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Evaluation of the Age Dependence of Conventional and Novel Photoplethysmography Parameters

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Abstract

Background Cardiovascular (CV) mortality increases with age partly due to physiological ageing of the CV system. Early vascular ageing raises CV risks. Personalizing CV risk assessment by defining CV age could reduce CV events. Photoplethysmography (PPG), which analyses the peripheral arterial pulse wave, may be an effective method for estimating CV age. Ageing index (AGEi) and some other PPG parameters were proven to have age correlation; however, the age dependence of many other pulse wave parameters remains unclear. We aimed to identify age correlations of PPG indices and pulse rate variability (PRV) parameters including a few novel parameters which were calculated to further investigate the various aspects of ageing.

Our study included 118 healthy (M/F: 53/65, mean age: 31.8 ± 11.8 SD) volunteers for PPG parameter calculation and 106 (M/F: 44/62, mean age: 32.6 ± 12.2 SD) for PRV parameters (age: 19–74). 2-min pulse wave recording was obtained using a pulse oximeter. An automated, proprietary software evaluated PPG and PRV parameter values, which were compared with chronological age (Pearson correlation and non-linear analysis).

Results PPG parameters describing various time-dependent aspects of cardiac ejection positively correlated with age, while those indicating arterial elasticity showed negative correlation. Composite PPG parameters proposed as indicators of CV health and fitness had negative, non-linear correlation. Most PRV parameters exhibited negative correlation, indicating reduced adaptive capacity due to ageing ($p < 0.05$, $|r| > 0.3$).

Conclusions PPG-based pulse waveform analysis provides a wide range of age-related parameters which display different patterns of age correlation, making it a promising method for estimating cardiovascular age. Future studies will include subjects with vascular ageing conditions beyond physiological values (e.g., hypertension, heart failure, coronary artery disease).

Keywords Photoplethysmography, Vascular ageing, Pulse wave analysis, Pulse rate variability

1 Introduction

Cardiovascular (CV) diseases, including atherosclerosis and stroke are major public health challenges, consistently ranking among the leading causes of death worldwide in recent decades, especially in the elderly population [1, 2]. Age-related phenotypic alterations in the CV system, and more importantly their accelerated development brought about by CV risk factors, are among the most relevant (patho)physiological changes that drive these diseases [3, 4]. Therefore, identifying

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new, affordable biomarkers that reflect (CV) aging is critical for improving treatments and preventive strategies.

Peripheral pulse wave analysis may offer a valuable method for monitoring CV health and predicting disease progression [5, 6]. Calculating heart rate from continuous pulse wave recordings may have relevance in diagnostics, as pulse rate variability (PRV) is an important indicator of various diseases [7–9]. Beyond PRV, the morphological characteristics of pulse waves have yielded considerable attention, with numerous studies suggesting that these parameters may be associated with CV disease states such as atherosclerosis and heart failure [5, 10, 11].

Photoplethysmography (PPG) is a simple, easily accessible, and highly repeatable method for real-time monitoring of pulse waves [12]. This non-invasive technique involves illuminating the skin and tissues below, typically the finger, with an LED and measuring the intensity of the reflected or transmitted light, which corresponds to pressure changes in the vascular system. Importantly, PPG has no known adverse effects [13].

The promising results from previous studies suggest that PPG-based pulse wave analysis could gain traction in CV diagnostics and home monitoring in the near future [14]. While it holds potential as a tool for assessing CV aging, its broader use is constrained by the limited investigation of age-related correlations in most PPG-derived parameters. Although some parameters have been linked to age-related changes, most studies have focused on the age dependence of individual or a few selected parameters, leaving the majority unexplored [6, 15–17].

However, a combination of parameters or composite measures derived from multiple parameters might better capture age-related changes than single parameters alone. PPG-based monitoring devices, equipped with advanced algorithms, enable the simultaneous assessment and complex analysis of numerous parameters [5, 18]. Consequently, research aimed at identifying a set of simultaneously recorded PPG features with the strongest correlation to CV age could significantly enhance the potential of PPG-based pulse wave analysis. Additionally, most published studies have assumed linear age dependence of parameters [15–17], which may not accurately reflect reality. Many parameters could exhibit non-linear relationships with age, particularly in women, where CV changes accelerate after menopause.

The primary goal of our research was to identify age-dependent changes in a large set of simultaneously recorded pulse wave parameters, including PRV parameters, pulse morphology parameters and newly developed composite score parameters, aiming to establish the utility of PPG-based pulse wave analysis as a tool to assess CV aging. For this purpose, we utilized an efficient, automated software that enables accurate, rapid, and reproducible evaluation of large datasets; and a comprehensive database of pulse wave data from a healthy adult population was established. To better characterize age-dependent parameter changes, we used both linear and non-linear analyses to describe age-related trends.

2 Methods

Participants were required to meet specific inclusion criteria, including self-reported good physical and mental health, absence of CV disease, no use of CV medications, non-pregnancy, a BMI between 18 and 26 kg/m^2, non-smoker status, negligible alcohol consumption, and no reported history of chronic or cancerous diseases.

Subjects were primarily recruited from among the healthy employees, relatives of employees, and students of Semmelweis University. Recruitment was facilitated by the University's Occupational Health Service and social networking platforms. All tests were conducted in the laboratory facilities of Semmelweis University. The study protocol was designed in accordance with the Declaration of Helsinki and approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (approval number: 120/2018).

Participants provided informed consent and completed a health questionnaire, which collected personal and health-related data, including medical history, lifestyle, and medication use. Blood pressure (BP) was measured three times using an automatic sphygmomanometer. Subjects with systolic BP higher than 140, and/or diastolic BP exceeding 90 mmHg were excluded from the study. All data was recorded anonymously.

Pulse wave recordings were obtained using a Berry BM 1000B pulse oximeter placed on the right index finger. This non-invasive device, certified by the manufacturer, recorded pulse waves for 140 s while the participant remained seated and still. The pulse oximeter transmitted data via Bluetooth to a mobile application (SCN4ALL/HeartReader), developed by E-Med4All Europe Ltd. (Budapest, Hungary), which uploaded the recordings to a secure online database. The studies for the repeatability and reliability of the measurements, along with the detailed description of signal processing methods of the system have already been published [19, 20]. Briefly, the measurement takes 140 s to be completed. Due to filtering and preprocessing reasons discussed in detail by Kulin et al. [19], 120 s of the recording is used for further analysis. Parameters were defined for each individual cycle that met certain predefined signal quality criteria, and the average of these values was reported.

The proprietary software used for analysis identified fiducial points on the pulse wave, allowing for the calculation of both classical and novel pulse wave parameters (PPG parameters), including pulse rate variability (PRV

parameters) metrics. The primary criterion for selecting parameters was to choose those that, according to the literature, describe various aspects of CV function—such as temporal relationships, arterial elasticity, and autonomic function—and have previously been reported to correlate with CV age, mortality, and (severity) of various CV diseases. Table 1. shows the parameters and their descriptions.

The parameter values obtained from the pulse waveform analysis were compared with the age (in years) of the volunteers (JASP 0.19.1 software, JASP Team (2024)) using Pearson correlation and Generalised Additive Models (GAM) analysis (Google Colaboratory. Retrieved December 14, 2024, from https://colab.research.google.com/). GAM is an advanced statistical modelling method designed to capture both linear and non-linear relationships between variables. (see the 'Additional file1.docx' for a more detailed description of the model). A p value of $<=0.05$ was accepted as significant throughout.

During the preparation of this work the author(s) used ChatGPT and Grammarly to improve the readability and find shorter expressions to fit word limit. After using these tools/services, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

3 Results

Our study included 118 healthy (M/F: 53/65, mean age: 31.8 ± 11.8 SD) volunteers for PPG parameter calculation and 106 (M/F: 44/62, mean age: 32.6 ± 12.2 SD) for PRV parameters. Participants were aged between 19 and 74 years.

The relationship between age and CV function may encompass both linear and non-linear factors. To comprehensively evaluate this, we performed two distinct analyses: a Pearson correlation to assess linear associations and a GAM analysis to capture potential non-linear trends.

Tables 2. and 3. summarize the results of Pearson correlation and GAM analysis between PPG and PRV parameters and age.

3.1 Pearson Correlation Analysis

Among the conventional PPG morphology parameters that significantly correlated with age, AGEi (r = 0.485), SysAlpha (r = − 0.418), and d/a (r = − 0.376) (Fig. 1A) demonstrated the strongest age dependence. Additionally, time-related parameters of the PPG curve that characterize ejection-related ventricular activity, such as ET(PPG) (r = 0.589), Crest Time (r = 0.570), LVETi (r = 0.539), and the proprietary parameters eLVET1* (r = 0.548) and eLVET2* (r = 0.450), also exhibited strong correlations with age (Table 2., Fig. 2.).

Furthermore, age correlation was observed in other novel parameters, including DNi* (r = -0.517) and c-d incidence* (r = 0.419) (Fig. 1B). Finally, all proprietary score parameters demonstrated significant correlations with age: Heart Fitness Score (r = − 0.493), CV Health Score (r = − 0.450), and Total Score (r = − 0.301) ($p < 0.001$ for all cases).

Several of the PRV parameters exhibited a moderate, but significant negative correlation with age (Table 3. and Fig. 3.). The cTotalPower (r = − 0.325) (Fig. 3A) and cSDRR (r = − 0.401) parameters (Fig. 3B) exhibited the strongest age dependence ($p < 0.001$) among frequency-domain and time-domain measures, respectively. The age correlation of non-linear PRV parameters proved to be weaker, except for cSD2 (r = − 0.428).

3.2 GAM Analysis

The GAM analysis allowed the identification of non-linear trends. Similar to the Pearson correlation analysis, this analysis also found significant correlations ($p < 0.05$) between age and PPG parameters, except for Si and b/a parameters. Among the PRV parameters, cSDRR, cTotalPower, cHFpow and cSD2 were significantly correlated with age based on GAM analysis. The GAM analysis confirmed linear (for AGEi, LVETi, eLVET2*, DNi*, SysAlpha) or near-linear (for b/a, d/a, Ri, Si) relationship between most PPG parameters and age. However, for some parameters, a non-linear trend with age was observed.

All Score parameters demonstrated a clear non-linear decline, especially after the age of 40. (Fig. 4A and B). The eLVET1* and c-d incidence* parameters showed a moderate non-linear upward trend followed by a plateau.

Crest Time exhibited extreme non-linearity with multiple inflection points (Fig. 4C).

For PRV parameters, cTotalPower and cSDRR showed a clear linear decrease with age. The cMHR did not have a significant correlation with age (nor did it when Pearson correlation analysis was performed) (Fig. 4D).

4 Discussion

From a public health perspective, addressing the assessment and monitoring of CV ageing is crucial, as CV diseases continue to be the leading cause of mortality, particularly in older populations. As the global population ages, the demand for reliable, non-invasive methods to meet this need is increasing. Photoplethysmography (PPG) appears to be a promising tool in this regard, as it offers a simple but effective way to monitor CV function by pulse wave analysis. Although the age correlation of some PPG parameters has been investigated, the full scope of age-related changes in pulse wave characteristics is not yet fully evaluated. [21–23] This study, by

Table 1 PPG and PRV parameter names and descriptions

PPG/PRV parameters	Abbreviations/ parameter names	Descriptions
Stiffness index	Si	Si = h/ PTT (m/s); h is the height of the person in meters. PTT is the pulse transit time in seconds [6].
b/a	b/a	The ratio of the first two inflection points of the second derivative of the pulse wave. Correlates with the elasticity of the large arteries and the contractility of the left ventricle [6].
d/a	d/a	The ratio of the first and fourth inflection points of the second derivative of the pulse wave. Independent cardiovascular risk factor [6].
Ageing-index	AGEi	The value derived from the second derivative of the pulse wave. AGEi = b-c-d-e/a [6].
Reflection index	Ri	The ratio of the amplitude of the diastolic peak to the amplitude of the systolic peak [6].
Systolic slope inclination	SysAlpha	The angle between the maximal inclination of systolic upstroke and the horizontal axis [37].
c-d point detection ratio *	c-d incidence *	c-d point detection ratio specifies the percentage of those pulse cycles in the recording in which c and d points of the second derivative of the pulse wave curve are successfully identified by the algorithm over all identified heart cycles
Left ventricular ejection time index	LVETi	Left ventricular ejection time indexed for heart rate (LVETi) was calculated from sex-specific resting regression equations LVETi(male) = 1,7 × heart rate + ET, LVETi(female) = 1,6 × heart rate + ET [26].
Dicrotic notch index *	DNi *	Describes the relative position of the diastolic peak to the dicrotic notch (the valley induced by the aortic valve closure before the diastolic peak)
Early left ventricular ejection time 1 and Early left ventricular ejection time 2	eLVET1 * eLVET2 *	The early left ventricular ejection time 1 and 2 are the two-time components of "Crest Time". eLVET1 is measured from the start of the period to the first peak of the first derivative of the pulse, whereas eLVET2 is defined as the time duration from the first peak of the first derivative PTG to the peak of the systolic wave
Crest Time	Crest Time	The time elapsed between the beginning of the period (foot) and the maximum systolic amplitude (peak) [6].
Left ventricular ejection time	ET(PPG)	The ejection time is the time elapsed between the beginning of the pulse period and the aortic valve closure (dicrotic notch/e-point) [38].
Score parameters: Scores were calculated based on the 30 + parameters derived from the proprietary analysis of the 2 min pulse-wave recording. The max. value is 100. Values below 70 might indicate that there is reason to evaluate details and to consult professionals for a more thorough health check		
Scores *	Total Score *	Calculated on the basis of the all 30 + cardiovascular and pulse rate variability parameters derived from the proprietary analysis of the 2 min pulse-wave recording. The Total Score is the master of all the other sub-scores, which can help to identify stronger and weaker aspects of the subject's CV status/health
	CV Health Score *	Obtained from the parameters that correspond with the function of the heart and the condition and aging of the arteries
	Heart Fitness Score *	Certain pulse wave parameters are influenced by the athletic lifestyle and athletic capabilities of the subject, so these aspects are marked by this score. This score provides information mostly about the health level of the HEART
PRV Time-domain parameters		
correctedMHR	cMHR	PRV Time-domain parameter. The mean heart rate. Corrected: see comment at "cTotal-Power"

Table 1 (continued)

PPG/PRV parameters	Abbreviations/ parameter names	Descriptions
correctedMNN	cMRR	PRV Time-domain parameter. The mean normal-to-normal interbeat interval [39]. Corrected: see comment at "cTotalPower"
corrected SDNN	cSDRR	PRV Time-domain parameter. The standard deviation of the interbeat intervals (ms). Its value is influenced by all cyclic components affecting heart rate variability and can be considered a quasi-summative autonomic nervous system index. Corrected: see comment at "cTotalPower" [39].
correctedrMSSD	crMSSD	PRV Time-domain parameter. The square root of the mean squared differences of successive interbeat intervals. Its value provides information primarily about the parasympathetic regulation of the heart and used to estimate the vagally mediated changes. The value of rMSSD could refer to the quality of electrical stability of the heart [39]. Corrected: see comment at "cTotalPower"
corrected pNN50	cpNN50	PRV Time-domain parameter. The proportion of differences of successive IBIs exceeding 50 ms. It characterizes parasympathetic activity.[39] Corrected: see comment at "cTotalPower"
PRV Frequency-domain parameters		
corrected Total Power (ms2)	cTotalPower	PRV Frequency-domain parameter. It specifies the area under the complete frequency-domain analysis curve. This reflects the activity of the entire autonomic nervous system. Corrected: automatic detection of irregular cycle lengths and application of cubic spline interpolation applied [39].
corrected HF Power	cHFpow	PRV Frequency-domain parameter. Absolute power of the high-frequency band (0.15–0.4 Hz). HF power is the marker of parasympathetic activity [39]. Corrected: see comment at "cTotalPower"
corrected LF Power	cLFpow	PRV Frequency-domain parameter. Absolute power of the low-frequency band (0.04–0.15 Hz). LF power is a marker of both sympathetic and parasympathetic activity. The LF band mainly reflects fluctuations in baroreceptor activity during resting conditions. LF power value correlates with the progression of atherosclerosis [40]. Corrected: see comment at "cTotalPower"
PRV Non-linear-domain parameters		
corrected SD1	cSD1	PRV Non-linear parameter. Standard deviation 1 of the Poincaré plot representing the length of the ellipse fitted to the plot [39].Corrected: see comment at "cTotalPower"
corrected SD2	cSD2	PRV Non-linear parameter. Standard deviation 2 of the Poincaré plot representing the width of the ellipse fitted to the plot [39]. Corrected: see comment at "cTotalPower"

*These parameters are developed by our research group. Most of them are not yet validated in clinical studies

Table 2 Results of correlation analysis of PPG parameters and age

PPG parameters	Correlation values of PPG parameters with age		Results of GAM analysis of the relationship between age and PPG parameters		
	Pearson's r	*p*	Deviance explained	EDOF	*p*
Conventional PPG parameters					
ET(PPG)	0.589	< .001	0.4000	5.6458	< .001
Crest Time	0.570	< .001	0.5092	12.4659	< .001
LVETi	0.539	< .001	0.2944	2.5483	< .001
AGEi	0.485	< .001	0.2385	2.5483	< .001
SysAlpha	-0.418	< .001	0.1834	2.5483	< .001
d/a	-0.376	< .001	0.1540	2.5483	< .001
b/a	0.207	0.025	0.0487	2.5483	0.052
Si	0.181	0.050	0.0708	2.7463	0.099
Ri	-0.159	0.085	0.0635	2.8567	0.010
Novel PPG parameters					
eLVET1*	0.548	< .001	0.3574	5.6458	< .001
DNi*	-0.517	< .001	0.2693	2.5483	< .001
eLVET2*	0.450	< .001	0.2063	2.5483	< .001
c-d incidence*	0.419	< .001	0.2459	5.6458	< .001
PPG Score parameters					
Heart Fitness Score*	-0.493	< .001	0.3310	3.3728	< .001
CV Health Score*	-0.450	< .001	0.2253	2.7463	< .001
Total Score*	-0.301	< .001	0.1815	3.3728	< .001

EDOF effective degrees of freedom, *ET(PPG)* left ventricular ejection time measured by PPG, *LVETi* left ventricular ejection time index, *AGEi* ageing-index, *SysAlpha* systolic slope inclination, *d/a and b/a* ratios of the different inflection points of the second derivative of the pulse wave, *Si* stiffness index, *Ri* reflection index, *eLVET1* and eLVET2** the early left ventricular ejection time 1 and 2 are the two-time components of "Crest Time", *DNi** dicrotic notch index, *c-d incidence** c-d point detection ratio, *Score parameters* scores were calculated based on the 30 + parameters derived from the proprietary analysis of the 2 min pulse-wave recording

* These parameters are developed by our research group. Most of them are not yet validated in clinical studies

For more information on GAM and an explanation of its measured values, see the Additional file1.docx

For a more detailed description of the PPG parameters, see Table 1

examining both conventional and novel PPG parameters, as well as PRV characteristics, provides a more comprehensive understanding of the effects of chronological ageing on the pulse waveform morphology. The importance of our research is emphasized by the fact that age is arguably the most significant risk factor for CV morbidity and mortality. This is supported by the results of Pencina et al. who found that age, sex, and race capture 63% to 80% of the prognostic performance of CV risk models [24]. This is further emphasized in the Framingham risk score, where age contributes more to the total risk score than any other variable. [25] Our study identified a diverse set of simultaneously recorded PPG parameters including ones that are related to cardiac ejection time, arterial elasticity and loss of PRV. These findings highlight the correlation of PPG parameters with chronological age, suggesting their potential use for monitoring age-related CV changes and evaluating CV health across different age groups. In addition, a major strength of this study lies in the use of a proprietary, automated software system capable of analyzing large datasets with high efficiency that enhance reliability, ensures the reproducibility of study's results [19].

Among the 16 PPG morphology parameters, ET, including its subcomponent eLVET1, as described by our research group, and LVETi, as described by Weber et al., demonstrated the strongest correlations with age, indicating a gradual decline in CV efficiency as individuals age [21, 26, 27]. Using GAM analysis, an extreme nonlinear relationship with multiple inflection points was observed between crest time and age. This is probably due to sparse sampling in older age groups. This highlights the sensitivity of nonlinear models to small sample sizes and outliers.

Arterial stiffening due to loss of arterial elasticity and structural changes in the vascular wall, such as increased collagen deposition and reduced elastin, is a hallmark of CV aging and contributes to elevated CV risk [28]. Therefore, reliable characterization of arterial distensibility by easily accessible biomarkers is an important step toward early detection and prevention of CV diseases, as well as the assessment of vascular aging [5, 29].

Our results also confirmed the findings of previous studies describing age-dependent changes in the AGEI. AGEi is a parameter derived from the second derivative of the pulse contour wave, and its correlation with age and arterial stiffness is widely recognized (as noted by Takazawa and colleagues) [15].

While pulse wave velocity (PWV) is often considered a better measure for assessing CV aging because of its broader predictive power at the population level, AGEi shows considerable potential as a complementary tool, particularly in individual risk assessment. The strong correlation between the second-derivative PPG signal parameters, particularly AGEi and PWV, has been published in several publications [16, 30]. These results highlight the potential of AGEi as a practical, non-invasive measure of individual risk stratification, especially when measurement of PWV is less accessible. The sensitivity of AGEi to age-related vascular changes is a valuable addition to CV diagnostics, complementing PWV's population-level insights. Our study has also shown that DNi has stronger age dependence than AGEi suggesting that it may have relevant potential in monitoring a progressive decline in arterial distensibility (DNi, a proposed

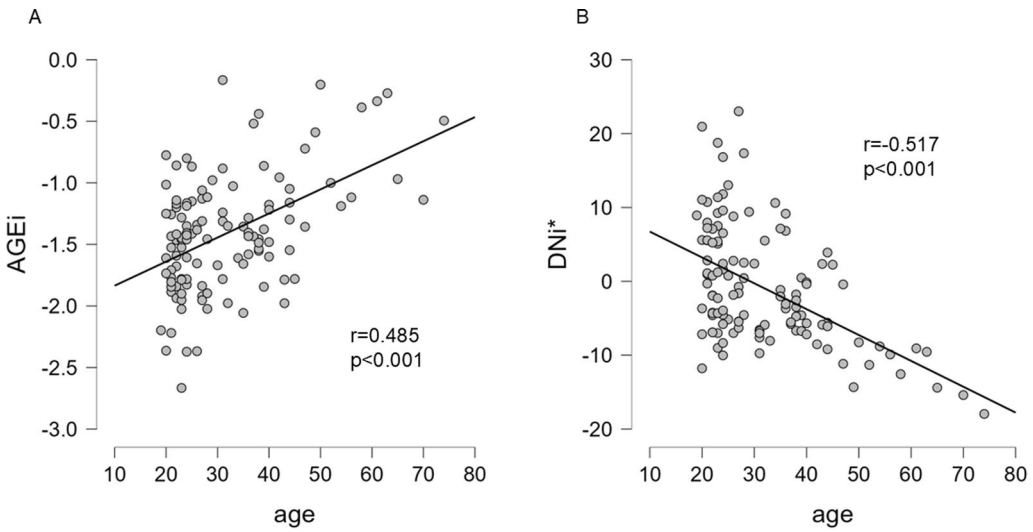

Fig. 1 Scatter plots of correlation results between age and PPG parameters (AGEi and DNi*). **A** The scatter plot of the correlation analysis between age and AGEi, and **B** the scatter plot of the correlation analysis between age and DNi* parameters

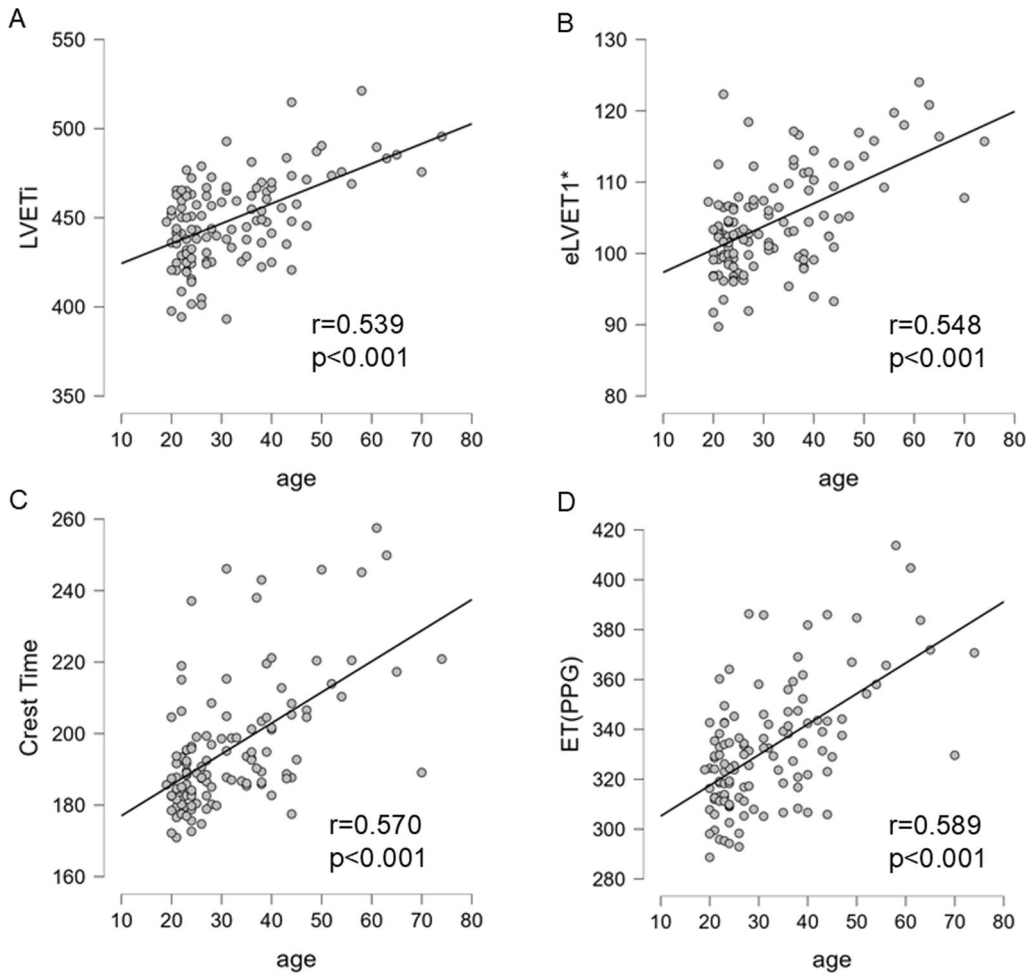

Fig. 2 Scatter plots of correlation results between age and the ejection-related PPG parameters. **A** The scatter plots of the correlation analysis between LVETi, **B** eLVET1, **C** Crest Time and **D** ET(PPG) and age

Table 3 Results of correlation analysis of PRV parameters and age

	Correlation values of PRV parameters with age		Results of GAM analysis of the relationship between age and PRV parameters		
	Pearson's r	p	Deviance Explained	EDOF	*p*
Time domain parameters					
cSDRR	– 0.401	< .001	0.1627	2.5413	< .001
crMSSD	– 0.266	0.006	0.0807	2.5413	0.058
cpNN50	– 0.225	0.021	0.0940	2.9638	0.080
cMRR	0.082	0.404	0.0628	3.7356	0.413
cMHR	– 0.109	0.264	0.0711	3.7356	0.472
Frequency domain parameters					
cTotalPower	– 0.325	< .001	0.1065	2.5413	0.028
cHFpow	– 0.299	0.002	0.0902	2.5413	0.035
cLFpow	– 0.277	0.004	0.0768	2.5413	0.270
Non-linear parameter					
cSD2	– 0.428	< .001	0.1887	2.5413	< .001
cSD1	– 0.266	0.006	0.0807	2.5413	0.058

EDOF Effective degrees of Freedom, *cSDRR* The standard deviation of the interbeat intervals (ms), *crMSSD* The square root of the mean squared differences of successive interbeat intervals, *cpNN50* the proportion of differences of successive IBIs exceeding 50 ms, *cMRR* the mean normal-to-normal interbeat interval, *cMHR* the mean heart rate, *cTotalPower* It specifies the area under the complete frequency-domain analysis curve, *cHFpow* absolute Power of the high-frequency band, *cLFpow* absolute power of the low-frequency band; cSD1 and cSD2: standard deviation 1 and 2 of the Poincaré plot representing the length and width of the ellipse fitted to the plot. The c in front of the parameter name stands for: corrected: automatic detection of irregular cycle lengths and application of cubic spline interpolation applied

For more information on GAM and an explanation of its measured values, see the Additional file1.docx

For a more detailed description of the PRV parameters, see Table 1

marker of aortic distensibility and coronary flow pressure gradient). Si is another PPG parameter proposed by several authors to characterize arterial stiffening. Based on the previous publication of Millasseau (Determination of age-related increases in large artery stiffness by digital pulse contour analysis), PWV and Si are significantly correlated with each other, and both are correlated with age. Interestingly, the Si showed a weak correlation with age in our study [31]. One possible explanation for this may be the different age and sex distribution of the two studies. In the study of Millaseau et al., 29 of the 87 participants were women; the mean age was 47 years, with a range of 21–68 years. Whereas our study age distribution for females found to contain a higher proportion of women mostly in premenopausal age. These observations emphasize that precise characterization of age correlation may require accounting for sex-specific differences and other confounding factors in the analysis; however, this necessitates analysis performed on large datasets.

In addition to the individual parameters, "composite scores" of multiple PPG parameters, such as the Total Score, Heart Fitness Score and CV Health Score, also showed significant correlations with age, both using Pearson correlation and GAM analysis. This supports the unpublished observations of the manufacturer that suggested strong age dependence of these parameters in a large inhomogeneous patient population coming from real-world data of more than 98 000 processed measurements from more than 5 800 individuals in various age, sex and health status [32]. The composite scores were developed to simplify the interpretation of CV health indicators by aggregating multiple PPG-derived parameters into a single, more user-friendly metric. This

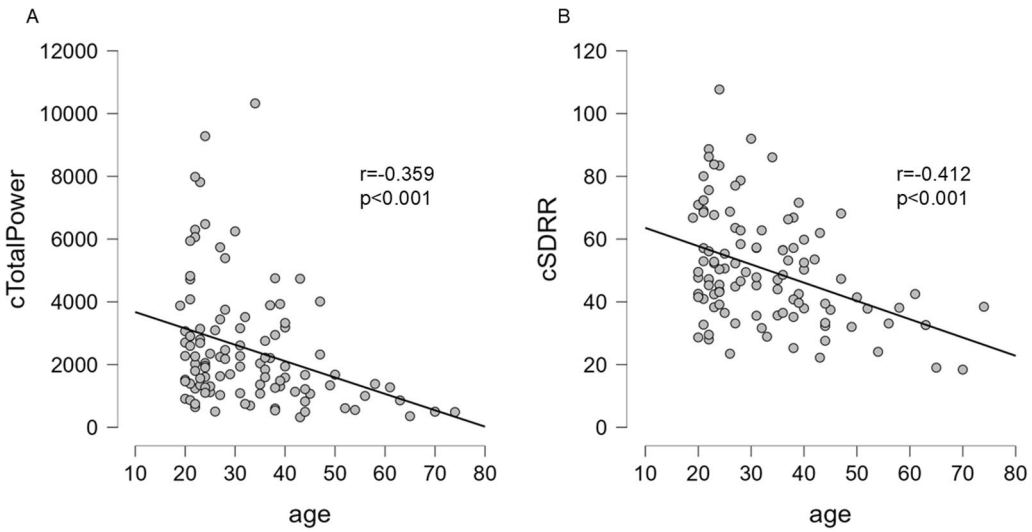

Fig. 3 Scatter plots of correlation results between age and PRV parameters **A** The scatter plot of the correlation analysis between age and cTotalPower, and **B** the scatter plot of the correlation analysis between age and cSDRR parameters

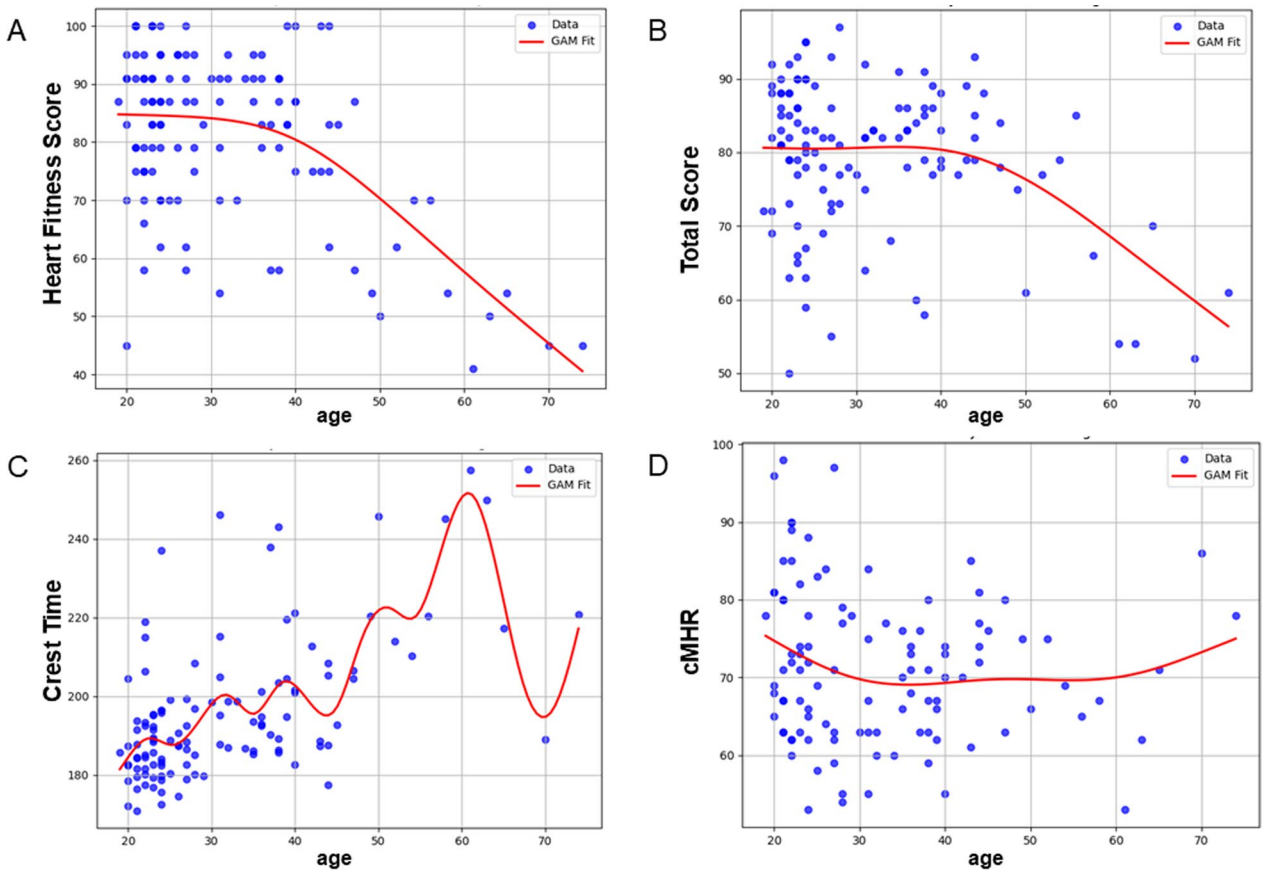

Fig. 4 Plots of GAM analysis. **A, B** The plot of the GAM analysis between age and Heart Fitness and Total Score parameters, **C** the plot of the GAM analysis between age and Crest Time PPG parameter and **D** the plot of the GAM analysis between age and cpNN50 PRV parameter

approach can make it easier for end-users to track and understand their metrics, especially for non-specialists for whom interpretation of multiple individual parameters (e.g. 15–20) can be challenging. While the exact calculation methods for these scores are proprietary, they are based on established PPG signal features associated with vascular and cardiac health. These include parameters related to arterial stiffness, pulse wave characteristics, and temporal signal dynamics, all of which are linked to age-dependent CV changes. The validation of these composite scores as independent predictors of CV health. requires further studies. However, preliminary findings suggest that they could support CV risk evaluations. All score parameters in this study showed a clear non-linear, decreasing relationship with age, especially after age 40. This sharp decline is consistent with published data showing accelerated ageing during middle age [33].

Some PRV parameters, such as total power (cTotalPower) and SDNN (cSDRR), showed a significant correlation with age. Both parameters showed a decrease with increasing age; this could indicate a less sensitive autonomic nervous system, which may contribute to the reduced cardiovascular adaptive capacity observed in the elderly. This finding is consistent with the existing literature, which suggests that decreased heart rate variability reflects reduced autonomic control of the CV system, and highlights the importance of monitoring autonomic function through PRV parameters as part of a comprehensive CV health assessment. [7–9, 34].

In summary, our results reveal a set of PPG and PRV parameters associated with age-related changes with distinct differences between parameters in the aspect of linearity, emphasizing the potential of simultaneous recording and analysis of multiple PPG parameters in CV prevention, though further research is required. Additionally, combining different PPG parameters has yielded composite scores with unique age-dependent patterns which might reflect the non-linear trends of ageing, which may prove useful in identifying age-related CV events or conditions. We believe that our study may serve as a foundational step in developing personalized PPG-based CV age assessment tools. However, future research should explore whether individuals positioned above or

below the correlation trend line represent distinct CV aging phenotypes, such as early vascular aging or supernormal vascular aging. [35, 36].

5 Limitations of the study

A limitation of our study is that the age distribution of the sample population is not fully uniform and may not be fully representative of the general population. Future research should, therefore, be extended to a wider, more diverse cohort to further verify these results.

Clinical validation of the proprietary PPG parameters introduced could be a critical next step towards their wider use and clinical utility. Although the aim of this study was primarily to explore the age dependence of these parameters, it is important to outline possible avenues for future validation. Future studies are planned to focus on the correlation of the new PPG composite scores with widely accepted CV risk scores such as the Framingham Risk Score or the HeartScore (European Society of Cardiology), as well as with established measures such as lipid profiles, hs-CRP, plasma creatinine, carotid Doppler and echocardiography results, and pulse wave velocity (PWV). Further validation efforts include analysing how composite scores interact with clinical and lifestyle factors, including patient history and modifiable risk behaviours, to increase their predictive accuracy. In addition, to ensure wider applicability, we plan to evaluate the performance of these scores in different patient subgroups, including individuals with different CV risk profiles and comorbidities. These studies may be beneficial to further refine the interpretation of the identified age-related indicators, as different PPG parameters may be more relevant in certain pathological contexts, such as hypertension or heart failure.

6 Conclusion

This study has successfully identified age-related linear and non-linear correlations across both conventional and novel PPG parameters, highlighting their potential as valuable indicators of CV ageing. The findings demonstrate that parameters related to cardiac ejection time, arterial elasticity, and PRV, among others, consistently correlate with age, offering a comprehensive view of how the CV system evolves over time. The introduction of novel composite PPG score parameters, which showed notable age correlations, may complement traditional metrics, although further validation is needed to confirm their specific contributions. The clinical relevance of these findings is that they draw attention to the potential of pulse wave analysis to monitor CV ageing non-invasively and position PPG as a promising tool in both clinical and preventive cardiology. However, translation of this method to clinical settings requires further research in patients with various CV conditions and comorbidities.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s44200-025-00068-w.

Below is the link to the electronic supplementary material.Supplementary file1 (DOCX 24 KB)

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Author Contributions

F.A. and D.K. designed the study and conducted the data collection; furthermore, they drafted the first version of the manuscript. S.K. contributed to the analysis and interpretation of the results. Z.M. provided critical revisions to the manuscript. All authors read and approved the final manuscript.

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Data Availability

The datasets generated and analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Declarations

Conflict of interest

F.A., D.K. and S.K. had financial relationships with E-Med4All Europe Ltd. (D.K. and S.K. as co-owners; F.A. is a former employee who worked during the data collection period). Z.M. is the PhD supervisor of D.K. and F.A. Z.M. did not receive any compensation for their contributions.

Ethical approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. All tests were conducted in the laboratory facilities of Semmelweis University. IRB approval number: 120/2018. Written informed consent was obtained from all participants involved in the study.

Consent for publication

Participants provided written consent for the publication of study results as part of their agreement to participate in the study.

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