Reliability of Laser Doppler Flowmetry Curve Reading for Measurement of Toe and Ankle Pressures: Intra- and Inter-observer Variation

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WHAT THIS PAPER ADDS

Peripheral arterial disease can be diagnosed non-invasively by measuring an ankle-brachial index or toe-brachial index. Laser Doppler flowmetry is considered the reference standard for distal pressure measurements in many vascular laboratories. Distal limb pressures are subject to substantial variation between repeated measurements, and an important source of variation is attributed to observer variation when reading the generated flow curve profiles. This study investigates the diagnostic agreement and variation in pressures when reading the flow curves using laboratory technologists as observers, and suggests influence of diabetes and chronic kidney disease on reproducibility.

Objectives: To assess the intra- and inter-observer variation in laser Doppler flowmetry curve reading for measurement of toe and ankle pressures.
Methods: A prospective single blinded diagnostic accuracy study was conducted on 200 patients with known or suspected peripheral arterial disease (PAD), with a total of 760 curve sets produced. The first curve reading for this study was performed by laboratory technologists blinded to clinical clues and previous readings at least 3 months after the primary data sampling. The pressure curves were later reassessed following another period of at least 3 months. Observer agreement in diagnostic classification according to TASC-II criteria was quantified using Cohen's kappa. Reliability was quantified using intra-class correlation coefficients, coefficients of variance, and Bland—Altman analysis.
Results: The overall agreement in diagnostic classification (PAD/not PAD) was 173/200 (87%) for intra-observer ($\kappa = .858$) and 175/200 (88%) for inter-observer data ($\kappa = .787$). Reliability analysis confirmed excellent correlation for both intra- and inter-observer data (ICC all $\geq$.931). The coefficients of variance ranged from 2.27% to 6.44% for intra-observer and 2.39% to 8.42% for inter-observer data. Subgroup analysis showed lower observer-variation for reading of toe pressures in patients with diabetes and/or chronic kidney disease than patients not diagnosed with these conditions. Bland—Altman plots showed higher variation in toe pressure readings than ankle pressure readings.
Conclusions: This study shows substantial intra- and inter-observer agreement in diagnostic classification and reading of absolute pressures when using laboratory technologists as observers. The study emphasises that observer variation for curve reading is an important factor concerning the overall reproducibility of the method. Our data suggest diabetes and chronic kidney disease have an influence on toe pressure reproducibility.

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INTRODUCTION

Diagnosis of peripheral arterial disease (PAD) is a strong predictor of risk for cardiovascular disease and mortality.[1] The disease can be diagnosed non-invasively by measuring the blood pressure at ankle or toe level and calculating a ratio to the brachial pressure, known as the ankle-brachial index or the toe-brachial index.[2] Laser Doppler flowmetry (LDF) has received increasing attention for distal pressure assessment, and is considered the method of reference by many vascular laboratories.[3,4] The method is based on measurement of capillary flow by the emission of laser light carried by a fibre-optic probe. The light hits moving blood cells, which causes alteration in the

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wavelength (the Doppler Shift) and the back-scatter is subsequently detected by a sensor.[4] The LDF method is based on manual or automated reading of the derived flow-signal. This method has been shown to be highly sensitive for the detection of low pressures (reduced signal) and thereby leads to a high completion rate.[5,6] Measurement of blood pressure in the lower limbs is, however, subject to substantial variation attributed to biological as well as methodological factors.[7] The LDF method has been characterised by quantifying correlation with other methods, as well as reproducibility.[5,6,8] However, a major source of variation is attributed to interpretation of the generated curves.[9,10] This is also the case in other methods used for measurement of distal pressures such as strain gauge plethysmography.[10,11] The quality of the LDF signal can be influenced by pathophysiological and external factors such as limb tremor, sudden movement, hyperaemia, or oedema.[3,12] The aim of the present study was to assess intra- and inter-observer variation among laboratory technologists for assessing the LDF curves.

METHODS

Subjects

A total of 200 consecutive patients participated in a trial performed at the Department of Clinical Physiology, Viborg, Denmark. The patients were recruited for a double-blinded diagnostic accuracy study of LDF versus strain gauge plethysmography.[13] The study protocol was approved by the Central Denmark Region Committees on Biomedical Research Ethics and the Danish Data Protection Agency.

Experimental procedure

The patients rested in a supine position for at least 15 minutes prior to the measurements in a room with temperatures at 25.4 °C (±0.6). The lower limbs were covered with heating overlays prior to testing (Action Shear Smart, Action Products Inc., Hagerstown, MD, USA) at 35—40 °C. Toe pressures were assessed by laser Doppler flowmetry as well as by strain gauge plethysmography in both limbs followed by ankle pressure measurements by both methods in a randomised sequence. The measurements were performed by two operators blinded to the results of the other test. Pressure measurements at the toe or ankle level were conducted in both limbs simultaneously. Data for the strain gauge plethysmography method is not part of the data analysis in this paper.[8] All measurements were made at least twice at each measuring site. Measurements were repeated until two readings were obtained with a maximum of 10 mmHg of difference. A maximum of five measurements were performed at each site.

Measurements with laser Doppler flowmetry

The MoorVMS-LDF (Moor Inc, Axminster, Devon, UK) system was used for the LDF measurements. The two probes (VP-1, Moor Inc, Axminster, Devon, UK) were embedded in a moulded flexible socket and secured using adhesive discs. The tubes from the occlusion cuffs were connected to the pressure controller (MoorVMS-PRES, Moor Inc, Axminster, Devon, UK). Following the positioning of the probe, an automated protocol was initiated which inflated the occlusion-cuff (inflation time approximately 3 seconds) to a pressure selected by the operator (150—250 mmHg), well above the systolic arm pressure. After a hold period of 10 seconds, the proximal cuff deflated automatically (3 mmHg/s) with the probe measuring skin blood-flow throughout the deflation period with a sampling rate of 40 Hz. The integrated software contained an algorithm that allows automatic determinations of systolic pressure readings. However, the algorithm did not work properly with the current hold-and-release settings, and many readings were clearly wrong (data not shown). Thus, no comparison of automatic versus manual readings was performed.

Brachial blood pressure

Brachial blood pressures were measured in the supine position using an automated device (Digital Blood Pressure Monitor, UA-852, A&D Instruments, Abingdon, UK). The blood pressure was measured in both arms, and the side with the highest systolic pressure was selected as the reference for calculation of the ankle-brachial index and toe-brachial index. The brachial pressure was acquired simultaneously with all separate measurements of toe and ankle pressures, allowing for the calculation of the ankle-brachial index and the toe-brachial index independent of brachial blood pressure variation.

Co-morbidity

Information regarding patient demographics, medication, and medical history was registered by a questionnaire. Presence of diabetes was defined according to anti-diabetic medication, and presence of chronic kidney disease was identified if blood tests showed an estimated glomerular filtration rate of <60 mL/min/1.73 m^2 for a period of more than 3 months.[14]

Operators

The operators consisted of 10 laboratory technicians who routinely perform distal blood pressure measurements at our department. They had from 2.8 to 29.3 years (median 4.8 years) of experience with the distal pressure measurements. Two of these laboratory technicians (observer A and observer B) were assigned for the secondary rereading of the curves used in this paper; they both had an experience of 3.4 years with the strain gauge plethysmography method but limited experience with the LDF method. The observers received supervised training in LDF curve interpretation prior to the primary data sampling (data not used in this paper) and additional training prior to the readings for this study.

Reading of pressure curves

Following the primary data sampling, the pressure curves were made fully anonymous and no alterations were