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Reproducibility and reliability of the ankle–brachial index as assessed by vascular experts, family physicians and nurses

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Abstract: The reliability of ankle–brachial index (ABI) measurements performed by different observer groups in primary care has not yet been determined. The aims of the study were to provide precise estimates for all effects influencing the variability of the ABI (patients' individual variability, intra- and inter-observer variability), with particular focus on the performance of different observer groups. Using a partially balanced incomplete block design, 144 unselected individuals aged ≥ 65 years underwent double ABI measurements by one vascular surgeon or vascular physician, one family physician and one nurse with training in Doppler sonography. Three groups comprising a total of 108 individuals were analyzed (only two with $ABI < 0.90$). Errors for two repeated measurements for all three observer groups did not differ (experts 8.5%, family physicians 7.7%, and nurses 7.5%, $p = 0.39$). There was no relevant bias among observer groups. Intra-observer variability expressed as standard deviation divided by the mean was 8%, and inter-observer variability was 9%. In conclusion, reproducibility of the ABI measurement was good in this cohort of elderly patients who almost all had values in the normal range. The mean error of 8–9% within or between observers is smaller than with established screening measures. Since there were no differences among observers with different training backgrounds, our study confirms the appropriateness of ABI assessment for screening peripheral arterial disease (PAD) and generalized atherosclerosis in the primary care setting. Given the importance of the early detection and management of PAD, this diagnostic tool should be used routinely as a standard for PAD screening. Additional studies will be required to confirm our observations in patients with PAD of various severities.

Key words: ankle–brachial index; peripheral arterial disease; precision; reproducibility; screening

Introduction

Coronary heart disease and stroke as manifestations of atherosclerosis are among the leading causes of death. Consequently, there has been an intensive search for methods of measuring atherosclerosis 'burden'

that may indicate the cardiovascular and also overall risk of the individual, particularly asymptomatic patient.¹

A large body of evidence has been gathered on the ankle–brachial index (ABI), which represents the ratio of the ankle to brachial systolic pressure.^{2,3} In the supine position, the pressure in the arm artery should be somewhat lower than in the ankle arteries, with a resulting ABI ratio of about 1.10.^{4,5} However, if atherosclerotic stenosis occurs in the lower extremity, the decreased pressure in the ankle arteries leads to lower ABI. Conventionally, ABI values below 0.90 are considered pathological, indicating peripheral arterial disease (PAD).⁶ Compared with angiography, the sensitivity of a low ABI for leg artery stenosis of $\geq 50\%$ is about 90%, and the specificity is about 98%.⁷

In a series of large-scale epidemiological studies in various settings and patient populations, it has consistently been shown that a decrease in ABI is associated with a substantially elevated risk of coronary death, cerebrovascular death and death from any cause.^{8–13}

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In a recent systematic review, the specificity of a low ABI for predicting future cardiovascular outcomes was high (e.g. 88% for cardiovascular mortality).⁹

Major guidelines and consensus statements recommend the ABI as a tool for the assessment of cardiovascular risk.^{1,3,6,14} It is non-invasive and generally regarded as easy to learn and apply with inexpensive equipment in the office or clinical setting. However, it is not clear whether the ABI can be reliably determined by non-experts such as family physicians or nurses, or whether its use should be restricted to specialists in vascular medicine. To date, methodological work on this topic is limited.

We therefore aimed to provide exact estimates of all effects influencing the variability of the ABI measurements. In particular, the study was to quantify intra-observer variability (same individual, same observer) as well as inter-observer variability (same individual, different observers) for ABI measurements when performed by vascular surgeons or vascular physicians, family physicians, or nurses.

Methods

Study population

Details on the study methods have been published previously.¹⁵ Volunteers were eligible for inclusion in the study if they were members of a public health insurance plan (BKK Hoechst), aged 65–70 years, resident in Frankfurt-Hoechst, ambulatory without wheelchair or walking aids, able to understand the study and able to provide written informed consent. Exclusion criteria were serious diseases such as cancer, any amputation of the upper or lower extremities, and a history of stroke with hemiplegia.

Observers

For the study, six experts, six family physicians and six nurses were recruited. Experts (vascular surgeons or internists with a specialization in vascular medicine) were selected from the co-ordinating and training centers of the German Epidemiological Trial on Ankle Brachial Index (getABI) study, which is a 5-year study on the prognosis for elderly patients with a low ABI compared to those with a normal ABI.¹³ Family physicians, all of whom with at least 3 years of residency training after medical school, were also getABI investigators. Nurses, who had received general training in assistance and technical support for medical devices such as ECG, X-ray or ultrasound (but no formal training on ABI), were from the offices of the experts. For the purpose of the getABI study, family physicians and nurses had received one-time training at investigator meetings on Doppler measurements and ABI calculations before the start of the study in 2001. On that occasion, the experts had demonstrated the correct use of the handheld Doppler devices

(on healthy volunteers) and the ABI measurements to the family physicians. As each vascular physician had ‘trained’ about 10 family physicians and their staff on that day and there were also a number of talks with discussion time, it seems that the actual average ‘hands-on’ training time for each family physician was only a few minutes.

Primary variables

The aim of the study was to estimate three variables, namely the true differences in ABI between patients, the measurement error resulting from repeated measurements in the same patients by the same observer (intra-observer variability), and the additional error obtained from repeated measurements on the same patient by a different observer (inter-observer variability). A design was used that is tailored for comparison between the groups of observers (experts, family physicians, nurses).^{15,16} Following this approach, each participant had a double measurement by one expert, one family physician and one nurse, respectively. A complete set of measurements in each volunteer consisted of six ABI measurements. To realize one ‘run’ of this plan, a sample of 36 patients was required. In each run of 36 probands any of the 36 possible pairs of observers from two different groups assessed one proband together. Thanks to this ‘group divisible partially balanced incomplete block’ design, it was not necessary for all 18 observers to perform two measurements on each of the 4×36 participants (the usual procedure for duplicate measurements), which would have resulted in a total of 5184 ABI measurements, but only on 4×6 participants, which resulted in 864 measurements (16.7% of 5184), sufficient to provide the same information with the desired precision.

Sample size considerations

In a previous study, the difference between the standard deviations of the most and least experienced observers was found to be 0.05 ABI points (standard deviations of 0.07 and 0.12 respectively).¹⁷ However, the present study was intended to allow for a somewhat finer discrimination, and therefore a two-way difference of half this amount (0.025 ABI points, 0.07 versus 0.095) was decided to be the minimal difference worthy of detection. Given a sample size of 108 (three runs of the design), the power for this comparison in an F-test was calculated as 93%, which was considered acceptable.

Study conduct

Figure 1 displays the study flow. A total of 1062 volunteers meeting the inclusion criteria received an invitation letter from the health insurance fund of the chemical company Hoechst and were invited to participate in the study. For the study, the first 100 men and 100 women to respond were chosen.

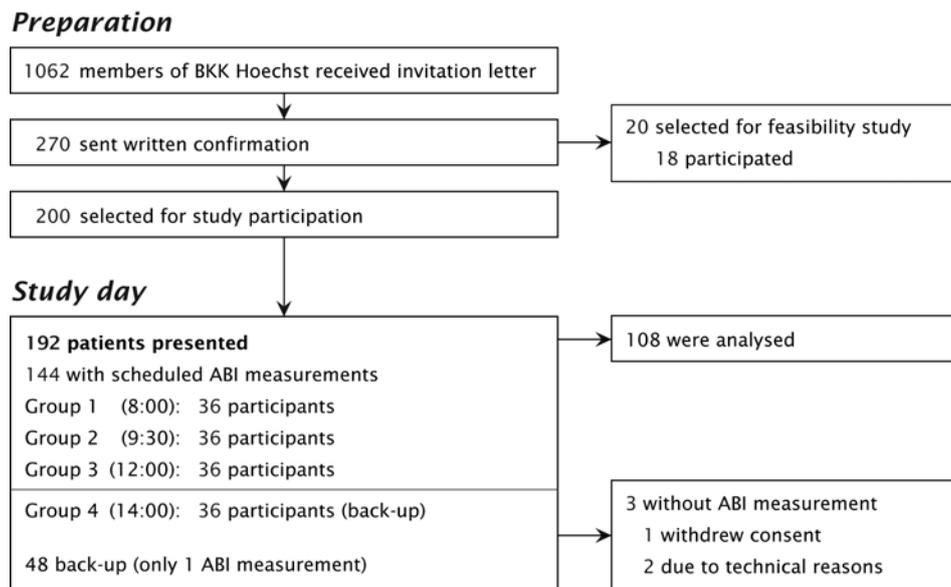


Figure 1 Patient disposition and study flow.

On the study day (December 12, 2005), the first 36 consecutive volunteers were enrolled for ABI measurements, and the remaining 14 volunteers were registered as stand-by probands ('back-up', not used in this study). This procedure was followed for three groups.

All volunteers underwent a physical examination by the vascular physicians or family physicians before the initiation of ABI measurements. Further, height, weight (for calculation of body mass index: BMI), and waist and hip circumference (for calculation of the waist-hip ratio) were measured. The volunteers were questioned about risk factors for atherosclerotic complications (smoking, hypertension, lipid disorders, diabetes mellitus, symptomatic PAD) and these were recorded on case record forms. For the ABI repeat measurements, each participant was measured exactly by one observer from each of the three observer groups, and each observer measured six of the 36 participants in a group.

The study was approved by the Institutional Review Board of the Ruhr-University Bochum and conducted in accordance with the 'Good Epidemiological Practice' recommendations issued by the 'German Working Group Epidemiology'.¹⁸

Doppler measurements and ABI determination

For ABI determinations, the same Doppler ultrasonic device as in the getABI study was used (Kranzbühler 8 MHz, Solingen, Germany). Measurements and calculations were performed according to the recommendations of the American Heart Association.¹ After an initial 10-minute rest of the volunteer in the supine position with the upper body as flat as possible, the blood pressure cuff was used to measure systolic blood

pressure in the brachial artery in both arms, with the Doppler detector in the antecubital fossa. It was then applied to the ankle, and the Doppler probe was used to determine systolic blood pressure at the left and right posterior and anterior tibial arteries. All pressures were measured to the nearest 2 mmHg. The volunteers remained lying on the bed until the next ABI measurement, with a rest period of at least 10 minutes between each observer measurement. Measurements were supervised and recorded by assistants, who ensured the correct order of measurements and the blinding of the observer to his/her previous measurements on the same volunteer. Pressures in each leg were measured and the ABIs calculated separately for each leg.

During the study, only raw blood pressure values were recorded. The ABI values were calculated post hoc by statisticians. The ABI for each leg equals the ratio of the higher of the two systolic pressures (anterior tibial and posterior tibial) above the ankle to the average of the right and left brachial artery pressures, unless there is a discrepancy ≥ 10 mmHg in blood pressure values between the two arms. In such a case, the higher reading was used for the ABI.

Data processing and statistical analysis

All data were double-punched to ensure accuracy of data entry. The main variables to be estimated were the standard deviation of repeated measurements in the same volunteer by the same observer (intra-observer variability), the standard deviation of measurements in the same volunteer by different observers (inter-observer variability), and the standard deviations of the true ABI values in the different volunteers. Bland Altman plots were used to assess the repeatability of the ABI by comparing repeated measurements on a

series of participants.¹⁹ Analyses were performed using a mixed model (Proc Mixed, SAS Version 9.13) with two random factors (observers [18 levels] and volunteers [108 levels]) and their interaction.

Total variation of the ABI values was separated into four variance components: (a) intra-observer variance; (b) additional variance due to bias between observers; (c) additional variance due to the interaction between patients and observers; and (d) inter-individual variance. From this, inter-observer variance was calculated as the sum of intra-observer variance plus additional variance due to bias between observers plus additional variance due to the interaction between patients and observers. Standard deviations are the square roots of these numbers.

In order to summarize these numbers in a single value, the intra-class correlation coefficient (ICC) was used. This coefficient calculates the fraction of the total variation of the ABI measurements (sum of components (a) + (b) + (c) + (d)) caused by the medically meaningful information (component (d), inter-patient variation).

In addition to the global numbers, separate estimates of intra-observer variance were obtained for each individual observer. Averaging these for all observers of one of the three qualifications, the average quality of the measurements of the three groups could be estimated.

Statistical differences between these groups were investigated by ANOVA. Here, the sum of squares for observers was divided into the part due to differences between the groups and the part due to individual differences between observers.

Results

Proband disposition and characteristics

Figure 1 shows patient disposition at various stages of the study. Of the 200 invited volunteers, 192 (96%) were present at the study day. Volunteers in all groups were similar in terms of characteristics and vascular risk factors (data not shown). In 189 volunteers, all ABI measurements could be obtained. Statistical analysis was performed on three groups with a total of 108 volunteers (58 females, 50 males).

Individuals in these three groups were 68.6 (± 1.5) years old, female in 53.7%, and had a mean BMI of 29.0 (± 4.3) kg/m². A total of 9.2% and 40.7%, respectively, were active or former smokers, 58.0% were hypertensive, 54.8% were dyslipidemic, and 15.7% had diabetes mellitus. The mean ABI was 1.10 (± 0.1), and only two (1.85%) volunteers had an ABI < 0.90. No elevated ABI values > 1.40 were recorded, i.e. a ratio that is associated with medial calcification and incompressible arteries. Further details about patient characteristics have been reported elsewhere.¹⁵

Components of variability

The mean variation (standard deviation) within volunteers, between observers, and between volunteers is shown in Table 1. Intra-observer variability was 0.087 ABI points (expressed by standard deviation divided by mean: 8%). Figure 2 shows the distribution of the intra-observer errors in all measurements.

Table 1 Primary parameters: underlying factors of variability of ABI determinations.

Component		Variance	Standard deviation	95% confidence intervals for SD
(a)	Variation within volunteers σ (<i>intra-observer</i> variation)	0.008	0.087	[0.081; 0.095]
(b)	Variation due to observer bias λ	0.001	0.029	[0.019; 0.058]
(c)	Variation due to observer-patient interaction φ <i>Inter-observer</i> variation (sum of variances (a) and (b) and (c))	0.002	0.046	[0.036; 0.067]
(d)	Variation between volunteers τ	0.011	0.103	[0.076; 0.107]

Within volunteer variation (*intra-observer* variability, expressed as standard deviation) was 0.087 ABI points. In order to calculate the standard deviations of two measurements by two different observers (*inter-observer* variability), intra-observer variance and the two between-observer variances (bias and interaction) have to be added. On doing this, inter-observer standard deviation was calculated as 0.103 ABI points.

$$\text{SD, standard deviation (inter-observer variability)} = \sqrt{\sigma^2 + \lambda^2 + \varphi^2} = 0.103$$

Variation among volunteers was 0.09 ABI points, almost identical to the value of intra-observer standard deviation. Placing this in relation to total variation (true value and error) the ICC (intra-class correlation-coefficient) was calculated as 0.423:

$$\text{ICC} = \frac{\tau^2}{\sigma^2 + \lambda^2 + \varphi^2 + \tau^2} = 42\%.$$

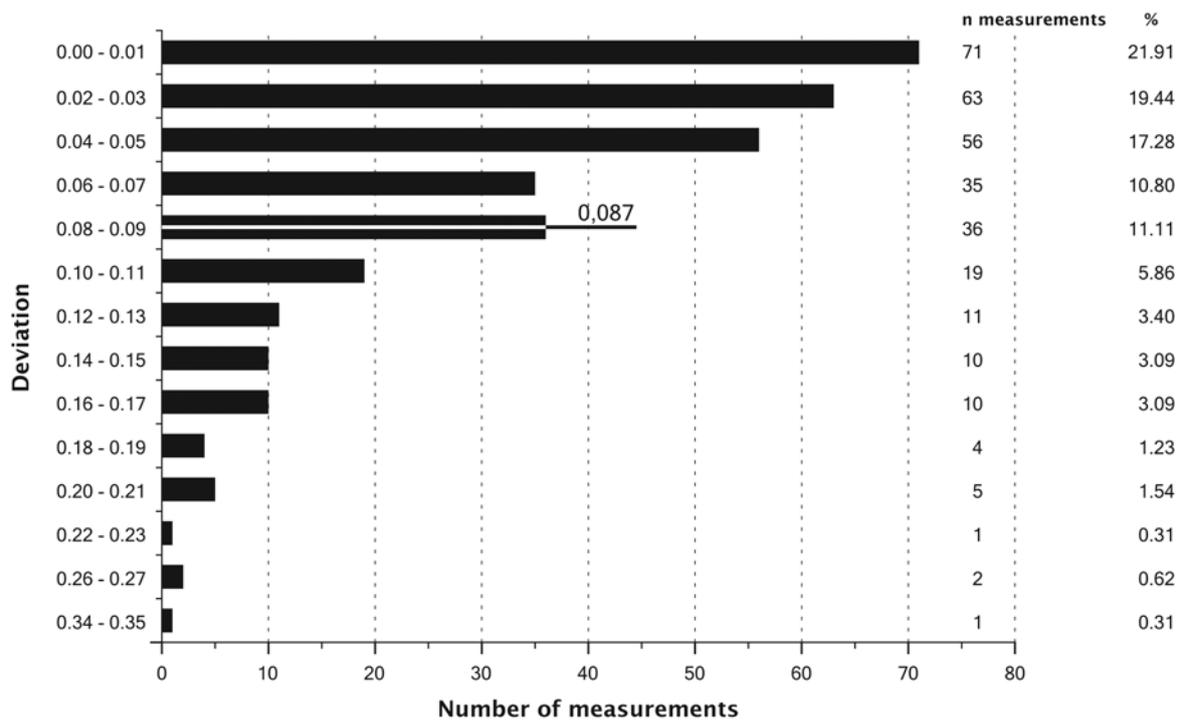


Figure 2 Variability of ABI measurements. The frequency plot shows the distribution of the intra-observer error in 324 ABI determinations ($n = 108$ volunteers, with duplicate measurements by three observers each). Observers represented all three groups (experts, family physicians, nurses). The horizontal line at 0.08–0.09 represents the mean of all measured observer errors.

Inter-observer standard deviation was calculated as 0.103 ABI points (i.e. 9%).

Comparison of observers by training

Figure 3 shows a scatter diagram of the inter-observer variability in the three observer groups. Variations in measurements are summarized in Table 2. Errors for two repeated measurements for all three observer groups did not differ (experts 8.5%, family physicians 7.7%, and nurses 7.5%; F-test $p = 0.39$). In addition, there was no systematic bias among groups (i.e. observers measured the same mean values, $p = 0.58$).

Discussion

This is the first large-scale study investigating the components of variability in ABI measurements. As key outcomes, both intra-observer and inter-observer errors for determination of the ABI were low, meaning that reproducibility of the ABI measurement is high. Further, there were no differences in terms of ABI determination among observers with different training backgrounds.

Despite the frequent use of the ABI in epidemiological studies and the recommendations to use it as a screening tool, the available evidence with regard to its reliability and reproducibility is limited, particularly in apparently ‘healthy’ individuals. In the last

20 years, to our knowledge only four studies have addressed this issue. Fowkes et al reported a study with four observers (newly recruited physiology measurement technicians who received training in ABI measurements) and 24 patients with symptomatic PAD and 12 healthy volunteers.²⁰ The 95% confidence limits of one measurement of the ABI were estimated to be $\pm 16\%$, decreasing to $\pm 10\%$ for the mean of four measurements taken by two observers on 2 days. Analysis of variance indicated that the variability in the measurement of ABI attributable to observers, days, timing of measurements on the same day, and repeat measurements was considerably less than the ‘biological’ variability among individuals and legs.

In the study by Mätzke et al, seven measurers with variable experience repeatedly measured ABI in 19 PAD patients. A total of 16% of the ABI values differed by 0.15 or more from the median and the mean coefficient of variation was 56.1. In the subsequent part of the study with two experienced observers, the difference between measurements did not exceed 0.14, with a mean coefficient of variation of 3.2.²¹

Jeelani et al found that the mean ABI difference measured by two observers (physician and technician, using sphygmomanometry or a semi-automated device) in 14 patients was 0.05, with a 20% margin of error.²²

Finally, Kaiser et al reported a study with 24 less experienced and two experienced observers measuring ABI in six patients. The overall intra-observer variability estimate was 11.8%; the intra-observer variability

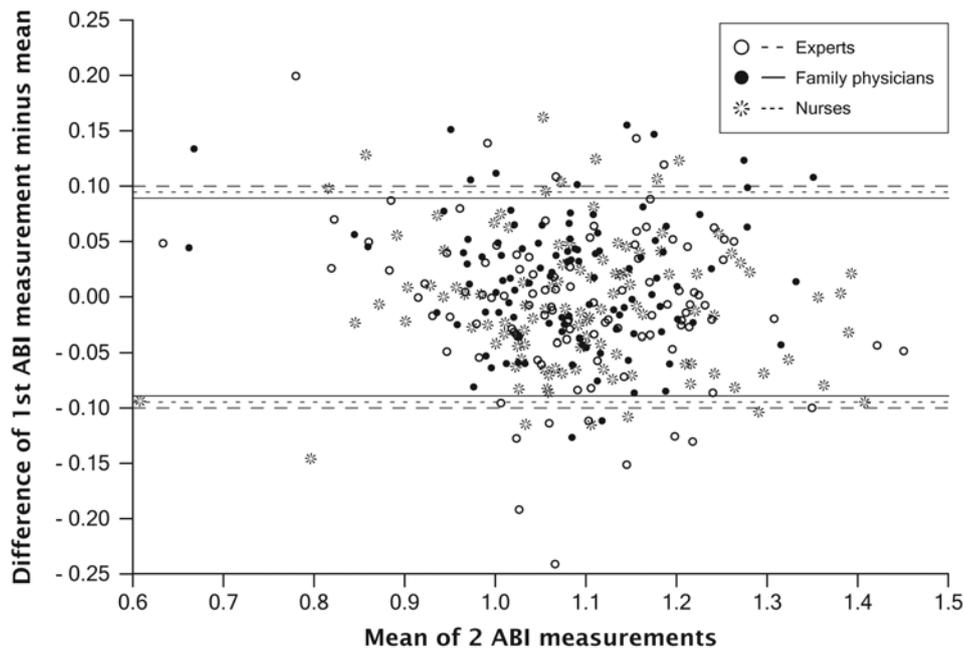


Figure 3 Inter-observer variability in the three observer groups. The graph displays a scatter diagram (three observers \times 108 volunteers = 324 measurements) of the differences between pairs of ABI measurements of the same observer, plotted against the averages of the two ABI measurements. The parallel horizontal lines (see key in the graph) indicate the mean standard deviation of measurements of the respective observer group. The mean difference between the first and second measurements was less than 0.01 in all groups combined (i.e. no bias). Of the 324 double ABI measurements, 15 (from 10 patients) were <0.9 and three ABI measurements (of two patients) were >1.4 . As mean values were calculated across all three observers, two patients had an ABI <0.9 and no patient had an ABI >1.4 (maximum mean value was: 1.37).

differed significantly among experienced observers (7.3%) and less experienced observers (12.0%).¹⁷

Direct comparisons between these studies are difficult as different statistical approaches were used. Further, one or more major methodological limitations applied (e.g. small samples of observers or patients, selection of symptomatic PAD patients). The latter is of importance, as intra-observer variability has been reported to differ between diseased and normal individuals.^{20,23} In contrast, our study was performed under conditions similar to the primary care setting, focusing on elderly individuals who are most likely to be screened. Importantly, almost all had no PAD (only two with ABI <0.9).

We report intra- and inter-individual errors of ABI measurements of 8% and 9% respectively, which is low compared to widely used screening measures. For example, mammography,²⁴ cervical cytological and histological interpretations,²⁵ or fecal occult blood testing,²⁶ all used for cancer screening, have considerable variability in interpretation and at most moderate reproducibility. Despite the high accuracy, however, physicians must be aware that a measured ABI measurement of 0.90 represents a 'true value' in a statistical sense in a range between 0.80 (per definition PAD) and 1.00 (per definition normal finding). In cases close to the 0.90 threshold it should be kept in mind that the mortality and cardiovascular risk

Table 2 Comparison of observer groups.

	Standard deviation within volunteers (ABI points)	Systematic error of observer group (bias) (ABI points)
Specialists in vascular medicine	0.094	0.000 (defined as standard)
Family physicians	0.085	0.011
Technicians	0.082	-0.008

There were no relevant differences between measurements of the three observer groups ($p = 0.39$ for standard deviations, $p = 0.58$ for bias, ANOVA F-tests).

across the ABI spectrum operates on a continuum.¹² Repeated ABI measurements or further diagnostic procedures are mandatory, especially if the PAD status is uncertain.

An important point is that experts, family physicians, and nurses measured identical mean ABI values. The absence of systematic bias across observer groups indicates that comparisons of ABI values across different settings and studies, at least epidemiological studies with a large proportion of healthy individuals, is possible.

Certain limitations have to be taken into account when assessing our study. We had expected on the basis of the ABI study that about every fifth elderly patient would present with an ABI below 0.9, but in our volunteer sample all but two had values in the normal range. Reproducibility of ABI may be easier for 'non-experts' in normal arteries, compared with arteries that are hard to find or if the pressure is lower. Thus, strictly speaking, our results apply to normal individuals and have to be confirmed in PAD patients. Similarly, no information about post-exercise ABI was collected. Further, the present study does not allow inference about the validity of the ABI determinations, defined as the agreement between the measurements and the true value. Determining the true value is difficult, because the ABI is based on indirect blood pressure measurements and composed of readings whose accuracy and reproducibility depend on many factors. For example, length of the rest period, patient-observer interaction, cuff placement, cuff size, inflation/deflation rates influence blood pressure readings.²⁷ In addition, blood pressure changes physiologically from minute to minute,²⁷ and differences of 7 mmHg between duplicate readings of the brachial blood pressure on the same visit have been reported.²⁸

In summary, our study confirms that ABI determinations are highly reproducible and reliable under routine conditions in primary care, and that the measurement can be done with little training, even by people other than physicians. Hence, the practicability of the ABI is similar to that of simple blood pressure measurements. This is mandatory (besides reimbursement) for establishing the ABI as a widely used screening tool for PAD. Given the undisputed importance of early detection and management of PAD, the ABI should be used routinely as a standard for atherosclerosis screening. Further studies should be conducted to confirm our observations in patients with PAD of various grades of severity.

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no influence on the scope, conduct and interpretation of the study.

References

- Greenland P, Abrams J, Aurigemma GP et al. Prevention Conference V. Beyond secondary prevention: identifying the high-risk patient for primary prevention. Noninvasive tests of atherosclerotic burden. *Circulation* 2000; **101**: E16–22.
- Mohler ER III. Peripheral arterial disease: identification and implications. *Arch Intern Med* 2003; **163**: 2306–14.
- Belch JFF, Topol EJ, Agnelli G et al. Critical issues in peripheral arterial disease detection and management: A call to action. *Arch Intern Med* 2003; **163**: 884–92.
- McDermott MM, Criqui MH, Liu K et al. Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior tibial arterial pressures, and association with leg functioning in peripheral arterial disease. *J Vasc Surg* 2000; **32**: 1164–71.
- Resnick HE, Lindsay RS, McDermott MM et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. *Circulation* 2004; **109**: 733–39.
- Dormandy J, Rutherford R. Management of peripheral arterial disease (PAD). TASC Working Group. TransAtlantic Inter-Society Consensus (TASC). *J Vasc Surg* 2000; **31**: S1–296.
- Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg* 1969; **56**: 676–79.
- Feringa HHH, Bax JJJ, van Waning VH et al. The long-term prognostic value of the resting and postexercise ankle-brachial index. *Arch Intern Med* 2006; **166**: 529–35.
- Doobay AV, Anand SS. Sensitivity and specificity of the ankle-brachial index to predict future cardiovascular outcomes: a systematic review. *Arterioscler Thromb Vasc Biol* 2005; **25**: 1463–69.
- Lee AJ, Price JF, Russell MJ, Smith FB, van Wijk MCW, Fowkes FGR. Improved prediction of fatal myocardial infarction using the ankle brachial index in addition to conventional risk factors: The Edinburgh Artery Study. *Circulation* 2004; **110**: 3075–80.
- Murabito JM, Evans JC, Larson MG, Nieto K, Levy D, Wilson PWF. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: The Framingham Study. *Arch Intern Med* 2003; **163**: 1939–42.
- O'Hare AM, Katz R, Shlipak MG, Cushman M, Newman AB. Mortality and cardiovascular risk across the ankle-arm index spectrum: results from the Cardiovascular Health Study. *Circulation* 2006; **113**: 388–93.
- Diehm C, Lange S, Darius H et al. Association of low ankle brachial index with high mortality in primary care. *Eur Heart J* 2006; **27**: 1743–49.
- American Diabetes Association. Peripheral arterial disease in people with diabetes. *Diabetes Care* 2003; **26**: 3333–41.
- Endres HG, Hucke C, Holland-Letz T, Trampisch HJ. A new efficient trial design for assessing reliability of ankle-brachial index measures by three different observer groups. Full text available at: <http://www.biomedcentral.com/1471-2261/6/33>. *BMC Cardiovasc Disord* 2006; **6**: 33–43.
- Street A, Street D. *Combinatorics of experimental design*. Clarendon Press, 1987: section 11.3.

- 17 Kaiser V, Kester AD, Stoffers HE, Kitslaar PJ, Knottnerus JA. The influence of experience on the reproducibility of the ankle-brachial systolic pressure ratio in peripheral arterial occlusive disease. *Eur J Vasc Endovasc Surg* 1999; **18**: 25–29.
- 18 Leitlinien und Empfehlungen zur Sicherung von Guter Epidemiologischer Praxis (GEP). Available at: http://www.gmds.de/texte/onlinedocs/empfehlungen/empf_gep_langfassung.htm, Arbeitsgruppe Epidemiologische Methoden der Deutschen Arbeitsgemeinschaft Epidemiologie (DAE).
- 19 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **i**: 307–10.
- 20 Fowkes FG, Housley E, Macintyre CC, Prescott RJ, Ruckley CV. Variability of ankle and brachial systolic pressures in the measurement of atherosclerotic peripheral arterial disease. *J Epidemiol Community Health* 1988; **42**: 128–33.
- 21 Matzke S, Franckena M, Alback A, Railo M, Lepantalo M. Ankle brachial index measurements in critical leg ischaemia – the influence of experience on reproducibility. *Scand J Surg* 2003; **92**: 144–47.
- 22 Jeelani NU, Braithwaite BD, Tomlin C, MacSweeney ST. Variation of method for measurement of brachial artery pressure significantly affects ankle-brachial pressure index values. *Eur J Vasc Endovasc Surg* 2000; **20**: 25–28.
- 23 Osmundson PJ, O’Fallon WM, Clements IP, Kazmier FJ, Zimmerman BR, Palumbo PJ. Reproducibility of noninvasive tests of peripheral occlusive arterial disease. *J Vasc Surg* 1985; **2**: 678–83.
- 24 Kerlikowske K, Grady D, Barclay J et al. Variability and accuracy in mammographic interpretation using the American College of Radiology Breast Imaging Reporting and Data System. *J Natl Cancer Inst* 1998; **90**: 1801–809.
- 25 Stoler MH, Schiffman M. Interobserver reproducibility of cervical cytologic and histologic interpretations: realistic estimates from the ASCUS-LSIL Triage Study. *JAMA* 2001; **285**: 1500–505.
- 26 Walsh JM, Terdiman JP. Colorectal cancer screening: scientific review. *JAMA* 2003; **289**: 1288–96.
- 27 Grim C, Grim C. Blood pressure management. American Heart Association Hypertension Primer. The essentials of high blood pressure. Basic science, population science, and clinical management. Lippincott Williams & Wilkins, 1999: 295–98.
- 28 Armitage P, Fox W, Rose GA, Tinker CM. The variability of measurements of casual blood pressure. II. Survey experience. *Clin Sci* 1966; **30**: 337–44.