Ankle-brachial index as a predictor of all-cause and cardiovascular disease mortality in 3733 Chinese patients with high cardiovascular risk

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Objective  To assess the association between 1-year risk of all-cause and cardiovascular disease (CVD) mortality and ankle-brachial index (ABI) in Chinese patients who were at high CVD risk.

Methods  Totally 3733 patients with high CV risk had bilateral ABI measurements at baseline and were followed up for 1-1.5 years. Patients were divided to four groups: 1) coronary heart disease (CHD); 2) ischemic stroke (IS); 3) diabetes mellitus (DM); 4) very high risk group (VHR), low ABI was defined as <0.9.

Results  A total of 3179 patients were analyzed. The prevalence of low ABI was 28.1%. At 1 year, all-cause mortality was 8.7%, and 27.6% was attributable to CVD; mortality due to CV events was 4.8% and 1.5%. After adjusting other risk factors the hazard ratio of low ABI was 1.623 for all-cause mortality and 2.304 for CVD mortality.

Similar in patient with and without low ABI, respectively were found in four groups.

Conclusion  ABI is a strong and independent predictor of mortality. Patients with a low ABI have a substantially increased risk of all-cause mortality and CVD mortality (J Geriatr Cardiol 2010; 7:17-20).

Keywords  ankle-brachial index; peripheral arterial disease; Chinese; mortality

Introduction  Cardiovascular disease is the leading cause of death in the world. The presence of peripheral arterial disease (PAD) is an indicator of widespread atherosclerosis in other vascular territories such as the coronary, carotid, and cerebrovascular arteries. There is substantial evidence that PAD is a predictor of future cardiovascular outcomes such as myocardial infarction, stroke, and death.¹⁻¹⁰ The ankle–brachial index (ABI) is the ratio of the ankle to brachial systolic blood pressure, and a value of <0.90 indicates the presence of PAD. ABI is a simple and noninvasive test that can be performed in the office or clinic setting. The goal of the present longitudinal part of the China Epidemiological Study on Ankle–brachial Index, was to assess the 1-year risk of all-cause and cardiovascular mortality associated with an ABI<0.9 in Chinese patients at high CV risk.

Methods

Study Population  The China Epidemiological Study is a large-scale epidemiological study in China with both a cross-sectional and a longitudinal part. The methods and design of the study have been described elsewhere in greater detail.¹ In this study, 3733 Chinese hospitalized patients over 50-year-old with two or more CVD risk factors were investigated using ABI measurement and clinical data were collected from medical records. Risk factors included obesity, smoking, diabetes, hypertension, lipid disorders, and history of coronary artery disease, stroke and PAD. Patients with cerebral disease of non-atherothrombotic origin (i.e., primary intracranial haemorrhage) or with neurological signs and symptoms due to a non-ischemic cause such as tumors or degenerative disease were excluded. We divided patients into four groups: 1) CHD only group; 2) stroke only group; 3) diabetes only group; and 4) very high risk group.

Very high risk was defined as the presence of established CHD plus one or more of the following: (1) multiple major risk factors (especially diabetes), (2) severe and poorly controlled risk factors (especially continued cigarette smoking), (3) multiple risk factors of the metabolic syndrome, and (4) acute coronary syndrome. The presence of underlying CHD was defined as a history of a physician-diagnosed heart attack, evidence of prior myocardial infarction by electrocardiogram or self-reporting of a prior coronary revascularization procedure (coronary artery intervention,
PCI or coronary-artery bypass surgery, CABG). Stroke was defined as a report of incident stroke or stroke and transient ischemic attack together. Type 2 diabetes was defined as a fasting plasma glucose concentration of >7.0 mmol/L in the absence of treatment and/or a plasma glucose concentration of ≥11.0 mmol/L 2h after a 75g oral glucose load, or being treated with glucose-lowering drugs. Hypertension was defined as a systolic blood pressure (SBP) of ≥140 mmHg, a diastolic blood pressure (DBP) of ≥90 mmHg or the current use of antihypertensive drugs to control hypertension. Lipid disorder was defined as TC >5.7 mmol/L, TG >1.7 mmol/L, LDL-C >3.6 mmol/L, HDL-C <0.9 mmol/L or treatment with antihyperlipidemic agents.

All-cause mortality and cardiovascular mortality were distinguished from each other, and cardiovascular mortality included atherosclerotic causes of death such as fatal myocardial infarction or stroke but did not include thromboembolic or aneurysmal causes.

Ankle-brachial index measurement

All patients were evaluated in the supine position after at least 5 minutes of rest. Systolic blood pressure was measured in arms and in the right and left posterior tibial and dorsalis pedis artery; a Doppler ultrasonic instrument (Nicolet Vascular, Elite 100R, USA, 5Hz) was used to detect flow in the arteries. The resting ABI was determined for each leg by dividing the systolic blood pressure at the ankle by the brachial pressure; the lower of the ABI values obtained in each leg was used in the data analysis. PAD was defined as an ABI of <0.9 in at least one leg.

Follow-up

The mean follow-up time was 13.3 ± 1.1 months. During the follow-up, 275 patients died from all causes, and of these 76 patients died from cardiovascular causes. Death was confirmed from hospital records or by contact with participants and their families. Cause of death was investigated using medical records and interviews. All materials were reviewed independently by a physician of the ABI cohort study to confirm the cause of death.

Statistical analysis

Data were analyzed using the software program SPSS13.0 (Chicago, IL, USA). Continuous variables are expressed as mean ± SD, and categorical variables as a percentage. Independent samples t-test and Chi-square test were used to compare continuous and categorical differences, respectively. A P value < 0.05 was considered statistically significant. The relationship between ABI and deaths from all-cause and CVD were adjusted for potential confounders, including age, gender, hypertension, dyslipidemia, diabetes, and smoking status.

Results

Baseline characteristics

Table 1 shows baseline characteristics by ABI group. Compared with participants with normal ABI at baseline, those with low ABI were significantly older and had more hypertension, lower HDL cholesterol.

All-cause and CVD mortality

The rate of all-cause mortality was 14.2% in the low-ABI group, and 6.5% in the normal-ABI group. In the CHD patients (n=840), the rate was 17.2% and 5.3% (RR 1.862, 95% CI 1.011-3.425); In the diabetics (n=505), the rate was 11.2% and 4.8% (RR 2.817, 95% CI 1.19-6.667); In the stroke patients (n=382), the rate was and 8.5 (RR 1.511, 95% CI 0.7-3.257); In the very high risk patients (n=1446), the rate was 13.1% and 7.6% (RR 1.456, 95% CI 0.972-2.183).

Table 1 Baseline characteristics of the study population (n = 3179)

<table>
<thead>
<tr>
<th>Item</th>
<th>ABI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>≥ 0.9 (n=895)</td>
<td>0.9-1.4 (n=2284)</td>
</tr>
<tr>
<td>Men (%)</td>
<td>49.1</td>
<td>54.6</td>
</tr>
<tr>
<td>BMI (≥±)</td>
<td>24.0±13.705</td>
<td>24.5±13.601</td>
</tr>
<tr>
<td>HBP (%)</td>
<td>80.6</td>
<td>72.0</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>143.27±25.502</td>
<td>138.80±22.694</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80.63±13.230</td>
<td>80.57±12.712</td>
</tr>
<tr>
<td>Dislipid (n, %)</td>
<td>47.7</td>
<td>44.1</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>4.68±1.204</td>
<td>4.610±1.122</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.74±1.333</td>
<td>1.667±1.111</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.769±0.889</td>
<td>2.733±0.853</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.172±0.384</td>
<td>1.209±0.420</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>42.6</td>
<td>38.8</td>
</tr>
<tr>
<td>All-cause mortality (% n)</td>
<td>14.2 (127)</td>
<td>6.5 (148)</td>
</tr>
<tr>
<td>CVD mortality (% n)</td>
<td>6.6 (59)</td>
<td>2.5 (57)</td>
</tr>
</tbody>
</table>
shows adjusted relative risks for all-cause mortality (ABI <0.9 and ABI 0.9~1.4) of each group in the ABI Cohort Study during 13-month follow-up (n=3179).

The rate of CVD mortality was 4.8% in the low-ABI group, and 1.5% in the normal-ABI group. In the CHD patients (n=840), the rate was 9.4% and 2.2% (RR 2.725, 95% CI 1.134-6.536). In the diabetics (n=505), the rate was 4.7% and 0.8% (RR 10.309, 95% CI 1.792-14.286). In the stroke patients (n=382), the rate was 8.0% and 5.1% in the normal-ABI group (RR 1.335, 95% CI 0.475-3.745). In the very high risk patients (n=1446), the rate was 5.9% and 2.6% (RR 2.309, 95% CI 1.212-4.405).

Association between ABI and mortality

When ABI groups were examined in relation to mortality in Cox regression models that adjusted for multiple CVD risk factors, low-ABI group was significantly associated with both all-cause mortality and CVD mortality. Low ABI was associated with adjusted all-cause and CVD mortality risk of 1.69 (95% CI 1.34 to 2.14) and 2.52 (95% CI 1.74 to 3.64), respectively (Fig.3 and Fig.4).

Discussion

Our previous studies 2,3 suggested that measurements of ABI might be useful indicators of systemic atherosclerosis in Chinese patients with cardiovascular risk factors and PAD is prevalent in Chinese high CV risk patients. Consistent with other studies 4-20 results of the present study showed that ABI is a strong and independent predictor of mortality, and patients with a low ABI have a substantially increased risk of all-cause mortality and CVD mortality, suggesting that low ABI is useful for identifying patients at excess risk.

Compared with participants with normal ABI, those with low ABI were significantly older and had more hypertension, lower HDL cholesterol. After adjusting for age, gender, hypertension, dyslipidemia, diabetes, smoking status, the hazard ratio (95% CI) of low ABI was 1.623 (1.228-2.146) for all-cause mortality and 2.304 (1.504-3.529) for CVD mortality. Similarly, for patients with CHD only, stroke only, diabetes only, very high risk, CVD mortality and all-cause mortality were significantly higher in lower ABI than those in normal ABI group.

It is possible that diabetic patients with low ABI are more susceptible to CVD death. Other possibilities related to our results included different ethnic groups and different duration of follow-up. However, an ABI of 0.90 was independently associated with a high risk of all-cause and CVD mortality.

All-cause and CVD mortalities were 14.2% and 4.8% in the low-ABI group, twice as high as those with normal ABI. Compared with the normal ABI group, the adjusted RR after 13-month follow-up was 1.623 (95% CI 1.228-2.146) for all
cause and 2.304 (95% CI 1.504-3.529) for CVD death in Chinese high risk patients. In diabetic patients, RR 2.817 (95%CI 1.19-6.667) for all-cause death, RR 10.309 (95%CI 1.792-14.286) for CVD death, higher than that in other groups. It is possible that diabetic patients with low ABI are more susceptible to CVD death.

Our findings of an independent relationship between low ABI and mortality risk is consistent with findings from other large studies of CVD. The Edinburgh Artery Study\(^7\), for example, showed 5-year relative risks of all-cause and CVD mortality of 1.58 and 1.85 for persons aged 55 to 74 years with an ABI <0.90. Similarly, in a study of older adults without prevalent CVD,\(^8\) the 6-year relative risk of death associated with an ABI <0.90 was 1.62. In studies with selected patient populations, however, a low ABI may be more strongly predictive of death. For instance, in older adults with systolic hypertension and no baseline CVD,\(^9\) an ABI <0.90 was associated with a 4-year relative risk of total mortality of 3.0 in men and 2.7 in women. Lately study\(^10\) 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), showed that 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. Our results showed 1-year relative risks of all-cause and CVD mortality of 1.623 and 2.304 for Chinese hospitalized patients over 50-year-old with two or more CVD risk factors with an ABI <0.90.

There are certain limitations to our study. We measured resting ABI in our study, ABI may be normal at rest despite hemodynamically significant arterial stenosis, yet decline following calf muscle exercise. For this reason, ABI should be measured following exercise. Because our study population consisted only of relatively old hospitalized patients, it is not fully generalizable to the population at large.

In summary, our results show an association between ABI and mortality, with significantly increased risk in the <0.90 group. Our findings further supported that ABI should be promoted as an ideal tool to predict mortality in high risk patients. Regular PAD screening in high risk patients and then intensive management of vascular risk factors should be encouraged in clinical experience.

The numbers of patients with cardiovascular disease has been increasing in China due to changes in diet and lifestyle. Atherosclerotic risk factors such as diabetes, hypercholesterolemia, and hypertension can and should be treated adequately, and smoking should be strongly advised against.

Acknowledgments

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References

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