Hypertension

ORIGINAL ARTICLE

Clinical Validation of Carotid-Femoral Pulse Wave Velocity Measurement Using a Multi-Beam Laser Vibrometer: The CARDIS Study

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BACKGROUND: Carotid-femoral pulse wave velocity (cfPWV) is the gold standard for noninvasive arterial stiffness assessment, an independent predictor of cardiovascular disease, and a potential parameter to guide therapy. However, cfPWV is not routinely measured in clinical practice due to the unavailability of a low-cost, operator-friendly, and independent device. The current study validated a novel laser Doppler vibrometry (LDV)-based measurement of cfPWV against the reference technique.

METHODS: In 100 (50 men) hypertensive patients, cfPWV was measured using applanation tonometry (Sphygmocor) and the novel LDV device. This device has 2 handpieces with 6 laser beams each that simultaneously measure vibrations from the skin surface at carotid and femoral sites. Pulse wave velocity is calculated using ECG for the identification of cardiac cycles. An ECG-independent method was also devised. Cardiovascular risk score was calculated for patients between 40 and 75 years old using the WHO risk scoring chart.

RESULTS: LDV-based cfPWV correlated significantly with tonometry (r=0.86, $P<0.0001$ ECG-dependent [$cfPWV_{LDV\_ECG}$] and r=0.80, $P<0.001$ ECG-independent [$cfPWV_{LDV\_w/oECG}$] methods). Bland-Altman analysis showed nonsignificant bias (0.65 m/s) and acceptable SD (1.27 m/s) between methods. Intraobserver coefficient of variance for LDV was 4.7% (95% CI, 3.0%–5.5%), and interobserver coefficient of variance was 5.87%. CfPWV correlated significantly with CVD risk (r=0.64, $P<0.001$; r=0.41, $P=0.003$; and r=0.37, $P=0.006$ for tonometry, LDV-with, and LDV-without ECG, respectively).

CONCLUSIONS: The study demonstrates clinical validity of the LDV device. The LDV provides a simple, noninvasive, operator-independent method to measure cfPWV for assessing arterial stiffness, comparable to the standard existing techniques.

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Key Words: cardiovascular diseases ■ carotid-femoral pulse wave velocity ■ optics and photonics ■ risk factors ■ vascular stiffness

The distensibility of the aorta allows it to decrease the load on the left heart and increase coronary perfusion by reducing pressure and flow during systole and increasing it during diastole. This distensibility reduces with age and in the presence of cardiovascular risk factors such as hypertension and diabetes.[1,2] An increase in aortic stiffness is associated with the development of cardiovascular disease and the risk of cardiovascular death, myocardial infarction, and stroke.[3,4]

Pulse wave velocity (PWV) is an indicator of arterial stiffness, and its relationship to the elasticity of the arteries is quantified by the Moens-Korteweg equation.[5]

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NOVELTY AND RELEVANCE

What Is New?

Novel laser Doppler vibrometer-based device provides valid measurement of carotid-femoral pulse wave velocity.

What Is Relevant?

Use of carotid-femoral pulse wave velocity is recommended by the European Society of Hypertension guidelines for the assessment of hypertension-mediated organ damage. However, it is not extensively used because of the lack of user-friendly devices.

Clinical/Pathophysiological Implications?

Laser Doppler vibrometer-based devices measuring carotid-femoral pulse wave velocity have the potential to be developed for use in primary health care settings for early diagnosis and prevention of cardiovascular disease.

Nonstandard Abbreviations and Acronyms

cfPWV	carotid-femoral pulse wave velocity
$cfPWV_{LDV\_ECG}$	carotid-femoral pulse wave velocity using LDV-ECG dependent method
$cfPWV_{LDV\_w/oECG}$	carotid-femoral pulse wave velocity using LDV-ECG independent method
$cfPWV_{tono}$	carotid-femoral pulse wave velocity using tonometry
CV	coefficient of variation
InSiDe	Integrated Silicon photonics for Cardiovascular Disease monitoring
LDV	laser Doppler vibrometry
PWV	pulse wave velocity

Measurement of PWV of the carotid-femoral arterial segment (cfPWV) is the current gold standard for assessing central/aortic arterial stiffness.[6] The clinical value of cfPWV has been recognized by the European Society of Hypertension and the European Society of Cardiology, which recommend its use in guidelines for hypertensive organ damage assessment.[7,8]

Despite its relevance in risk screening, cfPWV is not commonly used as a routine measurement in primary care settings. The current reference method for noninvasive measurement of cfPWV is applanation tonometry,[9] which requires partial flattening of the arterial wall against the tip of the probe to eliminate tangential forces for accurate measurement of pressure waveforms. The available devices for measuring cfPWV use pressure sensors, requiring attachments around the neck to hold the probe in place and palpation of the arteries in the neck and groin, which may cause discomfort to the patient. Furthermore, the morphology of the pressure waveform and the estimated PWV are extremely sensitive to the positioning of the probe and therefore require experienced operators. Finally, these devices are expensive and designed for clinical research use rather than clinical practice. Therefore, to use arterial stiffness as a screening tool in primary care, there is a need to develop a low-cost, reliable, operator-independent, and noninvasive device.

Palpation of vibrations from the skin surface induced by arterial (eg, peripheral pulse) and cardiac (eg, apex beat) motion has been used for millennia during clinical examinations and provides crucial information about cardiovascular health. A laser Doppler vibrometer (LDV) is a device that detects displacement/vibrations from a moving target surface by measuring the shift in frequency or phase between the transmitted and reflected laser beam.[10,11] In a study performed on a sample of 14 healthy subjects, pulse transit time from the carotid to femoral sites was found to be comparable between a noncontact optical laser-based vibrocardiograph and applanation tonometry.[12] Based on this proof of principle, we have developed a working prototype of an LDV device that allows measurement of cfPWV by simultaneously measuring the skin vibrations from the carotid and femoral arterial sites with 6 laser beams in each of 2 handpieces[13] during the EU H2020-funded CARDIS (Cardio Vascular Disease Detection with Integrated Silicon Photonics) project.[14] The device is developed on a silicon-based photonic integrated circuit platform, a technology that has the potential to be low-cost in scale production. Additionally, we hypothesized that the multibeam system can simplify the measurement of PWV by increasing the sites from which the signal is captured for each artery and reducing operator dependence.

The objective of the current study was to evaluate the clinical validity of using LDV-based measurements of cfPWV. The LDV measurements were compared with the current gold standard reference methods using applanation tonometry. Additionally, an exploratory analysis was performed to evaluate the association between cfPWV and the 10-year cardiovascular disease risk.

METHODS

Data Availability

The data that support the findings of the study are available from the corresponding author upon reasonable request. A total of 100 patients of both sexes, aged between 18 and 85 years and diagnosed with mild to moderate essential hypertension (systolic blood pressure [BP] 140–179 mm Hg and diastolic BP 90–109 mm Hg),[7] were recruited among the patients referred by the Hypertension and Pharmacology units of the Georges Pompidou European Hospital to the vascular laboratory for the assessment of cfPWV by applanation tonometry as part of routine clinical care (Figure 1). Patients were divided into 3 groups according to age (≤30 years, >30 to <60 years, and ≥60 years) following the 2010 International Guidelines for PWV Device Validation.[15] Patients with secondary hypertension, established cardiovascular disease such as a history of acute heart failure, unstable coronary heart disease, peripheral arterial disease, stroke or arrhythmias, and chronic inflammatory or chronic infectious diseases were excluded from the study.

This study was approved by the National Ethics Committee (Comité de Protection des Personnes; ClinicalTrials.gov ID NCT03446430). Written informed consent was obtained from all the participants before the start of the study. LDV and applanation tonometry measurements were performed sequentially in a random order by a single trained investigator (H.K.) on the same day in a dedicated room in the pharmacology unit.

All measurements were taken with the subjects in a supine position after a 10-minute rest period. Three consecutive measurements of BP and heart rate were performed using a validated brachial cuff oscillometric device (Colin press mate BP monitor) according to the European Society of Hypertension (ESH-ESC 2018 recommendations.[16] The average values were reported.

The measurements for the test and reference methods were made over the same path (carotid and femoral sites). Three measurements of cfPWV were made with the reference method (tonometry), and 4 measurements were made with the test method (LDV).

Arterial Stiffness Measurements

Reference Method: Applanation Tonometry

A Sphygmocor system (Atcor Medical, Australia) device was used to measure cfPWV using tonometry ($cfPWV_{tono}$). The tonometer probe was sequentially placed at the site where the right carotid and femoral arteries were best palpable. Lead-II ECG was simultaneously acquired to time the pressure pulses using R-wave gating. The foot-to-foot pulse transit time was calculated using the intersecting tangent algorithm built within the Sphygmocor system. The direct distance between the carotid and femoral sites was determined using a tape measure and corrected by a factor of 0.8 as recommended by the expert consensus document on the measurement of aortic stiffness.[17] The PWV was calculated as the distance/pulse transit time.

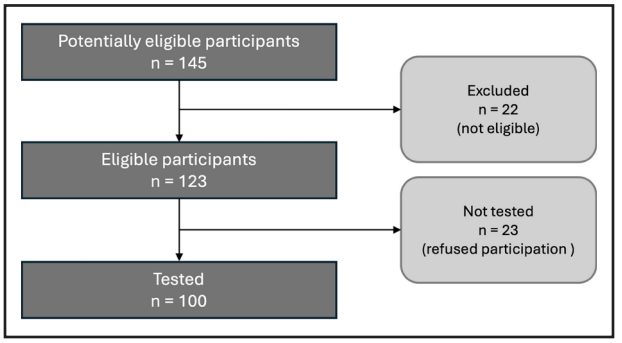

Figure 1. Flow chart showing the patient recruitment and exclusions.

Test Method: LDV

Signal Acquisition

To perform the LDV measurement, a retroreflective patch (3M Scotchlite High Gain Reflective Sheeting 7610) was first attached to a Tegaderm 3M film and carefully applied to the right side of the neck in the region of the common carotid artery and slightly below the inguinal hollow in the region of the femoral artery, where the pulses were felt the strongest. The LDV device comprises 2 handpieces (main and secondary sensors), each with 6 laser beams in a straight line, spaced 5 mm apart. They are connected to a data acquisition rack and a computer. Each of the sensors generates and receives the optical beams and converts the optical beams into electric signals. A detailed description of the device has been published previously.[13] One of the handpieces is directed toward the carotid artery, while the other is at the femoral artery for 20 seconds to simultaneously acquire the displacement signals from the skin from the carotid and femoral sites (Figure 2). Four 20-second recordings (3 during normal breathing and 1 during breath holding) were acquired. For optimal recording of the skin displacement, the probe is positioned at the focal distance from the skin surface, using a spacer; great care was taken not to press the skin with the spacer. Lead-II ECG was simultaneously acquired for the ECG-based estimation of cfPWV. Details of data processing and PWV estimation from the LDV signals are described in the Supplemental Material.

Agreement Between Reference and Test Device

In accordance with international recommendations,[17] for applanation tonometry, 3 PWV measurements were taken, and the average of the 3 was used if the difference was <0.5 m/s. Otherwise, the median of the measurements was considered the PWV of that individual. For the LDV, a total of 3+1 measurements were taken, the first 3 with normal breathing and an additional 1 during which the patients were asked to hold their breath for the recording period (20 seconds) to minimize movement artifacts. The median of the measurements was used as the PWV for that patient. Finally, the PWV obtained from applanation tonometry was compared with ECG-dependent and ECG-independent PWV calculations using the LDV.

Repeatability and Reproducibility of the Test Measurement

The repeatability of the LDV measurements was calculated from the coefficient of variation (CV) between the first 3

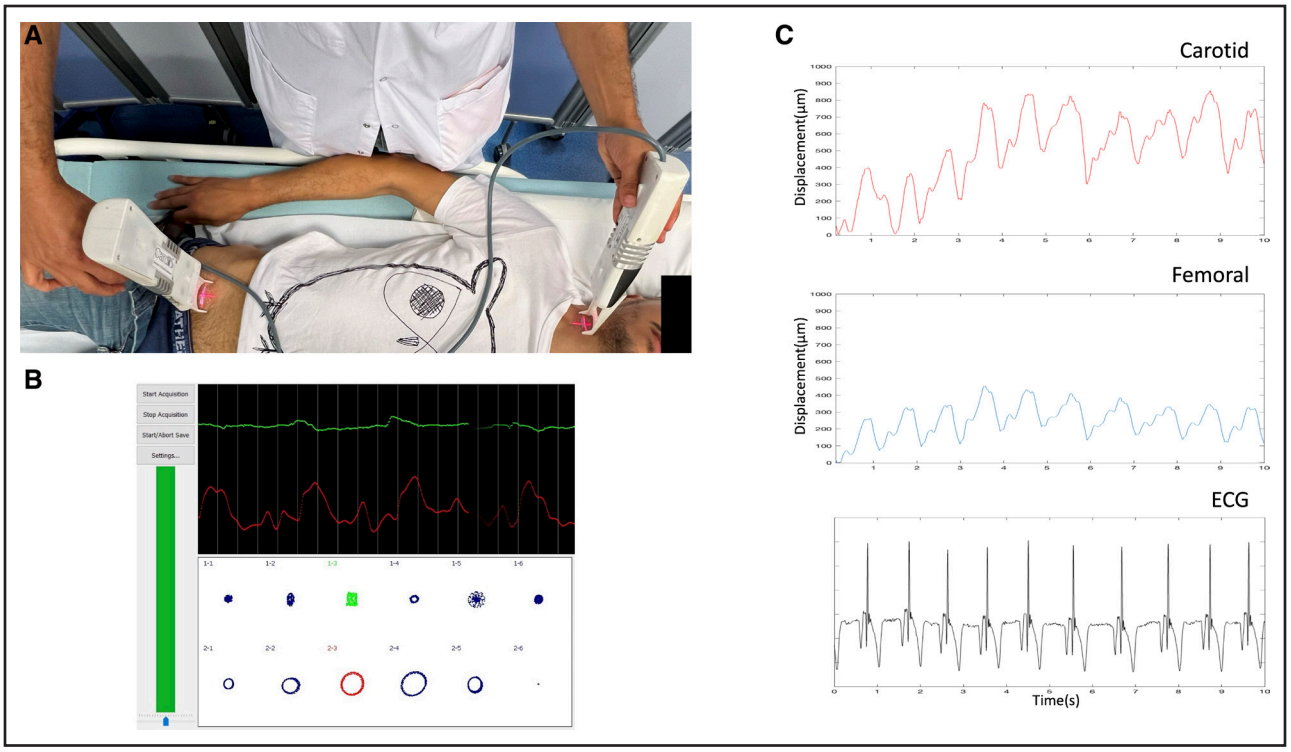

Figure 2. The acquisition and pattern of signals obtained using the laser Doppler vibrometry device.
A, Simultaneous acquisition of vibrations from the skin surface from the carotid and femoral arteries using the 2 handpieces of the laser Doppler vibrometry device. The operator presses a trigger on the main handpiece (at the femoral site) to start the acquisition. **B**, Custom made graphical user interface showing the displacement signal from the carotid (green) and femoral (red) sites. The lower panels provide feedback from each of the 6 beams in the 2 handpieces (beams 1–1 to 1–6 are from the Carotid site, and beams 2–1 to 2–6 are from Femoral). The signal quality from the respective beam is better when the signals are more circular and larger in diameter. **C**, Example of the displacement signals obtained for a carotid-femoral measurement by the laser Doppler vibrometry device (1 beam per location channel 13 [Carotid] and channel 24 [Femoral]).

measurements performed during normal breathing for each participant. To evaluate the potential effect of movement artifacts during breathing, the CV for each participant between normal breathing (median of the 3 measurements) and breath-hold measurement was calculated. Finally, the median CV and 95% CI of the population were calculated. A CV <10% is generally considered very good, >10% to <20% good, >20% to <30% acceptable, and >30% nonacceptable.

Interobserver reproducibility of the LDV measurements was evaluated in 10 subjects. Three measurements of cfPWV with the LDV, of 20 seconds each, were made by 2 independent observers (H.K. and S.B.) in random order. The median of the 3 measurements was used as the final cfPWV for that subject for each observer, and the CV between the 2 observers was calculated.

Association With Cardiovascular Risk

The cardiovascular risk score was calculated using WHO non-laboratory-based Western Europe charts for participants aged 40 to 75 years based on age, sex, systolic BP, body mass index, and smoking history.[18]

Statistical Methods

Data were analyzed using NCSS 11.0.13 software. Gaussian data were expressed as mean with SD and data with skewed distribution as median with interquartile range. As the distributions were not Gaussian, differences between the age groups were assessed using the Kruskal-Wallis test for comparison of a continuous dependent variable by a categorical independent variable, with Dunn's post hoc correction for multiple comparisons. Correlations were assessed using the Spearman test. Bland-Altman analysis was used to compare the LDV-based calculations of PWV with those of tonometry. The CV was calculated from the SD between measurements divided by the mean of the measurements and expressed as a percentage. The unpaired *t* test or Mann-Whitney *U* test (for non-Gaussian data) was used to compare the pulse wave velocities in patients with a high (≥10) versus those with a low (<10) cardiovascular disease risk score.

RESULTS

A total of 100 patients (50 males and 50 females) were recruited. Their median (IQR) age was 42 (28–65) years. The median duration of hypertension in the study population was 3 (1–9) years. Of all participants, 45% were on calcium channel blockers, 36% on angiotensin receptor blockers, 10% on angiotensin-converting enzyme inhibitors, 10% on beta-blockers, 24% on diuretics, 15% on statins, 11% on antiplatelet drugs, and 4% were not receiving any drug therapy for hypertension. Of the total, 16 patients had diabetes and 36 had dyslipidemia. The demographic and hemodynamic parameters of the study population are presented in the Table.

Table. Demographic and Hemodynamic Parameters in the Study Population

Parameters	All, n=100	≤30 y, n=29	>30 to <60 y, n=37	≥60 y, n=34	*P* value
Age, y	42 (28–65)	26 (23–28)	41(35–52)*	68 (65–73)*†	<0.001
Sex, m/f	50/50	16/13	17/20	17/17	0.758
BMI, kg/m^2	23.1 (20.6–26.0)	19.8 (21.2–23.7)	21.2 (23.6–25.9)	25.5 (22.3–28.0)*	0.002
Heart rate, beats/min	63 (59–67)	63 (59–67)	64 (59–67)	63 (60–71)	0.555
SBP, mm Hg	108.0 (114.5–129.3)	108.0 (105.3–113.5)	109.0 (114.5–130.3)*	121.5 (114.8–132.3)*	<0.001
MBP, mm Hg	81.5 (75.0–90.5)	75.0 (73.2–78.7)	83.5 (75.7–91.2)*	88.0 (78.0–93.2)*	<0.001
DBP, mm Hg	65.0 (58.0–72.0)	58.5 (56.2–64.0)	66.5 (59.7–73.2)*	68.0 (60.7–75.2)*	<0.001
$cfPWV_{tono}$, m/s	7.12(6.10–8.86)	6.00 (5.32–6.50)	6.92(6.34–7.84)	9.42 (8.32–10.0)*†	<0.001
$cfPWV_{LDV\_ECG}$, m/s	6.63 (5.80–7.96)	5.63 (5.09–6.16)	6.58 (5.81–7.23)	8.03 (7.44–9.12)*†	<0.001
$cfPWV_{LDV\_w/oECG}$, m/s	6.49 (5.78–7.70)	5.66 (5.03–6.22)	6.48 (5.75–7.13)	8.23 (7.00–9.08)*†	<0.001

Data are expressed as median (Interquartile range). BMI indicates body mass index; $cfPWV_{tono}$, carotid-femoral pulse wave velocity using tonometry; $cfPWV_{LDV\_ECG}$, carotid-femoral pulse wave velocity using LDV-ECG dependent method; $cfPWV_{LDV\_w/oECG}$, carotid-femoral pulse wave velocity using LDV-ECG independent method; DBP, diastolic blood pressure; LDV, laser Doppler vibrometry; MBP, mean blood pressure; and SBP, systolic blood pressure.

*Significant difference with age group ≤30 years.

†Significant difference with age group >30 to <60 years.

Of the participants, ECG during LDV could not be obtained in 5 because of technical failure, whereas it was possible to analyze the LDV signals in all patients. Therefore, $cfPWV_{LDV\_ECG}$ is described for 95 participants, and $cfPWV_{LDV\_w/oECG}$ is described for 100 participants.

CfPWV was significantly higher in the older age groups when measured with both tonometry and LDV. Furthermore, the PWV estimated using the ECG-dependent and ECG-independent methods was comparable (Figure 3; Table). A significant association was seen between PWV with age and brachial mean BP ($cfPWV_{tono}$ [r=0.84 and 0.64; *P*<0.001, respectively], $cfPWV_{LDV\_ECG}$ [r=0.79 and 0.61; *P*<0.001, respectively], and $cfPWV_{LDV\_w/oECG}$ [r=0.74 and 0.55; *P*<0.001, respectively]).

Comparison Between Reference and Test Device

PWV calculated by the algorithms using ECG ($cfPWV_{LDV\_ECG}$) and without ECG ($cfPWV_{LDV\_w/oECG}$) using the test LDV device showed a significant association with cfPWV measured by the reference method (r=0.86 and 0.80, respectively; *P*<0.001 for both; Figure 4A and 4B). The corresponding Bland-Altman plots are shown in

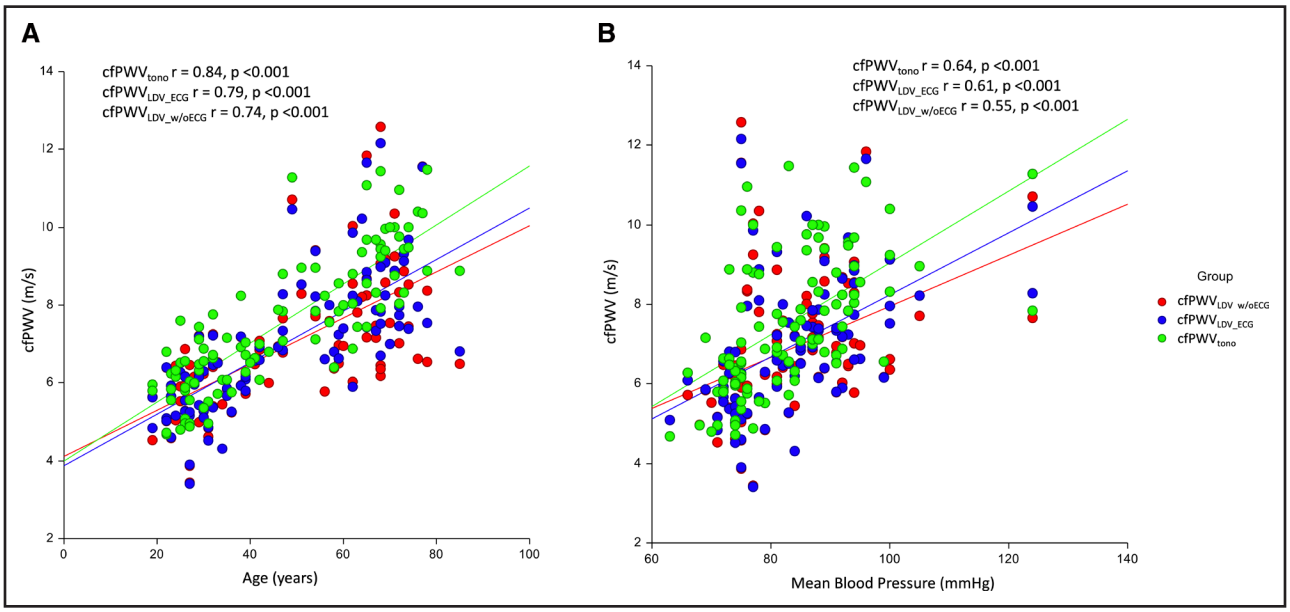

Figure 3. Correlation (Spearman) analysis between carotid-femoral pulse wave velocity (cfPWV) measured by applanation tonometry (green) and laser Doppler vibrometry device (red and blue).

A, Age (r=0.84, 0.79, and 0.74; *P*<0.001 for cfPWVtono, cfPWVLDV_withECG, and cfPWVLDV_w/oECG, respectively) and (**B**) mean blood pressure (r=0.64, 0.61, and 0.55; *P*<0.001 for cfPWVtono, cfPWVLDV_withECG, and cfPWVLDV_w/oECG, respectively). $cfPWV_{tono}$ indicates carotid-femoral pulse wave velocity using tonometry; $cfPWV_{LDV\_ECG}$, carotid-femoral pulse wave velocity using LDV-ECG dependent method; and $cfPWV_{LDV\_w/oECG}$, carotid-femoral pulse wave velocity using LDV-ECG independent method.

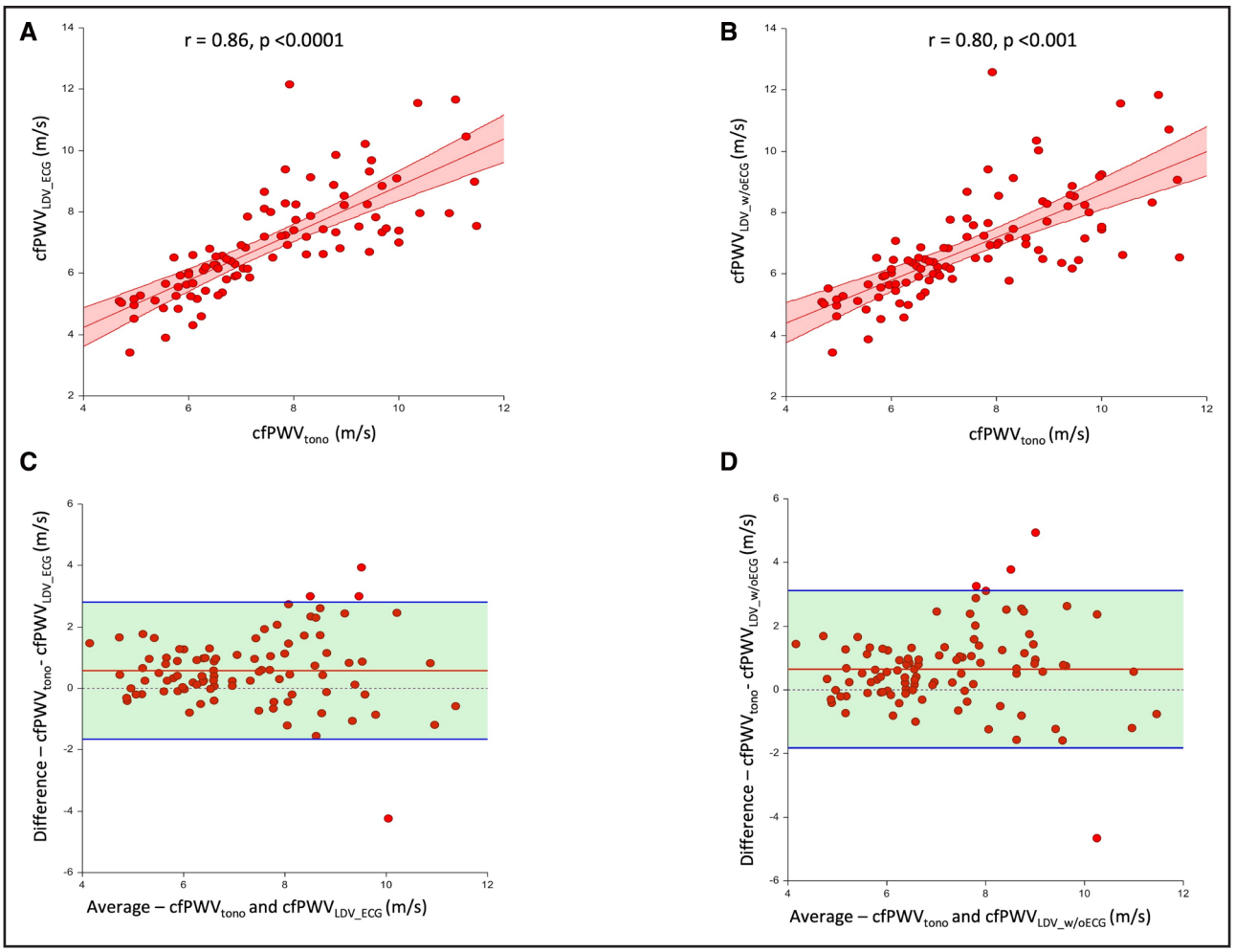

Figure 4. Results of correlation and Bland-Altman analysis between the reference and the test methods.
Calculation of carotid-femoral pulse wave velocity (PWV) using (**A**) laser Doppler vibrometry (LDV) with ECG (cfPWVLDV_withECG) correlates significantly (r =0.86, *P*<0.0001) and (**B**) LDV without ECG (cfPWV$_{LDV_w/oECG}$) correlates significantly (r =0.80, *P*<0.001) with tonometry (cfPWV$_{tono}$). (**C**) Shows a good agreement (bias 0.58±1.14m/s) between LDV with ECG (cfPWVLDV_withECG) and tonometry (cfPWV$_{tono}$) and (**D**) shows good agreement (bias 0.65±1.27m/s) between LDV without ECG (cfPWV$_{LDV_w/oECG}$) and tonometry. The red line in the Bland-Altman plots (**C** and **D**) represents the mean difference, and the blue lines indicate the 95% limits of agreement.

Figure 4C and 4D. For the LDV calculation using ECG (cfPWV$_{LDV_ECG}$), the bias against the reference method was 0.58±1.14 m/s, and the lower and upper 95% limits of agreement were −1.66 and 2.82 m/s, respectively. For the LDV calculation without ECG (cfPWV$_{LDV_w/oECG}$), the bias was 0.65±1.27 m/s, and the lower and upper 95% limits of agreement were −1.83 and 3.13 m/s, respectively.

Comparison between reference and test devices in different age groups are reported in the Supplemental Material (Table S2; Figure S3) and show no significant bias in any age category, though, as expected,[19,20] a higher dispersion is present in older individuals.

Repeatability and Reproducibility of the Test Device

The intraoperator CV between the three 20-second measurements during normal breathing was 4.2% for the ECG-based (cfPWV$_{LDV_ECG}$) calculation of PWV (95% CI, 2.6%–5.2%) and 4.7% (95% CI, 3.0%–5.5%) for the ECG-independent (cfPWV$_{LDV_w/oECG}$) calculation of PWV. The interoperator CV between measurements made by the 2 observers was 5.87%.

The CV between measurements made with normal breathing and breath holding was 4.9% (95% CI, 4.0%–6.0%) and 5.4% (95% CI, 3.9%–8.5%) for the ECG-dependent and the ECG-independent calculations, respectively. Additional comparison between normal breathing and breath-hold methods has been described in Supplemental Material (Figure S1 and S2; Table S1). A significant correlation was seen between the normal breathing and the breath-hold methods with a nonsignificant bias on Bland-Altman analysis.

Association With Cardiovascular Disease Risk Score

Of the total study population, 49 patients were within the 40- to 75-year age range. A significant correlation was

observed between PWV measured by all methods and the cardiovascular risk score (Figure 5).

DISCUSSION

This study evaluated the clinical validity of PWV measured using a novel technology based on LDV. The correlation test and the Bland-Altman analysis showed good agreement between the test and the reference methods. Both accuracy and precision were assessed and proved to correspond to the standards requested by international recommendations[9]; in particular, we demonstrated an acceptable agreement with the reference tonometric technique and a low intraoperator CV. The interoperator variability was similar to that reported for Sphygmocor.[21] The accuracy and precision were comparable for LDV measurements with and without ECG, indicating that the device has the potential to become fully contactless. Finally, an association with clinical variables such as age, BP, and 10-year CV risk has been demonstrated. These findings constitute a major advancement in the technical development of biomarkers for risk reclassification, making them possible for wider use in clinical practice.

Technical Advances and Validation

The device utilizes a novel approach based on silicon photonics to detect vibrations from the skin surface. The LDV device, a prototype developed in the CARDIS project, has many technical characteristics that constitute a major breakthrough compared with the currently available devices for arterial stiffness assessment. The 6 sensor beams are arranged in a line and oriented perpendicular to the long axis of the artery, thus ensuring that the vibrations from the artery are detected without the need to aim precisely over the vessel, in contrast to its mandatory requirement with tonometry. This multibeam system allows the LDV-based device to potentially simplify the acquisition of high-quality signals and reduce the dependence on operator skills.

Despite robust evidence indicating the utility of PWV in risk reclassification,[22,23] the complexity of the current devices to assess arterial stiffness, the skills required, and acceptability are major barriers to the wide implementation of arterial stiffness measurement in clinical practice. These barriers can be overcome by LDV technology. Furthermore, the low CV between normal breathing and breath-holding recordings shows that slow respiratory movements do not affect the measurement of PWV, making protocol acquisition simpler for the operator and patient. The CV of PWV measured by LDV is comparable to that of other tonometry-based PWV measurement methods.[24,25]

The current CARDIS prototype uses reflective stickers, which may restrain skin motion and must be put in contact with the patient's skin. However, an updated device currently being developed under European funding in the InSiDe (Integrated Silicon photonics for Cardiovascular Disease monitoring) project (grant number 871547) will measure signals directly from the bare skin surface.[26] The device incorporates additional features, such as being lightweight and wireless, with ameliorations aimed at improving user experience (both for patients and physicians). The objective of the InSiDe project is to lead the development of an LDV device to a stage that allows scaled industrial production.

Another major advantage of the LDV device is simultaneous signal acquisition from the carotid and femoral arteries. This can potentially reduce the time required for the measurement. Importantly, simultaneous

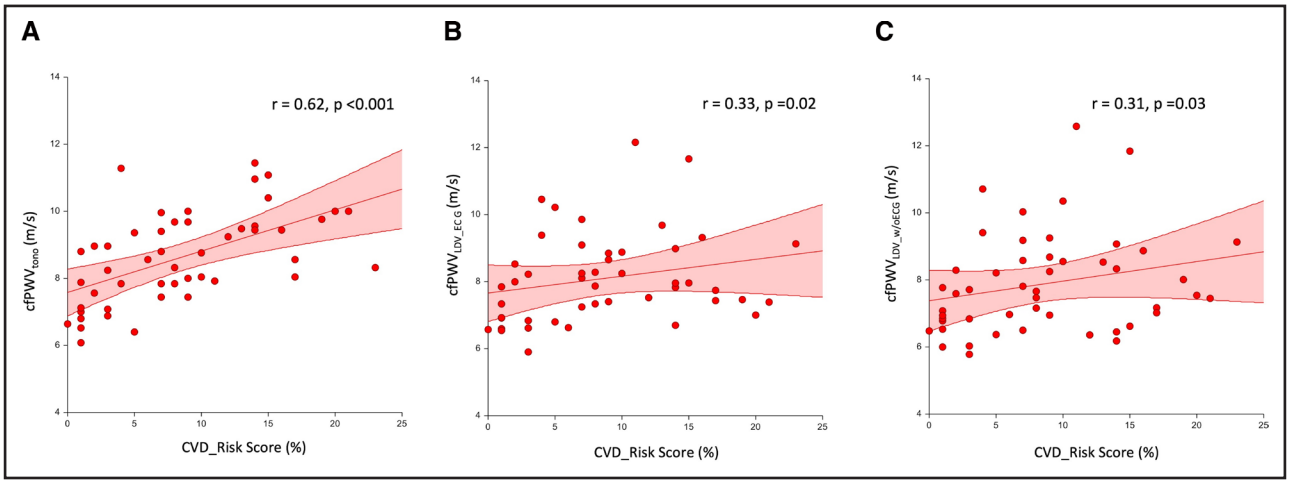

Figure 5. Correlation between 10-year cardiovascular risk and carotid-femoral pulse wave velocity (PWV). Measured by (**A**) applanation tonometry (cfPWVtono; r=0.64; *P*<0.001), (**B**) laser Doppler vibrometry (LDV) PWV with ECG (cfPWVLDV_withECG; r=0.33; *P*=0.02), and (**C**) LDV PWV without ECG (cfPWVLDV_w/oECG; r=0.31; *P*=0.03). cfPWV$_{tono}$ indicates carotid-femoral pulse wave velocity using tonometry; cfPWV$_{LDV_ECG}$, carotid-femoral pulse wave velocity using LDV-ECG dependent method; and cfPWV$_{LDV_w/oECG}$, carotid-femoral pulse wave velocity using LDV-ECG independent method.

measurement eliminates potential error due to heart rate differences and its consequential effect on the isovolumetric contraction period between the carotid and femoral signals. The ECG-independent calculation of PWV also ensures that arterial stiffness can be assessed even in cases where the R wave is not clearly discernible, as is the case for some tonometry devices, thus increasing ease of use.

The new Medical Device Regulation highlights the need for rigorous clinical validation and evidence for the safety and utility of the device.[27,28] Furthermore, the accuracy and precision of a new measurement system must be assessed according to recommended standards. In this case, the LDV device was compared with the noninvasive gold standard recommended by international guidelines for measuring cfPWV.[9] The LDV-based PWV measurements were found to be repeatable, and the within-observer variability was comparable to that observed with the reference technique.[21]

Clinical Relevance

CfPWV measured by applanation tonometry increased with age and BP. Additionally, an exploratory analysis showed a significant correlation of cfPWV with the CVD risk score. Similar results were observed with cfPWV measured using LDV, calculated both with and without the ECG signal. PWV measurement is clinically relevant because of its close relationship with cardiovascular disease risk and its risk reclassification power,[29–31] thus providing the opportunity to initiate and assess the efficacy of therapies set to modify those risk factors.[32–34] A wider application, that is, in a primary care setting, is advisable to help identify people at risk of cardiovascular disease. This is particularly relevant for a younger population, where traditional risk scores cannot be applied.[35] Indeed, traditional cardiovascular risk scores could not be calculated for a portion of the population recruited for the current study because of their young age. Furthermore, early lifestyle and risk factor modifications can have beneficial effects on vascular aging, which are not completely captured by classical scores, as well as negative effects of unknown and nonconventional risk factors.[35] Techniques that directly assess arterial health, such as PWV, may thus provide a unified measurement of the impact of multiple factors on the vasculature and may provide actionable guidance needed in clinical decision-making.

Strengths and Limitations

One of the strengths of this study is that the population is evenly distributed across both sexes and age ranges. Additionally, the inclusion of mild to moderate hypertensives made it possible to evaluate the expected physiological associations between PWV measured by the novel LDV device and BP. The study further validated an ECG-independent method of calculating PWV using LDV, which will make it possible to measure PWV even in conditions with ectopic heart beats in the ECG. Furthermore, as breath movements might have been a potential source of artifacts, the study compared the PWV measured by the LDV device during normal breathing with breath-holding and found minimal difference, as assessed by CV, between the 2 methods. Finally, the study found an association of PWV measured by the novel LDV device with age, BP, and 10-year cardiovascular risk score, confirming its potential clinical relevance.

Several limitations must be acknowledged. Owing to procedural and ethical considerations, intra-arterial validation with pressure waveforms recorded invasively from the aortic valve and above the aortic bifurcation has not been performed. However, comparison with the tonometric system has been recommended as an acceptable reference for device validation by the ARTERY guidelines.[9] A limitation of the current study is that it was validated in a general population of hypertensive individuals; further studies are needed to validate its use in special populations such as obese individuals, as recommended by validation guidelines.[9,36]

In its present form, the device is bulky and requires a retroreflective patch to enhance reflections from the skin. The next version of this device, which is currently under development in the InSiDe project, will be lightweight, wireless, and use laser wavelengths that allow for measurements without a patch. Furthermore, the association with cardiovascular risk was only performed as an exploratory analysis. It does not provide information about the reclassification power of cfPWV measured by the test device, which was beyond the scope of this study and needs to be confirmed in larger studies. However, this exploratory analysis highlights the clinical relevance of LDV-measured PWV.

Finally, in 2024, new guidelines for the validation of PWV devices has been released, which recommend some changes in patient recruitment and data analysis.[36] Since the protocol was designed well before this study, our protocol is not fully in accordance with procedures recommended in [36] in terms of acquisition protocol, age, PWV groups of participants, and other important protocol characteristics that make the cutoff for validation proposed in that paper to be inapplicable. However, the 2010 protocol was respected, and the LDV device shows an acceptable agreement with the reference method.

Perspectives

The current validation study shows that an LDV-based device can be used for accurate assessment of arterial stiffness. The LDV system provides a simple, noninvasive, operator-independent method to measure cfPWV.

Future versions of this technology will provide easy, user-friendly, and patient-friendly measurement of cfPWV and can potentially be used in primary care settings as a screening tool for cardiovascular disease.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Figure S1–S3
Table S1 and S2

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