Different Calculations of Ankle-Brachial Index and Their Impact on Cardiovascular Risk Prediction

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**Background**—An ankle-brachial index (ABI; ratio of ankle and brachial systolic blood pressure) <0.9 indicates peripheral arterial disease (PAD) and is a strong predictor of cardiovascular events. The aim of the present study was to address the prognostic value of different methods of ABI calculation.

**Methods and Results**—In 831 patients admitted with chest pain for diagnostic heart catheterization, blood pressure of both anterior and posterior tibial arteries was measured. ABI was calculated for each leg with the higher of the 2 ankle pressures (current definition of the American Heart Association) or with the lower of the 2 ankle pressures (modified definition) in relation to the higher of the left or right brachial systolic blood pressure. For each patient, the lower ABI from both legs was used for further evaluation. Fifteen patients (1.8%) with ABI >1.5 were excluded. We compared patients with ABI <0.9 according to the current definition (with PAD, n=204 [25.0%]), those with ABI ≥0.9 according to the modified definition (without PAD, n=524 [64.2%]), and those with ABI <0.9 according to the modified definition and ≥0.9 according to the current definition (suspected PAD, n=88 [10.8%]). Follow-up data (median 6.6 years) were available for 812 patients (99.5%); 157 patients (19.3%) experienced cardiovascular events (cardiovascular death, myocardial infarction, or stroke). Patients without PAD had the lowest cardiovascular event rate, whereas event rates were comparable for patients with PAD and those with suspected PAD (14.8% versus 28.4% versus 25.0%, respectively). In a fully adjusted Cox regression analysis that included patients without PAD as the reference group, the hazard ratio (95% CI) was 1.56 (0.97 to 2.53) for patients with suspected PAD and 1.67 (1.16 to 2.40) for patients with PAD.

**Conclusions**—When the higher ankle pressure is used for ABI calculation, a group of patients at high risk for cardiovascular events is overlooked. With a simple modification of ABI (use of the lower instead of the higher ankle pressure), more patients at risk could be identified. (Circulation. 2008;118:961-967.)

**Key Words:** ankle-brachial index ■ peripheral vascular disease ■ prognosis

Peripheral arterial disease (PAD) is highly prevalent in the United States and Europe.1–3 The presence of PAD is a predictor of cardiovascular events such as myocardial infarction, stroke, and cardiovascular death.4–6 A minority of PAD patients present with typical symptoms, such as intermittent claudication, ulcers, or rest pain.1–3 Nevertheless, cardiovascular risk is increased in both symptomatic and asymptomatic patients with PAD.7 Therefore, it appears of prognostic importance to screen patients with atherosclerotic risk factors or coronary artery disease (CAD) for PAD. Clinical examination that includes detection of femoral bruit or pulse abnormalities is not sufficiently sensitive to detect PAD.8 The ankle-brachial index (ABI) is regarded as an easy, reliable, and noninvasive measure of the presence and severity of lower-extremity PAD. Measurement of ABI allows the identification of both symptomatic and asymptomatic patients with PAD. Therefore, ABI measurement is widely recommended for PAD screening.6

**Clinical Perspective p 967**

According to the current guidelines of the American Heart Association (AHA) and the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II), ABI is defined as the ratio of the higher of the systolic blood pressures of the 2 ankle arteries of that limb (either the anterior or the tibial artery) and the higher of the 2 systolic blood pressures of the upper limbs.6,9,10 Usually, an ABI between 0.9 and 0.4 is interpreted as mild to moderate PAD and an ABI of <0.4 as severe PAD.6 The inverse relationship between ABI and atherosclerotic risk factors, as well as its relationship with the presence of both cardiovascular and cerebrovascular disease, has been well established.11,12 More-
over, recent investigations revealed a strong correlation between ABI and cardiovascular events.\textsuperscript{11–15} However, the current AHA and TASC II calculation of ABI by use of the higher ankle pressure is not widely accepted. Several authors preferred the average of both ankle pressures, and others even recommend that the lower of the 2 ankle pressures be used for ABI calculation.\textsuperscript{16,17} Recently, Schrör et al\textsuperscript{16} reported a stronger association with PAD prevalence using ABI based on the lower of the 2 ankle pressures than with the current AHA and TASC II definition in a systematic duplex sonographic evaluation.

The ABI measurement based on the higher of both ankle pressures appears to underestimate the true prevalence of PAD. Data on the prognostic impact of different ABI calculations on cardiovascular prognosis are scant. To the best of our knowledge, the present work for the first time evaluates whether a modified definition for ABI calculation that uses the lower instead of the higher of the 2 ankle pressures increases prognostic value with regard to cardiovascular events.

**Methods**

**Study Population**

Between November 1996 and July 1998, a total of 1168 consecutive patients were admitted to the Medical Department II of the University Hospital of Mainz, Germany, for diagnostic heart catheterization. Patient selection has been described in a previous publication.\textsuperscript{8} In a subgroup of 831 patients (71.1%), additional Doppler evaluation of leg perfusion and duplex sonography of the carotid arteries were performed. Presence of carotid artery stenosis was defined according to a previous publication.\textsuperscript{3} In total, 276 (33.2%) of these 831 patients presented in the hospital with an acute coronary syndrome, defined as unstable angina (Braunwald classification class B or C), acute ST-segment elevation, or non–ST-segment–elevation myocardial infarction. The remaining 555 patients (66.8%) had stable angina pectoris. Patients were considered to have CAD after coronary artery bypass surgery or in the presence of at least 1 stenosis with a diameter >30% according to coronary angiography by visual assessment in a major coronary artery after sublingual administration of 0.8 mg of nitroglycerin. After coronary angiography, CAD could be diagnosed in 726 patients (87.4%). In the remaining 105 patients (12.6%) with angiographically excluded CAD, symptoms were related to hypertensive or valvular heart disease. The history of classic risk factors was assessed as follows: Patients who had received antihypertensive treatment or who had received a diagnosis of hypertension (blood pressure >160/90 mm Hg) were considered to have hypertension. Patients were defined as diabetic if they had fasting blood glucose levels >125 mg/dL or if they were receiving dietary treatment or medication for diabetes. In general, study participants were German nationals and, particularly, were inhabitants of the Rhine-Main Area. The study was approved by the Ethics Committee of the University of Mainz. Participation was voluntary, and each study subject provided written informed consent.

**ABI Measurement**

The ABI measurement was performed in accordance with previous publications.\textsuperscript{17,18} For ABI measurement, a continuous phlygymnometer and a Doppler device (continuous-wave Doppler ultrasound device, Kretztechnik GmbH, Marl, Germany) with an 8-MHz continuous-wave probe was used. Measurement of upper- and lower-extremity blood pressure was performed after at least 30 minutes of rest. During the measurement, the participant was in a supine position. The blood pressure cuffs were placed over each brachial artery and above each malleolus. The cuff was inflated rapidly to 20 mm Hg above the audible systolic pressure of each arm and deflated in 2-mm/s increments. The systolic pressure was measured once in each of the following arteries: right and left brachial artery, right and left anterior tibial artery (probe position at dorsalis pedis artery), and right and left posterior tibial artery. The systolic pressure recorded was the pressure at the point it first became audible.

ABI was first calculated according to the AHA definition as the quotient of the higher of the systolic blood pressures of the 2 ankle arteries of that limb (either the anterior tibial artery or the posterior tibial artery) and the higher of the 2 brachial systolic blood pressures (current ABI definition). The second ABI was calculated as the quotient of the lower of the systolic blood pressures of the 2 ankle arteries of that limb (either the anterior tibial artery or the posterior tibial artery) and the higher of the 2 brachial systolic blood pressures (modified ABI definition).

PAD was defined as being present if ABI was <0.9 in at least 1 leg by the current or modified ABI definition. The incidence of cardiovascular events and cardiovascular mortality was evaluated with regard to the presence or absence of PAD by the different definitions. In accordance with previous publications, 15 patients (1.8%) with ABI values >1.5 in at least 1 leg were considered to have calcified atherosclerosis.\textsuperscript{19} These patients were excluded from further evaluation, and a total of 816 (98.2%) of 831 patients were included for further evaluation.

**Patient Follow-Up**

Follow-up information was available for 812 patients (99.5%) of the 816 study patients. The median follow-up period was 6.6 years (minimum 3.8 years, maximum 7.7 years). Cardiovascular events were defined as death of cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. Follow-up information was obtained from the admitting hospital or general practitioner charts.

**Laboratory Methods**

Blood samples were drawn from each subject after an overnight fasting period under standardized conditions. Serum was centrifuged at 4000g for 10 minutes, immediately divided into aliquots, and frozen at −80°C until analysis. Lipid serum levels, blood glucose, and insulin were measured immediately.

**Statistical Analysis**

ABI measurements were performed by 2 different investigators. The intraclass correlation coefficient for interobserver variability (n = 40; 2 investigators) was 0.994 (95% CI 0.991 to 0.997), and for intraobserver variability (n = 40), it was 0.995 (95% CI 0.992 to 0.998). Differences between patients were tested by 2-sample t test (2 groups) or 1-way ANOVA (3 groups) for approximately normally distributed variables, by Mann-Whitney test (2 groups) or Kruskal-Wallis test (3 groups) for skewed variables, and by Fisher’s exact test (2 groups) or χ² test (3 groups) for categorical variables. First, a comparison of all 3 groups was performed for each variable. If the resulting probability value was <0.05, all pairwise comparisons of the groups were performed. Survival was estimated by the Kaplan–Meier method and compared with the log-rank test. In survival analyses, the end point was cardiovascular events. Data on patients who died of other causes were censored at the time of death. Hazard ratios (HRs) and the corresponding 95% CI for cardiovascular events were estimated by Cox regression analysis adjusted for potential confounders. Because probability values are not adjusted for multiple testing, they must be considered as descriptive. All analyses were performed with SPSS software, version 12.0.1 (SPSS Inc, Chicago, Ill) or R 2.1.0 (R Development Core Team, 2005).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

**Results**

**Prevalence of PAD**

The mean ABI±SD (minimum, maximum) was 0.99±0.23 (0.21, 1.38) with the current definition and 0.92±0.23 (0.10, 1.35) with the modified definition. Among all study individu-
uals, 204 patients (25.0%) had an ABI <0.9 according to the current definition, and 292 (35.8%) had an ABI <0.9 according to the modified definition. On the basis of these results, patients were divided into 3 groups (Figure 1): (1) PAD (n=204, 25.0%): ABI <0.9 according to the current definition; (2) no PAD (n=524, 64.2%): ABI ≥0.9 according to the modified definition; and (3) suspected PAD (n=88, 10.8%): ABI <0.9 according to the modified definition and ABI ≥0.9 according to the current definition.

Baseline characteristics of the 3 patient groups are displayed in Table 1. There were only a minority of PAD patients with typical intermittent claudication (n=52, 6.4%). No patient had peripheral ulcerations or leg pain at rest. When we compared patients with PAD and those without PAD, patients with PAD were significantly older, were more often smokers, and had a higher prevalence of concomitant CAD and carotid artery disease than patients without PAD. When patients with PAD and with suspected PAD were compared, there were only a few differences in baseline characteristics.

**PAD and Cardiovascular Events**

Follow-up data (median 6.6 years) were available for 812 patients (99.5%). In total, 118 patients (14.5%) died, 83 (10.2%) of cardiovascular causes. In addition, 30 patients had a nonfatal stroke, and 44 had a nonfatal myocardial infarction. In total, 157 patients (19.3%) experienced cardiovascular events (death, myocardial infarction, or stroke). The event rate was higher in patients with an ABI <0.9 than in patients with an ABI ≥0.9 according to the current and modified ABI definitions (event rate by current definition: ABI <0.9=28.1% versus ABI ≥0.9=16.3%; by modified definition: ABI <0.9=27.4% versus ABI ≥0.9=14.8%).

The incidence of cardiovascular events for the 3 PAD groups (PAD, no PAD, and suspected PAD) is shown in Figure 2. The highest total cardiovascular event rate was found in patients with PAD according to the current definition. Results were similar with regard to total mortality and cardiovascular mortality. Patients with PAD according to the current ABI definition had higher overall and higher cardiovascular mortality than patients with PAD identified only by the modified ABI definition (suspected PAD), but the total cardiovascular event rate was similar for both groups. In general, patients with suspected PAD experienced more cardiovascular events than patients without PAD.

Kaplan–Meier analysis was performed for the end point of cardiovascular events according to the prevalence of PAD (Figure 3). There was a significant difference in event-free survival between patients without PAD and those with PAD (P log-rank <0.0001), as well as between patients without PAD and those with suspected PAD (P log-rank=0.002). During follow-up, there was no significant difference between patients identified as having PAD by the current ABI definition and those identified as having PAD only by the modified ABI definition (suspected PAD; P log-rank=0.56).

**Prognostic Value of PAD Based on Both ABI Definitions**

To compare the prognostic value of each ABI definition, we performed a backward stepwise Cox regression analysis using 2 models that included all confounding factors and PAD defined as ABI <0.9 based on the current ABI definition in 1 model (Table 2) and PAD defined as ABI <0.9 based on the modified ABI definition in the other model (Table 3). The level of significance was 5% for the inclusion and 10% for the exclusion of variables. Among the 12 test variables (age [5-year increase], gender, body mass index, presence or absence of hypertension, diabetes mellitus, high-density lipoprotein cholesterol [1-SD increase], smoker [current or former], CAD, carotid artery stenosis, acute coronary syndrome, statin, and PAD [ABI <0.9 by the current or modified definition]), 5 (PAD, prevalence of diabetes, smok-
ing, high-density lipoprotein cholesterol, and age) were identified as predictors of cardiovascular events in both models.

In addition, a Cox regression analysis was performed to compare patients with PAD, those with suspected PAD, and those without PAD. Results of the analysis are shown in Figure 4. With the inclusion of patients without PAD as the reference group, the HR (95% CI) was 1.56 (0.97 to 2.53) for patients with suspected PAD ($P=0.07$) and 1.67 (1.16 to

![Figure 2. Cardiovascular events according to PAD by use of both ABI definitions. PAD indicates ABI current definition $<$0.9; suspected PAD, ABI current definition $\geq$0.9 and ABI modified definition $<$0.9; and no PAD, ABI modified definition $\geq$0.9.](image-url)
2.40) for patients with PAD according to the current ABI
definition \( (P < 0.006) \), in a fully adjusted model (adjusted for
age, gender, body mass index, presence or absence of
hypertension, presence or absence of diabetes, high-density
lipoprotein cholesterol, smoking, CAD, carotid artery steno-
sis, acute coronary syndrome, and statin medication).

**Discussion**

Atherosclerotic disease involves the entire arterial vessel tree,
and PAD can be considered a marker of generalized athero-
sclerosis. The presence and severity of atherosclerosis in the
lower extremities has a high correlation to cardiovascular
prognosis. There is a strong association between athero-
sclerotic disease in the coronary and carotid arteries, as well
as in the lower-extremity arteries. Therefore, it makes sense
to screen patients with atherosclerotic risk factors for PAD.
Measurement of ABI is widely used for PAD screening, and
ABI is inversely correlated to cardiovascular events.

Guidelines on ABI measurement do not uniformly define
whether the higher or the lower ankle pressure should be
applied for the calculation. The AHA recently published PAD
guidelines with an ABI calculation that used the higher of the
2 ankle pressures, and the same definition is recommended by
the Society of Interventional Radiology. In contrast, a
recent study shows that the lower ankle pressure is more
sensitive than the higher ankle pressure for PAD detection by
ABI calculation. Different studies comparing ABI and
cardiovascular prognosis used either the lower or higher
ankle pressure for ABI calculation. One study
included the average of the anterior and posterior tibial artery
pressures for ABI calculation. To date, no data have been
available to compare the prognostic impact of ABI by
different calculation models.

In the present study, we were able to demonstrate that the
use of the higher of the 2 ankle pressures underestimates the
risk for cardiovascular events. We focused in particular on
those patients identified as having PAD only with the lower
of the 2 ankle pressures (suspected PAD). This group of 88
patients was similar with regard to baseline characteristics as
patients identified as having PAD with the higher ankle
pressure, and the cardiovascular event rate was nearly the
same in both groups (25% versus 28%).

The AtheroGene study population of patients who already
have atherosclerosis is very suitable for use in ABI studies
because of the high prevalence of PAD. In the present study,
the prevalence of PAD was 25% when the higher ankle

![Figure 3. Cardiovascular event-free survival as life-table analysis (Kaplan-Meier) according to PAD by use of different ABI definitions. Probability values describe comparison of PAD vs no PAD; suspected PAD vs no PAD; and PAD vs suspected PAD by log-rank test. PAD indicates ABI current definition <0.9; suspected PAD, ABI current definition $\geq 0.9$ and ABI modified definition <0.9; and no PAD, ABI modified definition $\geq 0.9$.](image)

### Table 2. Backward Stepwise Cox Regression Analysis for Cardiovascular Risk Predictors With Current ABI Definition

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 5-year increase)</td>
<td>1.25 (1.13–1.39)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.69 (1.21–2.36)</td>
<td>0.002</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.54 (1.10–2.16)</td>
<td>0.01</td>
</tr>
<tr>
<td>HDL cholesterol (per 1-SD increase)</td>
<td>0.77 (0.65–0.93)</td>
<td>0.005</td>
</tr>
<tr>
<td>PAD (ABI &lt;0.9 using current definition)</td>
<td>1.50 (1.08–2.10)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Twelve variables were introduced into a multiple stepwise regression model: age (5-year increase), sex, body mass index, presence or absence of hypertension, diabetes mellitus, HDL cholesterol (1-SD increase), smoker (current or former), CAD, carotid artery stenosis, acute coronary syndrome, statin use, and PAD (ABI <0.9 by the current ABI definition). The Table shows all variables selected as predictors of cardiovascular events.

### Table 3. Backward Stepwise Cox Regression Analysis for Cardiovascular Risk Predictors With Modified ABI Definition

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 5-year increase)</td>
<td>1.25 (1.13–1.38)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.67 (1.19–2.33)</td>
<td>0.003</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.53 (1.10–2.14)</td>
<td>0.01</td>
</tr>
<tr>
<td>HDL cholesterol (per 1-SD increase)</td>
<td>0.77 (0.65–0.93)</td>
<td>0.006</td>
</tr>
<tr>
<td>PAD (ABI &lt;0.9 using modified definition)</td>
<td>1.62 (1.17–2.23)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Twelve variables were introduced into a multiple stepwise regression model: age (5-year increase), sex, body mass index, presence or absence of hypertension, diabetes mellitus, HDL cholesterol (1-SD increase), smoker (current or former), CAD, carotid artery stenosis, acute coronary syndrome, statin use, and PAD (PAD defined as ABI <0.9 by the modified ABI definition). The Table shows all variables selected as predictors of cardiovascular events.
pressure was used and 36% when the lower ankle pressure was used. Only 13% of the patients identified as having PAD had intermittent claudication. In population-based studies such as the German GetABIB trial (German Epidemiological Trial on ABI), PAD prevalence was between 15% and 20% in individuals older than 65 years. In the AGATHA study (A Global ATHerosclerosis Assessment), a European multicenter study that included patients with atherosclerotic manifestations, the prevalence of PAD was higher. In that trial, PAD was found in 31% of patients with risk factors and in 41% of patients with atherosclerotic manifestations. This might be explained by the study population, one third of which consisted of patients with known PAD or cerebrovascular disease. In contrast, the MONICA (Monitoring of trends and determinants in Cardiovascular disease) Augsburg Survey, which included patients after myocardial infarction, found that only 4% of the patients had an ABI <0.9 with the lower ankle pressure. The explanation for the higher prevalence of PAD in the present study is the lower age of the patients (mean age 50 years) in the MONICA Augsburg Survey.

Limitations of the present study should be considered. Despite the high prevalence of PAD, the present study did not include a population-based cohort and may not necessarily be representative of other populations. The results of the present study must be confirmed by population-based trials.

In conclusion, this is the first study to compare the lower and higher of the 2 ankle pressures in the context of cardiovascular prognosis. Use of the higher of the 2 ankle pressures may be superior to the lower ankle pressure to address leg perfusion, and in patients with an ABI <0.9 by use of the higher ankle pressure, a more detailed examination of leg perfusion should be discussed, particularly in the presence of clinical symptoms. With regard to cardiovascular prognosis, the true prevalence of PAD is underestimated by use of the higher ankle pressure. With a simple modification (use of the lower instead of the higher ankle pressure), more patients at risk could be identified. On the basis of the present data, use of the lower of both ankle pressures for ABI calculation should be considered for cardiovascular risk prediction.

Disclosures

None.

References

Peripheral arterial disease (PAD) is highly prevalent in the United States and Europe, and these patients are at increased risk for cardiovascular events. The ankle-brachial index (ABI; ratio of ankle and brachial systolic blood pressure) is regarded as an easy, reliable, and noninvasive measure to identify symptomatic and asymptomatic patients with PAD. Usually, systolic blood pressure of both anterior and posterior tibial arteries and both brachial arteries is measured. According to the current guidelines of the American Heart Association, the higher of both ankle pressures and the higher of both arm pressures should be used for ABI calculation, and PAD is considered present if an ABI <0.9 is detected in at least 1 leg. This concept has been challenged by recent studies that suggest the use of the lower ankle pressure for ABI calculation. In the present study, we compared the prognostic value of different models for ABI calculation with regard to cardiovascular events. In total, 812 patients were included, and cardiovascular events (cardiovascular death, stroke, and myocardial infarction; n=157; 19.3%) were evaluated after a median of 6.6 years. We found that using the higher of both ankle pressures for ABI calculation, a group of patients at high risk for cardiovascular events is overlooked. With a simple modification of ABI (use of the lower instead of the higher ankle pressure), more patients at risk could be identified. On the basis of the present data, use of the lower of both ankle pressures for ABI calculation should be considered for cardiovascular risk prediction.
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