WHAT THIS PAPER ADDS
According to current guidelines, the highest systolic ankle blood pressure (BP) should be used for ankle brachial index (ABI) calculation. This study is the first to evaluate impact on cardiovascular events of using the lowest BP for ABI calculation in a population based setting. With this modification of ABI calculation, 70% more patients were identified, who would have been overseen. These subjects had higher event rates than references, with similar levels as the traditionally diagnosed subjects during the first years. The traditional ABI calculation concept of using the highest BP should be challenged to identify more subjects at risk who would benefit from preventive measurements.

Objective: The aim of this study was to estimate the prevalence and predictive accuracy for cardiovascular (CV) morbidity by using different ankle brachial index (ABI) calculation methods in the general population.

Methods: ABI measurements and questionnaire data were collected from 5,080 randomly selected citizens aged 60—90 years. A 10 year follow up with data from Swedish national health registries was carried out. ABI was calculated using as numerator the highest (ABI-HI) or the lowest (ABI-LO) ankle BP obtained in each leg. Subjects were defined as references or having peripheral arterial disease (PAD) based on ABI-LO (Group 1) or ABI-HI (Group 2). Prevalence, mortality, CV events and risk were then analysed for these three groups, and their predictive power by using the area under the curve (AUC).

Results: A total of 4,909 inhabitants were included in the cohort (References: 83.8%, Group 1: 6.7% and Group 2: 9.6%). The prevalence of PAD was 16% using ABI-LO, and 9.6% using ABI-HI. The 10 year all cause mortality for references and Groups 1 and 2 was 27.6%, 48.8%, and 67.2%, respectively. The overall age adjusted hazard ratio (95% confidence interval) for the composite outcome of CV mortality and a non-fatal CV event was 1.25 (1.06—1.49) for Group 1 and 2.11 (1.85—2.39) for Group 2. The prediction accuracy for ABI < 0.9 in predicting CV event measured with AUC was 0.60 for ABI-HI and 0.62 for ABI-LO.

Conclusion: An ABI < 0.9 should be considered a strong risk marker for future CV morbidity. Applying the traditional ABI calculation method of using the highest measured ankle BP, a group of subjects with high CV risk may be overlooked for intervention, and this why the lowest ankle BP should be the preferred for risk stratification. However, as a single predictive tool an ABI < 0.9 cannot adequately discriminate which individual will have a future CV event regardless of calculation method used.

Keywords: Ankle brachial index, Cardiovascular events, Mortality, Risk assessment, Risk marker

INTRODUCTION
Cardiovascular (CV) diseases have a malicious natural history and considerably impact societal resources as well as the health and quality of life of patients. Today medical care focuses mainly on disease treatment, which is often more costly than prevention. It is suggested that more than 80% of CV disease occurring in subjects below the age of 75
years is preventable.\textsuperscript{1,2} A key issue, however, is how to identify individuals at risk.

Ankle brachial index (ABI) measurement for peripheral arterial disease (PAD) was first described by Winsor in 1950\textsuperscript{3} and has since then been regarded as a key diagnostic test. In recent years a lowered ABI has gained increased attention as a marker for general atherosclerosis and CV risk.\textsuperscript{4–8}

The test is claimed to be reliable with a high specificity (83\% – 99\%) but a rather low sensitivity (69 – 89\%),\textsuperscript{8,9} and is known to be influenced by the method of calculation used.\textsuperscript{11,12} When using the lowest measured ankle blood pressure (BP), the prevalence increases by between 30\% and 500\%, depending on the study population, compared with using the highest ankle pressure. Data on the impact of using the higher or lower ankle BP for predicting CV events, as well as the potential as a predictive tool are scarce.\textsuperscript{13,14} In the studies of Niazi \textit{et al.}\textsuperscript{13} and Espinola-Klein \textit{et al.},\textsuperscript{14} the cohorts included 831 and 1 223 subjects, respectively, but neither cohort was strictly population based. Despite this, current guidelines recommend calculating ABI employing the highest BP in each leg and the highest systolic BP in the arm for diagnosis and risk assessment.\textsuperscript{15–17} By using the lower ankle BP, more subjects will be identified, but may potentially cause over diagnosis. A consequence of this could be increased resource utilisation and excessive costs. Conversely, subjects at risk may be neglected and experience a preventable CV event when using the higher ankle BP.

The aim of this study was to estimate prevalence and CV morbidity by using different ABI calculation methods in the general population. A secondary aim was to assess predictive accuracy for CV events by using different methods of ABI calculation.

\section*{Materials and Methods}

\subsection*{Study population}

The study population was described in detail 2007.\textsuperscript{15} Briefly, to make study results generalisable for the entire Swedish population, four regions were selected that covered different geographic and demographic areas. Subjects aged 60 – 90 years were then randomly selected from all inhabitants in these regions and screened for ABI measurements in specially assigned rooms at primary health care centres with as constant temperature as possible. From 8 000 invited individuals 5 080 agreed to participate (Fig. 1). Follow up information was collected from Swedish national registries.\textsuperscript{16} Observation time was from the autumn of 2005 until 31 December 2015. The study was originally designed to estimate the point prevalence of different PAD stages, risk factors, the natural history for limb and life and to evaluate how different methods of ABI calculation affect prevalence and CV risk over time.

\subsection*{ABI measurements and calculations}

ABI was determined by measuring the BP in the right arm using a 12 cm wide BP cuff with the patient in a sitting position. This was followed by ankle BP measurement using the lowest ankle pressure (AP): $\text{ABI} = \frac{\text{AP}}{\text{BP}} = 0.91$

\begin{tikzpicture}
    \node at (0,0) {\textbf{ABI calculation and definition:}};
    \node at (2,0) {Brachial pressure (BP)};
    \node at (2,-1) {120 mmHg};
    \node at (2,-2) {Left-arm systolic pressure};
    \node at (0,-2) {Modified ABI - using the lowest ankle pressure (AP)};
    \node at (2,-3) {BP};
    \node at (2,-4) {\text{ABI-LOW} = \frac{\text{AP}}{\text{BP}} = 0.33};
    \node at (2,-5) {\text{Traditional ABI} - using the highest AP};
    \node at (2,-6) {\text{ABI-HI} = \frac{\text{AP}}{\text{BP}} = 0.91};
    \node at (5,-2) {\text{AP}};
    \node at (5,-3) {40 mmHg};
    \node at (5,-4) {110 mmHg};
    \node at (5,-5) {\text{BP}};
    \node at (5,-6) {120 mmHg};
    \node at (2,-7) {DP};
    \node at (2,-8) {PT};
    \node at (5,-8) {110 mmHg};
    \node at (2,-9) {40 mmHg};
    \node at (5,-9) {120 mmHg};
    \node at (0,1) {Randomly selected - 8 000 inhabitants aged 60 – 90 years};
    \node at (3,0) {\text{5 080 Participants}};
    \node at (5,0) {\text{201 subjects were excluded:}};
    \node at (7,0) {\text{Missing values (n = 109)}};
    \node at (9,0) {\text{ABI measurement discrepancy (n = 50)}};
    \node at (11,0) {\text{ABI-HI > 1.4 (n = 42)}};
    \node at (2,-10) {\text{4 879 included for analyses}};
    \node at (0,-11) {\text{References}};
    \node at (2,-12) {\text{Group 1}};
    \node at (3,-12) {\text{ABI > 0.9 despite method}};
    \node at (5,-12) {\text{ABI-HI > 0.9 but ABI-LOW < 0.9}};
    \node at (7,-12) {\text{n = 4 081 (83.6\%)});
    \node at (9,-12) {\text{n = 330 (6.7\%)});
    \node at (11,-12) {\text{n = 469 (9.5\%)});
    \node at (2,-13) {\text{Group 2}};
    \node at (3,-13) {\text{ABI < 0.9}};
    \node at (5,-13) {\text{ABI-HI < 0.9}};
    \node at (7,-13) {\text{n = 4 879 (83.6\%)});
    \node at (9,-13) {\text{n = 330 (6.7\%)});
    \node at (11,-13) {\text{n = 469 (9.5\%)});
    \node at (0,-14) {\text{All cause mortality}};
    \node at (2,-14) {\text{CV mortality}};
    \node at (4,-14) {\text{CV events}};
    \node at (6,-14) {\text{10 years}};
    \node at (7,-14) {\text{Figure 1. Visual illustration of the study design, including total study population, follow-up duration and primary outcomes, as well as the different ankle-brachial index (ABI) calculation methods including the use of the highest ankle and arm pressure (ABI-HI) vs. the lowest ankle and arm pressure (ABI-LO) in this prevalence study evaluating peripheral arterial disease and cardiovascular (CV) risk in randomly selected Swedish citizens between 60 and 90 years of age. BP = brachial pressure, AP = ankle pressure, DP = dorsalis pedis artery, PT = posterior tibial artery.}};
\end{tikzpicture}
a pocket continuous wave (CW) doppler (8 MHz Doppler probe, Hadeco, Sweden) and the same BP cuff. Ankle BPs were obtained with the subject in supine position by insonating the posterior tibial and dorsalis pedis arteries. Pressures were obtained twice in each vessel, and the mean value of the two measured ankle BPs in each artery was then used to calculate the ABI in two different ways. First, the traditional way according to European Society for Vascular Surgery guidelines divides the highest ankle systolic BP by the arm systolic BP and recommends using the ABI in the leg with the lowest value (corresponding to ABI-HI in this study — Fig. 1). A second calculation was performed using the lowest obtained ankle BP (ABI-LO). The formulas are presented in the supplementary material (Supplementary Fig. S1).

Exclusion criteria, measurements discrepancy, and missing data

If BPs were not measurable in any vessel or if the two BP measurements in the same vessel differed more than 20 mmHg (Supplementary Table S2), subjects were excluded to avoid uncertainties in the classification to the two groups, i.e., it is not known whether the lack of BPs are a consequence of true grave PAD, hypoplasia, a coding error, or technical measurement problems. Also, all cases with an ABI > 1.4 were excluded, to avoid influence of high ABI results, for which the analyses in this study were not designed.

Subgroup classification — definitions

Subjects were allocated to three groups: Reference group: ABI ≥ 0.9 according to both ABI-HI and ABI-LO definitions (no PAD); Group 1: ABI > 0.9 according to the ABI-HI definition, but ABI < 0.9 according to ABI-LO definition; Group 2: ABI < 0.9 according to ABI-HI definition (i.e., the traditional definition of ABI).

Subject characteristics and follow up

All cause and CV deaths were retrieved from the Cause of Death Register as described previously. For CV events and death, the following International Classification of Diseases 10th edition codes were used: I10-15, I20-25, I50-51, I60-69, and I70-73 (Supplementary Table S3). Non-fatal CV events were collected from the Swedish National Patient Register, which covers > 99% of all somatic and psychiatric hospital discharges.

The study was approved by local ethics committees in Stockholm (KI 03-538 and Dnr 2014/2070-32), Umeå University (Dnr 03-459), Lund University (832-0), Uppsala University (Dnr 03-564), and Örebro (Dnr 374-03). Informed consent was obtained from each participant.

Statistics

Baseline characteristics were presented as descriptive statistics with mean and standard deviations for continuous data and absolute and relative frequencies for category data. Since ABI group is an ordinal variable with progressively more severe disease with increasing levels of events, Cuzick’s trend test was used for group differences. This is because it is more powerful than a test for unordered group variables. For regression analyses and age adjusted survival plots, Cox or Royston—Parmar models were used to investigate risk of a CV event in the three ABI groups. The proportional hazards requirement of the Cox model was employed using Schoenfeld residuals for baseline age and graphical methods for ABI group. When non-proportional hazards were indicated, Royston—Parmar models was used with three degrees of freedom for the baseline hazard and three degrees of freedom for the hazard ratio (HR) of time dependent variables. To test equality of the adjusted survival curves a composite test for equal hazards in all three groups was used. Histograms were used to illustrate the distribution of ABI values in subjects with and without CV events. The predictive power of ABI for subsequent CV events was evaluated by the AUC statistic for receiver operating characteristic (ROC) curves, with tests between AUC for ABI-LO and ABI-HI using the method of Delong. All analyses were carried out in Stata (version 16.1), StataCorp LP, College Station, TX, and all tests and confidence intervals were two sided.

Terminology definitions

Risk marker: A variable associated with an increased risk of disease but not necessarily the cause of the disease. Predictor: A risk marker used in a prediction model. A good predictor should provide incremental prognostic information when used in a model together with other predictors. Single predictor: A risk marker used as the only predictor in prediction modelling. A good single predictor should have the ability to foresee a future event and discriminate which individuals will or will not have the event. A good single predictor would be useful in a screening situation.

RESULTS

Cohort

Of the 5 080 subjects in the cohort at baseline, 4 879 were included for analyses. The reason for excluding 201 subjects were missing values (n = 109), ABI measurement discrepancy (n = 50), and ABI-HI > 1.4 (n = 42). Of the included subjects, 4 081 (83.6%), 329 (6.7%), and 469 (9.6%) were classified as Reference, Group 1 and Group 2, respectively. The PAD prevalence in the population when using ABI-HI was 9.6% (n = 469) and for ABI-LO 16.3% (n = 799). Therefore, 70% (number of subjects with ABI-LO [n = 799] subtracted by the number of subjects with ABI-HI [n = 469] then divided by the number of subjects with ABI-LO) more subjects at risk were identified with ABI-LO. The prevalence was higher in women than in men according to both definitions (Fig. 2).
Subjects in Groups 1 and 2 were older than Reference (74.6, 77.0, and 69.9 years, respectively). Comorbidities, except for hypertension, were significantly more common in Group 1 than in Reference (Table 1). Smoking history was similar (54% vs. 51%, p = .46). In Group 2, smoking history, coronary artery disease, cerebrovascular disease, and diabetes were more frequent among men, while women more often suffered from hypertension (Table 1). Use of CV preventive medications was generally low. In PAD subjects, antiplatelet therapy was more common in Group 2 than in Group 1 (46% vs. 31%, p < .001). A similar pattern was noted for lipid lowering drugs (27% vs. 20%, p < .001) (Table 1 and Supplementary Table S1).

**All cause mortality, cardiovascular mortality and non-fatal cardiovascular events**

During the 10 year follow up the unadjusted all cause mortality for Reference, Groups 1 and 2 was 27.6%, 48.8%, and 67.2%, respectively. The corresponding CV mortality was 13.8%, 20.1%, and 24.7%. When compared with Reference, the frequency of non-fatal CV events was doubled for Group 2 (33.8% vs. 67.2%) and increased 1.5

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**Table 1.** Baseline demographics of 4909 randomly selected Swedish citizens between 60 and 90 years of age, classified into three groups according to their ankle-brachial index (ABI) measurements the highest ankle and arm systolic blood pressure (ABI-HI), and the lowest ankle pressure and arm systolic blood pressure (ABI-LO)

<table>
<thead>
<tr>
<th>Variables</th>
<th>ABI-HI ≥ 0.9 and ABI-LO ≥ 0.9 (Group 1)</th>
<th>ABI-HI ≥ 0.9, ABI-LO &lt; 0.9 (Group 1)</th>
<th>ABI-HI and ABI-LO &lt; 0.9 (Group 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 4081)</td>
<td>Male (n = 1882)</td>
<td>Female (n = 2199)</td>
</tr>
<tr>
<td>Age</td>
<td>69.9 ± 7.5</td>
<td>69.5 ± 7.3</td>
<td>70.2 ± 7.6</td>
</tr>
<tr>
<td>Smoking history</td>
<td>2091 (51.2)</td>
<td>1176 (62.5)</td>
<td>915 (41.6)</td>
</tr>
<tr>
<td>CAD</td>
<td>618 (15.1)</td>
<td>349 (18.5)</td>
<td>269 (12.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>360 (8.8)</td>
<td>177 (9.4)</td>
<td>183 (8.3)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>246 (6.0)</td>
<td>141 (7.5)</td>
<td>105 (4.8)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>80 (2.0)</td>
<td>49 (2.6)</td>
<td>31 (1.4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1420 (34.8)</td>
<td>619 (32.9)</td>
<td>801 (36.4)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>127 (3.1)</td>
<td>86 (4.6)</td>
<td>41 (1.9)</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>840 (20.6)</td>
<td>465 (24.7)</td>
<td>375 (17.1)</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>622 (15.2)</td>
<td>320 (17.0)</td>
<td>302 (13.7)</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>1528 (37.4)</td>
<td>695 (36.9)</td>
<td>833 (37.9)</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or mean ± standard deviation. CAD = coronary artery disease; TIA = transient ischaemic attack. The trend test p-value for group differences was <.001 for all variables except for smoking history in women and anticoagulation therapy in men. The statistical differences between groups are presented in the Supplement Table 1.
times in Group 1 (33.8 vs. 45.9). The unadjusted CV event-free survival for Reference at one, five, and 10 years was 95.2%, 78.2%, and 57.8%, respectively. Corresponding figures for Group 1 are 89.1%, 63.8%, and 41.9%, and for Group 2 are 86.0%, 50.1%, and 21.3% (see Fig. 3).

The overall age adjusted HR for any CV event (95% CI) for Groups 1 and 2 was 1.25 (1.06–1.49) and 2.11 (1.85–2.39), respectively. Results separated by sex are presented in Table 2.

**Prediction measurements and accuracy**

The predictive ability of an ABI < 0.9 in predicting an individual’s subsequent CV event after five and 10 years of observation was low according to both ABI-HI and ABI-LO. The analyses with ROC curves gave an AUC = 0.60 for ABI-HI and AUC = 0.62 for ABI-LO. Using ABI < 0.9 as a cut-off point, there was a similar frequency of false positives and negatives for prediction of an event for both calculation methods, as shown in the distribution of CV events by ABI in 10 years (Fig. 4). Raw data histograms were performed for all years and revealed similar patterns (Supplementary Fig. S2). The p value for comparing AUC for ABI-HI and LO was .18 at 10 years.

**DISCUSSION**

In this decade long follow up, the impact of using different ABI calculation methods on PAD prevalence and CV risk was assessed. By using the lowest measured ankle BP

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Group</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference group</td>
<td>4 081</td>
<td>3 885</td>
<td>3 192</td>
</tr>
<tr>
<td>Group 1</td>
<td>329</td>
<td>293</td>
<td>264</td>
</tr>
<tr>
<td>Group 2</td>
<td>469</td>
<td>405</td>
<td>313</td>
</tr>
</tbody>
</table>

Figure 3. Cumulative Kaplan-Meier estimates of the unadjusted and age-adjusted (dashed lines) cardiovascular (CV) event-free survival rates of 4909 randomly selected Swedish citizens between 60 and 90 years of age, classified into three groups according to their ankle-brachial index (ABI) measurements, where the reference group represents individuals with an ABI ≥ 0.9, both calculated using the highest ankle and arm systolic blood pressure (SBP) (ABI-HI), as well as using the lowest ankle pressure and arm SBP (ABI-LO). Group 1 defined as participants with an ABI-HI ≥ 0.9, but an ABI-LO < 0.9, and Group 2 defined by an ABI-HI and ABI-LO < 0.9. The composite test of equality of the adjusted curves obtained a p value < .001.

Table 2. Crude and age-adjusted hazard ratio risks for non-fatal and fatal cardiovascular events according to the ankle brachial index (ABI) measured using the highest ankle and arm pressure (ABI-HI) versus the lowest ankle and arm pressure (ABI-LO), for the reference population (ABI-HI and ABI-LO > 0.9), group 1 (ABI-HI > 0.9 and ABI-LO < 0.9) and group 2 (ABI-HI and ABI-LO < 0.9), for the whole cohort and by gender

<table>
<thead>
<tr>
<th></th>
<th>Crude HR (95% CI)</th>
<th>p value</th>
<th>Adjusted HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference group</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>1.65 (1.39–1.95)</td>
<td>&lt;.001</td>
<td>1.25 (1.06–1.49)</td>
<td>.009</td>
</tr>
<tr>
<td>Group 2</td>
<td>3.01 (2.66–3.41)</td>
<td>&lt;.001</td>
<td>2.11 (1.85–2.39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference group</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>1.90 (1.50–2.41)</td>
<td>&lt;.001</td>
<td>1.41 (1.11–1.80)</td>
<td>.005</td>
</tr>
<tr>
<td>Group 2</td>
<td>2.64 (2.20–3.17)</td>
<td>&lt;.001</td>
<td>2.04 (1.69–2.46)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference group</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>1.62 (1.28–2.06)</td>
<td>&lt;.001</td>
<td>1.22 (0.96–1.55)</td>
<td>.107</td>
</tr>
<tr>
<td>Group 2</td>
<td>3.61 (3.05–4.28)</td>
<td>&lt;.001</td>
<td>2.26 (1.90–2.71)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CI = confidence interval.
(ABI-LO) for ABI calculation 70% more subjects were identified with a PAD diagnosis than if using the traditional method with ABI-HI. These additional subjects identified in Group 1 would possibly be overlooked for preventive measures, despite the fact that they also had significantly higher mortality and risk of non-fatal CV events rates compared with references. During the first years of follow up, they faced a similar risk to Group 2. It is thought that this is the first time the predictive value of different modes of ABI calculation to foresee a future individual CV event has been evaluated in a population based setting. While having an ABI < 0.9 is a well known risk marker for adverse CV events, it was found that this test was not able to foresee which individual subject would be affected by a future CV event. The interpretation of this is that having a low ABI is a risk marker among others such as a history of smoking or CV disease, but of limited value as a single predictor.

In the literature, risk assessment and prediction are often used interchangeably, which may cause confusion. In this paper, prediction is interpreted as the ability of a test to foresee a future event and discriminate which individuals will or will not have the event, while the risk refers to a general increased threat.

The way to calculate ABI is a neglected factor in PAD research focusing on prevalence, CV risk and prevention. The American Heart Association performed a literature study with the perspective of ABI assessment and found that only one of 16 studies included in their review specified the ABI calculation method employed. Occasionally, however, the calculation method has been scrutinised. For example, by using arterial duplex ultrasonography and digital subtraction angiography as gold standard the predictive ability of using ABI-LO and ABI-HI to detect PAD was evaluated and found to be adequate. In these studies, ABI-LO demonstrated a higher sensitivity than ABI-HI (0.84 vs. 0.89), and a lower specificity (0.64 vs. 0.93). ABI-LO also had a better overall accuracy.

The prevalence varies with the method of calculation used, and in this cohort it ranged from 9.6% using the highest ankle BP to 16.3% with the lowest ankle BP. Similar variations have been reported by others. For example, in the Multi-Ethnic Study of Atherosclerosis, the prevalence among women and men was, almost, respectively four and three times higher when using ABI-LO. Despite using the same recommended ABI threshold of 0.90, such prevalence variations will influence risk group size and thus resource allocations. This emphasises the importance of consistency.
in reporting the methodology for ABI calculations in future studies.

A key purpose of ABI is to identify populations at risk of CV morbidity. Risk assessment comparing ABI-LO and ABI-HI has previously been studied in high CV risk populations. In a hospital based setting of patients with chest pain eligible for diagnostic heart catheterisation, Espinola-Klein et al. demonstrated a slightly higher risk of a CV event for the ABI-HI than in the ABI-LO group. They found that by employing ABI-LO a HR of 1.56 was observed. Their corresponding figure for ABI-HI was 1.67. Another study reported similar results in patients undergoing coronary artery bypass surgery. In the population based setting, subjects with ABI-LO had a 25% higher risk of a fatal or non-fatal CV event than an age adjusted reference group. Accordingly, also in population based groups, using ABI-LO increases the size of the groups identified, a group with a consistent increased risk of a CV event.

ABI measurements have proven valuable for identification of groups of subjects with an increased CV risk, and several population based studies confirm that having an ABI < 0.9 should be regarded as an independent risk marker for future CV events and death. Accordingly, a low ABI may be considered an additional tool to improve the predictive performance of different prognostic models. This is especially true for individuals at intermediate risk. For example, by adding ABI to the Framingham Risk score, one in five men and one in three women were re-classified as having a substantial risk. While ABI measurements should be evaluated as an addition to improve other risk assessment tools such as the SCORE and ASCVD, this was not a goal of this study.

On the other hand, as a secondary aim, the aim was to evaluate whether an ABI < 0.9 could also predict individual risk. As shown in Figure 4, the isolated fact of having an ABI < 0.9 was not a reliable way to discriminate subjects who will or will not have a CV event. Regardless of calculation method used the ROC curve analysis showed a similar low AUC for ABI-HI and ABI-LO in the cohort. Accordingly, the intrinsic prognostic value of ABI does not appear to depend on the calculation method. However, 70% more subjects at risk were identified using ABI-LO than ABI-HI. Corresponding results have previously been described by Le Bivic et al. emphasising this finding.

**Limitations**

One limitation of this study was a possible selection bias. An analysis of the non-participants in this study was made, and these subjects were older and more severely ill than the enrolled subjects. Thus, the prevalence of PAD in this cohort is likely to be underestimated as well as the incidence of CV events. Subjects with an ABI > 1.4 (n = 42, 0.86%) were excluded from the analyses, mainly due to the inability to assign subjects into the groups of ABI-HI and ABI-LO. Furthermore, the increased CV risk of subjects with incompressible vessel is well described and therefore not the main target group for the research question. Regardless, it is unlikely that assignment of these 42 subjects to either group would significantly alter the results. Another limitation is that the systolic brachial BP was only measured in the right arm for practical purposes. This may potentially have influenced PAD prevalence and the number of subjects at risk among those with left, unilateral upper extremity ischaemia. This is fortunately a rare circumstance and is not assumed to considerably alter the results. Finally, an inaccuracy is that the registers only capture in hospital diagnosed CV events. The latter is probably of minor importance, however, since most CV events need in patient care.

**Conclusion**

The prevalence of PAD was 16% using ABI-LO and 9.6% using ABI-HI. An ABI < 0.9 should be considered a strong risk marker for future CV morbidity. Applying the traditional ABI calculation method of using the highest measured ankle BP, a group of subjects with high CV risk may be overlooked for intervention, which is why the lowest ankle BP should be preferred for risk stratification. However, as a single predictive tool a measured ABI < 0.9 cannot adequately discriminate which individual will have a future CV event regardless of calculation method used.

**CONFLICT OF INTEREST**

None.

**FUNDING**

The original study was supported by unrestricted grants from the Swedish Heart Lung Foundation, Värmland’s County Research Council, Sanofi-Aventis, and Astra Zeneca.

**DATA AVAILABILITY STATEMENT**

The data underlying this article will be shared on reasonable request to the corresponding author.

**APPENDIX A. SUPPLEMENTARY DATA**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2022.05.001.

**REFERENCES**

10 Shabani Varaki E, Gargiulo GD, Penkala S, Breen PP. Peripheral
14 Espinola-Klein C, Rupprecht HJ, Bickel C, Lackner K, Savvidis S,
13 Le Bivic L, Magne J, Guy-Moyat B, Wojtyna H, Lacroix P,
12 Niazi K, Khan TH, Easley KA. Ten year mortality in
16 The National Board of Health and Welfare (Socialstyrelsen). Available at: https://www.socialstyrelsen.se [Accessed 11 May 2022].