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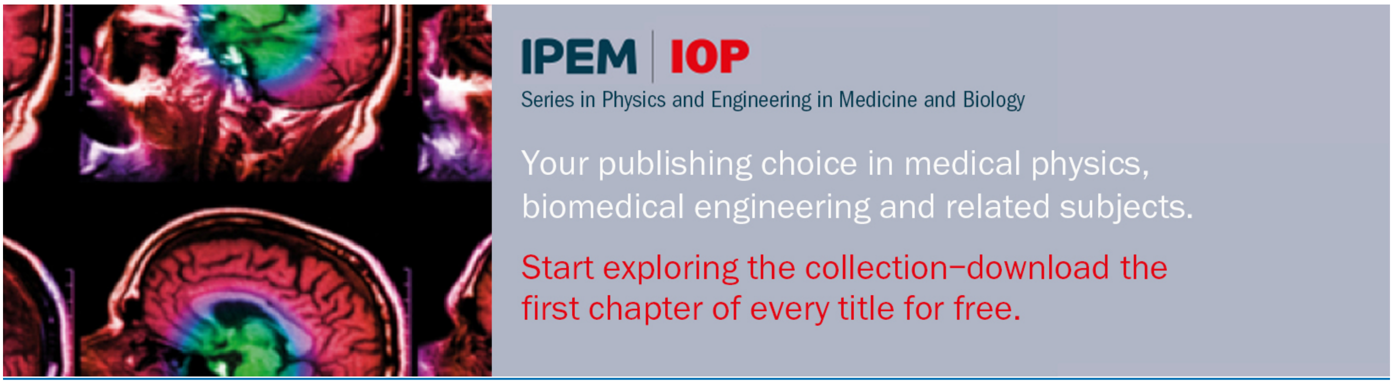

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PAPER

Estimation of carotid-femoral pulse wave velocity from finger photoplethysmography signal

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Abstract

Objective. This project compared a new method to estimate the carotid-femoral pulse wave velocity (cf-PWV) to the gold-standard cf-PWV technique. *Approach*. The cf-PWV was estimated from the pulse transit time (FPS-PTT) calculated by processing the finger photoplethysmographic signal of Finapres (FPS) and subject's height only (brief mode) as well as along with other variables (age, heart rate, arterial pressure, weight; complete mode). Doppler ultrasound cf-PWVs and FPS-PTTs were measured in 90 participants equally divided into 3 groups (18–30; 31–59; 60–79 years). Predictions were performed using multiple linear regressions (MLR) and with the best regression model identified by using MATLAB Regression Learner App. A validation set approach (60 training datasets, 30 testing datasets; VSA) and leave-one-out cross-validation (LOOCV) were used. *Main results*. With MLR, the discrepancies were: 0.01 ± 1.21 m s^{-1} (VSA) and 0.001 ± 1.11 m s^{-1} (LOOCV) in brief mode; -0.02 ± 0.83 m s^{-1} (VSA) and 0.001 ± 0.84 m s^{-1} (LOOCV) in complete mode. Using a linear support vector machine model (SVM) in brief mode, the discrepancies were: 0.01 ± 1.19 m s^{-1} (VSA) and -0.01 ± 1.06 m s^{-1} (LOOCV). Using an Exponential Gaussian process regression model (GPR) in complete mode, the discrepancies were: -0.03 ± 0.79 m s^{-1} (VSA) and 0.01 ± 0.75 m s^{-1} (LOOCV). *Significance*. The cf-PWV can be estimated by processing the FPS-PTT and subjects' height only, but the inclusion of other variables improves the prediction performance. Predictions through MLR qualify as acceptable in both brief and complete modes. Predictions via linear SVM in brief mode improve but still qualify as acceptable. Interestingly, predictions through Exponential GPR in complete mode improve and qualify as excellent.

Introduction

The aortic stiffness is an independent predictor of cardiovascular mortality (Cavalcante *et al* 2011). The non-invasive gold-standard measure to assess the aortic stiffness is the carotid-femoral pulse wave velocity (cf-PWV) measurement (Cavalcante *et al* 2011). This technique determines the velocity of the blood volume wave propagating over the arterial tree by dividing the pulse transit distance for the pulse transit time between the common carotid artery and the common femoral artery. The cf-PWV assessment has become a common procedure in clinical practice since it can be performed quickly and non-invasively through various techniques and devices (Jatoi *et al* 2009, Wilkinson *et al* 2010). Several cut-off values have been proposed to score the cardiovascular risk according to the subjects' characteristics (Mattace-Raso *et al* 2010, Ranjith *et al* 2014). However, this technique has several limitations. These include the long training time and the operator's skill dependency, the relatively long time needed to perform the measurement, the need to undress the patient to expose the groin, a great variability between operators in the measure of the transit distance, and the inability to obtain continuous beat-to-beat measurements over time (Parati and De Buyzere 2010).

Previous studies have used the finger photoplethysmographic signal (FPS) to estimate central arterial stiffness. Particularly, a recent study proposed a novel approach to estimate the aortic pulse wave velocity (aPWV), a surrogate index of aortic stiffness related to cf-PWV (Pilt *et al* 2011). This method applies the oscillometric working principle of the Arteriograph device (TensioMed Kft, Budapest, Hungary) to the FPS of the Finapres device (Finapres Medical System BV, The Netherlands) and determines the aortic pulse transit time by detecting specific features on the first- and second-order derivatives of the FPS (Pilt *et al* 2011). Another investigation showed that the PPGAI index, which is also determined by processing the FPS, is strongly correlated to the aortic augmentation index and able to discriminate individuals with augmented arterial stiffness compared to healthy individuals (Pilt *et al* 2014). For the assessment of peripheral arterial stiffness, the transient time from the R wave of ECG signal to the foot of the pressure wave recorded through finger photoplethysmography has been widely used in research as an index of upper limb arterial stiffness (Liu *et al* 2011, Ouyang *et al* 2021, Charlton *et al* 2022). Pulse wave velocity measurements by photoplethysmography have also been performed between other points, such as from ear to finger, ear to toe, and finger to toe (Liu *et al* 2011, Obeid *et al* 2017, Ouyang *et al* 2021, Charlton *et al* 2022). Interestingly, the subject's height is proportional to the carotid-femoral length and has been used to estimate the pulse travel distance via mathematical equations (Van Bortel *et al* 2012). Previous studies have also shown a relationship between the cf-PWV and age (Baier *et al* 2018, Pucci *et al* 2020), heart rate (Haesler *et al* 2004), arterial pressure (Tan *et al* 2016, Pucci *et al* 2020), and body weight (Logan *et al* 2020, Patil *et al* 2021), suggesting that these variables may be co-variants of the cf-PWV. Indeed, these variables have been integrated into mathematical equations to improve the accuracy of the cf-PWV estimation and used to estimate the cf-PWV or its surrogates (Van Bortel *et al* 2012, Greve *et al* 2016, 2017, Baier *et al* 2018, Schwartz *et al* 2019).

This project aims to evaluate a new method to estimate the cf-PWV from multiple input variables. It is tested whether the cf-PWV can be estimated from the pulse transit time calculated by processing the FPS signal of Finapres (FPS-PTT) and subjects' height only, the two main variables needed to determine the PWV (time interval and distance, respectively). It is also tested whether the inclusion of other input variables (age, heart rate, arterial pressure, weight) improves the accuracy of the cf-PWV prediction. Predictions are obtained through multiple linear regressions and also by using the best regression model identified with the Regression Learner App of MATLAB (MATLAB, MathWorks, US). Estimated measures will be compared to the gold-standard ones.

Methods

Measures were performed in 90 participants meeting inclusion (>18 years old) and exclusion criteria (atrial fibrillation and cardiac valve disease, not in sinus rhythm, pacemaker-dependent, pregnancy, BMI $> 30\ \mathrm{kg/m^2}$, known significant carotid or femoral artery stenosis, impalpable arterial pulse) (Wilkinson *et al* 2010). Subjects were divided into 3 groups by age as shown in table 1 (18–30 y.o.; 31–59 y.o.; 60–79 y.o.; 15 men and 15 women within each group). Personal data (age, weight, height) were recorded before starting the test. Subjects were connected to the input channel of the 3-lead electrocardiograph integrated into the ultrasound scanner (LOGIQ S7 pro, GE, Milwaukee, USA) through the use of skin electrodes. Moreover, subjects were instrumented with the beat-by-beat finger blood pressure monitoring system Finapres on the third medial phalanx of the right hand. The Finapres analog output was connected to an analog-to-digital converter (ESP32, AZDelivery, Germany) sampling at 1 kHz. Finapres data were saved into .txt files. The cf-PWV assessment was performed complying strictly with the recommendations on user procedures previously indicated (Van Bortel *et al* 2012). After 10 min of supine and quiet rest, 3 arterial pressure measurements were taken using the Riva-Rocci method on the left arm and averaged to obtain systolic (SAP) and diastolic (DAP) arterial pressure values, whereas the resting heart rate (HR) was read from the Finapres serial monitor. Then, the following measures were performed.

FPS-derived pulse transit time

The FPS-PTT was calculated complying strictly with the procedure previously indicated by Pilt *et al* (2011) with a slight modification (details below). The algorithm proposed by Pilt *et al* has been explained in detail in their article (Pilt *et al* 2011) and has been integrated into a MATLAB sketch by ourselves for being used in our project. The software has been implemented by ourselves with a user-friendly graphical interface to graphically detect the FPS-PPT (figure 1) to further simplify the signal analysis. The procedure for calculating the FPS-PTT is as follows. After running the MATLAB sketch, a pop-up window allows to upload the .txt file containing the numerical data of the Finapres signal to be analyzed. The software automatically filters the data through high-

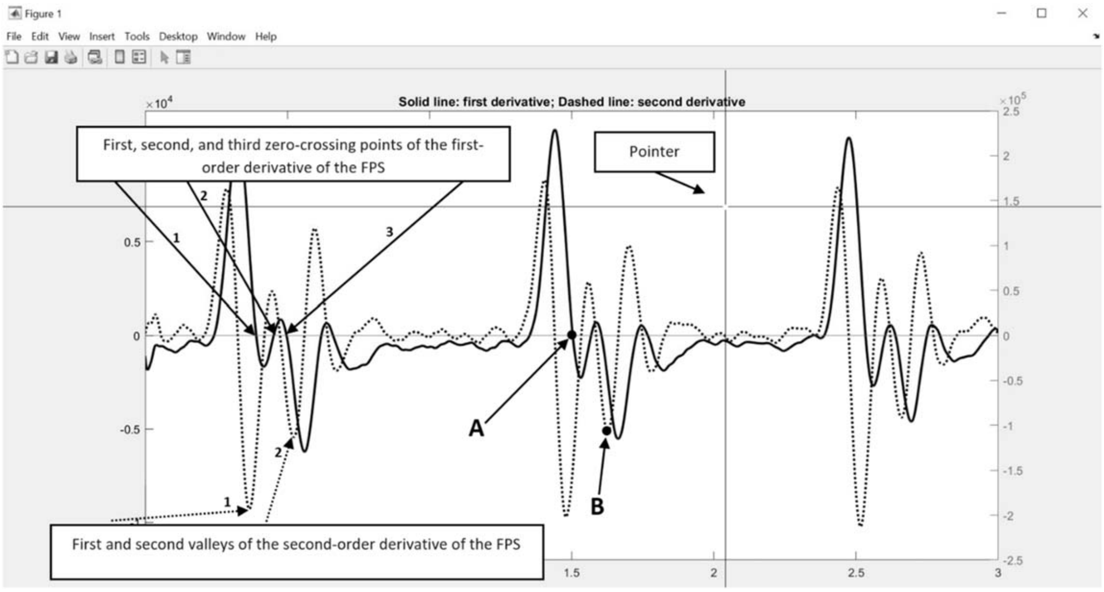


Figure 1. The figure shows the graphical interface with the first- (solid line) and second- (dashed line) order derivatives of the finger photoplethysmographic signal (FPS) with their zero-crossing points and valleys. To determine the FPS-derived pulse transit time, the software requires to click the pointer on the first zero-crossing point of the first-order derivative (A) and on the second valley of the second-order derivative (B).

Table 1. Characteristics of groups (mean ± standard deviation; 15 men and 15 women within each group).

Groups	18–29 Y.O.	30–59 Y.O.	60–79 Y.O.
Age (years)	24.0 ± 2.4	44.8 ± 10.4	68.1 ± 4.9
Weight (Kg)	67.9 ± 11.3	71.7 ± 9.8	77.1 ± 8.5
Height (cm)	1.74 ± 0.10	1.71 ± 0.06	1.70 ± 0.07
Systolic BP (mmHg)	114.7 ± 9.2	129.1 ± 10.9	137.9 ± 10.4
Diastolic BP (mmHg)	67.4 ± 6.2	74.4 ± 8.3	81.2 ± 6.9
Resting heart rate (HR)	60.8 ± 9.5	64.5 ± 8.9	67.2 ± 6.8
FPS-PTT (s)	0.17 ± 0.01	0.15 ± 0.02	0.12 ± 0.02
Doppler cf-PWV (m/s)	5.4 ± 0.6	6.9 ± 1.1	8.8 ± 1.4

and low-pass filters. Cut-off frequencies are 0.1 Hz and 30 Hz, respectively. Then, a graphical interface showing the first- and second-order derivatives of FPS appears on the screen. The user needs to click the pointer on the first zero-crossing point of the first-order derivative and on the second valley of the second-order derivative to determine the FPS-PTT, as shown in figure 1. The resolution to measure the time delay between the two points is 1 ms. The graphical interface shows the entire signal divided into subsequent 3 s windows to allow 15 consecutive measurements. When the 15 measures are completed, the software returns the average value of FPS-PTT on the screen. The original algorithm proposed by Pilt *et al* (2011) requires selecting the first zero-crossing point of the first-order derivative and, if visible, the third zero-crossing point of the first-order derivative. If the latter is not visible, the second valley of the second-order derivative needs to be selected. Indeed, the FPS-PTT may slightly change with aging and the third zero-crossing point of the first-order derivative may not be visible (Pilt *et al* 2011) (figure 2). Our modification consists of the standardization of the selection of the second valley of the second-order derivative across all subjects, even if the third zero-crossing point of the first-order derivative is visible, since these two points are almost coincident (figure 2, left panel). This change also simplifies signal analysis and technique teaching.

Doppler ultrasound cf-PWV measure

Details and graphical description about this procedure have been previously described (Calabia *et al* 2011, Van Bortel *et al* 2012). Briefly, scanning of the carotid artery at the supraclavicular level followed by another scanning

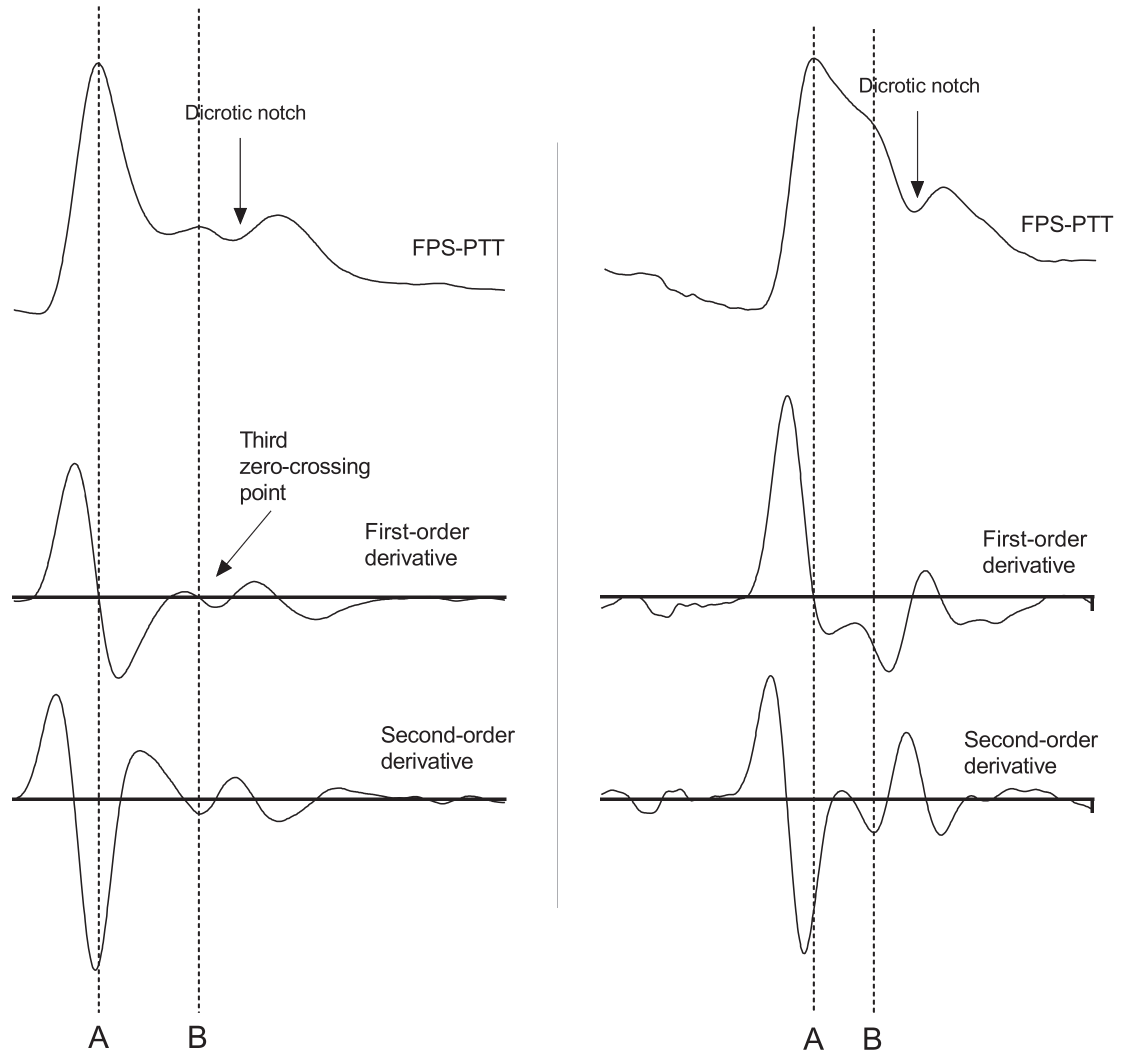


Figure 2. FPS-PTT, first-order derivative of FPS-PTT, and second-order derivative of FPS-PTT on a 20 years old men (left panel) and a 65 years old men (right panel). 'A' represents the first zero-crossing point of the first-order derivative, while 'B' represents the second valley of the second-order derivative. The third zero-crossing point of the first-order derivative is visible on the young men, but not on the older one.

of the common femoral artery in the groin were performed in B-mode using the pulsed Doppler function of our ultrasound scanner with a Linear Array (6.6 MHZ) probe synchronized with ECG. The pulse transit times at the carotid and femoral arteries were identified by measuring the time elapsed from the R peak of the ECG signal to the foot of the Doppler flow waves at the carotid and femoral recordings, respectively, as graphically shown in the paper by Calabia *et al* (2011). The foot of the Doppler flow wave defines the point where the steep rise of the waveform begins. Pulse transit times were measured offline using the proprietary software integrated into our ultrasound scanner. The software returns the time delay between two points of interest after positioning two movable cursors in correspondence of such points. The resolution to measure the time delay between the two points is 1 ms. The average values of the pulse transit times at the carotid and femoral arteries over 15 subsequent cycles were calculated. The pulse transit time was calculated by subtracting the average pulse transit time at the carotid artery from the average pulse transit time at the femoral artery (Van Bortel *et al* 2012). The cf-PWV was calculated as 0.8 times the direct body surface distance from the common carotid artery to the common femoral artery at the groin divided by the pulse transit time (Van Bortel *et al* 2012). Ultrasound measures were performed by an expert sonographer with >500 h of experience.

Validation methods

Two validation methods were used. First of all, we proceeded with a validation set approach (VSA). Data from 60 random participants (20 per group) were used for training, whereas the data of the other 30 participants were used for testing. Importantly, the training and testing datasets were determined once and then used to train and test all regression models. Secondly, we proceeded with a leave-one-out cross-validation (LOOCV). Repeatedly, each subject was excluded from the complete dataset, model training was performed with the data of the other 89 subjects and used to predict the cf-PWV of the excluded subject.

Multiple linear regression analysis

The relationship between independent variables (FPS-PTT, height, age, heart rate, weight, and systolic and diastolic arterial pressure) and the dependent variable (Doppler cf-PWV) was assessed by multiple linear regressions. It was obtained a mathematical equation to predict the cf-PWV from FPS-PTT and subjects' height only (brief mode), as well as another equation by also including age, heart rate, arterial pressure, weight as input variables (complete mode).

Analysis via MATLAB regression learner app

The Regression Learner App of MATLAB was used to assess and choose the multiple regression model with the best performance in predicting the cf-PWV. After entering input and target data, this App trains a wide range of regression models and compares their validation errors side-by-side. Thus, the regression model with the best performance can be chosen, exported, and used to make predictions by entering new input data via MATLAB code. It was chosen the regression model with the best performance using FPS-PTT and subjects' height only as inputs, as well as the best one using all input variables.

Statistics

The relationship between each independent variable and the Doppler cf-PWVs was assessed via linear regression. Predicted cf-PWVs were compared with the Doppler cf-PWVs through Bland–Altman plots and linear regression. Data analysis was performed by using MATLAB. GraphPad Prism 8 (GraphPad Software, San Diego, United States) was used for statistical analysis and graphs. To improve the fairness of the comparison between previous results and our own, we repeated the comparison between estimated cf-PWV and Doppler cf-PWV on a subset of subjects reporting similar features to those recruited in similar previous studies. Once the target features (number of subjects, sex distribution, age range, mean age) to be obtained in the new group were set, the subjects to be included were randomly chosen from the full dataset through MATLAB.

Results

The relationship between each independent variable and the Doppler cf-PWVs along with their coefficient of determination is shown in figure 3.

Multiple regression analysis

By using VSA, the bias of the technique was 0.01 m s^{-1} and the SD of bias was 1.21 m s^{-1} in the brief mode, whereas the bias of the technique was −0.02 m s^{-1} and the SD of bias was 0.83 m s^{-1} in the complete mode. The regression equations obtained were:

- $\text{cfPWV} = +12.097 + \text{height} * 1.748 - \text{FFSPTT} * 55.624$
- $\text{cfPWV} = -2.572 + \text{age} * 0.056 - \text{weight} * 0.012 + \text{SIS} * 0.028 - \text{DIA} * 0.015 + \text{HR} * 0.013 + \text{height} * 4.02 - \text{FFSPTT} * 15.45$

By using LOOCV, the bias of the technique was 0.001 m s^{-1} and the SD of bias was 1.11 m s^{-1} in the brief mode, whereas the bias of the technique was 0.001 m s^{-1} and the SD of bias was 0.84 m s^{-1} in the complete mode.

Analysis via MATLAB regression learner app

With VSA, the best regression model for the brief mode was a linear support vector machine, which led to a bias between the techniques of 0.01 m s^{-1} and a SD of bias of 1.19 m s^{-1}. The best regression model for the complete mode was an Exponential Gaussian process regression, which led to a bias between the techniques of −0.03 m s^{-1} and a SD of bias of 0.79 m s^{-1}.

With LOOCV, for each subject, the best regression models were Linear support vector machine and Exponential Gaussian process regression for the brief and complete modes, respectively. By using LOOCV, the bias of the technique was −0.01 m s^{-1} and the SD of bias was 1.06 m s^{-1} in the brief mode, whereas the bias of the technique was 0.01 m s^{-1} and the SD of bias was 0.75 m s^{-1} in the complete mode.

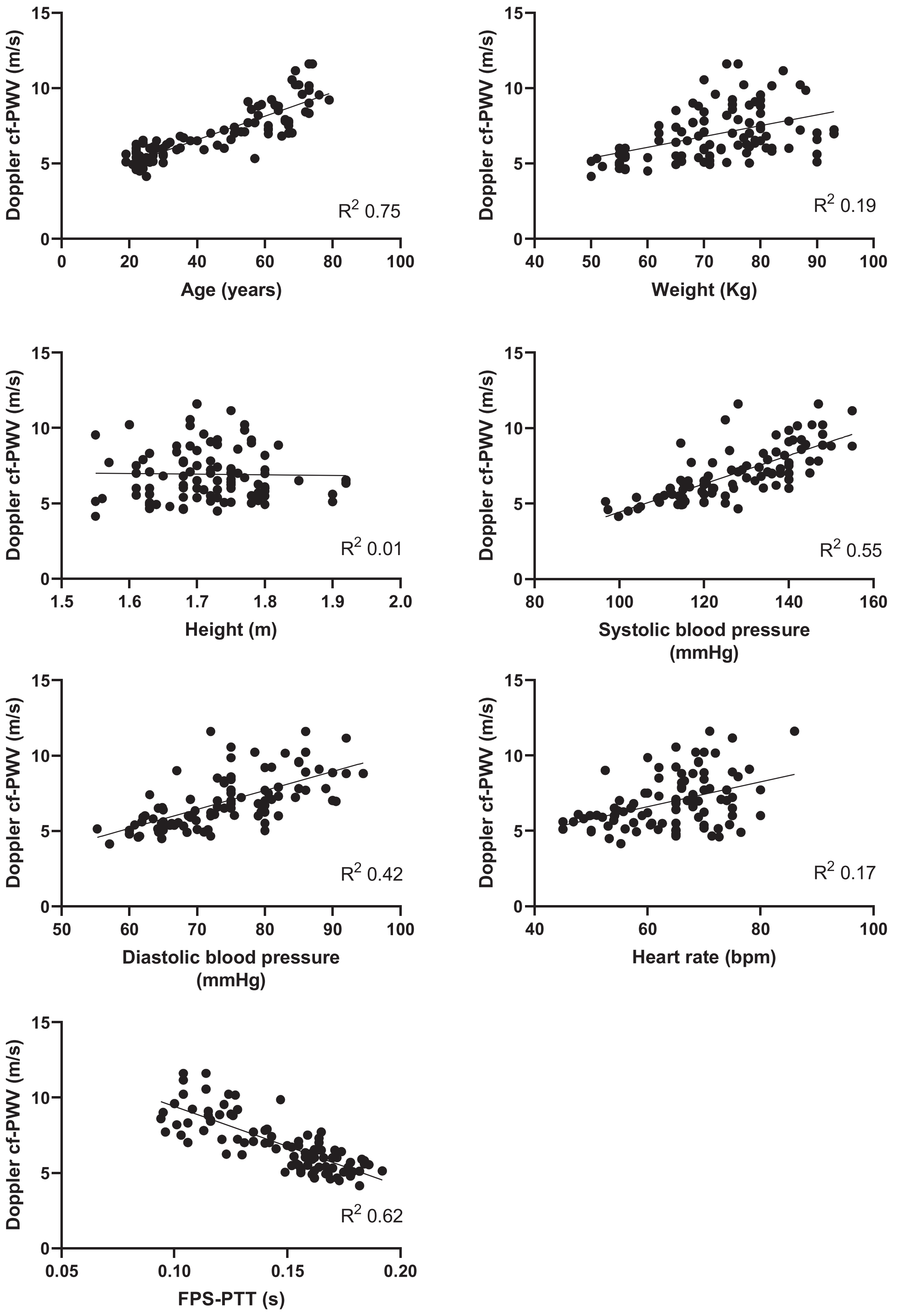
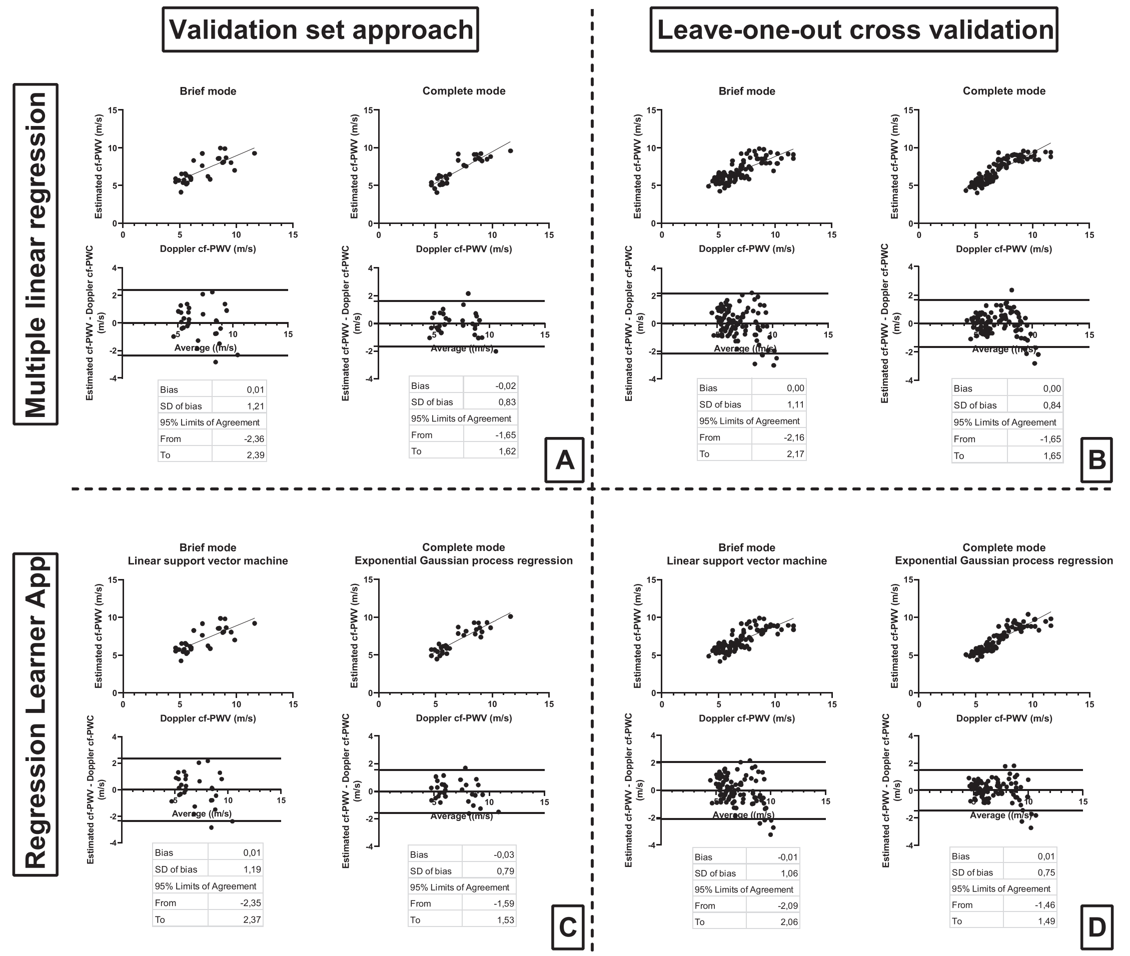


Figure 3. Relationship between input variables and cf-PWV.

Subgroup results

To improve the comparison between the results by Pilt *et al* (2011) and our own, we created a random subset of 23 healthy subjects (18 men and 5 women; age range: 20–64 y.o.; mean age: 34.3 ± 12.5 y.o.) from the full dataset. In this subgroup, the discrepancies between estimated cf-PWVs and Doppler cf-PWVs are as follows (bias ± SD; MLR and VSA: brief mode 0.23 ± 0.97 m s^{-1}, complete mode −0.04 ± 0.62; MLR and LOOCV:



Bias	0,01
SD of bias	1,21
95% Limits of Agreement	
From	-2,36
To	2,39

Bias	-0,02
SD of bias	0,83
95% Limits of Agreement	
From	-1,65
To	1,62

Bias	0,00
SD of bias	1,11
95% Limits of Agreement	
From	-2,16
To	2,17

Bias	0,00
SD of bias	0,84
95% Limits of Agreement	
From	-1,65
To	1,65

Bias	0,01
SD of bias	1,19
95% Limits of Agreement	
From	-2,35
To	2,37

Bias	-0,03
SD of bias	0,79
95% Limits of Agreement	
From	-1,59
To	1,53

Bias	-0,01
SD of bias	1,06
95% Limits of Agreement	
From	-2,09
To	2,06

Bias	0,01
SD of bias	0,75
95% Limits of Agreement	
From	-1,46
To	1,49

Figure 4. Comparison of the estimated cf-PWVs with the gold-standard measures. The cf-PWVs were estimated with multiple linear regression (A), (B) and with the best regression model identified with MATLAB regression learner App (C), (D) with a validation set approach (A, C; $n = 60$ training dataset and $n = 30$ testing dataset) and leave-one-out cross-validation (B), (D).

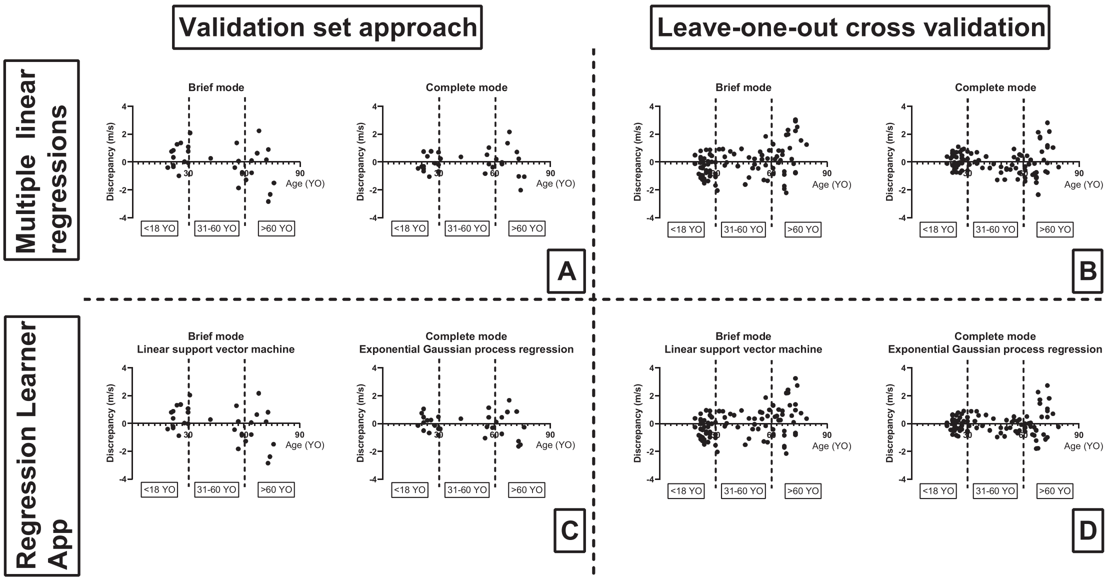


Figure 5. Discrepancy between the precicted cf-PWV and the gold-standard cf-PWV measures over age.

brief mode 0.11 ± 0.86, complete mode 0.07 ± 0.61; Linear support vector machine and VSA: brief mode 0.22 ± 0.95; Exponential Gaussian process regression and VSA: complete mode 0.05 ± 0.61; Linear support vector machine and LOOCV: brief mode 0.05 ± 0.85; Exponential Gaussian process regression and LOOCV: complete mode −0.01 ± 0.54).

Discussion

We sought to evaluate a new method to estimate the cf-PWV from multiple variables. We tested whether the cf-PWV can be estimated from the pulse transit time (FPS-PTT) calculated by processing the FPS of Finapres and the subjects' height only (brief mode). We also tested whether the inclusion of other input variables (age, heart rate, arterial pressure, weight; complete mode) improves the accuracy in the cf-PWV prediction. Predictions were made using multiple linear regressions, as well as with the best regression model identified with the MATLAB Regression Learner App. We used a VSA (60 subjects for training; 30 subjects for testing), as well as LOOCV (89 subjects for training; 1 subject for testing) as validation methods. According to the guidelines for validation of non-invasive arterial pulse wave velocity (Wilkinson *et al* 2010), the accuracy of the test device is scored as 'excellent' when the bias from the gold-standard measure is <0.5 m s^{-1} and the SD is <0.8 m s^{-1}, and 'acceptable' when the bias from the gold-standard measure is <1.0 m s^{-1} and the SD is <1.5 m s^{-1}.

Multiple linear regression is a simple, widely-used function to predict a target variable from independent variables through a mathematical equation. This function is integrated into user-friendly calculation systems such as Microsoft Excel (Microsoft Corporation, US). The Regression Learner App of MATLAB is a powerful tool that compares multiple regression models and allows to choose the one with the best performance. The best model is exported as a MATLAB file and used along with new input data to make predictions in new subjects via MATLAB code. Although the Regression Learner App could find regression models with greater performance than multiple linear regressions, it does not provide mathematical equations and requires substantial MATLAB coding skills to use the exported models and make predictions with new input data. Therefore, the use of multiple linear regressions would allow the use of the technique to a wider audience. The VSA provides a unique model or equation based on a portion of available data. The use of LOOCV allows the use of a larger training dataset compared to VSA since it repeatedly fits a model to a dataset that contains a number of observations equal to the total sample size minus 1. Furthermore, the use of LOOCV allows a final comparison of the techniques on a greater number of data points compared to VSA.

We used a new approach to calculate a variable related to the carotid-femoral pulse transit time, the FPS-PTT. It was calculated by applying the oscillometric working principle of Arteriograph to the FPS of Finapres as recently proposed by Pilt *et al* (2011). The oscillometric algorithm of Arteriograph assumes to determine the aortic pulse transit time by detecting the time elapsed between the first wave ejected from the left ventricle to the aortic root and its reflection from the aortic bifurcation as the second systolic wave (Baulmann *et al* 2008, Segers *et al* 2009). Subsequent research has questioned the existence of a discrete arterial reflection site and supported the notion of the presence of an effective reflection site that conceptually includes the integration of all scattered reflections that take place over the arterial tree, without connecting it to a precise anatomical location (Segers *et al* 2009, 2012). Such an effective reflection site is linked to the path traveled by the diffuse waves across the various segments of the arterial tree, whose length shows a certain degree of proportionality with the body height (Segers *et al* 2009, Van Bortel *et al* 2012, Westerhof *et al* 2020). Arteriograph underwent both noninvasive (Baulmann *et al* 2008, Rajzer *et al* 2008, Jatoi *et al* 2009, Nemes *et al* 2011, Ring *et al* 2014, Milan *et al* 2019) and invasive comparisons (Horváth *et al* 2010) against gold-standard cf-PWV methods, although there has been some debate regarding whether it measures the aortic stiffness directly or indirectly by measuring the axillo-brachial stiffness (Trachet *et al* 2010). Interestingly, as shown in figure 3, the FPS-PTT shows a relationship with the cf-PWV and tends to decrease with aging. This would be consistent with a faster pulse wave velocity in the elderly compared to young individuals (Baier *et al* 2018, Pucci *et al* 2020). The algorithm proposed by Pilt *et al* (2011) has been integrated and implemented into MATLAB software by ourselves. The software provides a graphical interface to quickly determine the FPS-PTT by clicking on specific features of the first- and second-derivative of the FPS with the mouse pointer as shown in figure 1. Specifically, the first zero-crossing point of the first-order derivative and the second valley of the second-order derivative need to be selected as these points are visible across all subjects regardless of the age (figure 2). The graphical detection of the FPS-PTT allows fast training to inexperienced users with little operators' skill dependency.

Linear multiple regression analysis

As shown in figure 4, the cf-PWV predictions from FPS-PTT and subjects' height only via VSA qualify as acceptable. The bias between the gold-standard values of cf-PWV and those predicted in 30 new subjects is close to 0 m s^{-1}. This result is relevant as it arises from the interaction between a time interval and a length only, in a

Table 2. Discrepancy (m/s) between the precicted cf-PWV and the gold-standard cf-PWV measures in both sexes (MLR: multiple linear regression; SVM: support vector machine; GPR: Gaussian process regression).

			Men	Women	Men versus Women (*p*-value)
VSA	Brief mode	MLR	−0.1 ± 1.4	0.1 ± 1.0	$p = 0.58$
		SVM	−0.1 ± 1.4	0.2 ± 1.0	$p = 0.53$
	Complete mode	MLR	0.1 ± 0.8	−0.1 ± 0.8	$p = 0.68$
		GPR	0.0 ± 0.8	0.0 ± 0.8	$p = 0.94$
LOOCV	Brief mode	MLR	−0.1 ± 1.2	0.1 ± 1.1	$p = 0.66$
		SVM	0.1 ± 1.4	0.2 ± 1.4	$p = 0.65$
	Complete mode	MLR	−0.1 ± 0.9	0.1 ± 0.8	$p = 0.46$
		GPR	0.0 ± 0.8	0.0 ± 0.8	$p = 0.90$

group of 30 new test subjects not used to develop the regression model. The carotid-femoral length has been shown to be proportional to subjects' height (Van Bortel *et al* 2012). This result implies that the FPS-PTT also be proportional to the carotid-femoral pulse transit time. The inclusion of other input variables (age, heart rate, arterial pressure, weight) improves the accuracy in the cf-PWV prediction via VSA compared to the brief mode. Indeed, the SD of bias decreases from 1.21 to 0.83 m s^{-1}. The complete mode still qualifies the prediction as acceptable, however, such results are close to the threshold to qualify the prediction as excellent (SD $=$ 0.80 m s^{-1}). The cf-PWV prediction in the brief mode slightly improves by using LOOCV compared to the VSA, although it still qualifies as acceptable. In the complete mode, the cf-PWV predictions with LOOCV compared to the VSA remain similar, suggesting that a multiple regression model fitted on more than 60 subjects does not necessarily improve accuracy in the cf-PWV prediction.

Analysis via MATLAB regression learner app

The regression models identified by MATLAB's Regression Learner App have improved cf-PWV prediction performance compared to multiple linear regressions, but only to a minimal extent. The cf-PWV prediction in brief mode with a Linear support vector machine model still qualifies as acceptable both with a VSA and LOOCV. In the cf-PWV prediction in complete mode with an Exponential Gaussian process regression model and VSA, although the bias does not change markedly, the SD of bias diminishes from 0.83 to 0.79 m s^{-1}. With the use of LOOCV, the SD of bias diminishes to 0.75 m s^{-1}. Under such circumstances, the cf-PWV predictions would qualify as excellent. With the threshold for the 'excellent' set at an SD of bias of 0.80, however, it might be more prudent to qualify the predictions between excellent and acceptable in practice. Therefore, the use of the MATLAB Regression Learner App has identified regression models with better performance than multiple linear regressions in predicting the cf-PWV. Despite the difference in prediction being pretty small, such a difference could improve the qualification of the prediction performance from acceptable to excellent in some circumstances.

Comparison with previous device validation results

In the study by Pilt *et al* (2011), the aPWV calculated by processing the Finapres signal was compared to the aPWV of Arteriograph on 23 subjects (age distribution not indicated), showing a bias between the techniques of 0.07 m s^{-1} and a SD bias of 0.51 m s^{-1}. Consistent with the previous study, our results from the full dataset show a small bias between the techniques but a slightly higher SD of bias. This discrepancy might be due to the different age distribution of the subjects. As shown in figure 5, the discrepancy between the techniques is much greater in subjects older than 59 and the inclusion of such subjects in the analysis may therefore increase the SD of bias. Indeed, the SD of bias diminished when we repeated comparisons on a subset of subjects with similar ages to those included in the study by Pilt *et al* (2011), showing values of SD ranging from 0.54 and 0.97 m s^{-1} depending on the condition. Conversely, the bias of the technique slightly increased in this subgroup in a range between −0.01 and 0.23 m s^{-1} depending on the condition. A previous study tested the agreement of the cf-PWV values assessed via Doppler Ultrasound against those assessed via the Complior device (Artech Medical, Pantin, France) in 40 subjects (Calabia *et al* 2011). The bias between the devices was 0.13 m s^{-1}, the limits of agreement were approximately (graphic data provided only) by 2 m s^{-1} (SD approximately 1 m s^{-1}), and $R = 0.91$. Regardless of the regression model and validation method chosen, our technique in complete mode provided a greater agreement with the Doppler cf-PWV values. At values higher than 8–10 m s^{-1}, however, our predicted cf-PWVs appear to be underestimated and a wider scatter is present. These trends were also found while comparing Arteriograph to Sphygmocor (Ring *et al* 2014) and to Complior (Horváth *et al* 2010). The reasons responsible for such behaviors at higher PWV values have not been elucidated (Baulmann *et al* 2008, Ring *et al* 2014), however, it has been speculated that these might derive from the fact that the aorta is to a variable degree increasing in length with aging. The ascending aortic length increases with aging up to double from 20 to 80 years of age, whereas the length of the other aortic segments increases or decreases to a lower extent (Sugawara *et al* 2008). The impact of age-related increases of the ascending aorta on cf-PWV is small because this tract is not considered in the carotid-femoral length (Sugawara *et al* 2008). However, it could affect the PWV assessed through the oscillometric algorithm of Arteriograph, because this method considers the pulse transit time from the left ventricle outflow tract to an effective reflection site conceptually located after the heart, over the arterial tree (Baulmann *et al* 2008). Any elongations of the aorta would result in a longer pulse transit time and, consequently, in an underestimation of velocity. Between-equipment divergences in the PWV calculation are well known and accepted across devices and have been mainly attributed to differences in calculating the travel distance rather than to differences in calculating the transit time (Rajzer *et al* 2008). The need to moderate any results to the device used and to use the same device for repeated measurements has indeed been suggested (Rajzer *et al* 2008). A detailed review between the agreements of different commercial devices for measuring cf-PWV is reported in the recent paper by Milan *et al* (2019).

Strengths and limitations of the technique

The strengths of our method are manifold. It adds important functionality to Finapres, a device commonly found in physiology laboratories. The bias against the gold-standard measure is close to 0 regardless of the mode used. As shown in table 2, our data reveal no overt sex differences. Data collection and analysis are simple to perform and take less than a couple of minutes. It is not necessary to uncover the groin as required for the gold-standard cf-PWV measure since data are taken from the subjects' fingers. The method does not require measuring the pulse transit distance. Full training to novice operators can be provided quickly within approximately one hour. This method has the potential to estimate cf-PWV beat-to-beat and under dynamic conditions, such as during exercise. As limitations, the software MATLAB and MATLAB coding knowledge are required to determine the FPS-PTT and to make predictions with MATLAB models. Moreover, this study compared the estimated cf-PWV values to the gold-standard ones in healthy subjects only. Further verification using multi-center data and data in other cohorts are required before considering this technique valid for use in research or clinical practice.

Conclusion

Our data suggest that the cf-PWV can be estimated through the FPS-PTT and subjects' height only, showing an acceptable agreement compared to the gold-standard Doppler cf-PWV measure. The inclusion of other variables (age, heart rate, arterial pressure, weight) improves the accuracy in the cf-PWV estimation up to excellent according to the regression model chosen. Predictions through the use of multiple linear regression qualify as acceptable in both brief and complete mode. The use of MATLAB's Regression Learner App has identified regression models with greater performance than multiple linear regressions. The cf-PWV predictions improve using a linear support vector machine model in the brief mode, despite predictions still qualify as acceptable. Interestingly, cf-PWV predictions via the Exponential Gaussian process regression model improve in the complete mode, qualifying as excellent via both VSA and LOOCV.

Software and data availability

The (a) MATLAB software to determine the FPS-PTT, (b) MATLAB file containing the linear support vector machine model (60 training dataset) for the cf-PWV prediction from FPS-PTT and subject's height only, and (c) MATLAB file containing the Exponential Gaussian process regression model (60 training subjects) for the cf-PWV prediction from FPS-PTT, subject's height, age, HR, weight, and SAP and DAP are available from the corresponding author upon reasonable request.

Declaration of conflicting interests

None declared.

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Ethical approval of studies and informed consent

The Ethics Board of the University of Verona approved all procedures involving human subjects (3293CESC). Each participant provided written informed consent. Our project was conducted in accordance with the principles embodied in the Declaration of Helsinki.

Authors' contributions

Study concept and design (AG); software development (AG); experiment execution and data collection (AG); data analysis (AG, CT, AC); data interpretation (AG, AC, CT, AVT, FS); original draft preparation (AG); review and critical revision of the manuscript (AG, AC, CT, AVT, FS); Supervision: AC, CT, FS; all authors approved the final version of this manuscript.

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