Relationship of Ankle Blood Pressures to Cardiovascular Events in Older Adults

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Background and Purpose—Low values of ankle–arm systolic blood pressure ratio predict mortality and cardiovascular events. High values, associated with arterial calcification, also carry risk for mortality. We focus on the extent to which low and high ankle–arm index values as well as noncompressible arteries are associated with mortality and cardiovascular events, including stroke in older adults.

Methods—We followed 2886 adults aged 70 to 79 for a mean of 6.7 years for vital status and cardiovascular events (coronary heart disease, stroke, and congestive heart failure).

Results—Normal ankle–arm index values of 0.91 to 1.3 were found in 80%, low values of ≤0.9 were found in 13%, high values of >1.3 were obtained in 5%, and noncompressible arteries were found in 2% of the group. Increased mortality was associated with both low and high ankle–arm index values beginning at levels of <1.0 or ≥1.4. Subjects with low ankle–arm index values or noncompressible arteries had significantly higher event rates than those with normal ankle blood pressures for all end points. For coronary heart disease, hazard ratios associated with a low ankle–arm index, high ankle–arm index, and noncompressible arteries were 1.4, 1.5, and 1.7 (P<0.05 for all) after controlling for age, gender, race, prevalent cardiovascular disease, diabetes, and major cardiovascular risk factors. Noncompressible arteries carried a particularly high risk of stroke and congestive heart failure (hazard ratio=2.1 and 2.4, respectively).

Conclusions—Among older adults, low and high ankle–arm index values carry elevated risk for cardiovascular events. Noncompressible leg arteries carry elevated risk for stroke and congestive heart failure specifically. (Stroke. 2008;39:863-869.)

Key Words: age ■ mortality ■ peripheral artery disease ■ stroke

Low ankle blood pressures are known to be a measure of subclinical atherosclerosis and as such have been consistently related to subsequent cardiovascular morbidity and mortality.1–7 In healthy individuals, ankle systolic blood pressures are slightly higher than the systolic blood pressure measured in the arm. As occlusive disease to the lower extremities develops, the systolic pressure at the level of the ankles decreases. An ankle systolic pressure that is ≥90% than that in the arm (an ankle-to-arm systolic blood pressure ratio of ≤0.9) has traditionally been the cut-point at which occlusive disease to the lower extremities is diagnosed.8,9 While this is a standard cut point for the purpose of clinical decision-making, the lower the ankle pressure, the greater the severity of occlusive disease and the higher the risk of cardiovascular events.6

It has been recognized for some time that systolic pressures at the level of the ankles can also be elevated in comparison to pressures measured in the arm. This is usually attributed to calcification of the arteries, which prevents arterial compression and results in a falsely elevated pressure measurement. This has been considered a disadvantage of ankle blood pressures, and values that are 30% to 50% more than the corresponding arm pressures (ratios of ≥1.3 to ≥1.5) are usually considered missing and excluded from analyses.

Recently, several studies have evaluated mortality rates across the full spectrum of ankle–arm index values and have shown that both elevated ankle pressures and low ankle pressures are associated with increased mortality. This was first reported in a cohort of Japanese hemodialysis patients10 and in the Strong Heart Study,11 a cohort of Native Ameri-
cans. These findings were then generalized to a broader population of older adults enrolled in the Cardiovascular Health Study. It has been suggested that an ankle–arm index value of 1.3 is the cut point at which the ankle–arm index reflects arterial stiffness and thus elevated risk. However, data from the Strong Heart study and the Cardiovascular Heart Study suggest that the cut point should be slightly higher at 1.4.

While associations between high ankle blood pressures and increased total mortality have been consistent in these studies, the associations with cardiovascular mortality and specific cardiovascular events such as stroke and coronary heart disease are less clear. In Cardiovascular Heart Study, the association between high ankle pressures and cardiovascular mortality did not reach statistical significance in adjusted models, and an association with cardiovascular events was not significant in either unadjusted or adjusted models. A noted limitation by the authors was the inability to identify subjects with noncompressible arteries. In the Strong Heart Study, high ankle blood pressure values (ankle–arm index >1.4) were strongly associated with cardiovascular mortality. However, much of this association was accounted for by study subjects with noncompressible arteries. The Strong Heart Study did not include information on stroke, coronary heart disease, or congestive heart failure.

Thus, to complete a full picture, more information is needed regarding the risks associated with high ankle pressures versus noncompressible arteries in a more general population, and the association of ankle blood pressures to specific cardiovascular events such as stroke, congestive heart failure, and coronary heart disease. The purpose of this study was to determine the extent to which low and high ankle–arm index values as well as noncompressible arteries are associated with mortality and specific cardiovascular events in a broad population of older adults.

**Patients and Methods**

**Study Sample**

The Health, Aging, and Body Composition Study is a community-based prospective study of the impact of changes in weight and body composition on age-related physiological and functional changes. Participants, aged 70 to 79 years, were recruited from March 1997 to July 1998, at 2 field centers located in Pittsburgh, Pennsylvania, and Memphis, Tennessee. Participants were drawn from a random sample of Medicare beneficiaries residing in zip codes from the metropolitan areas surrounding Pittsburgh and Memphis. Eligible participants reported no difficulty walking 3 miles, climbing 10 steps, or performing basic activities of daily living. Participants also reported no difficulty walking 3 miles, climbing 10 steps, or performing basic activities of daily living. Participants also reported no difficulty walking 3 miles, climbing 10 steps, or performing basic activities of daily living. Participants also reported no difficulty walking 3 miles, climbing 10 steps, or performing basic activities of daily living.

**Ankle–Arm Index**

All participants enrolled in The Health, Aging, and Body Composition Study are eligible for ankle–arm index measurement except for those with open wounds including venous stasis ulcers, rashes, those with bilateral amputations, or those who are unable to lie at 45 degrees or less. Trained, certified technicians measured the pressures in the right or left arm and both ankles (posterior tibial artery), according to standard protocol described previously. Briefly, the participant was asked to lie recumbent or semirecumbent for at least 5 minutes before measuring blood pressure. After this, appropriately sized blood pressure cuffs were applied to the right arm and each ankle (midpoint of the over the posterior tibial artery, with the lower end of the bladder ∼3 cm above the malleolus). If blood pressures could not be obtained in the right arm, then the left arm was used (50 cases). After palpation of the arteries, ultrasound gel was applied and an 8-MHz pencil Doppler probe (Parks Medical Electronics, Inc) was used with a standard manometer to measure systolic blood pressures. The systolic blood pressure of the ankle was divided by the systolic blood pressure of the arm to create the ankle–arm index. Measures were performed twice and the results were averaged; the lower average value between the two legs was used to define an individual’s ankle–arm index. Intermittent claudication was defined by the Rose questionnaire.

**Laboratory Values**

Fasting blood samples were obtained for assay. HDL, triglycerides, and glucose were assayed using a colorimetric technique on a Johnson and Johnson Vitros 950 analyzer. HDL was assayed after a magnetic precipitation of LDL, VLDL, and chylomicrons. LDL was estimated using the Friedewald equation. Insulin was assayed using a microparticle enzyme immunoassay (Abbott IMx analyzer) and for Hemoglobin Alc, ion exchange high-performance liquid chromatography was used (BioRad Variant analyzer). Creatinine values of 132.6 μmol/L (1.5 mg/dL) for men and ≥115 μmol/L (1.3 mg/dL) for women were considered elevated.

**Participant Follow-Up and Cardiovascular Events**

Participants were contacted every 6 months, alternating clinic visits and phone interviews. Vital status, functional limitations, all hospitalizations, and selected outpatient events were ascertained. Date of death was verified and deaths were reviewed for immediate and underlying cause using death certificates, hospital records, and a proxy interview. Standardized algorithms, designed by The Health, Aging, and Body Composition Study investigators who are clinicians, were used for adjudication of cause of death.

We evaluated mortality as both total mortality and cardiovascular mortality, which was defined as athrosclerotic cardiovascular disease (definite fatal myocardial infarction, definite fatal cardiovascular heart disease, or possible fatal cardiovascular heart disease), stroke, atherosclerotic disease other than coronary or cerebrovascular, and other cardiovascular disease (eg, valvular heart disease). We also analyzed the association between ankle–arm index and cardiovascular morbidity defined as incident cardiovascular heart disease, including coronary death or any overnight hospitalization in an acute care hospital for acute myocardial infarction or angina; stroke, defined as fatal and nonfatal stroke events; and congestive heart failure, defined as any overnight hospitalization in an acute care hospital for congestive heart failure during the follow-up. Follow-up time was calculated as months between the first clinic visit and date of event or date of last follow-up for censored participants.

**Statistical Methods**

Among the 3075 participants in The Health, Aging, and Body Composition Study, revascularization for peripheral arterial disease was reported in 57, and these participants were excluded from the analyses. Of the remaining 3018 participants, ankle–arm index measures were available in 2823 (93.5%). Ankle–arm index values ranged from 0.24 to 2.98, with a median value of 1.09. Among the 195 participants with missing data, an inability to compress the artery was listed as the reason for 63 subjects, and these individuals were added back to the analysis. Thus, data outcomes are presented for a total of 2886 participants. The average time on study for these participants was 6.7 years.
Descriptive analysis was performed using increments of 0.10 in ankle–arm index values, to evaluate cut-offs at which the risk for mortality increased significantly. After this, ankle–arm index was grouped into 4 categories: low (ankle–arm index <0.9), normal (0.91 to 1.3), high (ankle–arm index ≥1.31), and noncompressible arteries (ie, pulse could not be obliterated with pressures ≥250 mm Hg) to form exposure categories. Baseline demographic and key characteristics of the study sample have been presented as descriptive statistics (eg, means, medians, SDs, ranges) by these categories of ankle–arm index. The normal ankle–arm index group served as reference for all analyses and each of the other ankle–arm index categories (low, high, and noncompressible) were compared with this group, in separate models. Differences in baseline characteristics were assessed using χ² test for categorical variables and Student t test for continuous variables. Associations between mortality and morbidity and ankle–arm index categories were assessed using the Cox proportional hazards model, after assessing the proportionality assumption; both unadjusted and adjusted hazard ratios and 95% CI are reported. A value of P <0.05 was considered statistically significant.

SAS version 8.0 for Windows was used for all analyses (SAS, version 8.02; SAS Institute Inc).

Results

Of the 2886 participants analyzed, normal ankle–arm index values of 0.91 to 1.3 were found in 2299 (79.6%) partic-
Participants, low values of ≤0.9 were found in 383 (13.3%) participants, high values of >1.3 were obtained in 141 (4.9%) participants, and participants with noncompressible arteries represented 2.2% of the group. Baseline characteristics differed significantly across the four ankle–arm index groups (Table 1). As expected, elevated cardiovascular risk factors were associated with abnormal ankle–arm index findings. Interestingly, the specific risk factors tended to differ by type of ankle–arm index abnormality. Men had a higher prevalence of high ankle–arm index values and noncompressible arteries compared with women. White participants were more likely to have high ankle–arm index values, whereas black participants had significantly lower ankle–arm index values and noncompressible arteries. Low physical activity and positive history of smoking were primarily associated with low ankle–arm index values. Prevalent cardiovascular disease as well as elevated systolic blood pressure was strongly associated with all ankle–arm index abnormalities.

When evaluating total mortality rates across the range of ankle–arm index values, a clear U-shape relationship is seen with high mortality being associated with both low and high ankle–arm index values (Figure 1). On the low side of the distribution, mortality rates begin to increase when the ankle–arm index value decreases to 1.0 or lower. On the high side of the distribution, mortality rates begin to rise when ankle–arm index values are >1.31.

When evaluating Kaplan–Meier estimates of both total and cardiovascular mortality over an average 6.7-year period, participants with low ankle blood pressure values or noncompressible arteries had higher mortality than those with normal or high ankle–arm index values (Figure 2). When evaluating fatal plus nonfatal events individually (Figure 3), more of a differential effect is seen. For cardiovascular heart disease and congestive heart failure, subjects with noncompressible arteries had the highest event rates, followed by those with a low ankle–arm index. For stroke, both a low ankle–arm index and noncompressible arteries carry similarly high risk.

When these associations are controlled for potential confounding variables, they persist (Table 2). Subjects with low ankle–arm index values or noncompressible arteries had significantly higher event rates than those with normal ankle blood pressures, and this was true for each of the end points evaluated. These associations remained significant after controlling for age, gender, race, systolic blood pressure, and site. The addition of prevalent cardiovascular disease or diabetes and other cardiovascular risk factors related to mortality reduced these associations slightly, but they remained significant for all end points. The only end point for which high
ankle blood pressures remained an independent predictor of outcome was fatal or nonfatal coronary heart disease. For this end point, subjects with any ankle–arm index abnormality had a higher risk of an event in comparison to those with a normal ankle pressure. Noncompressible arteries carried the highest risk (hazard ratio=1.7), followed by a high ankle–arm index (hazard ratio=1.5), and then a low ankle–arm index (hazard ratio=1.4). When the analyses were repeated using the highest rather than lowest leg ankle–arm index, the results did not change substantially (data not shown).

**Discussion**

These data show clearly that both low ankle blood pressures and noncompressible leg arteries are associated with an elevated risk of mortality and cardiovascular events in comparison to normal ankle blood pressures. Participants with noncompressible arteries had the highest risk, particularly with respect to stroke, congestive heart failure, and cardiovascular mortality. When evaluating coronary heart disease events, high ankle blood pressures also carried a significantly elevated risk. Compared with normal ankle pressures, there is a 41% higher risk associated with low ankle pressures, a 50% higher risk associated with high ankle pressures, and a 65% higher risk associated with noncompressible arteries. In addition, these data show that noncompressible arteries are associated with an elevated risk of stroke and congestive heart failure specifically. These associations remained significant even after controlling for age, gender, race, and other cardiovascular risk factors.

These data are the first to our knowledge to show the prognostic significance of high ankle pressure and noncompressible arteries on specific cardiovascular events. In addition, these data confirm the recently published data from the Strong Heart Study and the Cardiovascular Health Study. For total mortality, our data are strikingly similar to data in both these studies in that increases in risk are apparent with ankle–arm index values >1.4 and <1.1. In all studies, on the low side of the distribution, the elevation in risk appears to begin with the “low normal” group with values of 1.01 to 1.09. This is consistent with data from the Multi-Ethnic Study of Atherosclerosis, which found that other measures of subclinical atherosclerosis were elevated among individuals with borderline ankle–arm index values of 0.90 to 0.99.

The ankle–arm index is a particularly useful test because the 2 ends of the ankle–arm index distribution convey complimentary information about the vasculature. Low ankle pressures are indicative of atheroma or atherosclerosis, which has reached the point at which blood flow to the lower extremities is impeded. High ankle pressures, however, provide an indication of arterial stiffness, or arteriosclerosis of the vessel wall. These 2 vascular processes both carry separate risk. Atherosclerosis in the lower extremities is likely marker for lesions in the coronary and intracranial vessels. Arterial stiffening, however, is a marker for vascular aging. The accompanying hemodynamic consequences of arterial stiffening include increases in cardiac after load, reduced coronary filling, and exposure of the brain and kidneys to damaging pressures. Specifically, it has been suggested that the loss of buffering capacity of the aorta can lead to microvascular damage to the brain. This likely explains the particularly strong association between noncompressible arteries and the outcomes of stroke and congestive heart failure. Thus, our data suggest that ankle blood pressures are a simple measure that can detect both the atherosclerosis (plaque) and arteriosclerosis (arterial stiffening) components of vascular damage.

When evaluating cardiovascular mortality, our data suggest that the elevated risk in the upper end of the ankle–arm index distribution is primarily restricted to noncompressible arteries. This may be why the Cardiovascular Heart Study data failed to show a significant association between high ankle–arm index values and cardiovascular mortality in adjusted models, whereas the Strong Heart Study did. For coronary heart disease events, our data show significant associations for both high ankle pressure values and noncompressible arteries, whereas the Cardiovascular Heart Study data do not.

When evaluating the baseline characteristics of participants across the range of high ankle–arm index values, it is interesting to note that the group with high ankle–arm index values actually had lower blood pressure and lower cholesterol values than participants with normal ankle pressures,
which seems inconsistent with a higher risk group. However, it should be pointed out that among older individuals, higher cholesterol is not associated with mortality or cardiovascular disease events, possibly because chronic inflammation reduces lipid levels in older individuals. With respect to systolic blood pressure, it is possible that this group has lower systolic blood pressure, site-adjusting for this did not totally account for this difference. It is also possible that the use of a cut-point of 1.3 to define high pressures has resulted in a number of inaccurately categorized participants. If a cut-point of 1.4 is used to define a high ankle–arm index, then the difference in systolic blood pressure between the normal and high group is no longer significant.

Previous analyses of ankle–arm index data have excluded those with high values because it is not possible to either diagnose or rule out arterial occlusion. If diagnosis of occlusive disease is the goal of testing, then individuals with a high ankle–arm index should be referred for further testing. Regardless of the true rate of occlusion, these individuals are at higher risk for mortality and cardiovascular events and should be managed appropriately with aggressive cardiovascular disease risk factor reduction. These data are important because they lend clinical value to ankle–arm index values that previously have been disregarded as erroneous.

Our data suggest that a simple ankle blood pressure can be tremendously useful from a clinical perspective. Despite this, in clinical practice, ankle blood pressures are underutilized because they lend clinical value to ankle–arm index values that previously have been disregarded as erroneous.

Conclusions

In conclusion, older adults have a high prevalence of both low and high ankle blood pressures, and these findings have a high risk for cardiovascular events. Older individuals with noncompressible leg arteries are at particularly high risk for stroke, congestive heart failure, and cardiovascular mortality.
Sources of Funding
This work was supported through the National Institute on Aging, contract numbers N01-AG-6-2106, N01-AG-6-2101, and N01-AG-6-2103. This research was supported in part by the Intramural Research Program of the National Institutes of Health, National Institute on Aging.

Disclosures
None.

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Stroke. 2008;39:863-869; originally published online February 7, 2008;
doi: 10.1161/STROKEAHA.107.487439

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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