COMPARISON OF THE AUTOMATED OSCILLOMETRIC BLOOD PRESSURE METHOD WITH THE DOPPLER ULTRASOUND METHOD FOR MEASUREMENT OF THE ANKLE-BRACHIAL INDEX

Jonas DELFORCHE

Promoter: Prof. Dr. T. De Backer

Dissertation presented in the 2nd Master year in the programme of

Master of Medicine in Medicine
“The author and the promoter give the permission to use this thesis for consultation and to copy parts of it for personal use. Every other use is subject to the copyright laws, more specifically the source must be extensively specified when using results from this thesis.”

Date

Signature (student) (promoter)

Name (student) (promoter)
Preface – word of thanks

First of all, I would like to thank my promoter, Prof. Dr. Tine De Backer, for her continuous accompaniment and support, for the evening sessions where constructive discussions arose and for the astounding availability she expressed throughout the 2 years we’ve spent working on this experimental study.

Secondly, I would like to say thank you to Dr. Laurence Campens, who recruited subjects in the years 2010-2011, was always available for meetings, responded comprehensively to any question concerning the methods used and played an important role in the realization of this thesis.

I wish to thank my fellow students, responding immediately to my request of contributing to my thesis by volunteering for the inter-observer study.

I also would like to thank Prof. Vermassen, who allowed me to take measurements at the Department of Thoracic and Vascular Surgery at the Ghent University Hospital.

A big thank you goes out to the personnel at the Department of Cardiology at the Ghent University Hospital where I’ve spent several weeks collecting data. A special thanks for Tamara Leune, head nurse of the Cardiology ward, who always treated me with respect and indulgence and aided me in approaching patients and other personnel.

I wish to thank Rik Vuylsteke, vascular technician, for introducing me to the Doppler technique and ABI determination with clarity.

I would like to thank Prof. George Van Maele, who was a big help in the statistical analysis and interpretation.

Last but not least, I would like to thank my parents and brothers, who I can always count on, for their patience, confidence and support, and for allowing me to enrich myself in 7 years of education.
# Table of contents

Abstract ........................................................................................................................................... 1  
List of acronyms and abbreviations ................................................................................................. 3  
1. Introduction ................................................................................................................................... 4  
   1.1 Peripheral artery disease (PAD) ................................................................................................. 4  
      1.1.1 Etiopathogenesis of PAD ................................................................................................... 4  
      1.1.2 Epidemiology ..................................................................................................................... 4  
      1.1.3 Clinical presentation and symptomatology .......................................................................... 4  
      1.1.4 Consequences of PAD ....................................................................................................... 6  
      1.1.5 Risk factors for developing PAD ......................................................................................... 7  
      1.1.6 Treatment of PAD ............................................................................................................. 7  
      1.1.7 Detection of PAD with the ankle-brachial index ................................................................. 8  
   1.2 Indications for ABI measurement ............................................................................................. 8  
   1.3 How is the ABI measured? ....................................................................................................... 9  
   1.4 How is the ABI interpreted? ................................................................................................... 11  
   1.5 Objective .................................................................................................................................. 12  
2. Methods ....................................................................................................................................... 13  
   2.1 Introduction ............................................................................................................................. 13  
   2.2 Literature study ........................................................................................................................ 13  
   2.3 Ethical committee .................................................................................................................... 13  
   2.4 Participant recruitment ............................................................................................................ 13  
   2.5 ABI measurement .................................................................................................................... 14  
      2.5.1 The Doppler ultrasound method (golden standard) ............................................................ 14  
      2.5.2 The automated oscillometric blood pressure method ....................................................... 15  
   2.6 Questionnaire .......................................................................................................................... 15
2.7 Statistical methods................................................................. 15

3. Results ...................................................................................... 17
  3.1 Study Population .................................................................... 17
  3.2 Cardiovascular risk factors in PAD ........................................... 18
  3.3 Correlation of measurements of both methods ......................... 19
    3.2.1 Bland Altman plot ......................................................... 20
    3.2.2 Intraclass correlation coefficient (ICC) ........................... 22
  3.4 Agreement of both methods on PAD diagnosis ....................... 23
  3.5 Agreement between different observers (Inter-observer study) .... 25
  3.6 Comparison of time required for Doppler and oscillometric method 26
  3.7 Conclusion ........................................................................... 29

4. Discussion .................................................................................. 30
  4.1 Limitations of the ABI ............................................................. 31
  4.2 Alternative tests for detecting PAD non-invasively ...................... 33
  4.3 Limitations with the Doppler method .......................................... 34
  4.4 Limitations with the automated oscillometric method .................. 34
  4.5 Study limitations .................................................................. 34
  4.6 Alternative calculations of the ABI ............................................. 35
  4.7 Future prospective .................................................................. 36

5. References .................................................................................. 37

6. Appendix .................................................................................... I
Nederlandstalige samenvatting

Titel: Vergelijking van de automatische bloeddrukmeting met de doppler bloeddrukmeting voor het bepalen van de enkel-arm index.

Achtergrond: Omdat perifeer arterieel vaatlijden (peripheral arterial disease, PAD) frequent voorkomt, ernstige gevolgen kan hebben (hoog risico op myocardinfarct, cerebrovasculair accident en sterfte, risico op amputatie), grote kosten met zich meebrengt en vaak aanwezig is bij asymptomatische patiënten, is het sterk aangeraden om te screenen voor PAD. De enkel-arm index (ankle-brachial index, ABI) is een eenvoudige, betrouwbare manier om PAD op te sporen. PAD wordt vermoed als de ABI ≤ 0.90.

Objectieven: De Doppler ABI test kan tijdrovend zijn en opleiding in het correct gebruik van de Doppler techniek is een vereiste. Daarom wordt de automatisch oscillometrische bloeddrukmeting voorgesteld voor het meten van de ABI. Op deze manier kan zowel het technische aspect als de benodigde tijd voor het meten van de ABI sterk verminderd worden. Deze studie onderzoekt de overeenkomst van metingen enerzijds via de automatisch oscillometrische methode (ABIosc) en anderzijds via de gouden standaard Doppler methode (ABIdop) en vergelijkt de benodigde tijd voor het uitvoeren van beide methodes.

Design: Observatieveel cross-sectioneel onderzoek.


Resultaten: De twee ABI metingen (ABIdop en ABIosc) bleken goed te correleren (Spearman correlatie coëfficiënt \( r_s \) van 0.604). Intra-class correlation coëfficient (ICC) werd berekend op 0.665 en een Bland Altman plot toonde weinig verschil en geen opmerkelijke systematische bias tussen metingen van beide methodes. Desondanks had de automatisch oscillometrische methode wel de neiging om de ABI te onderschatten of overschatten wanneer de ABI gemeten door Doppler respectievelijk hoog of laag was. De gemiddelde benodigde tijd voor het meten van de
ABI met de Doppler methode was 12 minuten 22 seconden, de gemiddelde benodigde tijd met de oscillometrische methode was slechts 4 minuten 59 seconden.

**Conclusie:** Uit deze gegevens kan de automatisch oscillometrische methode beschouwd worden als vrij goed overeenkomend met de Doppler ABI methode wat betreft de gemeten ABI waarden en als een eenvoudigere en snellere manier voor het meten van de ABI voor screeningsdoeleinden. Verder grootschalig onderzoek dient hierover een meer definitief oordeel te vormen.

**Keywords:** Bloeddrukmeting, enkel-arm index, oscillometrie, Doppler, perifeer arterieel vaatlijden,…
Abstract

Title: Comparison of the automated oscillometric blood pressure method with the Doppler ultrasound method for measurement of the ankle-brachial index.

Background: Because peripheral artery disease (PAD) is highly prevalent, has serious consequences (high risk of myocardial infarction, stroke and death, risk of amputation), implicates high economic costs and, more worrisome, is often present in absence of symptoms, it is strongly advised to screen for PAD. The ankle-brachial index (ABI) represents a simple, reliable method for detecting PAD. PAD is suspected when the ABI ≤ 0.90.

Objective: The Doppler ABI test may be time-consuming and technical instruction on accurate use of the Doppler technique is necessary. This is why the use of automated oscillometric blood pressure measurement is proposed to measure the ABI. In this way, the technical aspect and time for measurement could be reduced greatly. This study investigates the agreement between the automated oscillometric ABI determination (ABIdopsc) and the golden standard Doppler ABI determination (ABIdop) while also comparing time needed to perform each measurement method.

Design: Observational cross-sectional study.

Study population: Hundred ninety-eight (198) participants were recruited at the Departments of Cardiovascular Diseases and Thoracovascular Surgery at the Ghent University Hospital between January 2010 and November 2013. In 39 subjects (19.7%), PAD was detected by Doppler method (ABIdop ≤0.9). In 2 subjects the ABI could not be determined due to incompressible arteries.

Results: The two ABI measurements (ABIdop and ABIdopsc) were found to be correlating well (Spearman’s correlation coefficient (r_s) of 0.604). Intra-class correlation coefficient (ICC) was calculated at 0.665 and a Bland Altman plot showed little difference and no obvious systematic bias between measurements of the two methods. However, the automated oscillometric method was likely to underestimate or overestimate the ABI when the ABI measured by Doppler method was either high or low respectively. The average time to perform the Doppler method was
12 minutes, 22 seconds compared to only 4 minutes, 59 seconds needed to perform the oscillometric method.

**Conclusion:** From these data, the automated oscillometric method for measuring the ABI for screening purposes can be considered as having an acceptable agreement on its values with the Doppler ABI method and as being more efficient in terms of easiness and time consumption. Further large population based studies could give a more definite view on this subject.

**Keywords:** Blood pressure measurement, ankle-brachial index, Doppler, oscillometry, peripheral arterial disease…
# List of acronyms and abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABI</strong></td>
<td>Ankle-Brachial (Arm) Index</td>
</tr>
<tr>
<td><strong>ABIdop</strong></td>
<td>ABI measured by Doppler</td>
</tr>
<tr>
<td><strong>ABIosc</strong></td>
<td>ABI measured by automated oscillometric device</td>
</tr>
<tr>
<td><strong>CI</strong></td>
<td>95% confidence interval</td>
</tr>
<tr>
<td><strong>CLI</strong></td>
<td>Critical limb ischemia</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>Computed tomography</td>
</tr>
<tr>
<td><strong>CVD</strong></td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td><strong>ICC</strong></td>
<td>Intra class correlation coefficient</td>
</tr>
<tr>
<td><strong>ABIdop1</strong></td>
<td>ABIdop measured by first observer</td>
</tr>
<tr>
<td><strong>ABIdop2</strong></td>
<td>ABIdop measured by second observer</td>
</tr>
<tr>
<td><strong>LEAD</strong></td>
<td>Lower extremity artery disease</td>
</tr>
<tr>
<td><strong>LR-</strong></td>
<td>Likelihood ratio for a negative result</td>
</tr>
<tr>
<td><strong>LR+</strong></td>
<td>Likelihood ratio for a positive result</td>
</tr>
<tr>
<td><strong>MeanABI</strong></td>
<td>The mean of ABIdop and ABIosc</td>
</tr>
<tr>
<td><strong>MR</strong></td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>Negative predictive value</td>
</tr>
<tr>
<td><strong>PAD</strong></td>
<td>Peripheral arterial (artery) disease</td>
</tr>
<tr>
<td><strong>PADdop</strong></td>
<td>PAD diagnosed by Doppler method</td>
</tr>
<tr>
<td><strong>PADosc</strong></td>
<td>PAD diagnosed by automated oscillometric method</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>Positive predictive value</td>
</tr>
<tr>
<td><strong>PVR</strong></td>
<td>Pulse volume recording</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>Standard Deviation</td>
</tr>
<tr>
<td><strong>κ</strong></td>
<td>Kappa coefficient</td>
</tr>
</tbody>
</table>
1. Introduction

“Cardiovascular disease (CVD) is the leading cause of death and disability in Europe, posing a great social and economic burden” stated the European Society for Cardiology in their latest guidelines for peripheral artery diseases. (1) Because CVD can be, at least partially, prevented by appropriate care, it is important to detect risk factors and early stages of the disease.

1.1 Peripheral artery disease (PAD)

1.1.1 Etiopathogenesis of PAD

Atherosclerosis plays an important role in the development of CVD. Atherosclerosis is a systemic disease that is characterized by the narrowing and stiffening of blood vessels through the process of plaque forming within these vessels throughout the body. It can lead to serious problems such as coronary artery disease, carotid artery disease and peripheral artery disease (PAD). PAD is a condition where arterial blood vessels to the head, organs and limbs are narrowed due to atherosclerosis. This narrowing can reduce the blood flow. Atherosclerosis more frequently affects the arteries of the legs compared to the arteries of the arms. (1) PAD in the legs is also known as lower extremity artery disease (LEAD).

1.1.2 Epidemiology

PAD has shown to be prevalent. In a recent German study called the Heinz Nixdorf recall study, 4,814 subjects aged 45-75 years were screened for PAD. Overall, PAD affected 6.4% among men and 5.1% among women and became much more prevalent in older individuals: 18.2% in those aged 70-75 years. (2) In an American study, the National Health and Nutrition Examination Survey study, including 2174 participants, the prevalence of PAD in the United States among adults aged 40 years and over was 4.3%. Among those aged 70 years or over, the prevalence of PAD was 14.5%. Furthermore, this study found that black people are almost 3 times as much affected (odds ratio = 2.83) as white people. (3)

1.1.3 Clinical presentation and symptomatology

PAD can lead to different manifestations depending on the site and the severity of the disease. The symptoms are caused by a reduced blood flow in the affected arteries. Especially during physical activity, insufficient oxygen is supplied to muscles and organs which results in ischemic
symptoms. Signs and symptoms include: pain, numbness, achiness or heaviness in the leg muscles when walking or climbing stairs; weak or absent pulses in the legs or feet; sores or wounds on the toes, feet, or legs that heal slowly, poorly, or not at all; a pale or bluish colour to the skin; a lower temperature in one leg than the other leg; poor nail growth on the toes and decreased hair growth on the legs.(4) A classic symptom of PAD is painful cramping of leg muscles after walking a distance that is relieved by rest called intermittent claudication. The site of claudication is distal to the diseased arterial segment. For example, buttock, hip, and thigh claudication are seen with aortoiliac disease and calf claudication with femoral-popliteal disease.

With severe PAD, patients may present with signs and symptoms of critical limb ischemia (CLI). These include rest pain, cold, pallor, paraesthesia or numbness, weak or absent pulses in the leg or feet, with or without tissue loss (nonhealing ulcers or gangrene). The symptoms of CLI are often referred to as “the six P’s” occurring in the affected leg: paraesthesia (altered sensation), pain, pallor (mottled colouration), pulselessness, paralysis, poikilothermia (coolness). Rest pain usually occurs at night (because of the horizontal position, which deprives the patient of the effect of gravity on blood flow through the tight lesions) and improves when the legs are in a dependent position. Rest pain is a sign of more severe or multilevel arterial occlusions.(5)

The presentation of PAD is categorized according to the Fontaine or Rutherford classification.(Table 1)
**Table 1.** Classification of PAD: Fontaine and Rutherford classification.(6)

<table>
<thead>
<tr>
<th>Fontaine classification</th>
<th>Rutherford classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication (&gt;200m)*</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate to severe claudication (&lt;200m)*</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: leg pain can occur after walking a longer distance (>200 meters) or after walking a relatively short distance (<200 meters).

However, most patients do not have the typical intermittent claudication; they have atypical leg symptoms or no symptoms at all.(7) About 60% of the PAD patients was asymptomatic in a population-based study.(8) ‘Importantly, even with a similar extent and level of disease progression, symptoms and their severity may vary from one patient to another.’(1)

In addition to leg symptoms, symptomatic patients often report poor quality of life related to their limited mobility and subsequent decline in overall functional capacity.(9, 10)

**1.1.4 Consequences of PAD**

The prognosis for PAD patients with claudication is bad: about 30% can be expected to die within 5 years, and 1-3% will undergo major amputation.(11) Other and more than the risk to lose a limb, PAD is associated with a very high risk of myocardial infarction, stroke and death.(1, 7, 11-14) The progression of PAD is predictive for cardiovascular disease morbidity and mortality.(15) Because of the grave consequences, PAD is also a big economic burden. Smolderen et al. calculated that the two-year hospitalization costs were highest for patients with
PAD (approximately 2953 euro) compared to the costs for cerebrovascular disease and coronary artery disease. This high cost for PAD was explained mainly because of the high expenses on peripheral revascularizations and amputations.(16)

1.1.5 Risk factors for developing PAD

Table 2. Risk factors for PAD

<table>
<thead>
<tr>
<th>Risk factors for PAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Family history of premature CVD</td>
</tr>
<tr>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Hypercholesterolemia (dyslipidaemia)</td>
</tr>
<tr>
<td>Low kidney function</td>
</tr>
</tbody>
</table>

Risk factors for PAD (table 2) include: advanced age, (family) history of premature CVD, cigarette smoking, diabetes mellitus, hypertension, hypercholesterolemia and low kidney function.(3) While the risk factors for PAD are similar to those for atherosclerotic disease in general as in coronary artery disease and cerebrovascular disease, diabetes(17) and cigarette smoking(1, 17) have a particularly strong association with PAD. Smoking is the most important risk factor for the progression of local disease in the legs, with an amputation rate 11 times greater in smokers than in non-smokers.(11) Diabetes, male gender, and hypertension are also important risk factors for progression of PAD.(11)

1.1.6 Treatment of PAD

Management of PAD includes aggressive management of atherosclerotic risk factors, a structured exercise program, use of antiplatelet agents and, when indicated, percutaneous or surgical revascularization.(5)
1.1.7 Detection of PAD with the ankle-brachial index

Because PAD is highly prevalent, has serious consequences (not only amputation, but also and mainly myocardial infarction, stroke and death), implicates high economic costs and, more worrisome, often can be present in absence of symptoms, it is strongly advised to screen for PAD.

This demands for adequate diagnostic and prognostic tools. ‘Although other methods exist to assess the peripheral vasculature more objectively, the ankle-brachial index (ABI) represents a simple, reliable method for detecting PAD.’ (18) PAD is suspected when ABI is 0.90 or lower (≤0.90). The ABI test is inexpensive, accurate, and relatively easy to perform so that the ABI has achieved a major role in screening patients for PAD. (19, 20)

1.2 Indications for ABI measurement

The ABI can be used to confirm the diagnosis in patients with symptoms suggestive of PAD or it can be used to screen for asymptomatic PAD. The question is: Who should be screened for PAD?

Specific clinical information should be used to identify individuals who should undergo ABI examination. ‘Clinical data that should guide this assessment includes: the presence of atherosclerosis risk factors (especially age, smoking, and diabetes), clinical history (a history of atherosclerotic coronary artery, carotid artery, or renal artery disease and lower extremity symptoms), and an abnormal lower extremity pulse examination.’ (21) Recommendations on screening asymptomatic patients with PAD vary across current guidelines. Ferket et al. (22) compared 8 leading guidelines of which 7 were developed in North America and 1 was developed by an international collaboration (Europe, Japan, North America, Australia and South Africa). Target groups in these guidelines generally comprised middle-aged persons with one or more cardiovascular risk factors and the elderly. (22) In the most recent American College of Cardiology–American Heart Association (ACC/AHA) Practice Guidelines, high-risk patients who should undergo ABI testing were identified as follows (table 3).
Table 3. Who Should Undergo screening with Ankle-Brachial Index Testing?

<table>
<thead>
<tr>
<th>Age ≥ 70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age = 50-69 years with history of diabetes or smoking</td>
</tr>
<tr>
<td>Age ≤ 49 years with diabetes and one additional risk factor (smoking, diabetes, hypertension, or elevated cholesterol levels)</td>
</tr>
<tr>
<td>Individuals who present with claudication or more severe limb ischemic symptoms</td>
</tr>
<tr>
<td>Abnormal lower extremity pulse examination</td>
</tr>
<tr>
<td>Known atherosclerotic disease elsewhere (coronary, carotid or renal arteries)</td>
</tr>
</tbody>
</table>

Furthermore, ABI measurement is also indicated for assessment of healing potential and evaluation of vascular compromise in patients with trauma of the lower legs. Follow-up evaluation with ABI is advised in graft surveillance, worsening of ischemic symptoms and assessment of revascularization therapy.(18, 23)

1.3 How is the ABI measured?

Figure 1. The ankle-brachial index test. As the blood pressure cuff deflates, the systolic blood pressure is recorded. Reprinted with permission, National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.(24)
Blood pressure is measured at both arms (brachial artery) and ankles (posterior tibial artery and dorsal pedis artery) with a Doppler probe and a sphygmomanometer. The ABI is then calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure at the arm. The higher of the two ankle pressures (posterior tibial artery or dorsal pedis artery) is used as the numerator and the higher of the two arm pressures is used as the denominator for both limbs. (Figure 2) If the index is 0.9 or less in either lower extremity, the diagnosis of PAD is put forward. Further investigation is then advised. Recently, some alternative calculations of the ABI
1.4 How is the ABI interpreted?

There is a U-shaped relationship between the ABI and mortality risk.(Figure 3)

![Figure 3](image)

**Figure 3.** The U-shaped relationship between ankle-brachial index and death. This data was gained from 4,393 patients in the Strong Heart Study. Patients were followed for a mean of 8.3 years. All-cause (white bar) and cardiovascular-disease-related (black bar) mortality rates were lowest in people with values of 1.0 to 1.4. Adapted from the Strong Heart Study.(28)

With a patient at rest, results ranging from 0.91 to 1.30-1.40 are normal. Readings below 0.91 indicate PAD and are associated with an increased risk of cardiovascular morbidity and mortality.(1, 7, 11-14). An ABI < 0.50 indicates a high risk of amputation.(1) On the other hand, readings above 1.30-1.40 are suggestive of stiffened and thus incompressible arteries in the ankles. This is often seen in elderly patients, patients with diabetes, or patients with end-stage renal failure requiring dialysis.(18) These patients also have an increased cardiovascular and overall mortality.(28) ‘Importantly, a substantial proportion of patients with an elevated ABI have been proposed. These are reviewed in the discussion. Moreover, measuring the ABI after exercise might diagnose PAD in patients with normal or borderline ABI at rest.(26, 27)
actually do have occlusive artery disease. Alternative tests such as measurement of the toe systolic pressures and Doppler waveform analysis are useful to unmask LEAD’. (1) These alternative tests are covered in the discussion.

Another important question is: “What is known about the sensitivity and specificity of the ABI?” Suggested PAD diagnosis by ABI can be verified objectively by non-invasive imaging techniques such as Duplex-, computed tomography- (CT-) or magnetic resonance- (MR-) angiography. A standard contrast angiogram, the golden standard for imaging PAD, is an invasive intravascular perfusion study that uses X-rays. Nowadays, it is only performed when surgical revascularization is considered. (29) Specificity and sensitivity of the ABI to detect PAD have been estimated on 441 patients, respectively at 96% and 79% (obtaining the best results when defining PAD as an ABI $\leq 0.9$). (19) A more recent review by Dachun et al., comprising 2043 patients, reported a high specificity (83.3–99.0%) and accuracy (72.1–89.2%), but a sensitivity that varied greatly (15–79%). Sensitivity was low, especially in elderly individuals and patients with diabetes. (20) Here, falsely elevated ABIs can occur due to stiffening of the arteries at the ankles, thereby lowering the sensitivity of the ABI test for PAD.

1.5 Objective

While the disease is relatively easy to detect, PAD is still underdiagnosed in primary care. This may be a barrier to effective prevention and treatment of the high ischemic cardiovascular risk associated with PAD. (7) Preferably, a screening test should be cheap, broadly applicable, quick and easy to execute, sensitive and specific. The ABI test is cheap, broadly applicable, quite sensitive (aside from patients with stiffened arteries) and specific. The ABI test may be, however, time-consuming and technical instruction on accurate use of the Doppler technique is necessary. This is why the use of automated (oscillometric) blood pressure measurement is proposed to measure the ABI. In this way, the technical aspect and time for measurement could be reduced greatly. This paper investigates the agreement between the automated oscillometric ABI determination and the golden standard Doppler ABI determination while also comparing time needed to perform each measurement method.
2. Methods

2.1 Introduction

To identify the agreement between the automated oscillometric measurement of the ABI and the golden standard Doppler ultrasound measurement of the ABI, both measurements were performed consecutively on the same patient in a randomized order. Patients were examined in supine position after resting quietly for 5 to 10 minutes in a room with ambient temperature. A questionnaire was taken to evaluate cardiovascular risk profile. Time needed to perform each method of measuring ABI was recorded.

2.2 Literature study

First, a literature study was performed to gain insight in the pathology of PAD and the diagnostic approach with Doppler device and automated oscillometric device. The search engine ‘Pubmed’ was searched by using MeSH terms ‘Ankle-brachial index’ (subheadings: methods, instrumentation), ‘Peripheral arterial disease’, ‘Oscillometry’ and others. Hundred and seven (107) articles were found in this manner. After reading the abstracts, 24 articles were selected. Snowball method (following references of selected articles) was used to collect 19 more articles of interest. Endnote X7 was used to collect, adjust and insert references into Word.

2.3 Ethical committee

Before starting the experimental phase of this study, permission was granted by the ethical committee of the Ghent University Hospital on 26 October 2012, Project number EC 2009|S90.(Attachment 1)

2.4 Participant recruitment

Participants were recruited at the Departments of Cardiovascular Diseases and Thoracovascular Surgery at the Ghent University Hospital between January 2010 and November 2013. An informed consent (attachment 2) was signed prior to the tests. A total of 198 subjects with various cardiovascular risk profiles (table 5) were recruited. All subjects were included, however, missing values are present in some cases of which in 2, ABI could not be determined because of incompressible arteries.
2.5 ABI measurement

The ankle-brachial index is measured in two ways: firstly using a handheld Doppler probe (Hadeco Bidop ES-100V3, Inc., Kawasaki, Japan) and sphygmomanometer, and secondly using a validated automated blood pressure device (Datascope Acutorr Plus, Paramus, NJ, USA), both with an appropriately sized blood-pressure cuff.

Measurements were performed by 2 operators, one a doctor already acquainted with Doppler method and I, who received a short training in Doppler handling and ABI measurement by an experienced vascular technician at the Ghent University Hospital

2.5.1 The Doppler ultrasound method (golden standard)

The blood-pressure cuff is placed on the patient’s upper arm and gel is applied at the level where the brachial pulse is palpated. A Doppler auditory signal is obtained by placing the Doppler probe (Hadeco Bidop ES-100V3, Inc., Kawasaki, Japan) towards the patient’s head in a 45- to 60-degree angle with respect to the artery, against the arterial current. Next, the cuff is inflated rapidly to 30 mm Hg above the point of cessation of brachial artery flow (silence on the Doppler machine). Then, the blood pressure cuff is slowly deflated until, again, a Doppler signal is being received. At this moment, the systolic pressure for the brachial artery is noted. The same sequence is repeated on the other arm.

After measuring the systolic pressure at both arms, the cuff is placed above the ankle. The posterior tibial artery is palpated and gel is applied on this area. Once again, the cuff is inflated rapidly to 30 mm Hg above the level at which flow ceases, then deflated slowly until a Doppler signal is being received and the systolic pressure for the posterior tibial artery is noted. Finally, the dorsalis pedis artery is palpated and the same sequence is followed. The same routine is then repeated on the other leg.

The ABI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure at the arm. (Figure 2) The higher of the two ankle pressures (posterior tibial or dorsalis pedis artery systolic blood pressure) is used as the numerator and the higher of the two arm pressures is used as the denominator for both limbs. If the ABI is 0.9 or lower in either lower extremity, the diagnosis of peripheral artery disease (PAD) is put forward.
2.5.2 The automated oscillometric blood pressure method

A validated automated blood-pressure device (Datascope Acutorr Plus, Paramus, NJ, USA) was used as an alternative method to obtain the ABI. ‘Oscillometers measure the magnitude of the pressure oscillation in the limb as the cuff is deflated from suprasystolic pressures. As the pressure in the cuff decreases and approaches systolic blood pressure, oscillation rapidly increases and eventually reaches a peak after which lowering the cuff pressure causes the oscillation to decrease. Systolic blood pressure is calculated when the oscillation increases rapidly, the diastolic pressure is calculated when the oscillation decreases rapidly.’ (30) This measurement is a lot easier to perform than the Doppler method. The cuff is placed consecutively on both arms and ankles, the systolic (and diastolic) blood pressures are noted, and the ABI is calculated in the same way as the Doppler method. With the oscillometric device, diagnosis of PAD is also put forward when ABI is ≤ 0.9.

2.6 Questionnaire

A questionnaire on cardiovascular risk factors (attachment 3) was filled in. Significant risk factors for PAD were subsequently investigated in this study population.

2.7 Statistical methods

ABI measured by Doppler (ABIdop) and ABI measured by oscillometric device (ABIosc) were calculated and dichotomized at the value of 0.91 to diagnose respectively PADdop and PADosc in subjects. All ABIdop and ABIosc were set out in pairs per limb to be investigated for correlation using the Spearman correlation coefficient and for agreement using the Bland Altman plot and intraclass correlation coefficient (ICC). Analysis of the differences between both methods was conducted to see whether these measures varied systematically over the range of ABI. Diagnostic accuracy (the agreement between PAdosc and PADdop per patient) was evaluated by kappa coefficient, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio.

To estimate the average time that can be saved by measuring the ABI with an automated oscillometric device instead of a Doppler device, time needed to perform each method was compared by Wilcoxon paired test and a boxplot was used for visual representation. Finally, an inter-observer agreement study was performed.
Significance or $\alpha$ level was set to 0.05 and all P-values were calculated 2-tailed. All analyses were conducted using SPSS version 22.
3. Results

3.1 Study Population

The study population comprised 198 subjects. In 39 subjects (19.7%), PAD was detected by Doppler method (ABIdop ≤ 0.9), leaving 157 where PAD was not detected (ABIdop between 0.91 and 1.39) and 2 subjects of whom the ABI could not be determined due to incompressible arteries.

In the PAD group, the mean age was 67 years (standard deviation, SD=13.8 years), maximum age was 84 years old and minimum age was 19 years old. For the no-PAD group, subjects were significantly younger (cfr. infra) with a mean age of 53 (SD= 18.6 years), a maximum age of 85 and a minimum age of 19.(Appendix)

Of the 39 participants suspected of having PAD, only 51.3% experienced symptoms of the disease.(Table 4) This is in accordance with Sigvant et al., who reported 60% of PAD patients to be asymptomatic.(8)

Table 4. Fontaine classification of participants in the PAD group versus the no PAD group.

<table>
<thead>
<tr>
<th>Fontaine stage</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>1</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate to severe intermittent claudication occurring after a &lt;200m walk</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>No PAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>145</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication occurring after &gt;200meters walk</td>
<td>7</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate to severe claudication occurring after a &lt;200m walk</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>157</td>
</tr>
<tr>
<td>PAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>19</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild intermittent claudication occurring after &gt;200meters walk</td>
<td>6</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate to severe claudication occurring after &lt;200m walk</td>
<td>5</td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
<td>6</td>
</tr>
<tr>
<td>IV</td>
<td>Trophic lesions (ulceration, gangrene...)</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>39</td>
</tr>
</tbody>
</table>
### 3.2 Cardiovascular risk factors in PAD

Table 5 shows prevalence of some important cardiovascular risk factors in subjects with PAD (defined by ABI measured by Doppler ≤0.9) compared to subjects without PAD. P value is also noted, resulting from a Mann-Whitney U test. Significance or α level is set to 0.05 (2-sided) with the null hypothesis that the reported cardiovascular risk factors have equal presence among subjects of both groups. Consequently, a significant difference between the two groups is acknowledged when P value is < 0.05.

#### Table 5. Cardiovascular risk profiles for PAD and no-PAD subjects

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>PAD (N=39)</th>
<th>No PAD (N=157)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67 (SD=13.8)</td>
<td>53 (SD=18.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Min: 19</td>
<td>Min: 19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Max: 84</td>
<td>Max: 85</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>25 (64%)</td>
<td>73 (46%)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>14 (36%)</td>
<td>84 (54%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>15 (38.5%)</td>
<td>28 (17.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>28 (71.8%)</td>
<td>53 (33.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethylism (more than 3 consumptions a day)</td>
<td>4 (10.3%)</td>
<td>1 (0.6%)</td>
<td>0.695</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13 (33.3%)</td>
<td>31 (19.7%)</td>
<td>0.073</td>
</tr>
<tr>
<td>Overweight (BMI &gt;25)</td>
<td>10 (25.6%)</td>
<td>47 (29.9%)</td>
<td>0.717</td>
</tr>
<tr>
<td>Obese (BMI &gt; 30)</td>
<td>9 (23.1%)</td>
<td>24 (15.3%)</td>
<td>0.252</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>24 (61.5%)</td>
<td>51 (32.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiovascular disease (CVD)**</td>
<td>18 (46.2%)</td>
<td>58 (36.9%)</td>
<td>0.305</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>14 (35.9%)</td>
<td>26 (16.6%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Family history of CVD**</td>
<td>10 (25.6%)</td>
<td>45 (28.7%)</td>
<td>0.946</td>
</tr>
</tbody>
</table>
*: Office systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg or patients taking blood pressure lowering medication.

**: History of angor pectoris, stroke, transient ischemic attack (TIA), acute coronary syndrome (ACS), carotid artery stenosis, bypass or stent or dilatation of leg arteries, heart transplantation, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).

Cardiovascular risk factors, significantly (P < 0.05) more present in the PAD group versus the no PAD group, were: advanced age, smoking, hypertension, hypercholesterolemia and renal insufficiency. Diabetes showed a trend with a P-value of 0.073.

3.3 Correlation of measurements of both methods

To assess how well the automated oscillometric method correlates with the Doppler method, ABI measured by Doppler (ABIdop) and ABI measured by oscillometric device (ABIsoc) were investigated in pairs per patient. A scatterplot of ABIdop and ABIsoc gives a quick perception of the correlation between both methods.(Figure 4).

![Figure 4. Scatter plot. Correlation between ABIsoc and ABIdop](image-url)
To evaluate correlation between ABI<sub>dop</sub> and ABI<sub>osc</sub>, Spearman correlation coefficient was determined. (Table 6) The Spearman correlation coefficient was chosen over the Pearson correlation coefficient because variables ABI<sub>dop</sub> and ABI<sub>osc</sub> were not normally distributed. (Appendix 3, Appendix 4)

Table 6. Spearman correlation coefficient of ABI<sub>dop</sub> and ABI<sub>osc</sub>.

<table>
<thead>
<tr>
<th>ABI measured by Doppler</th>
<th>ABI measured by Oscillometric device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation Coefficient</td>
<td>1</td>
</tr>
<tr>
<td>P-value</td>
<td>.004</td>
</tr>
<tr>
<td>N</td>
<td>385</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>.604</td>
</tr>
<tr>
<td>P-value</td>
<td>.000</td>
</tr>
<tr>
<td>N</td>
<td>387</td>
</tr>
</tbody>
</table>

Note that per patient, 2 ABI<sub>dop</sub> (right ABI<sub>dop</sub> and left ABI<sub>dop</sub>) and 2 ABI<sub>osc</sub> (right ABI<sub>osc</sub> and left ABI<sub>osc</sub>) were compared. That is why N is now theoretically 396 (the number of limbs) instead of 198 (the number of subjects).

The Spearman correlation coefficient ($r_s$) is 0.604 with $P < 0.001$. However, correlation does not give adequate information on agreement between both (linear) variables. (31, 32) Therefore, Bland Altman plot and ICC (intraclass correlation coefficient) were used to illustrate agreement.

3.2.1 Bland Altman plot

The Bland Altman method can generally be used to assess agreement between two methods of clinical measurement and can also be used to determine whether these methods vary systematically. If methods vary systematically, measurements can not be used interchangeably and systematic adaptation of one method should be considered. An important remark is that neither one of the methods is required to have perfect sensitivity, nor specificity in order to compare the two methods. Although the Doppler method is referred to as the ‘golden standard’ in measuring the ABI, the true golden standard for detecting PAD would be invasive contrast angiography. Doppler-based ABI is thus far from perfect in diagnosing PAD and therefore in measuring the ABI accurately. The same applies for the oscillometric-based ABI. The Bland
Altman plot has the ability to compare these two imperfect methods. (Figure 5) To construct a Bland Altman plot, the mean of the two measurements (MeanABI) should be assigned to the x-axis and the difference between the two values (ABI\textsubscript{dop}-ABI\textsubscript{osc}) to the y-axis.

Figure 5. Bland Altman plot of the differences between both methods against their mean showing good agreement and no obvious systematic difference between ABI\textsubscript{dop} and ABI\textsubscript{osc}. Mean ± 1.96SD and mean – 1.96SD form the 95% limits of agreement.

No obvious systematic difference in ABI between both methods is detected. This is also shown in figure 6, showing frequencies of the differences between the two measurements distributed around zero, relatively following the Gaussian curve. However, as mean ABI gets bigger, the difference between ABI\textsubscript{dop} and ABI\textsubscript{osc} becomes more positive. This means that higher values of the ABI more frequently are underestimated by the oscillometric method. As mean ABI gets smaller, the difference between ABI\textsubscript{dop} and ABI\textsubscript{osc} becomes more negative. This means that lower values of the ABI more frequently are overestimated by the oscillometric method. The latter can lead to false negative results: patients with PAD would not be detected by the automated oscillometric method.
Figure 6. Histogram of the distribution of differences between ABIdop and ABIosc with Gaussian curve and limits of agreement (95% confidence interval, CI).

The mean difference between ABIdop and ABIosc is only 0.0026, making a systematic bias between the two methods very unlikely. Mean + 1.96SD and mean – 1.96SD form the 95% limits of agreement. Differences outside this 95% confidence interval (CI) (between values -0.2768 and 0.2775) are significantly different from each other and therefore unacceptable. Only 20 limbs were found to be measured significantly different in both methods. Because most of the differences between both methods lie between these limits, good agreement between both methods can be expected.

3.2.2 Intraclass correlation coefficient (ICC)

As a third method to evaluate ABIosc against ABIdop, an intraclass correlation coefficient (ICC) was calculated. (Table 7) Intraclass correlation coefficients are measures of the relative similarity of quantities which share the same observational units of a sampling and/or measurement process. The closer the value of ICC is to 1, the less variability and the more similarity there is between both methods’ measurements.
Table 7. Intraclass correlation coefficient (ICC) of ABIsoc and ABIdop.

<table>
<thead>
<tr>
<th></th>
<th>Intraclass Correlation</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>Single Measures</td>
<td>.665</td>
<td>.605</td>
</tr>
<tr>
<td>Average Measures</td>
<td>.799</td>
<td>.754</td>
</tr>
</tbody>
</table>

‘Single measures ICC’ (reliability of single measures) can be used when only one measurement of the ABI is performed. ‘Average measures ICC’ (reliability of averages of measures) can be used when a mean of different ABI measurements is used.(33) In this case, ABI was mostly measured only once. The single measure ICC is always lower than the average measures ICC. The single measures ICC value is 0.665 (CI: 0.605 to 0.717) which is an adequate to good relative reliability, according to Fleiss.(34) (Table 8)

Table 8. Relative reliability according to Fleiss.(34)

<table>
<thead>
<tr>
<th>Value of ICC</th>
<th>Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 0.75</td>
<td>excellent</td>
</tr>
<tr>
<td>0.40 – 0.75</td>
<td>adequate</td>
</tr>
<tr>
<td>&lt; 0.40</td>
<td>poor</td>
</tr>
</tbody>
</table>

3.4 Agreement of both methods on PAD diagnosis

In order for the oscillometric method to be reliable, it should identify true patients as having PAD and healthy subjects as having no PAD. Unfortunately, the true golden standard to which diagnosis of PAD should be compared to, invasive contrast angiography, was not performed in this study. The next best thing to compare it to is the suspected diagnosis by the Doppler-based ABI. To evaluate how both methods agree on PAD diagnosis, a 2x2 cross table is shown (table 9) and diagnostic performance (table 10) and kappa coefficient were calculated.
Table 9. 2x2 cross table of PAD diagnosed by oscillometric device and PAD diagnosed by Doppler.

<table>
<thead>
<tr>
<th></th>
<th>Peripheral artery disease diagnosed by oscillometric device</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No PAD</td>
<td>PAD</td>
</tr>
<tr>
<td>Peripheral artery disease diagnosed by Doppler</td>
<td>No PAD</td>
<td>153</td>
</tr>
<tr>
<td></td>
<td>PAD</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
<td>30</td>
</tr>
</tbody>
</table>

In 15 subjects, PAD classification differed between both methods. The diagnostic performance of the automated oscillometric device method, assuming the Doppler method to be the golden standard was (table 10): sensitivity 69.23% (CI: 52.27% to 82.45%), specificity 98.08% (CI: 94.04% to 99.50%), accuracy 92.30% (CI: 87.70% to 94.50%), positive predictive value (PPV) 0.90% (CI: 0.723% to 0.973%) and negative predictive value (NPV) 0.92% (CI: 0.873% to 0.960%). The likelihood ratio for a positive result (LR+) was 36.00 (CI: 11.51 to 112.6), the likelihood ratio for a negative result (LR-) was 0.31 (CI: 0.196 to 0.503).

Table 10. Diagnostic performance of the automated oscillometric device method.

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>69.23%</td>
<td>52.27% to 82.45%</td>
</tr>
<tr>
<td>Specificity</td>
<td>98.08%</td>
<td>94.04% to 99.50%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>92.30%</td>
<td>52.27% to 82.45%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>90%</td>
<td>72.3% to 97.3%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>92%</td>
<td>87.3% to 96.0%</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>36.00</td>
<td>11.51 to 112.6</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.31</td>
<td>0.196 to 0.503</td>
</tr>
<tr>
<td>Kappa coefficient</td>
<td>0.737</td>
<td>0.581 to 0.813</td>
</tr>
</tbody>
</table>

The Kappa coefficient (κ) is 0.737 with P < 0.001. κ=0.737 can be considered as a substantial agreement according to Landis & Koch.(35) (Table 11)

Table 11. Agreement according to Landis & Koch.(35)

<table>
<thead>
<tr>
<th>Value of Kappa</th>
<th>Statistical Strength of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.81 – 1.00</td>
<td>excellent</td>
</tr>
<tr>
<td>0.61 – 0.80</td>
<td>substantial</td>
</tr>
<tr>
<td>0.41 – 0.60</td>
<td>moderate</td>
</tr>
<tr>
<td>0.21 – 0.40</td>
<td>fair</td>
</tr>
<tr>
<td>0.00 – 0.20</td>
<td>slight</td>
</tr>
<tr>
<td>&lt; 0.00</td>
<td>poor</td>
</tr>
</tbody>
</table>

24
3.5 Agreement between different observers (Inter-observer study)

Since 2 observers collected data, an inter-observer study is desirable. While differences in blood pressure measurements done with an automated oscillometric device by different observers will be less likely due to differences in technical skills and experience, measurements done with Doppler can be affected more by inter-observer bias. To evaluate these differences, 10 subjects were measured by Doppler consecutively by the 2 observers. Measurements I personally performed were noted as ABIdop measured by observer 1, measurements performed by the doctor were noted as ABIdop measured by observer 2. Oscillometric method comparison was not performed because measurements were expected to be very alike.

![Scatterplot for Doppler ABI measured by observer 1 and Doppler ABI measured by observer 2.](image)

**Figure 7.** Scatterplot for Doppler ABI measured by observer 1 and Doppler ABI measured by observer 2.

The scatterplot (figure 7) looks rather random, but notice that the scale is fairly small, which results in seemingly big differences. An ICC was calculated to evaluate the inter-observer reliability more objectively. (Table 12)
### Table 12. ICC of ABIdop1 and ABIdop2

<table>
<thead>
<tr>
<th></th>
<th>Intraclass Correlation</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Bound, Upper Bound</td>
</tr>
<tr>
<td>Single Measures</td>
<td>.138</td>
<td>-.314, .538</td>
</tr>
<tr>
<td>Average Measures</td>
<td>.242</td>
<td>-.915, .700</td>
</tr>
</tbody>
</table>

Only one measurement was taken for both ABIdop1 and ABIdop2 and no averages were calculated so that the ICC, again, is a single measures ICC. The single measures ICC represents the consistency in ABI measurements between the 2 observers. The closer the value of ICC is to 1, the less variability and the more agreement there is between both observers’ measurements. In this inter-observer study, the ICC is 0.138 (CI: -0.314 to 0.538), which is a poor reliability according to Fleiss. (34) (Table 8)

Kappa calculation was found invaluable because no subjects were diagnosed with PAD by any of the observers.

This unfortunately low similarity between both observers’ measurements can be partially explained by the small number of test subjects in this inter-observer study. The fact that all 10 subjects were healthy and no one was diagnosed incorrectly puts the low reliability in perspective. The maximum difference in ABI between the observers is 0.15 which has little meaning in healthy patients falling in the normal ABI range and an ABI change of >0.15 is generally required to consider worsening of limb perfusion over time, or improving after revascularization. (36) Of course, overall, this small difference in ABI measurement between different investigators can cause serious bias. Ideally, the inter-observer study should have been performed on a larger group of not exclusively healthy subjects in order to properly estimate the inter-observer variability.

#### 3.6 Comparison of time required for Doppler and oscillometric method

To estimate the average time that can be saved by measuring the ABI with an automated oscillometric device instead of a Doppler device, time needed to perform the examination using each method was compared. (Figure 8)
Figure 8. Box-and-whisker plot of time needed to perform the Doppler method and time needed to perform the oscillometric method.

Table 13. Descriptive statistics of time needed to measure the ABI for both methods.

<table>
<thead>
<tr>
<th></th>
<th>Time consumed for Doppler measurement (minutes:seconds)</th>
<th>Time consumed for oscillometric measurement (minutes:seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Valid 84 Missing 114</td>
<td>84 114</td>
</tr>
<tr>
<td>Mean</td>
<td>12:22 4:17</td>
<td>4:59 1:09</td>
</tr>
<tr>
<td>SD</td>
<td>4:17 1:09</td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>3:51 3:02</td>
<td>3:02</td>
</tr>
<tr>
<td>Maximum</td>
<td>26:00 9:00</td>
<td>9:00</td>
</tr>
</tbody>
</table>

Note that only for 84 subjects time could be compared for both methods. The mean time needed to measure the ABI with Doppler device (TimeDop) was 12 minutes and 22 seconds, the mean
time needed to measure the ABI with an automated oscillometric device (TimeOsc) was much less: only 4 minutes and 59 seconds. (Table 13) This means that the average time gained if oscillometric measurement is used instead of Doppler measurement in this study population is 7.4 minutes per subject. Also, a much bigger range of time needed to measure the ABI with Doppler can be illustrated. This can be explained by the frequent difficulties in using the Doppler technique on some subjects, resulting in big maximum values. Problems on Doppler usage are covered in the discussion.

A Wilcoxon paired test revealed a P value <0.001 so that the null hypothesis (TimeDop equals TimeOsc) could be rejected. This means that there was a (very) significant difference between the time needed for Doppler ABI measurement and time needed for oscillometric ABI measurement.

Another important observation is that there is a learning curve in handling the Doppler device efficiently: time needed for ABI measurements decreases with practice. (Figure 9) Measurements performed by an investigator with little experience with Doppler device will take much longer than an investigator with ample experience. This observation was not so obvious in the oscillometric method. (Figure 10)
‘Nr’ represents the sequence in which subjects were investigated. For the first 98 subjects, time was unfortunately not recorded. So only the last 100 subjects, measured by the second observer (myself) are shown. It is clear that, even after measuring about 200 limbs, there is still a large range in time needed to measure the ABI in different subjects, which is also acknowledged by experienced investigators.

3.7 Conclusion

In this paper, the automated oscillometric device method was compared to the golden standard Doppler method to measure the ABI. Investigating 198 subjects consecutively with Doppler and oscillometric device in a randomized order, the two ABIs (ABIdop and ABIosc) were found to be correlating well with a Spearman's correlation coefficient ($r_s$) of 0.604. There was also an adequate to good ICC of 0.665 and a Bland Altman plot showed little difference and no obvious systematic bias between measurements of the two methods. However, the automated oscillometric method was likely to underestimate or overestimate the ABI when the ABI measured by Doppler method was either high or low respectively.

Both methods seem to be agreeing well on PAD diagnosis. A substantial Kappa coefficient ($\kappa$) of 0.737 was calculated. Diagnostic performance of the automated oscillometric method versus the Doppler method was good: sensitivity 69.23% (CI: 52.27% to 82.45%), specificity 98.08% (CI: 94.04% to 99.50%), accuracy 92.30% (CI: 87.70% to 94.50%), PPV 0.90 % (CI: 0.723% to 0.973) , NPV 0.92% (CI: 0.873% to 0.960%), LR+ 36.00 (CI: 11.51 to 112.6) and LR- 0.31 (CI: 0.196 to 0.503).

Significant difference between both methods in time needed to measure the ABI was found: a mean of 12 minutes and 22 seconds for the Doppler method versus a mean of 4 minutes and 59 seconds for the automated method. A learning curve for the Doppler method could be illustrated.

Unfortunately the inter-observer study on 10 healthy subjects revealed poor similarity (ICC= 0.138) between both investigators’ Doppler measurements. However, this should be seen in the light of a small sample size, a relatively narrow range within normal ABI values and different experience level between the two observers.

Taking into consideration all pros and cons, the automated oscillometric method can be suggested for measuring the ABI for screening purposes.
4. Discussion

Because of its serious health consequences, high economic costs and given the fact that it is often present in the absence of symptoms, screening for PAD is strongly advised, especially in certain risk groups (table 3). While the disease is relatively easy to detect by the ABI test, PAD still remains underdiagnosed in primary care. The main limitations in assessing the ABI in daily practice are time constraints, lack of reimbursement and staff availability.(37) Also lack of education in Doppler handling and ABI calculation and too low awareness of PAD may also play a role. In this thesis, the Doppler method was challenged by the automated oscillometric method for measuring the ABI because the latter method is supposed to relieve some of these above mentioned constraints. Measurements of the automated oscillometric method were compared to the golden standard Doppler method and reasonable advantages (in time and technique) in favour of the automated oscillometric method were demonstrated in a group of 198 volunteers.

While Doppler-based ABI is the golden standard for measuring the ABI, invasive contrast angiography is the golden standard in diagnosing PAD. Because invasive contrast angiography or other imaging techniques were not performed in this setting, diagnostic performance of the automated oscillometric method could only be assessed using the Doppler-based ABI as a reference.

Diagnostic performance of the automated oscillometric method versus Doppler method (PADosc compared to PADdop) found in this study population is comparable to studies on the same subject. In this study, sensitivity was 69.23% (CI: 52.27% to 82.45%), specificity 98.08% (CI: 94.04% to 99.50%), PPV 90% (CI: 72.3% to 97.3%) and NPV 92% (CI: 87.3% to 96.0%). Beckman et al. reported a sensitivity of 73-88%, specificity of 85-95%, PPV of 65-88% and NPV of 88-96%, depending on which leg was compared.(30) The most recent assessment of sensitivity and specificity of oscillometric versus Doppler method was performed by Verberk et al. in a large meta-analysis comprising 25 studies and a total of 4186 subjects. The average sensitivity and specificity of the oscillometric ABI estimation in PAD diagnosis found in this meta-analysis was 69% (SD 6%) and 96% (SD 1%), respectively (with Doppler-based ABI as reference).(38) This is very much in line with our results.
Because the automated oscillometric device is proposed to be used for screening purposes, it is important to have a substantial specificity in order to correctly identify healthy persons. A false positive result could imply that the screened subject could possibly be submitted to costly investigations, subjected to unnecessary fear or maybe even be overtreated.

Although ABIsosc and ABIdop were found to agree well in this study, the automated oscillometric method was likely to underestimate or overestimate the ABI when the ABI measured by Doppler method was either high or low respectively. Accordingly, Verberk et al. and Jönsson et al. both reported that in general, the oscillometric devices tend to overestimate the ankle pressure in patients with moderate to severe PAD, giving a falsely high ABI.(38, 39) This means that the oscillometric method would yield more false negatives and would therefore have a lower sensitivity.

In this study population, especially in subjects with a low ABI, the oscillometric device seemed to overestimate the ABI.(Figure 4) In the view of screening, this can be tolerated. However, for precise assessment of the ABI in PAD patients, for e.g. making a decision whether a patient needs invasive treatment, post-treatment evaluation, follow-up, etc., automated oscillometric measurement might lose its advantages over the Doppler method due to its lesser agreement at low ABI values. Automated oscillometric measurement of the ABI is thus preferably only suggested for screening purposes.

4.1 Limitations of the ABI

The reasons that ABI is rarely used in routine clinical practice include time constraints, lack of reimbursement and staff availability.(37) This study confirms that ABI measurement by Doppler can indeed be time consuming. In this study, on average, a Doppler ABI measurement was performed in 12 minutes and 22 seconds. An automated ABI measurement only took 4 minutes and 59 seconds on average, demonstrating an important advantage for the latter method in measuring the ABI.

For an ABI to be measured properly, training is advised on how to correctly use a Doppler device for blood pressure measurement on peripheral blood vessels. It is important how the Doppler device is held (preferably at a 45-60-degree angle towards the blood flow) and where it is located (placing the probe, after applying some gel, where the pulse is felt). This sometimes can be
difficult, even for experienced investigators. The learning curve (figure 9) also illustrates that, even after the observer went through quite some practice, he/she might need notably more time for certain patients compared to others. (Figure based on my own results.) This can be explained by the common difficulties in measuring the systolic blood pressures with a Doppler device as I have experienced myself during the recordings: incompressible or hardly palpable arteries, anatomical variations of arteries, a loud environment so that the Doppler signal can not be heard on time.

Inaccurate measurements can occur. As noted in the introduction, the ABI test is a non-invasive tool for detecting PAD with its own diagnostic accuracy. A recent review reported a high specificity (83.3–99.0%) and accuracy (72.1–89.2%), but a sensitivity that varied greatly (15–79%). Sensitivity was low, especially in elderly individuals and patients with diabetes.(20) Here, falsely elevated ABIs can occur due to stiffening of the arteries in the ankles, thereby lowering the sensitivity of the ABI test for PAD. ‘Importantly, a substantial proportion of patients with an elevated ABI actually do have occlusive artery disease’.(1) These patients also have an increased cardiovascular and overall mortality.(28)(Figure 3) Other diagnostic tests (e.g. toe systolic pressures, pulse volume recording, duplex ultrasonography, MR-angiography, and CT-angiography) are recommended for those with calcified vessels (e.g., older individuals, those with long-standing diabetes or end-stage renal disease) suspected of having PAD and/or having a resting ABI value of more than 1.3.

The shortcomings of the ABI test also include the potential to miss mild proximal disease of the aorta and iliac arteries in those with well-developed collaterals. An exercise ABI (cfr. infra) should be determined when the resting ABI value is normal and there is a high clinical suspicion for PAD.

Some articles use different cut-off points for the ABI to suspect PAD. Sometimes PAD is suspected when ABI <0.90, while in other articles, PAD is already suspected when ABI <0.91. Consensus should be made to define universal cut-off points.
4.2 Alternative tests for detecting PAD non-invasively

In subjects with an ABI > 1.3, different alternative tests can be used to diagnose PAD.

1) **Toe systolic pressures.** Toe systolic pressures are used instead of ankle systolic pressures to calculate the ABI because the smaller arteries in the toes are less susceptible to calcification.(40)

2) **Pulse volume recording (PVR).** Pulse volume recordings are obtained with partially inflated segmental blood pressure cuffs that detect volume changes sequentially down a limb. Volume changes beneath the cuffs resulting from systole and diastole cause small pressure changes within the cuffs, which, with the use of appropriate transducers, can be displayed as arterial waveforms. Characteristics of the arterial waveforms reveal any occlusions within the investigated arteries.

3) **Duplex ultrasonography.** Duplex ultrasonography incorporates both echo (grayscale ultrasound) to visualize the blood vessel architecture (measurement of the intima-media thickness and tracking of atherosclerosis) and colour-Doppler ultrasound to visualize the flow within the blood vessel.

4) **MR-angiography and CT-angiography.** These imaging techniques are less invasive than contrast angiography, although CT-angiography carries risks related to ionising radiation, and both contrast enhanced MR-angiography and CT-angiography carry risks associated with the use of contrast agents.

The last 3 techniques have the ability to identify the location and severity of arterial narrowing and occlusion.

In subjects with a normal resting ABI but a high clinical suspicion of PAD, an exercise ABI is recommended.

**Exercise ABI.** The ABI is measured after exercise (mostly) on a treadmill. This could yield a better sensitivity for detecting PAD.(26, 27) Moreover, it can assess the functional status of a patient with PAD. “*How long can the patient walk before ischemic symptoms occur?*” And it provides important prognostic information on long-term outcome.(27) However, other studies report that it does not lead to more patients being detected.(41)
4.3 Limitations with the Doppler method

Errors in ABI measurement with the Doppler device are frequently due to an incorrect positioning angle of the Doppler probe, a loud environment so that the Doppler signal can not be heard on time, not applying enough gel on the spot where the Doppler probe makes skin contact, too much pressure on the artery by the Doppler probe, …

4.4 Limitations with the automated oscillometric method

The main problem with this technique is that the amplitude of the oscillations depends on several factors other than blood pressure, most importantly the stiffness of the arteries. Oscillometric devices tend to overestimate the ABI in PAD-affected limbs.(38, 39)

While a validated oscillometric device was used, some ankle pressures could not be measured because of unknown reasons. Kim et al.(25) indicated that the inconsistency between different validation studies of oscillometric ABI measurement is likely because the devices were designed for measuring blood pressure in non-obstructed arms, not in the legs, and especially not in diseased legs. Also, simultaneous oscillometric arm-leg measurements have more accuracy in measuring the ABI than sequential oscillometric measurements as performed in this study.(38)

4.5 Study limitations

Measurements were taken by 2 observers. Although methods on measurement were matched beforehand and training was received, an inter-observer study revealed a substantial inter-observer bias. However, this should be seen in the light of a small sample size, a relatively narrow range within normal ABI values and different experience level between the two observers. Ideally, the inter-observer study should have been performed on a larger group of not exclusively healthy subjects in order to properly estimate the inter-observer variability.

Investigating the intra- and inter-observer variability of Doppler-based ABI, inconsistencies between articles were encountered. On the one hand, Richart et al. concluded that Doppler technique requires trained investigators because of an intra-observer variability of approximately 10%.(42) On the other hand, a study by Holland-Letz et al. that focused solely on intra- and inter-observer bias in ABI measurement reported an intra- and inter-observer variability of 8% and 9%
respectively and a fairly high ICC of 0.423. Upon these results, Holland-Letz et al. concluded that ABI determinations are highly reproducible and reliable under routine conditions and that ABI measurements can be performed with little training, even by people other than physicians. However, in this particular study population, only 2 out of 108 subjects had an ABI ≤ 0.9 which makes these observations less reliable.

The automated oscillometric method was not tested for inter-observer variability because results were expected to be much more solid. However, it would have been interesting to see how oscillometric measurements agreed within the 2 different observers and to have compared this result with the Doppler inter-observer variability. The only thing that might be supposed is that the inter-observer variability of the oscillometric method would probably be much less than the inter-observer variability of the Doppler method.

More intense training on Doppler technique could have improved the accuracy of Doppler measurements. By measuring blood pressures multiple times and calculating the mean, more accurate results could have been achieved in both Doppler method and oscillometric method. It is also generally suggested to reassess the ABI within different visitations over time, before diagnosing peripheral artery disease and before making therapeutic decisions.

In 84 participants out of 198, time needed for performing the ABI test with each method was measured. Results show a clear advantage for the oscillometric method.

Standardized questionnaires to screen and diagnose intermittent claudication such as the Edinburgh Claudication Questionnaire were not used. Instead, a questionnaire was created to get a more global view on the patients’ cardiovascular risk profiles.

4.6 Alternative calculations of the ABI

The higher of the two brachial pressures is used as the denominator to account for the possibility of subclavian artery stenosis, which can decrease the blood pressure in the upper extremity and thus falsely elevate the ABI.

Ankle pressures used for the ABI calculation can be chosen differently from the pressures in the classical calculation of the ABI using the highest ankle pressure of either the posterior tibial artery or the dorsal pedis artery for each limb.
Various articles report a higher sensitivity in detecting PAD by using an alternate calculation of the ABI. One method uses the mean of the pressures in the dorsal pedis and posterior tibial arteries in each leg. (45) Others suggest that for situations in which the pressures in the two ankle arteries are different, the lower value may be of benefit, raising the diagnostic sensitivity. (46, 47)

4.7 Future prospective

Implications of this study include that screening patients for PAD by measuring the ABI could be performed by the automated oscillometric device instead of the Doppler device with more ease and in a shorter time. Hopefully, measuring the ABI will become more of a routine test in vascular investigation and cardiovascular risk assessment once oscillometric devices are fully validated for this purpose.

The implementation of automated oscillometric devices in routine ABI assessments beyond screening requires further demonstration of concordance with the golden standard Doppler-based ABI. Large population based studies could give a more definite view on this subject.

This study can be considered as an asset and already demonstrates some advantages of automated ABI determination.
5. References


6. Appendix

Appendix 1. Summary of descriptive characteristics for continuous variable age for no PAD and PAD group.

<table>
<thead>
<tr>
<th></th>
<th>No PAD</th>
<th>PAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>153</td>
<td>39</td>
</tr>
<tr>
<td>Valid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Mean</td>
<td>53,38</td>
<td>66,77</td>
</tr>
<tr>
<td>Median</td>
<td>55</td>
<td>68</td>
</tr>
<tr>
<td>SD</td>
<td>18,579</td>
<td>13,800</td>
</tr>
<tr>
<td>Range</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>Minimum</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Maximum</td>
<td>85</td>
<td>84</td>
</tr>
<tr>
<td>Percentiles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>39,00</td>
<td>60,00</td>
</tr>
<tr>
<td>Q3</td>
<td>70,00</td>
<td>78,00</td>
</tr>
</tbody>
</table>
Appendix 2. Histogram of ABI_dop, not normally distributed.

Shapiro-wilk test: p < 0.001

Appendix 3. Histogram of ABI_oscc, not normally distributed.

Shapiro-wilk test: p < 0.001
Attachment 1: Ethical Committee

Universitair Ziekenhuis Gent

Hart- en Vaatziekten
Dr. Tine DE BACKER
ALHIER

CONTACT                  TELEFOON      FAX            E-MAIL
Secretariaat            +32 (09) 332 56 13 +32 (09) 332 49 62 ethisch.comite@ugent.be

UW KENMERK                ONS KENMERK      DATUM            KOPIE
2012/721                  26-oct-12

BETREFT
Advies voor monocentric studie met als titel:
Acuutafhankelijk van automatische bloeddrukmeting bij het bepalen van de enkel/arm (E/A) index - Scriptie Jonas Dolfcorche

Belgisch Registratienummer: BE70201215327

* Begeleidende brief dd. 20/09/2009
* (Patienten)informatie- en toestemmingssformulier dd. 16/10/2009
* Protocol dd. 18/10/2009 (versie 1)
* Adviesaanvraagformulier dd. 17/10/2012 (document E)
* Informatie- en waarschuwingennota over de verwerking van informatie voor medisch-wetenschappelijk onderzoek dd. 24/10/2012
Jonas Dolfcorche

Advies werd gevraagd door:
Dr. T. DE BACKER; Hoofdontedezoeker

BOVENVERMELDE DOCUMENTEN WERDEN DOOR HET ETHISCH COMITÉ BEoordEELD.
ER WERD EEN POSITIEF ADVIES GEGEVEN OVER DIT PROTOCOL OP 26/10/2012. INDIEN DE STUDIE NIET WORDT OPGESTART VOOR 25/10/2013, VERVALT HET ADVIES EN MOET HET PROJECT TERUG INGEDEED WORDEN.

THE ABOVE MENTIONED DOCUMENTS HAVE BEEN REVIEWED BY THE ETHICS COMMITTEE.
A POSITIVE ADVICE WAS GIVEN FOR THIS PROTOCOL ON 25/10/2012. IN CASE THIS STUDY IS NOT STARTED BY 25/10/2013, THIS ADVICE WILL BE NO LONGER VALID AND THE PROJECT MUST BE RESUBMITTED.

DIT ADVIES WORDT OPGENOMEN IN HET VERSLAG VAN DE VERGADERING VAN HET ETHISCH COMITE VAN 20/11/2012

THIS ADVICE WILL APPEAR IN THE PROCEEDINGS OF THE MEETING OF THE ETHICS COMMITTEE OF 20/11/2012

Het Ethical Comité werkt volgens "ICP Good Clinical Practice"- regels
Het Ethical Comité bekleedt uiteen een gunstig advies met betrekking tot het Comité de verantwoordelijkheid voor het onderzoek op zich neemt. Beoordelingen die u over te voeren dat U enz. als betrouwbare onderzoeker worden vooropgezet in publicaties, rapporten voor de overheid enz., die het resultaat zijn van dit onderzoek.
In het kader van "Good Clinical Practice" moet de mogelijke bestaan dat het proces van de dataverzameling en de autoriteiten inzake. Krijgen van de originele data. In dit verband dienen de onderzoekers emotie in zaken dat, dat gebeurt zonder schending van de privacy van de proefpersonen.
Het Ethical Comité benadrukt dat het de promotor is die garanteriet te staan voor de conformiteit van de onderliggende informatie- en zorginstellingen met de nationale wetgeving.
Geen enkele onderzoeker betrokken bij deze studie is lid van het Ethical Comité.
Alle leden van het Ethical Comité behouden dit project beoordelings. (De ledenlijst is bijgevoegd)

Universitair Ziekenhuis Gent
De Pintelaan 185-B- 9000 Gent
www.ugent.be

Veerle De Rouck
09/332 22 06
veerle.derouck@ugent.be
The Ethics Committee is organized and operates according to the 'ICH Good Clinical Practice' rules.

The Ethics Committee stresses that approval of a study does not mean that the Committee accepts responsibility for it. Moreover, please keep in mind that your opinion as investigator is presented in the publications, reports to the government, etc., that are a result of this research.

In the framework of 'Good Clinical Practice', the pharmaceutical company and the authorities have the right to inspect the original data. The investigators have to ensure that the privacy of the subjects is respected.

The Ethics Committee stresses that it is the responsibility of the promoter to guarantee the conformity of the non-Dutch informed consent forms with the Dutch documents.

None of the investigators involved in this study is a member of the Ethics Committee.

All members of the Ethics Committee have reviewed this project. (The list of the members is enclosed)

Namens het Ethisch Comité / On behalf of the Ethics Committee
Prof. dr. Q. MATTHYS
Veegmeester / Chairman

CC: UZ Gent - Beheer en algemene directie
FAGG - Research & Development, Victor Hortaaplein 40, postbus 40 1080 Brussel
Attachment 2: Informed Consent

Informatiebrief voor de deelnemers aan experimenten

1 Titel van de studie:

Accuraatheid van automatische bloeddrukmeting bij het bepalen van de enkel/arm index (E/A index).

2 Doel van de studie:

Men heeft u gevraagd om deel te nemen aan een studie.

Deze studie wordt uitgevoerd om te bepalen of een automatische bloeddrukmeter kan worden gebruikt om uit te maken of er vernauwingen aanwezig zijn in de onderste ledematen. De aanwezigheid van deze vernauwingen is een belangrijke risicofactor voor hart- en bloedvaten. Deze alternatieve methode met automatische bloeddrukmeter zal worden vergeleken met een reeds bestaande standaard methode (Doppler) hieronder verder beschreven.

3 Beschrijving van de studie:

Het gaat om een éénmalig onderzoek waarbij de enkel/arm index via twee verschillende methodes zal worden gemeten.

Er zal u worden gevraagd om eerst vijf minuten in een rustige onderzoekskamer neer te liggen vooraleer het onderzoek met de metingen plaatsvindt. Om de twee onderzoeksmethodes te kunnen vergelijken, zal er in een willekeurige volgorde een bloeddrukmeter, die manueel wordt opgeblazen en een bloeddrukmeter die automatisch
opblaast, worden aangelegd. De bloeddrukmeter wordt afwisselend ter hoogte van beide armen en vervolgens ter hoogte van de beide enkels aangebracht. Bij de manuele bloeddrukmeter wordt er met een toestelletje geluidssignalen opgevangen van de bloedvaten en kan de bloeddruk worden bepaald (Doppler methode). De andere methode bestaat erin om een bloeddrukmeter aan te leggen die automatisch opblaast en automatisch de bloeddruk bepaalt ter hoogte van beide armen en enkels. Tussen de beide onderzoeken wordt er vijf minuten gepauzeerd.

De resultaten van deze beide methodes zullen worden vergeleken om te zien of de te testen methode evenwaardig is aan de reeds bestaande methode.

De verwachte totale duur van de studie is 30 minuten
Er zullen in totaal 60 personen aan deze studie deelnemen.

4 Wat wordt verwacht van de deelnemer?

Voor het welslagen van de studie, is het uitermate belangrijk dat u volledig meewerkt met de onderzoeker en dat u zijn/haar instructies nauwlettend opvolgt.

5 Deelname en beëindiging:

De deelname aan deze studie vindt plaats op vrijwillige basis.

Uw deelname in de studie kan helpen om in de toekomst patiënten beter te kunnen helpen.
U kan weigeren om deel te nemen aan de studie, en u kunt zich op elk ogenblik terugtrekken uit de studie zonder dat u hiervoor een reden moet opgeven en zonder dat dit op enigerlei wijze een invloed zal hebben op uw verdere relatie en/of behandeling met de onderzoeker of de behandelende arts.

Uw deelname aan deze studie zal worden beëindigd als de onderzoeker meent dat dit in uw belang is. U kunt ook voortijdig uit de studie worden teruggetrokken als u de in deze informatiebrief beschreven procedures niet goed opvolgt of u de beschreven items niet respecteert.

Als u deelneemt, wordt u gevraagd het toestemmingsformulier te tekenen.

5.1 Procedures:

Om de enkel/arm index te bepalen zal volgens een willekeurige volgorde achtereenvolgens gebruik worden gemaakt van een automatische bloeddrukmeter en van een manuele bloeddrukmeter en een doppler toestel.

5.2 Studieverloop:

Het gaat om een éénmalige meting waarbij de enkel/arm index via de twee verschillende methodes zal worden bepaald.

6 Risico’s en voordelen:

Er zijn geen risico’s verbonden aan dit onderzoek.

Deelname aan deze studie brengt voor u geen onmiddellijk therapeutisch voordeel.
Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent en wordt uitgevoerd volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki opgesteld ter bescherming van mensen deelnemend aan klinische studies. In geen geval dient u de goedkeuring door de Commissie voor Medische Ethiek te beschouwen als een aanzet tot deelname aan deze studie.

7 Kosten:

Uw deelname aan deze studie brengt geen extra kosten mee voor U.

8 Vergoeding:

Er wordt geen vergoeding voorzien.

9 Vertrouwelijkheid:

In overeenstemming met de Belgische wet van 8 december 1992 en de Belgische wet van 22 augustus 2002, zal u persoonlijke levenssfeer worden gerespecteerd en zal u toegang krijgen tot de verzamelde gegevens. Elk onjuist gegeven kan op uw verzoek verbeterd worden.

Vertegenwoordigers van de opdrachtgever, auditoren, de Commissie voor Medische Ethiek en de bevoegde overheden hebben rechtstreeks toegang tot Uw medische dossiers om de procedures van de studie en/of de gegevens te controleren, zonder de vertrouwelijkheid te schenden. Dit kan enkel binnen de grenzen die door de betreffende wetten zijn toegestaan. Door het toestemmingsformulier, na voorafgaande uitleg, te ondertekenen stemt U in met deze toegang.
Als u akkoord gaat om aan deze studie deel te nemen, zullen uw persoonlijke en klinische gegevens tijdens deze studie worden verzameld en gecodeerd (hierbij kan men uw gegevens nog terug koppelen naar uw persoonlijk dossier). Verslagen waarin U wordt geïdentificeerd, zullen niet openlijk beschikbaar zijn. Als de resultaten van de studie worden gepubliceerd, zal uw identiteit vertrouwelijke informatie blijven.

10 Letsels ten gevolge van deelname aan de studie:

De onderzoeker voorziet in een vergoeding en/of medische behandeling in het geval van schade en/of letsel ten gevolge van deelname aan de studie. Voor dit doeleinde is een verzekering afgesloten met foutloze aansprakelijkheid conform de wet inzake experimenten op de menselijke persoon van 7 mei 2004. Op dat ogenblik kunnen uw gegevens doorgegeven worden aan de verzekeraar

11 Contactpersoon:

Als er letsel optreedt tengevolge van de studie, of als U aanvullende informatie wenst over de studie of over uw rechten en plichten, kunt U in de loop van de studie op elk ogenblik contact opnemen met:

Dr. T. De Backer  
Cardioloog UZ Gent  
09/332.34.71
Toestemmingsformulier


Ik heb een kopij gekregen van dit ondertekende en gedateerd formulier voor “Toestemmingsformulier”. Ik heb uitleg gekregen over de aard, het doel, de duur, en de te voorziene effecten van de studie en over wat men van mij verwacht. Ik heb uitleg gekregen over de mogelijke risico’s en voordelen van de studie. Men heeft me de gelegenheid en voldoende tijd gegeven om vragen te stellen over de studie, en ik heb op al mijn vragen een bevredigend antwoord gekregen.

Ik stem ermee in om volledig samen te werken met de toeziende onderzoeker. Ik zal hem/haar op de hoogte brengen als ik onverwachte of ongebruikelijke symptomen ervaar.

Ik ben me ervan bewust dat deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent en dat deze studie zal uitgevoerd worden volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki, opgesteld ter bescherming van mensen deelnemend aan experimenten. Deze goedkeuring was in geen geval de aanzet om te beslissen om deel te nemen aan deze studie.

Ik mag me op elk ogenblik uit de studie terugtrekken zonder een reden voor deze beslissing op te geven en zonder dat dit op enigerlei wijze een invloed zal hebben op mijn verdere relatie met de onderzoeker. Men heeft mij ingelicht dat zowel persoonlijke gegevens als gegevens aangaande mijn gezondheid, ras en seksuele leven worden verwerkt en bewaard gedurende minstens 30 jaar. Ik stem hiermee in en ben op de hoogte dat ik recht heb op toegang en verbetering van deze gegevens. Aangezien deze gegevens verwerkt worden in het kader van medisch-wetenschappelijke doeleinden, begrijp ik dat de toegang tot mijn gegevens kan uitgesteld worden tot na beëindiging van het onderzoek. Indien ik toegang wil tot mijn gegevens, zal ik mij richten tot de toeziende onderzoeker, die verantwoordelijk is voor de verwerking.

X

Ik ben bereid op vrijwillige basis deel te nemen aan deze studie.

Naam van de vrijwilliger: ________________________

Datum: _________________________________________

Handtekening:

Ik bevestig dat ik de aard, het doel, en de te voorziene effecten van de studie heb uitgelegd aan de bovenvermelde vrijwilliger.

De vrijwilliger stemde toe om deel te nemen door zijn/haar persoonlijk gedateerde handtekening te plaatsen.

Naam van de persoon die voorafgaande uitleg heeft gegeven: ________________________

Datum: _________________________________________

Handtekening:
Attachment 3: Questionnaire

VRAGENLIJST STUDIE ENKEL ARM INDEX

Via deze vragenlijst willen we een overzicht krijgen van uw risicofactoren op het ontwikkelen van perifeer vaatlijden.

Uw gegevens worden enkel gebruikt in het kader van deze studie en zullen niet worden gedeeld met derden.

1) Wat is uw leeftijd?

2) Gewicht:

3) Lengte:

4) Rookt u? Zo ja, Hoeveel?:

of Heeft u ooit gerookt? Hoelang bent u gestopt?

5) Heeft u suikerziekte?

6) Heeft u teveel cholesterol of neemt u medicatie om de cholesterol te verlagen? ja/nee

7) Heeft u hypertensie of neemt u bloeddrukverlagende medicatie? Ja/nee

XII
8) Hoeveel glazen alcohol consumeert U gemiddeld per dag (beschouwd over 1 week)?:

9) Hoeveel keer per week heeft u beweging of doet u aan sport?

10) Bent u gekend met nierinsufficiëntie?

11) Ervaart u pijn/last in de benen na een afstand stappen? Ja/nee

Indien ja:
    - Gaat de pijn over indien u stil staat?
    - Na welke afstand stappen begint de pijn? </> dan 200m
    - Heeft u ook pijn in rust?

12) Heeft u ooit een ingreep ondergaan thv de bloedvaten van uw benen (ballondilatatie, stent, overbrugging)?
13) Ervaart u soms een druk op de borstkas bij inspanning?

Indien ja:

- Gaat de pijn over wanneer u rust?

- Indien u deze druk ervaart, straalt deze dan uit naar de arm, hals?

- Neemt u hiervoor medicatie, zo ja: welke?

14) Heeft u een voorgeschiedenis van hartinfarct en/of heeft u ooit een ingreep gehad van de bloedvaten van uw hart (ballondilatatie, stent, overbrugging)?

15) Bent u gekend met een vernauwing thv de halsvaten of heeft u hiervoor reeds een ingreep ondergaan?

16) Heeft u een voorgeschiedenis van TIA of hersentrombose?
17) Zijn er mensen in uw familie die problemen hebben van het hart en/of de bloedvaten op jonge leeftijd (< 65j)? Zo ja, welke aandoeningen? (hartinfarct, hersentrombose, plotse dood? hypertensie?)

18) Welke medicatie neemt u?

Dank voor uw deelname.

Jonas Delforche, student Master Geneeskunde

Dr T. De Backer – Dr L. Campens – Dr. M. De Pauw

Dienst Cardiologie

UZ Gent

XV