Smartwatches in Clinical Pre-diagnosis: Enhancing Tilt Test Analysis for Prolonged COVID-19 Symptoms

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Abstract

Technological advancements have transformed smartwatches into versatile tools for real-time biomedical data collection. We developed a specialized smartwatch app tailored for clinical pre-diagnosis, targeting individuals with Long-COVID-19 and post-COVID-19 symptoms. Our app measures heart rate and utilizes accelerometer data to assess autonomic responses. In a study involving 46 participants (31 in the study group, 15 in the control group) undergoing a 50-minute tilt-test protocol, we compared the app's results with data from ECG monitoring. The comparison revealed a strong correlation (r=0.98) between the smartwatch and ECG data, highlighting the app's accuracy in capturing physiological parameters. Furthermore, our analysis unveiled significant differences in HRV parameters between the study and control groups, indicating potential autonomic dysfunctions in post-COVID-19 patients (p<0.05). Looking ahead, the app holds promise for facilitating 'at-home tilt-tests,' detecting conditions like Postural Orthostatic Tachycardia Syndrome (POTS) in Long-COVID-19/post-COVID-19 patients. This innovation enhances accessibility to clinical assessments and potentially improves patient outcomes through proactive monitoring and early intervention.

1. Introduction

The technological advances in recent decades have revolutionized the field of health, especially regarding continuous and personalized monitoring. In this context, smartwatches have emerged as multifunctional devices that offer the opportunity to collect biomedical data non-invasively and in real time[1,2].

Most modern smartwatches incorporate optical heart rate sensors, based on photoplethysmographic technology. These sensors emit LED light through the skin, capture reflected light, and, based on variations in light absorption by the blood, estimate heart rate[3]. This non-invasive approach allows for continuous real-time monitoring of heart rate, serving as the basis for subsequent HRV analysis[2].

In addition to heart rate acquisition, modern smartwatches also incorporate accelerometers, allowing the measurement of acceleration and, therefore, determining body position. This technological addition enables a comprehensive understanding of postural changes throughout the day, including tests such as the "Tilt Test" and transitions between sitting, standing, lying down, and standing[2].

The advanced signal processing algorithms present in smartwatches can analyze both heart rate data and acceleration data, providing an integrated view of cardiovascular health and postural behavior. Several applications have been developed for smartwatches, focused on the joint analysis of HRV and acceleration. However, conventional applications are not suitable for diagnosing or analyzing heart rate variability due to the low sampling rate[1].

In this context, we emphasize the need to develop and validate an application designed for a smartwatch with a significantly higher sampling frequency, making it suitable for more accurate clinical pre-diagnoses.

1.1. Hypothesis

Signal processing algorithms in smartwatches can improve our understanding of cardiovascular health and postural behavior.

1.2. Objective

Validate an application for smartwatches that focuses on clinical pre-diagnostic evaluation, particularly for the Tilt Test, while also considering a broader perspective with an

emphasis on Long-COVID19 and post-COVID symptoms.

2. Materials and Methods

2.1. Participants

Forty-six participants were initially evaluated based on specific inclusion and exclusion criteria, leading to the inclusion of 44 individuals. These volunteers, comprising both sexes and aged between 20 and 70 years old with a mean age of 41.0 ± 13.3 years, participated in the study." enrolled in the Brazilian public health system (SUS) participated in the study. (Table 1) Research Location: Polyclinic Hospital / University of Mogi das Cruzes (UMC), Dom Antônio Cândido de Alvarenga Street, 170 - Centro, Mogi das Cruzes, SP, Brazil. The protocol was approved by the Ethics Committee of the UMC (process # 5.770.826, CAAE register 64561022.7.0000.5497). All participants were informed and signed the consent form, which described the study in detail in accordance with the Helsinki Declaration.

Table 1. Clinical Profile. M: mean value. SD: Deviation. DBP: Diastolic blood pressure. SBP: Systolic blood pressure. (*) $p<0.05$.

	Study Group (SD)	Control Group (CG)	*p*
Participants n (%)	31 (70.73%)	15 (29.27%)	
Female (%)	15(83.34%)	3(16.66%)	0.117
Age, years (M ± SD)	44.4 ± 12.0	33.7 ± 13.5	0.01*
Weight, kg (M ± SD)	81.4 ± 15.0	77.1 ± 14.5	0.342
Height, cm (M ± SD)	167.0 ± 5.95	171.4 ± 9.8	0.519
BMI, kg/m^2 (M ± SD)	28.7 ± 4.35	26.5 ± 17.5	0.483
DBP, mmHg (M ± SD)	77.0 ± 7.3	68.9 ± 3.9	0.003*
SBP, mmHg (M ± SD)	120.9 ± 14.4	116.7 ± 9.4	0.502
HR, bpm (M ± SD)	66.6 ± 9.3	61.9 ± 7.2	0.825

2.2. Developing an App for smartwatches

The smartwatches used in the research were the Samsung Galaxy Watch 4 BT model. An application for the smartwatch was developed using *Android Studio Electric Eel version 2022.1.1 Patch 2* to collect and send data from the accelerometer, gyroscope, gravity acceleration, and heart rate to the predefined local server IP. The sampling frequency was 40Hz. Data processing was performed in Python (Google Colab). HR values that were captured as null (zeros) by the smartwatch were interpolated using the *Cubic Spline* library, and the signal was oversampled to 80Hz. The angle of movement was calculated according to the following equation:

$$\theta = 180 * \frac{arctan\left(-\frac{gravx}{gravy}\right)}{\pi} \qquad (1)$$

A proprietary program developed in Python was used to calculate RR intervals and HRV parameters were subsequently computed in the time-, frequency-domain, and non-linear parameters. Data acquisition was synchronized with the collection of ECG data, which served as the gold standard.

2.3. Data acquisition ECG

Data collection was carried out using the PC1000 ECG model from TEB (Brazilian Electronic Technology) with software for processing Heart Rate Variability (HRV); an arm blood pressure monitor from OMRON, model Hem-7320-Br; and a Samsung Galaxy Watch 4 BT 44 mm smartwatch.

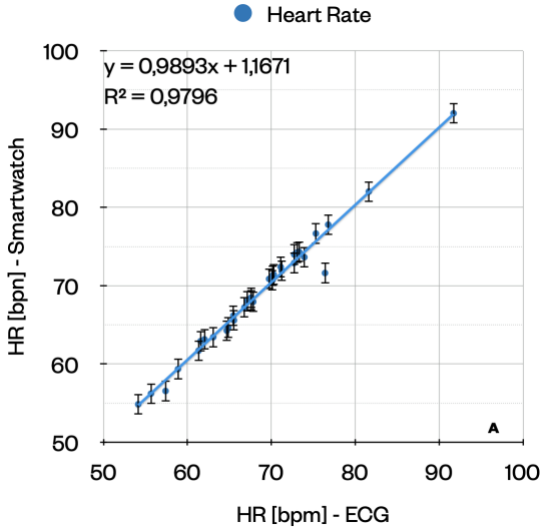
2.4. Statistic

To ensure app accuracy, we conducted calibration tests, including linear regression and the Bland-Altman test to analyze result concordance. Data normality was evaluated using the Shapiro - Wilk goodness-of-fit test. Our null hypothesis was that there is no difference among groups. The Mann-Whitney test was used to assess differences between group followed by the Bonferroni post-hoc test, p values < 0.05 were considered statistically significant.

3. Results

3.1. Calibration

The data collected by the smartwatch was compared with ECG, showing close results (R=0.98) and a concordance error of approximately 1bpm (Figure 1). The importance of applications with higher sampling frequency for accurate clinical pre-diagnosis is emphasized.



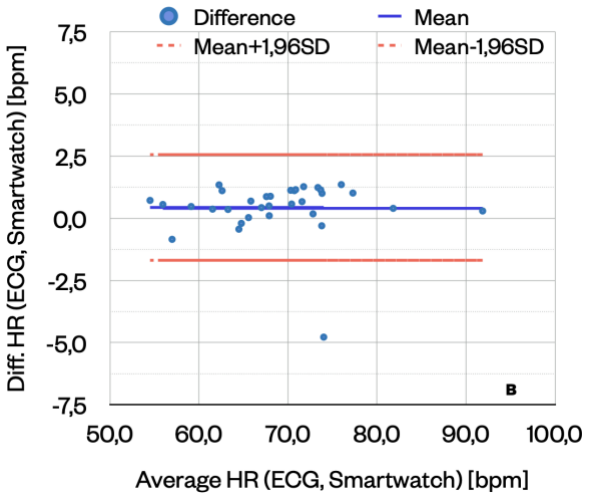


Figure 1. Smartwatch vs ECG Calibration: A) HR Correlation. B) HR Bland-Altman Plot.

3.2. Tilt-Test ECG vs Smartwatch

Heart Rate, Blood Pressure, and Angle was collected using a 50-minute tilt-test protocol divided into 3 phases: 1st phase: Horizontal (15 minutes); 2nd phase: Inclined at 70 degrees from horizontal (15 minutes); 3rd phase: Horizontal (20 minutes). Figure 2 shows the Heart Rate signals acquired by both the ECG and Smartwatch simultaneously.

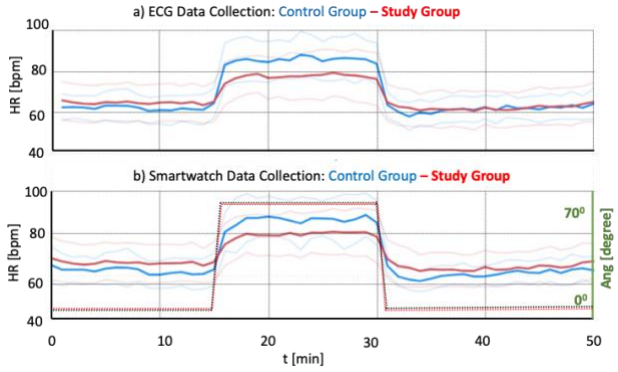


Figure 2. Data acquisition of Tilt-Test by ECG vs Smartwatch in CG (n= 31) and SG (n=15) participants. Angle: dashed blue line (CG), dashed line red (SG).

Data from the smartwatch were compared with ECG data, showing a high correlation. The result reported in Figure 2 enables the application of the signal analysis procedure in the time- and frequency-domain for HRV analysis.

3.2. HRV analysis

We conducted an analysis of HR analysis to time-, and frequency-domain, and HR, BPS, BPD variance. The spectral density across three distinct bands: Very Low Frequency (VLF) [0.0033, 0.04] Hz, which pertains to hormonal regulation, thermoregulation, respiration, and various bodily functions; Low Frequency (LF) [0.04, 0.15] Hz, primarily linked to sympathetic nervous system activity but also influenced by the parasympathetic nervous system; and High Frequency (HF) [0.15, 0.4] Hz, primarily associated with parasympathetic nervous system activity, although it can also be influenced by the sympathetic nervous system(4). Figure 2 illustrates the typical response for both groups, as recorded by the ECG and Smartwatch. Notably, there is a significant reduction in heart rate response. This decrease may signify the impact of viral infection on the autonomic nervous system. The LF/HF ratio, which signifies the sympathetic vs. parasympathetic relationship, exhibited a significant difference (3.95 ± 7.48 for SG vs. 1.27 ± 0.98 for CG, $p<0.05$), while the HR variance (HR var) served as a notable index for distinguishing between groups: 71.52 ± 60.78 for the study group and 143.83 ± 112.17 for the control group ($p<0.001$). Conversely, activity in the VLF and LF bands did not display significant changes. In the time domain, parameters like SDNN, NN50, pNN50, and RMSSD not exhibited significant differences between the groups, suggesting that individuals affected by SARS-CoV-2 respond to postural changes within a narrow range of heart frequencies (see Table 2).

Table 2. HRV statistical analysis. (*) $p < 0.05$.

	Study Group	**Control Group**	***p***
	mean ± SD	mean ± SD	
Time domain			
HR mean [bpm]	68.38 ± 896	71.47 ± 808	0.315
NN mean [ms]	969.9 ± 397.90	872.10 ± 102.68	0.418
SDNN [ms]	477.4 ± 1821.1	151.00 ± 62.01	0.258
NN50	459.69 ± 283.00	591.00 ± 423.663	0.326
pNN50 [%]	16.62 ± 17.02	17.55 ± 12.87	0.586
RMSSD	4.6e+3 ± 1.9e+3	85.30 ± 50.12	0.351
Triang. index	22.32 ± 9.54	22.85 ± 8.17	0.638
Frequency domain			
VLF [s^2]	8.1e+8 ± 4.4e+9	4691.7 ± 7647.1	0.845
LF [s^2]	2.9e+6 ± 1.5e+7	7512.4 ± 12721.6	0.980
HF [s^2]	8e+4 ± 3.8e4	5312.46 ± 9101.9	0.433
LF/HF ratio	3.95 ± 7.48	1.27 ± 0.98	0.013*
Variance			
HR var	71.52 ± 60.78	143.83 ± 112.17	0.013*
SBP var	34.12 ± 27.44	28.87 ± 18.57	0.607
DBP var	30.38 ± 15.89	37.49 ± 17.74	0.200

Based on the angle signal, it was possible to segment the HR signal into the three phases of the tilt test. No significant differences were observed in phases 1 and 3 between both groups. However, when comparing phase 2, it confirms the results obtained in Table 2, LF/HF ratio 4.0 ± 7.5 to SG vs 1.3 ± 0.6 to CG, $p<0.05$. This result suggests dysregulation of heart rate by the sympathetic / parasympathetic system during postural position changes.

4. Discussion

Data collected by the smartwatch were compared with ECG data, showing close results (r=0.98). Statistical analyses highlighted significant differences between study and control groups ($p<0.05$). The importance of apps with higher sampling frequencies for accurate clinical pre-diagnosis is emphasized.

Through continuous monitoring of HR, HRV, and body position, smartwatches offer a approach to health management, particularly for individuals experiencing Long-COVID19 or post-COVID symptoms. By enabling at-home tilt-tests and providing real-time information into cardiovascular health and postural behavior, smartwatches empower patients to actively engage in their healthcare journey. This not only enhances accessibility to clinical pre-diagnosis but also facilitates timely interventions and personalized care strategies. The integration of advanced algorithms and specialized smartwatch apps showcases the potential of leveraging digital technologies to enhance public health. This advancement enables a new approach, where volunteers can perform a "home tilt-test" or activities of daily living, such as lying down, standing, sitting, more simply using just a smartwatch in the comfort of their homes, expanding accessibility to clinical pre-diagnosis through the use of smartwatches, aligning with the WHO Global Strategy on Digital Health 2020-2025.

During the protocol, the device faced a limitation in battery consumption, with approximately 40% of its total charge being used over the 50-minute test. It's conceivable that newer versions could address this limitation for continuous monitoring.

Some potential clinical consequences of the previous findings include: i) Increased risk of cardiac arrhythmias: The alteration in autonomic modulation of heart rate, as indicated by the change in LF/HF ratio (Table 2); ii) Autonomic dysfunction: Reduced heart rate variability (HRV), evidenced by lower heart rate variance (Var HR), may indicate autonomic dysfunction, which can predispose to a range of cardiovascular complications, such as hypertension, metabolic syndrome, and adverse cardiovascular events (Figure 2 and Table 2); iii) Increased cardiovascular risk: Autonomic dysfunction and alteration in autonomic modulation of heart rate are associated with an increased cardiovascular risk, including events like myocardial infarction, stroke, and heart failure; iv) Reduced quality of life: Changes in autonomic modulation of heart rate and HRV may be associated with symptoms such as fatigue, lack of energy, and decreased ability to perform physical activities, resulting in a reduced quality of life for affected individuals. One limitation of our approach is the sampling frequency set at 80Hz, the recommendation is to use 250Hz(2,3). But, as we are monitoring 11 variables (linear acceleration: a_x, a_y, a_z; gravity: g_x, g_y, g_z; angular velocity, ω_x, ω_y, ω_z; HR, time), there is a practical limit on how fast we can sample.

It is important to note that these consequences may vary depending on the severity of COVID-19, the presence of underlying comorbidities, and other individual factors. Furthermore, further research is needed to fully understand the clinical implications of these findings and to develop appropriate intervention strategies to mitigate potential negative impacts on the cardiovascular health of patients who had COVID-19.

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References

1. Goda MÁ, Charlton PH, Behar JA. pyPPG: a Python toolbox for comprehensive photoplethysmography signal analysis. Physiol Meas. 2024;45(4):045001.
2. Charlton PH, Marozas V. Wearable photoplethysmography devices. In: Photoplethysmography. Elsevier; 2022 p. 401–39. https://linkinghub.elsevier.com/retrieve/pii/B9780128233740000116
3. Avram R, Ramsis M, Cristal AD, Nathan V, Zhu L, Kim J, et al. Validation of an algorithm for continuous monitoring of atrial fibrillation using a consumer smartwatch. Heart Rhythm. setembro de 2021;18(9):1482–90.
4. M. Camargo S, M. Silva B, W. U. Pereira M, L. G. Dos Santos A, T. Maximo S, T. Watanabe W, et al. Assessing Autonomic Nervous System Imbalance in Post-COVID-19 Patients through Heart Rate Variability During Tilt Testing. In: https://www.cinc.org/archives/2023/pdf/CinC2023-411.pdf

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