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Original Article

A validation study of a smartphone application for heart rate variability assessment in asymptomatic adults

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Abstract: Background: Assessment of heart rate variability (HRV) is an effective non-invasive tool to obtain data on cardiac autonomic modulation and may be assessed by a range of devices, including mobile applications. *Objective:* This study aimed to validate a smartphone application by comparing the R-R intervals (RRi) obtained by the app with a classic electrocardiogram (ECG)-derived reference condition Methods: Fifteen asymptomatic adults (24.9±3.4 years) underwent an orthostatic challenge during which RRi were simultaneously recorded by a freeware smartphone application and by an ECG recorder. Pearson correlation coefficients (*r*) and coefficients of determination (r^2) were calculated to determine the degree of association between the two electronic devices. Two-way repeated measures analysis of variance and Bland-Altman analysis were used to calculate the measurement consistency and agreement, respectively, between the two methods. Effect size was also used to estimate the magnitude of the differences. Results: The number of RRi from asymptomatic adults recorded by the ECG and by the free smartphone application was similar at rest in supine position (13,149 vs. 13,157; *P* = 0.432) and during orthostatic challenge (10,666 vs. 10,664 *P = 0.532).* RRi in milliseconds from both devices presented a near perfect correlation in the supine position (*r* = 0.999; Confidence Interval [CI] at 95%: 0.999-0.999; P < 0.0001) and during orthostatic challenge (r = 0.988; 95% CI: 0.988-0.989; P < 0.0001). A negative bias of -0.526 milliseconds (95% limits of agreement [LoA] from -4.319 to 3.266 milliseconds) was observed in supine position between ECG and the smartphone application. On the other hand, a positive bias of 0.077 milliseconds (95% LoA from -10.090 to 10.240 milliseconds) during the orthostatic challenge was observed. Conclusions: Our results cross-validated a freeware smartphone application with the ECG-derived reference condition for asymptomatic adults at rest in the supine position and during orthostatic challenge.

Keywords: Autonomic nervous system, heart rate, electrocardiography, mobile applications

Introduction

An increasing number of smartphone applications has been recently designed for health purposes and are widely used by healthcare providers to aid in diagnosis, prognosis, and treatment of medical conditions [1, 2]. Approximately 80% of undergraduate medical stu-

dents and 75% of graduate students own smartphones [3]. It is expected that this trend grows as this handheld device allows portable computation of the data obtained from inbuilt sensors. A smartphone application may also be custom-made, as it may run third-party software.

The assessment of consecutive heartbeat intervals is an emergent property of interdependent regulatory systems operating on different time scales in order to adapt to challenges such as mental stress, breathing and metabolic alterations [4-6]. Some studies [6-10] have found a close relationship between the R-R intervals (RRi) from electrocardiogram (ECG) and the parasympathetic branches of autonomic nervous system in different physiological conditions and heart diseases.

In this context, heart rate variability (HRV) assessment is an effective non-invasive tool to obtain data on cardiac autonomic modulation and may be assessed by a range of devices [8]. Although HRV has been largely employed in hospitals and clinics using data obtained from high-quality electrocardiogram (ECG) recorders [11, 12], a number of studies [13-18] have demonstrated that some heart rate monitoring applications are user-friendly, have low cost and are indeed effective in assessing HRV. In addition, these studies have emphasized the accuracy of the mobile devices for heart rate or pulse rate monitoring and HRV measurements.

In this regard, free mobile applications have been widely used to collect HRV data by acquiring the R-R intervals (RRi) in distinct populations [19-25]. In recent years, a freeware smartphone application (the Elite HRV smartphone app) has gained popularity as wellness telehealth application for diagnosing psychological stress indicators. The app was also devised as a mobile tool to capture HRV data from compatible heart rate monitors via Bluetooth. The application is available for free on compatible Apple iOS and Android devices.

Currently, however, there appears to be no consensus on the use of the Elite HRV smartphone app to evaluate HRV data by acquiring the RRi in diseased or healthy populations. Perrotta AS, Jeklin AT, Hives BA, Meanwell LE, & Warburton DE, [26], in a study involving recreational athletes, have demonstrated a strong discrepancy between the app and the Kubios HRV for the root mean square of difference of successive NN intervals (rMSSD) parameter. On the other hand, Guzik P, Piekos C, Pierog O, Fenech N, Krauze T, Piskorski J, & Wykretowicz A, [27] have observed that measurements for the same HRV parameters derived from ECG-derived reference condition and Elite HRV smartphone app were not equivalent in a population of young healthy adults. Additionally, several studies [20, 21], [25, 28] have addressed the effectiveness of mobile technology-derived approaches to measure HRV in athletes, healthy young and middle-age individuals, but their findings remain controversial.

Therefore, this study aimed to determine measurement consistency and agreement between HRV data by ECG-derived reference condition and the Elite HRV freeware smartphone app. We hypothesized that the measurements using smartphone application would be comparable to the findings obtained from the reference condition.

Materials and methods

Participants

The sample was composed by fifteen asymptomatic adults (8 males; age 24.9±3.4 years). All of them were fully functional in the performance of activities of daily living and were not using any prescription drugs. Participants self-reported no smoking or regular drinking and non-use of illicit drugs. The experiment was approved by the Research Ethics Committee of University of Pernambuco (CEP-UPE) and all participants signed a written consent form before the tests. The research was conducted in the Human Performance Research Laboratory (LAPEDH) from UPE and the sample size was justified by the method proposed by Liao JJ [29]. All participants were interviewed and examined by the medical staff before the test protocol to assess their clinical stability and health status.

Testing procedures

All participants were instructed to avoid caffeinated and alcoholic beverages as well as strenuous exercise on the day preceding the test protocol. They were also instructed to have a light meal at least 2 hours prior to the test.

The experiments were carried out in the afternoon in climate-controlled conditions (22 to 24°C) with relative air humidity of 40 to 50%

Anthropometric measurements were undertaken, and participants were familiarized with the equipment and the experimental procedures to reduce anxiety. For each test, a full demonstration was provided, and two practice trials were allowed before the actual test began. After this procedure, resting measurements were conducted in supine position (30-degree head elevation) followed by an active orthostatic challenge [30]. The participants rested comfortably in a quiet laboratory room during the recording for at least 10 min in the supine position and 10 min in the orthostatic challenge. All participants were instructed to breathe spontaneously in these two moments. All participants were evaluated for in a randomized order and the random sequence was generated by an online software (www.random.org).

The skin of each subject was cleaned and prepared for the attachment of surface electrodes (Red Dot™ 2560, 3M, Sumaré, SP, Brazil) before the 20-min recording, according to the manufacturer's instructions The white electrode was placed on the center of manubrium, the red electrode on xiphoid process, the black electrode was placed on left anterior axillary line on sixth rib and the green electrode was placed on right anterior axillary line on sixth rib. The ECG electrodes were placed in standardized positions in such way as to avoid interference from the installation of the elastic electrode belt Polar H7 (Polar Electro Oy, Kempele, Finland). The electrode belt was placed at the xiphoid level just below the chest muscles with a conductive gel applied as described by the manufacturer.

The RRi were simultaneously recorded with the free smartphone application (Elite HRV LLC, Asheville, NC, USA, Release 4.0.2, 2018) for Android via Bluetooth 4.0, using a SM-G935F (Samsung, Manaus, MA, Brazil) by elastic electrode belt Polar H7 (Polar Electro Oy) and a 3-channel ECG recorder (Cardiomapa, Cardios, São Paulo, SP, Brazil) at a sampling frequency of 800 Hz during supine position and orthostatic challenge.

Subsequently to the data collection, the raw RRi data from ECG were exported into ASCII format by a software supplied by the manufacturer. In the same way, the raw RRi data from the smartphone application were exported from the server database. The RRi derived from ECG and from the smartphone application were not cleaned or corrected for ectopic beats or signal noise. No filters were used for cleaning or correction of artifacts. The same raw and uncorrected sequences from the smartphone application and ECG were selected for all participants.

The signals from the reference condition and from the smartphone application were synchronized using the same time frame for analysis into Kubios HRV Standard software (Kubios Oy, Kuopio, Finland, release 3.1.0.1, 2018) for macOS (Apple Inc., Cupertino, CA, USA, Release 10.13.4, 2018). The pair of continuous 512 beats series were randomly chosen for 10 minutes in supine position and 10 minutes in orthostatic challenge. The same series were used for time and frequency domain analysis, and for quantitative beat-to-beat analysis [11, 31].

Heart rate variability analysis

For time domain analysis the following calculations were performed: the mean NN interval, the standard deviation of all NN intervals (SDNN), the rMSSD, and the proportion of differences between adjacent NN intervals of more than 50 milliseconds (pNN50) [11].

Frequency domain analysis was performed using the Fast Fourier Transform test for previously selected RRi sequences of 512 sample segments with 4-Hz interpolation and 50% overlap. Two main spectral components were selected for analysis: low frequency [sympathetic and parasympathetic components (LF, from 0.04 to 0.15 Hz)] and high frequency (parasympathetic component (HF, from 0.15 to 0.50 Hz). The spectral components were expressed as normalized units (LF [nu] and HF [nu]) and ratio (LF/HF). Normalization consisted of dividing the power of a given spectral component (HF or LF) by the total power minus the power below 0.04 Hz and multiplying this ratio by 100. All the participants presented a respiratory rate within the HF range.

Quantitative beat-to-beat analysis were performed using the Poincaré plot [31]. The

Poincaré plot provides both a qualitative and a quantitative analysis of HRV. The shape of the plot can be used not only to classify the signal into one of various classes, but also to fit an ellipse, which enabled us to quantify the standard deviation of the instantaneous variability of the beat-to-beat interval (SD1) and the long-term variability of the continuous R-R intervals (SD2) parameters. SD1 represents the dispersion of the points perpendicular to the line of identity, and it is thought to be an index of the instantaneous beat-to-beat variability of the data, while SD2 represents the dispersion of the points along the line of identity and represents the slow variability of heart rate.

Statistical analysis

Data were processed and analyzed using SPSS (SPSS Inc., Chicago, IL, USA, Release 16.0.2, 2008) and Prism (GraphPad Inc., San Diego, CA, USA, Release 6.01, 2012) software's. Initially, Shapiro-Wilk's test and Bartlett's criteria were used for descriptive statistics. Homogeneity of variances and homoscedasticity were determined by Levene's test. Continuous variables were presented as mean and standard deviation (SD), while categorical variables were expressed as percentage and frequency. Pearson correlation coefficient[s] (r) and coefficients of determination (r^2) were calculated to determine the degree of association between HRV indices calculated from both electronic devices. A two-way repeated measures (RM) analysis of variance (ANOVA) was used to test the overall effect, with adjustments for covariates and using the multiple measurements for each subject. Effect size (ES) was used to estimate the magnitude of the differences from reference condition and smartphone application [32]. Finally, Bland-Altman plots of all measures from both systems were constructed and the 95% limits of agreement (LoA) were computed [33]. All statistical methods were two-tailed, P values were calculated, with a 95% confidence interval and significance level was set as $P \leq 0.05$.

Results

R-R intervals

The total number of RRi collected from all participants during the 10 minutes rest in supine position was 13,149 intervals for ECG and 13,157 intervals for smartphone application (Δ = 8 intervals; P = 0.990). During orthostatic challenge (Δ = 2 intervals; P = 0.998), the number of RRi detected in 10 minutes was 10,666 intervals (ECG) and 10,664 intervals (smartphone application).

The high consistency between the two electronic devices analyzed was also demonstrated by the two-way RM ANOVA, which did not reveal any statistical interaction between the selected 512 pairs of RRi acquired by ECG and the smartphone used at rest in the supine position (F(511,7154) = 1.009; P = 0.432). In the same way, the two-way RM ANOVA did not show any statistical interaction during orthostatic challenge when the devices were compared (F(511,7154) = 0.9935; P = 0.532). **Figure 1** shows the 512 beat-to-beat analysis at rest in the supine position and during the orthostatic challenge for both HRV recorders and the overlapping results.

The relationship between the RRi acquired by smartphone application and the reference condition (**Figure 2**) presented near perfect correlations at rest in the supine position (r = 0.9985; CI [confidence interval] 95%: 0.9985-0.9986; P < 0.0001) and during the orthostatic challenge (r = 0.9881; 95% CI: 0.9876-0.9886; P < 0.0001).

The results for the Bland-Altman analysis of RRi acquired by ECG and smartphone application also presented high agreement (**Figure 3**). Only 43 (0.56%) and 86 (1.12%) data points of the residuals fell outside the 95% LoA for the supine position and orthostatic challenge, respectively. Furthermore, a negative bias of -0.526 milliseconds (95% LoA from -4.319 to 3.266 milliseconds) was observed in supine position between RRi ECG-derived reference condition and smartphone application. In the other hand, a positive bias of 0.077 milliseconds (95% LoA from -10.090 to 10.240 milliseconds) were observed when the RRi obtained by reference condition was compared to the smartphone application during orthostatic challenge.

Time domain analysis and frequency domain analysis

Finally, no significant differences were found for time domain analysis, frequency domain analy-

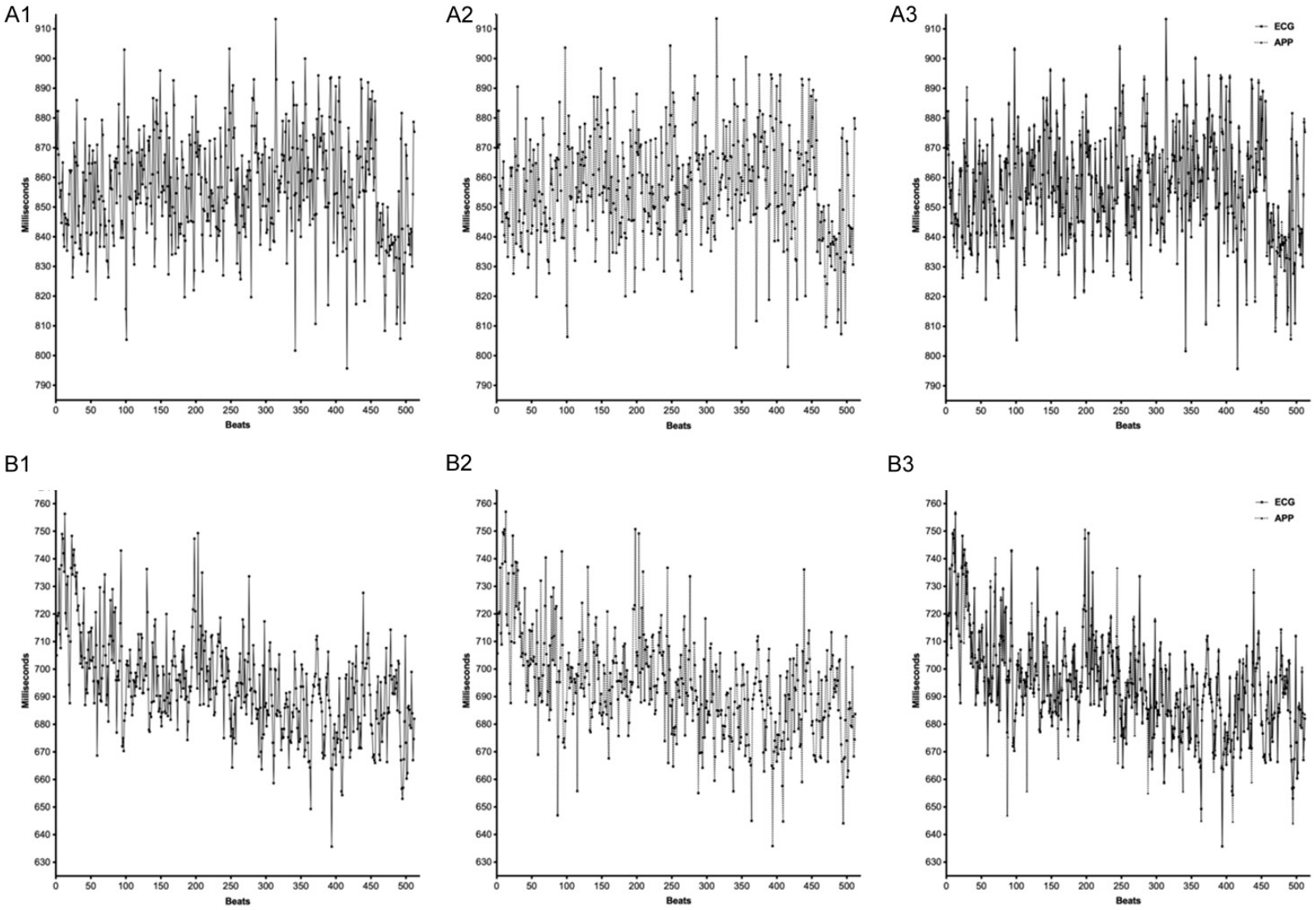

Figure 1. R-R intervals at rest in supine position and during an orthostatic challenge. A1, B1: Reference condition (ECG); A2, B2: Smartphone application (APP); A3, B3: Superposed results from ECG and APP.

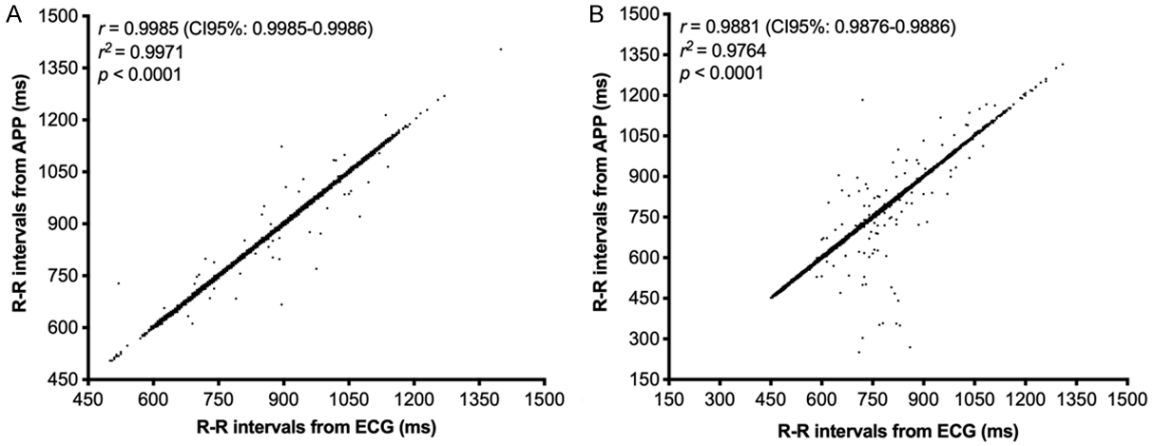

Figure 2. Relationship between R-R intervals acquired by reference condition (ECG) and smartphone application (APP). A: At rest in supine position; B: During the orthostatic challenge.

sis, or quantitative beat-to-beat analysis obtained from reference condition and the smartphone application at rest in the supine position and during the orthostatic challenge (**Table 1**).

Discussion

This study validated a free Elite HRV smartphone app for assessing the R-R intervals in a supine position and during orthostatic challenge in asymptomatic adults. We found solid measurements of consistency and agreement between the smartphone application and the reference condition. In the same way, results from the Bland-Altman analysis demonstrated very low discrepancies at rest in supine position and during orthostatic challenge.

In line with these findings, Perrotta AS, Jeklin AT, Hives BA, Meanwell LE, & Warburton DE, [26] have demonstrated a strong correlation between the rMSSD parameter derived from the Elite HRV app and from Kubios HRV in recreational athletes. Furthermore, Flatt AA, & Esco MR, [20], Peng RC, Zhou XL, Lin WH, & Zhang YT, [28], Plews DJ, Laursen PB, Stanley J, Kilding AE, & Buchheit M, [21] and Bánhalmi A, Borbás J, Fidrich M, Bilicki V, Gingl Z, & Rudas L, [25] have also shown the effectiveness of mobile applications regarding HRV assessment in healthy subjects. In this sense, the validation of a freeware smartphone application is very important for healthcare providers to aid in diagnosis, prognosis, and treatment of medical conditions, since it is a low-cost alternative and a user-friendly tool to monitor the physical workload and cognitive task performance of the patients.

Unlike the research carried out by Guzik P, Piekos C, Pierog O, Fenech N, Krauze T, Piskorski J, & Wykretowicz A, [27], which did not evaluate RRi, in this study we compared the same RRi sequences acquired in the data collection performed concomitantly by ECG-derived reference condition and the smartphone application. In this manner, the data captured by the mobile technology derived approach was not modified nor underwent any filtering process. In addition, besides calculating rMSSD and SDNN parameters and the mean RRi [27], we also calculated pNN50, NN50, Poincaré plot indexes and frequency domain analysis. Our findings indicate that the RRi obtained by mobile technology may be used to evaluate the behavior of heart beats in asymptomatic individuals.

Gamelin FX, Berthoin S, & Bosquet L, [14] have observed higher correlations when the RRi and the subsequent HRV data obtained from a heart rate monitor was compared to an ECG recorder. These authors validated a heart rate monitor for HRV analysis among healthy young adults to be used at rest in the supine position, demonstrating a small effect size and low discrepancies for time and frequency domain indexes. In the present study, we also demonstrated small effect sizes for the same indexes in a similar sample. A study carried out by de Rezende Barbosa MPDC, Silva NTD, de Azevedo FM, Pastre CM, & Vanderlei LCM, [15], also

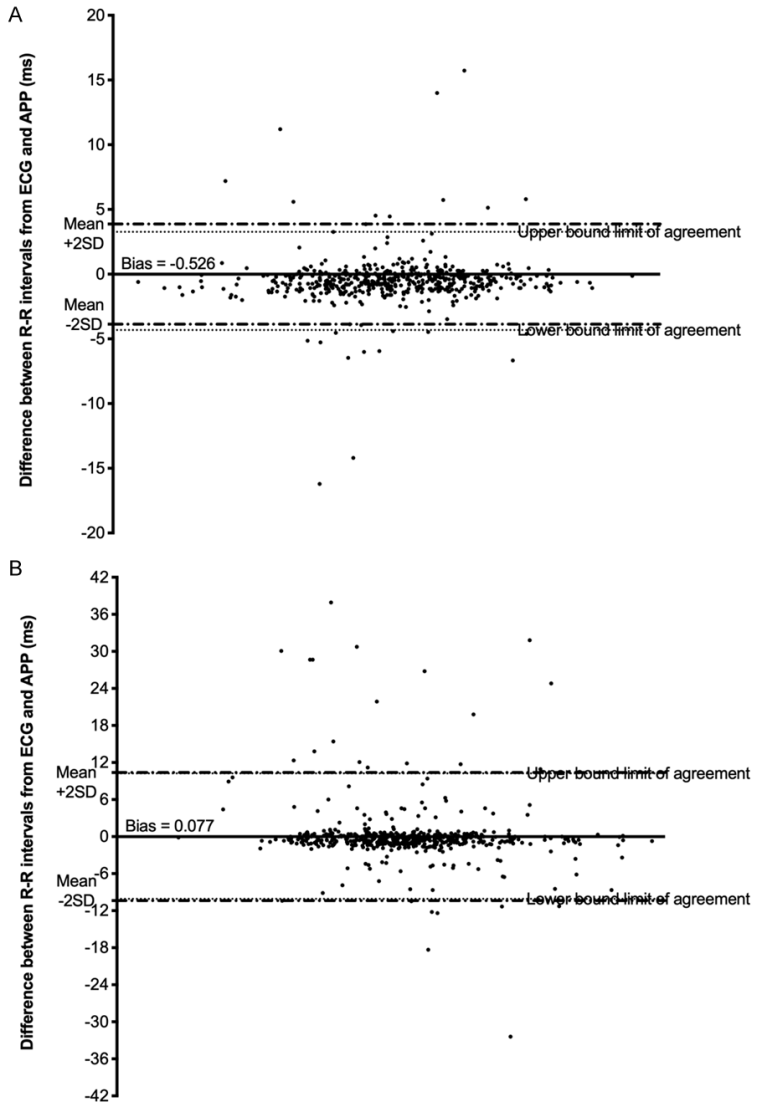

Figure 3. Bland-Altman plot for R-R intervals acquired by reference condition (ECG) and from smartphone application (APP). Center solid line is equal to the mean difference between the two devices to detect R-R intervals, regular dot-dash lines are equal to 95% limits of agreement, and outer bold thickness is equal to 2 standard deviations (SD) of the mean. A: Supine position; B: Standing position.

involving healthy young adults, have looked at the effectiveness of wearable fitness devices for HRV measurement at rest. The study validated two heart rate monitors for assessing HRV and found a high correlation coefficient between the data obtained from the smartwatches and by the ECG recorder at rest in supine and sitting positions.

Vanderlei LCM, Silva RA, Pastre CM, Azevedo FMD, & Godoy MF, [16] have compared the HRV of healthy young adults at rest and during exercise by collecting data from a heart rate monitor and from an ECG recorder. The authors did not observe significant differences when comparing the values obtained from the two electronic devices at rest or during physical exercise. Weippert M, Kumar M, Kreuzfeld S, Arndt D, Rieger A, & Stoll R, [34] have also compared the data extracted from heart rate monitors with data acquired by an ECG recorder. The researchers found that the wearable fitness device to be reliable and useful for the extraction of normalized RRi for HRV analysis in males aged between 22 and 31 years old. In line with these findings, Kingsley M, Lewis MJ, & Marson RE, [13] have found no significant differences between RRi extracted from a digital ECG and from a heart rate monitor at any relative intensity of physical exercise. They also found the heart rate monitor to be a reliable device for obtaining the RRi. Similarly, the RRi recorded by the smartphone application in the present study also provided reliable information with high level of agreement about the interaction between autonomic nervous system and heart in supine position and during orthostatic challenge among asymptomatic adults. Our findings demonstrate that the RRi acquired by the Elite HRV smartphone app is reliable, precise and accurate for further analysis in the time domain, frequency domain and quantitative beat-to-beat.

A number of studies have already demonstrated the advantages of using heart rate monitors to assess HRV and the body's responses to physical and mental workloads, thus enabling a more effective control and adjustment of the physical and emotional symptoms of stress [4, 13-17, 34-36]. Actually, HRV emerges a nonin-

Table 1. Concordance between HRV signals (mean ± SD) obtained from reference condition (ECG) and the freeware smartphone application (APP) in supine position and during orthostatic challenge

Parameters	ECG	APP	Correlation		Bias	(LoA)	Magnitude of the Bias	
			r*	r^2			ES	Interpretation
Supine position								
RRi (ms)	856.06±123.40	856.58±123.40	1.000	1.000	-0.455	(-0.915 to 0.005)	-0.004	Small
SDNN (ms)	55.47±25.23	55.53±25.25	1.000	1.000	-0.066	(-1430 to 1298)	-0.003	Small
RMSSD (ms)	60.15±34.86	60.44±34.70	0.999	0.999	-0.286	(-3833 to 3260)	-0.008	Small
NN50 (count)	163.13±113.95	162.60±114.85	1.000	1.000	0.533	(-6251 to 7318)	0.005	Small
pNN50 (%)	31.92±22.30	31.82±22.47	1.000	1.000	0.104	(-1223 to 1432)	0.005	Small
LF (ms^2)	1182.65±748.72	1190.64±759.80	1.000	1.000	-7.982	(-54.53 to 38.56)	-0.011	Small
HF (ms^2)	2192.09±2104.99	2196.46±2097.75	0.999	0.999	-4.366	(-137.8 to 129.1)	-0.002	Small
LF (nu)	43.15±15.16	43.20±15.08	0.999	0.999	-0.047	(-1644 to 1550)	-0.003	Small
HF (nu)	56.61±15.24	56.58±15.16	0.998	0.998	0.039	(-1606 to 1684)	0.003	Small
Total power (ms^2)	3463.37±2715.63	3474.61±2715.99	0.999	0.999	-11.24	(-186.6 to 164.1)	-0.004	Small
LF/HF	0.89±0.55	0.89±0.55	0.998	0.998	0.000	(-0.065 to 0.064)	-0.001	Small
SD1 (ms)	42.58±24.67	42.78±24.56	0.999	0.999	-0.203	(-2713 to 2308)	-0.008	Small
SD2 (ms)	65.41±27.11	65.42±27.19	1.000	1.000	-0.008	(-0.762 to 0.746)	0.000	Small
Orthostatic challenge								
RRi (ms)	694.89±119.65	694.31±119.18	1.000	0.999	0.586	(-5.829 to 7.002)	0.005	Small
SDNN (ms)	45.97±24.05	48.04±28.35	0.993	0.985	-2.066	(-12.550 to 8.418)	-0.080	Small
RMSSD (ms)	38.07±38.24	41.98±45.61	0.995	0.991	-3.911	(-20.360 to 12.540)	-0.093	Small
NN50 (count)	60.40±94.96	66.73±101.75	0.992	0.984	-6.333	(-33.870 to 21.200)	-0.064	Small
pNN50 (%)	12.19±18.81	13.06±19.91	0.998	0.995	-0.870	(-4.226 to 2.486)	-0.045	Small
LF (ms^2)	1171.56±772.06	1282.79±963.60	0.901	0.811	-111.235	(-952.800 to 730.300)	-0.127	Small
HF (ms^2)	1068.08±1838.86	1230.66±2242.65	0.991	0.983	-162.579	(-1112.000 to 786.800)	-0.079	Small
LF (nu)	71.10±22.85	71.39±22.20	0.997	0.994	-0.291	(-4.020 to 3.438)	-0.013	Small
HF (nu)	28.77±22.68	28.43±21.92	0.995	0.991	0.334	(-4.072 to 4.740)	0.015	Small
Total power (ms^2)	2338.03±2319.41	2623.11±3056.00	0.974	0.949	-285.084	(-2151.000 to 1581.000)	-0.105	Small
LF/HF	6.09±7.43	6.27±7.73	0.999	0.998	-0.177	(-1.076 to 0.723)	-0.023	Small
SD1 (ms)	26.95±27.07	29.71±32.28	0.995	0.991	-2.766	(-14.400 to 8.868)	-0.093	Small
SD2 (ms)	57.76±24.55	59.45±27.94	0.988	0.977	-1.683	(-11.960 to 8.598)	-0.064	Small

*$P < 0.00001$ for all correlation coefficients; SD: standard deviation; LoA: limits of agreement; ES: effect size.

vasive methodology to identify patients at risk of cardiac disorders [37], and multiple HRV measurements have been designed to achieve a better risk stratification. In this context, the contemporary therapeutic use for the HRV analysis works as risk stratification tool for patients with post-myocardial infarction or heart failure who are prone to have arrhythmic death and who would benefit from implantable cardioverter-defibrillators. Additionally, it is critical to evaluate and monitor these variables throughout cardiac rehabilitation in order to establish parameters to demonstrate to the patients that such therapeutic approach is effective [38].

Studies dealing with time and frequency domain analysis during active orthostatic challenge seem to be absent in the relevant literature. In this sense, we found that the free smartphone application may be an effective and practical tool for monitoring R-R intervals during an orthostatic test. As already mentioned, the Elite HRV smartphone app was also cross-validated in the present study to acquire RRi at rest in the supine position and for the further HRV time-domain, frequency-domain, and non-linear metrics. However, Guzik P, Piekos C, Pierog O, Fenech N, Krauze T, Piskorski J, & Wykretowicz A, [27] have compared three HRV parameters from young adults obtained at rest in supine position by ECG-derived reference condition to the Elite HRV smartphone app and concluded that the measurements obtained are not equivalent. These results deserve attention, but in their study the authors analyzed the 3rd release of the free smartphone application (released before 2017) and calculated the HRV parameters using only 168 RRi for each participant (4,872 pairs of RRi). On the other hand, we followed the international standards of measurement for HRV [11], analyzing 512 RRi for each participant (7,680 pairs of RRi) and used the 4th version of the mobile application (released in 2018). Currently the app remains on the 4th release, working with Android 7.0 and above (October 2019) and the 7.1 release for Apple iOS (November 2019).

Finally, the absence of patients with cardiovascular, respiratory and/or other diseases may well be a limitation of this study. We recommend further studies to fine-tune our approach by repeating the procedure with other populations and other working environments (hospitals and clinics). Our findings support the use of smartphone application specifically for asymptomatic adults.

Conclusions

In this study, we cross-validated a freeware smartphone application with the ECG-derived reference condition for asymptomatic adults at rest in the supine position and during orthostatic challenge. The positive and negative biases presented by the smartphone application for supine position and orthostatic challenge, respectively, were not clinically significant.

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Disclosure of conflict of interest

None.

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