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A hybrid CAVI-ML algorithm reducing blood pressure dependence in arterial stiffness assessment

Lilia Radjef[1], Tahar Omari[2], Karim Baiche[1]
[1]Systems Engineering and Telecommunications Laboratory (LIST), Department of Electrical Systems Engineering, Faculty of Technology, University M'hamed BOUGARA, Boumerdès, Algeria
[2]Department of Electrical Engineering, Faculty of Technology, University of Ain Temouchent, Ain Temouchent, Algeria

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ABSTRACT

This article introduces a hybrid cardio-ankle vascular index–machine learning method (CAVI-ML) that combines the classical non-invasive CAVI with a random forest (RF) model to reduce CAVI's residual dependence on systolic blood pressure (SBP) and the pressure gradient. The key change is replacing the standard coefficients a and b with RF-predicted apred and bpred. Using a synthetic pulse wave database (PWDB) of 4,374 virtual pulse waves (ages 25–75), classical CAVI was computed via the Bramwell–Hill equation, and 11 non-invasive hemodynamic features per subject were used to train an RF regressor (100 trees; 63.2% bootstrap samples; 3 variables per split). We then used tree-averaged apred and bpred to calculate normalised CAVIDyn. We compared performance with classical CAVI and the gold standard carotid-femoral pulse wave velocity (cfPWV) using the metrics: R^2, root mean square error (RMSE), mean absolute error (MAE) and mean absolute percentage error (MAPE). CAVI-ML reduced correlation with SBP by 59% ($r = 0.613 \rightarrow 0.251$) and with diastolic pressure by 73% ($r = 0.735 \rightarrow 0.201$), and was 62% less blood-pressure-dependent than cfPWV ($r = 0.662$). CAVI-ML improves independence from instantaneous blood pressure and shows promise for non-invasive arterial stiffness estimation and cardiovascular risk prediction, but requires validation on clinical data.

Corresponding Author:

Lilia Radjef
Systems Engineering and Telecommunications Laboratory (LIST)
Department of Electrical Systems Engineering, Faculty of Technology, University M'hamed BOUGARA
Cité Frantz Fanon, 35000, Boumerdès, Algeria
Email: l.radjef@univ-boumerdes.dz

1. INTRODUCTION

Arterial stiffness is recognised as an independent predictor of cardiovascular events [1], [2]. It is closely linked to stroke [3], heart failure [4], hypertension [5] and kidney disease [6]. An early sign of structural or functional changes in the arteries [7], [8], reflecting a loss of distensibility [9]. This phenomenon is due to changes in the elastin-to-collagen ratio [10], medial calcification [11], and lipid accumulation [12]. Carotid-femoral pulse wave velocity (cfPWV) is the gold standard for measuring central arterial stiffness [13]. However, it has several limitations: dependence on instantaneous blood pressure [14], [15], operator-related variability [16], and overestimation or underestimation of propagation time in obese subjects [17].

To overcome these drawbacks, the cardio-ankle vascular index (CAVI) was proposed by Hayashi *et al.* [18] and formalised by Shirai *et al.* [19]. This biomarker reflects the stiffness of the entire arterial segment extending from the origin of the aorta to the ankle (including the aorta, femoral and tibial arteries). It is calculated from the pulse wave velocity between the heart and the ankle pulse wave velocity (haPWV) and

the blood pressure measured in the arm, based on the stiffness parameter β and the modified Bramwell-Hill equation [20]. In practice, a CAVI of around 8 corresponds to normal stiffness; between 8 and 9, stiffness is considered borderline; above 9, stiffness is high. Its most important characteristic is its independence from blood pressure at the precise moment of measurement [21], [22]. Conventional pulse wave velocity (PWV) increases mechanically when blood pressure rises during the examination. In contrast, the CAVI reflects the intrinsic stiffness of the arterial wall [23], [24]. However, the fact that it is constantly dependent on blood pressure distorts the interpretation of vascular status in patients with hypertension and the monitoring of the actual effect of antihypertensive treatments on the arteries. A change in the CAVI may reflect a change in blood pressure rather than a genuine alteration in the properties of the vascular wall [25]-[27]. Despite its advantages, several studies show that the CAVI remains dependent on blood pressure [28]-[30]. Researchers [28], [30] report correlations of the order of $r = 0.15 - 0.25$ with systolic pressure and $r = 0.20 - 0.35$ with pulse pressure. This persistent dependence can be explained by several factors: the log-linear model is only an approximation of the pressure-volume relationship; the brachial-ankle pulse wave velocity (baPWV) incorporates mixed arterial segments (elastic aorta, muscular arteries). Previous approaches aimed at adjusting CAVI for its dependence on blood pressure have relied on parametric regression models [30]. Finally, the classical CAVI uses fixed empirical coefficients a and b, calibrated on an average population [31], [32]. Machine learning-based approaches have recently demonstrated their potential for improving arterial stiffness estimation [33], [34]. However, to our knowledge, none had yet directly incorporated machine learning into the calculation of the CAVI index.

Our objective is to provide a non-invasive, accurate approach to facilitate early detection and assessment of arterial stiffness and cardiovascular disease prevention. We propose a new CAVI-ML algorithm, combining the classical CAVI with random forest (RF) regression. This innovative approach enables: (i) the customisation of the coefficients apred and bpred according to individual hemodynamic parameters, (ii) exploration of the relationships among the 11 hemodynamic parameters using a "RF" model, and (iii) reduction of pressure dependence compared to classical CAVI and gold standard cfPWV.

The remainder of the article is organised as follows: section 2 details the conventional CAVI framework, presents the database used, and describes the CAVI-ML algorithm. Section 3 presents the results and comparisons. Section 4 discusses the clinical implications, limitations and prospects.

2. MATERIALS AND METHODS

2.1. Study design

We propose a hybrid CAVI-ML algorithm that combines the conventional CAVI method with a RF regression model. This method reduces pressure dependence compared to the conventional CAVI method and cfPWV by replacing the fixed coefficients a and b of the CAVI method with a_{pred} and b_{pred} parameters using 11 individual hemodynamic parameters derived from arterial pulse wave analysis.

2.2. Database

We used the pulse wave database (PWDB), which contains 4,374 virtual arterial pulse waves from several measurement sites (aorta, carotid, brachial, radial, digital, femoral and tibial). It comprises subjects aged between 25 and 75 years (divided into 10-year age groups, with 100 subjects per group), generated using a validated cardiovascular simulation model that incorporates heart rate, arterial stiffness, peripheral resistance, and vascular geometry [35]. Table 1 summarises the characteristics of the study population.

2.3. Classical CAVI framework

The CAVI reflects the stiffness of the complete arterial segment from the aortic root to the ankle [36], [37]. In theory, the CAVI is derived from the stiffness parameter β (proposed by Hayashi) and the Bramwell-Hill equation. Whilst the original β parameter applied only to a local segment of the artery, the CAVI adapts it to measure stiffness across a long section of the arterial tree [27], [38]:

$$\beta = ln(\frac{P_s}{P_d}) \times \frac{D}{\Delta D} \quad (1)$$

where: P_s and P_d are systolic and diastolic blood pressures (DBP) in Pa. D is the arterial diameter, and ΔD is the pressure-induced diameter change. Applying the modified Bramwell-Hill:

$$PWV^2 = \frac{\Delta P}{\rho} \times \frac{V}{\Delta V} \approx \frac{\Delta P}{\rho} \times \frac{D}{2\Delta D} \quad (2)$$

$\Delta P = P_s - P_d$ is pulse pressure, and $\rho \approx 1050$ Kg/m^3 is the density of blood. The formula in the original (CAVI) article is expressed as [37]:

$$CAVI = a \times \left(2\rho \,. \frac{ln(^{P_s}/_{P_d})}{\Delta P} . haPWV^2 \right) + b \quad (3)$$

The haPWV and baPWV are often considered identical or very similar (difference < 1 m/s, r > 0.95), since baPWV approximates heart-to-ankle PWV using brachial measurements [30]. Hence:

$$CAVI = a \times \left(2\rho \,. \frac{ln(^{P_s}/_{P_d})}{\Delta P} . baPWV^2 \right) + b \quad (4)$$

$$CAVI = a \times [CAVI_0] + b \quad (5)$$

The CAVI score is a dimensionless and standardised measure of overall arterial stiffness; a and b are empirical adjustments of the $CAVI_0$ constants in Table 2 [39].

Table 1. Population characteristics (n = 4,374)

Parameters	Mean ± σ
Age (years)	55.2 ± 15.8
cfPWV (m/s)	8.5 ± 2.1
Aortic PWV (aPWV) (m/s)	7.2 ± 1.8
Brachial ankle PWV (baPWV) (m/s)	12.4 ± 2.9
Augmentation index (AIx) %	28.5 ± 12.3
Pulse pressure amplitude (PPamp) (mmHg)	45.2 ± 8.7
Systolic blood pressure (SBP) (mmHg)	128.5 ± 14.2
DBP (mmHg)	78.3 ± 9.1
Pulse pressure (PP) (mmHg)	50.2 ± 10.5
Mean blood pressure (MBP) (mmHg)	95.0 ± 10.5
Aortic SBP (mmHg)	108.6±14.8
Aortic DBP (mmHg)	74.5±7.8
Aortic MBP (mmHg)	92.8±8.0
Aortic PP (mmHg)	92.8±8.0
Brachial SBP (mmHg)	117.6±13.9
Brachial DBP (mmHg)	72.0±7.8
Brachial MBP (mmHg)	92.6±8.1
Brachial SBP (mmHg)	45.6±16.3

Table 2. The a and b coefficients values in the CAVI formula [30]

	$CAVI_0 < 7.34875$	$7.34875 \leq CAVI_0 < 10.30372$	$10.30372 \leq CAVI_0$
Coefficient a	0.85	0.658	0.432
Coefficient b	0.695	2.103	4.41

2.4. CAVI-ML algorithm

2.4.1. Algorithm pipeline

The proposed hybrid CAVI-ML algorithm reduces blood pressure dependence in arterial stiffness assessment and comprises four principal steps: importing data from the PWDB database, preprocessing and preparation, machine learning, and output and validation. Figure 1 shows the flowchart of the proposed algorithm.

- Raw CAVI calculation: we calculate the raw CAVI using Shirai *et al.* [19] in (4)
- Ideal physiological target definition: we calculate the mean value of the raw index CAVI based on a healthy reference subpopulation (normal blood pressure, non-diabetic, non-smokers, and BMI < 25 kg/m²). This serves as an ideal physiological target:

$$CAVI_{Target} = \overline{CAVI}_{Healthly} \quad (6)$$

– Identification of the optimal coefficients a_{opt} and b_{opt}: for each subject i, we identify the coefficients ($a_{opt(i)}$ and $b_{opt(i)}$) that minimise the difference between the raw ($CAVI_{Raw}$) and the physiological $CAVI_{Target}$, using Ridge regression with L2 regularisation (λ = 0.01):

$$(a_{opt(i)}, b_{opt(i)}) = argmin\, ||CAVI_{Target(i)} - (a \times CAVI_{Raw}(i) + b)||^2 + \lambda (a^2 + b^2) \quad (7)$$

– Predictive features construction: the training features of the RF model are shown in Table 3.

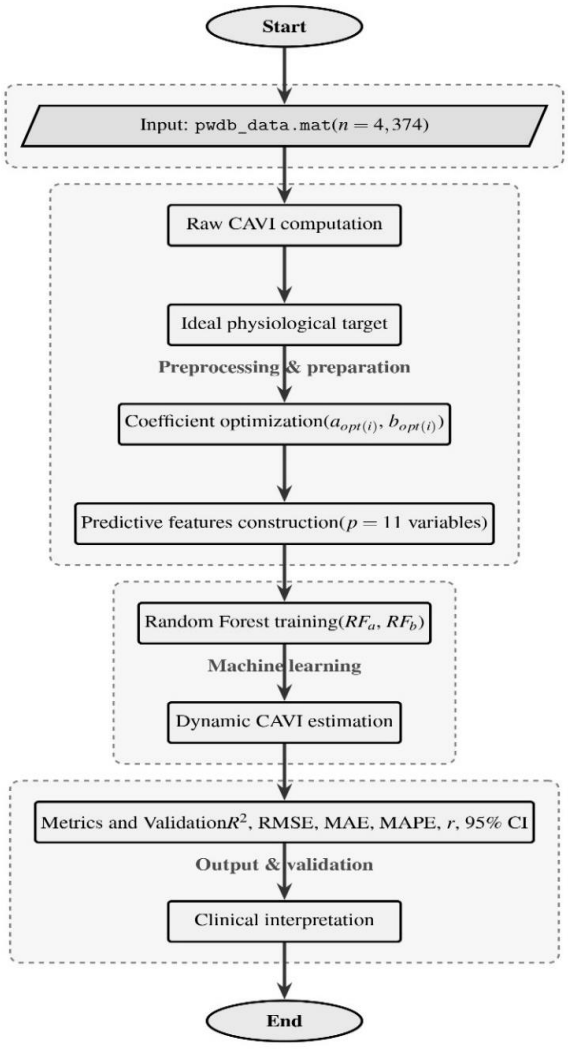

Figure 1. Dynamic normalisation pipeline of the (CAVI –ML) algorithm

Table 3. Training features of the RF model

Features	Physiological role
Age	Primary risk factor
SBP	Left ventricular load
DBP	Coronary perfusion pressure
PP	Reflects aortic stiffness
MBP	Infusion pressure indicator
cfPWV	Gold standard for central stiffness
aPWV	Direct indicator of aortic stiffness
faPWV	Lower limb stiffness
Aix	Percentage increase in central blood pressure resulting from the reflected wave
PP_{amp}	Peripheral hemodynamics

– RF model training: we chose the 'RF' model given its ability to capture non-linear relationships among hemodynamic parameters and its robustness against overfitting. We trained the RF models (RF_a and RF_b) (number of trees = 100, minimum leaf size = 10, number of features per split = 3) as:

$$a_{pred} = RF_a\ (Age, SBP, DBP, PP, MBP, PWV, AIx,\ PP_{amp}) \quad (8)$$

$$bpred\ =\ RFb\ (Age, SBP, DBP, PP, MBP, PWV, AIx, PPamp) \quad (9)$$

Table 4 summarises the optimal hyperparameters for the RF models (RF_a and RF_b).

Table 4. RF model hyperparameters

Hyperparameters	Explored values	Selected value
Number of trees (n-estimators)	[50,100,200,500]	100
Maximum depth (max-depth)	[10,20,30]	30
Minimum samples to split a node (min-samples-split)	[2,5,10]	5
Min samples per leaf node(min-samples-leaf)	[1,2,5,10]	10
Features considered for best split (max-features)	$[\sqrt{(n-features)}]$	3

Train/test separation: 80% / 20% (3 500 / 874 subjects)

– Dynamic CAVI calculation: once the RF models have predicted the coefficients, we calculate the dynamic value ($CAVI_{Dyn}$) as:

$$CAVI_{Dyn}\ =\ a_{pred}\ \times\ CAVI_{Raw}\ +\ b_{pred} \quad (10)$$

– Metrics and validation: to evaluate the models' performance, we calculated the performance metrics using the equations shown in Table 5.

Table 5. Models' performance evaluation metrics.

Metrics	Equation
Coefficient of determination (R^2)	$R^2 = 1 - \frac{\sum(y-\hat{y})^2}{\sum(y-\bar{y})^2}$ (12)
Root mean square error (RMSE)	$RMSE = \sqrt{\frac{\sum(y-\hat{y})^2}{n}}$ (13)
Mean absolute error (MAE)	$MAE = \sum\frac{\lvert y-\hat{y}\rvert}{n}$ (14)
Mean absolute percentage error (MAPE)	$MAPE = 100 \times \sum\frac{\frac{\lvert y-\hat{y}\rvert}{y}}{n}$ (15)
Pearson's correlation coefficient r with 95% CI (Fisher's transformation)	$r = \frac{\mathrm{cov(X,Y)}}{\sigma_X\sigma_Y}$ (16) $IC = \tanh(0.5\ln(\frac{1+r}{1-r}) \pm \frac{1.96}{\sqrt{n-3}})$ (17)

where:$\hat{y}$ is the target value of the variable of interest; y is the mean of observed values, and n *is* the number of observations (sample size)

– Clinical interpretation: The clinical interpretation compares $CAVI_{Dyn}$ with $CAVI_{Target}$ based on the following reasoning:

$$\mathrm{CAVI_{Dyn}}\ \approx\ \mathrm{CAVI_{Target}}\ \text{Normal arterial stiffness} \quad (11)$$

$$\mathrm{CAVI_{Dyn}} > \mathrm{CAVI_{Target}}\ \text{Accelerated vascular ageing} \quad (12)$$

$$\mathrm{CAVI_{Dyn}} < \mathrm{CAVI_{Target}}\ \text{Lower than normal stiffness} \quad (13)$$

The standardised deviation, or Z-score, is defined as:

$$\mathrm{Z_{CAVI(i)}} = \frac{CAVI_{Dyn(i)} - CAVI_{Target}}{\sigma_{Residual}} \quad (14)$$

where $\sigma_{Residual}$ is the standard deviation of the residuals in the healthy population. A $Z_{CAVI} > 1.96$ value greater than 1.96 indicates abnormally high stiffness ($p < 0.05$).

2.4.2. Algorithm description

The CAVI-ML algorithm provides a personalised estimation of arterial stiffness based on the cardio-ankle vascular dynamic index ($CAVI_{Dyn}$). The process begins by calculating the raw ($CAVI_{Raw}$) using the original formula by Shirai *et al.* [19]. A healthy reference subpopulation (normotensive, non-diabetic, non-smokers, BMI < 25 kg/m²) defines the ideal physiological target ($CAVI_{Target}$). A Ridge regression (λ = 0.01) applied to this subgroup minimises the difference between $CAVI_{Target}$ and the linear transformation of the raw CAVI. For all subjects in the cohort, we identify the individual coefficients $a_{opt(i)}$ and $b_{opt(i)}$. Then, when applied to $CAVI_{Raw}$, they yield a corrected value consistent with the physiological relationship established in healthy subjects. A set of hemodynamic parameters: age, systolic and DBPs, pulse pressure, mean arterial pressure, central and peripheral pulse wave velocities, the rise index, and the amplitude of pulse pressure serves as training features for two RF models, RF_a and RF_b, each comprising 100 trees, with a minimum leaf size set to 10 and 3 variables tested per node. These models are trained on 80 % of the cohort (3,500 subjects) to predict the coefficients a_{pred} and b_{pred}, with the remaining 20 % reserved for testing. Once these coefficients have been predicted, the $CAVI_{Dyn}$ is calculated for each individual using (11). The predictive performance of the models is assessed using standard metrics Table 5. The clinical interpretation compares $CAVI_{Dyn}$ with $CAVI_{Target}$; a higher value indicates accelerated vascular ageing. A Z-score is calculated to quantify this deviation, using (14), with a threshold of 1.96 ($p < 0.05$), to identify abnormally high arterial stiffness.

3. RESULTS

3.1. Pressure dependence

The main advantage of CAVI-ML is its relative independence from blood pressure during the measurement. Figure 2 illustrates the correlation coefficient r of the CAVI-ML approach compared to the raw CAVI and the gold standard cfPWV. Raw CAVI exhibits substantial correlations with SBP: r = 0.613 and pulse pressure (PP: r = 0.735), confirming its residual dependence on blood pressure despite theoretical attempts at normalisation. In contrast, the proposed dynamic CAVI significantly reduces these correlations to r = 0.251 for SBP and r = 0.201 for PP, corresponding to a relative reduction of 59% and 73%, respectively. Compared to the gold-standard cfPWV, which shows correlations of r = 0.662 with SBP and r = 0.733 with PP. The CAVI-ML algorithm is 62% less dependent on blood pressure.

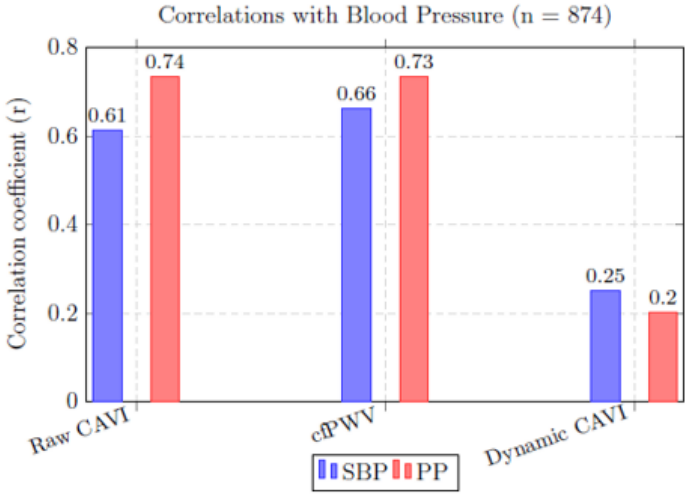

Figure 2. Comparison of the correlations observed between raw CAVI, cfPWV, and dynamic CAVI and blood pressure

3.2. Feature importance analysis

We used permutation importance analysis to improve the interpretability of the CAVI-ML algorithm and to identify the impact of hemodynamic parameters in the RF model. Higher importance indicates a greater predictive contribution from the corresponding parameters. The results of this analysis are presented in Figure 3.

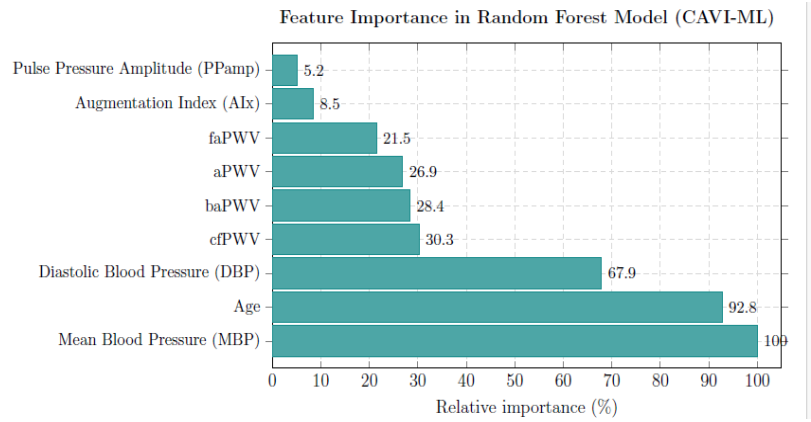

Figure 3. Importance of parameters in the RF model

Analysis of parameter importance using the RF method (Figure 3) reveals that MBP is the dominant predictor (100% relative importance), followed by age (92.8%) and DBP (67.9%). The contributions of pulse wave velocities are moderate but balanced: cfPWV (30.3%), baPWV (28.4%), aPWV (26.9%) and femoral ankle pulse wave velocity (faPWV) (21.5%). Supplementary indices such as the augmentation index (AIx) and pulsed pressure amplitude (PPamp) contribute marginally (<10%), suggesting that they do not significantly improve the reduction in persistent dependence.

3.3. Arterial stiffness categories

We reclassified the 4,374 subjects using the new algorithm into five categories normal, borderline, moderate, advanced, and high risk, as shown in Figure 4. The CAVI-ML shifts patients toward normal and borderline categories (↑ normal: +2.9%, ↑ borderline: +2.4%), while reducing classification in higher severity categories (↓ moderate: -3.1%, ↓ advanced: -1.6%, ↓ high risk: -0.6%).

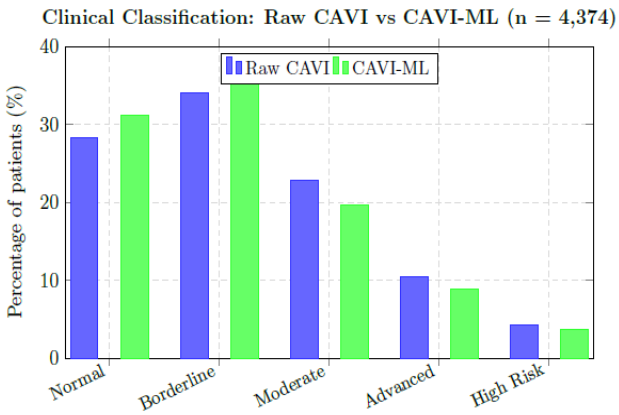

Figure 4. Clinical reclassification of subjects' arterial stiffness categories using (CAVI-ML) compared to raw CAVI

3.4. Age and arterial stiffness correlation

Age plays a physiological role in arterial stiffness. This section examines the relationship between age and the raw CAVI, and between age and CAVI-ML. Figure 5 shows a strong linear correlation between age and raw CAVI, and between age and CAVI-ML (CAVI-ML, r = 0.91 vs 0.88 for raw CAVI). This linear relationship indicates that the older the participants, the higher the arterial stiffness index, confirming that ageing is a major non-modifiable risk factor. The algorithm (CAVI-ML) does not eliminate any biologically significant signal whilst effectively correcting for pressure-induced bias. The results of the RF model's performance are summarised in Table 6.

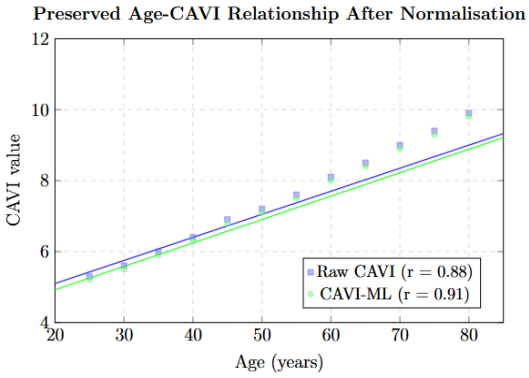

Figure 5. Analysis of the positive correlation between age, the raw CAVI and the CAVI-ML

Table 6. Performance metrics of CAVI–ML algorithm

Metrics	Value
R^2	0.978
RMSE	0.123
MAE	0.098
MAPE	1.24%
Pearson's r (CAVI brut **vs**CAVI-ML)	0.989
IC 95% (Fisher's transformation)	0.986 –0.992

4. DISCUSSION

4.1. Principal finding

The hybrid algorithm CAVI-ML operates as a machine learning model that complements a physical model based on individual data. This design preserves the physiological interpretability of the CAVI model whilst flexibly correcting the residual dependence on blood pressure. The reduction in correlation with SBP from r = 0.613 to r = 0.251 (a 59% decrease) and with PP from r = 0.735 to r = 0.201 (a 73% decrease) confirms that personalised normalisation effectively isolates arterial stiffness from acute pressure variations.

The most significant predictive factor is mean arterial pressure (MAP) (100%), followed by age (92.8%) and DBP (67.9%). These results are clinically consistent, as age reflects cumulative structural and functional changes in the arteries. DBP, which reflects the baseline tension of the arterial wall during the cardiac cycle, is significantly higher than SBP.

The predictive value of pulse wave velocities cfPWV, baPWV, aPWV and faPWV is moderate (21–30%). aPWV measures aortic arterial stiffness, whilst baPWV provides an assessment of overall arterial stiffness, but is influenced by both central and peripheral vascular resistance. faPWV assesses peripheral arterial stiffness, and cfPWV reflects central stiffness. Although AIx and PPamp provide useful information on the interaction between incident and reflected waves, they are not a direct measure of arterial stiffness. Multiple factors influence them, including heart rate, left ventricular ejection time and peripheral resistance. These results suggest that the algorithm (CAVI-ML) effectively extracts the most physiologically relevant parameters, whilst minimising the influence of less informative characteristics.

Clinical interpretation compares $CAVI_{Dyn}$ with $CAVI_{Target}$ values: normal arterial stiffness and good elasticity result in $CAVI_{Dyn} \approx CAVI_{Target}$. This reflects a normal elastin-to-collagen ratio, preserved damping function (Windkessel effect) and pulse wave reflection during diastole. Accelerated vascular ageing is characterised by a $CAVI_{Dyn}$ value > $CAVI_{Target}$, resulting from pathophysiological processes (extracellular matrix remodelling, medial calcification and endothelial dysfunction). These changes lead to an increase in the pressure gradient, left ventricular afterload and premature reflection of the arterial pulse wave. A value of $CAVI_{Dyn} < CAVI_{Target}$ is generally observed in young people, athletes or those undergoing vasoprotective treatment, indicating good arterial compliance. However, conditions such as severe hypotension, low-output heart failure or certain valvular heart diseases reduce the measured stiffness.

The high predictive accuracy R^2 = 0.978, RMSE = 0.123 further supports the reliability of the correction. Importantly, the physiological relationship with age is preserved: the correlation between CAVI and age remains strong for raw CAVI: r = 0.88; CAVI-ML: r = 0.91, reflecting the well-known progressive loss of arterial elasticity with ageing. This indicates that CAVI-ML does not artificially eliminate a biologically significant signal, but specifically targets pressure-induced artefacts.

4.2. Literature comparison

We compared our results against those of studies in the literature as shown in Table 7. Compared to the fixed-coefficient method of Shirai *et al.* [19] and the multiple regression approach of Spronck *et al.* [40], which achieved approximately 30% reduction in pressure dependence, CAVI-ML more than doubles this improvement (up to 73%). Notably, Giudici *et al*. [41] subsequently demonstrated that $CAVI_0$ may enhance pressure-independent assessment, particularly in populations with large inter-individual blood pressure differences. Our RF model, trained on a simulated dataset (n = 4,374), achieves a quantifiable and substantial reduction, positioning CAVI-ML as the most effective normalisation strategy reported to date.

Table 7. Comparison of standardisation approaches

Study	Method	Dependency reduction	Population	Key contribution / Limitation
Shirai *et al.* [19] (2006)	Fixed coefficients	Reference	Japanese (n = 500)	Original CAVI formulation; persistent BP dependence acknowledged
Spronck *et al.* [40] (2017)	Multiple regression	≈30%	European (n = 300)	Significant reduction vs. original CAVI; linear correction only
Giudici *et al.* [41] (2021)	Review/validation of $CAVI_0$	Contextual (no new quantification)	Multi-Population review	Confirmed $CAVI_0$ improves pressure independence, especially with large inter-individual BP differences
CAVI-ML (2026)	RF	59–73%	Simulation (n = 4,374)	A significant improvement on previous methods; a quantised, non-linear correction

4.3. Limitations, prospects, and clinical implications

The PWDB database contains only simulated data from healthy adults. Pathological cases (for example, patients with high blood pressure, diabetes or end-stage renal failure) or the effects of medication are not included. Prospects and clinical implications:

- Validation of the algorithm CAVI-ML on prospective clinical datasets PhysioNet, MIMIC-IV: a comprehensive database comprising cardiovascular case studies, reflecting the diversity of populations in terms of age, sex, ethnic origin and comorbidities.
- Development of deep learning architectures 1D CNN, LSTM that directly use raw arterial pulse wave signals, without the need for manual feature extraction.
- Integration of the CAVI-ML algorithm into a portable, real-time embedded device, for example, an ambulatory cardiology clinic.
- Prospective studies comparing CAVI-ML with imaging biomarkers (carotid intima-media thickness, coronary calcium score) to demonstrate its clinical utility and predictive value.
- Deployment in telemedicine for remote cardiovascular monitoring.

4. CONCLUSION

This article presented an innovative approach, CAVI-ML, a hybrid algorithm that combines the classical framework CAVI with an 'RF' regression model. We used the open-access PWDB database, which contains pulse waves from 4,374 virtual subjects, to obtain a personalised estimate of arterial stiffness, independent of blood pressure. The innovative aspect of this study is the a_{pred} and b_{pred} coefficients customisation for each subject according to their age and hemodynamic parameters. The model achieved excellent accuracy (R^2 = 0.978, RMSE = 0.123) and a significant reduction in pressure dependence: 59% for systolic pressure and 73% for differential pressure. This resulted in greater independence from the gold standard cfPWV (a 62% reduction in dependence). The permutation importance analysis confirms that MAP (100%) and DBP (67.9%) are the most important predictors of the RF models. The CAVI-ML algorithm provided a robust, interpretable measurement that is significantly less dependent on blood pressure, outperforming both raw CAVI and cfPWV. These findings enable more accurate and personalised assessment of arterial stiffness in clinical and epidemiological settings and improve the prediction of cardiovascular diseases.

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AUTHOR CONTRIBUTIONS STATEMENT

This journal uses the Contributor Roles Taxonomy (CRediT) to recognize individual author contributions, reduce authorship disputes, and facilitate collaboration.

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Lilia Radjef	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Tahar Omari	✓	✓		✓	✓	✓			✓	✓	✓	✓		
Karim Baiche	✓	✓		✓	✓	✓			✓	✓	✓		✓	

C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
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Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

CONFLICT OF INTEREST STATEMENT

The authors state no conflict of interest.

DATA AVAILABILITY

The PWDB is publicly available at https://peterhcharlton.github.io/pwdb/.

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BIOGRAPHIES OF AUTHORS

Lilia Radjef received her Master's degree in Biomedical Engineering in 2021. In March 2022, she was admitted to the national Doctoral programme in Biomedical Engineering at M'Hamed Bougara University of Boumerdes, Algeria. She is a member of the Systems and Telecommunications Engineering Laboratory (LIST) at the Faculty of Technology. Her doctoral research focuses on arterial stiffness assessment and biomedical signal processing. Since July 2023, she has gained professional experience as a biomedical maintenance engineer and medical physicist in medical imaging at Tizi Ouzou Hospital. Her research interests include arterial stiffness estimation, physiological signal processing, biomedical data analysis, medical instrumentation, artificial intelligence applications in biomedical engineering, medical device technologies, and medical imaging. She can be contacted at email: l.radjef@univ-boumerdes.dz.

Tahar Omari the Engineer degree in Biomedical Engineering in 2006, the M.Sc. degree in 2009, and the Ph.D. degree in 2017 from the University of Tlemcen, Algeria, followed by the Habilitation (HDR) in 2019 from the same institution. He is currently an Associate Professor at the University of Ain Temouchent, Algeria, where he teaches programming and biomedical instrumentation. His research covers cardiovascular monitoring, non-invasive blood pressure estimation, pulse transit time analysis, and arterial stiffness assessment. He can be contacted at email: tahar.omari@univ-temouchent.edu.dz.

Karim Baiche Received the Engineer degree in Electronics and Control Engineering in 1992 from the University of Setif, Algeria. The M.Sc. (Magister) degree in Applied Automation from the Institute of Hydrocarbons and Chemistry (INHC)-Boumerdes in 1998, and received his Ph.D. from the University of M'Hamed Bougara, Boumerdes, Algeria in 2014. He obtained the Habilitation (HDR) in Electrical Engineering, Control Engineering and Signal Processing from the same university in 2019. He is currently a full Professor at the University of M'Hamed Bougara, Boumerdes, Algeria, where he is involved in teaching and practical training in telecommunications and biomedical instrumentation. His main current research interests include signal processing, system diagnostics and evolutionary computation and metaheuristics. He can be contacted at email: kbaiche@univ-boumerdes.dz.