The use of smart watch for early detection of paroxysmal atrial fibrillation

（スマートウォッチを用いた発作性心房細動の早期発見）

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BACKGROUND

Atrial fibrillation (AF) is the most common arrhythmia that afflicts approximately 34 million people worldwide. AF is a well-known risk factor for stroke, with almost 1/3 of all strokes being attributed to this arrhythmia [1-5]. Moreover, nearly 1/3 of patients with paroxysmal AF are asymptomatic [1,4-6], and thus obscuring the diagnosis of this arrhythmia; in fact, up to 50% of patients with stroke caused by AF are diagnosed with AF after the onset of a stroke event [7-9].

With the advent of mobile devices and wearable sensors, it has become possible to continuously monitor health in daily life. Over 450 million wearable devices have been sold, and the current sales growth rate of these devices is approximately 20% per year [10]. Amongst these devices, the smart watch has been gaining attention for its potential usefulness as a wristband-type continuous pulse measurement terminal. This device carries a photoplethysmograph (PPG), a photodetector that uses infrared light emitting diode optical sensors to monitor blood volume changes of the microvasculature [10].

PPG allows pulse rate to be passively and continuously computed on the smart watch. Each pulse signal captured by PPG can be interpreted as an R-wave on the electrocardiogram [10]. If the R-wave in AF can be detected with high precision using PPG, it would be possible to diagnose AF based on the pulse rate [11-13]. Therefore, an algorithm to detect AF using PPG would be an attractive alternative to existing electrocardiography (ECG)-based monitoring, which have limitations particularly in patients with asymptomatic paroxysmal AF [14].

The clinical applicability of PPG has been addressed in many studies, with most studies demonstrating high accuracy in PPG-based pulse measurement among healthy subjects who have no arrhythmia [15-17]. However, ambiguities exist regarding the accuracy of the pulse measurements in patients with an arrhythmia, particularly AF. Additionally, the usefulness of PPG as a diagnostic tool for detecting AF has remained inconclusive, as most reports were based on a short observation period and under resting conditions in patients suffering from persistent AF [18]. Importantly, those studies have not taken into account motion artifacts and other noises that may occur regularly in daily life [19]. Characteristic signals or patterns suggesting the onset and offset of AF have also not been determined [18-21].

The primary purpose of this study was to develop a method for immediate detection of paroxysmal of AF using PPG technology and determine whether PPG-based diagnosis of

paroxysmal AF is feasible in clinical practice. To achieve this, we divided the study into 2 parts: (1) validation of precision and accuracy of data acquired from PPG; and (2) development of an algorithm for on-the-spot detection and diagnosis of paroxysmal AF. This paper, which represents the first part of this study, compares the diagnostic performance of 2 major PPG-integrated smart watches, Apple Watch Series 3 (Apple Watch; Apple Inc., Cupertino, USA) and Fitbit Charge HR (Fitbit; Fitbit Inc., San Francisco, USA), and assesses whether pulse rate values and variations obtained from the PPG devices can help detect paroxysmal AF. Given the high incidence of paroxysmal AF in patients early after cardiac surgery [22-24], those patients were chosen as our study subjects.

METHODS

This study was approved by the Clinical Research Ethics Committee of Chiba University Hospital (Protocol No. UMIN000028403; approved July 27, 2017). All study subjects provided written informed consent that allowed data monitoring, which was performed by Chiba University Hospital Clinical Trials Data Center, and data registration and management, which were undertaken by University of Tokyo. An independent data monitoring committee was also established within the Clinical Trials Division, Chiba University.

From September 2017 to March 2018, 40 subjects from patients scheduled for cardiac surgery at a single center were recruited for Part 1 of this study. The exclusion criteria for this study were history of permanent pacemaker implantation, skin disorder at the wristband attachment site, rubber allergy, and postoperative pacemaker requirement.

Study Protocol

After obtaining written informed consent, the 40 subjects were given a pair of smart watches, Apple Watch and Fitbit, which were worn side-by-side on one forearm. A fully charged extra pair of smart watches was made available at all times in case an exchange is needed and to prevent data loss. The exchange was always carried out by a doctor to ensure data continuity. The smart watches were given to the subjects when the subjects were freed from intensive care (usually on the next day after surgery). The watches were worn continuously until discharge or for 2 weeks, unless the study was aborted for clinical or personal reasons.

Apple Watch offers 2 functional modes with different algorithm settings, the standby (S) mode and the workout (W) mode. Each mode also differs in the algorithm for pulse rate

measurements (as described below), and the subjects were monitored using one of the 2 modes depending on when the device was given. Subjects who started wearing the device before November 2017 were monitored with the S mode until the end of their observation period; from November 2017, the W mode was used instead. The following groups were thus formed: 40 subjects with Fitbit (group FBT), 18 subjects with Apple Watch S mode (group AWS), and 22 subjects with Apple Watch W mode (group AWW).

Central ECG monitoring using a telemetry system (DynaBase CVW-7000, FUKUDA DENSHI, Tokyo, Japan) was continued in all patients until discharge. If AF was suspected, 12-lead ECG was performed for confirmation. AF was diagnosed based on guided diagnostic criteria by a qualified physician. When AF was confirmed, its onset and offset were recorded by reviewing the telemetry data. These procedures were repeated whenever AF was suspected on the central monitor. Any drug therapy that was initiated after AF occurrence was also recorded.

Heart rate and pulse rate measurements

Heart rate data were obtained from the telemetric electrocardiograph, which calculates heart rate every second based on the immediately preceding RR interval.

Pulse rate data were obtained from the PPG-integrated smart watches, although the algorithm for pulse measurements differs slightly between devices. Fitbit calculates the pulse rate by taking the average of the pulse signals captured between 2 and 5 seconds. Apple Watch has 2 functional modes with different algorithm settings; on S mode, the pulse rate (average of pulse signals) is computed at roughly every 6 minutes, and on W mode, the rate is calculated every 5 to 6 seconds. In addition, Apple Watch has an automatic optimization function that increases the luminance of the light emitting diode and sampling rate to compensate for low signal levels (e.g., low perfusion states and dark skin tones); therefore, the time interval (Δt) between each pulse rate calculation on Apple Watch may fluctuate depending on conditions. [25].

Both heart rate and pulse rate data were outputted as a comma-separated values (CSV) file for subsequent analyses.

Cross-correlation analysis

To validate the data obtained from the PPG devices for the detection of AF, the pulse rate data from the PPG devices were compared with the heart rate data from telemetric ECG. Given the variability in the time interval (Δt) for pulse rate calculation as opposed to the time

interval, which is constant at 1 second, for heart rate calculation, we created a time-series graph (Figure 1A) showing the pulse rate {px, p(x+1), p(x+2),…} and the corresponding heart rate {hx, h(x+1), h(x+2),…} at each time point {tx, t(x+1), t(x+2),…} when the pulse rate was calculated. To adjust for the differences in the time intervals, we took the average of all pulse rates calculated within a time frame {e.g., t(x-10) to t(x)} and compared that with the average of the corresponding heart rates calculated within the same time frame. The comparison was repeated by shifting the time frame forward by one time point {t(x-9) to t(x+1), t(x-8) to t(x+2),…}. Thus, a similar time-series graph (Figure 1B) that compared the averages of the pulse rates {Px, P(x+1), P(x+2),…} and the averages of the corresponding heart rates {Hx, H(x+1), H(x+2),…} can be drawn. Those averages were used to analyze for similarities in various trend patterns in the trend curves of the heart rate and the pulse rate by determining their cross-correlation functions (CCF), which range between -1 and 1. In general, the closer the CCF value is to 1, the more similar the patterns are.

In this CCF analysis, the time frame to determine the averages of the calculated rates was set to contain 10 consecutive pulse rate measurements. This time frame corresponded to approximately 1 minute of recording time. Datasets (1 set = 10 pulse/heart rate data) that largely deviated from this 1-minute time frame were excluded from this analysis. After creating the time-series trend curves from the averaged rates, a CCF analysis was performed as follows: 1) apply single regression analysis to each time-series data; 2) calculate the residuals at each time point; and 3) calculate the correlation coefficient by using the residuals of each time-series data [26,27].

Simple linear regression analysis

To evaluate the accuracy of the pulse rates based on PPG measurement in reference to the heart rates based on ECG during AF, a simple linear regression analysis was performed using the same datasets created for the CCF analysis. The mean and the standard deviation of all average pulse rates {Px, P(x+1), P(x+2),…} during AF were compared with the mean and the standard deviation of the corresponding average heart rates {Hx, H(x+1), H(x+2),…}.

Other statistical analyses

Summary statistics were constructed using frequencies and proportions for categorical data and mean ± standard deviation for continuous data. Comparisons between groups were carried out using Student's t test, analysis of variance (ANOVA), or nonparametric tests for

continuous data, and Pearson's chi-squared test for categorical data. *P* values <0.05 were considered statistically significant.

All statistical analyses were performed using SAS version 9.4 for Windows (SAS Institute Inc., Cary, NC).

RESULTS

The demographics of the 40 study subjects are shown in Table 1.

The number of times pulse rate was calculated on the PPG devices was 23,665, 1,758,226, and 4,791,577 in groups AWS, AWW, and FBT, respectively. The time interval (Δt) between each pulse rate calculation was (in seconds) 393.6 ± 525.7, 6.2 ± 6.1, and 3.5 ± 2.6 in groups AWS, AWW, and FBT, respectively. In particular, Δt for pulse rate varied from 1 second to 39 minutes in group AWS with no noticeable increase in the sampling rate during AF.

AF occurred in 24 (60%) subjects. We detected 33 AF events, which included 5 in group AWS, 28 in group AWW, and 33 in group FBT, all confirmed by 12-lead ECG as per guidelines. For validation purposes, very brief episodes of AF and AF events with unclear onset or offset were excluded. Also excluded were AF events that contained device-related noises and interruptions, and those with wide Δt causing deviation from the CCF analysis criteria. After the exclusion process, 23 AF events were considered fit for this validation study.

Validation of precision of detecting AF

Table 2 shows the results of the CCF analysis. The table lists the 23 AF events that can be used for the analysis. As shown, there were 20 and 16 events in groups FBT and AWW, respectively, and none in group AWS that met the analysis criteria.

Of the 20 AF events in group FBT, 9 showed a very weak or a negative correlation between pulse rate trend patterns and heart rate trend patterns. Of the 16 AF events in group AWW, 2 showed a very weak or a negative correlation between the 2 trend patterns. A comparison of the 2 groups by AF events (no. 8-11, 14, 15, 17-23 on Table 2) showed a stronger correlation with group AWW. Regarding group AWS, all 5 events that were confirmed positive for AF were excluded from the analysis because of the very low number of pulse rate measurement per given time frame.

Figures 2A and 2B represent an event (no. 18) and show the two time-series curves, one representing heart rate trend and the other representing pulse rate trend, related to this event. The CCF analyses revealed that the trend patterns during this event were almost identical between Apple Watch W mode and ECG (Figure 2A; CCF 0.83, P <0.001), and similar as a whole but having brief episodes of negative correlation (or inaccurate pulse rate measurements) between Fitbit and ECG (Figure 2B; CCF 0.55, P <0.001).

Figure 3 also represents an event (no. 22) and shows the trend curves that resulted as a negative correlation for both Apple Watch W mode and Fitbit (CCF, -0.02 and -0.62, respectively; P value, 0.283 and <0.001, respectively). Note that the negative correlation was stronger and significant with Fitbit. The subject patient who experienced this event was hypotensive (systolic pressure of 80-85) at the time of the event and had low left ventricular ejection fraction (34%) before surgery. Soon after this event, the same patient had another AF event (no. 23), which similarly showed a very weak or a negative correlation for both devices.

Validation of accuracy of PPG-based pulse rates during AF

The formulas for the fitted regression lines for both the mean and the standard deviation of all average pulse rates and all corresponding average heart rates were obtained using the linear regression model. The scatter plots and the regression lines derived from the regression analysis are shown in Figures 4A and 4B.

Where X denotes the mean of all average pulse rates during AF and Y denotes the mean of all corresponding average heart rates during AF, the regression formulas for Apple Watch W mode and Fitbit were $X = 14.203 + 0.841Y$ and $X = 58.225 + 0.228Y$, respectively, and the coefficient of determination (R^2) were 0.685 and 0.057, respectively (P value, <0.001 and 0.285, respectively).

Where A denotes the standard deviation of all average pulse rates during AF and B denotes the standard deviation of all corresponding average heart rates during AF, the regression formulas for Apple Watch W mode and Fitbit were $A = 5.178 + 0.778B$ and $A = 5.610 + 0.522B$, respectively, and R^2 were 0.572 and 0.255, respectively (P value, 0.002 and 0.017, respectively).

From these analyses, the pulse rate data obtained from Apple Watch W mode significantly reflected the heart rate data from ECG, whereas this correlation was not found with Fitbit. However, an incremental increase in the difference between the pulse rate and the heart rate was observed as the rate increased in the AWW group.

DISCUSSION

Despite the rapid growth and improvement in PPG technology, there has been no direct comparison between long-term monitoring of pulse rates using a PPG device and that of heart rates by ECG in patients with paroxysmal AF. Studies have shown that the risk of stroke associated with AF rises with time and sharply over 24 hours [29]. However, paroxysmal AF is often asymptomatic [1,4-6], leading to unawareness for what may be at risk and limitations for preventive therapy. In this context, the significance of early detection and diagnosis of AF is unquestionable.

This project was started to evaluate the diagnostic feasibility of PPG-integrated smart watches for paroxysmal AF and to develop an algorithm for immediate detection and diagnosis of the arrhythmia using those smart watches as wearable monitoring terminals. To do these, we first performed a validation study to test the precision and accuracy of PPG-based measurements during AF. This was done by using time-series data of the pulse rates and matching those with corresponding time-series data of the heart rates. Due to the difference in the algorithm for pulse measurements between devices, we also compared the two most common devices for their precision and accuracy.

The main findings of this validation study were: 1) paroxysmal AF can be detected with sufficient precision from the trends of the pulse rates, although adjustments are required (e.g., during unstable hypotensive states); 2) pulse rates based on PPG measurements can be matched with heart rates from ECG with sufficient accuracy, although adjustments are required (e.g., during tachycardia); and 3) Apple Watch W mode has the highest precision and accuracy in regards to AF detection and pulse measurement during AF compared to Fitbit and the S mode of Apple Watch. Other notable characteristics of this study were: a) the study was performed under an environment where the subjects were allowed ambulation; b) the comparison between PPG-based data and ECG-based data was done continuously over a long observation period; and c) the onsets and offsets of AF were analyzed with respect to AF detection using PPG. These characteristics were important for the next step of this ongoing project.

In this validation study, a positive correlation was found between the trend patterns of the heart rates and the pulse rates during AF, suggesting that AF can be tracked and possibly alerted at onset on the smart watches. However, there were incidents where an inverse correlation was found, conveying a potential limitation with these devices under certain

conditions. One such condition is low systemic blood pressure, which may weaken the pulse signals that can be recognized by PPG. Clinically, rapid AF is also known to adversely affect cardiac output, thus causing malperfusion of the peripheral vasculature [30-32].

Regarding accuracy of the pulse measurements during AF, the regression line formulated from the linear regression model suggested that, when Apple Watch W mode is being used, a near linear relationship between pulse rates and hearts rates may exists. However, there was an incremental increase in discrepancy between the estimated pulse rate and the heart rate as the rate increased, implying that there may be a limit for which pulse rate computed on the smart watch can accurately reflect the heart rate on ECG.

Previous related studies have reported similar findings. In a study using a different model of Apple Watch and Fitbit, Koshy et al. [21] demonstrated that a rate of >100 beats per minute would result in a difference of 40% and 85% for Apple Watch and Fitbit, respectively, between heart rate and pulse rate. Similarly, other studies [33] have shown a discrepancy between electrical ventricular rate and pulse rate during AF in clinical practice, likely reflecting an occasional absence of aortic valve opening during rapid conduction of electrical impulse within the ventricular myocardium. In an animal model of AF, this discrepancy accounted for a 96.8% reduction of effective ventricular rate, or pulse rate, when the electrical ventricular rate was 80 beats per minute, and a 92.5% reduction when the rate was 120 beats per minute [34].

PPG is affected by multiple factors, including measurement location, skin conditions, and tightness of skin contact. In this validation study, the differences in results between devices were unlikely due to those factors, as the devices were worn side-by-side and on the same side of the wrist. Apple Watch has 4 PPG sensors and the automatic luminance regulation system [25] and Fitbit has only 2 sensors and does not have an auto-adjustment function, and thus it is likely that device performance itself was responsible for the differences.

This study has a number of limitations. The sample size was small and the subjects of this study were elderly patients who required cardiac surgery. All of the subjects were on medications with some subjects in unstable hemodynamic conditions. Thus, the study was directed at people with limited movement and low activity and did not account for motion artifacts in daily life. However, all those issues will be addressed in our next study.

In recent years, industries have begun shifting their production towards wearable devices equipped with a portable electrocardiograph. The new Apple Watch Series 4 carries an electrical heart sensor that, when used with an app, generates a single-lead electrocardiogram capable of diagnosing AF [35]. The electrocardiogram is generated by bringing both hands

(the wrist and a finger) in contact with the device; thus, the diagnosis of AF is possible only when AF is present. This feature is particularly useful when AF can be detected on-the-spot using PPG. Combining these with the rapidly evolving telemedical services and the emergence of direct oral anticoagulants that do not require routine blood monitoring, public health care may enter a new era encompassing efficiency and efficacy, particular in regards to stroke prevention.

CONCLUSION

This first part of the 2-phase study showed that PPG-integrated smart watches can reliably detect AF under controlled conditions. Based on this study, Apple Watch W mode was considered most suitable for the detection of paroxysmal AF. The device demonstrated optimal performance in both detection precision and measurement accuracy when AF occurred. Our next step is to use these data to achieve our purpose of this study - the development of an algorithm for on-the-spot detection and diagnosis of paroxysmal AF.

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DISCLOSURES

The authors declare no conflicts of interest.

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FIGURE

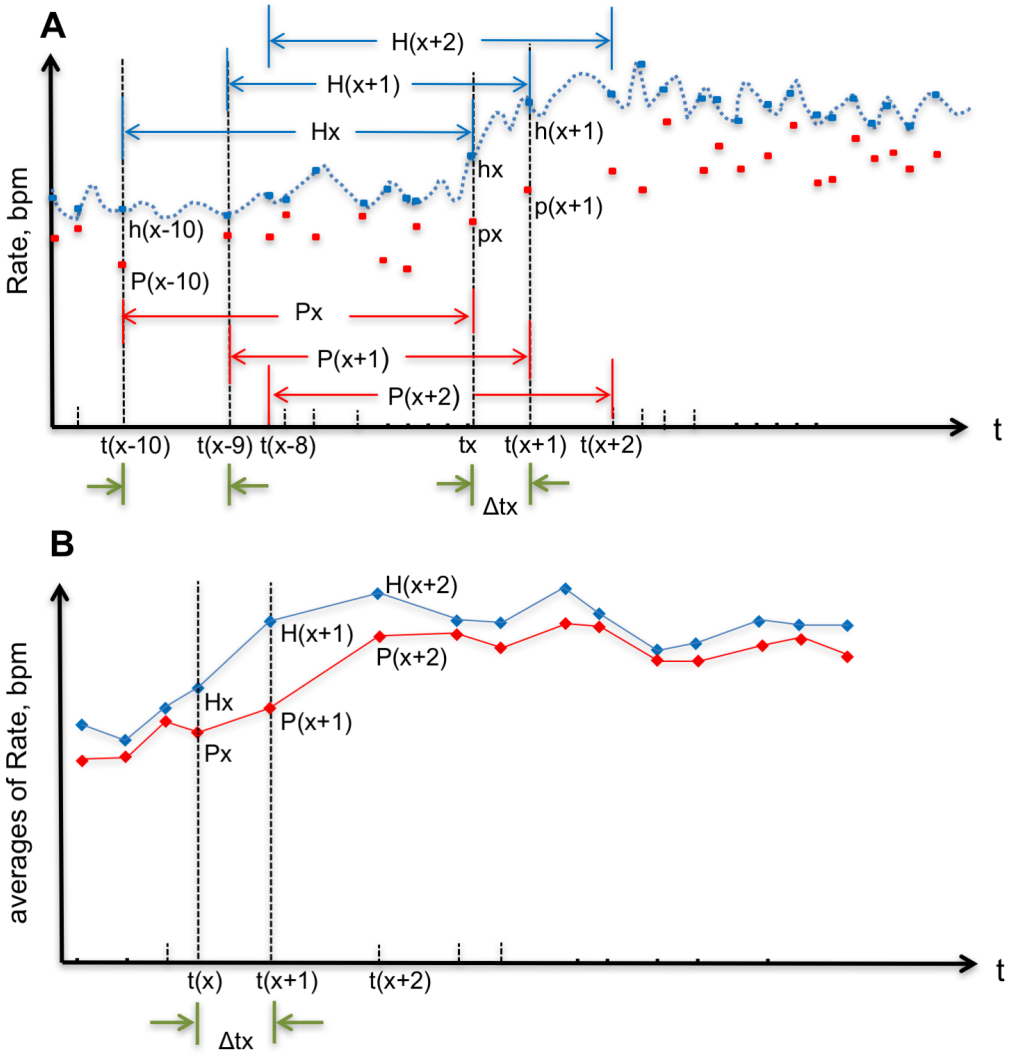

Figure 1. Schematic diagram of time-series curves with matching measurement intervals

Figure 1A shows the pulse rates (px) calculated on the smart watches and the corresponding heart rates (hx) on the electrocardiographic monitor at each time point (tx) when the pulse rate was calculated. The time interval (Δt) shown on this graph is dependent on the pulse rate measurements. The averages of 10 consecutive pulse rates and 10 corresponding heart rates are Px and Hx, respectively.

Figure 1B shows the trend curves formed by plotting the averages of the pulse rates (Px) and the averages of the corresponding heart rates (Hx). These trend curves were used for subsequent analyses.

Red dot represents pulse rate, and blue dot represents heart rate (bolded blue dot represents corresponding heart rate). bpm, beats per minute; t, time.

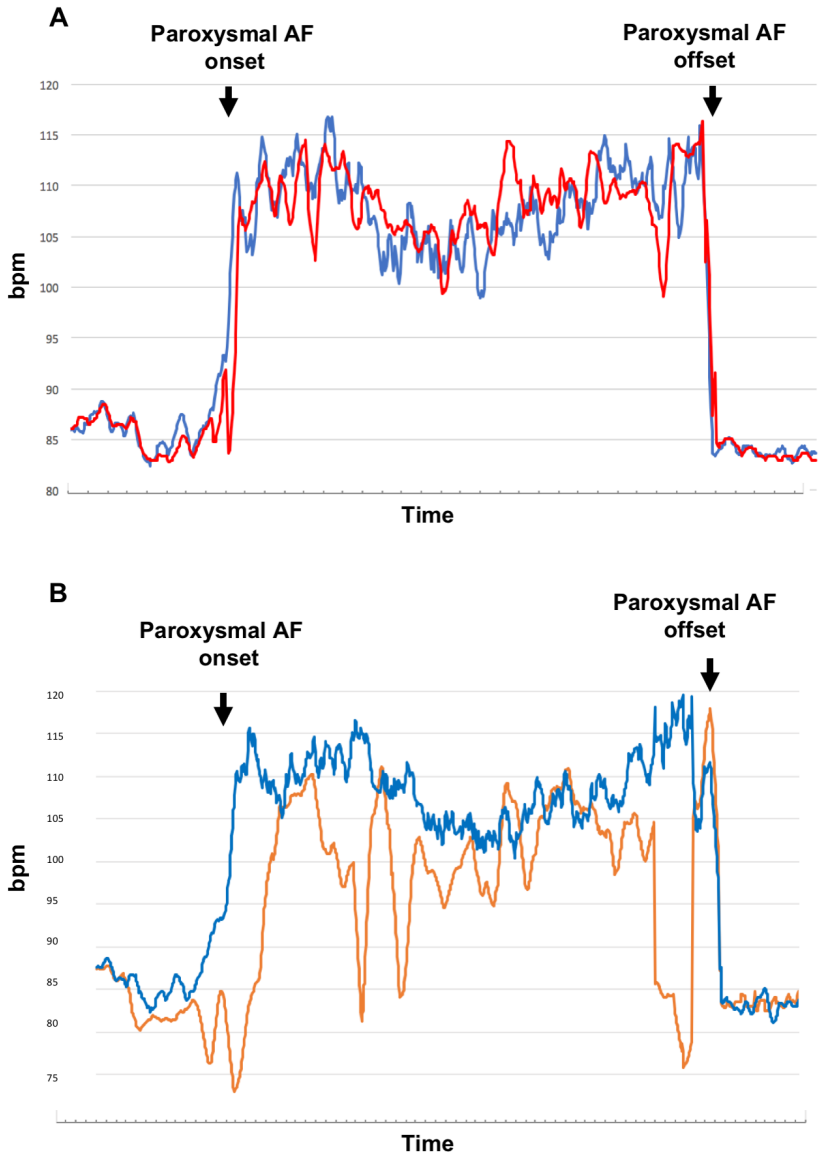

Figure 2. Time-series trend curves during atrial fibrillation (event no. 18)

Figures 2A and 2B represent a same event (event no. 18). Note that the 2 graphs differ in time intervals.

Figure 2A compares the trend curve of the Apple Watch W mode pulse rate (red curve) with that of the ECG-based heart rate (blue curve). The 2 trend curves follow a similar pattern and therefore appears almost identical (CCF 0.83, P <0.001).

Figure 2B compares the trend curve of the Fitbit pulse rate (orange curve) with that of the ECG-based heart rate (blue curve). Although the trends were statistically similar as a whole, brief episodes of an inverse correlation were present, thus weakening the correlation between the two curves (CCF 0.55, P <0.001).

bpm, beats per minute.

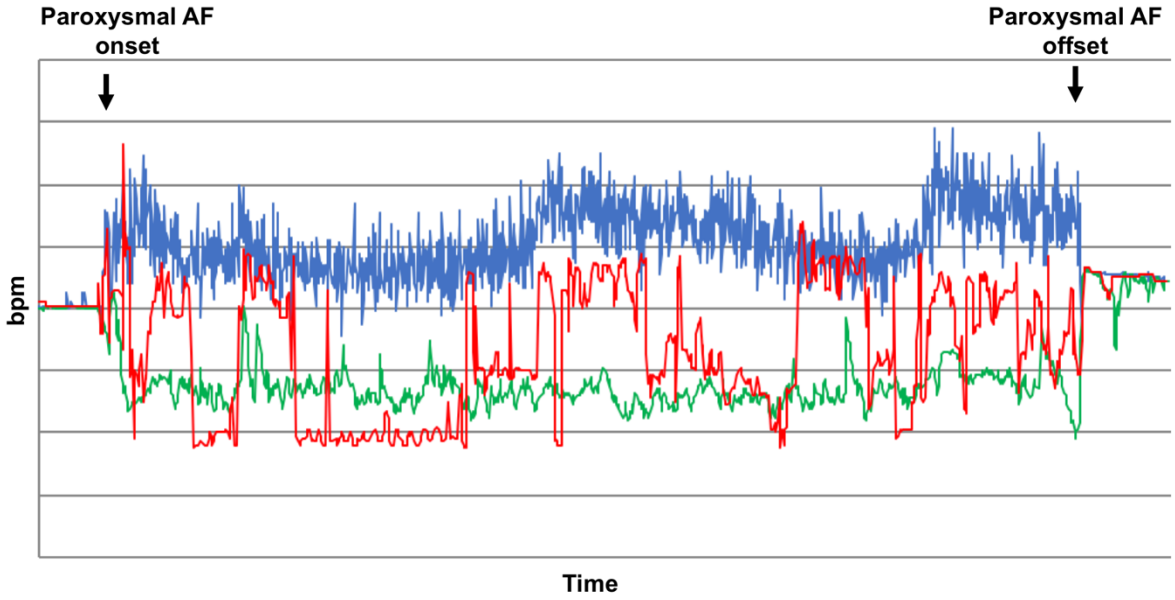

Figure 3. Time-series trend curves during atrial fibrillation (event no. 22)

The 3 trend curves (ECG heart rate, blue curve; Apple Watch W mode pulse rate, red curve; and Fitbit pulse rate, green curve) were compared for similarity. The subject patient who experienced this event was hypotensive at the time of the event. Both Apple Watch W mode and Fitbit showed a negative correlation for pulse rate trends when compared with the heart rate trend (CCF, -0.02 and -0.62, respectively; *P* value, 0.283 and <0.001, respectively). Note that the negative correlation was stronger and significant with Fitbit.

bpm, beats per minute.

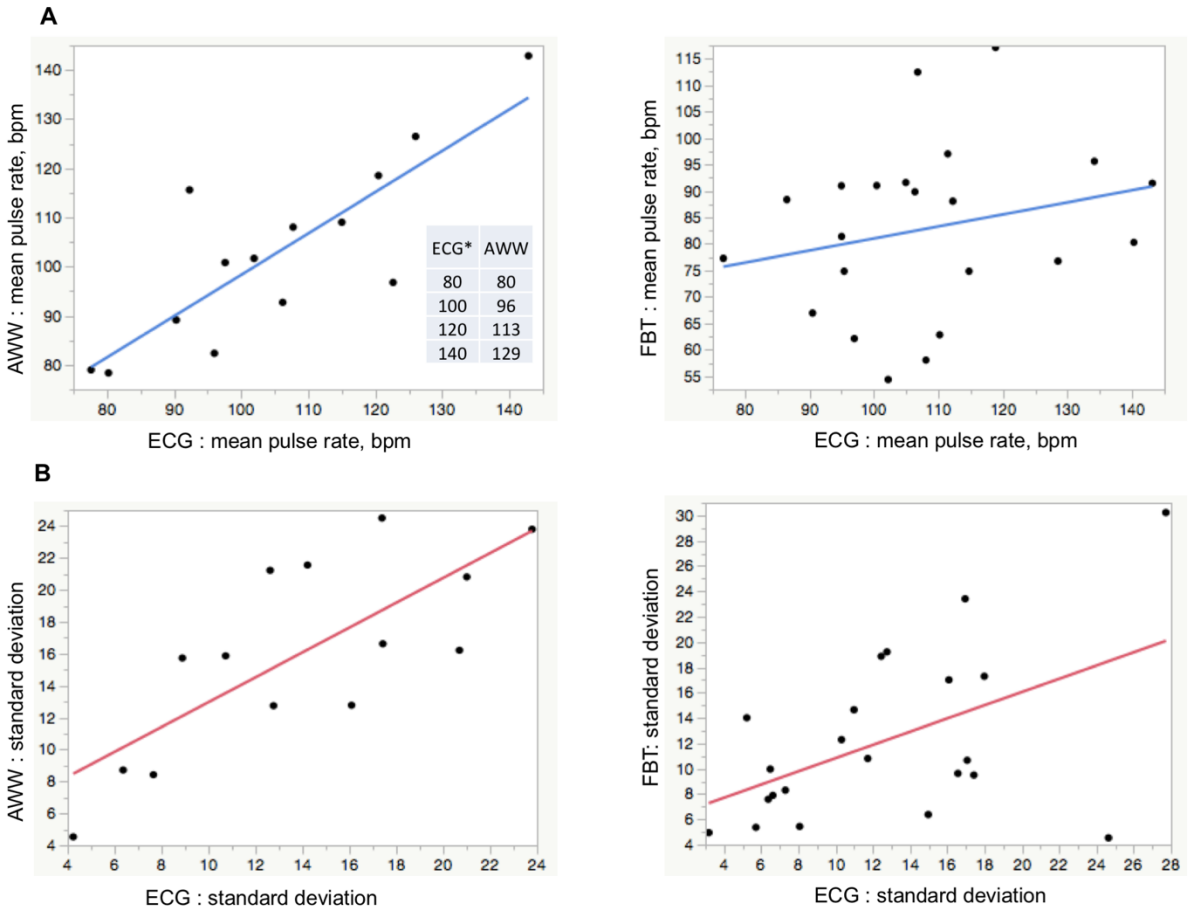

Figure 4. Scatter plot and simple linear regression analysis

AF, atrial fibrillation; AWW, Apple Watch work out mode; BPM, beat per minutes; ECG, electrocardiography; FBT, Fitbit Charge HR; SD, standard deviation.

Table1. Characteristics of patients in each group

	AWS n=18	AWW n=22	FBT n=40	*P* Value*
Age, years	71.0 ± 11.9	70.7 ± 10.6	70.9 ± 11.1	0.94
Male, n (%)	11 (61.1)	16 (72.3)	27 (67.5)	0.44
LVEF	57.7 ± 13.2	61.1 ± 10.2	59.5 ± 11.6	0.37
OPCAB, n (%)	3 (16.7)	5 (22.7)	7 (17.5)	0.63
Valve surgery, n (%)†	14 (77.8)	13 (59.0)	27 (67.5)	0.21
Other surgery, n (%)‡	2 (11.1)	3 (13.6)	6 (15)	0.81
Postoperative stay, days	24.1 ± 17.5	17.5 ± 8.3	20.7 ± 13.6	0.09
Monitoring period, days	12.4 ± 2.1	10.3 ± 2.1	11.3 ± 2.7	0.01
Use of antiarrhythmic drugs before event, n (%)§	16 (88.9)	22 (100)	38 (95)	0.11
Use of antiarrhythmic drugs after event, n (%)‖	18 (100)	22 (100)	40 (100)	-

Values are presented as mean ± standard deviation or number (%) of subjects. AWS, Apple Watch standby mode; AWW, Apple Watch work out mode; FBT, Fitbit Charge HR; LVEF, left ventricular ejection fraction; OPCAB, off pump coronary artery bypass grafting.

* Note that statistical comparison on this table is made only between Apple Watch standby mode and Apple Watch work out mode because of overlaps.

† Included concomitant surgeries.

‡ Included 2 thoracic surgery,1 atrial septal defect closure, and 3 on pump beating coronary artery bypass grafting.

§, ‖ Types of antiarrhythmic drugs included pilsicainide, amiodarone, verapamil, and beta-blockers.

Table2. Time series correlation of pulse change in paroxysmal Atrial Fibrillation

Event Number.	Cross-correlation function			
	Apple Watch Work out mode	*P* Value	Fitbit Charge HR	*P* Value
1	-	-	0.13	<0.001
2	-	-	0.54	<0.001
3	-	-	-0.04	0.039
4	-	-	0.20	<0.001
5	-	-	0.49	<0.001
6	-	-	0.25	<0.001
7	-	-	0.02	<0.001
8	0.81	<0.001	0.62	<0.001
9	0.71	<0.001	-0.08	0.001
10	0.68	<0.001	0.41	<0.001
11	0.79	<0.001	0.37	<0.001
12	0.45	<0.001	-	-
13	0.23	<0.001	-	-
14	0.36	<0.001	0.13	<0.001
15	0.59	<0.001	0.02	0.059
16	0.51	<0.001	-	-
17	0.64	<0.001	0.39	<0.001
18	0.83	<0.001	0.55	<0.001
19	0.83	<0.001	0.71	<0.001
20	0.78	<0.001	0.38	<0.001
21	0.85	<0.001	-0.35	<0.001
22	-0.02	0.284	-0.62	<0.001
23	0.02	0.218	-0.38	<0.001

For reference, the strength of each correlation [28] has been classified in the literature as: <0.19, very weak; 0.20 to 0.39, weak; 0.40 to 0.59; moderate; 0.60 to 0.79, strong; and >0.80, very strong.