Training to Perform Ankle-Brachial Index: Systematic Review and Perspectives to Improve Teaching and Learning

S. Chaudru, Pierre-Yves de Müllenheim, Alexis Le Faucheur, A. Kaladji, V. Jaquinandi, G Mahé

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Training to perform Ankle-Brachial Index

Systematic Review and perspectives to improve teaching and learning

Authors

Chaudru S. (MSc)\textsuperscript{1}, de Müllenheim P.-Y. (MSc)\textsuperscript{2}, Le Faucheur A. (PhD)\textsuperscript{1,2,3}, Kaladji A. (MD, MSc)\textsuperscript{4}, Jaquinandi V. (MD, PhD)\textsuperscript{5}, Mahé G. (MD, PhD)\textsuperscript{1,6}

Affiliations

\textsuperscript{1} INSERM, Centre d’Investigation Clinique, CIC 1414, F-35033 Rennes. FRANCE.

\textsuperscript{2} Movement, Sport and Health laboratory. EA 1274. UFR APS, University of Rennes 2. Rennes, F-35000. FRANCE.

\textsuperscript{3} Department of sport sciences and physical education. ENS Rennes, Campus de Ker Lann. Bruz, F-35170. FRANCE.

\textsuperscript{4} University of Rennes 1, INSERM U1099, Signal and Image Processing Laboratory, F-35000, Rennes, FRANCE.

\textsuperscript{5} Cabinet d’angiologie, 6 rue de Bellinière. Trélazé, F-49800.FRANCE.

\textsuperscript{6} CHU Rennes, Imagerie Cœur-Vaisseaux, F-35033 Rennes. FRANCE.

Corresponding author

Guillaume MAHE.

Pôle imagerie médicale et explorations fonctionnelles. Hôpital Pontchaillou, 2 rue Henri Le Guilloux. Rennes, F-35033. France. Tel: +33 (0)2 9928 4321. Fax: +33 (0)2 9928 4364

E-mail: maheguillaume@yahoo.fr

2560 words
Ankle-brachial index is widely used to diagnose peripheral artery disease. To date no review has been performed on medical education and ankle-brachial index teaching. Our systematic review focuses on the impact of training programs on ABI performance by medical students, doctors or primary care providers. Using different databases we found that only five studies have addressed the impact of such training programs. We underline that the literature is sparse whereas, without a good teaching, a task cannot be well performed.

High quality studies are required to define the best training program for ABI teaching and learning.
ABSTRACT

Objective: To conduct a systematic review focusing on the impact of training programs on Ankle-brachial Index (ABI) performance by either medical students, or doctors or primary care providers. Lower extremity peripheral artery disease (PAD) is a highly prevalent disease affecting ~ 202 million people worldwide. ABI is an essential component of medical education because of its ability to diagnose PAD, and since it is a powerful prognostic marker for overall and cardiovascular-related mortality.

Design: Systematic review.

Materials: Medline, Embase, and Web of Science databases.

Methods: A systematic search was conducted (up to May 2015).

Results: Five studies have addressed the impact of a training program on ABI performance by either medical students, or doctors or primary care providers. All were assigned at low quality regarding to GRADE system. The components of the training vary greatly either in substance (what was taught) or in form (duration of the training, type of support which was used). No consistency was found in the outcome measures.

Conclusion: According to this systematic review, only few studies, with a low quality rating, have addressed which training program should be performed to provide the best way of teaching how to perform ABI. Futures high quality level researches are required to define objectively the best training program to facilitate ABI teaching and learning.

Keywords: peripheral arterial disease, training program, diagnosis, curriculum, vascular medicine
INTRODUCTION

Ankle-brachial index (ABI) is the recommended method for the diagnosis of lower extremity peripheral artery disease (PAD), a highly prevalent disease affecting ~ 202 million people worldwide.\textsuperscript{1,2} It is an objective test initially proposed by Winsor\textsuperscript{3} which has high specificity and sensitivity, provided that is performed by well-trained health professionals.\textsuperscript{4} Besides its ability to diagnose PAD, ABI is of interest since it is a marker for overall and cardiovascular-related mortality.\textsuperscript{2,5–7}

Although used as a medical procedure since more 50 years ago, the method for measuring, calculating and interpreting the ABI is standardized and guidelines have been published in 2012.\textsuperscript{2} A summary of these guidelines is presented in Figure 1.

Despite its noninvasive nature and inexpensive cost, a significant proportion of individuals with PAD (over 44%) remain undiagnosed in clinical practice.\textsuperscript{8–10} Different factors have been proposed to explain why ABI is underused. For instance, it is reported by some physicians that performing ABI is time consuming whereas others found the equipment expensive.\textsuperscript{11,12} A lack of knowledge and technical expertise can represent another barrier to use the ABI for diagnosing PAD and stratifying cardiovascular risk.\textsuperscript{13–15}

Although ABI is of importance in medical care, only a few studies have addressed which training program should be performed to provide the best way of teaching how to perform ABI. Our aim is to conduct a systematic review focusing on the impact of training programs on ABI performance by either medical students, or doctors or primary care providers.
MATERIALS AND METHODS

The literature was systematically reviewed and synthesized according to the method below.

Search Strategy

Electronic search was performed using Medline, Embase, and Web of Science databases, (updated May 2015). This search was conducted by two independent investigators (SC and GM). Search using the following key terms: “Ankle Brachial Index”, “Arterial occlusive diseases/diagnosis”, “Vascular Diseases/diagnosis”, “Peripheral Arterial Disease/diagnosis”, “Educational measurement”, "Teaching", "Clinical competence" "Training", “Students medical”, "Internship”, “residency”, “undergraduate”, “residents”, “GPs”, and "general practitioners".

This combination aimed to focus on articles dealing with the impact of training programs on improving ABI performance. No filter was used.

Selection criteria

Two investigators (SC and GM) read titles and abstracts of the articles yielded by the computer-assisted search to select articles for full-text reading. An article was considered suitable for full text reading if the abstract focused on the impact of a training program on ABI performance. Further, through checking reference lists of related papers, other new relevant references were identified and selected applying the same selection strategy. Studies that did not report the training methodology were excluded.

Data extraction and critical appraisal

For the study selection a third investigator (VJ) was consulted to resolve discrepancies through discussion and consensus. SC and GM extracted information about study design, participants’ characteristics, intervention components, outcome measures, and main findings.
Study quality

Study quality was rated by SC and GM using the GRADE system. This one assigned a quality rating for each study based on the study design: “high” for randomized controlled trials and “low” for observational studies. Observational studies were upgraded if there was a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. The rating was downgraded for the following study limitations criteria: risk of bias, inconsistency, indirectness and imprecision.

RESULTS

Our initial search strategy identified 62 articles (Figure 2). After screening the titles and abstracts on the basis of our inclusion and exclusion criteria, 3 articles were selected. From reading articles, two other relevant references were identified. Finally, five studies were included in this analysis. Among the five studies included in this systematic review, none was randomized and all were assigned a “low” quality rating. Table 1 summarizes the study design, participants’ characteristics and intervention components of each study.

Participant’s characteristics

In two studies a training program was addressed for internal medicine residents. For other studies, it concerned either general practitioners, primary care provider, or junior doctors. According to the identified studies, the total number of participants (receiving ABI teaching) ranged from 1 to 53.

 Intervention components

Some training programs took the form of theoretical courses while others proposed practice sessions under supervision with direct feedback. Practice was performed either on healthy
subjects or on PAD patients. Some training programs included only four-hour session when others lasted 4 weeks without any detail about the duration per week.

Outcome measures

Table 2 summarizes the outcome measures and the main findings of each study.

Outcome measures took a variety of forms. Four studies evaluated general competence outcomes (ability to measure correctly ABI) and one evaluated task-specific competence outcomes (ability to perform each task of the ABI procedure: measurement, calculation, interpretation). In two studies, trainee’s competency was objectively assessed through comparisons of ABI values obtained in PAD patients between trainees and trainers. In two other studies, competency was assessed through comparisons between ABI values obtained in primary care practice and vascular laboratory. In other cases, trainee’s competency was assessed through observation of ABI performance in healthy subjects and completion of a scoring sheet awarding marks for correct completion of the critical elements in ABI measurement.

Main findings

Wyatt et al. (2010) reported that at baseline 4% of residents correctly measured the ankle and brachial pressures, 10% correctly calculated the ABI, and 45% correctly interpreted the ABI. Following the training program, 50% of these residents correctly measured the ankle and brachial pressures, 75% correctly calculated the ABI, and 88% correctly interpreted the ABI.

Willigendael et al. (2005) reported that, following the training program, the number of patients referred for PAD to a vascular out-patient clinic with a correct ABI measurement performed prior to referral increased almost six fold.
DISCUSSION

This is the first systematic review assessing the impact of a training program on ABI performance. One interesting result that emerged in the early stages of this systematic review was that only 5 studies have addressed the impact of a training program on ABI performance by either medical students, doctors or primary care providers, whereas there are more than 4000 papers about ABI in PubMed database. This is surprising since without a good teaching a task cannot be well performed. Recent guidelines published in 2012 from the AHA only insist on the didactic learning without any reference demonstrating that the literature is poor on this topic.²

Components of the training

This systematic review also highlights a lack of uniformity in the components of the training either in substance (what was taught) or in form (training duration, type of support used). The choice of an adequate training program is yet essential for learning.

In 2015, a document entitled “COCATS (COre CArdiovascular Training Statement) 4 Task Force 9: Training in vascular medicine” was endorsed by the American Society for Vascular Medicine.²¹ In this document, ABI procedure is considered as a level I training. Moreover, the authors emphasize that training for noninvasive vascular tests should include case presentations and formal lectures and at least 2 months of exposure to vascular medicine services. They indicate that training may occur either in dedicated rotation or throughout the cardiovascular clinical training period in which trainees should encounter and receive instruction in the bedside evaluation of patients with PAD. In this systematic review, only two studies used a bedside procedure.¹⁸,²⁰ Ray et al. ²⁰ compared two different bedside procedures of teaching: a “role model” and a “direct supervision after formal initial training session”.

During a “role model”, trainees observe the procedure conducted by the trainers. During “direct supervision”, the trainee who performs the procedure is observed by the trainers, who
can coach and inform him of any flaws. Ray et al. have shown that the latter bedside procedure offered better results in the learning process than “role model” strategie. In their guidelines, the COCATS 4 also highlights that feedbacks should be an essential part of the teaching and learning process. Feedback is a time of exchanges and explanations between trainers and trainees. It helps students to understand the subject being studied, gives them clear guidance on how to improve their learning, and encourages active reflective practices. Moreover, feedback can improve student’s confidence, self-awareness and enthusiasm for learning. Interestingly, only two studies of this systematic review reported the use of feedback.

Outcome measures
This systematic review highlights the lack of uniformity regarding the outcome measure to evaluate ABI performance. Only two out of five studies have used the same outcome measure which was the difference between ABI measurement performed in primary care practice and in vascular laboratory. It is interesting to discuss the choice of this outcome measure. Indeed, the second measurement performed in the vascular laboratory, which is the benchmark, was not immediately performed after the first measurement. Between these two measurements, it cannot be excluded that the disease state has changed either positively or negatively. There is also a day-to-day spontaneous variability in ABI measurements caused by for example caffeine or tobacco. Finally, Baker et al. have shown that in PAD patients, ABI must change by at least 0.15 before this can be considered as significant. Unfortunately, results for ABI measurement variations were not presented in these studies and they did not assess subjects who were not considered as suspected PAD patients in primary care practice. One study examined the effectiveness of teaching ankle-brachial index on all the components of ABI performance which includes measurement, calculation and interpretation.
evaluation was performed through a questionnaire. Most of the common mistakes in the ABI procedure include errors in technical aspect of the measurement (such as locating ankle pulses, maintaining the position of the Doppler probe), but deviations from guidelines in calculation and interpretation are also commonplace, then leading to misdiagnoses. As mentioned by Wyatt et al. it seems important to evaluate each task that together makes up ABI procedure (measurement, calculation, interpretation). However, in this study, Wyatt et al. have not considered the reliability of their questionnaire and have attributed the improvement of ABI performance only to the training program and not to a potential test-retest variability in questionnaire results.

Main considerations for the teaching procedure

Whatever the components of the training, all selected studies noticed an improvement after the training program. However, it appears that, in spite of a training program, mistakes regarding ABI guidelines were still present. Wyatt et al. have shown that half of the residents repeated the initial errors they had performed at the beginning of the training, even after errors had been explained and corrected by the trainers. It suggests that ABI training required time. These results are in agreement with the findings of Georgakarakos et al. who highlighted that, after a basic training course, trainees correctly measured ABI in patients with mild to moderate PAD but tended to overestimate ABI in patients with severe PAD. They demonstrated that the completion of 20 measurements in PAD patients was required to achieve enough competencies to avoid misdiagnosing patients.

Limitations

All identified studies in this present systematic review were rated as “low” quality. This low quality level was mainly due to no randomization procedure, non-blinding of outcome
assessors, small sample sizes, and limited generalizability of the results (because most studies recruited participants from a single center and characteristics of the trainees greatly varied). However, this systematic review emphasizes the paucity of the literature on this topic. ABI teaching remains a significant challenge and definition of sound training programs in medical school with appropriate standardized methodology are needed.

**Perspectives**

Based on this systematic review, we propose a summary of the recommendations to improve the learning and teaching of ABI performance in students (Table 3). It appears that initial ABI training should include methodological requirements for accurate and reproducible ABI measurement, as well as theoretical basis and limitations of the test. It should be done by a vascular expert. Indeed, Lazarides et al. highlighted that learning is strongly influenced by the interest of the trainers.26

The initial training should be completed with practical measurement by students on healthy subjects in order to achieve competency such as familiarization with the technical aspect of the measurement (location of the pulses, proper application of the Doppler probe whilst inflating the blood pressure cuff, detection of an audible Doppler signal). Nevertheless, the best way for students to improve competency should be performing bedside training in a vascular laboratory where they should: i) be exposed to an environment with a sufficient number of vascular cases, ii) received practical instruction regarding the ABI test, iii) practiced ABI on patients.21

Training on simulators may be an alternative solution offering the opportunity for students to perform ABI procedure through “virtual” patients or legs. Unfortunately, such a “virtual” device is not currently available.
CONCLUSION

ABI has high specificity and sensitivity for PAD diagnosis provided that is evaluated by well-trained health professionals. There are evidences that training of medical students and doctors during their early residency is rather limited, leading to unreliable and false measurements. Given its importance in the diagnosis of PAD and in the prediction of cardiovascular morbidity and mortality, an inadequate medical education could lead to a misuse of the ABI in clinical routine. Only few studies have addressed which training program should be performed to provide the best way to teach how to perform ABI, and the quality of each study was poor. Future high level quality researches are required to define objectively the best training program to facilitate ABI teaching and learning.
ACKNOWLEDGMENTS

None.
REFERENCES


Tables Legends

Table 1: Study design, participants’ characteristics and intervention components of each study.

Table 1 legend: ABI = ankle-brachial index; PAD = Peripheral Artery Disease; GP = General practitioner; CD = Compact Disc.

Table 2: Summary of outcomes measures and main findings of the studies.

Table 2 legend: ABI = ankle-brachial index; PAD = Peripheral Artery Disease; GP = General practitioner

Table 3: Summary of the suggestions to improve the learning and teaching of ABI performance in students.
<table>
<thead>
<tr>
<th>Study</th>
<th>Total n</th>
<th>Study design, participants’ characteristics and intervention components of each study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wyatt et al., 2010 (USA)</td>
<td>24</td>
<td>Non-randomized longitudinal cohort study Low quality rate: Training program combining: - direct feedback to participants on their individual errors and on the most common errors of the group; - presentation of an internet video that included demonstration of an ABI measurement performed by an experienced vascular specialist and instructions regarding ABI calculation and interpretation. No information about duration of the training.</td>
</tr>
<tr>
<td>Georgakarakos et al., 2013 (Greece)</td>
<td>5</td>
<td>Non-randomized longitudinal cohort study Low quality rate: 26 hours training program combining: - 13h of theoretical lessons, - 13h of clinical practice. Twice per week, for 2 consecutive weeks, students received basic training course and demonstration of ABI procedure (proper application of the Doppler apparatus, choice of the appropriate size of sphygmomanometer cuff and technical tips such as gradual inflating and deflating the cuff while detecting the audible Doppler signal) given by an experienced vascular surgeon</td>
</tr>
<tr>
<td>Willigendael et al., 2005 (Netherlands)</td>
<td>53</td>
<td>Non-randomized longitudinal cohort study Low quality rate: 4 hours training program combining: - plenary introduction on PAD - theoretical introduction and training in i) performing ABI ii) PAD diagnosis iii) treatment and vascular risk factor management given by a vascular surgeon and a GP. All participants received the course book and a CD with ABI instructions on video.</td>
</tr>
<tr>
<td>Coe et al., 2014 (USA)</td>
<td>1</td>
<td>Non-randomized longitudinal cohort study Low quality rate: 4 weeks training program: 1&lt;sup&gt;st&lt;/sup&gt; week: observe a vascular technologist in the offices of a cardiologist, a vascular surgeon or at the hospital laboratory. 2&lt;sup&gt;nd&lt;/sup&gt; week: perform ABIs procedure and interpret results to become proficient in the technique. 3&lt;sup&gt;rd&lt;/sup&gt; week: shadow vascular surgeon who was performing PAD examination to become proficient in listening to the wave sounds. 4&lt;sup&gt;th&lt;/sup&gt; week: perform vascular assessment and ABI indices with interpretation that are evaluated by nurse practitioners or physicians on proficiency of performing and interpreting ABIs before performing them independently.</td>
</tr>
<tr>
<td>Ray et al., 1993 (Great Britain)</td>
<td>4</td>
<td>Two arms, non-randomized longitudinal cohort study Low quality rate: Training program: Experiment 1: an expert showed the doctors once how to perform Doppler ultrasonographic systolic arterial blood pressure measurements. Experiment 2: during 40 min an expert instructed doctors in the use of Doppler flowmeters and in the measurement of ankle systolic blood pressures. The doctors then practiced ABI under expert supervision which informed the doctor of any flaws.</td>
</tr>
<tr>
<td>Study</td>
<td>Outcome measures, follow up</td>
<td>Main findings</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Wyatt et al., 2010 | 1/ABI measurement: in a standardized environment, participants were given written instructions directing them to perform an ABI measurement on a healthy subject. Performance was observed and scored by a trained observer using a standardized template.  
2/ABI calculation: participants were instructed to select the appropriate numerator and denominator required to calculate the right and left ABI for a hypothetical patient.  
3/ABI interpretation: participants were given a worksheet listing six ABI values with the appropriate interpretation.                                                                                     | At baseline, 4% of residents correctly measured the ABI, 10% correctly calculated the ABI and 45% correctly interpreted the ABI. Performance was unaffected by year of residency.  
Following the training program, 50% of residents correctly measured the ABI, 75% correctly calculated the ABI and 88% correctly interpreted the ABI.  
The mean score for the tasks of ABI measurement, calculation and interpretation between baseline and post education were 4.6 ± 3 and 13.9 ± 1.6 (p < 0.001), 1 ± 0.9 and 2.3 ± 1.2 (p = 0.002) and 4.9 ± 1.6 and 5.9 ± 0.3 (p=0.008) respectively. |
| Georgarakos et al., 2013 | Comparison of ABI values between trainees and trainer in the 13 limbs of severe PAD, 11 limbs of mild to moderate PAD and 4 normal limbs.                                                                                                                                                                                                               | At the intervention end-point there was no difference in ABI values between trainees and trainer for subjects with mild to moderate PAD (0.70 ± 0.22 vs 0.77 ± 0.19, p= 0.95). In the 4 normal limbs, ABI was 1.37 ± 0.12 and 1.16 ± 0.11 as measured by the trainer and the trainees (p < 0.0001). In subjects with severe PAD, trainees tended to overestimate ABI (0.32 ± 0.23 vs 0.23 ± 0.07 p = 0.0002). |
| Willigendael et al., 2005 | Comparison of ABI measurement and adequate diagnosis between GPs and a vascular laboratory specialist. Outcomes assessed at baseline and six months after completion of the training session.                                                                                                               | At baseline, 40% of GPs correctly measured ABI. Following the training program, the number of patients referred for PAD to a vascular out-patient clinic with a correct ABI measurement performed prior to referral increased almost six fold. |
| Coe et al., 2014    | Comparison of adequate diagnosis between trainee and specialist of the hospital vascular laboratory.                                                                                                                                                                                                                                                     | At baseline, 61% of the ABI tested positive. Following the training program, the skill and competence of the primary care provider increased. There was an increase in identification of positive ABIs from 61% to 71%. |
| Ray et al., 1993    | Comparison of ABI values between trainees and trainers in PAD patients.                                                                                                                                                                                                                                                                                  | The mean difference in ABI measurement between the trainees and the trainer in Experiment 1 was greater than that in Experiment 2.  
Nearly 30% of the trainees’ ABI measurements in Experiment 1 differed from those of the trainer by more than 0.15, in comparison with only 15% of the measurements performed in Experiment 2.  
In the Experiment 2, through the 6 weeks, difference between values of the trainees and the trainers don’t decrease even if trainers gave feedback. |
Table 3: Summary of the suggestions to improve the learning and teaching of ABI performance in students.

<table>
<thead>
<tr>
<th>Current suggestions to improve ABI performance in students based on the available literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Training program should be supervised by an experienced vascular professional interested by the subject. (Lazarides et al., 2006)</td>
</tr>
<tr>
<td>2. Training program should begin with case representation and formal lectures. (Ray et al., 1994)</td>
</tr>
<tr>
<td>3. Training program should include exposure to vascular medicine services where trainees should encounter and receive instructions (role model and/or direct supervision) in the bedside evaluation of patients with PAD (e.g. normal patients, patients with a range of abnormal or low ABI, patients with incompressible vessels). (Creager et al., 2015; Ray et al., 1994)</td>
</tr>
<tr>
<td>4. Feedback to the trainees should be provided after each training program. (Creager et al., 2015)</td>
</tr>
<tr>
<td>5. At least 20 bedside procedures should be completed by the trainee. (Georgakarakos et al., 2013)</td>
</tr>
<tr>
<td>6. Each task that together makes up ABI procedure (measurement, calculation, interpretation) should be evaluate. (Wyatt et al., 2010)</td>
</tr>
<tr>
<td>7. A long term follow-up should be organized to determine whether improved ABI measurement is durable.</td>
</tr>
</tbody>
</table>
Figure Legends

Figure 1: How to perform Ankle-Brachial Index (ABI) in clinical practice according to American Heart Association (AHA) recommendations.

Figure 1 legend: *For the right arm, average the 1\textsuperscript{st} and 2\textsuperscript{nd} measurement except if the difference exceeds 10mmHg. In that case, the 1\textsuperscript{st} measurement must be disregarded.

Figure 2: Flow diagram of the systematic review process.
Conditions:
• Room with comfortable temperature (19°C–22°C).
• Patient at rest for 5 to 10 min in supine position, relaxed, head and heels supported.

1. Sphygmomanometer (the cuff should have a width at least 40% of the limb circumference). Ankle cuff is placed just above the malleoli.
2. 8 to 10 MHz Doppler probe with Doppler gel applied over the probe. Probe is placed in the area of the pulse at 45° to 60° angle to the surface of the skin.
3. Inflate the cuff up to 20 mmHg above flow signal disappearance and then deflate slowly to detect the pressure level of flow signal reappearance. ▲ The cuff should not be applied over a distal bypass or over ulcers.

Sequence of pressure measurements (from 1 to 7):

For peripheral artery disease (PAD) diagnosis:

\[
\text{ABI}_{\text{right}} = \frac{\text{Higher of the PT or DP systolic pressure in right ankle}}{\text{Higher of the left or right brachial systolic pressure}}
\]

\[
\text{ABI}_{\text{left}} = \frac{\text{Higher of the PT or DP systolic pressure in left ankle}}{\text{Higher of the left or right brachial systolic pressure}}
\]

For cardiovascular risk assessment:
The lower of the ABIs of the left and right leg should be used.

<table>
<thead>
<tr>
<th>Right brachial artery</th>
<th>120 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right PT artery</td>
<td>60 mmHg</td>
</tr>
<tr>
<td>Right DP artery</td>
<td>76 mmHg</td>
</tr>
<tr>
<td>Left PT artery</td>
<td>110 mmHg</td>
</tr>
<tr>
<td>Left DP artery</td>
<td>110 mmHg</td>
</tr>
<tr>
<td>Left brachial artery</td>
<td>120 mmHg</td>
</tr>
<tr>
<td>Right brachial artery</td>
<td>116 mmHg</td>
</tr>
</tbody>
</table>

For diagnosis:
\[
\text{ABI}_{\text{right}} = \frac{76}{120} = 0.63
\]
\[
\text{ABI}_{\text{left}} = \frac{110}{120} = 0.92
\]

For cardiovascular risk assessment:
\[
\text{ABI} = 0.63
\]

When the ABI initially determined is
• between 0.80 and 1.00, repeat the measurement.
• ≥ 1.40 with a clinical suspicion of PAD, a toe brachial index should be used.
An ABI decrease of > 0.15 over time can be effective to detect significant progression.

▲ Risk of falsely normal ABI among patients with diabetes, chronic renal failure or advanced age due to calcification of the arterial wall.

Interpretation:

<table>
<thead>
<tr>
<th>ABI</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.40</td>
<td>Severe PAD</td>
</tr>
<tr>
<td>0.41 – 0.90</td>
<td>Mild to moderate PAD</td>
</tr>
<tr>
<td>0.91 – 1.00</td>
<td>Borderline</td>
</tr>
<tr>
<td>1.01 – 1.40</td>
<td>Normal</td>
</tr>
<tr>
<td>&gt;1.40</td>
<td>Incompressible artery</td>
</tr>
</tbody>
</table>
Figure 2. Flow diagram of the systematic review process.