The Ankle-Brachial Index in the Elderly and Risk of Stroke, Coronary Disease, and Death

The Framingham Study

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Background: A low ankle-brachial index (ABI) is associated with an increased risk of death and cardiovascular disease. Limited data exist regarding the relation between a low ABI and stroke. We sought to examine the relation between a low ABI and stroke, coronary heart disease, and death in the elderly.

Methods: We examined 251 men and 423 women with a mean age of 80 years who had a Framingham Study examination from 1994 to 1995. A low ABI was defined as less than 0.9. Persons were followed up for 4 years for occurrence of stroke or transient ischemic attack, coronary disease, and death. Cox proportional hazards models were used to assess the relation between a low ABI and each outcome after adjusting for age, sex, and prevalent cardiovascular disease.

Results: A low ABI was detected in 20% of our sample. Only 18% of the participants with a low ABI reported claudication symptoms. One third of those with a normal ABI and 55% of those with a low ABI had cardiovascular disease at baseline. Results of multivariable Cox proportional hazards analysis demonstrated a statistically significant increase in the risk of stroke or transient ischemic attack in persons with a low ABI (hazards ratio, 2.0; 95% confidence interval, 1.1-3.7). No significant relation between a low ABI and coronary heart disease (hazards ratio, 1.2; 95% confidence interval, 0.7-2.1) or death (hazards ratio, 1.4; 95% confidence interval, 0.9-2.1) was observed.

Conclusions: A low ABI is associated with risk of stroke or transient ischemic attack in the elderly. These results need to be confirmed in larger studies.

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LOW ankle-brachial index (ABI) is common in the elderly and the prevalence exceeds 25% in persons older than 85 years.1-4 In middle-aged and older adults a low ABI has been reported to be associated with an increased risk of death, total cardiovascular disease (CVD), coronary heart disease (CHD), congestive heart failure, and symptomatic peripheral arterial disease.5-12 Risk for all-cause mortality is increased 2- to 4-fold in persons with a low ABI6 while risk of death from coronary disease is increased more than 6-fold in middle-aged adults6 and more than 3-fold in older adults.7,8 Peripheral arterial disease that is symptomatic and severe increased cardiovascular and CHD mortality 15-fold.8 Limited data are available on the relation between ABI and risk of stroke. Studies of men with symptoms of lower extremity arterial disease have reported an increased risk of stroke death.13-15 Decreasing ABI levels have been associated with a higher prevalence of self-reported stroke or transient ischemic attack (TIA) in middle-aged adults.16 The Honolulu Heart Program recently reported an increased risk of stroke with declining ABI levels in elderly men.17 We had the opportunity to examine the relation between low ABI and risk of stroke, CHD, and death in elderly adults participating in the Framingham Heart Study.

METHODS

Our study sample included surviving members of the original cohort who had a Framingham Heart Study routine research examination between 1993 and 1995. Participants have been examined every 2 years since the study inception in 1948. Informed consent for this study was obtained from participants at the time of their examination. The institutional review board of the Boston University School of Medicine approved the examination content, which included a standardized medical history and physical examination, an electrocardiogram, noninvasive cardiovascular testing, and phlebotomy for measurement of blood lipids and glucose levels.

Trained technicians obtained ankle-brachial systolic blood pressure measure-
ments according to a standardized protocol. Blood pressure cuffs were applied to both arms and both ankles and the systolic blood pressure was measured twice at each site using an 8-MHz Doppler pen probe and an ultrasonic Doppler flow detector (Parks Medical Electronics Inc, Shaw Aloha, Ore). A third measurement was taken when the initial and second blood pressure measurements differed by more than 10 mm Hg at any site. If the posterior tibial pulse could not be located by palpation or with the Doppler probe, measurement was taken from the dorsalis pedis artery.

To calculate the ABI ratio, the average systolic blood pressure measurement in the ankle was divided by the average systolic blood pressure measurement in the arm. The mean pressure of the higher arm was used to calculate the ABI separately for each leg. A low ABI was defined as less than 0.9 in either leg. We excluded 11 participants with insufficient blood pressure data. An additional 18 participants with an ABI greater than 1.5 were also excluded.

Intermittent claudication was ascertained using a standardized physician-administered questionnaire. The specific questions were about exertional leg discomfort that was related to ground steepness or rapidity of walking and relieved with rest. Participants were queried at each examination about cigarette smoking. The examining physician measured resting blood pressure twice and the average of the 2 readings was used to determine the presence of hypertension. Hypertension was defined as a blood pressure of 140/90 mm Hg or greater or the use of antihypertensive medications. Diabetes mellitus was considered present if a random glucose reading was 140 mg/dL (7.77 mmol/L) or greater, or if the participant took insulin or oral hypoglycemic medications.

Participants were followed up for 4 years for the occurrence of stroke, TIA, fatal and nonfatal CHD (angina pectoris; coronary insufficiency; myocardial infarction; and CHD death, sudden and nonsudden), and death from all causes. Using previously established criteria, a panel of neurologists made the final determination of the occurrence of stroke or TIA. A separate panel of senior physician investigators determined all CHD end points and causes of death. Among those with a low ABI, one third had CHD, 15% had experienced a stroke or TIA, and a few more than half had CVD (CHD, stroke or TIA, or intermittent claudication). Nearly 70% of those with a normal ABI and only 18% reported symptoms of intermittent claudication at the baseline examination. The baseline prevalence of CHD, stroke or TIA, and CVD was substantial (Table 1). Among those with a low ABI, one third had CHD, 15% experienced a stroke or TIA, and a few more than half had CVD (CHD, stroke or TIA, or intermittent claudication). Nearly 70% of those with a normal ABI and 86% of those with a low ABI had hypertension. Although the prevalence of current smoking was low, more than half of the participants were former smokers.

During 4 years of follow-up, 12% of subjects with a low ABI had a CHD event, 13% had a stroke or TIA, and 23% died (Table 2). Corresponding events in subjects with a normal ABI were 9%, 5%, and 14%. Of the 47 stroke or TIA events that occurred during follow-up, 17 were atherothrombotic brain infarctions, 14 were TIAs, 12 were cerebral emboli, and 4 were intracranial hemorrhages. There was no significant relation between a low ABI and CHD (hazards ratio [HR], 1.2; 95% confidence interval [CI], 0.7-2.1) or death (HR, 1.4; 95% CI, 0.9-2.1) (Table 3). There was, however, a significant 2-fold risk for stroke or TIA in persons with a low ABI (HR, 2.0; 95% CI, 1.1-3.7). The relation between ABI level and stroke or TIA revealed an increasing hazard as the ABI level decreased (Figure 1). Compared with the referent group.
of persons with an ABI greater than 1.0, persons with an ABI of 0.9 to 1.0 had an HR of 1.5 while persons with an ABI less than 0.9 had an HR of 2.2 (test for trend across ABI levels, \( P = .02 \)).

The relation between a low ABI and risk for stroke or TIA was consistent in persons with and without baseline CVD (Figure 2). The HR was 2.2 (95% CI, 1.1-4.4) when persons with stroke or TIA at baseline were excluded. In persons free of baseline CVD or atrial fibrillation the HR was also 2.2 but the relation was no longer significant owing to the small number of stroke events \( (P = .11) \). Similarly, in persons with CVD at baseline, the HR was 1.8; again, the number of events was small, which limited our power to detect a significant relation \( (P = .15) \).

**COMMENT**

A low ABI was associated with risk of stroke or TIA in this sample of elderly persons but not with risk of coronary disease or death. The ABI was both independently and inversely related to risk of stroke or TIA. The association between low ABI and stroke or TIA was consistent in persons with and without CVD at baseline. Our findings are remarkably similar to those recently reported by the Honolulu Heart Program Study,\(^{17}\) the first study to describe an independent association between ABI and stroke in the elderly. In elderly Japanese men free of stroke, CHD, and history of lower extremity vascular surgery at baseline, a low ABI was associated with twice the hazard for total and thromboembolic stroke.\(^{23}\) Furthermore, in that study, a low ABI was related to an increased stroke risk both before and after risk factor adjustment.

Studies of the relation between ABI and incident stroke in middle-aged populations have suggested a positive association.\(^{23-25}\) In middle-aged adults (45-64 years) a low ABI was found to be strongly associated with ischemic stroke in men and women as well as in blacks and whites, but the relationship was attenuated and not significant after risk factor adjustment.\(^{23}\) In that study, the HR for stroke in the group with the lowest ABI \(<0.8\), however, was nearly 2.0 (95% CI, 0.8-4.7), which is consistent with our findings and those of the Honolulu Heart Program Study. The Edinburgh Artery Study\(^{24}\) reported an increased relative risk of stroke in persons with a low ABI (relative risk, 1.98; 95% CI, 1.05-3.77), as did a Swedish study\(^{25}\) of 68-year-old men with asymptomatic carotid stenosis (relative risk, 2.0; 95% CI, 1.1-3.7). Although the Cardiovascular Health Study\(^{6}\) did not find a significant relation between a low ABI and stroke in persons free of baseline CVD, the incidence of stroke was higher in persons with a low ABI. The incidence of stroke at 6 years was 21.2 per 1000 person-years in those with a low ABI compared with 9.1 per 1000 person-years in those with a normal ABI.\(^{9}\) These findings from the Cardiovascular Health Study are consistent with results from the Honolulu Heart Program Study\(^{26}\) and our study.

Low ABI levels have been shown to be an important marker of generalized atherosclerosis through a positive association with CVD risk factors and outcomes as well as measures of subclinical atherosclerotic disease. Population-based studies of middle-aged and older adults have demonstrated a positive correlation between low ABI and ultrasound-detected carotid atherosclerosis, the latter being defined by measurement of carotid stenosis or carotid intima-media thickness.\(^{27,28}\) In addition, elderly persons with peripheral arterial disease have increased aortic and common carotid artery stiffness compared with persons without peripheral arterial disease.\(^{29}\) Atherosclerosis and vascular stiffness may explain in part the underlying pathologic mechanisms mediating the relation between ABI and stroke risk.

Many studies have reported a 2- to 4-fold increase in mortality associated with a low ABI.\(^{5,9,30}\) In contrast, we did not find a relation between a low ABI and mortality in our sample. The disparity in findings may be age related, as the average age of our subjects, which exceeded 80 years, was much higher than that of subjects in most prior reports. In addition, most deaths in our sample (62%) were from noncardiovascular causes. On the other hand, the SHEP (Systolic Hypertension in the Elderly Program) study,\(^{8}\) with participants only slightly younger than those in our sample, reported a positive association between mortality and a low ABI. Most of the deaths that occurred in the SHEP study, a trial of blood pressure treatment in older adults with isolated systolic hypertension, resulted from CVD. Other population-based studies have reported that deaths from causes other than CVD were not significantly increased in persons with...
a low ABI5,7 or in persons with a low ABI and baseline CVD.9 Our findings therefore are not inconsistent with prior reports.

A low ABI has been shown to increase risk for CHD mortality.5,6,8 Criqui et al6 were the first to demonstrate a significant increase in CHD deaths in both men and women with large-vessel peripheral arterial disease. In that study of predominantly white upper-middle-class adults with a mean age of 66 years, CHD deaths were increased more than 6-fold in those with peripheral arterial disease. Subsequently, the SHEP study9 and an ancillary study to the Multicenter Study of Osteoporotic Fractures10 demonstrated a more than 3-fold risk for coronary disease mortality in older adults with a low ABI. There were too few CHD deaths in our sample to evaluate this relationship (only 9 deaths during follow-up were attributable to coronary disease). However, although the occurrence of coronary disease was higher in persons with a low ABI (12% vs 9%), we did not observe a relation between a low ABI and a composite of nonfatal and fatal CHD events. Others have reported a nonsignificant increase in risk of nonfatal myocardial infarction11,12 and total myocardial infarction and angina in persons with a low ABI.13 In the Cardiovascular Health Study9 a low ABI was positively related to risk of total myocardial infarction and angina; however, after multivariate adjustment, the risk ratios were reduced and no longer significant. The lack of an association between a low ABI and coronary disease in our study may in part be related to the small number of coronary events.

In conclusion, a low ABI is associated with risk of stroke or TIA in the elderly. The ankle-brachial blood pressure measurement is a simple test that can be used to identify stroke-prone elderly persons, who can then be considered for more aggressive preventive interventions. Others have shown that peripheral arterial disease often goes unrecognized in primary care practice, which may present a barrier to secondary prevention of cardiovascular events.31 These findings need to be confirmed in larger studies.

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