Research

Comparison of Peak-to-Peak Interval Calculated from Photoplethysmograms Measured on The Forearm and Finger: The Effect of Measurement Positions

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Abstract

Wearable devices mainly use photoplethysmography (PPG) to measure physiological information, and PPG measurements may differ depending on the physiological characteristics of the measurement site. This study aimed to quantitatively evaluate the impact of different measurement sites on the peak-to-peak interval (PPI), focusing on one type of PPG data, PPI. Twenty-one healthy adults were included in this study. PPG was measured at the fingertips and forearms, and the R–R interval (RRI) was calculated by measuring electrocardiograph simultaneously. The PPIs and RRI were measured continuously for 5 minutes in the resting state and 10 minutes during the color-word conflict test (CWT). To examine the reliability of PPI, the intraclass correlation coefficient (ICC) with the RRI was calculated. Furthermore, to evaluate the accuracy and error of PPI measurement, Bland–Altman analysis was performed with RRI to verify the limits of agreement and fixed and proportional bias. ICCs in finger and forearm PPI were highly correlated (ICC > 0.9) at both resting and CWT, and finger PPI tended to be more consistent with RRI, both at rest and during the CWT. The results of this study suggest that PPI calculated from PPG may be influenced by the physiological characteristics of the measurement site.

Key words: Photoplethysmography, peak-to-peak interval, electrocardiograph, intraclass correlation, bland–altman plot

Introduction

Wearable devices paired with various applications play an essential role as health management tools in the information society. The technology employed in wearable devices to obtain physiological information is primarily based on photoplethysmography (PPG), which uses near-infrared light to detect hemoglobin flow in the blood through the skin. This involves illuminating the skin surface with near-infrared light and detecting the reflected light with a photodetector, which allows for capturing blood flow information as a waveform [1]. Studies using PPG have been reported on the evaluation of exercise therapy for patients with hemiplegia after stroke [2]. Furthermore, PPG has been reported to be capable of not only measuring heart rate (HR) but also calculating the pulse rate variability (PRV) indices from the peak-to-peak interval (PPI), which allows for the evaluation of autonomic nervous system indices with an accuracy equivalent to that of an electrocardiograph (ECG) [3-8]. Therefore, PPG, which evaluates physical and psychological aspects with a low-cost and noninvasive technique, is attracting attention as an alternative to ECG [9,10]. PPG can be measured using noninvasive measurement techniques, such as fingers, wrists, ears, or anywhere that can be touched with a measuring device. On the other hand, it has been reported that the waveform of PPG and PRV differ depending on the measurement sites [11,12]. In other words, when PPG is measured at different sites, physiological data calculated from PPG may differ depending on the physiological factors at the site where it was measured. A deeper understanding of PPG data obtained from different measurement sites will contribute to improved clinical diagnosis and health monitoring accuracy utilizing PPG. In previous studies, to the best of the author's knowledge, it has not been clarified how dif-

ferent measurement sites affect PPI. This study focused on PPI, one of the physiological data calculated from PPG, and aimed to clarify the influence of physiological differences in measurement sites on measurement results by quantitatively evaluating differences in pulse intervals measured at different sites (finger and forearm). The study's findings indicate that finger and forearm PPIs showed a high correlation and concordance with the RRI. However, there were differences in the error characteristics when comparing PPI and RRI, which differed between the finger and forearm. Therefore, this study suggests that the PPI calculated from PPG is affected by the physiological characteristics of the measurement site. In other words, by selecting the measurement site based on the subject's situation, it is possible to measure physical and psychological aspects of the subject under various circumstances. This study reveals that PPG has the potential to contribute to health management and disease prevention based on the subject's situation.

Materials and Methods

This study conducted the following investigations:

1) To clarify the reliability of each PPI, we calculated the intraclass correlation coefficient (ICC) of the PPI and R–R interval (RRI) in the resting state and during the color-word conflict test (CWT).

2) Bland-Altman analysis was performed using the PPI and RRI to verify the measurement error of each PPI in the resting state and during the CWT.

Participants

The inclusion criteria for this study were healthy adults aged 18–60 years. The exclusion criteria were people with diabetes, any type of vascular disease, dyschromatopsia, and pregnant women. This study was conducted in accordance with the Helsinki Declaration after obtaining the approval of the Ethics Committee of Iryo Sosei University (approval number 21-20). All participants' informed consent was obtained in writing before participating in the study. The participants were informed that they could withdraw from the study at any time.

Experimental design

After entering the laboratory, participants received an explanation of the survey. The survey was conducted with participants who had agreed to participate in the study. First a questionnaire survey on participant characteristics was performed. After answering the questionnaire, the measurement equipment was attached. The probes of the Bacs Advance (TAOS Institute, Inc., Kanagawa, Japan) were attached to the second fingers of the left and right hands. The Polar OH1 (Polar Electro Oy, Kempele, Finland) was then attached to the left and right forearms. The LRR-05 electrocardiograph (GMS Co., Ltd.) was attached with three-point induction. After attaching each measuring device, participants were asked to rest in a seated posture for 5 minutes (resting state). The PPI and RRI were continuously measured for 5 minutes during that time. Next, the CWT was conducted for 10 minutes to induce a state of psychological stress (confusion). The PPI and RRI were measured for 10 minutes from the start of the CWT (state of psychological stress, hereinafter referred to as the "during the CWT"). Data analysis was performed using data measured on the nondominant side. Polar OH1 [13,14], Bacs

Advance [15,16], and LRR-05 [17,18] are measurement devices that have already been used in scientific investigations. Figure 1 shows the experimental environment.
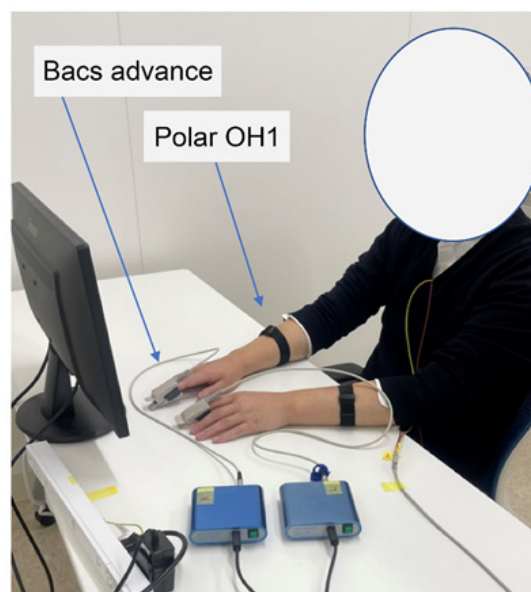

Figure 1. Experimental environment

Mental stress test

The Stroop CWT is a human defensive response model that includes sensory rejection in the human recognition process, which was developed by Stroop [19]. In the CWT, words written in red, blue, green, and yellow appear, but the word names are written in one of the four colors, and the words' names and colors do not match. The subject must recognize the color of the word, not the word's name. This cognitive process creates stress that leads to changes in HR [20]. In this study, the CWT was conducted using the application Hacaro–Stroop Test (Digital Standard Co., Ltd.) to apply psychological stress on the subject and measure the accompanying changes in biological information.

Data acquisition

The data measured by the Polar OH1 was analyzed using the Polar Sensor Logger App via Bluetooth to calculate the PPI (forearm PPI). The data measured by the Bacs Advance was analyzed on a computer using the accompanying software to calculate the PPI (finger PPI). If the PPI value showed a difference of >8% compared with the median of three consecutive PPI, it was clearly judged to be noise, and a median filter was applied before and after to interpolate the median of the data [7].

Statistical analysis

In this study, statistical analysis was performed using SPSS version 28 for Windows. The ICC and its confidence interval (CI) were calculated for the measurement results of each PPI and RRI. The ICC ware classified as poor (<0.5), moderate (0.5–0.75), good (0.75–0.9), and excellent reliability (>0.9) [21]. In addition, Bland-Altman plots were created to validate the bias of each PPI and RRI. Bias in the Bland–Altman analysis was defined as the mean difference between the two variables being compared, and the 95% limit of agreement (LOA) was defined as the mean difference $\pm 1.96 \times$ the standard deviation. Subject characteristics are shown as the mean $\pm$ standard deviation; the other data are shown as the median, first quartile (25%), and

third quartile (75%). The level of significance was set at p<0.05 for all tests, and two-tailed tests were conducted.

Results

Based on the measurement results of 21 participants, the number of subjects required for statistical processing was calculated. The required number of subjects was six, based on the error of 0.05, the statistical power of 0.95, the effect size (ICC) of 0.9

Table 1. Participant characteristics

Participant	21 (Male: 15, Female: 6)	
	Average ± Standard Deviation	
Age (y)	35.3	13.0
High (cm)	169.5	9.6
Weight (kg)	68.4	19.9
BMI (kg/m2)	23.6	5.5

Table 2. The ICCs for each PPI and the RRI in the resting state

	ICC	95% CI
Forearm PPI	0.994*	0.994–0.994
Finger PPI	0.996*	0.970–0.999

Abbreviations: ICC, intraclass correlation coefficient: CI, confidence interval, PPI, peak-to-peak interval, RRI, R–R interval
*p < 0.01

Table 3. The ICCs for each PPI and the RRI during the CWT

	ICC	95% CI
Forearm PPI	0.990*	0.989–0.990
Finger PPI	0.988*	0.988–0.989

Abbreviations: ICC, intraclass correlation coefficient: CI, confidence interval, PPI, peak-to-peak interval, RRI, R–R interval, CWT, color-word conflict test
*p < 0.01

calculated from the results of the ICC of each PPI and RRI. The sample size was calculated using the statistical power analysis software G*power 3.1.9.7. This study was carried out based on the measurement results of 21 subjects who had already been measured.

Participants characteristics

The participants were 21 healthy people, and their characteristics are in Table 1.

With one participant, noticeable noise was observed from small body movements during the CWT. Therefore, using data from 21 participants in the resting state and 20 participants during the CWT. Reliability assessment of HR intervals and each pulse interval

Table 2 shows the ICCs for the PPI and each RRI in the resting state.

In the resting state, the ICC between each PPI and the RRI was >0.9. Table 3 shows the ICCs for the PPI and each RRI during the CWT. During the CWT, the ICC between each PPI and the RRI was >0.9.
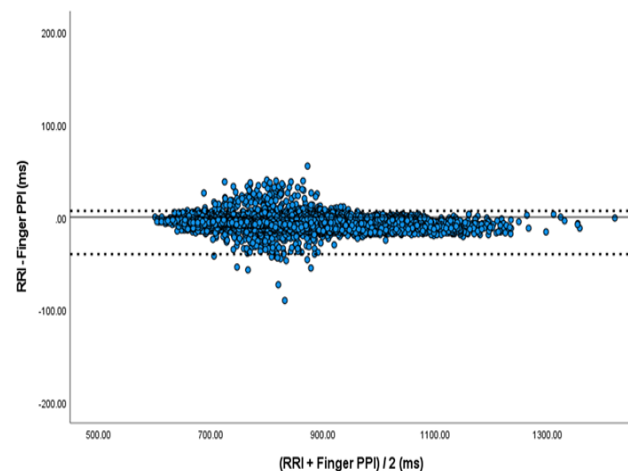
Consistency assessment of HR intervals and each pulse interval.

Figure 2 shows the Bland–Altman plot using the forearm PPI and the RRI in the resting state.

In the resting state, the bias between the RRI and the Forearm PPI was −0.03 ms, and the 95% LOA ranged from −24.5 ms to 24.5 ms.
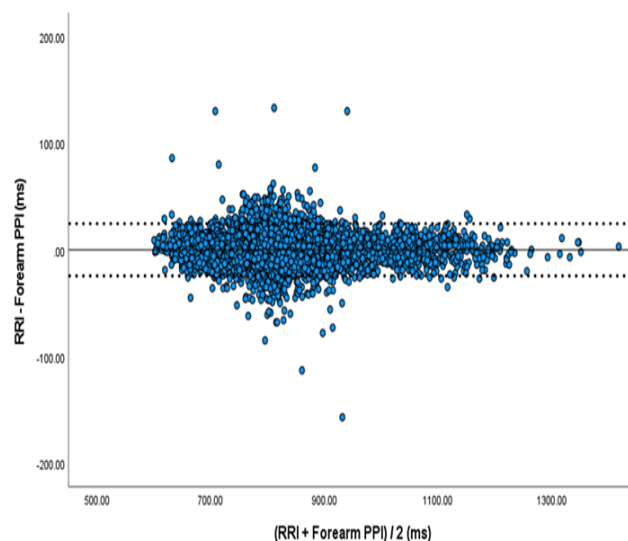
Figure 2. Bland–Altman plot for the forearm peak-to-peak interval (PPI) and R–R interval (RRI) in the resting state


Figure 3. shows the Bland–Altman plot using the finger PPI and the RRI in the resting state

In the resting state, the bias between the RRI and the finger PPI was -6.96 ms, and the 95% LOA ranged from -20.6 ms to 6.7 ms.

The Table 4 shows the LOA and measurement error of the forearm PPI and finger PPI in the resting state.

According to the Bland–Altman analysis, fixed bias was observed for finger PPI with a 95% CI of −7.11 ms~−6.80 ms in resting state. While proportional bias was observed in both forearm PPI and finger PPI in the resting state, the regression coefficient of proportional bias in forearm PPI was −0.004, and in finger PPI was −0.008. Figure 4 shows the Bland-Altman plot using the forearm PPI and the RRI during the CWT.

During the CWT, the bias between the RRI and the Forearm
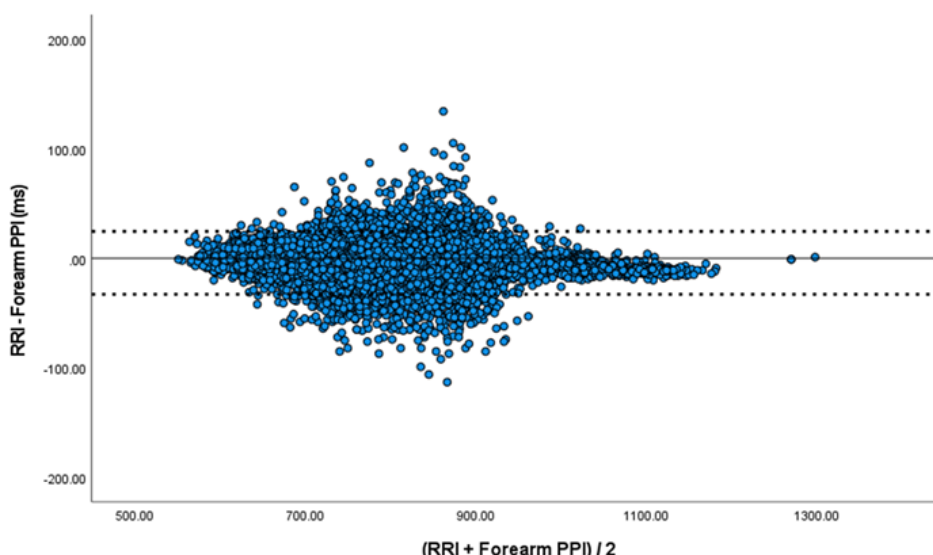
Figure 4. Bland–Altman plot for the forearm peak-to-peak interval (PPI) and R–R interval (RRI) during the color-word conflict test
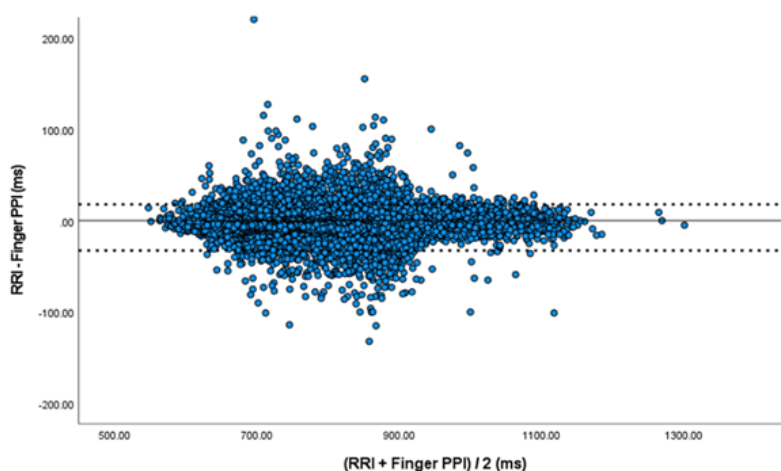
Figure 5. Bland–Altman plot for the finger peak-to-peak interval (PPI) and R–R interval (RRI) during the color-word conflict test

Table 4. Bland–Altman analysis of each PPI and the RRI in the resting state

	Bias	LOA	Fixed bias	Proportional bias			
			95%CI	Y/N	Linear Regression Slope		Y/N
Forearm PPI	−0.03	−24.5~24.5	−0.30~0.25	N	−0.004	0.002	Y
Finger PPI	−6.96	−20.6~6.7	−7.11~−6.80	Y	−0.008	<.001	Y
Abbreviations: LOA, limit of agreement: CI, confidence interval: Y, Yes: N, No, PPI, peak-to-peak interval, RRI, R–R interval							

Table 5. Bland-Altman analysis of each PPI and the RRI during the CWT

	Bias	LOA	Fixed bias	Proportional bias			
			95%CI	Y/N	Linear Regression Slope		Y/N
Forearm PPI	−4.18	−32.8~24.5	−4.40~−3.95	Y	−0.012	p < 0.001	Y
Finger PPI	−2.49	−32.8~17.8	−2.74~−2.25	Y	−0.001	p = 0.564	N
Abbreviations: LOA, limit of agreement: CI, confidence interval: Y, Yes: N, No, PPI, peak-to-peak interval, RRI, R–R interval, CWT, color-word conflict test							

PPI was −4.18 ms, and the 95% LOA ranged from −32.8 ms to 24.5 ms. Figure 5 shows the Bland–Altman plot using the finger PPI and the RRI during the CWT.

During the CWT, the bias between the RRI and the finger PPI was −2.49 ms, and the 95% LOA ranged from −32.8 ms to 17.8 ms.

The Table 5 shows the LOA and measurement error of the forearm PPI and the finger PPI during the CWT.

According to the Bland-Altman analysis, fixed bias was observed in both forearm PPI and finger PPI during the CWT, the 95% CI in forearm PPI was −4.40 ms~−3.95 ms, and in finger PPI was −2.74 ms~−2.25 ms. Proportional bias was observed in forearm PPI during the CWT, the regression coefficient of proportional bias was −0.012.

Discussion

The noninvasive and simple PPG technology is drawing attention and is expected to be used increasingly for health management and clinical diagnosis and disease prevention in the future. PPG can be measured at various locations, such as the fingers, wrists, and ears. Still, previous studies have reported that PPG waveform varies depending on where on the body it is measured. If the PPG waveform differs depending on the measurement site, the PPI calculated based on the PPG may also differ. This study focused on PPI, which is one of the physiological data calculated from PPG, and quantitatively evaluated the error in PPI measured at two sites, the finger and forearm, to clarify how physiological differences of the measurement site affect PPI.

We calculated the ICC with RRI to compare the accuracy of PPI measured on the finger and the forearm. We also created Bland–Altman plots using RRI and various PPI to evaluate for measurement error patterns. PPI (finger/forearm) had a high ICC with RRI at rest and during CWT. This suggests that PPI measured at both the finger and forearm have the precision (reliability) to accurately capture HR variability.

Bland–Altman analysis was conducted in this study to clarify measurement errors [22]. A Bland–Altman plot that shows a particular distribution in some direction may indicate a proportional bias. The additive bias is a bias that occurs in a specific direction, regardless of the magnitude of the measured value. In statistical terms, a 95% CI of the average difference between two measurements that do not include 0 suggests that the measurements are distributed in a certain direction, indicative of an additive bias. Proportional bias is a bias that increases (or decreases) in proportion to the measured value. Statistically, a proportional bias is deemed present in the case of a significant difference confirmed using the Bland–Altman plot regression test. The LOA at rest ranged between −24.5 ms and 24.5 ms for forearm PPI and between −20.6 ms and 6.7 ms for finger PPI. At rest, the finger PPI had a narrower LOA range, suggesting that the finger PPI may provide results that correspond to RRI more consistently. The LOA during CWT was in the range between −32.8 ms and 24.5 ms for forearm PPI and between −32.8 ms and 17.8 ms for finger PPI. This suggested that the finger PPI had a narrower LOA range during CWT, suggesting that the finger PPI could provide results corresponding to RRI more consistently, similar to measurements taken at rest. A comparison of the additive bias and proportional bias of each PPI at rest and during CWT rendered different results. Fixed bias at rest was observed in finger PPI. Furthermore, fixed bias during CWT was confirmed for both forearm and finger PPI. In this study, forearm PPI did not produce any fixed bias at rest but did during CWT. In forearm PPI, the 95% CI of the fixed bias that occurred when imple-

menting CWT was in the negative range. Fixed biases occurred in the finger PPI at rest and during CWT, and its 95% CI was in the negative range. In other words, the results of this study can be interpreted to mean that measured values tended to be larger for finger PPI during rest and for forearm and finger PPI during CWT than for RRI. Next, proportional biases at rest were confirmed for both forearm and finger PPI. Proportional errors during CWT were confirmed only in forearm PPI. However, both of the confirmed regression coefficients of proportional biases showed only slightly negative values. Since a statistically significant difference was confirmed, a linear relationship between the bias (each PPI and RRI) and mean (of each PPI and RRI) is suggested. Still, the small regression coefficient value implies that both forearm and finger PPI have little influence on the error with RRI and that the proportional biases confirmed by this study were all small. It is clear that the waveform of the pulse wave differs depending on the measurement site [23]. Differences in blood vessel diameters in each part of the artery and complex structures of the blood vessels and arterial walls in each part may explain the difference in conduction velocity of pulse waves between different blood vessels under the control of autonomic nerves [24,25]. Furthermore, factors that cause pulse waves to differ depending on the measurement site include differences in skin pigmentation and tissue thickness [26], high sensitivity of cutaneous vascular walls of the fingers to blood volume fluctuations (being innervated by alpha-adrenergic receptors, they are sensitive to blood volume fluctuations) [27], and a wide vascular bed in the distal region [28]. This study revealed that the errors produced in forearm and finger PPIs differ from RRI. On the other hand, in this study, the physiological characteristics that cause errors in PPI measurements for each region were not fully understood. Future studies should clarify the effects of various conditions on PPI, such as the load caused by exercise and the effects of temperature on the body, to further interpret PPG data for each region. Such studies should provide a more detailed understanding of the relationship between PPI measurements and physiological characteristics.

It is important to understand the physiological characteristics of each measurement site and interpret the data based on such understanding when measuring PPG. Furthermore, this study's finding that PPG data differs depending on the measurement site suggests that there may be physiological information in PPG data that cannot be captured from specific sites. Our future challenge is, therefore, to investigate PPG data further to reveal physiological information that cannot be obtained from RRI and to pursue its potential for application to health management. After interpreting the calculated LOA range, measurement errors, and the ICC value, it was determined that the PPI measured at both the finger and the forearm were sufficiently accurate. Measurements of pulse waves in previous studies were often taken at the finger. However, the results of this study showed that the pulse interval measured on the forearm in both resting and stressed states was accurate enough to be used for scientific research. The findings obtained in this study are particularly useful when measuring PPG using a fingertip is not feasible, such as in patients with peripheral hyperkinesia or involuntary movements or during clinical interventions when devices cannot be attached to the fingertip. This study revealed that PPG has

the potential to be a flexible technology that enables applications in health management and disease prevention by selecting the measurement site according to the subject's situation.

There were several limitations to this study. The sampling rates of the various measurement devices were different: for example, the Polar OH1 used to record pulse waves was 135 Hz, the sampling rate of Bacs Advance was 1024 Hz, and the sampling rate of LRR-05 was 1000 Hz. The pulse wave signals and ECGs from different regions were recorded simultaneously. Still, because each signal was recorded with a separate device, the precise timing of the signals could not be adjusted to the millisecond level. Thus, accurate analysis of the pulse wave signal with perfectly synchronized recordings at different sites is required to identify a more accurate mechanism. This study was not conducted to compare and examine algorithms for calculating PP interval from pulse waveforms. Therefore, different calculation algorithms for the PP interval may yield different results.

Conclusions

PPI was calculated from pulse wave signals measured at two different sites and was then compared with RRI. The reliability of PPI and correspondence with RRI were high for measurements taken at both sites. However, comparing the CIs showed that correspondence with RRI was higher for measurements taken at the finger. These findings suggest that PPI is influenced by local physiological factors according to the site of measurement. Furthermore, these results suggest not only the potential of PPI as an alternative to RRI but also the importance of research on physiological data obtained from PPI at sites for which data cannot be obtained by RRI.

Abbreviations

CI: confidence interval; CWT: color-word conflict test; HR, heart rate; ICC, intraclass correlation coefficient; LOA, limit of agreement; PPI, peak interval; PRV, pulse rate variability

Acknowledgements

Conflicts of Interest

The authors declare no conflict of interest.

Data Availability Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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31. Terminology used in literature are waba (Epidamic), waba umoomi (Pandamic), waba shadeed (severe Pandamic)

32. Galen, 129 AD 210 AD worked on padamic called Antonine Plaque of 165 to 180 AD also known as plaque of Galen.

33. Treatise on Small Pox and Melesies, Kitab-al-hawi, Fial-tibb translated in 1279 AC by Mohd. Ibn Zakiria Al Razi (854 to 925 ce). b) the canon of medicine c) Zakira khwarazam shai in 1110 AC.

34. Annexture in the Supporting Information is enclosed to this paper giving details of drug composition of BSAPM Unani

35. Scientists call the poly-protein a "single reading frame", containing several "open reading frames", namely those that contain a start code and end with a stop code, each containing the relevant protein to be expressed by the host cell.

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41. Immunity is the balanced state of multicellular organisms having adequate biological defenses to fight infection, disease, or other unwanted biological invasion, while having adequate tolerance to avoid allergy, and autoimmune diseases.]