Diagnostic accuracy of laser Doppler flowmetry versus strain gauge plethysmography for segmental pressure measurement

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Objective: **To assess the diagnostic accuracy of laser Doppler flowmetry (LDF) with mercury-in-silastic strain gauge plethysmography (SGP) as a reference test for measuring the toe and ankle pressures in patients with known or suspected peripheral arterial disease (PAD).**

Methods: **This was a prospective, randomized, blinded diagnostic accuracy study. Toe and ankle pressures were measured using both methods in 200 consecutive patients, who were recruited at our vascular laboratory over a period of 30 working days. Classification of PAD and critical limb ischemia (CLI) was made in accordance with TASC-II criteria.**

Results: **The LDF method demonstrated 5.8 mm Hg higher mean toe pressures than the SGP method for the right limb and 7.0 mm Hg for the left limb (both $P < .001$). There were no significant differences in the mean ankle pressures (both $P > .129$). The limits of agreement for the differences (SGP − LDF) were −31.7 to 20.2 mm Hg for right toe pressures, −28.0 to 14.0 mm Hg for left toe pressures, −25.5 to 22.8 mm Hg for right ankle pressures, and −26.9 to 24.6 mm Hg for left ankle pressures. A correlation analysis of the absolute pressures using the two methods showed an intraclass correlation coefficient of 0.902 (95% confidence interval [CI], 0.835-0.938) for right toe pressures, 0.919 (95% CI, 0.782-0.960) for the left toe pressures, 0.953 (95% CI, 0.937-0.965) for right ankle pressures, and 0.952 (95% CI, 0.936-0.964) for left ankle pressures. Cohen's Kappa showed an agreement in the diagnostic classification of $\kappa = 0.775$ (95% CI, 0.631-0.919) for PAD and $\kappa = 0.780$ (95% CI, 0.624-0.936) for CLI.**

Conclusions: **LDF showed a good correlation with SGP over a wide range of toe and ankle pressures, as well as substantial agreement for the diagnostic classification of PAD including CLI. (J Vasc Surg 2013;58:1563-70.)**

The diagnosis of peripheral arterial disease (PAD) is a well-described indicator for increased risks of cardiovascular disease and death,[1] even in the absence of other cardiovascular risk factors.[2] According to intersociety consensus guidelines, PAD can be diagnosed non-invasively by measuring the ankle-brachial index (ABI) or the toe-brachial index (TBI).[3,4] Furthermore, measuring the toe and ankle pressures can disclose important information and aid in selecting the optimal treatment regime for patients with critical limb ischemia (CLI).[5] Because these patients have low distal limb pressures, it is imperative to have reliable methods for pressure measurements. Currently, a number of different techniques are used for this purpose in vascular laboratories and have substantial differences in their methodologies.[6] Factors such as edema, wounds, hyperemia, and tremor are often present in patients with PAD, and can influence measurements.[7] The various methods in use have different strengths regarding these entities, which makes diagnostic accuracy studies using an appropriate patient pool essential to assess interchangeability.[8]

One of the methods for distal pressure measurements is the mercury-in-silastic strain gauge plethysmography (SGP). This method is based on detection of volume change and was introduced in the 1960s. It is still considered the method of reference in many vascular laboratories in northern Europe, due to the ample validation against intra-arterial pressure and angiographic findings.[9] Another method in use is laser Doppler flowmetry (LDF), which has been applied in micro-vascular research for cutaneous flow measurement for three decades.[10] LDF has increasingly been used for distal pressure measurements over the last 10 years. LDF allows measuring capillary flow via the emission of laser light carried by a fiber-optic probe. The light hits moving blood cells, which leads to a change in the wavelength (the Doppler shift), and the scatter is detected by a sensor. This method has been shown to be highly sensitive for the detection of low pressures (reduced signal).[11,12] The LDF method has previously been compared with the SGP method in a small study with acceptable agreement.[13] However, it remains unclear

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whether these two techniques are fully interchangeable in a clinical setting using patients with a broad disease spectrum.

METHODS

Design. The study was performed as a prospective, randomized, blinded study following the recommendations of Standards for Reporting Diagnostic Accuracy Studies (STARD)[14] and Cochrane Diagnostic Test Accuracy (DTA)[15] requirements in one center (Department of Clinical Physiology, Viborg Regional Hospital, Denmark).

Recruitment of patients. Consecutive patients referred for distal blood pressure measurements in the Spring of 2012 were screened for inclusion in the trial. Two hundred patients were scheduled for inclusion in the study. The eligibility criteria were age >18 years and the mental capacity for complying with the study procedures. Patients were excluded if time constraints from other procedures in the lab interfered with the study procedure. The study protocol was approved by the Central Denmark Region Committee on Biomedical Research Ethics (M-20110286) and the Danish Data Protection Agency (2007580010).

Demographics. Patient demographics, medication, and medical history were obtained by a questionnaire. The patients' medical files were reviewed for prior vascular surgery. The presence of diabetes, chronic kidney disease, and hypercholesterolemia were established based on biochemical data, current medication, and/or patient records.

Experimental procedure. The patients rested in a supine position for at least 15 minutes prior to the measurements. Adequate limb temperature was provided by heating the lower extremities with heating overlays (Action Shear Smart; Action Products Inc, Hagerstown, Md) at 35°C to 40°C. Room temperature was maintained at an average of 25.4°C (±0.6). Eligible patients were randomized for measurements by both techniques in one of the two sequences: (1) $SGP_{toe\ pressures}$–$LDF_{toe\ pressures}$–$SGP_{ankle\ pressures}$–$LDF_{ankle\ pressures}$ or (2) $LDF_{toe\ pressures}$–$SGP_{toe\ pressures}$–$LDF_{ankle\ pressures}$–$SGP_{ankle\ pressures}$. All patients were randomized in blocks of four by using opaque, sealed envelopes to determine the sequence. Measurements by the two methods were performed by two different operators blinded to the results of the other test. Pressure measurements at the toe or ankle level were conducted in both limbs simultaneously. The same occlusion cuffs were used by both systems, and there was no repositioning of the cuffs between tests. The occlusion cuffs were connected to pressure controllers specific for each device. Appropriately sized pneumatic occlusion cuffs, ranging from 90 to 130 mm × 15 to 25 mm, were used for the toe pressure measurement, and cuffs ranging from 290 to 420 mm × 120 mm were used for the ankle pressure measurements. Throughout the measurements, the detectors (strain gauge or LDF probe) were placed on the pulp of the toe. The preferred site for the detectors was the first toe. If amputations or other restrictions existed that prevented applying the cuff to the first toe, measurements were performed on the second toe. All measurements were at least made in duplicate at each measuring site. The measurements were repeated until two readings were obtained with a maximum of 10 mm Hg of difference. A maximum of five measurements was performed at each site. Following the measuring sequence, the segmental pressures were calculated as an average of the two measurements with ≤10 mm Hg in difference. In cases with three pressures obtained with a difference ≤20 mm Hg between the highest and lowest value, an average of the three was used. The skin temperature of the first toe was measured using an infrared thermometer (TN1 thermometer; Electronic Temperature Instruments Ltd, Worthing, UK). The operators consisted of 10 laboratory technicians who routinely perform distal blood pressure measurements in the lab. Their experience with the SGP method ranged from 2.8 to 29.3 years (median, 4.8 years). They had no prior experience with LDF but received detailed training before and during the study. In situations where measurements could only be obtained by one method, that particular measuring site was excluded from the comparative analysis.

Diagnostic criteria. PAD was diagnosed according to the TASC-II criteria as ABI ≤ 0.90 or TBI < 0.70.[3] Findings of low segmental blood pressure (toe pressure <30 mm Hg and/or ankle pressure <50 mm Hg) and concurrent clinical findings of ischemia (chronic ischemic rest pain, ulcers, or gangrene [ie, Fontaine III-IV]) defined CLI.[3]

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 the ABI and TBI calculations. The brachial pressure was acquired concurrently with all separate measurements of the toe and ankle pressures.

Measurements with the index test (LDF). The Moor VMS-LDF (Moor Inc, Axminster, Devon, UK) system was used for the LDF measurements. The two probes (VP-1; Moor Inc) were embedded in a molded flexible socket and secured using adhesive discs. The tubes from the occlusion cuffs were connected to the pressure controller (Moor VMS-PRES; Moor Inc). Following the positioning of the probe, an automated protocol was initiated that inflated the occlusion cuff (inflation time, approximately 3 seconds) to a pressure selected by the operator (150-250 mm Hg), well above the systolic arm pressure. After a hold period of 10 seconds, the proximal cuff deflated automatically (3 mm Hg/sec) with the probe measuring skin blood flow throughout the deflation period with a sampling rate of 40 Hz. At least 3 months after the completion of the study, two independent technicians reanalyzed the LDF curves without information about patient history, signs, or symptoms. The observers received supervised training in LDF curve interpretation during the

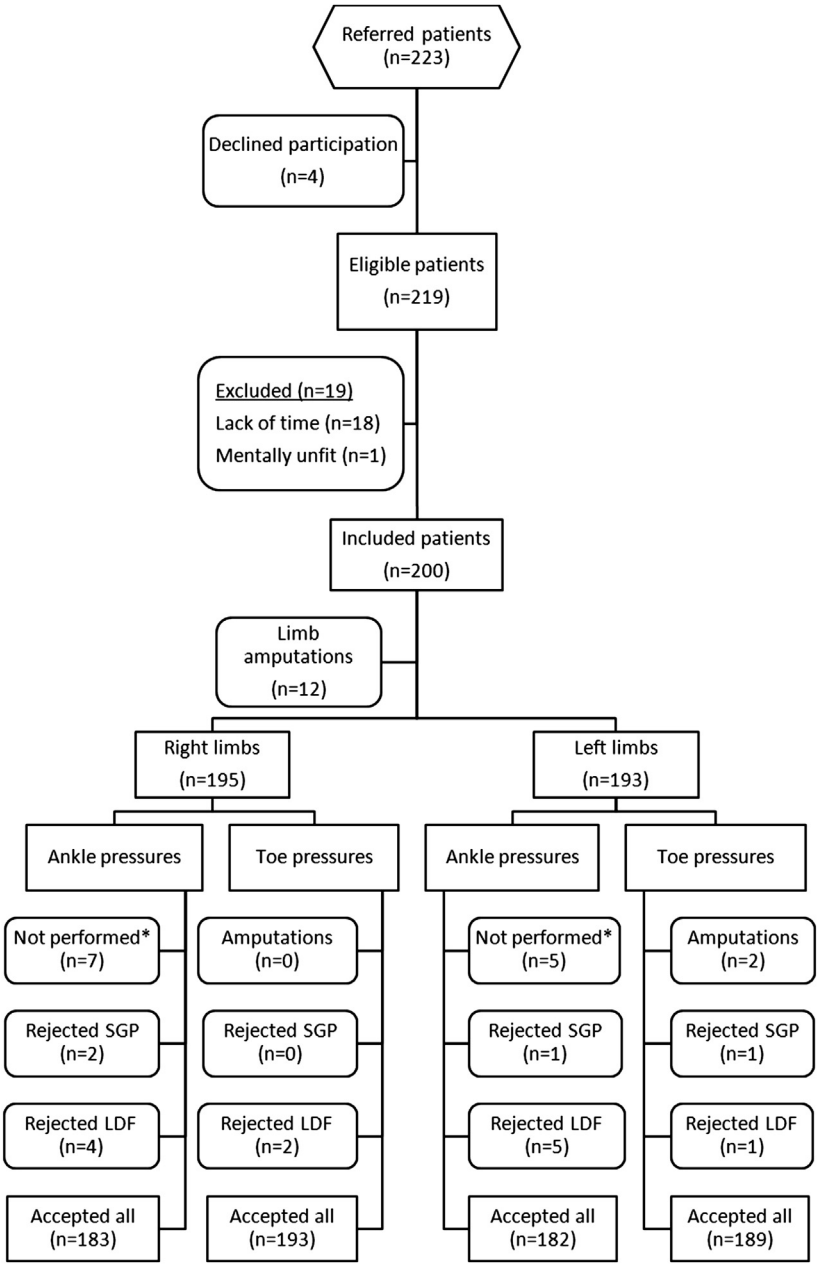

Fig 1. Flow diagram showing patient recruitment. *Not performed due to recent vascular surgery, major wounds, or fracture. *LDF*, Laser Doppler flowmetry; *SGP*, strain gauge plethysmography.

study period and additional training prior to the readings. If one of the two LDF readers deemed the curves for a measuring site unacceptable, this dataset was rejected. The pressure value used for comparison with the reference test was the average of the pressures found by the two observers. The curves were read to the nearest one millimeter of mercury.

Measurements with reference test (SGP). A Digitmatic DM2000 (Medimatic A/S, Hellerup, Denmark) was used for SGP. A mercury-in-silastic strain gauge was wrapped around the pulp of the toe for all SGP measurements. Prior to filling the occlusion cuff (inflation time, <1 second), 10 seconds of manual pressure was applied to the pulp of the toe to empty the vascular bed. Prior to inflation of the occlusion cuff at ankle level, the lower limbs were elevated at 50 to 70 cm for 30 seconds prior to inflation to reduce the peripheral blood volume. The deflation time for the occlusion cuff (average, 3 mm Hg/sec) and the sensitivity were adjusted appropriately by the primary technicians according to institutional practice. The pressures were assessed by reading the curves to the nearest 1 millimeter of mercury on site. Because identical

Table I. Patient demographics and clinical characteristics

	Total (n = 200)
Male/female	111/89
Age, years	71.2 ± 10.4
Caucasian race	198 (99)
BMI, kg/m^2	26.0 ± 5.4
BP systolic, mm Hg	144 ± 21
BP diastolic, mm Hg	77 ± 13
Diabetes	52 (26)
Chronic kidney insufficiency	49 (25)
Arterial hypertension	151 (76)
Hypercholesterolemia	167 (84)
Myocardial infarction	35 (18)
Smokers, current	55 (28)
Smokers, former	98 (49)
BMI >25 kg/m^2	102 (51)
Prior lower limb revascularization	
Total	94 (47)
<1 month	30 (15)
Amputations	
Toe	8 (4)
Lower limb	12 (6)
Symptoms	
Fontaine I	37 (18)
Fontaine II	81 (40)
Fontaine III	41 (21)
Fontaine IV	41 (21)
Department of referral	
Vascular surgery	159 (79)
General practitioners	30 (15)
Other	11 (6)

BMI, Body mass index; *BP,* brachial blood pressure; *SD*, standard deviation. Values are presented as mean ± SD or number (%).

results of the reading of SGP curves were recently shown in the clinical situation with blinded reading of SGP curves, blinded re-readings of the SGP curves were not made.[16]

Statistical analysis. The data are presented as the means ± standard deviations. Agreement in diagnostic classification (PAD/not PAD) was analyzed by using the Cohen Kappa (κ). A κ value ranging from 0.41 to 0.60 was considered to show moderate agreement, a value between 0.61 and 0.80 indicated substantial agreement, and a value between 0.81 and 0.99 indicated almost perfect agreement.[17] Agreement in pressure values and indices was assessed using an intraclass correlation coefficient (absolute agreement, single measures, two-way random model). Reproducibility was assessed using coefficient of variance. Difference-mean plots (Bland-Altman) were constructed to assess the discordance in the range of pressures.[18] Limits of agreement were compared by calculating a 95% confidence interval (CI) for upper and lower limits. A paired *t*-test was used to compare the means of the variables of the two techniques, and an unpaired *t*-test for intragroup comparisons. A P value < .05 was considered to be statistically significant. Statistical analysis was performed using SPSS software version 20.0 (SPSS Inc, Chicago, Ill).

RESULTS

Patients. A total of 223 patients were screened, and 200 patients (90% of referred patients) were included in the study. The recruitment period lasted 30 working days, from February 20 to April 10, 2012. The patient flowchart is presented in Fig 1. Patient demographics and clinical information are displayed in Table I. The skin temperatures averaged 30.8°C (± 1.9°C) during the toe pressure measurements and 29.8°C (± 1.8°C) during the ankle pressure measurements with no significant difference between the temperatures during the index and reference tests.

Rate of completion. It was possible to perform SGP measurements according to our reproducibility criteria in 373/376 (99.2%) of the ankle pressure measurements and in 385/386 (99.7%) of the toe pressure measurements. During the blinded reading of the LDF curves, both observers accepted the data quality in 367/376 (97.6%) of the ankle pressures and in 383/386 (99.2%) of the toe pressure measurements.

Variation in brachial blood pressures. The mean brachial blood pressure was 138 ± 20 mm Hg during the SGP toe pressure measurements and 138 ± 21 during the LDF toe pressure measurements with no significant difference between the methods ($P = .107$). The brachial blood pressure was significantly higher with SPG during the ankle measurements than with LDF (140 ± 21 mm Hg vs 137 ± 21 mm Hg; $P < .001$).

Agreement in segmental pressures and indices. The absolute pressures and pressure indices obtained using the two methods are compared in Table II. The LDF method measured significantly higher toe pressures than SGP on both sides, with a mean difference of 5.8 mm Hg for right limbs and 7.0 mm Hg for left limbs (both $P < .001$). There were no significant differences between the two methods regarding mean ankle pressures on either side (both $P > .129$). The LDF method showed higher values for TBI and ABI compared with SGP for both limbs (for all, $P < .002$). The Bland-Altman plots for toe and ankle pressure measurements (Fig 2) did not reveal a systematic difference in any pressure range.

A subgroup analysis was performed for agreement of pressures and indices in patients with diabetes (n = 52) vs nondiabetics (n = 148), overweight patients (body mass index >25 kg/m^2; n = 102) vs nonoverweight patients (body mass index <25 kg/m^2; n = 98), and patients with Fontaine I-II (n = 118) vs III-IV (n = 82), respectively. No statistically significant systematic bias was observed for the mean difference for the various comparisons in any of the four measuring sites (all $P > .131$) except for right toe pressures in overweight patients ($P = .042$). No significant differences were shown between the limits of agreement except for significantly higher variation in overweight vs nonoverweight patients for right toe pressures (−34.3-25.5 mm Hg vs −28.0-13.5 mm Hg) and right TBI (−0.28-0.21 vs −0.22-0.12).

A total of 10 ankle pressure measurements were classified as incompressible vessels using the SGP method (ABI >1.40). Two of these were likewise categorized as incompressible vessels by LDF, four were categorized as compressible, and four were rejected by at least one observer based on inadequate signal quality.

Table II. Strain gauge plethysmography (*SGP*) vs laser Doppler flowmetry (*LDF*)

	No.	*Mean ± SD*	*Limits of agreement*	*Mean differences ± SD_{diff}*	P[a]	*CV, %*	*ICC*	*95% CI*
SGP − LDF, mm Hg								
Right toe pressures	193	70.7 ± 31.1	−31.7 to 20.2	−5.8 ± 13.0	.001	10.1	0.902[b]	0.835-0.938
Left toe pressures	189	68.1 ± 30.6	−28.0 to 14.0	−7.0 ± 10.5	.001	11.6	0.919[b]	0.782-0.960
Right ankle pressures	181	110.8 ± 39.0	−25.5 to 22.8	−1.4 ± 12.1	.129	5.9	0.953[b]	0.937-0.965
Left ankle pressures	178	108.5 ± 41.0	−26.9 to 24.6	−1.2 ± 12.9	.225	6.9	0.952[b]	0.936-0.964
SGP − LDF, indices								
Right TBI	193	0.51 ± 0.22	−0.25 to 0.16	−0.04 ± 0.10	.001	12.0	0.869[b]	0.794-0.913
Left TBI	189	0.50 ± 0.22	−0.21 to 0.11	−0.05 ± 0.08	.001	12.2	0.904[b]	0.742-0.953
Right ABI	181	0.80 ± 0.27	−0.22 to 0.16	−0.03 ± 0.10	.001	6.1	0.935[b]	0.906-0.953
Left ABI	178	0.78 ± 0.28	−0.23 to 0.18	−0.02 ± 0.10	.002	7.7	0.933[b]	0.908-0.950

ABI, Ankle-brachial index; *CI,* confidence interval; *CV,* coefficienct of variance; *ICC,* intraclass correlation coefficienct; *SD*, standard deviation; SD_{diff}, standard deviation of mean differences; *TBI,* toe-brachial index.
Limits of agreement are defined as mean difference ± two standard deviations.
Incompressible vessels not included (n = 6).
[a]Paired *t*-test for mean differences.
[b]*P* value < .001 for the ICC.

Agreement in diagnostic classification. The two methods agreed in the diagnostic classification of PAD in 191 of 200 patients, as displayed in Table III. The Cohen Kappa showed an agreement of $\kappa = 0.775$ (95% CI, 0.631-0.919).

A total of 82 patients had Fontaine III or IV. Agreement in CLI diagnosis in terms of ankle pressures <50 mm Hg and/or toe pressures <30 mm Hg was found in 75 patients, as shown in Table IV. The agreement according to the Cohen Kappa was $\kappa = 0.780$ (95% CI, 0.624-0.936).

Reproducibility. For the LDF method, the number of measurements required to generate a dataset according to our reproducibility criterion was 2.4 ± 0.7 for toe pressures and 2.4 ± 0.6 for ankle pressure measurements. The required measurements for SGP were 2.4 ± 0.7 for toe pressures and 2.4 ± 0.7 for the SGP ankle pressures. Analysis of repeated measurements showed a mean coefficient of variance for the LDF method of 6.5% for the right toe, 7.2% for left toe pressures, 4.6% for right ankle pressures, and 4.0% for left ankle pressures. The corresponding numbers for SGP were 6.1% for right toe pressures, 7.1% for left toe pressures, 4.5% for right ankle pressures, and 4.0% for left ankle pressure measurements.

Noneligible patients. Noneligible patients (n = 23) did not show any statistically significant differences in the toe, ankle, or brachial pressures compared with eligible patients (data not shown).

DISCUSSION

In this paper, a diagnostic accuracy study in accordance with STARD and Cochrane DTA recommendations in a large cohort of patients with a broad disease spectrum was conducted. The LDF showed good correlation for toe and ankle pressure measurements with the well-validated SGP method over a wide range of pressures. The two methods showed substantial agreement in disease classification with respect to the diagnosis of PAD and CLI. Generally, the agreement between the methods was excellent, including subgroup analysis of diabetes, body mass index, or Fontaine classification.

Although the LDF method is increasingly used as a reference standard in vascular laboratories, few studies have been conducted to study the interchangeability with other methods on a large scale.[11-13,19,20] Previously, a small study pioneering the use of LDF in segmental pressure measurements by Andersson et al in 1986 compared the method with SGP.[13] The study included a small number of highly selected patients. The authors showed an excellent correlation between the two methods for both ankle and toe pressures when the methods were used simultaneously. However, the agreement was markedly reduced when the comparison was performed using successive measurements. The authors suggested that the variation in the comparison was caused by variation in the lower limb blood pressure. This finding is in agreement with the known test-retest variation, as shown in prior studies using SGP or LDF measurements.[12,21] Our setup did not allow for simultaneous measurements because of the incompatibility between the systems. For this reason, we did not expect perfect agreement between the methods. In our study, the LDF method systematically yielded results that were 5 to 7 mm Hg lower than the SGP method at the toe level but were only 1 to 2 mm Hg lower than SGP at the ankle level. However, the mean brachial pressures were 3 mm Hg higher during ankle pressure measurements made by SGP compared with LDF. The instantaneous inflation of the occlusion cuff used by the SGP method may induce discomfort, particularly in patients with leg ulcers. This discomfort may have induced elevated systemic arterial pressure and potentially masked a greater true difference between the methods.[22] In agreement with this finding, both the TBI and ABI values were significantly lower for SGP than for LDF. It could be hypothesized that the flow changes (LDF) after deflation can be detected prior to the detection of volume changes (SGP). The cost of the equipment varies depending on manufacturer and model.

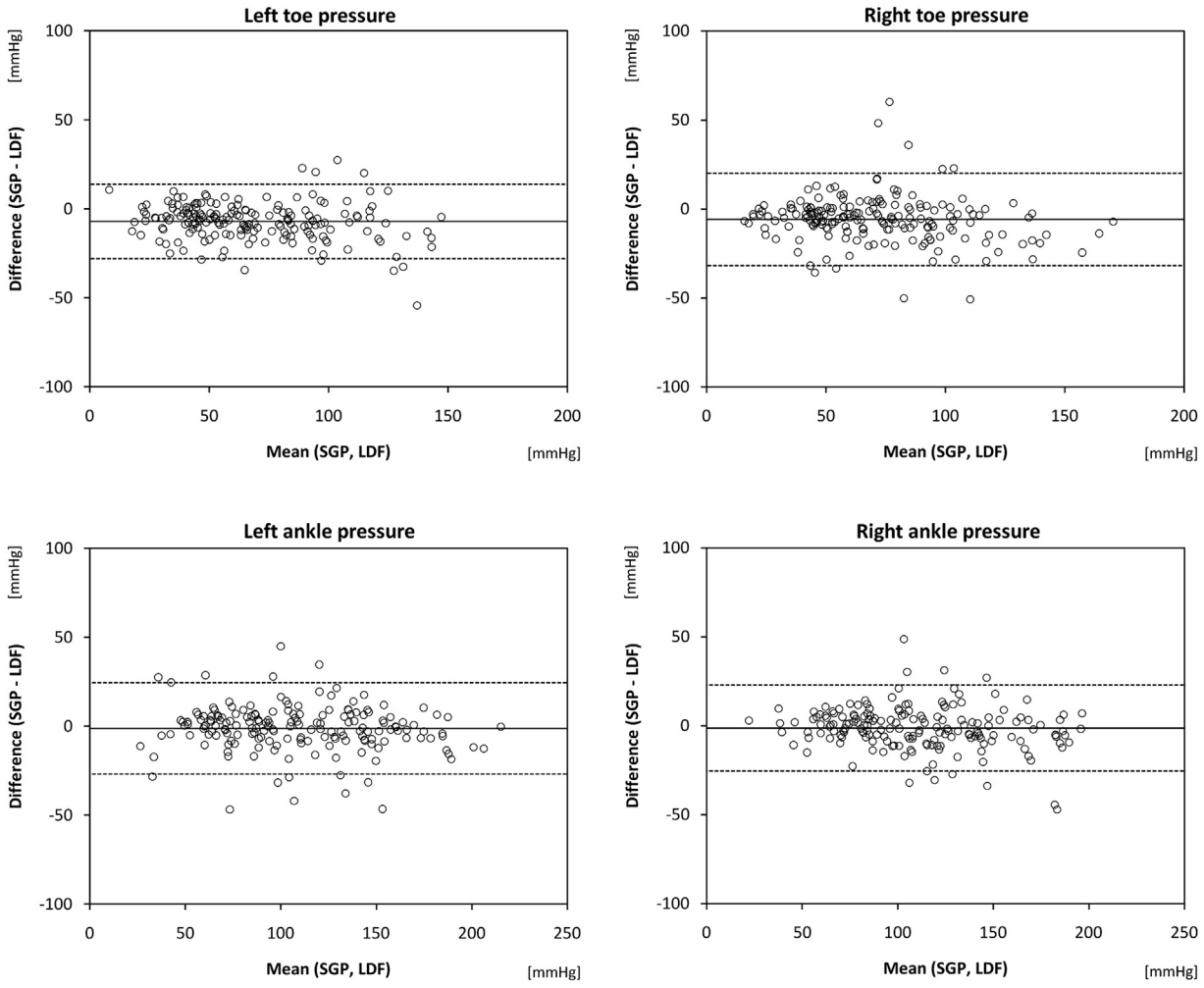

Fig 2. Bland-Altman plots showing the difference in toe pressures (*top row*) and ankle pressures (*bottom row*) obtained by strain gauge plethysmography (*SGP*) vs laser Doppler flowmetry (*LDF*) for left limbs (*left side*) and right limbs (*right side*), respectively. The lines show the mean (*full line*) ± two standard deviations (*dotted line*).

Table III. Agreement in diagnostic classification of peripheral arterial disease (*PAD*)

	LDF		
SGP	*PAD*	*Not PAD*	*Total*
PAD	173	6	179
Not PAD	3	18	21
Total	176	24	200

LDF, Laser Doppler flowmetry; *SGP*, strain gauge plethysmography.

Table IV. Agreement in diagnostic classification of critical limb ischemia (*CLI*) for patients with Fontaine III-IV

	LDF		
SGP	*CLI*	*Not CLI*	*Total*
CLI	18	5	23
Not CLI	2	57	59
Total	20	62	82

LDF, Laser Doppler flowmetry; *SGP*, strain gauge plethysmography.

Cost of common LDF equipment ranges from $20,000 to $50,000 USD. In comparison, the cost of various models for SGP measurements is approximately $35,000 to $70,000 USD. The time to completion of a measurement was not recorded in this study. The time to obtain one measurement was very similar for LDF and SGP, the latter recently being reported.[22]

Previous studies on LDF toe pressure measurements have shown good correlation with other methods, such as photo-plethysmography.[11,12,23,24] In most of these studies, LDF was shown to produce slightly higher pressure readings than photo-plethysmography. In general, the studies showed a more pronounced variation between the methods than we encountered in our study. The approach to limb heating

prior to the tests in the mentioned studies is markedly different. Measurements of toe pressures have been shown to be highly susceptible to distal temperature changes, and it has been argued that insufficient heating can lead to disease misclassification.[25] Thus, lower limb heating has been recommended to improve standardization.[25,26] The LDF signal can also be optimized by local heating in the vicinity of the probe, as shown by Ubbink et al in 2004.[11] However, the sole use of local heating would likely challenge the test-retest reproducibility due to the effects on limb temperature by hyperemia induced by inflammation, recent surgery, or seasonal temperature changes, as the measured toe pressures correspond to the limb temperature.[26] The impact of these laboratory and clinical conditions on disease classification (PAD/not PAD) remains largely unknown.

Although the mechanism behind the various blood flow detection systems differs, they share a signal curve that reflects changes in absolute blood flow/volume increment and return of pulsation.[10] It is likely that weak AC signals are better detected in some techniques than in others. In agreement with this, LDF has been shown to be a more sensitive detection method for low pressures (reduced signal) compared with photoplethysmography.[11,12] Accuracy in low pressures is vital because diagnosing CLI entails measuring toe pressures below 30 mm Hg.[3] In our study, which included a large proportion of patients with recent surgery and distal wounds, the completion rate for the LDF was comparable to that of SGP.

In guideline recommendations, the methods used for toe or ankle pressure measurements are generally considered fully interchangeable.[3,27] However, it is evident that a high level of variation is present among the different techniques. It remains undetermined whether that variation is due to biological blood pressure variation, experimental test conditions, or technical variation in the different detection systems. These features complicate the identification of an optimal laboratory reference standard for the measurement of segmental blood pressure. Additionally, in order to correctly interpret the readings from the various methods on patient management, future studies should include clinical outcome such as wound healing. SGP is the only method that has been subjected to comparison to the true reference standard, which is intra-arterial pressure measurement.[9,28] However, the findings of our study indicate a high degree of interchangeability between LDF and SGP for such measurements.

CONCLUSIONS

LDF showed good correlation with SGP over a wide range of toe and ankle pressures as well as substantial agreement in the diagnostic classification for PAD including CLI. The LDF method yielded systematically higher TBI and ABI, as well as higher toe pressure readings than SGP; however, no significant difference was found in absolute ankle pressure measurements.

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AUTHOR CONTRIBUTIONS

Conception and design: CH, JS, LP
Analysis and interpretation: CH, JS, JP, SP, LP
Data collection: CH, JP, SP
Writing the article: CH, JS, LP
Critical revision of the article: CH, JS, JP, SP, LP
Final approval of the article: CH, JS, JP, SP, LP
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REFERENCES

1. Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA 2008;300:197-208.
2. Aboyans V, McClelland RL, Allison MA, McDermott MM, Blumenthal RS, Macura K, et al. Lower extremity peripheral artery disease in the absence of traditional risk factors. The Multi-Ethnic Study of Atherosclerosis. Atherosclerosis 2011;214:169-73.
3. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg 2007;33(Suppl 1):S1-75.
4. Høyer C, Sandermann J, Petersen LJ. The toe-brachial index in the diagnosis of peripheral arterial disease. J Vasc Surg 2013;58:231-8.
5. Becker F, Robert-Ebadi H, Ricco JB, Setacci C, Cao P, de DG, et al. Chapter I: Definitions, epidemiology, clinical presentation and prognosis. Eur J Vasc Endovasc Surg 2011;42(Suppl 2):S4-12.
6. Alnaeb ME, Alobaid N, Seifalian AM, Mikhailidis DP, Hamilton G. Optical techniques in the assessment of peripheral arterial disease. Curr Vasc Pharmacol 2007;5:53-9.
7. Wahlberg E, Olofsson P, Swedenborg J, Fagrell B. Effects of local hyperemia and edema on the biological zero in laser Doppler fluxmetry (LD). Int J Microcirc Clin Exp 1992;11:157-65.
8. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529-36.
9. Carter SA, Lezack JD. Digital systolic pressures in the lower limb in arterial disease. Circulation 1971;43:905-14.
10. Wright CI, Kroner CI, Draijer R. Non-invasive methods and stimuli for evaluating the skin's microcirculation. J Pharmacol Toxicol Methods 2006;54:1-25.
11. Ubbink DT. Toe blood pressure measurements in patients suspected of leg ischaemia: a new laser Doppler device compared with photoplethysmography. Eur J Vasc Endovasc Surg 2004;27:629-34.
12. de Graaff JC, Ubbink DT, Legemate DA, de Haan RJ, Jacobs MJ. The usefulness of a laser Doppler in the measurement of toe blood pressures. J Vasc Surg 2000;32:1172-9.
13. Andersson S, Linderholm H, Rinnstrom O, Burlin L. A laser Doppler technique for measuring distal blood-pressure: a comparison with conventional strain-gauge technique. Clin Physiol 1986;6:329-35.
14. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Standards for Reporting of Diagnostic Accuracy. Clin Chem 2003;49:1-6.
15. Reitsma JB, Rutjes AWS, Whiting P, Vlassov VV, Leeflang MMG, Deeks JJ. Assessing methodological quality. In: Deeks JJ, Bossuyt PM, Gatsonis C, editors. Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. 1.0 edition. Oxford, UK: The Cochrane Collaboration; 2009.
16. Høyer C, Pavar S, Pedersen BH, Manresa JA, Petersen LJ. Reliability of mercury-in-silastic strain gauge plethysmography curve reading: influence of clinical clues and observer variation. Scand J Clin Lab Invest 2013;73:380-6.
17. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med 2005;37:360-3.

18. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999;8:135-60.
19. Beinder E, Hoffmann U, Franzeck UK, Huch A, Huch R, Bollinger A. Laser Doppler technique for the measurement of digital and segmental systolic blood pressure. Vasa 1992;21:15-21.
20. Perez-Martin A, Meyer G, Demattei C, Boge G, Laroche JP, Quere I, et al. Validation of a fully automatic photoplethysmographic device for toe blood pressure measurement. Eur J Vasc Endovasc Surg 2010;40: 515-20.
21. Arveschoug AK, Revsbech P, Brochner-Mortensen J. Sources of variation in the determination of distal blood pressure measured using the strain gauge technique. Clin Physiol 1998;18:361-8.
22. Høyer C, Sandermann J, Petersen LJ. Randomised diagnostic accuracy study of a fully automated portable device for diagnosing peripheral arterial disease by measuring the toe-brachial index. Eur J Vasc Endovasc Surg 2013;45:57-64.
23. Wahlberg E, Gush R. A new automated toe blood pressure monitor for assessment of limb ischemia. Eur J Vasc Endovasc Surg 2002;24: 304-8.
24. Widmer LW, Vikatmaa P, Aho P, Lepantalo M, Venermo M. Reliability and repeatability of toe pressures measured with laser Doppler and portable and stationary photoplethysmography devices. Ann Vasc Surg 2012;26:404-10.
25. McCollum PT, Stanley ST, Kent P, Grouden MC, Moore DJ, Shanik GD. Assessment of arterial disease using digital systolic pressure measurement. Ann Vasc Surg 1988;2:349-51.
26. Sawka AM, Carter SA. Effect of temperature on digital systolic pressures in lower limb in arterial disease. Circulation 1992;85: 1097-101.
27. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al; Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society for Vascular Medicine, Society for Vascular Surgery. 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients with Peripheral Artery Disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;58:2020-45.
28. Lezack JD, Carter SA. The relationship of distal systolic pressures to the clinical and angiographic findings in limbs with arterial occlusive disease. Scand J Clin Lab Invest Suppl 1973;128:97-101.

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