JMIR Cardio

Electronic, mobile, digital health approaches in cardiology and for cardiovascular health
Volume 4 (2020), Issue 1 ISSN 2561-1011 Editor in Chief: Andrew Coristine, PhD, Scientific Editor at JMIR Publications, Canada

Contents

Original Papers

Corrigenda and Addenda

Original Paper

Use of a Smart Watch for Early Detection of Paroxysmal Atrial Fibrillation: Validation Study

Tomohiko Inui[1], MD, PhD; Hiroki Kohno[1], MD, PhD; Yohei Kawasaki[2], PhD; Kaoru Matsuura[1], MD, PhD; Hideki Ueda[1], MD, PhD; Yusaku Tamura[1], MD, PhD; Michiko Watanabe[1], MD, PhD; Yuichi Inage[1], MD, PhD; Yasunori Yakita[1], MD; Yutaka Wakabayashi[1], MD; Goro Matsumiya[1], MD, PhD

[1]Department of Cardiovascular Surgery, University of Chiba, Chiba, Japan

[2]Clinical Research Center, University of Chiba, Chiba, Japan

Corresponding Author:
Tomohiko Inui, MD, PhD
Department of Cardiovascular Surgery
University of Chiba
1-8-1, Inohana, Chuo-ku
Chiba
Japan
Phone: 81 432262567
Email: nuinui5762@yahoo.co.jp

Abstract

Background: Wearable devices with photoplethysmography (PPG) technology can be useful for detecting paroxysmal atrial fibrillation (AF), which often goes uncaptured despite being a leading cause of stroke.

Objective: This study is the first part of a 2-phase study that aimed at developing a method for immediate detection of paroxysmal AF using PPG-integrated wearable devices. In this study, the diagnostic performance of 2 major smart watches, Apple Watch Series 3 and Fitbit (FBT) Charge HR Wireless Activity Wristband, each equipped with a PPG sensor, was compared, and the pulse rate data outputted from those devices were analyzed for precision and accuracy in reference to the heart rate data from electrocardiography (ECG) during AF.

Methods: A total of 40 subjects from patients who underwent cardiac surgery at a single center between September 2017 and March 2018 were monitored for postoperative AF using telemetric ECG and PPG devices. AF was diagnosed using a 12-lead ECG by qualified physicians. Each subject was given a pair of smart watches, Apple Watch and FBT, for simultaneous pulse rate monitoring. The heart rate of all subjects was also recorded on the telemetry system. Time series pulse rate trends and heart rate trends were created and analyzed for trend pattern similarities. Those trend data were then used to determine the accuracy of PPG-based pulse rate measurements in reference to ECG-based heart rate measurements during AF.

Results: Of the 20 AF events in group FBT, 6 (30%) showed a moderate or higher correlation (cross-correlation function>0.40) between pulse rate trend patterns and heart rate trend patterns. Of the 16 AF events in group Apple Watch (workout [W] mode), 12 (75%) showed a moderate or higher correlation between the 2 trend patterns. Linear regression analyses also showed a significant correlation between the pulse rates and the heart rates during AF in the subjects with Apple Watch. This correlation was not observed with FBT. The regression formula for Apple Watch W mode and FBT was X=14.203 + 0.841Y and X=58.225 + 0.228Y, respectively (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), and the coefficient of determination (R^2) was 0.685 and 0.057, respectively (P<.001 and .29, respectively).

Conclusions: In this validation study, the detection precision of AF and measurement accuracy during AF were both better with Apple Watch W mode than with FBT.

(JMIR Cardio 2020;4(1):e14857) doi:10.2196/14857

KEYWORDS

Apple Watch; Fitbit Charge HR; paroxysmal atrial fibrillation; photoplethysmography; mobile health; heart rate; validation; wrist-banded devices

Introduction

Background

Atrial fibrillation (AF) is the most common sustained arrhythmia that afflicts approximately 34 million people worldwide. AF is a well-known risk factor for stroke, with almost one-third of all strokes being attributed to this arrhythmia [1-5]. Moreover, nearly one-third of patients with paroxysmal AF are asymptomatic [1,4-6], 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 [10,11]. Among 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, a photodetector that uses infrared light-emitting diode optical sensors to monitor blood volume changes of the microvasculature [12].

Photoplethysmography (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 [12]. 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 [13,14]. Therefore, an algorithm to detect AF using PPG would be an attractive alternative to existing electrocardiography (ECG)–based monitoring, which has limitations, particularly in patients with asymptomatic paroxysmal AF [15-19].

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 [20-22]. However, ambiguities exist regarding the accuracy of the pulse measurements in patients with an arrhythmia, particularly AF. In addition, 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 [23]. Importantly, those studies have not taken into account motion artifacts and other noises that may occur regularly in daily life [24]. Characteristic signals or patterns suggesting the onset and offset of AF have also not been determined [23-26].

Objectives

The primary purpose of this study was to develop a method for immediate detection of paroxysmal AF using PPG technology and to 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, compared the diagnostic performance of 2 major PPG-integrated smart watches, Apple Watch Series 3 (Apple Inc) and Fitbit (FBT) Charge HR Wireless Activity Wristband (Fitbit Inc), and assessed 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 [27-29], those patients were chosen as our study subjects.

Methods

Study Protocol

This study was approved by the Clinical Research Ethics Committee of Chiba University Hospital (protocol number UMIN000028403; approved July 27, 2017) in accordance with all applicable regulations. All study subjects provided written informed consent that allowed data monitoring, which was performed by the Chiba University Hospital Clinical Trials Data Center, and data registration and management, which were undertaken by the 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 a history of permanent pacemaker implantation, skin disorder at the wristband attachment site, rubber allergy, and postoperative pacemaker requirement.

After obtaining written informed consent, the 40 subjects were given a pair of smart watches, Apple Watch and FBT, 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 was 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 1 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 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) was continued in all patients until discharge. If AF was suspected, a 12-lead ECG was performed for confirmation [30]. AF was diagnosed based on the 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. FBT 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 min, 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 (eg, 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 [31].

Both heart rate and pulse rate data were outputted as a comma-separated values 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 1) 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, for example, {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 1 time point {t(x-9) to t(x+1), t(x-8) to t(x+2),...}. Thus, a similar time series graph (Figure 2) 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 (CCFs), 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 min of recording time. Datasets (1 set =10 pulse/heart rate data) that largely deviated from this 1-min 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 [32,33].

Figure 1. Schematic diagram of time series curves with matching measurement intervals (Step1). The figure 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 average of 10 consecutive pulse rates and 10 corresponding heart rates is Px and Hx, respectively. bpm: beats per minute.

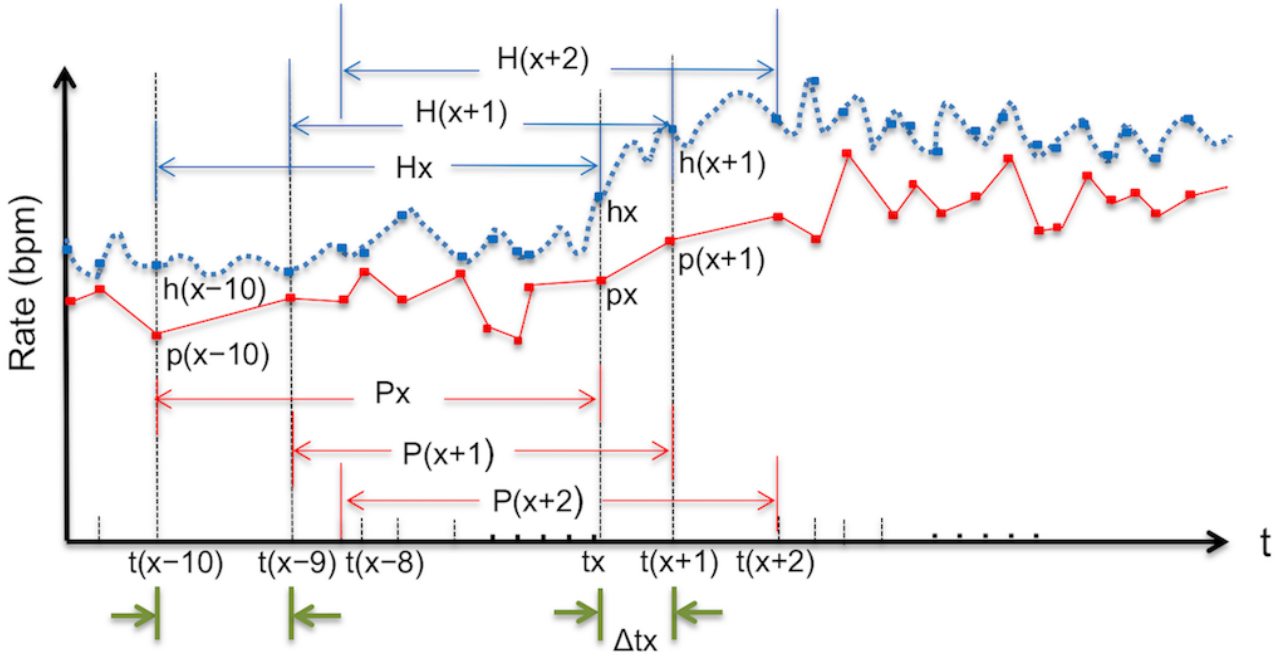
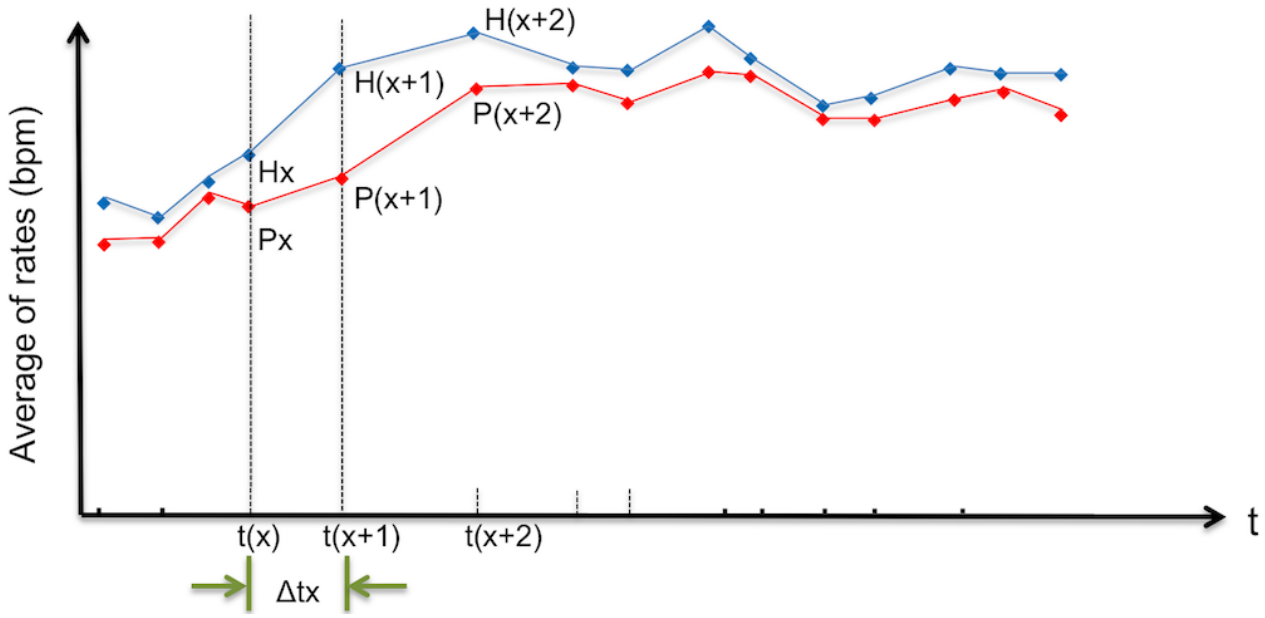


Figure 2. Schematic diagram of time series curves with matching measurement intervals (Step2). The figure shows the averages of the pulse rates (Px) and the averages of the corresponding heart rates (Hx). These trend curves were used for subsequent analyses. The red dot represents pulse rate, and the blue dot represents heart rate (bolded blue dot represents corresponding heart rate). bpm: beats per minute; t: time.



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 *t* test, analysis of variance, or nonparametric tests for continuous data and Pearson chi-square test for categorical data. *P* values less than .05 were considered statistically significant.

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

Results

Patient Demographics

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

Table 1. Characteristics of patients in each group (note that statistical comparison on this table is made only between Apple Watch standby mode and Apple Watch workout mode because of overlaps).

Demographics	Apple Watch standby mode (n=18)	Apple Watch workout mode (n=22)	Fitbit Charge HR (n=40)
Age (years), mean (SD)	71.0 (11.9)	70.7 (10.6)	70.9 (11.1)
Male, n (%)	11 (61)	16(72)	27 (68)
Left ventricular ejection fraction, mean (SD)	57.7 (13.2)	61.1 (10.2)	59.5 (11.6)
Off-pump coronary artery bypass grafting, n (%)	2 (11)	5 (23)	7 (18)
Valve surgery, n (%)[a]	14 (78)	13 (59)	27 (68)
Other surgery, n (%)[b]	2 (11)	4 (18)	6 (15)
Postoperative stay, days	24 (17.5)	17.5 (8.3)	20.7 (13.6)
Monitoring period, days	12.4 (2.1)	10.3 (2.1)	11.3 (2.7)
Use of antiarrhythmic drugs before event, n (%)[c]	16 (89)	22 (100)	38 (95)
Use of antiarrhythmic drugs after event, n (%)[d]	18 (100)	22 (100)	40 (100)

[a]Included multiple surgery.

[b]Included 2 thoracic surgeries, 1 atrial septal defect closure, and 3 on-pump beating coronary artery bypass graftings.

[c]Types of antiarrhythmic drugs included pilsicainide, amiodarone, verapamil, and beta-blockers.

[d]Types of antiarrhythmic drugs included pilsicainide, amiodarone, verapamil, and beta-blockers.

Heart Rate and Pulse Rate Measurements

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 min in group AWS with no noticeable increase in the sampling rate during AF.

AF occurred in 24 out of 40 (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 a 12-lead ECG as per guidelines. For validation purposes, very brief episodes of AF and AF events with unclear onset or offset were excluded. AF events that contained device-related noises and interruptions and those with wide Δt causing deviation from the CCF analysis criteria were also excluded. After the exclusion process, 23 AF events were considered fit for this validation study.

Validation of Precision of Detecting Atrial Fibrillation: Cross-Correlation Analysis

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 (numbers 8-11, 14, 15, and 17-23 in 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 3 and 4 represent an event (number 18) and show the 2 time series curves related to this event: one representing heart rate trend and the other representing pulse rate trend. The CCF analyses revealed that the trend patterns during this event were almost identical between AWW and ECG (Figure 3; CCF 0.83, $P<.001$) and were similar as a whole but having brief episodes of negative correlation (or inaccurate pulse rate measurements) between FBT and ECG (Figure 4; CCF 0.55, $P<.001$).

Figure 5 also represents an event (number 22) and shows the trend curves that resulted as a negative correlation for both AWW and FBT (CCF −0.02 and −0.62, respectively; $P=.28$ and <.001, respectively). Note that the negative correlation was stronger and significant with FBT. The subject patient who experienced this event was hypotensive (systolic pressure of 80-85 mmHg) at the time of the event and had low left ventricular ejection fraction (0.34) before surgery. Soon after this event, the same patient had another AF event (number 23), which similarly showed a very weak or negative correlation for both devices.

Table 2. Time series correlation of pulse change in paroxysmal atrial fibrillation.

Event number	Cross-correlation function			
	Apple Watch workout mode[a]	*P* value	Fitbit Charge HR[a]	*P* value
1	__[b]	—	0.13	<.001
2	—	—	0.54	<.001
3	—	—	−0.04	.04
4	—	—	0.20	<.001
5	—	—	0.49	<.001
6	—	—	0.25	<.001
7	—	—	0.02	.001
8	0.81	<.001	0.62	<.001
9	0.71	<.001	−0.08	<.001
10	0.68	<.001	0.41	<.001
11	0.79	<.001	0.37	<.001
12	0.45	<.001	—	—
13	0.23	<.001	—	—
14	0.36	<.001	0.13	<.001
15	0.59	<.001	0.02	.06
16	0.51	<.001	—	—
17	0.64	<.001	0.39	<.001
18	0.83	<.001	0.55	<.001
19	0.83	<001	0.71	<.001
20	0.78	<.001	0.38	<.001
21	0.85	<.001	−0.35	<.001
22	−0.02	.28	−0.62	<.001
23	0.02	.22	−0.38	<.001

[a]For reference, the strength of correlation [34] can be classified in the literature as: <0.19, very weak; 0.2 to 0.39, weak; 0.4 to 0.59, moderate; 0.6 to 0.79, strong; >0.8, very strong.

[b]Apple Watch workout mode was not used during the period when some events (numbers 1-7) occurred; hence the missing values for those events. Other missing values represent unavailable data.

Figure 3. Time series trend curves during atrial fibrillation (event number 18). The figure compares the trend curve of the Apple Watch W mode pulse rate (red curve) with that of the electrocardiography-based heart rate (blue curve). The 2 trend curves follow a similar pattern and therefore appear almost identical (cross-correlation function 0.83; *P*<.001). AF: atrial fibrillation; bpm: beats per minute.

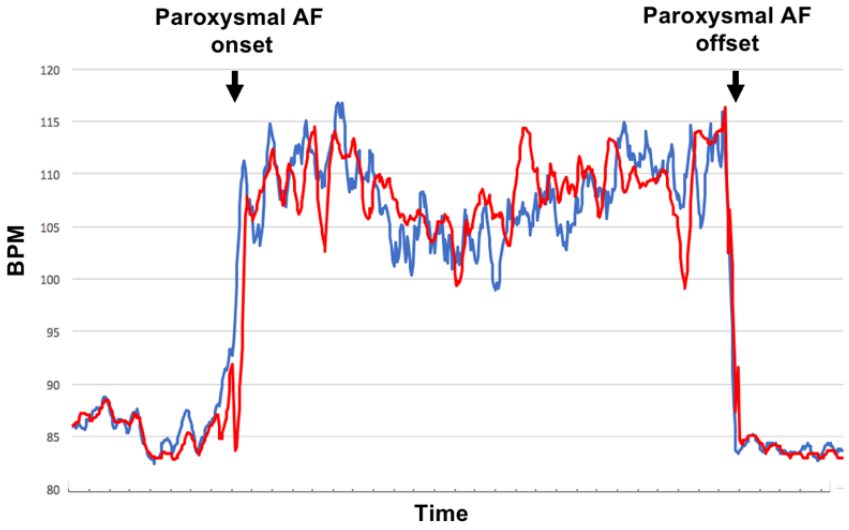


Figure 4. Time series trend curves during atrial fibrillation (event number 18). Figures 3 and 4 represent the same event (event number 18). Note that the 2 graphs differ in time intervals. This figure compares the trend curve of the Fitbit pulse rate (orange curve) with that of the electrocardiography-based 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 2 curves (cross-correlation function 0.55; *P*<.001). AF: atrial fibrillation; bpm: beats per minute.

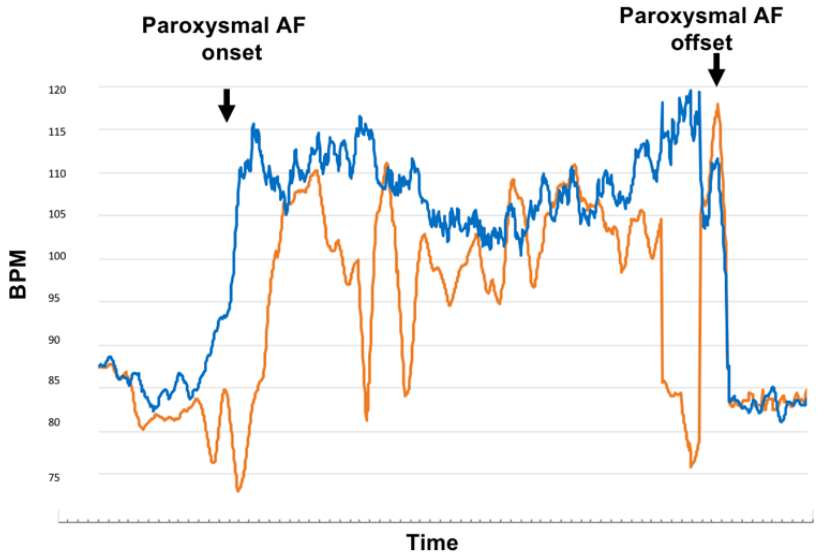
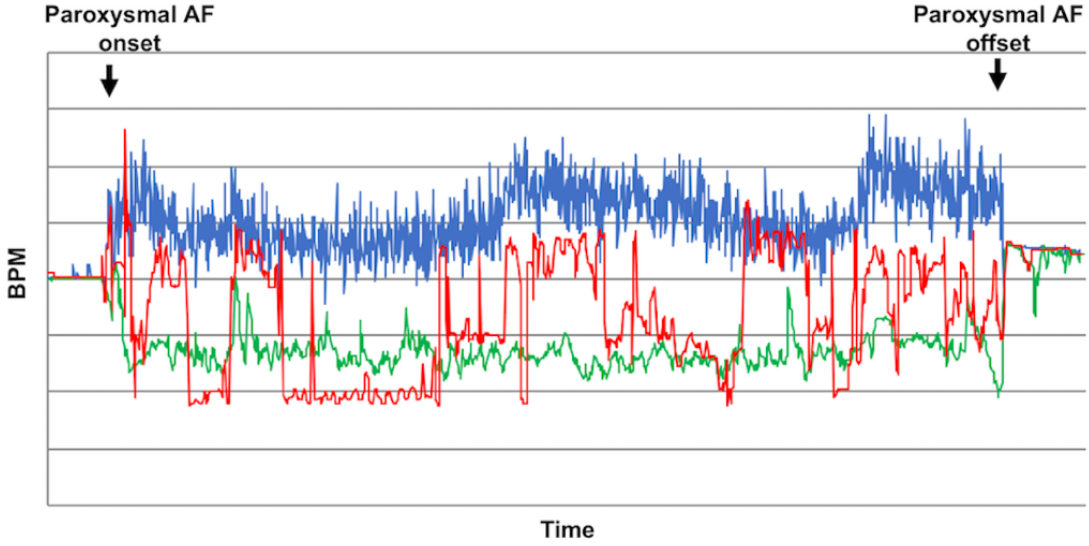


Figure 5. Time series trend curves during atrial fibrillation (event number 22). The 3 trend curves (electrocardiography heart rate, blue curve; Apple Watch W mode pulse rate, red curve; and Fitbit pulse rate, green curve) were compared for similarity. The subject patient who experienced this event was 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 (cross-correlation function −0.02 and −0.62, respectively; *P*=.28 and <.001, respectively). Note that the negative correlation was stronger and significant with Fitbit. AF: atrial fibrillation; bpm: beats per minute.



Validation of Accuracy of PPG-Based Pulse Rates During Atrial Fibrillation: Simple Linear Regression Analysis

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 6 and 7.

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 formula for AWW and FBT was $X=14.203 + 0.841Y$ and $X=58.225 + 0.228Y$, respectively, and the coefficient of determination (R^2) was 0.685 and 0.057, respectively (*P*<.001 and .29, 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 formula for AWW and FBT was $A=5.178 + 0.778B$ and $A=5.610 + 0.522B$, respectively, and R^2 was 0.572 and 0.255, respectively (*P*<.002 and .02, respectively).

From these analyses, the pulse rate data obtained from AWW significantly reflected the heart rate data from ECG, whereas this correlation was not found with FBT. 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.

Figure 6. Scatter plot and simple linear regression analysis for the mean of all average pulse rates and all corresponding average heart rates during atrial fibrillation. AWW: Apple Watch workout mode; bpm: beat per minutes; ECG: electrocardiography; FBT: Fitbit Charge HR.

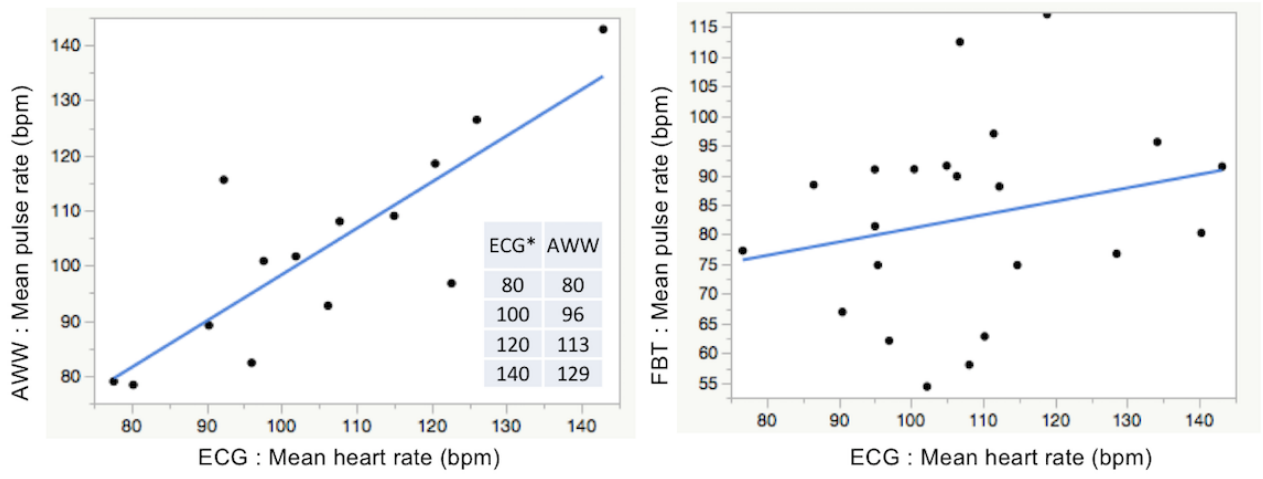
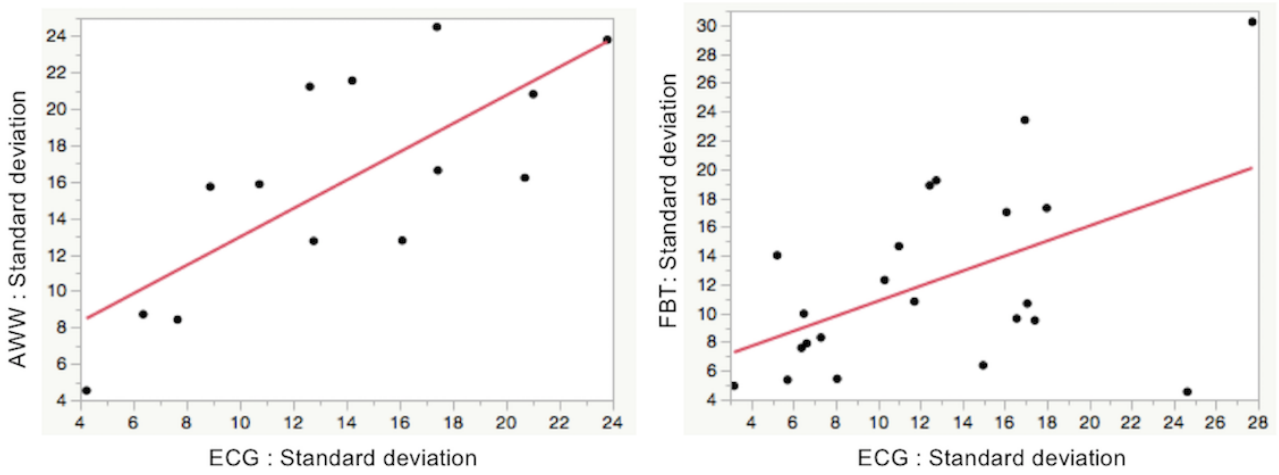


Figure 7. Scatter plot and simple linear regression analysis for the standard deviation of all average pulse rates and all corresponding average heart rates during atrial fibrillation. AWW: Apple Watch workout mode; bpm: beat per minutes; ECG: electrocardiography; FBT: Fitbit Charge HR.



Discussion

Principal Findings

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. In view of this, we have started a project that evaluated 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. The first part of the project was to conduct a validation study, a test of precision and accuracy of the PPG-based measurements during AF. This was done by using the time series data of the pulse rates and matching those with the corresponding time series data of the heart rates. Owing to the difference in the algorithm for pulse measurements between devices, we also compared the 2 most common devices currently available in the market.

The main findings of this validation study were as follows: (1) paroxysmal AF can be detected with sufficient precision from the trends of the pulse rates, although some adjustments may be required (eg, during unstable hypotensive states); (2) pulse rates based on PPG measurements can be matched with heart rates from ECG with sufficient accuracy, although some adjustments may be required (eg, during tachycardia); and (3) AWW has the highest precision and accuracy with regard to AF detection and pulse measurement during AF compared with FBT and the S mode of Apple Watch. It is important to note that these findings were accentuated by the following characteristics: (1) the study was performed under an environment where the subjects were allowed ambulation, (2) the comparison between PPG-based data and ECG-based data was done continuously over a long observation period, and (3) the onsets and offsets of AF were analyzed based on PPG data. These characteristics formed the backbone of this validation study and are crucial 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, implying that AF can be tracked with sufficient precision using a PPG device and that PPG device users can possibly be alerted at the onset of AF. However, there were incidents where an inverse correlation was found, suggesting a potential limitation to the reliability of the device if used under certain conditions. One such condition is low blood pressure. Reduced peripheral blood pressures may weaken the pulse signals that can be captured by PPG. Similarly, rapid AF is known to adversely affect cardiac output and cause malperfusion of the peripheral vasculature [35-37]; thus, further research may be required to test whether other pathophysiologic conditions, such as rapid AF, will compromise the diagnostic capability of PPG.

Regarding the accuracy of the pulse measurements during AF, the regression line formulated from the linear regression model showed that when AWW is used, a near linear relationship between pulse rates and hearts rates existed. 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 [38].

In this study, we also evaluated whether the dispersion of the pulse rates correlated with that of the heart rates during AF. This was done by comparing the standard deviations of both measurements. Unlike other arrhythmias with a fixed RR interval, AF exhibits standard deviations that are inconsistent and thus scattered when plotted on a time series scatter diagram. This inconsistency may help differentiate AF from other common arrhythmias in clinical practice. In terms of validation, we found a positive correlation in the standard deviations between AWW and ECG (Figure 7), thus adding to the suitability of this PPG device for further research.

Comparison With Prior Work

Previous related studies have reported similar findings. In a study using a different model of Apple Watch and FBT, Koshy et al [26] demonstrated that a rate of more than 100 beats per minute (bpm) would result in a difference of 40% and 85% for Apple Watch and FBT, respectively, between heart rate and pulse rate. Similarly, other studies [39] 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 bpm and a 92.5% reduction when the rate was 120 bpm [40].

Limitations

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 [41]. However, all of those issues will be addressed in our next study.

PPG is affected by multiple factors, including measurement location, skin conditions, and tightness of skin contact [42]. In this validation study, the differences in results between devices were unlikely to be because of 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 an automatic luminance regulation system [31], and FBT has only 2 sensors and does not have the auto adjustment function, and thus, it is likely that device performance itself was responsible for the differences.

Clinical Prospects

In recent years, industries have begun shifting their production toward 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 [43]. 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 [44]. By combining those technologies with the rapidly evolving telemedical services and artificial intelligence technology 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, particularly with regard to stroke prevention [43-48]

Conclusions

This first part of the 2-phase study showed that PPG-integrated smart watches can reliably detect AF under controlled conditions. On the basis of this study, AWW 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 using artificial intelligence technology to facilitate and enhance the detection performance.

Acknowledgments

The authors deeply thank Hideyuki Akashi, MD and CEO of MEDCARE Corporation for providing the monitoring equipment necessary for this study. The study equipment was borrowed from MEDCARE Corporation for clinical monitoring purposes only.

Conflicts of Interest

TI, HK, KM, HU, YT, MW, and GM received research funds administered by the Chiba University Graduate School of Medicine from Century Medical, Edwards Lifesciences, Astellas Pharma and TEIJIN Pharma. The remaining authors have no conflicts of interest to disclose.

References

1. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation 2014 Dec 02;130(23):2071-2104. [doi: 10.1161/CIR.0000000000000040] [Medline: 24682348]
2. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014 Feb 25;129(8):837-847 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.113.005119] [Medline: 24345399]
3. Xian Y, O'Brien EC, Liang L, Xu H, Schwamm LH, Fonarow GC, et al. Association of preceding antithrombotic treatment with acute ischemic stroke severity and in-hospital outcomes among patients with atrial fibrillation. J Am Med Assoc 2017 Mar 14;317(10):1057-1067. [doi: 10.1001/jama.2017.1371] [Medline: 28291892]
4. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, American Heart Association Stroke Council, Council on CardiovascularStroke Nursing, Council on Clinical Cardiology,Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014 Jul;45(7):2160-2236. [doi: 10.1161/STR.0000000000000024] [Medline: 24788967]

5. Friberg L, Rosenqvist M, Lindgren A, Terént A, Norrving B, Asplund K. High prevalence of atrial fibrillation among patients with ischemic stroke. Stroke 2014 Sep;45(9):2599-2605. [doi: 10.1161/STROKEAHA.114.006070] [Medline: 25034713]
6. Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012 Jan 12;366(2):120-129. [doi: 10.1056/NEJMoa1105575] [Medline: 22236222]
7. Senoo K, Suzuki S, Sagara K, Otsuka T, Matsuno S, Funada R, et al. Distribution of first-detected atrial fibrillation patients without structural heart diseases in symptom classifications. Circ J 2012;76(4):1020-1023 [FREE Full text] [doi: 10.1253/circj.cj-12-0105] [Medline: 22451452]
8. Hannon N, Sheehan O, Kelly L, Marnane M, Merwick A, Moore A, et al. Stroke associated with atrial fibrillation--incidence and early outcomes in the north Dublin population stroke study. Cerebrovasc Dis 2010;29(1):43-49 [FREE Full text] [doi: 10.1159/000255973] [Medline: 19893311]
9. Sposato LA, Cipriano LE, Saposnik G, Ruíz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. Lancet Neurol 2015 Apr;14(4):377-387. [doi: 10.1016/S1474-4422(15)70027-X] [Medline: 25748102]
10. Statista. 2019. Number of Connected Wearable Devices Worldwide From 2016 to 2022 URL: https://www.statista.com/statistics/487291/global-connected-wearable-devices/
11. Nagamine K. Business Wire. 2021. IDC Forecasts Shipments of Wearable Devices to Nearly Double by 2021 as Smart Watches and New Product Categories Gain Traction URL: https://www.businesswire.com/news/home/20171220005110/en/IDC-Forecasts-Shipments-Wearable-Devices-Double-2021
12. Allen J. Photoplethysmography and its application in clinical physiological measurement. Physiol Meas 2007 Mar;28(3):R1-39. [doi: 10.1088/0967-3334/28/3/R01] [Medline: 17322588]
13. Huang C, Ye S, Chen H, Li D, He F, Tu Y. A novel method for detection of the transition between atrial fibrillation and sinus rhythm. IEEE Trans Biomed Eng 2011 Apr;58(4):1113-1119. [doi: 10.1109/TBME.2010.2096506] [Medline: 21134807]
14. Li Y, Tang X, Wang A, Tang H. Probability density distribution of delta RR intervals: a novel method for the detection of atrial fibrillation. Australas Phys Eng Sci Med 2017 Sep;40(3):707-716. [doi: 10.1007/s13246-017-0554-2] [Medline: 28620839]
15. Camm AJ, Corbucci G, Padeletti L. Usefulness of continuous electrocardiographic monitoring for atrial fibrillation. Am J Cardiol 2012 Jul 15;110(2):270-276. [doi: 10.1016/j.amjcard.2012.03.021] [Medline: 22503584]
16. White RD, Flaker G. Smartphone-based arrhythmia detection: should we encourage patients to use the ECG in their pocket? J Atr Fibrillation 2017;9(6):1605 [FREE Full text] [doi: 10.4022/jafib.1605] [Medline: 29250298]
17. Cheung CC, Krahn AD, Andrade JG. The emerging role of wearable technologies in detection of arrhythmia. Can J Cardiol 2018 Aug;34(8):1083-1087. [doi: 10.1016/j.cjca.2018.05.003] [Medline: 30049358]
18. Turakhia MP, Kaiser DW. Transforming the care of atrial fibrillation with mobile health. J Interv Card Electrophysiol 2016 Oct;47(1):45-50. [doi: 10.1007/s10840-016-0136-3] [Medline: 27306552]
19. Steijlen AS, Jansen KM, Albayrak A, Verschure DO, Van Wijk DF. A novel 12-lead electrocardiographic system for home use: development and usability testing. JMIR Mhealth Uhealth 2018 Jul 30;6(7):e10126 [FREE Full text] [doi: 10.2196/10126] [Medline: 30061094]
20. Cadmus-Bertram L, Gangnon R, Wirkus EJ, Thraen-Borowski KM, Gorzelitz-Liebhauser J. The accuracy of heart rate monitoring by some wrist-worn activity trackers. Ann Intern Med 2017 Apr 18;166(8):610-612 [FREE Full text] [doi: 10.7326/L16-0353] [Medline: 28395305]
21. Wang R, Blackburn G, Desai M, Phelan D, Gillinov L, Houghtaling P, et al. Accuracy of wrist-worn heart rate monitors. JAMA Cardiol 2016 Oct 12;2(1):104-106. [doi: 10.1001/jamacardio.2016.3340] [Medline: 27732703]
22. Wallen MP, Gomersall SR, Keating SE, Wisløff U, Coombes JS. Accuracy of heart rate watches: implications for weight management. PLoS One 2016;11(5):e0154420 [FREE Full text] [doi: 10.1371/journal.pone.0154420] [Medline: 27232714]
23. Tison GH, Sanchez JM, Ballinger B, Singh A, Olgin JE, Pletcher MJ, et al. Passive detection of atrial fibrillation using a commercially available smartwatch. JAMA Cardiol 2018 May 01;3(5):409-416 [FREE Full text] [doi: 10.1001/jamacardio.2018.0136] [Medline: 29562087]
24. Eerik¨ainen L, Dekker L, Bonomi A, Vullings R, Schipper F, Margarito J, et al. Validating features for atrial fibrillation detection from photoplethysmogram under hospital and free-living conditions. Comput Cardiol 2017;44:1-4. [doi: 10.22489/cinc.2017.050-177]
25. Bonomi AG, Schipper F, Eerikäinen LM, Margarito J, van Dinther R, Muesch G, et al. Atrial fibrillation detection using a novel cardiac ambulatory monitor based on photo-plethysmography at the wrist. J Am Heart Assoc 2018 Aug 07;7(15):e009351 [FREE Full text] [doi: 10.1161/JAHA.118.009351] [Medline: 30371247]
26. Koshy AN, Sajeev JK, Nerlekar N, Brown AJ, Rajakariar K, Zureik M, et al. Smart watches for heart rate assessment in atrial arrhythmias. Int J Cardiol 2018 Sep 01;266:124-127. [doi: 10.1016/j.ijcard.2018.02.073] [Medline: 29887428]

27. Kaw R, Hernandez AV, Masood I, Gillinov AM, Saliba W, Blackstone EH. Short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2011 May;141(5):1305-1312 [FREE Full text] [doi: 10.1016/j.jtcvs.2010.10.040] [Medline: 21247589]
28. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. Ann Intern Med 2001 Dec 18;135(12):1061-1073. [doi: 10.7326/0003-4819-135-12-200112180-00010] [Medline: 11747385]
29. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, Investigators of the Ischemia ResearchEducation Foundation, Multicenter Study of Perioperative Ischemia Research Group. A multicenter risk index for atrial fibrillation after cardiac surgery. J Am Med Assoc 2004 Apr 14;291(14):1720-1729. [doi: 10.1001/jama.291.14.1720] [Medline: 15082699]
30. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016 Oct 07;37(38):2893-2962. [doi: 10.1093/eurheartj/ehw210] [Medline: 27567408]
31. Apple Inc. 2017. Heart Rate URL: https://support.apple.com/en-us/HT204666 [accessed 2019-05-20] [WebCite Cache ID 78VxgGKQ2]
32. Yuan N, Fu Z, Zhang H, Piao L, Xoplaki E, Luterbacher J. Detrended partial-cross-correlation analysis: a new method for analyzing correlations in complex system. Sci Rep 2015 Jan 30;5:8143 [FREE Full text] [doi: 10.1038/srep08143] [Medline: 25634341]
33. Chen Y. A new methodology of spatial cross-correlation analysis. PLoS One 2015 May 19;10(5):e0126158 [FREE Full text] [doi: 10.1371/journal.pone.0126158] [Medline: 25993120]
34. Ide K, Yamada H, Kawasaki Y, Yamanaka M, Kawakami N, Katsuyama Y, et al. Peripheral vitamin C levels in Alzheimer's disease: a cross-sectional study. J Nutr Sci Vitaminol (Tokyo) 2016;62(6):432-436 [FREE Full text] [doi: 10.3177/jnsv.62.432] [Medline: 28202849]
35. Clark DM, Plumb VJ, Epstein AE, Kay GN. Hemodynamic effects of an irregular sequence of ventricular cycle lengths during atrial fibrillation. J Am Coll Cardiol 1997 Oct;30(4):1039-1045 [FREE Full text] [doi: 10.1016/s0735-1097(97)00254-4] [Medline: 9316536]
36. Samet P. Hemodynamic sequelae of cardiac arrhythmias. Circulation 1973 Feb;47(2):399-407. [Medline: 4567870]
37. Rawles JM. What is meant by a "controlled" ventricular rate in atrial fibrillation? Br Heart J 1990 Mar;63(3):157-161 [FREE Full text] [doi: 10.1136/hrt.63.3.157] [Medline: 2183858]
38. Harju J, Tarniceriu A, Parak J, Vehkaoja A, Yli-Hankala A, Korhonen I. Monitoring of heart rate and inter-beat intervals with wrist plethysmography in patients with atrial fibrillation. Physiol Meas 2018 Jun 27;39(6):065007. [doi: 10.1088/1361-6579/aac9a9] [Medline: 29856730]
39. Gosselink AT, Blanksma PK, Crijns HJ, Van Gelder IC, de Kam PJ, Hillege HL, et al. Left ventricular beat-to-beat performance in atrial fibrillation: contribution of Frank-Starling mechanism after short rather than long RR intervals. J Am Coll Cardiol 1995 Nov 15;26(6):1516-1521 [FREE Full text] [doi: 10.1016/0735-1097(95)00340-1] [Medline: 7594079]
40. Liau CS, Chen MF, Lin FY, Tsai CH, Lee YT. Relationship between ventricular rate and cardiac output in mimic experimental atrial fibrillation. J Electrocardiol 1994 Apr;27(2):163-168. [doi: 10.1016/s0022-0736(05)80100-1] [Medline: 8201300]
41. Eerikäinen L, Dekker L, Bonomi A, Vullings R, Schipper F, Margarito J. Validating feature for atrial fibrillation detection from photoplethysmogram under hospital and free-living conditions. In: 2017 Computing in Cardiology. 2017 May 24 Presented at: Computing in Cardiology; September 24-27, 2017; Rennes, France p. 3 URL: http://www.cinc.org/archives/2017/pdf/050-177.pdf [doi: 10.22489/CinC.2017.050-177]
42. Shcherbina A, Mattsson CM, Waggott D, Salisbury H, Christle JW, Hastie T, et al. Accuracy in wrist-worn, sensor-based measurements of heart rate and energy expenditure in a diverse cohort. J Pers Med 2017 May 24;7(2):44-44 [FREE Full text] [doi: 10.3390/jpm7020003] [Medline: 28538708]
43. Bumgarner JM, Lambert CT, Hussein AA, Cantillon DJ, Baranowski B, Wolski K, et al. Smartwatch algorithm for automated detection of atrial fibrillation. J Am Coll Cardiol 2018 May 29;71(21):2381-2388 [FREE Full text] [doi: 10.1016/j.jacc.2018.03.003] [Medline: 29535065]
44. Giebel GD, Gissel C. Accuracy of mHealth devices for atrial fibrillation screening: systematic review. JMIR Mhealth Uhealth 2019 Jun 16;7(6):e13641 [FREE Full text] [doi: 10.2196/13641] [Medline: 31199337]
45. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014 Mar 15;383(9921):955-962. [doi: 10.1016/S0140-6736(13)62343-0] [Medline: 24315724]
46. Fan Y, Li Y, Li J, Cheng W, Shan Z, Wang Y, et al. Diagnostic performance of a smart device with photoplethysmography technology for atrial fibrillation detection: pilot study (pre-mAFA II registry). JMIR Mhealth Uhealth 2019 Mar 05;7(3):e11437 [FREE Full text] [doi: 10.2196/11437] [Medline: 30835243]
47. William AD, Kanbour M, Callahan T, Bhargava M, Varma N, Rickard J, et al. Assessing the accuracy of an automated atrial fibrillation detection algorithm using smartphone technology: The iREAD Study. Heart Rhythm 2018 Oct;15(10):1561-1515. [doi: 10.1016/j.hrthm.2018.06.037] [Medline: 30143448]

48. Turakhia MP, Desai M, Hedlin H, Rajmane A, Talati N, Ferris T, et al. Rationale and design of a large-scale, app-based study to identify cardiac arrhythmias using a smartwatch: The Apple Heart Study. Am Heart J 2019 Jan;207:66-75 [FREE Full text] [doi: 10.1016/j.ahj.2018.09.002] [Medline: 30392584]

Abbreviations

AF: atrial fibrillation
AWS: Apple Watch S mode
AWW: Apple Watch W mode
bpm: beats per minute
CCF: cross-correlation function
ECG: electrocardiography
FBT: Fitbit
PPG: photoplethysmography
S: standby
W: workout

Edited by M Focsa; submitted 03.06.19; peer-reviewed by M Lang, M Gaman; comments to author 25.06.19; revised version received 14.11.19; accepted 01.12.19; published 22.01.20.

Please cite as:
Inui T, Kohno H, Kawasaki Y, Matsuura K, Ueda H, Tamura Y, Watanabe M, Inage Y, Yakita Y, Wakabayashi Y, Matsumiya G
Use of a Smart Watch for Early Detection of Paroxysmal Atrial Fibrillation: Validation Study
JMIR Cardio 2020;4(1):e14857
URL: http://cardio.jmir.org/2020/1/e14857/
doi:10.2196/14857
PMID:32012044

Original Paper

The Added Value of In-Hospital Tracking of the Efficacy of Decongestion Therapy and Prognostic Value of a Wearable Thoracic Impedance Sensor in Acutely Decompensated Heart Failure With Volume Overload: Prospective Cohort Study

Christophe J P Smeets[1,2,3], MSc, PhD; Seulki Lee[2], PhD; Willemijn Groenendaal[2], PhD; Gabriel Squillace[2], MSc, PDEng; Julie Vranken[1,3], MSc; Hélène De Cannière[1,3], MSc; Chris Van Hoof[2,4], PhD; Lars Grieten[1,2], MSc, PhD; Wilfried Mullens[5], PhD, MD; Petra Nijst[5], PhD, MD; Pieter M Vandervoort[1,3,5], MD

[1]Mobile Health Unit, Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium

[2]Connected Health Solutions, Holst Centre/Interuniversity Microelectronics Center The Netherlands, Eindhoven, Netherlands

[3]Future Health Department, Ziekenhuis Oost-Limburg, Genk, Belgium

[4]Interuniversity Microelectronics Center, Heverlee, Belgium

[5]Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium

Corresponding Author:
Christophe J P Smeets, MSc, PhD
Mobile Health Unit
Faculty of Medicine and Life Sciences
Hasselt University
Martelarenlaan 42, 3500
Hasselt
Belgium
Phone: 32 89212011
Email: Christophe.smeets@uhasselt.be

Abstract

Background: Incomplete relief of congestion in acute decompensated heart failure (HF) is related to poor outcomes. However, congestion can be difficult to evaluate, stressing the urgent need for new objective approaches. Due to its inverse correlation with tissue hydration, continuous bioimpedance monitoring might be an effective method for serial fluid status assessments.

Objective: This study aimed to determine whether in-hospital bioimpedance monitoring can be used to track fluid changes (ie, the efficacy of decongestion therapy) and the relationships between bioimpedance changes and HF hospitalization and all-cause mortality.

Methods: A wearable bioimpedance monitoring device was used for thoracic impedance measurements. Thirty-six patients with signs of acute decompensated HF and volume overload were included. Changes in the resistance at 80 kHz (R_{80kHz}) were analyzed, with fluid balance (fluid in/out) used as a reference. Patients were divided into two groups depending on the change in R_{80kHz} during hospitalization: increase in R_{80kHz} or decrease in R_{80kHz}. Clinical outcomes in terms of HF rehospitalization and all-cause mortality were studied at 30 days and 1 year of follow-up.

Results: During hospitalization, R_{80kHz} increased for 24 patients, and decreased for 12 patients. For the total study sample, a moderate negative correlation was found between changes in fluid balance (in/out) and relative changes in R_{80kHz} during hospitalization (rs=-0.51, P<.001). Clinical outcomes at both 30 days and 1 year of follow-up were significantly better for patients with an increase in R_{80kHz}. At 1 year of follow-up, 88% (21/24) of patients with an increase in R_{80kHz} were free from all-cause mortality, compared with 50% (6/12) of patients with a decrease in R_{80kHz} (P=.01); 75% (18/24) and 25% (3/12) were free from all-cause mortality and HF hospitalization, respectively (P=.01). A decrease in R_{80kHz} resulted in a significant hazard ratio of 4.96 (95% CI 1.82-14.37, P=.003) on the composite endpoint.

Conclusions: The wearable bioimpedance device was able to track changes in fluid status during hospitalization and is a convenient method to assess the efficacy of decongestion therapy during hospitalization. Patients who do not show an improvement

in thoracic impedance tend to have worse clinical outcomes, indicating the potential use of thoracic impedance as a prognostic parameter.

(JMIR Cardio 2020;4(1):e12141) doi:10.2196/12141

KEYWORDS

congestive heart failure; electric impedance; prognosis

Introduction

Heart failure (HF) is a major and increasing public health problem worldwide and is characterized by frequent (re)hospitalizations that are mainly caused by congestion [1,2]. Congestion is related to water and sodium retention and is defined as a high left ventricular end-diastolic pressure (ie, pressure overload) followed by signs and symptoms such as dyspnea, rales, and edema (ie, volume overload) [3,4]. At present, a high dose of intravenously administered loop diuretics is the most widely used and effective therapy for fluid removal [4]. Accurately assessing a patient's congestion status and treatment efficacy remains difficult and is mainly done by physical examination (ie, dyspnea, orthopnea, edema) or radiographic signs on chest X-ray (ie, interstitial edema, pleural effusion). Unfortunately, physical examination results and radiographic signs have poor sensitivity and predictive value [5,6]. The current gold standard to assess pressure overload is measuring right atrial and pulmonary capillary wedge pressure via cardiac catheterization [7]. However, its invasive nature limits its routine use in daily practice. Guidelines or specific criteria to define treatment efficacy and discharge readiness of patients presenting with acute decompensated HF are vague or missing. Consequently, 30% of patients still have symptoms of congestion on discharge, which negatively influences their prognosis [8].

In recent years, thoracic impedance measurements, provided by implantable (ie, OptiVol and CorVue) or external devices, have been investigated as a tool to assess fluid status and detect volume overload [9-11]. Bioimpedance is an electrical parameter that represents the resistance opposing an electrical current passing through the body. Since blood and fluids have lower resistance to an electrical current than thoracic tissue, it is theoretically possible to measure thoracic fluid changes. An inverse correlation exists between bioimpedance and the amount of body fluid [11-13]. Several invasive and portable devices can measure bioimpedance. However, due to the invasive character of implantable devices, they are only used for a subset of eligible patients. Portable devices, such as the body composition monitor from Fresenius (Bad Homburg vor der Höhe, Germany) or the Bioscan 920-II device from Maltron (Essex, United Kingdom), are bulky and can only be applied by trained medical staff. The Edema Guard Monitor from CardioSet Medical (Bnei Brak, Israel) is a portable device that can be applied in the home environment. This device can be used to predict cardiogenic pulmonary edema, but only until 60 minutes before the appearance of clinical signs, and it can prevent hospitalizations for acute HF [14,15]. Non-invasive wearable devices for bioimpedance recordings provide an interesting alternative since they enable longitudinal monitoring and trend analysis in a comfortable way [12,13,16,17]. There exists only a handful of these devices: the Cova necklace from toSense (La Jolla, CA) [18], the AVIVO Mobile Patient Management System from Corventis (San Jose, CA) [19,20], and the wearable bioimpedance vest from Philips (Andover, MA) [13,17]. The Philips vest showed a strong correlation between bioimpedance and daily weight changes, and has been shown to be able to track recompensation during therapy for acute congestive HF [13]. Unfortunately, the form of the vest limits in-hospital use and is less convenient for continuous, long-term, in-home monitoring. In an article published 2 years later, the researchers suggested that wearable bioimpedance systems such as the vest could provide value beyond measuring clinical improvement and provide a prognostic assessment of patients admitted for HF [17]. However, more evidence on the use of bioimpedance to track fluid changes and the relationship with clinical outcome is needed to support the translation of this approach into clinical practice. In a previous study, we provided initial results on the feasibility of the wearable bioimpedance sensor and the correlations with clinical reference measures [12].

In the current study, we aimed to determine whether bioimpedance-based monitoring can be used to assess changes in a patient's fluid status (ie, the efficacy of decongestion therapy during hospitalization) and the relationships with both HF hospitalization and all-cause mortality. The research questions were *"Can a wearable bioimpedance sensor be used to measure changes in fluid status as a measure of the efficacy of decongestion therapy in patients hospitalized for acute decompensated HF?"* and *"Is there a relationship between changes in thoracic bioimpedance during hospitalization for acute decompensated HF and clinical outcome in terms of HF hospitalization and all-cause mortality?"*

Methods

Study Design

This was a prospective cohort study of patients admitted to a single tertiary care center (Ziekenhuis Oost-Limburg, Genk, Belgium). Consecutive patients admitted with signs of acute decompensated HF, for which diuretic therapy was started, were included. Diuretic therapy was initiated according to standard clinical practice. The initiation and continuation of the diuretic therapy were not dictated by the study protocol but were carried out according to standard care. Besides bioimpedance measurements, no additional tests nor treatments were performed beyond those of standard practice (eg, fluid balance, chest X-ray, echocardiographic examination). Bioimpedance measurement results were blinded for the treating physician. Patients were divided into two groups according to the change in bioimpedance during hospitalization and were clinically

followed for 12 months. Clinical outcome measures were assessed at 30 days and 1 year of follow-up and included all-cause mortality, HF hospitalization, and the composite of all-cause mortality and HF hospitalization. All participants provided written, informed consent. The study complied with the Declaration of Helsinki, and the study protocol was approved by the local committee on human research.

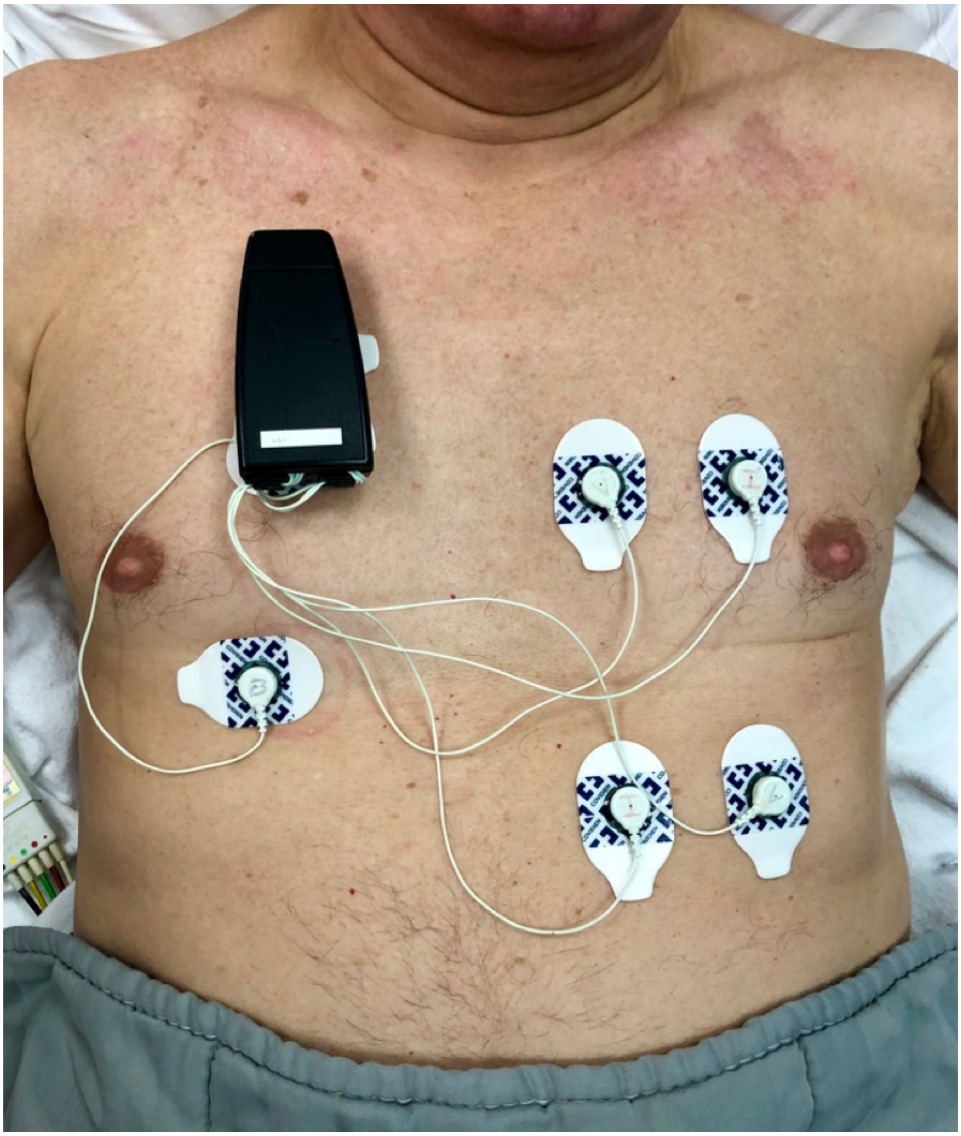
Study Population

Patients admitted to the emergency room with signs or symptoms of acute decompensated HF with volume overload, assessed by a dedicated HF specialist, were approached as soon as possible after triage. Symptoms of congestion were defined as pitting edema, worsening in shortness of breath or orthopnea, paroxysmal nocturnal dyspnea, wheezes, rales, or signs of congestion on chest X-ray such as the presence of pulmonary venous congestion, vascular redistribution, Kerley B lines, or blunted costophrenic angles. Patients were included only when the anticipated date of discharge was >48 hours after study screening (as estimated by the dedicated HF specialist). This study inclusion criterion was based on previous research in the field of bioimpedance monitoring in HF [11].

Wearable Bioimpedance Monitor

A novel, wearable, multi-parametric bioimpedance monitoring device from the Interuniversity Microelectronics Center (imec) the Netherlands (Eindhoven, The Netherlands) was used for local bioimpedance measurements (Figure 1). The device measures multi-frequency bioimpedance, non-standard one-lead electrocardiogram, and accelerometer data [12,16,21]. Analysis of the one-lead electrocardiogram data was out of scope for the current study since patients were monitored using a gold-standard, bedside, vital signs monitor according to standard care. Due to the dominant resistive component of fluid changes, changes in resistance at 80kHz (R_{80kHz}) were used for the analyses. At this frequency, the weighted sum of extracellular water and intracellular water resistivities is being measured. This is because the current passes through both intra- and extracellular fluid, although the proportion varies from tissue to tissue. To calculate the R value per session, only bioimpedance data recorded under the same posture and during periods of low movement intensity (as measured by the accelerometer) were selected for further analysis. Next, the median R value of the filtered data per measurement was used for analysis. Bioimpedance values are strongly dependent on patient-specific characteristics, such as body composition (ie, fat percentage, muscle percentage), the amount of body hair, and skin condition. Relative bioimpedance values were therefore used for more individualized analyses and to minimalize inter-individual variability. To do so, every measurement was divided by the baseline measurement (R_n/R_0; R_n corresponds to the resistance value at time point *n*, and R_0 corresponds to the resistance value at baseline). Patients were divided into two groups: those with a relative increase in R_{80kHz} and those with a relative decrease in R_{80kHz} from admission to coronary care unit discharge (ie, change in impedance between the very first and very last measurements). A fixed tetrapolar electrode configuration [12] was used to reduce the influence of the electrode-skin impedance.

Figure 1. Positioning of the wearable, multi-parametric bioimpedance monitoring device from imec the Netherlands.



Measurement Protocol for Patients with Decompensated Heart Failure

Using a fixed electrode position of the wearable device, thoracic impedance measurements were performed twice a day for about 10 minutes per measurement for at least 3 consecutive days (Figure 1). Between the consecutive measurements, the device was detached; however, whenever possible, the electrodes were left in place. A skin marker was used to mark the location of the electrodes when they were removed. To eliminate the possible influence of posture, patients were always placed in a 20-30-degree semi-Fowler's position and were asked not to move or talk during measurements. In addition, patients' input/output fluid balances were documented every hour as a reference measure for changes in fluid status. Fluid balance was chosen as the reference measure due to its objective nature and ease of measurement in a coronary care unit where patients are equipped with a urinal or bladder probe. Fluid balance information was available until patients moved from the coronary care unit to the low intensive care unit.

Statistical Analysis

Continuous variables are expressed as mean (SD), if normally distributed, or as median (IQR), if not normally distributed. Normality was assessed using the Shapiro-Wilk statistic. To identify statistical differences between the two groups, the independent samples student's *t* test and Mann-Whitney *U* test were used for normally and not normally distributed continuous variables, respectively, and the Chi-Square test was used for categorical variables. Correlation analysis between each consecutive measurement for changes in fluid balance and changes in thoracic impedance values was performed using the one-tailed Spearman correlation. Survival curves were constructed according to the Kaplan-Meier method, with the log-rank test used for comparison between the groups. Cox regression analysis with Firth's penalized likelihood correction was used to calculate hazard ratios. A multivariate Cox regression model was fitted with the following explanatory variables: baseline characteristics that were significantly different between the two groups (presence of atrial fibrillation and diuretic use), clinically relevant factors (age and left ventricular ejection fraction), and the group indicator. Next, backward model building was executed, removing the

explanatory variables not significant at a 5% level. A significance level of .05 was used for all tests. Cox regression with Firth's penalization was performed using SAS 9.4 (SAS Institute Inc, Cary, NC); all other statistical analyses were performed using SPSS release 24.0 (SPSS Inc, Chicago, IL).

Results

Study Sample

Thirty-six patients admitted to the cardiology ward with acute decompensated HF were included with the following characteristics: mean age 81 years (SD 8 years), left ventricular ejection fraction 45% (IQR 36-55), 14 (39%) with ischemic HF etiology. Eight patients were equipped with an implantable electronic cardiac device, of which 5 patients had a pacemaker and 3 patients had a cardiac resynchronization therapy device. The mean measurement duration was 5 days (SD 2 days).

Bioimpedance Changes

Thoracic impedance data showed an inverse relationship with fluid status for a representative patient with combined HF (Figure 2) and with isolated left-sided HF (Figure 3) during hospital admission, also visible by the observed strong correlation coefficients (r_s>0.700, *P*<.001). The correlation coefficient is higher for patients with isolated left-sided HF.

Figure 2. Relationship between thoracic impedance at 80 kHz (R_{80kHz}; black triangles) and fluid balance (blue squares) for a representative patient admitted with combined heart failure.

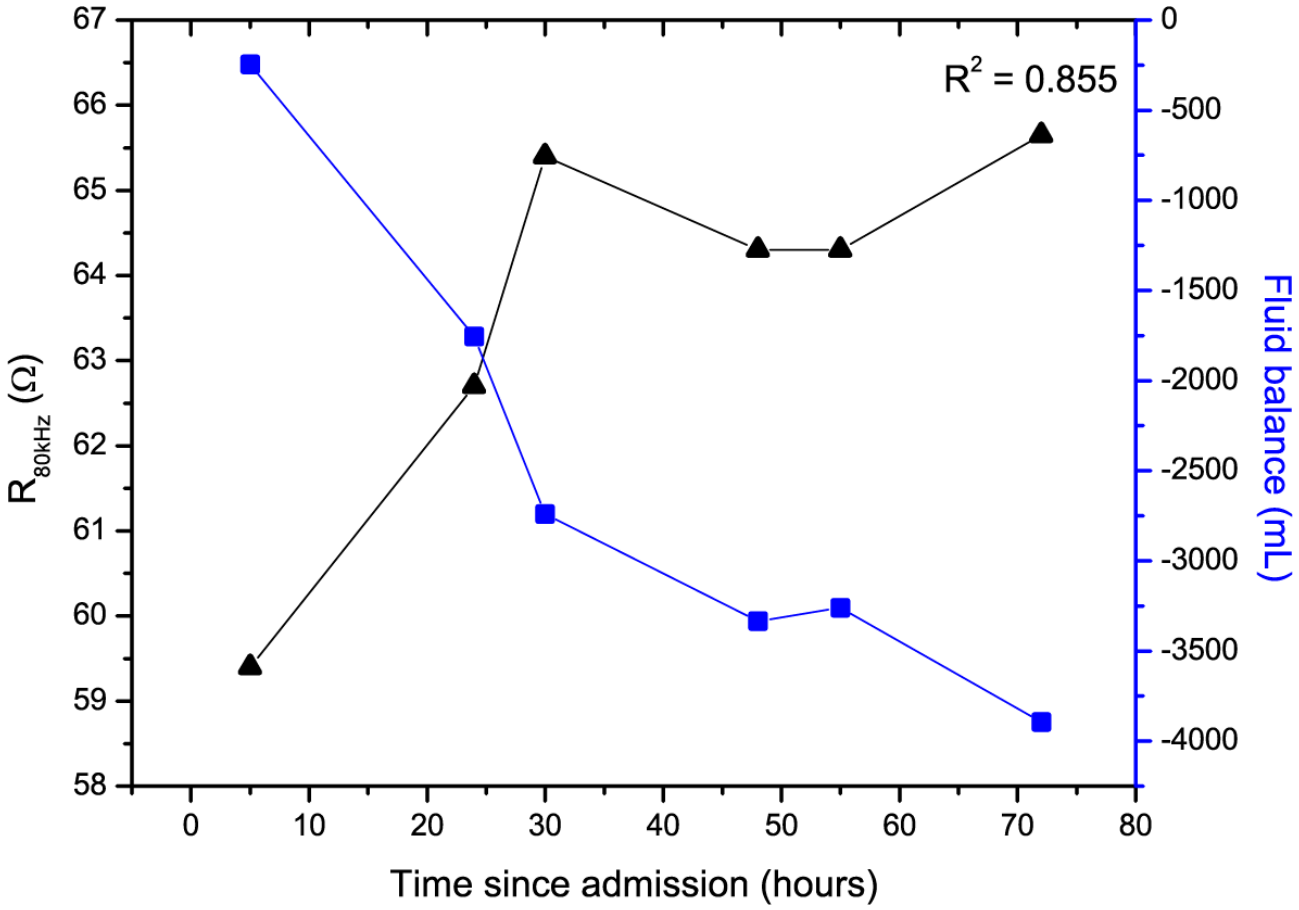
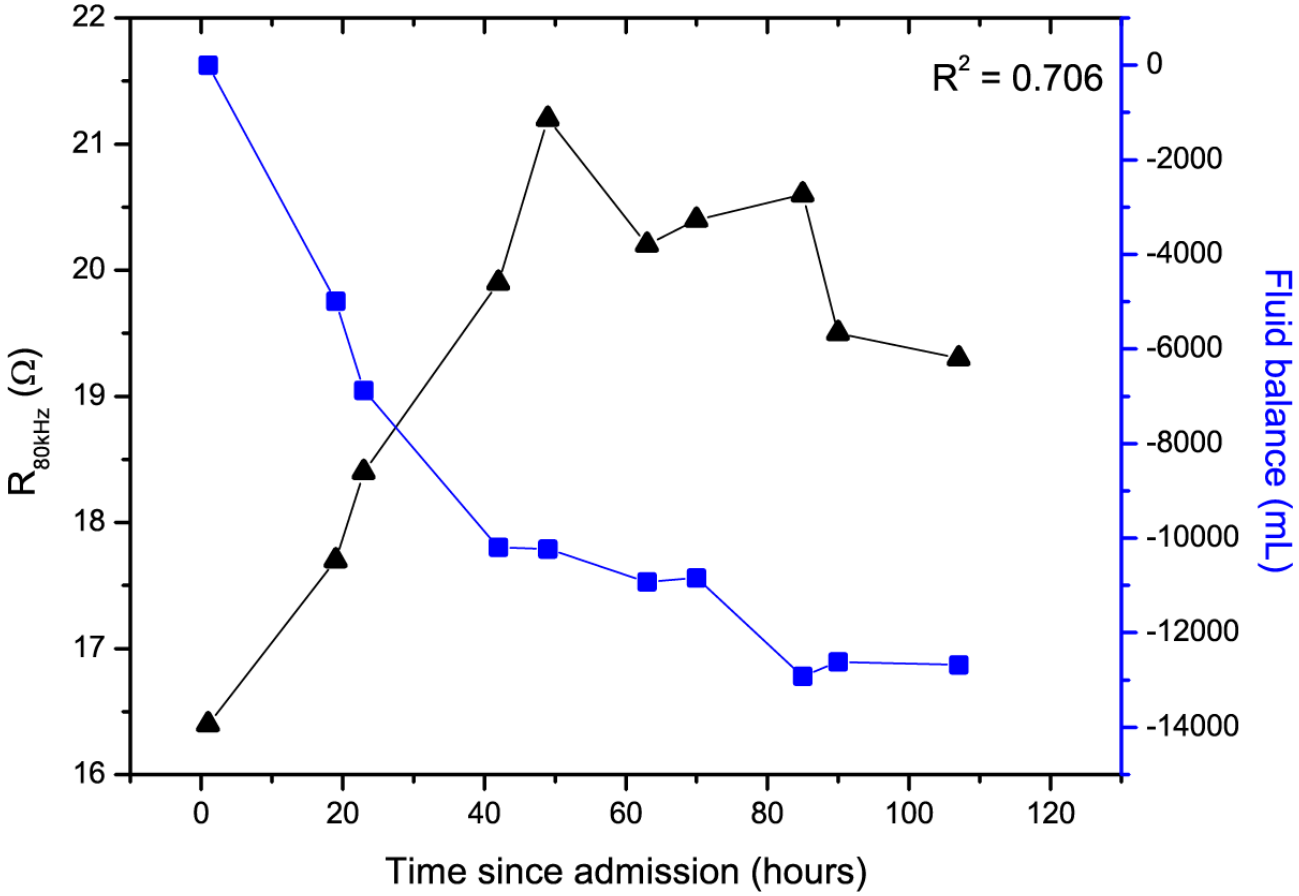


Figure 3. Relationship between thoracic impedance at 80 kHz (R_{80kHz}; black triangles) and fluid balance (blue squares) for a representative patient admitted with isolated left-sided heart failure.



For the total sample, a moderate negative correlation was found between changes in fluid balance and relative changes in R_{80kHz} (r_s= -0.51, P<.001). Patients were divided into two groups according to the relative change in R_{80kHz} from admission to coronary care unit discharge: patients with a relative increase in R_{80kHz} and patients with a relative decrease in R_{80kHz}. Baseline population characteristics are provided in Table 1. Of the 36 patients, 24 (67%) patients showed a relative increase in R_{80kHz}, and 12 (33%) patients showed a relative decrease in R_{80kHz} (Figure 4).

Table 1. Comparison of patient baseline characteristics at arrival at the emergency department, grouped according to the relative change in resistance at 80kHz (R_{80kHz}) from admission to coronary care unit discharge.

Variables	Patients with decompensated heart failure (n=36)		
	Increase in R_{80kHz} (n=24)	Decrease in R_{80kHz} (n=12)	*P* value
Age (years), mean (SD)	80 (9)	83 (6)	.24
Male sex, n (%)	10 (42)	6 (50)	.64
BMI (kg/m²), mean (SD)	31 (8)	30 (4)	.86
Left ventricular ejection fraction (%)[a], median (IQR)	55 (39 to 55)	44 (26 to 47)	.057
Heart rate (bpm), mean (SD)	86 (25)	90 (19)	.65
Systolic blood pressure (mm Hg), mean (SD)	144 (23)	147 (33)	.73
Diastolic blood pressure (mm Hg), mean (SD)	74 (18)	72 (26)	.86
Baseline NT-proBNP[b] (pg/mL)[c], median (IQR)	3,027 (1681 to 6161)	12,181 (3307 to 17,352)	.052
Total fluid balance during hospitalization (mL), median (IQR)	–3048 (–4396 to 1963)	–1298 (–2225 to 69)	.002
R_{80kHz} at admission (Ω), mean (SD)	42 (20)	46 (18)	.52
R_{80kHz} at coronary care unit discharge (Ω), mean (SD)	48 (22)	44 (18)	.60
Relative R_{80kHz} change from admission to coronary care unit discharge (%), median (IQR)	109 (105 to 122)	94 (85 to 97)	<.001
Heart failure etiology, n (%)			
Ischemic heart disease	10 (42)	4 (33)	.73
Dilated cardiomyopathy	0 (0)	1 (8)	.33
Valvular disease	5 (21)	3 (25)	1.00
Other	9 (38)	4 (33)	.26
Comorbidities, n (%)			
eGFR[d] <60 mL/min/1.73m²	15 (63)	11 (92)	.12
Atrial fibrillation	11 (46)	10 (83)	.03
Implantable electronic cardiac device	5 (21)	3 (25)	.55
Chronic obstructive pulmonary disease	1 (4)	3 (25)	.10
Diabetes	7 (29)	6 (50)	.28
Maintenance therapy, n (%)			
Renin-angiotensin system blocker	12 (50)	6 (50)	1.00
Beta blocker	16 (67)	7 (58)	.72
(Loop) diuretic	14 (58)	12 (100)	.02

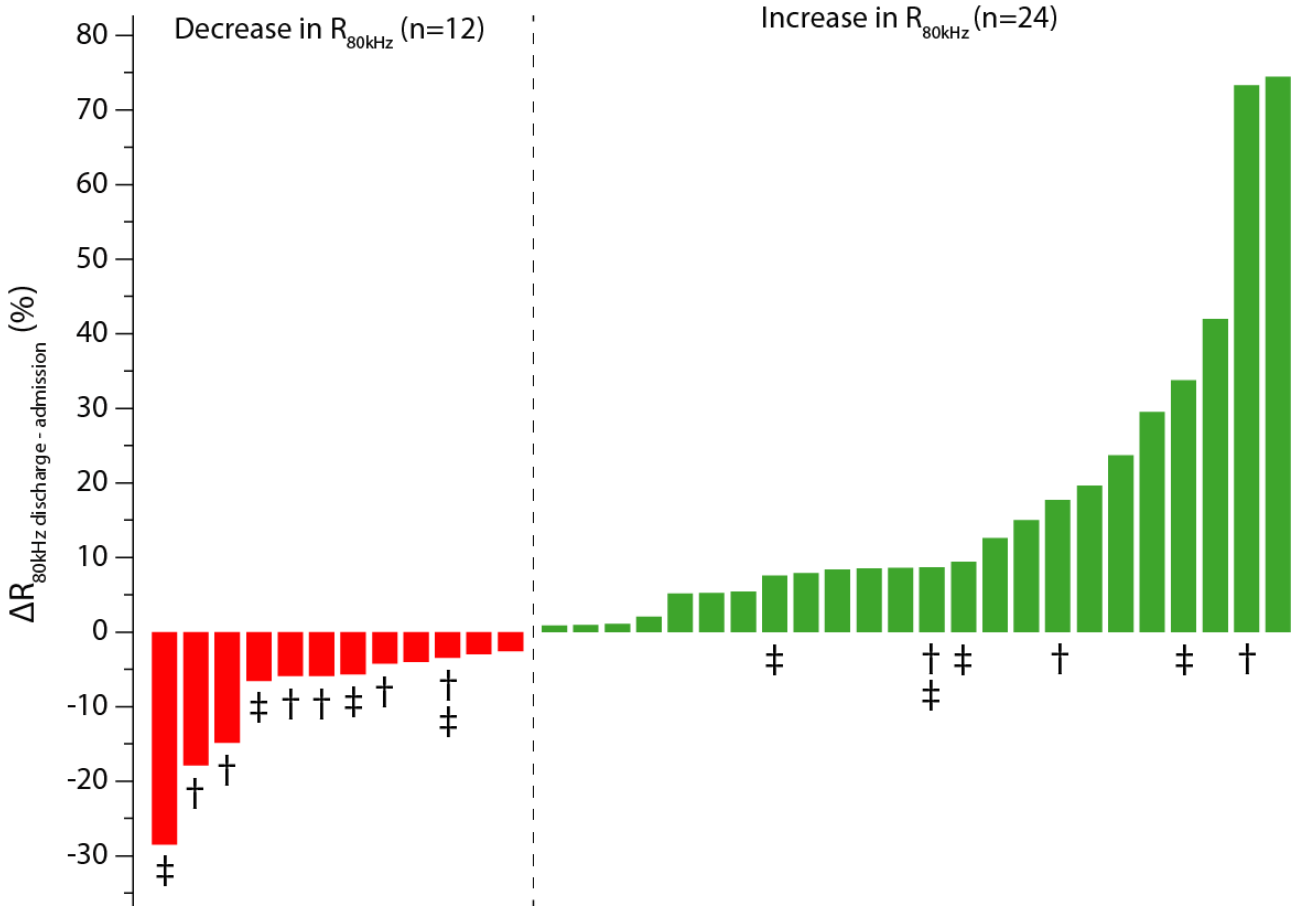
[a]n=31.

[b]NT-proBNP: N-terminal pro-brain natriuretic peptide.

[c]n=26.

[d]eGFR: estimated glomerular filtration rate.

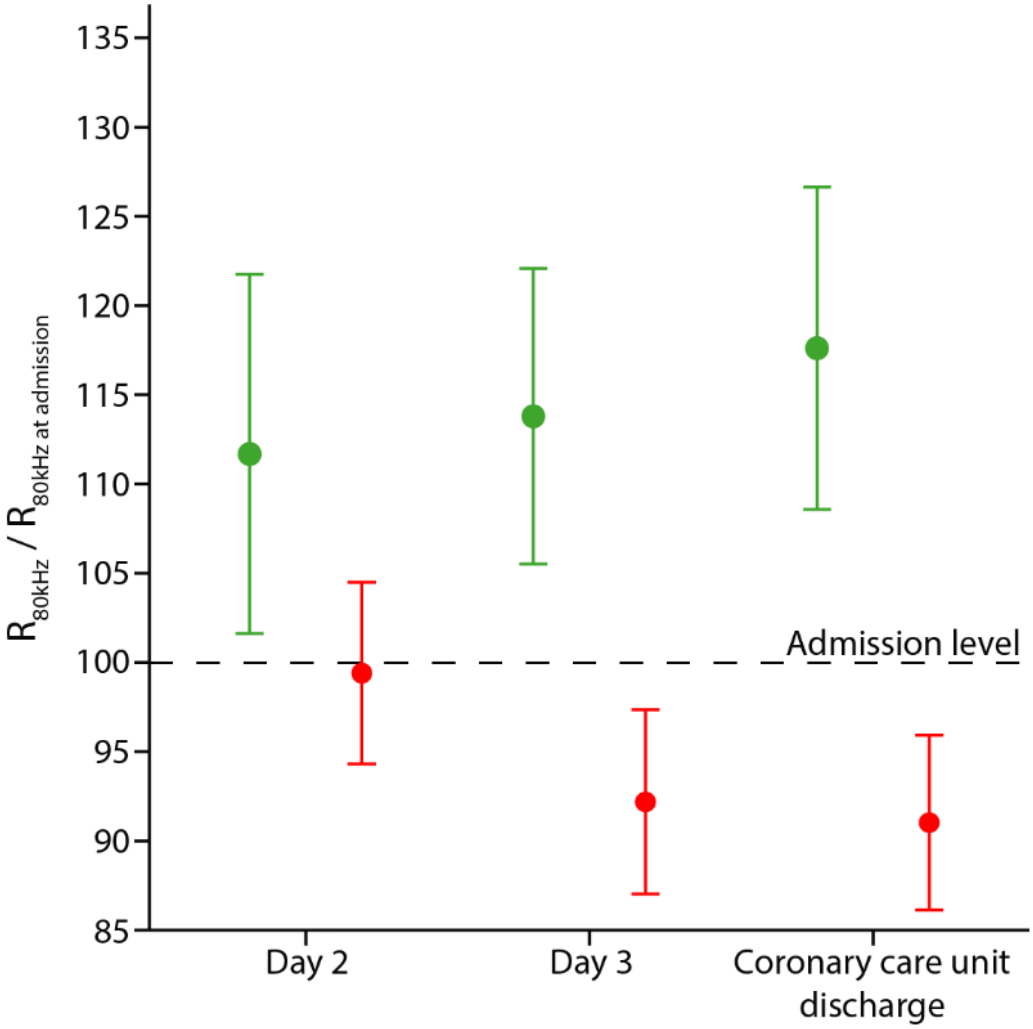
Figure 4. Changes in thoracic impedance at 80 kHz (R_{80kHz}) from admission to coronary care unit discharge by patient, including clinical outcome status († all-cause mortality and ‡ hospital admission with a primary diagnosis of heart failure).



The groups had similar baseline patient characteristics. Significantly fewer patients with atrial fibrillation or undergoing diuretic therapy were present in the group with a relative increase in R_{80kHz}. A significant difference in relative R_{80kHz} change from admission to coronary care unit discharge was observed for patients with an increase in R_{80kHz} (109%, IQR 105-122) compared with those with a decrease in R_{80kHz} (94%, IQR 85-97, *P*<.001).

In the patients with a relative increase in R_{80kHz}, the biggest change in R_{80kHz} was observed between the day of admission and the day after admission (+12%; Figure 5). During the subsequent days, smaller relative changes in R_{80kHz} of +2% (between day 2 and day 3) and +4% (between day 3 and the day of coronary care unit discharge) were observed. For patients with a relative decrease in R_{80kHz}, smaller relative changes in R_{80kHz} were observed (-0.5%, -7%, and -1%, respectively).

Figure 5. Relative changes in thoracic impedance at 80 kHz (R_{80kHz}) from admission to coronary care unit discharge (mean and two times standard error) for patients with a relative increase in R_{80kHz} (green; n=24) or relative decrease in R_{80kHz} (red; n=12).



Clinical Outcome

During follow-up, 9 of the 36 patients died, leading to a 1-year survival rate of 75%. Patients with a relative increase in R_{80kHz} had a significantly higher probability of survival (21/24, 88%) than patients with a relative decrease in R_{80kHz} (6/12, 50%, *P*=.01; Figure 6). This difference was already present at 30 days of follow-up (24/24, 100%, and 7/12, 58%, respectively, *P*<.001). After one 1 year of follow-up, 28 of the 36 patients (78%) had not been readmitted to the hospital with a primary diagnosis of HF, and this was not significantly different between patients with a relative increase in R_{80kHz} and patients with a relative decrease in R_{80kHz} (20/24, 83%, and 8/12, 67%, respectively, *P*=.28). At 30 days, these values were 23/24 (96%) and 11/12 (92%), respectively (*P*=.63). Finally, 21 of the 36 (58%) patients survived and had not been readmitted for HF at 1 year of follow-up: 75% of the patients with a relative increase in R_{80kHz} (18/24) and 25% of the patients with a relative decrease in R_{80kHz} (3/12, *P*=.01; Figure 7), compared with 96% (23/24) and 50% (6/12, *P*=.01), respectively, at 30 days of follow-up. Clinical outcome status is included in Figure 4. There were 28 cardiac-related hospitalizations for 42% (15/36) of the patients. Of the 28 hospitalizations, 27 (96%) were non-elective, and 13 (46%) were HF-related. Clinical outcome results are summarized in Table 2.

Figure 6. Freedom from all-cause mortality in patients with an increase in R_{80kHz} (green; n=24) versus patients with a decrease in R_{80kHz} (red; n=12).

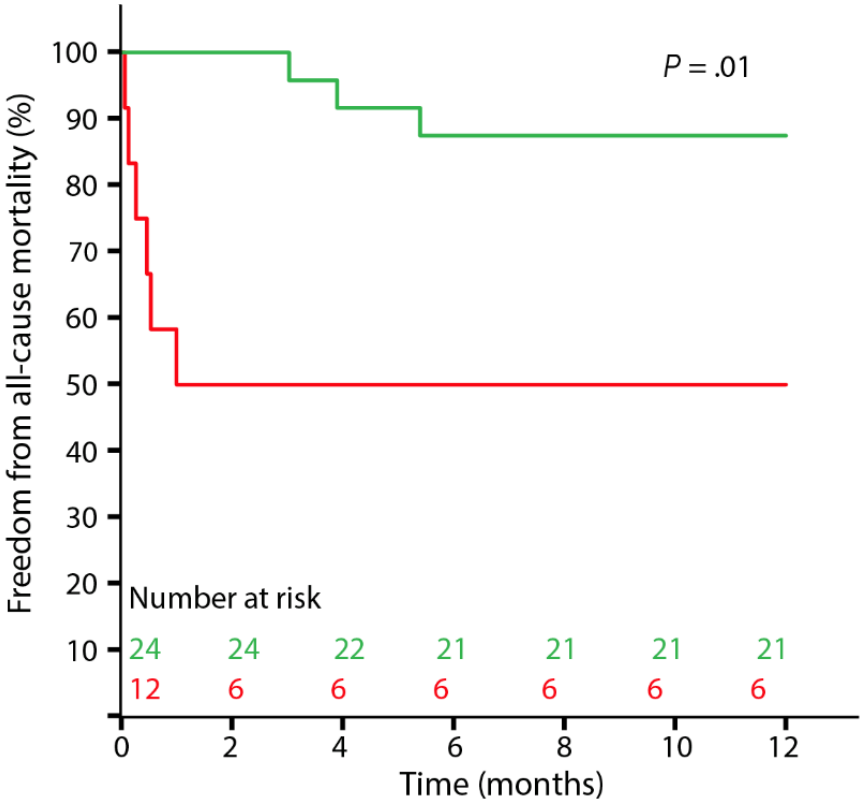


Figure 7. Freedom from all-cause mortality or hospital admission with a primary diagnosis of heart failure for patients with an increase in R_{80kHz} (green; n=24) versus patients with a decrease in R_{80kHz} (red; n=12).

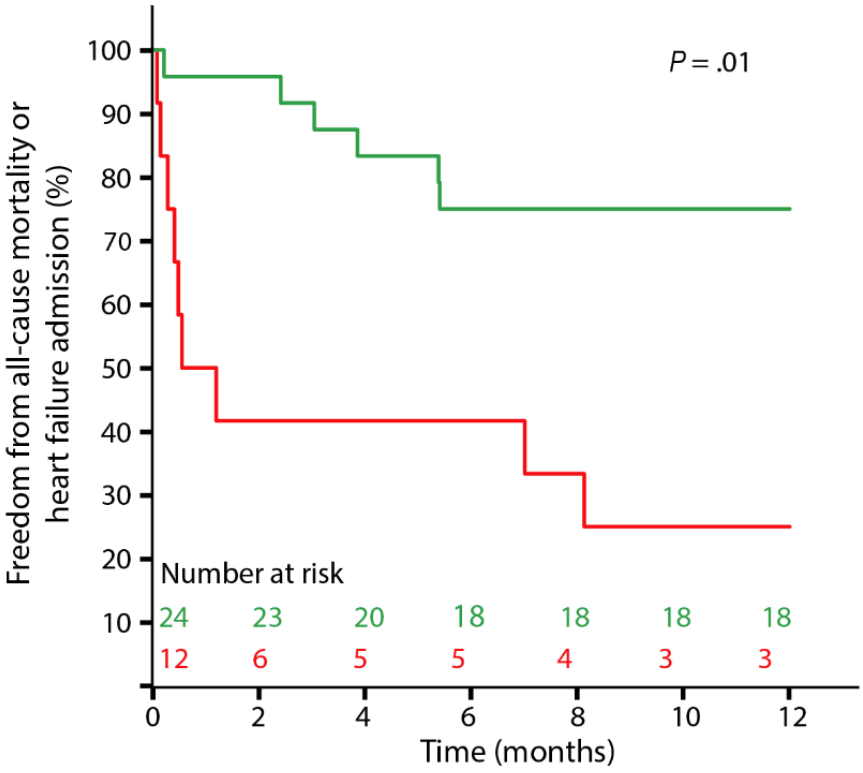


Table 2. Clinical outcome results at both 30 days and 1 year of follow-up.

Endpoint	30 days of follow-up			1 year of follow-up		
	Increase in R_{80kHz} (n=24)	Decrease in R_{80kHz} (n=12)	*P* value	Increase in R_{80kHz} (n=24)	Decrease in R_{80kHz} (n=12)	*P* value
Freedom from heart failure hospitalization and all-cause mortality, n (%)	23 (96)	6 (50)	.001	18 (75)	3 (25)	.001
Freedom from all-cause mortality, n (%)	24 (100)	7 (58)	<.001	21 (88)	6 (50)	.005
Freedom from heart failure hospitalization, n (%)	23 (96)	11 (92)	.63	20 (83)	8 (67)	.28

Table 3 provides an overview of the Cox regression analysis. A decrease in R_{80kHz} from admission to coronary care unit discharge resulted in a significant hazard ratio of 4.96 (1.82-14.37) for the combined endpoint, mainly driven by all-cause mortality. Multivariate analysis revealed that baseline characteristics that were significantly different between both groups (ie, presence of atrial fibrillation and diuretic use) and clinically relevant parameters (ie, age and left ventricular ejection fraction) had no significant influence on the clinical outcomes (after considering the group variable). Since no factor was significant in the model, the adjusted and unadjusted hazard ratios are the same.

Table 3. Cox regression analysis with Firth's penalization for clinical outcome measures.

Endpoint	Hazard ratio	95% CI	*P* value
Heart failure hospitalization and all-cause mortality	4.96	1.82-14.37	.01
All-cause mortality	5.51	1.55-23.32	.02
Heart failure hospitalization	2.10	0.54-8.14	.29

Discussion

Principal Findings

Different invasive and non-invasive bioimpedance applications have previously been studied for their potential applications in HF treatment and follow-up [9-13,16,17]. This study provides preliminary evidence about the potential in-hospital use and prognostic value of a wearable thoracic impedance sensor. Individualized bioimpedance monitoring was useful to assess the efficacy of decongestion therapy by tracking changes in a patient's fluid status. A significant inverse relationship was found between daily fluid balance and thoracic impedance measurements, especially on the individual level. Moreover, patients with an increase in thoracic impedance during initial treatment tended to have a better clinical outcome than patients without an increase in thoracic impedance.

Wearable bioimpedance devices enable longitudinal monitoring and trend analysis in a low-cost, feasible, reproducible, and non-invasive manner. In addition, thoracic impedance changes correlate well with a patient's fluid balance and could therefore be used to track volume overload [12]. Furthermore, Cuba-Gyllensten et al [13] found the highest correlation between daily fluid levels and thoracic impedance measurements compared to other clinical parameters. Due to the poor prognostic value, serial echocardiographs (eg, left ventricular ejection fraction, E/e' ratio) or serial biomarkers (eg, pro-BNP, troponins) were not collected as a reference in the current study [4,22-24]. Instead, due to its objective nature, we relied on fluid balance (in and out each hour) as a comparator for fluid status. In this study, the wearable bioimpedance sensor was also inversely related with fluid balance, as expected. Correlations for individual patients were higher than the correlation for the total study population. For the total study sample, a moderate negative correlation was found between changes in fluid balance and relative changes in R_{80kHz} from admission to coronary care unit discharge (r_s=-0.51, *P*<.001). In a previous study, in which invasive thoracic impedance monitoring was used to target one side of the thorax, the correlation between thoracic impedance and weight changes was –0.65 [11]. Other research on non-invasive bioimpedance monitoring targeting both lungs found even higher correlations [13]. This can be explained by the fact that changes in fluid level occur throughout the entire body, whereas thoracic impedance is a local measurement that, in the current study, only considered the basal part of the left lung. Therefore, when using a non-invasive wearable bioimpedance device, it is very important to consider that the correlation between bioimpedance and fluid balance strongly depends on the location of the excessive fluid and the measurement area of the device. Accordingly, correlations on the individual level can be higher than at the population level, as we demonstrated in our previous study [12]. Similarly, in the present study, a higher correlation coefficient was present for a representative patient with isolated left-sided HF than for a patient with combined HF. In a patient with isolated left-sided HF, most of the extracted fluid originates from the lung area (ie, the measurement location of our wearable device), while in combined HF, fluid is also extracted from the lower peripherals. Measuring a larger area could improve the correlation but limits the possibility of incorporating it in a wearable bioimpedance sensor. It is also important to remember that there are various influencing factors when dealing with non-invasive thoracic impedance measurements. This could further explain the lower correlation for the total study population than for the individual patients in our study. Potential influencing factors for non-invasive bioimpedance measurements include skin

conditions, body composition (eg, fat percentage, muscle percentage), food intake, air in the intestines, and pleural cavity fluid. Moreover, external influences can include body posture and electrode placement. Therefore, in our experience, bioimpedance measurements should be interpreted in an individualized longitudinal manner since absolute bioimpedance values exhibit high individual variability. Individually adjusted thresholds and trends, rather than absolute numbers, could help in clinical decision making based on bioimpedance measures.

For patients with an increase in R_{80kHz}, the highest change in R_{80kHz} was observed during the first day. This is in accordance with clinical findings from previous research, in which patients with acutely decompensated HF and under diuretic therapy had substantially higher urinary output during the first 24 hours after admission [25]. Interestingly, when compared with patients with a decrease in R_{80kHz}, for the patients with an increase in R_{80kHz}, a significant survival benefit was observed both for all-cause survival (21/24, 88%, and 6/12, 50%, respectively, *P*=.01) and the composite of all-cause mortality and HF hospitalization (18/24, 75%, and 3/12, 25%, respectively, *P*=.01) at 1 year of follow-up. This difference was already present at 30 days of follow-up. A decrease in R_{80kHz} resulted in a significant hazard ratio of 4.96 (1.82-14.37) for the combined endpoint, and the multivariate analyses, including baseline characteristics that were significantly different between both groups and clinically relevant parameters, revealed no significant influence of these parameters. Thus, the multivariate analysis indicated that the presence of atrial fibrillation, diuretic use, age, and left ventricular ejection fraction did not contribute to the observed differences in clinical outcome between the groups; therefore, this difference was mainly driven by the increase or decrease in thoracic bioimpedance during hospitalization. Effective decongestion, indicated by an increase in thoracic impedance during hospitalization, is thus pivotal for good clinical prognosis. Our wearable bioimpedance monitoring device provides an easy-to-use parameter in this context. The current preliminary results indicate that non-invasive bioimpedance changes early during hospitalization could possibly be used to determine the efficacy of decongestion therapy and improve resource allocation. Accordingly, patients that do not show an improvement in thoracic impedance during the first 48 hours of hospitalization tend to have a poor clinical outcome and require extra attention to optimize decongestion therapy (ie, increase diuretic dose, initiate dialysis therapy). Currently, the efficacy of congestion is mainly determined based on X-ray images or fluid balance information. However, X-ray images are usually only taken once every 24 hours in the acute setting, and although fluid in- and outtake information is recorded every hour, the actual fluid balance is only calculated once every 24 hours. Therefore, bioimpedance could be a more convenient and faster method to determine the efficacy of decongestion therapy. The technique could be easily integrated into existing bedside vital sign monitors for a more continuous recording of fluid status.

Longitudinal invasive hemodynamic monitoring (ie, pressure overload) has already shown its clinical relevance by improving HF management [26]. The proposed wearable bioimpedance monitoring device could be easily integrated in patch form or as textile sensors. It could provide an interesting, non-invasive alternative since it enables longitudinal monitoring of fluid volume in an easy, inexpensive, and comfortable way. Therefore, besides its in-hospital use as an indicator for the efficacy of decongestion therapy or as a prognostic parameter, it could be relevant for in-home monitoring for the early detection of volume overload. Therefore, it could address the increasing burden of worsening HF that requires hospital admission. To ensure patient compliance, a crucial consideration is the autonomous working principle of the wearable form factor, which minimizes patient burden. In the ideal setting, the patient must only attach the wearable device for about 5 minutes daily, during which the device automatically sends the information to the clinical call center. In addition, since the device also enables electrocardiogram data recording and is capable of measuring respiration using bioimpedance, additional parameters can be gathered to obtain a more complete overview of the patient's health status. In this way, the device could be used to predict upcoming HF decompensation using a multi-parameter approach. However, a new prospective study is needed to investigate its use in an in-home environment.

Study Limitations

This study should be interpreted in the light of some limitations. Since thoracic impedance measurements were performed on a confined area only covering the basal part of the left lung, changes in bioimpedance measured with the wearable device therefore can only approximate the fluid changes at the whole-body level. However, if both lungs are considered, the device loses the advantages of a comfortable miniaturized wearable device. In our center, the number of patients that are admitted to the coronary care unit for heart decompensation is quite low since we have a multidisciplinary HF clinic in which patients are closely followed. Although the sample size is small, it is comparable in size to other studies that assessed bioimpedance changes in HF patients, and we are convinced that the current findings are strong enough to encourage other research groups to further study the use of non-invasive bioimpedance devices in more detail [11,13,17]. Another limitation is the fact that baseline diuretic use prior to admission at the emergency room was significantly higher in the patients that showed a decrease in thoracic impedance during hospitalization. However, in the clinical outcome analysis, this factor was included in the multivariate analysis and showed no significant influence on the observed differences in clinical outcome. The current results related to clinical outcome are therefore hypothesis-generating, and larger studies are required to support these findings. Finally, serial echocardiographic parameters and biomarkers were not used as reference measures.

Conclusions

The current study shows that individualized bioimpedance monitoring can be used to track the efficacy of decongestion therapy by measuring changes in fluid status during hospitalization. Changes in fluid balance (in/out) and relative changes in R_{80kHz} from admission to coronary care unit discharge showed a moderate negative correlation on the sample level and higher correlations on the individual level. Early

decreases in R_{80kHz} were related with worse clinical outcomes both at 30 days and 1 year of follow-up. Future studies are required to confirm whether bioimpedance monitors could add value in diagnostic evaluation, longitudinal prognostication, therapeutic decision-making, and in-home monitoring for the early detection of volume overload.

Acknowledgments

This report is part of the Limburg Clinical Research Program (LCRP) UHasselt-ZOL-Jessa, supported by the foundation Limburg Sterk Merk (LSM), Hasselt University, Ziekenhuis Oost-Limburg and Jessa Hospital. We would like to thank the engineers from imec the Netherlands/Holst Centre for their technical support. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors contributed substantially to this work.

Conflicts of Interest

None declared.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016 Jul 14;37(27):2129-2200. [doi: 10.1093/eurheartj/ehw128] [Medline: 27206819]
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Oct 15;62(16):e147-e239 [FREE Full text] [doi: 10.1016/j.jacc.2013.05.019] [Medline: 23747642]
3. Adams KF, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, ADHERE Scientific Advisory Committee Investigators. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 2005 Feb;149(2):209-216. [doi: 10.1016/j.ahj.2004.08.005] [Medline: 15846257]
4. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JEA, Cleland JG, et al. Assessing and grading congestion in acute heart failure: a scientific statement from the acute heart failure committee of the heart failure association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. Eur J Heart Fail 2010 May;12(5):423-433 [FREE Full text] [doi: 10.1093/eurjhf/hfq045] [Medline: 20354029]
5. Stevenson LW, Perloff JK. The limited reliability of physical signs for estimating hemodynamics in chronic heart failure. JAMA 1989 Feb 10;261(6):884-888. [Medline: 2913385]
6. Chakko S, Woska D, Martinez H, de Marchena E, Futterman L, Kessler KM, et al. Clinical, radiographic, and hemodynamic correlations in chronic congestive heart failure: conflicting results may lead to inappropriate care. Am J Med 1991 Mar;90(3):353-359. [doi: 10.1016/0002-9343(91)80016-f] [Medline: 1825901]
7. Stevenson LW. Are hemodynamic goals viable in tailoring heart failure therapy? Hemodynamic goals are relevant. Circulation 2006 Feb 21;113(7):1020-7; discussion 1033. [doi: 10.1161/CIRCULATIONAHA.104.478321] [Medline: 16490837]
8. Fonarow GC. The Acute Decompensated Heart Failure National Registry (ADHERE): opportunities to improve care of patients hospitalized with acute decompensated heart failure. Rev Cardiovasc Med 2003;4 Suppl 7:S21-S30. [Medline: 14668697]
9. Yu C, Wang L, Chau E, Chan RH, Kong S, Tang M, et al. Intrathoracic impedance monitoring in patients with heart failure: correlation with fluid status and feasibility of early warning preceding hospitalization. Circulation 2005 Aug 9;112(6):841-848 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.104.492207] [Medline: 16061743]
10. van Veldhuisen DJ, Braunschweig F, Conraads V, Ford I, Cowie MR, Jondeau G, et al. Intrathoracic Impedance Monitoring, Audible Patient Alerts, and Outcome in Patients With Heart Failure. Circulation 2011 Oct 18;124(16):1719-1726. [doi: 10.1161/circulationaha.111.043042]
11. Whellan DJ, Droogan CJ, Fitzpatrick J, Adams S, McCarey MM, Andrel J, et al. Change in intrathoracic impedance measures during acute decompensated heart failure admission: results from the Diagnostic Data for Discharge in Heart Failure Patients (3D-HF) Pilot Study. J Card Fail 2012 Feb;18(2):107-112. [doi: 10.1016/j.cardfail.2011.10.017] [Medline: 22300777]
12. Lee S, Squillace G, Smeets C, Vandecasteele M, Grieten L, de Francisco R, et al. Congestive heart failure patient monitoring using wearable Bio-impedance sensor technology. Conf Proc IEEE Eng Med Biol Soc 2015 Aug;2015:438-441. [doi: 10.1109/EMBC.2015.7318393] [Medline: 26736293]
13. Cuba-Gyllensten I, Gastelurrutia P, Riistama J, Aarts R, Nuñez J, Lupon J, et al. A novel wearable vest for tracking pulmonary congestion in acutely decompensated heart failure. Int J Cardiol 2014 Nov 15;177(1):199-201. [doi: 10.1016/j.ijcard.2014.09.041] [Medline: 25499378]

14. Shochat M, Charach G, Meyler S, Meisel S, Weintraub M, Mengeritsky G, et al. Prediction of cardiogenic pulmonary edema onset by monitoring right lung impedance. Intensive Care Med 2006 Aug;32(8):1214-1221. [doi: 10.1007/s00134-006-0237-z] [Medline: 16775717]
15. Shochat MK, Shotan A, Blondheim DS, Kazatsker M, Dahan I, Asif A, et al. Non-Invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: A Randomized Controlled Trial (IMPEDANCE-HF Trial). J Card Fail 2016 Sep;22(9):713-722. [doi: 10.1016/j.cardfail.2016.03.015] [Medline: 27058408]
16. Lee S, Polito S, Agell C, Mitra S, Firat Yazicioglu R, Riistama J, et al. A Low-power and Compact-sized Wearable Bio-impedance Monitor with Wireless Connectivity. In: J. Phys. Conf. Ser. 2013 Apr 18 Presented at: 15th International Conference on Electrical Bio-Impedance (ICEBI) / 14th Conference on Electrical Impedance Tomography (EIT); 2013; Heilbad Heiligenstadt, Germany p. 012013. [doi: 10.1088/1742-6596/434/1/012013]
17. Gastelurrutia P, Cuba-Gyllensten I, Lupon J, Zamora E, Llibre C, Caballero A, et al. Wearable vest for pulmonary congestion tracking and prognosis in heart failure: A pilot study. Int J Cardiol 2016 Jul 15;215:77-79. [doi: 10.1016/j.ijcard.2016.04.024] [Medline: 27111163]
18. Khandwalla RM, Birkeland K, Zimmer R, Banet M, Pede S, Kedan I. Predicting Heart Failure Events With Home Monitoring: Use of a Novel, Wearable Necklace to Measure Stroke Volume, Cardiac Output and Thoracic Impedance. Journal of the American College of Cardiology 2016 Apr;67(13):1296. [doi: 10.1016/s0735-1097(16)31297-9]
19. Anand IS, Greenberg BH, Fogoros RN, Libbus I, Katra RP, Music Investigators. Design of the Multi-Sensor Monitoring in Congestive Heart Failure (MUSIC) study: prospective trial to assess the utility of continuous wireless physiologic monitoring in heart failure. J Card Fail 2011 Jan;17(1):11-16. [doi: 10.1016/j.cardfail.2010.08.001] [Medline: 21187259]
20. Anand IS, Tang WW, Greenberg BH, Chakravarthy N, Libbus I, Katra RP, Music Investigators. Design and performance of a multisensor heart failure monitoring algorithm: results from the multisensor monitoring in congestive heart failure (MUSIC) study. J Card Fail 2012 Apr;18(4):289-295. [doi: 10.1016/j.cardfail.2012.01.009] [Medline: 22464769]
21. Helleputte N, Konijnenburg M, Kim H, Pettine J, Jee D, Breeschoten A, et al. A multi-parameter signal-acquisition SoC for connected personal health applications. 2014 Presented at: IEEE International Solid-State Circuits Conference Digest of Technical Papers (ISSCC); Feb 2014; San Francisco, CA p. 9-13. [doi: 10.1109/isscc.2014.6757449]
22. Donal E, Lund LH, Oger E, Hage C, Persson H, Reynaud A, KaRen investigators. New echocardiographic predictors of clinical outcome in patients presenting with heart failure and a preserved left ventricular ejection fraction: a subanalysis of the Ka (Karolinska) Ren (Rennes) Study. Eur J Heart Fail 2015 Jul;17(7):680-688 [FREE Full text] [doi: 10.1002/ejhf.291] [Medline: 26033771]
23. Gromadziński L, Targoński R. Impact of clinical and echocardiographic parameters assessed during acute decompensation of chronic heart failure on 3-year survival. Kardiol Pol 2006 Sep;64(9):951-6; discussion 957 [FREE Full text] [Medline: 17054026]
24. Cleland JGF, Teerlink JR, Davison BA, Shoaib A, Metra M, Senger S, VERITAS Investigators. Measurement of troponin and natriuretic peptides shortly after admission in patients with heart failure-does it add useful prognostic information? An analysis of the Value of Endothelin Receptor Inhibition with Tezosentan in Acute heart failure Studies (VERITAS). Eur J Heart Fail 2017 Dec;19(6):739-747 [FREE Full text] [doi: 10.1002/ejhf.786] [Medline: 28296139]
25. Verbrugge FH, Nijst P, Dupont M, Penders J, Tang WHW, Mullens W. Urinary composition during decongestive treatment in heart failure with reduced ejection fraction. Circ Heart Fail 2014 Sep;7(5):766-772. [doi: 10.1161/CIRCHEARTFAILURE.114.001377] [Medline: 25037309]
26. Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet 2011 Feb 19;377(9766):658-666. [doi: 10.1016/S0140-6736(11)60101-3] [Medline: 21315441]

Abbreviations

BNP: brain natriuretic peptide.
eGFR: estimated glomerular filtration rate.
HF: heart failure.
R_{80kHz}: resistance at 80 kHz.

Edited by G Eysenbach; submitted 04.10.18; peer-reviewed by A Accardi, M Simons, H Wang; comments to author 25.02.19; revised version received 22.08.19; accepted 27.09.19; published 18.03.20.

Please cite as:
Smeets CJP, Lee S, Groenendaal W, Squillace G, Vranken J, De Cannière H, Van Hoof C, Grieten L, Mullens W, Nijst P, Vandervoort PM
The Added Value of In-Hospital Tracking of the Efficacy of Decongestion Therapy and Prognostic Value of a Wearable Thoracic Impedance Sensor in Acutely Decompensated Heart Failure With Volume Overload: Prospective Cohort Study
JMIR Cardio 2020;4(1):e12141
URL: https://cardio.jmir.org/2020/1/e12141
doi:10.2196/12141
PMID:32186520

Original Paper

Interdisciplinary Mobile Health Model to Improve Clinical Care After Heart Transplantation: Implementation Strategy Study

Mar Gomis-Pastor[1,2], DPharm, PhD; Sonia Mirabet[2], MD, PhD; Eulalia Roig[2], MD, PhD; Laura Lopez[2], MD; Vicens Brossa[2], MD; Elisabeth Galvez-Tugas[2], BSN; Esther Rodriguez-Murphy[1], BPharm; Anna Feliu[1], BPharm, PhD; Gerardo Ontiveros[3], FIB; Francesc Garcia-Cuyàs[4], MD, PhD; Albert Salazar[5], MD, PhD; M Antonia Mangues[1], BPharm, PhD

[1]Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[2]Heart Failure and Heart Transplant Unit, Cardiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[3]Information System Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[4]Deputy Medical Director, Hospital Sant Joan de Déu, Barcelona, Spain

[5]Director Manager, Hospital Universitari Vall Hebron, Barcelona, Spain

Corresponding Author:
Mar Gomis-Pastor, DPharm, PhD
Pharmacy Department
Hospital de la Santa Creu i Sant Pau
San Quintin no 87
Barcelona, 08041
Spain
Phone: 34 636060364 ext 31897
Email: mar@margomis.com

Abstract

Background: Solid organ transplantation could be the only life-saving treatment for end-stage heart failure. Nevertheless, multimorbidity and polypharmacy remain major problems after heart transplant. A technology-based behavioral intervention model was established to improve clinical practice in a heart transplant outpatient setting. To support the new strategy, the mHeart app, a mobile health (mHealth) tool, was developed for use by patients and providers.

Objective: The primary objective of this study was to describe the implementation of the mHeart model and to outline the main facilitators identified when conceiving an mHealth approach. The secondary objectives were to evaluate the barriers, benefits, and willingness to use mHealth services reported by heart transplant recipients and cardiology providers.

Methods: This was an implementation strategy study directed by a multidisciplinary cardiology team conducted in four stages: design of the model and the software, development of the mHeart tool, interoperability among systems, and quality and security requirements. A mixed methods study design was applied combining a literature review, several surveys, interviews, and focus groups. The approach involved merging engineering and behavioral theory science. Participants were chronic-stage heart transplant recipients, patient associations, health providers, stakeholders, and diverse experts from the legal, data protection, and interoperability fields.

Results: An interdisciplinary and patient-centered process was applied to obtain a comprehensive care model. The heart transplant recipients (N=135) included in the study confirmed they had access to smartphones (132/135, 97.7%) and were willing to use the mHeart system (132/135, 97.7%). Based on stakeholder agreement (>75%, N=26), the major priorities identified of the mHealth approach were to improve therapy management, patient empowerment, and patient-provider interactions. Stakeholder agreement on the barriers to implementing the system was weak (<75%). Establishing the new model posed several challenges to the multidisciplinary team in charge. The main factors that needed to be overcome were ensuring data confidentiality, reducing workload, minimizing the digital divide, and increasing interoperability. Experts from various fields, scientific societies, and patient associations were essential to meet the quality requirements and the model scalability.

Conclusions: The mHeart model will be applicable in distinct clinical and research contexts, and may inspire other cardiology health providers to create innovative ways to deal with therapeutic complexity and multimorbidity through health care systems. Professionals and patients are willing to use such innovative mHealth programs. The facilitators and key strategies described were needed for success in the implementation of the new holistic theory–based mHealth strategy.

(JMIR Cardio 2020;4(1):e19065) doi:10.2196/19065

KEYWORDS

cardiology; heart transplantation; implementation strategy; health care model; integrated health care systems; interdisciplinary health team; medication therapy management; health care technology; mHealth; eHealth

Introduction

Background

Solid organ transplantation could be the only life-saving treatment for end-stage heart failure [1]. Since the first heart transplant was performed in 1967, recipients' life expectancy has markedly increased [2-4], making heart transplant a chronic condition. Nevertheless, the improvement in survival has been accompanied by greater multimorbidity [5,6] and long-term complexity [7-9]. Five years posttransplant, 95% of heart recipients have hypertension, 81% have hyperlipidemia, 33% have chronic renal failure, and 32% have diabetes [7]. In addition, nonadherence to lifestyle recommendations (eg, diet, exercise, or blood pressure monitoring) is frequent after transplant, with serious consequences for survival [10,11].

Another challenge for heart transplant recipients is the lifetime need to rigorously follow a regimen of immunosuppressive therapy to avoid rejection and to take multiple drugs to treat comorbidities [12]. Five years posttransplant, heart recipients take an average of 10 drugs [13], with a third of them taking more than 16 medications per day [8]. These therapeutic complexity rates are high compared with those in other chronically ill populations [8,9,14,15], increasing the risk of poor therapeutic adherence [16], pharmacological interactions and medication adverse effects [17-19], impaired quality of life [20,21], hospital readmissions [22], and even mortality [23]. In particular, 20%-50% of recipients are nonadherent to immunosuppressive treatment [24,25], which is worrisome owing to the association between nonadherence and graft failure, rejection, and poor survival after heart transplant [10,24].

The search for clinical improvement practices to deal with multimorbidity and polypharmacy is currently a priority for heart transplant providers [26]. Longer morbidity-free survival rates and enhanced quality of life [2,27] could be achieved by improvements in healthy lifestyle habits, medication management, and quality of care [2,11]. Some promising strategies have already been tested in clinical practice and are ready to be applied in the heart transplant population.

First, integrated and comprehensive health care programs carried out by proactive teams could enhance health outcomes [28,29]. Well-trained interdisciplinary teams have been associated with better management of chronicity after heart transplant [30,31]. Second, the use of internet-based (eHealth) systems, including web and mobile health (mHealth) apps, has been reported to improve lifestyle and medication management in chronic conditions [32-42]. According to the International Society for Research on Internet Interventions (ISRII) statements [43] and other authors [44], internet-based models are an opportunity to deliver interventions to produce a cognitive and behavioral change in patients. Such interventions consist of "treatments, typically behaviorally based, that are operationalized and transformed for delivery via the internet" [43,45-47]. To increase their efficacy, these interventions are typically tailored to an individual's needs and environment, based on electronic patient-reported outcomes [36,40,48]. The establishment of new internet-based interventions in the field of transplantation is promising [26,49,50], but holistic models based on behavioral change technologies in heart transplant population are still scarce.

Based on these strategies, an internet- and theory-based holistic intervention model was implemented for the first time in the heart transplant outpatient clinic of a tertiary hospital. The new practice was designed to help health providers improve medication safety and effectiveness, patient-provider interactions, and comprehensive clinical care. The tool created to support the interventional program, the mHeart system, was a mobile app complemented by a website for use by patients and providers (Figure 1). Establishing the new model was costly and time-consuming and its implementation in usual practice posed several challenges to the multidisciplinary team in charge. The skills of the health providers in charge, such as patient engagement, motivational interviewing, and management [51], were essential to lead the implementation. The mHeart system and the theory-based interventional health care program were designed to offer a solid starting point to improve health outcomes in complex populations such as heart transplant patients.

Figure 1. The mHeart system menu, displaying the different app modules: Treatment, Agenda, Self-control, Symptoms, Messaging, Health Education and Advice, Personal and Clinical Data.

Outlining the methodology used, principal findings, and the barriers and facilitators encountered in usual clinical practice could be highly useful for new developers and could be generalizable in other contexts. Therefore, this article may guide other health providers in the implementation of holistic and interdisciplinary internet-based strategies to improve clinical practice.

Objectives

The main objectives of this study were (1) to describe the implementation of a holistic interdisciplinary technology-based behavioral intervention model to improve therapy management and the clinical care of heart transplant recipients, and (2) to outline the facilitators for future implementations based on the experience gained.

Secondary objectives were to assess patients' access to technology and willingness to use mHealth services, and to analyze stakeholders' opinions of the major gains and barriers to an mHealth approach.

Methods

Study Design and Setting

This study is based on an implementation strategy of a clinical practice improvement model. The study was conducted in a heart transplant outpatient setting of a cardiology unit of a tertiary university hospital between 2014 and 2017. A mixed methods design was applied and included several surveys, interviews, and focus groups. The study was approved by the institutional review board (IIBSP-MHE-2014-55). Participants

were adult outpatient heart transplant recipients; representatives of patient associations; health professionals; providers; and experts in quality, safety, or legal fields. Participants were informed of the study objectives and of the team conducting the study. All participants provided written consent.

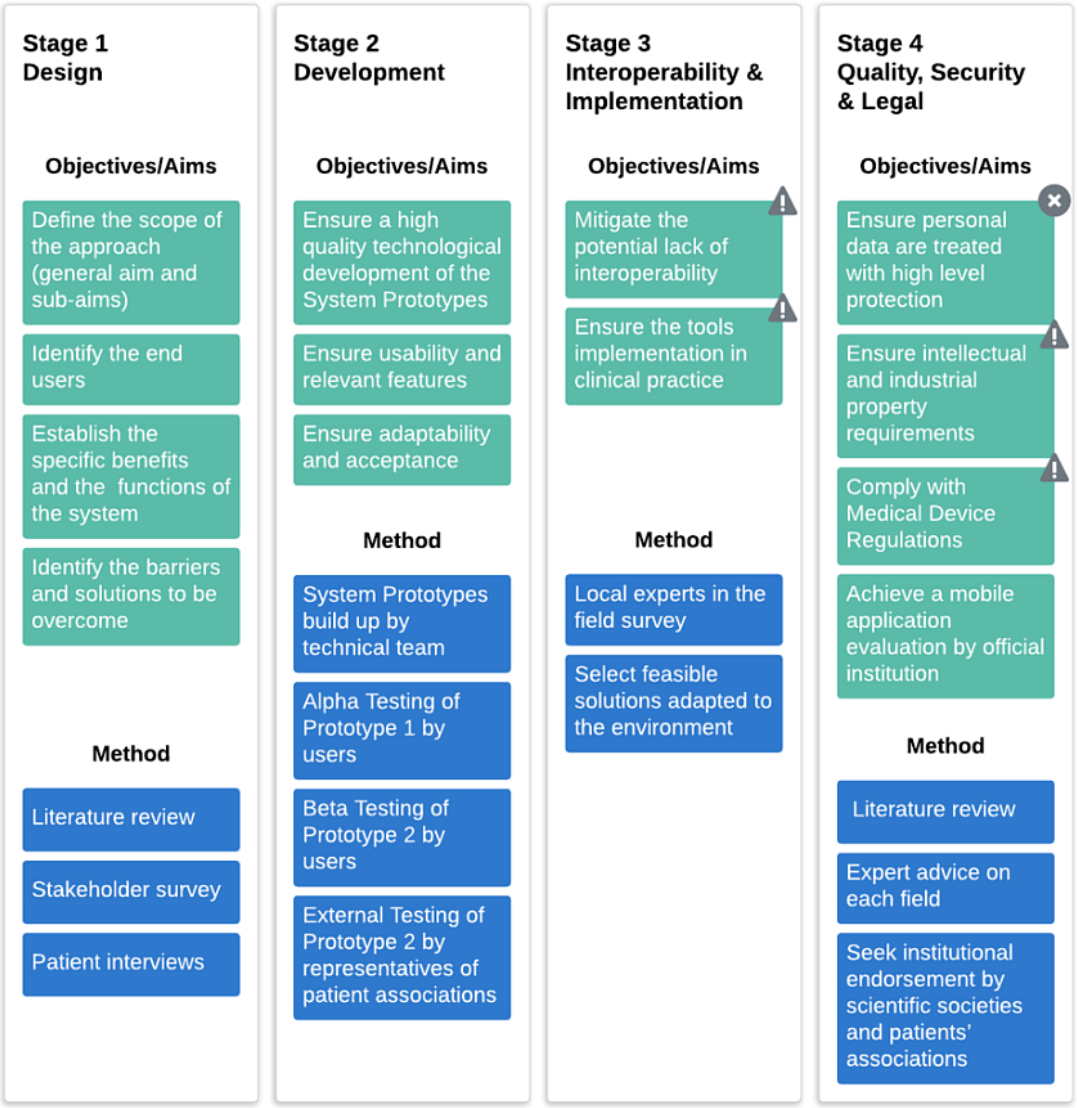
The Standards for Reporting Implementation Studies [52] were followed for transparent and accurate data reporting for the entire study. When the content analysis method was used from group discussions, the Consolidated Criteria for Reporting Qualitative Research (COREQ) [53] were applied. In addition, the directions for the ISRII [43] and the CONSORT-EHEALTH guidelines [47] were followed to report the internet-based interventional program, as appropriate.

Procedures

Phases and Team

The internet-based strategy was carried out in four stages, including design; development; interoperability and implementation; and quality, security, and legal requirements. A summary of the aims of the stages and the methodology used is provided in Figure 2.

Figure 2. Summary of the procedures and stages followed during implementation of the mHeart approach.



A warning sign indicates "plan from the beginning: time and effort consuming". A blade refers to a "mandatory requisite".
Definitions: System Prototype (each version of the software developed ready to be tested by end users); Interoperability (properties of systems, eHealth tools and electronic medical records, for data exchange); Users (patients and health providers).

The interdisciplinary clinical team in charge of the mHeart system was the hospital's scientific advisory team, composed of 4 cardiologists, 2 cardiology nurses, 1 cardiology psychologist, and 2 clinical pharmacists. All of them were female except for the male cardiologist. Among the pharmacists, one was a transplant pharmacist with experience in motivational interviewing and transplant therapeutics, while the other had broad experience of managerial skills. The transplant pharmacist

was assigned as the scientific coordinator and undertook the following tasks: facilitating procedures and meeting deadlines, prioritizing tasks, liaising with participants and the technical team, and reporting to the scientific advisory team.

Stage 1: Design

Stage 1 lasted from April 2, 2014 to March 15, 2015. During this period, distinct methodologies were combined to establish the following approach.

First, the software was categorized by the scientific advisory team as a behavior intervention technology to facilitate relevant overall goals: health behavior change (ie, increase patients' healthy behaviors and prevent the onset of disease) and targeted disease management (ie, facilitate therapeutic interventions and improve patients' self-management). The system was initially conceived of as an mHealth software based on a mobile app for heart transplant recipients in the outpatient setting. The software was interactive with additional human support (ie, a multidisciplinary heart transplant team) [43]; thus, a website was also designed for providers.

Second, the scientific advisory team reviewed design models for the development of behavior intervention technologies, mainly that of Mohr et al [54] but also several others [55-58], which served as a guide for how to combine technology engineering with behavioral science. Several expert reports on the efficacy of internet-based interventions and system engagement were also reviewed [35,43,45-47,59-61]. Behavior change theories were used as a framework to design the interventions and software components. The interventional program was based on human support, motivational engagement, and therapeutic alliance [62,63]. The strategies applied included tailored feedback, among others [44,64-67]. The taxonomy of Abraham and Michie [68] was used to standardize the theory-based interventions in terms of discrete techniques. These techniques are fully described to improve the future replication of the approach and its adoption in usual clinical practice or research (Multimedia Appendix 1). Interactive elements were also used as digital triggers to prevent the law of attrition in eHealth interventions (eg, alerts, prompts, reminders, notifications, messages, and video calls) [62,69]. The components of the system aimed to deliver personalized interventions using motivational interviewing techniques, according to common practice in heart transplant centers [25,70].

Third, the scientific advisory team performed a literature review to guide the specific clinical subaims and software functionalities that should be prioritized in the model [54] and identify the barriers to be overcome, including institutional reports such as those of the US Food and Drug Administration, European Union, and Pharmacist Associations statements about eHealth [37-39,71-77]; studies on improving polypharmacy and chronic disease management [34,36,40-42,48,78,79]; and studies or reports describing patient-reported outcome measures with an impact on survival in heart transplant [7,10,11,79-85].

Fourth, the opinions of end users (ie, providers and patients) were evaluated. To assess patients' access to technology and willingness to use mHealth services, the scientific coordinator performed a 45-minute, in-depth face-to-face interview with each adult chronic-stage (>1.5 years from heart transplant) recipient included in the study. The recipients were recruited consecutively in the Cardiology Outpatient Clinic from April 15, 2014 until April 2, 2015. The interviews aimed to determine patients' current access, knowledge, and use of technology and their willingness to use an mHealth approach. The interview was based on a questionnaire previously reported by McGillicuddy et al [86]. Sociodemographic and clinical variables were collected from the patients' electronic health records. The data collection sheet is provided in Multimedia Appendix 2.

To assess the stakeholders' agreement about the gains and barriers associated with an mHealth approach in the heart transplant population, the scientific coordinator invited a purposive sample of stakeholders to participate in a survey. The themes were previously identified in the literature review and were related with benefits and barriers associated with an mHealth approach directed to multimorbid patients with polypharmacy (Multimedia Appendix 2). The survey was sent by email on September 29, 2014. The results were used to indicate which clinical subaims of the approach should be prioritized and the software design solutions necessary to overcome the limitations identified. An agreement of >75% of the stakeholders was considered adequate [87].

The following stakeholders were eligible for selection: interdisciplinary transplant staff (n=21), with no distinction being made in terms of age, knowledge of technologies, or favorable or unfavorable personal opinions about eHealth programs; technology analysts (n=2); experts in mHealth (n=3) (ie, the Regional Health Department specialist in innovative health care projects, the manager of the mHealth.cat Regional Health Department, and the Director of the mHealth Competence Center at Mobile World Capital); the hospital manager (n=1); and the manager of the Regional Technology, Innovation, and Public Health Department (n=1).

Stage 2: Development

Stage 2 lasted from March 15, 2015 to June 2, 2016 and aimed to design the technology and to test mHeart. The development of the system was assigned to a health care system apps firm. The technical team consisted of 1 analyst, 5 developers (superior systems engineers), 1 designer, and 1 project leader. The scientific coordinator intervened throughout the process, providing advice to the technical team and consulting with other providers when necessary. Development and testing environments were used by the technical team to respectively produce and consolidate the system prototypes before end users were involved. First, a general software structure was set up (mHealthCare system) to then direct it to heart transplant specifications and obtain the mHeart tool. The system was built as three apps: web, Android, and iOS mobile apps. To increase the scalability of the approach and data transparency, an in-depth description of the system's technical details, the source code, and other relevant details are provided in an online dataset [88].

The mHeart prototypes were tested by end users in a Staging environment (alpha testing), followed by a Production environment (beta testing).

Alpha testing of Prototype 1 was performed to explore three domains: feature intuitiveness, esthetics, and new software elements or functions not considered during the design stage. With this aim, two distinct group sessions were held on September 15, 2015: one with the hospital's scientific advisory team (n=9) and the other with heart transplant recipient volunteers consecutively recruited from the Cardiology Outpatient Clinic (n=6). Each session lasted 3 hours and was led by the technical team and the scientific coordinator. A video of the prototype was played to guide the groups through each of the prototype modules and functions. Participants were then asked to complete the same tasks using the tool on their smartphones. Software usability issues, uncompleted tasks, and doubts arising during the sessions were noted. At the end of the session, the three domains were explored. Field notes were recorded by a nurse of the scientific advisory team during the session. Conclusions were provided to participants at the end of the session for comments or corrections.

Beta testing of Prototype 2 aimed to obtain user feedback simulating a real-world home-based 4-week follow-up (January 10, 2016 to February 10, 2016). Participants consisted of the scientific advisory team (n=9) and volunteer heart transplant recipients consecutively recruited from the Cardiology Outpatient Clinic (n=6). Each day, participants electronically completed a data collection sheet with the following domains: technical issues, amendments suggested by the participants, and additional features not included in the prototype. The test findings were analyzed by the scientific coordinator in consensus with the technical team to prioritize tasks.

Additionally, an external session was held in the offices of the local transplant organization on October 25, 2016. Participants consisted of representatives of patient associations (n=7) recruited via telephone by the organization. The scientific coordinator conducted a 2-hour session with a video demonstration of prototype 2. The participants were then asked to complete the same tasks using the tool on their smartphones. At the end of the session, the domains explored were the tool's acceptance, adaptability of the approach to other heart transplant centers, and any new queries or opinions. Field notes were recorded by a nurse of the scientific advisory team during the session. Conclusions were provided to participants at the end for comments or corrections.

Stage 3: Interoperability and Implementation

Stage 3 aimed to mitigate the potential lack of interoperability (the property of systems such as mHeart and medical records to exchange data) and to ensure the implementation of the approach in clinical practice. The survey designed is provided in Multimedia Appendix 2. Themes were identified in advance, including the available technical possibilities and resources to automatically transfer patients' sociodemographic data from electronic health records to mHeart, and to upload data recorded in mHeart to medical records. Purposive participants were recruited by phone by the scientific coordinator: these participants consisted of the manager of the Hospital Information Analysis Department and the manager of the mHealth.cat Regional Health Department. The survey was sent by email on February 16, 2016. The responses were analyzed, and feasible solutions were prioritized by the scientific coordinator in consensus with the technical team.

Stage 4: Quality, Security, and Legal Requirements

Stage 4 aimed to ensure the quality and security of the internet-based platform. The scientific coordinator sought the involvement of hospital experts or external consultation on the following domains: data protection and confidentiality policy (n=2), legal requirements (n=2), intellectual and industrial property (n=3) and an external consultant (n=1), and evaluation of mobile apps standards and certifications (n=1). Feasible solutions were applied based on the experts' requirements and technical possibilities. Finally, written endorsement of the quality content was requested from 1 regional health institution, 2 scientific societies, and 2 patient associations.

Data Recording and Statistical Analysis

To ensure data accuracy, data collected during the study stages were recorded electronically in the online database Clinapsis [89] by a pharmacist. A second review was independently performed by a pharmacist and a physician. None of the data coders was part of the hospital's scientific advisory team.

Statistical analysis was applied to analyze the results of patient interviews and stakeholder surveys. Categorical variables are reported as number and percentage. Quantitative variables are expressed as the mean and standard deviation. Nonnormally distributed variables are expressed as the median and interquartile range. The statistical analysis was performed with IBM SPSS (V22.0).

Results

Stage 1: Design

Regarding patient access to technology and willingness to use mHealth services, of the 158 recipients >1.5 years from heart transplant, 142 (89.9%) were assessed for eligibility and 135 (85.4%) were finally recruited and analyzed. Of the patients excluded, 5 were followed up in another transplant center, 5 had cognitive impairment, and 6 were palliative. Of the 7 recipients who declined to participate, the reasons were lack of interest (n=2), lack of time to complete the interview (n=4), and feeling too unwell to complete the interview (n=1).

Basic demographic and clinical data of the 135 chronic-stage heart transplant recipients interviewed are provided in Table 1. Briefly, the recipients' mean age was 57 (SD 14) years and 31% were women. The mean time since transplant was 12 (SD 7, range 2-31) years and was ≥15 years in 32% of the sample. The mean total number of drugs prescribed was 12 (SD 3, range 5-21) to treat 6 (SD 3, range 0-11) comorbidities posttransplant.

Respondents' access to technology and willingness to use mHealth services are described in Table 2. Patients' opinions led to the inclusion of the following elements: the figure of the tutor (a caregiver or a close family member), a proactive technical support service, and a website profile for patients to complement the initial mHealth system.

Table 1. Chronic heart transplant recipients' (>1.5 years from transplant) sociodemographic and clinical characteristics (N=135).

Variable	Value
Women, n (%)	41 (30.4)
Age at time of study inclusion (years), mean (SD)	57 (14)
Time since transplant at the time of study inclusion (years)	
Whole sample, mean (SD), range	12 (7), 2-31
>1.5-3, n (%)	11 (8.1)
3-5, n (%)	16 (11.9)
5-10, n(%)	27 (20.0)
10-15, n (%)	37 (27.4)
≥15, n (%)	43 (31.9)
BMI (kg/m^2), mean (SD)	27 (6)
Heart failure etiology, n (%)	
Coronary/ischemic	36 (26.7)
Cardiomyopathy	58 (43.0)
Other	41 (30.4)
Urgent heart transplant, n (%)	33 (24.4)
Educational attainment, n (%)	
No schooling	15 (11.1)
Middle school graduate	58 (43.0)
High school graduate	25 (18.5)
University graduate	36 (26.7)
Employment status, n (%)	
Disability	74 (54.8)
Retired	20 (14.8)
No previous employment	7 (5.2)
Currently working	33 (24.4)
Need or requirement for caregiver, n (%)	28 (20.7)
Lives with someone else, n (%)	115 (85.2)
Number of comorbidities, mean (SD), range	6 (3), 0-11
Patients with comorbidity posttransplant, n (%)	
High blood pressure	94 (69.6)
Dyslipidemia	73 (54.1)
Chronic kidney failure	58 (50.0)
Osteopathies and chondroplasties	52 (38.5)
Diseases of the nervous system	51 (37.8)
Mood and anxiety disorders	49 (36.3)
Digestive system diseases or disorders	42 (31.1)
Diabetes mellitus	42 (31.1)
Neoplasia	39 (28.9)
Arthropathies	27 (20.0)
Total number of drugs prescribed, mean (SD); range (IQR)	12 (3); 5-21 (9-14)

Table 2. Chronic heart transplant recipients' (>1.5 years from transplant) access to technology and willingness to use mobile health (mHealth) services (N=135).

Variable	Value
Number of devices per patient, mean (SD)	2.2 (0.7)
Types of devices owned by patients, n (%)	
Mobile phone	132 (97.8)
Computer	98 (72.6)
Tablet	60 (44.4)
Internet access on patients' devices, n (%)	
3G or 4G connection	112 (83.0)
Only connects to the internet using WiFi	18 (13.3)
Does not know/no response	5 (3.7)
Frequency of technology use, n (%)	
Often	87 (64.4)
Sporadically	35 (25.9)
Never	13 (9.6)
Internet usage for health-related purposes, n (%)	
Often	41 (30.4)
Sporadically	43 (31.9)
Never	51 (28.1)
Initial assessment of the mHealth approach, n (%)	
Not very useful	2 (1.5)
Useful	92 (68.1)
Very useful	40 (29.6)
Not yet known until the platform is tested	1 (0.7)
Initial assessment of mHeart type of platform, n (%) (multiple choice)	
Interested in using mHeart mobile app	81 (60.0)
Interested in using mHeart website	64 (47.4)
Not yet known until the platform is tested	40 (29.6)
Initially requires a tutor to use the platform, n (%)	30 (22.2)

According to stakeholder agreement about the benefits and barriers of an mHealth approach, of the 31 stakeholders invited to complete the survey, 2 nurses, 2 cardiologists, and 1 social worker did not respond. No reasons were reported. Finally, 26 stakeholders responded to the questionnaire, 17 (65%) were women with a mean age of 46 (SD 10) years. The profiles of the 26 participants were: 6 (23%) physicians, 3 (11%) nurses, 5 (19%) pharmacists, 2 (8%) psychologists, 2 (8%) technology analysts, 3 (11%) key representatives of local health authorities, 2 (8%) representatives of regional health authorities, and 3 (12%) experts in mHealth.

The main gains of the mHeart strategy according to stakeholders' opinions are detailed in Table 3. Consensus was strong for the use of mHealth to improve therapy management (>85%). In this sense, the mHeart key features were mainly designed according to the aims presented in Textbox 1. Strong agreement (>75%) was also achieved for several other comprehensive benefits. Thus, the software features design was also directed to promote patient-provider interactions and communication, and to empower patients to play a more active role in their lifestyle, treatment, and self-care. The major barriers of an mHealth approach identified by stakeholders are described in Table 3. Of note, agreement among stakeholders was weak for all items (<75%). Relevant barriers were prioritized to be overcome by the hospital's scientific advisory team due to their impact on implementation and scalability: (1) ensuring the system's legal requirements, quality, and data security; (2) mitigating end users' digital divide (providers and patients); (3) achieving system interoperability; and (4) building the mHeart software in a global structure that could be easily adapted to other complex diseases.

Table 3. Stakeholders' agreement on the benefits and limitations of a mobile health approach in multimorbid patients with polypharmacy such as the heart transplant population (N=26).

Statement for agreement	Stakeholders, n (%)
Benefits	
Improves patients' knowledge of therapy, management, and medication adherence	23 (88)
Improves the continuity of care and the flow of information between providers and levels of care	21 (81)
Allows patients to be empowered and actively manage their disease and treatment	20 (77)
Resolves patient and caregiver queries from home due to the two-way health care provider-patient communication	20 (77)
Monitoring and managing patient-reported outcomes such as symptoms and adverse effects to drugs	17 (65)
Focuses on health promotion and prevention to reduce the number of acute events	17 (65)
Increases the cost-effectiveness of resources by reducing both scheduled and urgent visits due to decompensation	17 (65)
Facilitates innovation in health and documentation of evidence that translates into measurable health outcomes	17 (65)
Reduces inequalities in access to the health system due to traveling difficulties or lack of resources	10 (38)
Improves patients' experience because of close communication with providers	4 (15)
Limitations	
Increase in workload for staff	15 (58)
Lack of institutional guidelines to set up and implement systems and accreditation of mobile health apps	14 (54)
Risk of not sharing the patient's registered information with other levels of care or with other apps (used to manage other health conditions)	13 (50)
Risk of not protecting confidential patient data	6 (23)
Risk of creating inequalities in patient care due to resistance to use technology or the digital divide	6 (23)
Lack of guarantee of the long-term economic sustainability of research projects for innovative technologies and companies that develop the systems	4 (15)

Textbox 1. Main aims of the mHeart strategy and software according to stakeholder's agreement.

- Improve therapy management (>85%)
  - Identify nonadherent patients and determinants of medication nonadherence.
  - Identify potential pharmacological interactions and adverse effects.
  - Improve patients' knowledge and management of regimens.
  - Reinforce patients' coresponsibility in their treatment.
  - To provide early medication adjustments and tailored interventions based on patient-reported outcomes.
- To promote patient-provider interactions and communication (>75%)
- To empower patients to play a more active role in their lifestyle, treatment, and self-care (>75%)

Stage 2: Development

As a result of the alpha testing with focus groups, additional features and improvements in functionality were implemented; the list is fully detailed in Multimedia Appendix 3. Beta testing feedback greatly improved usability, and the suggestions not affecting usability or security were postponed to subsequent mHeart improvement phases. New developers could incorporate these challenges described in Textbox 2 into their initial design of the system.

Textbox 2. Beta testing suggestions postponed to subsequent mHeart improvement phases; new developers could incorporate these challenges into the initial design of a new system.

- Automatic responses to consultations regarding interactions with concomitant therapies connected to the official database.
- Programming periodic changes to the mHeart questionnaire type or order of items (eg, adherence or general condition). This will prevent the patient from responding in a routine manner and the system from losing sensitivity in identifying nonadherent patients.
- Set up a discussion forum for patients.
- Enable patients at home to print the medication chart and the calendar with all tasks planned in the tool's agenda by providers and patients.
- Connecting the mHeart agenda with the hospital visit scheduling system to automatically download the appointment schedules on the mHeart system.
- Develop a decision support system based on artificial intelligence algorithms (patterns and prediction rules).
- Translating the platform into other languages to make the tool usable in other countries.

Important contributions were also obtained from patient association opinions. First, participants showed interest in using mHealth to manage their chronic comorbidities. Moreover, they highlighted their interest in two-way messaging with the clinical team. Participants also compared the tool with other free downloadable tools from online stores. Thus, the main additional value of mHeart noticed by the participants was primarily that it was adapted to their condition by transplant providers and that they could obtain clinical feedback on the activity recorded. Finally, they requested a patients' chat room and a patient-provider teleconference module.

The entire technical development and user testing processes resulted in the final prototype of mHeart primarily directed to carry out integral therapy management and clinical care in transplant populations, and specifically in heart transplant recipients. The system is a mobile phone app connected to a website [90] for use by providers and patients. The app can be downloaded free from the online Google [91] and Apple [92] stores. The general layout is represented in Figure 3 and is detailed in the online dataset [88]. From a clinical point of view, the tool can be simultaneously used on distinct devices to facilitate support from caregivers or tutors. The use of the platform by patients and the multidisciplinary team are summarized in Tables 4 and 5. The behavioral framework and theory-based interventions that could be delivered using the mHeart tool in future intervention studies are listed in Multimedia Appendix 1. More details about functionalities and a video of the clinical use of the mHeart mobile app are also provided in the online dataset [88].

Figure 3. Functional layers and cloud architecture of mHeart. HIS: hospital information system; LOPD: the Spanish Organic Data Protection Law; WS: web server; HL7: High Level-7.

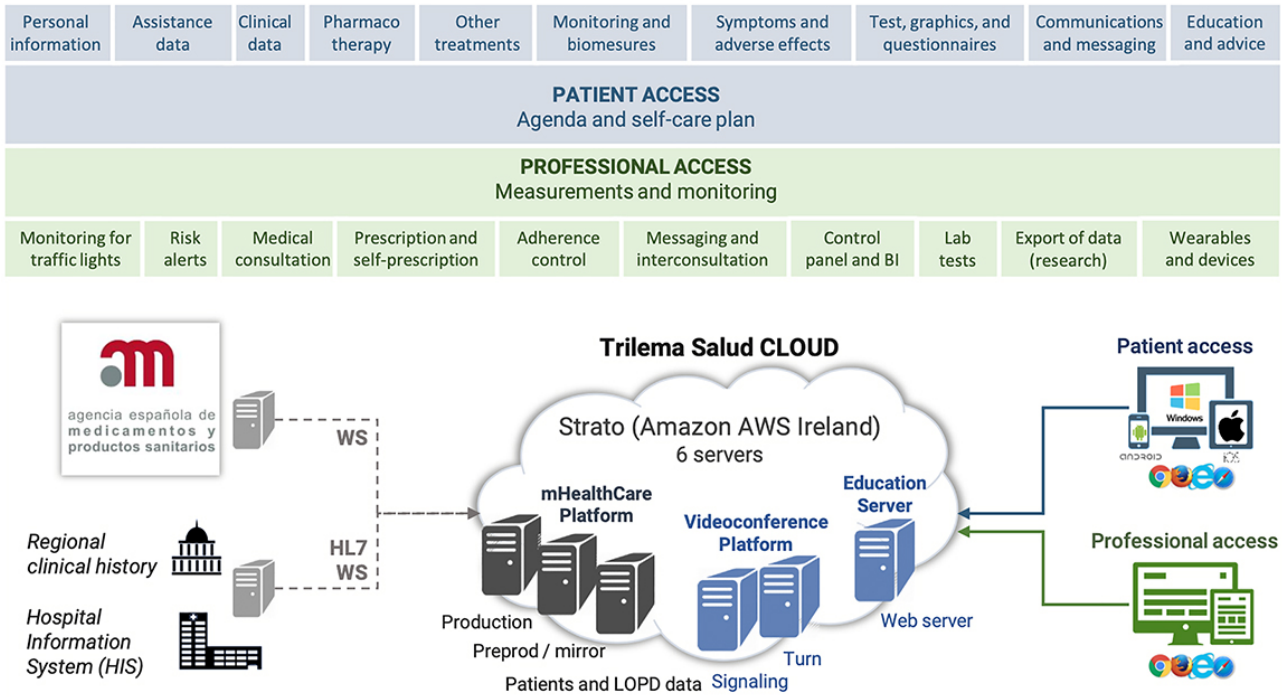


Table 4. mHeart patient profile modules, components, and clinical use.

Patient module	Components and clinical use
Treatment	Medication list including information on inactive drugs. Enquire about interactions consultation (ie, ask transplant pharmacist about new therapies).
Patient-Centered Module	Consulting and recording data (manually or using wearables). Reminders can be scheduled in the Agenda module. (1) Vital signs (ie, blood pressure, temperature, pulse and respiratory rate) and biomeasurements (ie, weight, height, glycemia). (2) Dietary intake, exercise data, and general wellness. Health instruments: adherence to medication (Haynes-Sachet [94] and Morisky-Green 4-item scale [95]), insomnia (Insomnia Severity Index [96]), and quality of life (EQ-5D-3L [97]). (3) Symptoms or adverse effects. The symptoms connected with an alert to clinicians were diarrhea, vomiting, fever, fainting episode, and syncope.
Agenda	The content of diverse modules is uploaded. A Push text alert can be activated on the patient's mobile phone. (1) Medication timing and consultation of recommendations. (2) Drug intake recording (single or several drugs at the same time) and reasons for nonadherence (drop-down list). (3) Nonpharmacological prescriptions (eg, relaxation practice according to the psychologist's prescription). (4) Tasks from the Patient-Centered Module programmed (eg, blood pressure monitoring 3 times per week). (5) Health reminders (eg, appointments, blood tests).
Communication Aids	(1) Teleconference: individual and group sessions. (2) A private patient-provider chat. Files can be attached.
Health Advice	Healthy lifestyle and health promotion information (eg, texts, photographs, or multimedia files).
Personal and Clinical Data	Sociodemographic data, documented allergies, and provider profiles (including affiliation and picture).
Help	(1) A help center service to solve both technical and functional problems (ie, telephone number, private message, and email). (2) Clinical contact data: medical team, pharmacist, transplant coordinator, patient appointment center, etc.
About	Information about the developers, aim of the tool, and team in charge.
Terms of Use and Privacy Policy	All the legal requirements already accepted should always be available for consultation.

Table 5. mHeart professional profile modules, components, and clinical use.

Provider Module	Component and clinical use
Patient View	List of active patient filters to organize the list and perform a rapid search.
Patient Registration	(1) The center identification number is used to download patient data from the hospital information system. (2) The patient receives a private message with login credentials. (3) Providers individualize the patient-reported outcome measures, schedule, and the treatment plan and recommendations for each new patient.
Treatment Prescription	(1) Pharmacological treatment is prescribed from a drop-down list of drugs updated from the Spanish National Formulary. Tailored recommendations can be added (eg, "Antirejection treatment. It is recommended that you take this on an empty stomach"). (2) Nonpharmacological therapies can be prescribed in free-form data entry by the multidisciplinary team (eg, nonsalty diet).
Patient-Centered Data Consultation	All data recorded in the Patient-Centered module can be tracked graphically in tables and diagrams. Timeframe filters can be used. mHeart platform features designed to follow medication adherence are adherence test results and drug intake registrations: (1) A traffic light system of alerts indicating a decrease in the patient's weekly adherence. List of patients can be sorted by adherence rate to prioritize interventions. (2) Adherence rates are presented graphically and through tables (for each drug and for the overall treatment).
Communication Aids	(1) Individual patient-provider chat. (2) Group messaging. Filters are available. Large-scale interventions can be scheduled (eg, preventive health promotions) for specific time periods. (3) Teleconsultation patient(s)-provider(s) for individual or group visit. (4) Teleconference for interdisciplinary communication and shared decision-making between providers.

Stage 3: Prototype Interoperability and Implementation

Diverse solutions to address implementation were settled by the scientific advisory team. First, mHeart was set up to be compatible with different systems and apps to ensure that users could employ their own phones, computers, or tablets. Second, technical support was outsourced (by the technological development firm) to provide initial training on mHeart skills to patients and providers as well as to solve queries. Finally, institutional protocols were created to standardize the new clinical workflows.

Additionally, based on participants' expertise (n=2, 100%), the pathways to overcome the lack of integration and communication between mHeart and electronic health records were separated into local and institutional solutions. Regarding local solutions, the strategies embedded allowed for two-way data exchange between mHeart and the hospital information system. First, the mHeart system requests sociodemographic patient data from the hospital information system. Data can refer to a new patient or an update on the patient's data. This is achieved via a synchronous high level-7 message patient query through the Simple Object Access Protocol. Second, once a week, a data report containing all of the mHeart patient-reported outcome measures is uploaded to the hospital information system. This is achieved via an implicit File Transfer Protocol over the Transport Layer Security server. A security process identifies the report and assigns it to the patient in the hospital information system. Only the latest report can be consulted as a clinical document. More details are also provided in the online dataset [88].

According to institutional solutions identified, the patient's data report could also be integrated with the regional electronic clinical record. With this report, any provider in the catchment area can monitor patients from any care level (eg, primary care, hospital care). In addition, in 2017, the regional health care system approved mHeart to be integrated with La Meva Salut, which is a patient health website allowing citizens to interact with the regional health care system.

Stage 4: Quality, Security, and Legal Requirements

Based on expert feedback, workable solutions were identified (listed in Textbox 3) to ensure legal, security, and data protection; medical technology intellectual property; medical device regulations; and quality evaluation. The solutions embedded could be used by other developers as a checklist to ensure minimum standards but are not limited to these solutions.

Textbox 3. Workable solutions to ensure the quality and security of the eHealth platform.

Processing personal data with confidentiality and security

- Comply with the national regulations on high-level confidential personal data.
- Obtain support from the hospital's Department of Data Confidentiality and Data Analysis.
- Ensure the quality of the Data Center through certification.
- Use secure connections for data integration between systems.
- Perform an annual audit of confidentiality and security by an external firm.
- Ensure users' duties: (1) patients should sign a nondisclosure agreement; (2) passwords require updating every 6 months; (3) acceptance of mHeart's conditions of use is a prerequisite and should always be available for future consultation by users.

Intellectual and industrial property recommendations

- Obtain support from experts on medical technology intellectual and industrial property.
- Sign a collaboration contract between the hospital and the developer's private firm.
- Register the platform trademark (eg, "mHeart").
- Register the platform content on intellectual property registers.

Medical device certificate

- Adopt the legislation requirements on medical device regulations [74,97]. CE marking as a class IIa medical device was obtained for mHeart.

Certification granted by a local institution

- Certificate of app quality by local institutions. AppSaludable [98] is already adopted for mHeart. AppSalut [99] is in the process of adoption by Fundació TicSalut (Regional Health Department). Some other options are British [100,101], iSYS Score [102], and uMARS [103,104].

Content quality

- Obtain institutional endorsement by scientific societies related to the population field. Written support for mHeart was provided by:
  - The regional transplant organization (OCATT) (October 31, 2016).
  - The regional transplant society (SCT) (October 10, 2017).
  - La Meva Salut homologation approval by the regional Health Government (October 20, 2016).
- Obtain written endorsement from patient associations and support groups. Written support for mHeart was provided by:
  - "Club de la Cremallera" Clinic Hospital (November 3, 2016).
  - "Cors Nous" Bellvitge Hospital (November 3, 2016).

Discussion

Principal Findings

The steps and key literature outlined in this paper resulted in the implementation of a holistic internet- and theory-based intervention model for the heart transplant population in the outpatient setting. After design of the mHeart system, several time-consuming issues remained to be resolved, such as interoperability, implementation, security, and quality. Moreover, the involvement of the interdisciplinary team, patients, and several experts was essential for the success of the platform but also required complex interactions.

Scalable, interactive apps directed to improve clinical practice are costly and time-consuming to produce [43]. We found several potential barriers when implementing the internet-based program in multimorbid patients, which are well known to lead to "dead ends" in real-world clinical practice [36,39,77]. Based on the experience gathered, the key points deemed essential in conceiving a new behavioral interventional model are outlined in Textbox 4. These recommendations could be used by future developers as a checklist to ensure minimum standards.

Textbox 4. Key recommendations for successful implementation of new eHealth strategies for new developers.

1. Avoid new developments from scratch. Tools that are already established and tested are an efficient starting point. This will help to allocate the economic resources on new features, facilitating the meeting of deadlines and achieving the expected quality of the system.
2. Before choosing the development company, determine that (i) it is a solvent and solid firm, (ii) its compliance with national standards of quality and safety, (iii) it has previous experience of clinically tested health care systems, (iv) it has favorable opinions of previous developers, and (v) it provides an excellent user help center.
3. Allocate resources to having expert advice on (i) legal, security, and data protection; (ii) medical technology intellectual property; and (iii) medical device regulations and quality evaluation.
4. Assign a provider as a part-time coordinator to facilitate procedures and deadlines, and to liaise with third parties. The recommended skills of the coordinator are a proactive approach; holistic vision; experience of research and innovative projects; ability to work in a team; and to have training in a specialty, medication management, behavioral change theories, and patient engagement.
5. First, design a general system structure and later adapt it to the target population needs. This will help to ensure end-user engagement while compensating for the implementation burden and ensuring the scalability of the model.
6. Base the design of the interventional model on already demonstrated major determinants of the efficacy of interventions and patient engagement: (i) proactive and trained multidisciplinary teams, (ii) active interaction with end users, (iii) behavioral change theories, and (iv) tailored interventions based on relevant patient-reported outcome measures.
7. Include in the design stage: (i) an analysis of end users' expectations, fears, and barriers; (ii) expert opinions on the interoperability of the system; and (iii) a plan for sustainability and reimbursement according to the interests of the center or health institution.
8. Join forces with patient associations and scientific societies during the design and testing stages to ensure content quality and scalability among centers.
9. Evaluate whether new features that may arise in the testing are (i) incorporated in the prototype (only recommended if they affect the usability and quality of the system), or (ii) addressed in subsequent phases of improvements.
10. Once the final prototype is established, resources should be allocated to provide continuous updates based on users' needs and feedback. This will ensure the system's usability, quality, and persistence over time.

Barriers and Facilitators to Implementing the mHeart mHealth Approach

Consideration of the issues to overcome during the implementation of mHeart could shorten the time period to reach the desired quality standards. Thus, it is critical for any new development to be based on an in-depth analysis of feasible solutions to overcome limitations. The first potential barrier to implementing an mHealth solution according to the opinion of 58% of the stakeholders was the *increase in clinicians workload*. However, in line with previous studies [36,45,105], the burden experienced during mHeart implementation was mainly derived from several other reasons such as achieving a well-designed theory-based framework of the intervention model, ensuring legal and security requirements, involving the health care team in training and workflow, and, ultimately, several organizational barriers. These tasks were highly demanding of time, and therefore it is strongly recommended that future developers perform an initial roadmap based on successful previous experiences. Moreover, an initial agreement with all of the parties involved on the stages and their responsibilities is also critical to reduce burden.

The second most widely agreed barrier, by 50% of respondents, was *lack of interoperability*, which has also been identified by other authors [33,39,77] as a major risk factor for unsuccessful eHealth approaches becoming isolated from the health care system. This challenge was technically demanding, but entails improvements in safety and quality. Indeed, mHeart testing of interoperability revealed that transcription errors could be avoided, the time spent typing patient data decreased, and better coordination among providers could be achieved.

Other well-established major barriers of eHealth strategies in clinical practice [72], and in line with respondents' opinions, were the *lack of models for funding* (15%) and *reimbursement for mHealth services by health systems* (54%). Although local guidance is fortunately growing [39,106], there is a delay in the implementation of new telemedicine laws [51]. This causes uncertainty about minimum quality standards and hinders scalability because of a lack of reimbursement models [38,73,107]. The initial mHeart funding was based on grants and has been detailed in the online dataset [88] to increase transparency and inspire new developers to overcome this barrier.

The risk of *patient'sresistance to using technology or the digital divide* was also a potential barrier according to 23% of the stakeholders, and is in agreement with a previous finding in multimorbid patients [33]. Nevertheless, almost all of the recipients in this study owned a cell phone and agreed on the utility of mHealth approaches such as mHeart. Thus, these data reinforce the idea of access, widespread use, and acceptance of technology in the heart transplant population, as previously observed in transplant recipients [86,108]. Nevertheless, high levels of attrition are a real issue in eHealth programs [62]. Thus, a persuasive design focused on enhancing user adherence is highly recommended [69,109,110]. Moreover, patients' opinions should also be carefully considered, with special emphasis on identifying potential barriers. In the mHeart interviews, up to 47% of recipients were interested in using a complementary website and 22% reported the need for a tutor to use the tool. Thus, a patient profile website was provided, and a help center was hired to provide human assistance and initial training to users; according to other authors [62], this

strategy has potential to increase user engagement without increasing provider burden.

Benefits of the mHeart Strategy in Multimorbid and Polypharmacy Populations Such As Heart Transplant Recipients

The information gathered from the opinions of patients and stakeholders allowed us to establish the aims of the mHeart clinical practice improvement model. Thus, the theoretical gains of mHealth described in the literature were translated into real-world strengths and the key software features were designed to achieve them. First, the *improvement in medication safety and efficacy* achieved the highest agreement by the stakeholders surveyed (88%), which supports previous studies [111-113] highlighting safety and efficacy as a major determinant in health outcomes. Thus, the main feature of mHeart was to provide pharmaceutical care, with particular emphasis on reducing the impact observed [10,24] of nonadherence to immunosuppressants after transplant. To succeed, the mHeart design combined multilevel strategies inspired by previous successful experiences [38,114,115], including educational, motivational, and tailored internet theory–based interventions to be delivered by a proactive team [12,25,41].

The two main strengths of the mHealth approach were *improving continuity of care and information flow* (81%) and *solving patient and caregiver queries* (77%). Indeed, based on the opinions of patient association representatives and in line with the findings of other authors [33,111], chronic patients are seeking more communication opportunities and better coordination among providers. In this sense, mHealth programs represent a unique opportunity to combine human support and new digital skills to reach a therapeutic alliance with the patient [109,110]. Software functions to promote patient-professional interaction [62,69] are therefore essential in a patient-centered model such as mHeart targeting the outpatient population.

Other relevant gains of mHealth reported by stakeholders were *enhancing patient's self-management* (77%), *early detection of symptoms or adverse effects* (65%), and *the use of patient-reported outcomes to allow preventive strategies* (65%). Indeed, the current scenario, in which patients are demanding coresponsibility [63], provides a strong opportunity to engage patients in electronically recorded patient-reported outcomes but also to train them in how to detect alarm symptoms and how to act when they arise. The use of patient-reported outcomes has previously shown an impact on medication efficacy and safety [36], patients' quality of life, and even survival [40]. Thus, it is expected that preventive internet-based interventions based on patient-reported outcomes will be a determinant to improve outcomes in outpatient care in the near future.

Opportunities Derived From Implementation of the mHeart Model

Successful eHealth interventions are commonly directed to specific population needs, such as mHeart in the heart transplant population [45,116]. This was indeed a particular strength highlighted by the patient associations during the testing of mHeart. Nevertheless, according to the ISRII experts, public dissemination of internet programs in different contexts is also highly valued [43]. Indeed, adapting the structure of the mHeart system to other population needs in the same health institution was an aid for recuperating the initial cost and implementation burden. Likewise, other institutions could profit from an already established clinically tested software as a starting point to avoid the burden of developing systems from scratch. An example is how the mHealthCare System, designed as a basis to develop mHeart, has been scaled to different populations by other health care centers (ie, MedPlan+, e-OncoSalud, ePrematur, Entrena EII, Gerar, RC Rehabilitación Cardiaca, and ICOnnecta, among others). Thus, any new upgrade on these apps improves the basis of the software and benefits several institutions.

The implementation of behavioral change technology models targeting complex populations demands a multidisciplinary approach to obtain the strategy benefit [37,51,115]. Operating this process was a highly demanding task, requiring managerial and coordinator profiles with certain skills. The leadership of mHeart implementation by a clinical pharmacist provided a strong opportunity to expand this role into the cardiology team, while making this provider visible to patients, families, and institutions. Likewise, eHealth has resulted in a valuable opportunity to expand the benefits of patient counseling and therapeutic drug monitoring by a multidisciplinary team in health care systems [37,117].

To scale any intervention model into research studies, and in line with the ISRII [43] and the CONSORT-EHEALTH reporting guidelines [47], it is vital to include an in-depth description of the strategy design. Thus, the theoretical framework, mode of delivery, and components of the intervention have been detailed for mHeart. Thereby, a behavioral-based design was used given the potential for providing a better understanding of how the intervention works on patient behaviors [118]. This has in turn been shown to increase efficacy, comparability, and scalability of the interventions performed [43,47]. Based on this background, a pilot study was performed to validate the mHeart tool to improve medication adherence in heart transplant patients. This exploratory study showed that the multilevel behavioral change intervention established (ie, the mHeart strategy) was highly effective since the improvement in adherence to immunosuppressive medication was 30%. Moreover, patient overall satisfaction with the mHeart approach was 9 (on a scale of 0-10) and the mHeart approach demonstrated its potential to overcome the limitations of traditional on-site methods [119]. Based on this experience and in line with other authors [25,70,120,121], it is highly recommended for future studies inspired on the mHeart model to count on providers properly trained in behavioral skills (eg, motivational interviewing) to deliver such theory-based interventions.

Limitations

This study has some limitations. First, we did not address the efficacy and sustainability of the mHeart approach over time, since the focus of the study was on the model implementation and scalability phases. Therefore, clinical applications of the mHeart strategy will provide information on the impact of its features on health outcomes. In future research conducted with this model, details should be provided by health providers on

when and under what conditions interventions will be delivered [54]. Second, based on ISRII recommendations [43], the validity of the electronic versions of the questionnaires used to measure diverse health domains in the mHeart system should also be evaluated before scaling up for larger research. The mHeart electronic questionnaires used to measure medication adherence have been validated and were proven to be as effective as the traditional on-site method in identifying nonadherent recipients in a pilot study [119]. This finding supports their widespread application in larger research and clinical practice. Third, in-depth analysis of the external validation was needed. In this regard, and to support the quality content of the mHeart platform, we obtained external feedback from patients' representatives of support groups from other centers and institutional endorsement by scientific societies related to the population field. Moreover, the mHeart validation study was also performed to compare the electronic mHeart approach versus the traditional (in-clinic) method to detect nonadherent heart transplant recipients and to improve medication adherence rates [119].

Conclusions

The experience gained during mHeart implementation has identified the facilitators and key strategies needed for success in new holistic theory–based internet models. It is recommended that future developers direct efforts to verify the experience of the technical team; ensure data confidentiality; and overcome workload, the digital divide, and interoperability. Heart transplant recipients' access to technology and willingness to use an mHealth approach were confirmed. An interdisciplinary team and a patient-centered design were vital to achieving a comprehensive mHealth approach directed to improve therapy management, patient empowerment, and patient-provider interactions. The mHeart model will be widely applicable in distinct clinical contexts, and may inspire other health providers to create innovative ways to deal with therapeutic complexity and multimorbidity in complex populations.

Acknowledgments

This work would not have been possible without the patients' contributions and willingness to achieve a patient-centered design. Furthermore, we would like to express our gratitude to the Catalan Transplant Organization (OCATT) and the Catalan Transplant Society (SCT) for their support and institutional vision, as well as to the representatives of the cardiac transplant patient support groups at Hospital Clínic ("Club de la Cremallera") and Bellvitge Hospital ("Cors Nous"). Stakeholder cooperation has also been essential (JT De Pourcq, A. Esquirol, A. Barata, A. Villalobos, D. Cebrian, E. Moreno, J. Cornet, C. Pratdepadua, R. Manté, J. Berdun, I. García-Cadenas, S. Novelli, V. Pellicer, N. Roser) in obtaining first-hand knowledge of the potential and expectations of mHeart in our environment, as well as its integration possibilities and available certifications. The authors are grateful to the experts involved in mHeart quality, implementation, and scalability, namely: J. Caparrus and N. Alberich as experts on data protection and confidentiality policy; V. Robert and the Information Systems Department for conducting platform interoperability; R. Mangues for his methodological advice as research projects coordinator; A. Ferrero for his statistical expertise; O. Pozas and F. Carbajo for their support from the legal department; D. Gallardo as an expert on intellectual property; and M. Ors, B. Monsalve, and N. Ichaso for their expertise from the Transference and Innovation Unite Research Institute. This work required many contributions and support from nonauthor members of the multidisciplinary Heart Failure and Heart Transplant team, and particularly D. Gil, S. Ros, M. Pirla, N. Mesado, E. Sole, J. Alvarez, M. Ribas, Y. Capape, M. Perez, J. Ruiz De Andres, and A. Blasco. The leadership of the project by the Pharmacy Department was possible thanks to the legacy left by many clinical pharmacists since 1967 in the hospital. All of them inspired this promising, innovative, and multidisciplinary clinical care line of research. This work was supported by the General Pharmaceutical Council of Barcelona (COFB; scientific research grant, 2016), Astellas Pharma S.L. (contribution to the institution aimed at reinforcing the resources to perform the project), and the Pharmacy Department of the Hospital de la Santa Creu i Sant Pau. The current sponsors Amgen S.L. have supported the hospital to continue in their efforts to investigate innovative mHealth solutions to improving patients' health outcomes. The above-mentioned funders and the firm in charge of the technological development of the software (Trilema Salud Group) played no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. The Hospital Research Institute owns the legal property of the mHeart national trademark and the intellectual property of the mHeart content.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Behavior change techniques designed to improve patients' medication and lifestyle habits, adapted to be delivered using the mHeart platform in interventional studies.
[PDF File (Adobe PDF File), 36 KB - cardio_v4i1e19065_app1.pdf]

Multimedia Appendix 2
Questionnaires and surveys designed to asses participants' data.
[PDF File (Adobe PDF File), 71 KB - cardio_v4i1e19065_app2.pdf]

Multimedia Appendix 3
Main areas for improvement in mHeart prototype 1 as a result of user feedback during alpha testing.
[PDF File (Adobe PDF File), 40 KB - cardio_v4i1e19065_app3.pdf]

References

1. Matesanz R, Domínguez-Gil B, Coll E, Mahíllo B, Marazuela R. How Spain Reached 40 Deceased Organ Donors per Million Population. Am J Transplant 2017 Jun 09;17(6):1447-1454. [doi: 10.1111/ajt.14104] [Medline: 28066980]
2. Wilhelm MJ. Long-term outcome following heart transplantation: current perspective. J Thorac Dis 2015 Mar;7(3):549-551. [doi: 10.3978/j.issn.2072-1439.2015.01.46] [Medline: 25922738]
3. González-Vílchez F, Almenar-Bonet L, Crespo-Leiro MG, Alonso-Pulpón L, González-Costelo J, Sobrino-Márquez JM, et al. Registro Español de Trasplante Cardiaco. XXIX Informe Oficial de la Sección de Insuficiencia Cardiaca de la Sociedad Española de Cardiología (1984-2017). Rev Español Cardiol 2018 Nov;71(11):952-960. [doi: 10.1016/j.recesp.2018.07.020]
4. Lund LH, Khush KK, Cherikh WS, Goldfarb S, Kucheryavaya AY, Levvey BJ, International Society for HeartLung Transplantation. The Registry of the International Society for Heart and Lung Transplantation: Thirty-fourth Adult Heart Transplantation Report-2017; Focus Theme: Allograft ischemic time. J Heart Lung Transplant 2017 Oct;36(10):1037-1046. [doi: 10.1016/j.healun.2017.07.019] [Medline: 28779893]
5. Mercer S, Furler J, Moffat K, Fischbacher-Smith D, Sanci L. Multimorbidity: Technical Series on Safer Primary Care. Geneva: World Health Organization; 2016:978-992.
6. Kernick D, Chew-Graham CA, O'Flynn N. Clinical assessment and management of multimorbidity: NICE guideline. Br J Gen Pract 2017 May;67(658):235-236 [FREE Full text] [doi: 10.3399/bjgp17X690857] [Medline: 28450343]
7. Lindenfeld J, Page RL, Zolty R, Shakar SF, Levi M, Lowes B, et al. Drug therapy in the heart transplant recipient: Part III: common medical problems. Circulation 2005 Jan 04;111(1):113-117. [doi: 10.1161/01.CIR.0000151609.60618.3C] [Medline: 15630040]
8. Bryant BM, Libby AM, Metz KR, Page RL, Ambardekar AV, Lindenfeld J, et al. Evaluating Patient-Level Medication Regimen Complexity Over Time in Heart Transplant Recipients. Ann Pharmacother 2016 Nov;50(11):926-934. [doi: 10.1177/1060028016657552] [Medline: 27371949]
9. Gomis-Pastor M, Roig Mingell E, Mirabet Perez S, Brossa Loidi V, Lopez Lopez L, Diaz Bassons A, et al. Multimorbidity and medication complexity: New challenges in heart transplantation. Clin Transplant 2019 Oct;33(10):e13682. [doi: 10.1111/ctr.13682] [Medline: 31368585]
10. De Geest S, Dobbels F, Fluri C, Paris W, Troosters T. Adherence to the therapeutic regimen in heart, lung, and heart-lung transplant recipients. J Cardiovasc Nurs 2005;20(5 Suppl):S88-S98. [doi: 10.1097/00005082-200509001-00010] [Medline: 16160588]
11. Brocks Y, Zittermann A, Grisse D, Schmid-Ott G, Stock-Gießendanner S, Schulz U, et al. Adherence of Heart Transplant Recipients to Prescribed Medication and Recommended Lifestyle Habits. Prog Transplant 2017 Jun;27(2):160-166. [doi: 10.1177/1526924817699959] [Medline: 28617170]
12. Denhaerynck K, Berben L, Dobbels F, Russell CL, Crespo-Leiro MG, Poncelet AJ, BRIGHT study team. Multilevel factors are associated with immunosuppressant nonadherence in heart transplant recipients: The international BRIGHT study. Am J Transplant 2018 Jun;18(6):1447-1460. [doi: 10.1111/ajt.14611] [Medline: 29205855]
13. Korb-Savoldelli V, Sabatier B, Gillaizeau F, Guillemain R, Prognon P, Bégué D, et al. Non-adherence with drug treatment after heart or lung transplantation in adults: a systematic review. Patient Educ Couns 2010 Nov;81(2):148-154. [doi: 10.1016/j.pec.2010.04.013] [Medline: 20627643]
14. Kamila P, Smith SG, Patzer R, Wolf MS, Marina S. Medication regimen complexity in kidney and liver transplant recipients. Transplantation 2014 Oct 15;98(7):e73-e74 [FREE Full text] [doi: 10.1097/TP.0000000000000403] [Medline: 25285955]
15. Libby AM, Fish DN, Hosokawa PW, Linnebur SA, Metz KR, Nair KV, et al. Patient-level medication regimen complexity across populations with chronic disease. Clin Ther 2013 Apr;35(4):385-398.e1 [FREE Full text] [doi: 10.1016/j.clinthera.2013.02.019] [Medline: 23541707]
16. Pantuzza LL, Ceccato MDGB, Silveira MR, Junqueira LMR, Reis AMM. Association between medication regimen complexity and pharmacotherapy adherence: a systematic review. Eur J Clin Pharmacol 2017 Nov 4;73(11):1475-1489. [doi: 10.1007/s00228-017-2315-2] [Medline: 28779460]
17. Schoonover H, Corbett CF, Weeks DL, Willson MN, Setter SM. Predicting potential postdischarge adverse drug events and 30-day unplanned hospital readmissions from medication regimen complexity. J Patient Saf 2014 Dec;10(4):186-191. [doi: 10.1097/PTS.0000000000000067] [Medline: 25408236]
18. Sevilla-Sanchez D, Molist-Brunet N, Amblàs-Novellas J, Roura-Poch P, Espaulella-Panicot J, Codina-Jané C. Adverse drug events in patients with advanced chronic conditions who have a prognosis of limited life expectancy at hospital admission. Eur J Clin Pharmacol 2017 Jan;73(1):79-89. [doi: 10.1007/s00228-016-2136-8] [Medline: 27704168]
19. Menditto E, Gimeno Miguel A, Moreno Juste A, Poblador Plou B, Aza Pascual-Salcedo M, Orlando V, et al. Patterns of multimorbidity and polypharmacy in young and adult population: Systematic associations among chronic diseases and drugs using factor analysis. PLoS One 2019 Feb 6;14(2):e0210701 [FREE Full text] [doi: 10.1371/journal.pone.0210701] [Medline: 30726245]

20. Montiel-Luque A, Núñez-Montenegro AJ, Martín-Aurioles E, Canca-Sánchez JC, Toro-Toro MC, González-Correa JA, Polipresact Research Group. Medication-related factors associated with health-related quality of life in patients older than 65 years with polypharmacy. PLoS One 2017 Feb 6;12(2):e0171320 [FREE Full text] [doi: 10.1371/journal.pone.0171320] [Medline: 28166266]
21. Ghimire S, Peterson GM, Castelino RL, Jose MD, Zaidi STR. Medication Regimen Complexity and Adherence in Haemodialysis Patients: An Exploratory Study. Am J Nephrol 2016;43(5):318-324. [doi: 10.1159/000446450] [Medline: 27166159]
22. Wimmer BC, Bell JS, Fastbom J, Wiese MD, Johnell K. Medication Regimen Complexity and Number of Medications as Factors Associated With Unplanned Hospitalizations in Older People: A Population-based Cohort Study. J Gerontol A Biol Sci Med Sci 2016 Jun;71(6):831-837 [FREE Full text] [doi: 10.1093/gerona/glv219] [Medline: 26707381]
23. Wimmer BC, Bell JS, Fastbom J, Wiese MD, Johnell K. Medication Regimen Complexity and Polypharmacy as Factors Associated With All-Cause Mortality in Older People: A Population-Based Cohort Study. Ann Pharmacother 2016 Feb 17;50(2):89-95 [FREE Full text] [doi: 10.1177/1060028015621071] [Medline: 26681444]
24. Dobbels F, De Geest S, van Cleemput J, Droogne W, Vanhaecke J. Effect of late medication non-compliance on outcome after heart transplantation: a 5-year follow-up. J Heart Lung Transplant 2004 Nov;23(11):1245-1251. [doi: 10.1016/j.healun.2003.09.016] [Medline: 15539122]
25. Senft Y, Kirsch M, Denhaerynck K, Dobbels F, Helmy R, Russell CL, BRIGHT study team. Practice patterns to improve pre and post-transplant medication adherence in heart transplant centres: a secondary data analysis of the international BRIGHT study. Eur J Cardiovasc Nurs 2018 Apr 01;17(4):356-367. [doi: 10.1177/1474515117747577] [Medline: 29231747]
26. Fleming JN, Taber DJ, McElligott J, McGillicuddy JW, Treiber F. Mobile Health in Solid Organ Transplant: The Time Is Now. Am J Transplant 2017 Sep 17;17(9):2263-2276. [doi: 10.1111/ajt.14225] [Medline: 28188681]
27. Karam V, Sebagh M, Rifai K, Yilmaz F, Bhangui P, Danet C, et al. Quality of life 10 years after liver transplantation: The impact of graft histology. World J Transplant 2016 Dec 24;6(4):703-711 [FREE Full text] [doi: 10.5500/wjt.v6.i4.703] [Medline: 28058221]
28. Damery S, Flanagan S, Combes G. The effectiveness of interventions to achieve co-ordinated multidisciplinary care and reduce hospital use for people with chronic diseases: study protocol for a systematic review of reviews. Syst Rev 2015 May 08;4(1):64 [FREE Full text] [doi: 10.1186/s13643-015-0055-x] [Medline: 25951820]
29. Damery S, Flanagan S, Combes G. Does integrated care reduce hospital activity for patients with chronic diseases? An umbrella review of systematic reviews. BMJ Open 2016 Nov 21;6(11):e011952 [FREE Full text] [doi: 10.1136/bmjopen-2016-011952] [Medline: 27872113]
30. Cajita MI, Baumgartner E, Berben L, Denhaerynck K, Helmy R, Schönfeld S, BRIGHT Study Team. Heart transplant centers with multidisciplinary team show a higher level of chronic illness management - Findings from the International BRIGHT Study. Heart Lung 2017 Sep;46(5):351-356. [doi: 10.1016/j.hrtlng.2017.05.006] [Medline: 28624338]
31. Costanzo MR, Dipchand A, Starling R, Anderson A, Chan M, Desai S, International Society of HeartLung Transplantation Guidelines. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. J Heart Lung Transplant 2010 Aug;29(8):914-956. [doi: 10.1016/j.healun.2010.05.034] [Medline: 20643330]
32. Comín-Colet J, Enjuanes C, Verdú-Rotellar JM, Linas A, Ruiz-Rodriguez P, González-Robledo G, et al. Impact on clinical events and healthcare costs of adding telemedicine to multidisciplinary disease management programmes for heart failure: Results of a randomized controlled trial. J Telemed Telecare 2016 Jul;22(5):282-295. [doi: 10.1177/1357633X15600583] [Medline: 26350543]
33. Melchiorre MG, Lamura G, Barbabella F, ICARE4EU Consortium. eHealth for people with multimorbidity: Results from the ICARE4EU project and insights from the "10 e's" by Gunther Eysenbach. PLoS One 2018;13(11):e0207292 [FREE Full text] [doi: 10.1371/journal.pone.0207292] [Medline: 30427924]
34. Martínez-Pérez B, de la Torre-Díez I, López-Coronado M, Herreros-González J. Mobile apps in cardiology: review. JMIR Mhealth Uhealth 2013 Jul 24;1(2):e15 [FREE Full text] [doi: 10.2196/mhealth.2737] [Medline: 25098320]
35. Kohl LFM, Crutzen R, de Vries NK. Online prevention aimed at lifestyle behaviors: a systematic review of reviews. J Med Internet Res 2013 Jul 16;15(7):e146 [FREE Full text] [doi: 10.2196/jmir.2665] [Medline: 23859884]
36. Lancaster K, Abuzour A, Khaira M, Mathers A, Chan A, Bui V, et al. The Use and Effects of Electronic Health Tools for Patient Self-Monitoring and Reporting of Outcomes Following Medication Use: Systematic Review. J Med Internet Res 2018 Dec 18;20(12):e294 [FREE Full text] [doi: 10.2196/jmir.9284] [Medline: 30563822]
37. Alexander E, Butler C, Darr A, Jenkins M, Long R, Shipman C, et al. ASHP Statement on Telepharmacy. Am J Health Syst Pharm 2017 May 01;74(9):e236-e241. [doi: 10.2146/ajhp170039] [Medline: 28438829]
38. Littauer SL, Dixon DL, Mishra VK, Sisson EM, Salgado TM. Pharmacists providing care in the outpatient setting through telemedicine models: a narrative review. Pharm Pract (Granada) 2017 Dec 31;15(4):1134-1134. [doi: 10.18549/pharmpract.2017.04.1134]
39. Vallespin B, Cornet J, Kotzeva A. Ensuring Evidence-Based Safe and Effective mHealth Applications. Stud Health Technol Inform 2016;222:248-261. [Medline: 27198107]

40. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J Clin Oncol 2016 Feb 20;34(6):557-565 [FREE Full text] [doi: 10.1200/JCO.2015.63.0830] [Medline: 26644527]
41. Park LG, Howie-Esquivel J, Dracup K. A quantitative systematic review of the efficacy of mobile phone interventions to improve medication adherence. J Adv Nurs 2014 Sep;70(9):1932-1953. [doi: 10.1111/jan.12400] [Medline: 24689978]
42. Piette JD, List J, Rana GK, Townsend W, Striplin D, Heisler M. Mobile Health Devices as Tools for Worldwide Cardiovascular Risk Reduction and Disease Management. Circulation 2015 Nov 24;132(21):2012-2027 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.114.008723] [Medline: 26596977]
43. Ritterband LM, Andersson G, Christensen HM, Carlbring P, Cuijpers P. Directions for the International Society for Research on Internet Interventions (ISRII). J Med Internet Res 2006 Sep 29;8(3):e23 [FREE Full text] [doi: 10.2196/jmir.8.3.e23] [Medline: 17032639]
44. Webb TL, Joseph J, Yardley L, Michie S. Using the internet to promote health behavior change: a systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. J Med Internet Res 2010 Feb 17;12(1):e4 [FREE Full text] [doi: 10.2196/jmir.1376] [Medline: 20164043]
45. Heron KE, Smyth JM. Ecological momentary interventions: incorporating mobile technology into psychosocial and health behaviour treatments. Br J Health Psychol 2010 Feb;15(Pt 1):1-39 [FREE Full text] [doi: 10.1348/135910709X466063] [Medline: 19646331]
46. Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, et al. The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: a systematic review. PLoS Med 2013 Jan 15;10(1):e1001362 [FREE Full text] [doi: 10.1371/journal.pmed.1001362] [Medline: 23349621]
47. Eysenbach G, CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. J Med Internet Res 2011 Dec 31;13(4):e126 [FREE Full text] [doi: 10.2196/jmir.1923] [Medline: 22209829]
48. Davidson T, McGillicuddy J, Mueller M, Brunner-Jackson B, Favella A, Anderson A, et al. Evaluation of an mHealth Medication Regimen Self-Management Program for African American and Hispanic Uncontrolled Hypertensives. J Pers Med 2015 Nov 17;5(4):389-405 [FREE Full text] [doi: 10.3390/jpm5040389] [Medline: 26593951]
49. DeVito Dabbs A, Song MK, Myers BA, Li R, Hawkins RP, Pilewski JM, et al. A Randomized Controlled Trial of a Mobile Health Intervention to Promote Self-Management After Lung Transplantation. Am J Transplant 2016 Jul 14;16(7):2172-2180. [doi: 10.1111/ajt.13701] [Medline: 26729617]
50. Rosenberger EM, DeVito Dabbs AJ, DiMartini AF, Landsittel DP, Pilewski JM, Dew MA. Long-Term Follow-up of a Randomized Controlled Trial Evaluating a Mobile Health Intervention for Self-Management in Lung Transplant Recipients. Am J Transplant 2017 May 31;17(5):1286-1293. [doi: 10.1111/ajt.14062] [Medline: 27664940]
51. Poudel A, Nissen L. Integr Pharm Res Pract 2016 Oct;5:75-82. [doi: 10.2147/iprp.s101685]
52. Pinnock H, Barwick M, Carpenter CR, Eldridge S, Grandes G, Griffiths CJ, StaRI Group. Standards for Reporting Implementation Studies (StaRI) Statement. BMJ 2017 Mar 06;356:i6795 [FREE Full text] [doi: 10.1136/bmj.i6795] [Medline: 28264797]
53. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007 Dec 16;19(6):349-357. [doi: 10.1093/intqhc/mzm042] [Medline: 17872937]
54. Mohr DC, Schueller SM, Montague E, Burns MN, Rashidi P. The behavioral intervention technology model: an integrated conceptual and technological framework for eHealth and mHealth interventions. J Med Internet Res 2014 Jun 05;16(6):e146 [FREE Full text] [doi: 10.2196/jmir.3077] [Medline: 24905070]
55. Ritterband LM, Thorndike FP, Cox DJ, Kovatchev BP, Gonder-Frederick LA. A behavior change model for internet interventions. Ann Behav Med 2009 Aug;38(1):18-27 [FREE Full text] [doi: 10.1007/s12160-009-9133-4] [Medline: 19802647]
56. Oinas-Kukkonen H. A foundation for the study of behavior change support systems. Pers Ubiquit Comput 2012 Jul 19;17(6):1223-1235. [doi: 10.1007/s00779-012-0591-5]
57. Oinas-Kukkonen H, Harjumaa M. Persuasive Systems Design: Key Issues, Process Model, and System Features. Commun Assoc Inf Syst 2009;24:28. [doi: 10.17705/1cais.02428]
58. Fogg BJ. A behavior model for persuasive design. 2009 Presented at: Persuasive Technology, Fourth International Conference, PERSUASIVE 2009; April 26-29, 2009; Claremont, CA. [doi: 10.1145/1541948.1541999]
59. Whittaker R, Merry S, Dorey E, Maddison R. A development and evaluation process for mHealth interventions: examples from New Zealand. J Health Commun 2012;17(Suppl 1):11-21. [doi: 10.1080/10810730.2011.649103] [Medline: 22548594]
60. Yen P, Bakken S. Review of health information technology usability study methodologies. J Am Med Inform Assoc 2012;19(3):413-422 [FREE Full text] [doi: 10.1136/amiajnl-2010-000020] [Medline: 21828224]
61. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JEWC. Persuasive system design does matter: a systematic review of adherence to web-based interventions. J Med Internet Res 2012 Nov 14;14(6):e152 [FREE Full text] [doi: 10.2196/jmir.2104] [Medline: 23151820]

62. Baumel A, Kane JM. Examining Predictors of Real-World User Engagement with Self-Guided eHealth Interventions: Analysis of Mobile Apps and Websites Using a Novel Dataset. J Med Internet Res 2018 Dec 14;20(12):e11491 [FREE Full text] [doi: 10.2196/11491] [Medline: 30552077]
63. Pagès-Puigdemont N, Mangues MA, Masip M, Gabriele G, Fernández-Maldonado L, Blancafort S, et al. Patients' Perspective of Medication Adherence in Chronic Conditions: A Qualitative Study. Adv Ther 2016 Oct 9;33(10):1740-1754 [FREE Full text] [doi: 10.1007/s12325-016-0394-6] [Medline: 27503082]
64. Davis R, Campbell R, Hildon Z, Hobbs L, Michie S. Theories of behaviour and behaviour change across the social and behavioural sciences: a scoping review. Health Psychol Rev 2015;9(3):323-344 [FREE Full text] [doi: 10.1080/17437199.2014.941722] [Medline: 25104107]
65. Conn VS, Enriquez M, Ruppar TM, Chan KC. Meta-analyses of Theory Use in Medication Adherence Intervention Research. Am J Health Behav 2016 Mar;40(2):155-171 [FREE Full text] [doi: 10.5993/AJHB.40.2.1] [Medline: 26931748]
66. Kok G, Schaalma H, Ruiter RAC, van Empelen P, Brug J. Intervention mapping: protocol for applying health psychology theory to prevention programmes. J Health Psychol 2004 Jan;9(1):85-98. [doi: 10.1177/1359105304038379] [Medline: 14683571]
67. Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From Theory to Intervention: Mapping Theoretically Derived Behavioural Determinants to Behaviour Change Techniques. Appl Psychol 2008;57(4):660-680. [doi: 10.1111/j.1464-0597.2008.00341.x]
68. Abraham C, Michie S. A taxonomy of behavior change techniques used in interventions. Health Psychol 2008 May;27(3):379-387. [doi: 10.1037/0278-6133.27.3.379] [Medline: 18624603]
69. Muench F, Baumel A. More Than a Text Message: Dismantling Digital Triggers to Curate Behavior Change in Patient-Centered Health Interventions. J Med Internet Res 2017 May 26;19(5):e147 [FREE Full text] [doi: 10.2196/jmir.7463] [Medline: 28550001]
70. Dobbels F, De Bleser L, Berben L, Kristanto P, Dupont L, Nevens F, et al. Efficacy of a medication adherence enhancing intervention in transplantation: The MAESTRO-Tx trial. J Heart Lung Transplant 2017 May;36(5):499-508. [doi: 10.1016/j.healun.2017.01.007] [Medline: 28162931]
71. Kay M, World Health Organization, Global Observatory for eHealth. mHealth: New horizons for health through mobile technologies. Global Observatory for eHealth series: Volume 3. 2011. URL: https://www.who.int/goe/publications/goe_mhealth_web.pdf [accessed 2020-11-14]
72. Green Paper on mobile health ("mHealth"). Brussels: European Comission; 2014. URL: https://ec.europa.eu/digital-single-market/en/news/green-paper-mobile-health-mhealth [accessed 2020-11-14]
73. Socio-economic impact of mHealth. An assessment report for the European Union. Pricewaterhouse Coopers Private Limited. India: GSMA; 2013. URL: https://www.gsma.com/iot/wp-content/uploads/2013/06/Socio-economic_impact-of-mHealth_EU_14062013V2.pdf [accessed 2020-11-14]
74. Policy for Device Software Functions and Mobile Medical Applications. Guidance for Industry and Food and Drug Administration Staff.: Food and Drug Administration, US Department of Health and Human Services, Center for Devices and Radiological Health. Center for Biologics Evaluation and Research; 2019. URL: https://www.fda.gov/media/80958/download [accessed 2020-11-14]
75. Cortez NG, Cohen IG, Kesselheim AS. FDA regulation of mobile health technologies. N Engl J Med 2014 Jul 24;371(4):372-379. [doi: 10.1056/NEJMhle1403384] [Medline: 25054722]
76. eHealth Action Plan 2012-2020 -Innovative healthcare for the 21st century Internet. European Commission. 2012. URL: https://ec.europa.eu/health/sites/health/files/ehealth/docs/com_2012_736_en.pdf [accessed 2020-11-11]
77. PLOS Medicine Editors. A reality checkpoint for mobile health: three challenges to overcome. PLoS Med 2013;10(2):e1001395 [FREE Full text] [doi: 10.1371/journal.pmed.1001395] [Medline: 23468597]
78. Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. J Med Internet Res 2015 Feb 24;17(2):e52 [FREE Full text] [doi: 10.2196/jmir.3951] [Medline: 25803266]
79. McGillicuddy JW, Gregoski MJ, Weiland AK, Rock RA, Brunner-Jackson BM, Patel SK, et al. Mobile Health Medication Adherence and Blood Pressure Control in Renal Transplant Recipients: A Proof-of-Concept Randomized Controlled Trial. JMIR Res Protoc 2013 Sep 04;2(2):e32 [FREE Full text] [doi: 10.2196/resprot.2633] [Medline: 24004517]
80. Rao S, Ghanta M, Moritz MJ, Constantinescu S. Long-Term Functional Recovery, Quality of Life, and Pregnancy After Solid Organ Transplantation. Med Clin North Am 2016 May;100(3):613-629. [doi: 10.1016/j.mcna.2016.01.010] [Medline: 27095649]
81. Dew MA, Goycoolea JM, Harris RC, Lee A, Zomak R, Dunbar-Jacob J, et al. An internet-based intervention to improve psychosocial outcomes in heart transplant recipients and family caregivers: development and evaluation. J Heart Lung Transplant 2004 Jun;23(6):745-758. [doi: 10.1016/j.healun.2003.07.002] [Medline: 15366436]
82. Berben L, Denhaerynck K, Dobbels F, Engberg S, Vanhaecke J, Crespo-Leiro MG, BRIGHT study consortium. Building research initiative group: chronic illness management and adherence in transplantation (BRIGHT) study: study protocol. J Adv Nurs 2015 Mar;71(3):642-654. [doi: 10.1111/jan.12519] [Medline: 25257974]

83. Hugon A, Roustit M, Lehmann A, Saint-Raymond C, Borrel E, Hilleret M, et al. Influence of intention to adhere, beliefs and satisfaction about medicines on adherence in solid organ transplant recipients. Transplantation 2014 Jul 27;98(2):222-228. [doi: 10.1097/TP.0000000000000221] [Medline: 24926826]
84. Kobashigawa J, Zuckermann A, Macdonald P, Leprince P, Esmailian F, Luu M, Consensus Conference participants. Report from a consensus conference on primary graft dysfunction after cardiac transplantation. J Heart Lung Transplant 2014 Apr;33(4):327-340. [doi: 10.1016/j.healun.2014.02.027] [Medline: 24661451]
85. Lee JL, Eaton C, Gutiérrez-Colina AM, Devine K, Simons LE, Mee L, et al. Longitudinal stability of specific barriers to medication adherence. J Pediatr Psychol 2014 Aug;39(7):667-676. [doi: 10.1093/jpepsy/jsu026] [Medline: 24824613]
86. McGillicuddy J, Weiland A, Frenzel R, Mueller M, Brunner-Jackson B, Taber D, et al. Patient attitudes toward mobile phone-based health monitoring: questionnaire study among kidney transplant recipients. J Med Internet Res 2013 Jan 08;15(1):e6 [FREE Full text] [doi: 10.2196/jmir.2284] [Medline: 23305649]
87. Viladrich C, Doval E. Medición: Fiabilidad y Validez. In: 5a ed Bellaterra: Laboratori d'estadística Aplicada i Modelització. Barcelona: Universitat Autónoma de Barcelona; 2011.
88. Gomis-Pastor M, Mangues M, Pellicer V. mHeart - mHealthCare Platform Adapted to the Heart Transplant Population - Technical Specifications and Software Source Code Internet. Mendeley Data. 2019. URL: https://data.mendeley.com/datasets/yf2dgcfmmh/4 [accessed 2020-11-14]
89. Clinapsis: Clinical Epidemiology and Healthcare Services. URL: http://www.clinapsis.com/index.php/auth/login/?l=en [accessed 2019-07-05]
90. mHealthCare Platform Trilema Salud Internet. Fundación Trilema. 2019. URL: https://salud.trilema.es/pages/users/login.jsp [accessed 2019-07-19]
91. mHeart - Google Play Mobile Applications Internet. Socioemprende SL (TrilemaSalud Group). URL: https://play.google.com/store/apps/details?id=nabelia.mheart&gl=ES [accessed 2019-07-20]
92. mHeart - App Store Mobile Applications Internet. Socioemprende S.L (TrilemaSalud Group). URL: https://apps.apple.com/us/app/mheart/id1449696988 [accessed 2019-07-20]
93. Sackett DL, Haynes RB, Fuyatt GH, Tungwell P. Ayudar a los pacientes a cumplir los tratamientos. In: Epidemiol clínica, Cienc básica para la Med clínica 2a ed. Madrid: Panamericana; 1994:249-278.
94. Carbonell Abella C, Guañabens Gay N, Regadera Anechina L, Marín Rives JA, Taverna Llauradó E, Ayechu Redín MP, ADHEPOR. [Analysis of therapeutic compliance in women with osteoporosis]. Reumatol Clin 2011 Sep;7(5):299-304 [FREE Full text] [doi: 10.1016/j.reuma.2010.12.003] [Medline: 21925445]
95. Fernandez-Mendoza J, Rodriguez-Muñoz A, Vela-Bueno A, Olavarrieta-Bernardino S, Calhoun SL, Bixler EO, et al. The Spanish version of the Insomnia Severity Index: a confirmatory factor analysis. Sleep Med 2012 Feb;13(2):207-210. [doi: 10.1016/j.sleep.2011.06.019] [Medline: 22172961]
96. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001 Jul;33(5):337-343. [doi: 10.3109/07853890109002087] [Medline: 11491192]
97. Regulatory framework: Internal Market, Industry, Entrepreneurship and SMEs Internet. European Commission. 2019. URL: https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en [accessed 2019-07-18]
98. AppSaludable Quality Seal Internet. Agencia de Calidad Sanitaria de Andalucía. 2012. URL: http://www.calidadappsalud.com/en/distintivo-appsaludable/ [accessed 2019-07-02]
99. Guidebooks for the accreditation process for health or wellness Apps. Fundació TIC Salut Social. Generalitat de Catalunya. URL: https://ticsalutsocial.cat/en/recursos/mhealth-en/apps-accreditation-guidebooks/ [accessed 2020-11-11]
100. Behaviour change: general approaches (PH6). National Institute for Health and Care Excellence (NICE). URL: https://www.nice.org.uk/guidance/ph6 [accessed 2019-07-02]
101. McMillan B, Hickey E, Patel MG, Mitchell C. Quality assessment of a sample of mobile app-based health behavior change interventions using a tool based on the National Institute of Health and Care Excellence behavior change guidance. Patient Educ Couns 2016 Mar;99(3):429-435. [doi: 10.1016/j.pec.2015.10.023] [Medline: 26607787]
102. Inscripción TOP20 Internet. iSYS Foundation. URL: https://www.fundacionisys.org/es/apps-de-salud/inscripcion-de-apps [accessed 2019-07-02]
103. Stoyanov SR, Hides L, Kavanagh DJ, Wilson H. Development and Validation of the User Version of the Mobile Application Rating Scale (uMARS). JMIR Mhealth Uhealth 2016 Jun 10;4(2):e72 [FREE Full text] [doi: 10.2196/mhealth.5849] [Medline: 27287964]
104. Domnich A, Arata L, Amicizia D, Signori A, Patrick B, Stoyanov S, et al. Development and validation of the Italian version of the Mobile Application Rating Scale and its generalisability to apps targeting primary prevention. BMC Med Inform Decis Mak 2016 Jul 07;16(1):83 [FREE Full text] [doi: 10.1186/s12911-016-0323-2] [Medline: 27387434]
105. Williams A, Low JK, Manias E, Dooley M, Crawford K. Trials and tribulations with electronic medication adherence monitoring in kidney transplantation. Res Social Adm Pharm 2016 Sep;12(5):794-800. [doi: 10.1016/j.sapharm.2015.10.010] [Medline: 26616159]
106. A quick guide to recommendations for the development of health and social care Apps. How to create an application secure, accessible mobile usable and interoperable. Fundació TIC Salut Social. Generalitat de Catalunya. 2018. URL: https:/

/ticsalutsocial.cat/en/recursos/mhealth-en/a-quick-guide-to-recommendations-for-the-development-of-health-and-social-care-apps/ [accessed 2020-11-11]
107. Summary report on public consultation on the green paper on mobile health. European Comission. URL: https://ec.europa.eu/digital-single-market/en/news/summary-report-public-consultation-green-paper-mobile-health [accessed 2020-11-11]
108. Israni A, Dean C, Kasel B, Berndt L, Wildebush W, Wang CJ. Why do Patients Forget to Take Immunosuppression Medications and Miss Appointments: Can a Mobile Phone App Help? JMIR Public Health Surveill 2016 Apr 04;2(1):e15 [FREE Full text] [doi: 10.2196/publichealth.5285] [Medline: 27227150]
109. Perski O, Blandford A, West R, Michie S. Conceptualising engagement with digital behaviour change interventions: a systematic review using principles from critical interpretive synthesis. Transl Behav Med 2017 Jun;7(2):254-267 [FREE Full text] [doi: 10.1007/s13142-016-0453-1] [Medline: 27966189]
110. Yardley L, Spring BJ, Riper H, Morrison LG, Crane DH, Curtis K, et al. Understanding and Promoting Effective Engagement With Digital Behavior Change Interventions. Am J Prev Med 2016 Nov;51(5):833-842. [doi: 10.1016/j.amepre.2016.06.015] [Medline: 27745683]
111. Molokhia M, Majeed A. Current and future perspectives on the management of polypharmacy. BMC Fam Pract 2017 Jun 06;18(1):70 [FREE Full text] [doi: 10.1186/s12875-017-0642-0] [Medline: 28587644]
112. Kim DH, Rich MW. Patient-Centred Care of Older Adults With Cardiovascular Disease and Multiple Chronic Conditions. Can J Cardiol 2016 Sep;32(9):1097-1107 [FREE Full text] [doi: 10.1016/j.cjca.2016.04.003] [Medline: 27378591]
113. García-Jiménez E, Amariles P, González M, Parras-Martín M, Espejo-Guerrero J, Faus M. Non-adherence, drug-related problems and negative outcomes associated with medication: Causes and outcomes in drug therapy follow-up. Ars Pharm 2008;49(2):145-157.
114. Sankaranarayanan J, Murante LJ, Moffett LM. A retrospective evaluation of remote pharmacist interventions in a telepharmacy service model using a conceptual framework. Telemed J E Health 2014 Oct;20(10):893-901 [FREE Full text] [doi: 10.1089/tmj.2013.0362] [Medline: 24611489]
115. Niznik JD, He H, Kane-Gill SL. Impact of clinical pharmacist services delivered via telemedicine in the outpatient or ambulatory care setting: A systematic review. Res Social Adm Pharm 2018 Aug;14(8):707-717. [doi: 10.1016/j.sapharm.2017.10.011] [Medline: 29100941]
116. Checchi KD, Huybrechts KF, Avorn J, Kesselheim AS. Electronic medication packaging devices and medication adherence: a systematic review. JAMA 2014 Sep 24;312(12):1237-1247 [FREE Full text] [doi: 10.1001/jama.2014.10059] [Medline: 25247520]
117. Strand M, Tellers J, Patterson A, Ross A, Palombi L. The achievement of public health services in pharmacy practice: A literature review. Res Social Adm Pharm 2016;12(2):247-256. [doi: 10.1016/j.sapharm.2015.06.004] [Medline: 26215337]
118. Michie S, Wood CE, Johnston M, Abraham C, Francis JJ, Hardeman W. Behaviour change techniques: the development and evaluation of a taxonomic method for reporting and describing behaviour change interventions (a suite of five studies involving consensus methods, randomised controlled trials and analysis of qualitative data). Health Technol Assess 2015 Nov;19(99):1-188. [doi: 10.3310/hta19990] [Medline: 26616119]
119. Gomis-Pastor M, Roig E, Mirabet S, T De Pourcq J, Conejo I, Feliu A, et al. A Mobile App (mHeart) to Detect Medication Nonadherence in the Heart Transplant Population: Validation Study. JMIR Mhealth Uhealth 2020 Feb 04;8(2):e15957-e1S274 [FREE Full text] [doi: 10.2196/15957] [Medline: 32014839]
120. Salvo MC, Cannon-Breland ML. Motivational interviewing for medication adherence. J Am Pharm Assoc (2003) 2015;55(4):e354-61; quiz e362. [doi: 10.1331/JAPhA.2015.15532] [Medline: 26161493]
121. Morton K, Beauchamp M, Prothero A, Joyce L, Saunders L, Spencer-Bowdage S, et al. The effectiveness of motivational interviewing for health behaviour change in primary care settings: a systematic review. Health Psychol Rev 2015 Feb 12;9(2):205-223. [doi: 10.1080/17437199.2014.882006] [Medline: 26209209]

Abbreviations

ISRII: International Society for Research on Internet Interventions
mHealth: mobile health

Edited by G Eysenbach; submitted 02.04.20; peer-reviewed by M Schuuring, R Treskes; comments to author 23.06.20; revised version received 05.07.20; accepted 16.09.20; published 24.11.20.

Please cite as:
Gomis-Pastor M, Mirabet S, Roig E, Lopez L, Brossa V, Galvez-Tugas E, Rodriguez-Murphy E, Feliu A, Ontiveros G, Garcia-Cuyàs F, Salazar A, Mangues MA
Interdisciplinary Mobile Health Model to Improve Clinical Care After Heart Transplantation: Implementation Strategy Study
JMIR Cardio 2020;4(1):e19065
URL: http://cardio.jmir.org/2020/1/e19065/
doi:10.2196/19065
PMID:33231557

Original Paper

“I Like the Idea of It…But Probably Wouldn’t Use It” - Health Care Provider Perspectives on Heart Failure mHealth: Qualitative Study

Jennifer Dickman Portz[1,2], MSW, PhD; Kelsey Lynett Ford[2], MPH; Kira Elsbernd[2], MPH; Christopher E Knoepke[3,4,5], MSW, PhD; Kelsey Flint[6], MD; David B Bekelman[1,6], MPH, MD; Rebecca S Boxer[7], MS, MD; Sheana Bull[2], MPH, PhD

[1]Division of General Internal Medicine, University of Colorado School of Medicine Anschutz Medical Campus, Aurora, CO, United States

[2]mHealth Impact Lab, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

[3]Division of Cardiology, University of Colorado School of Medicine Anschutz Medical Campus, Aurora, CO, United States

[4]Data Science to Patient Value (D2V) Initiative, University of Colorado School of Medicine Anschutz Medical Campus, Aurora, CO, United States

[5]Adult & Child Consortium for Outcomes Research & Delivery Science, University of Colorado School of Medicine Anschutz Medical Campus, Aurora, CO, United States

[6]Department of Medicine, Eastern Colorado Health Care System, Department of Veterans Affairs, Aurora, CO, United States

[7]Institute for Health Research, Kaiser Permanente Colorado, Aurora, CO, United States

Corresponding Author:
Jennifer Dickman Portz, MSW, PhD
Division of General Internal Medicine
University of Colorado School of Medicine Anschutz Medical Campus
Mailbox B180
12631 East 17th Avenue
Aurora, CO, 80045
United States
Phone: 1 303 724 4438
Email: Jennifer.Portz@cuanschutz.edu

Abstract

Background: Many mobile health (mHealth) technologies exist for patients with heart failure (HF). However, HF mhealth lacks evidence of efficacy, caregiver involvement, and clinically useful real-time data.

Objective: We aim to capture health care providers’ perceived value of HF mHealth, particularly for pairing patient–caregiver-generated data with clinical intervention to inform the design of future HF mHealth.

Methods: This study is a subanalysis of a larger qualitative study based on interviewing patients with HF, their caregivers, and health care providers. This analysis included interviews with health care providers (N=20), focusing on their perceived usefulness of HF mHealth tools and interventions.

Results: A total of 5 themes emerged: (1) bio-psychosocial-spiritual monitoring, (2) use of sensors, (3) interoperability, (4) data sharing, and (5) usefulness of patient-reported outcomes in practice. Providers remain interested in mHealth technologies for HF patients and their caregivers. However, providers report being unconvinced of the clinical usefulness of robust real-time patient-reported outcomes.

Conclusions: The use of assessments, sensors, and real-time data collection could provide value in patient care. Future research must continually explore how to maximize the utility of mHealth for HF patients, their caregivers, and health care providers.

(JMIR Cardio 2020;4(1):e18101) doi:10.2196/18101

KEYWORDS

heart failure; information technology; informatics; telemedicine; mHealth

Introduction

Nearly 6.5 million Americans have heart failure (HF), which is a leading cause of death, associated with high medical costs and poor quality of life [1]. In all its forms, HF is a chronic condition often characterized by an unpredictable clinical trajectory. HF therapies are complex, including as many as 5 categories of medications when optimized, on top of a variety of possible devices meant to prevent sudden death, improve quality of life and physical functioning, manage syndromes occurring secondary to HF, or some combination of all 3 objectives [2,3]. HF management is thus similarly complex, with alterations to treatment often occurring in response to unsuccessful trials of treatment combinations or hospitalizations, ultimately resulting in the consideration for transplant or mechanical circulatory support [2]. Consistent and ongoing patient-reported data are critical to understanding and predicting clinical decompensation, and methods of capturing such data have historically proven to be elusive [4,5].

The pace of technology continues to drive innovative HF management strategies [6,7]. Consumer-facing mobile technology (eg, wearables, mobile apps, and web-based platforms), known as mHealth (mobile health), offers a modern approach for HF symptom monitoring and psychosocial support. Some of these approaches show promise in improving health care services and health outcomes for patients with HF [8,9]. However, not all off-the-shelf technologies demonstrate evidence of effectiveness or successful adoption [7,10,11]. Despite mixed reviews on their efficacy, enthusiasm for emerging technologies continues among researchers and interventionists [12]. The popularity with real-time interventions, interoperability with electronic health records, and personalization features persist, generating voluminous amounts of data. The clinical usefulness of such robust data in practice remains continually debated [13].

This short paper describes preliminary findings from an ongoing larger mixed-methods research study [14] designed to develop an evidence-based HF mHealth intervention in partnership with all health care stakeholders (ie, patients, caregivers, and providers). The objective of this paper is to illustrate providers' specific perceived value of HF mHealth, particularly when pairing patient- and caregiver-generated data with meaningful, timely, and effective clinical intervention. Future steps include interviewing and co-designing with patients, health care providers, and family caregivers.

Methods

This study used a phenomenological [15] design to explore health care providers' experiences when developing HF mHealth. The qualitative study took place at the University of Colorado Anschutz Medical Campus within the University's health system—UCHealth. The research team consisted of 1 principal investigator (JDP) and 2 research assistants (KF and KE) experienced in qualitative methods. The study adhered to the Consolidated Criteria for Reporting Qualitative Research (COREQ) [16] and was approved by the Colorado Multiple Institutional Review Board.

Recruitment and Interview Procedure

Between September 2018 and February 2019, participants were purposefully recruited [17] to partake in semistructured interviews, which were audio-recorded and transcribed. Initially, 10 health care providers with expertise in the treatment of patients with HF were recruited, with snowball sampling methods used to identify an additional 15 providers. Of the 22 that agreed to participate, 20 health care providers from diverse specialties (physicians, nurses, social workers, therapists, and chaplains) participated in interviews. Semistructured interviews were held in a location convenient to the participant and lasted 30-60 minutes.

An 18-question interview guide probed experiences related to the discipline, training, and clinical work with HF. Graphical depictions (ie, "wireframes") of mobile app elements were created to solicit provider opinions and reactions [18]. Various in-app features included physiologic elements, psychosocial-spiritual assessments, and links to possible resources, beyond standard symptom monitoring. The research team asked about perceived usefulness of mHealth tools for care delivery and care coordination between family caregivers. Participants were incentivized with a US $25 coffee-shop gift card upon completion of the interview.

Analysis

Two research assistants (KF and KE) read all transcripts and performed double coding procedures. An iterative team-based approach was used to develop a codebook and coding structure based on the research assistants' epistemological position [19]. The codebook and coding structure were applied to the dataset using Dedoose software (v8.035). Ongoing analysis meetings occurred to validate findings and compare written notes and memos. This consensus-building process ensured the team bracketed their biases and remained reflexive throughout the study. Interrater reliability was calculated for 6 randomly selected transcripts (81% agreement, κ=0.725), reflecting adequate coding consistency. Additionally, during analysis, triangulation occurred to compile resources gathered from interviews (eg, health education materials, mobile app resources, and website suggestions). Until thematic saturation [20] was reached, the research team clustered the codes into categories using significant statements to describe the core essence among participants' perspectives and selected illustrative quotes reflective of each theme. Member-checking occurred with HF and digital health experts to determine trustworthiness of findings.

Results

Participants

The sample included diverse health care provider specialties, including advanced practice nurses (n=7), art/music therapists (n=2), chaplains/spiritual care (n=2), physicians (n=4), registered nurses (n=3), and social workers (n=2). Provider experience ranged from 2 to 17 years (mean 9.78, SD 3.75) working with advanced HF patients. All participants identified as White, 16 identified as female and 4 as male.

Summary of Significant Statements

A total of 5 thematic clusters resulted from the qualitative analysis. Summarized in Table 1, clusters include bio-psychosocial-spiritual remote monitoring, using sensors and mobile apps, interoperability, data sharing, and useful heuristic preferences.

Table 1. Summary of themes with supporting quotes from participant feedback.

Theme	Illustrative quote
Bio-psychosocial-spiritual remote monitoring	*There are a lot of patients, there are a lot of caregivers for whom that stuff is really important. And they do track things and I would imagine it could be really helpful for them going into their doctor to be able to have this information* [1012 – Spiritual Provider]
	For me, from a provider perspective, this would help me feel connected. So, if I know the person uses it, likes it, is comfortable with it, and I get immediate messaging about stuff going on, then I can intervene quickly. So, I think from a provider perspective, there's great comfort in knowing your patient is not heading to crisis. And so, the continual updates are helpful. Balancing that with a lot of unnecessary information. [1005 – Registered Nurse]
	So—because when I see people long-term, we both get to the point where we have trouble remembering what things were like six months ago. …And then you go, well, let's look. That's where I use data. Let's look two weeks ago. Two weeks ago, you were saying things were good. So, it hasn't been bad for six months. You were kind of good two weeks ago but now we're having a blip. And that will encourage—that will give two things. That will give people perspective on their disease, but it will also be huge for prognosis for a provider. [1005 – Registered Nurse]
	I think symptom tracking is good because a lot of times whether you're the patient or the caregiver, both want to know what symptoms to look out for to be causes of concern like when do I need to call my doctor, when do I need to get to an emergency room. [1016 – Social Worker]
Sensor technologies and potential of real-time data	*If that's one less thing the person has to enter, then I'm all for it.* [1005 – Registered Nurse]
	…for the most part I think that it's really good because it empowers the patient to take control of their self. [1019 – Advanced Practice Nurse]
	So if you had somebody that had really high heart rates and said they didn't feel well and that's for a step like who's going to read that data, who's going to get them in and is it the patient's responsibility to still call and say, 'Hey, I feel terrible.' [1011 – Advanced Practice Nurse]
Interoperability for a personalized experience	*…[if] they had a desire for [seeing a spiritual provider or social worker]; for there to actually be a vehicle where they're not dependent on someone asking or them to think to ask for it. Maybe they didn't even know they could.* [1012 – Spiritual Provider]
	So yeah, I don't necessarily have to have my diet fitness app integrated with my heart failure app, per se. I'm not sure there's huge advantage to that, unless you're linking them somehow. So OK; so now I'm figuring how much sodium there is and then my sodium on my fitness diet app is looking at my weight and saying, "Well as it turns out, you say your weight's going up and your sodium consumption over the last four days has been 4,000 milligrams a day, which is more," and then you're like giving real-time feedback to the patient about how, potentially, what they're doing in terms of their health behaviors is affecting their objective measures. That would be nice. That seems pretty complex, though." [1018 – Physician]
Tailored assessment and sharing of data	*So, I see how it could be helpful for sure. But I just see the patient as potentially having some problems with it. I see the caregiver as going oh, my gosh, aren't I doing enough? And so, there can be guilt that this could trigger. Used with the right people—and if you had the ability to (tailor) opt in or opt out of this feature, that's how you might be able to solve that. Some people would love it. I know they would. But I just don't have a good feel for the percentages on that and so maybe you just opt in or opt out.* [1005 – Registered Nurse]
	I think that's an individual thing. Some caregivers, family members want to know everything like this and some of them only want to know if something bad is going on. So, I guess that would be a decision between the patient and the caregiver about what they wanted to do from that. [1011 – Advanced Practice Nurse]
Usefulness of patient-reported outcomes in practice	*…in clinic now when I try to get a point across to the patients, I'll graph some of the data and you can see it taking off. And it's really—I don't know if it's motivating to them, but they're real interested in those trends.* [1020 – Registered Nurse]
	I think the way this could be useful is just looking at trends. You know, if you were able to say well on Monday this is how I felt and then on Thursday of that week, you don't really remember what you put for Monday and if you could track some sort of bar graph or something for your responses, all of a sudden you click on a summary and it's like oh, I've been a little tired for the last 12 days and I've been coughing and—or whatever it is. [1000 – Registered Nurse]
	…the problem is you have so many different users. You have users with visual impairment who listen to their smartphone through their ear… It'd be cool if you could design the app where it's sort of tailored to different disabilities like see this for visually impaired or see this for hearing… [1015 – Physician]

Bio-Psychosocial-Spiritual Remote Monitoring

Many health care providers, especially clinical providers (physicians and nurses), mentioned that some of their patients already tracked HF symptoms in a variety of ways, most commonly handwritten journals. In addition, several providers discussed the value of this information for caregivers and the utility of a mobile app for consolidating patient-reported monitoring metrics, thus helping family members and caregivers feel updated on their loved one's condition. Psychosocial assessments and questions about practical help, while less interesting to clinical providers, were recognized as a way to get a more well-rounded picture of patients with complex chronic illness. However, a few participants raised concerns about the utility of psychosocial assessment in a digital platform. Concerns included the ability of an app to link patients to reliable follow-up resources based on responses.

Sensor Technologies and Potential of Real-Time Data

Most providers were excited about sensor technology such as weight tracking, home blood pressure monitoring, and physical activity monitoring and its utility in minimizing patient-driven data collection. A few providers mentioned technical difficulties (eg, wireless access, end-user error) or practical challenges (eg, ability to fit sensor-generated data monitoring into the clinical workflow) in past experiences with sensor technology. While most providers agree that this type of information is useful during patient encounters, the ability to monitor the data was a concern. The technology allows an abundance of data to be collected 24 hours a day, 7 days a week via sensors with no associated plan as to how to monitor that data; this was consistently raised across provider specialties.

Interoperability for a Personalized Experience

Many providers discussed the potential to sync patient-generated data with the electronic health record and patient portal. However, many providers raised concerns about various limitations to make this information useful to the care team and caregivers. For example, a few providers reported that there are many symptom-tracking technologies, which collect patient-reported outcomes, currently linked to the electronic health record but are rarely monitored on the clinical side.

Beyond clinical interoperability, providers discussed the ability of HF mHealth to interface with other apps that provide psychosocial support, reporting it to be useful to sync with other commonly used apps (eg, mindfulness apps, music apps, Google calendars, and shared-list apps). Most providers recommended this would be more helpful than having an additional modality to find resources. Many providers discussed the many existing HF resources and raised the need for an app assessment to link to actionable resources (eg, ask patient about medical power of attorney and provide a web link to fulfill the need; provide functionality to request a spiritual provider or social worker based on remote monitoring responses). Such personalization appeared advanced to providers. However, most of them reported how interoperability would improve usability.

Tailored Assessment and Sharing of Data

Many providers reported reliance on caregivers during patient encounters as an additional perspective of patient health status and as a secondary source when discussing care plans. Thus, most providers agreed that caregivers having access to patient data would be helpful. However, concerns were raised around patient privacy and caregiver fatigue or guilt. Furthermore, providers discussed varying preferences for specific caregivers; and therefore, tailoring data-sharing options would be critical.

Usefulness of Patient-Reported Outcomes in Practice

Providers almost unanimously preferred graphs showing trends in HF symptoms and physiologic measures. Many providers were concerned with facilitating data collection in a patient-centered, noninvasive way that does not collect more data than used. Suggestions to improve accessibility, language, and literacy of assessment questions remained a key consideration. In addition, several providers brought up disabilities such as diminished eyesight or hearing among an older population and discussed advanced technology features such as voice activation integrated into an app to increase accessibility of mobile apps in this population.

Discussion

This study reports provider experiences and opinions regarding the development of HF mHealth that will maximize patient, family, and provider clinical utility. Our findings suggest providers remain interested in various innovative solutions for HF patients and their caregivers. The use of assessments, sensors, and real-time data collection could provide value in patient care. However, providers remained skeptical of the clinical usefulness of vast data and real-time patient reported outcomes [7,21].

Although HF mHealth is increasing in popularity, concerns with privacy, confidentiality, and overburden of electronic medical record alerts with interoperable technologies may only complicate the clinical practice [22,23]. This contradicts current endorsements of real-time data generation in mHealth (eg, just-in-time adaptive interventions and ecological momentary interventions) to inform clinical decision making [24]. Instead, we found that health care providers "…like the idea of it but, personally, probably wouldn't use it."

In conclusion, future HF mHealth research must consider its usefulness in practice for patients, caregivers, and health care providers. Although innovative mHealth technologies offer promise in improving HF outcomes and quality of life for patients, the interventions and tools must remain relevant and useful without causing an additional burden for the patient, caregiver, and care team. With the increasing adoption of HF mHealth, understanding multiple perspectives remains critical for sustained engagement, thus improving the impact of HF mHealth on patients, families, society, and the health care system.

Acknowledgments

This research is funded by a career development award (K76AG059934) and training support (T32AG044296) from the National Institute on Aging.

Conflicts of Interest

None declared.

References

1. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, American Heart Association Council on EpidemiologyPrevention Statistics CommitteeStroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. Circulation 2019 Mar 05;139(10):e56-e528. [doi: 10.1161/CIR.0000000000000659] [Medline: 30700139]
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Card Fail 2017 Aug;23(8):628-651. [doi: 10.1016/j.cardfail.2017.04.014] [Medline: 28461259]
3. Yancy CW, Januzzi JL, Allen LA, Butler J, Davis LL, Fonarow GC, et al. 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol 2018 Jan 16;71(2):201-230 [FREE Full text] [doi: 10.1016/j.jacc.2017.11.025] [Medline: 29277252]
4. Masterson Creber RM, Maurer MS, Reading M, Hiraldo G, Hickey KT, Iribarren S. Review and Analysis of Existing Mobile Phone Apps to Support Heart Failure Symptom Monitoring and Self-Care Management Using the Mobile Application Rating Scale (MARS). JMIR Mhealth Uhealth 2016 Jun 14;4(2):e74 [FREE Full text] [doi: 10.2196/mhealth.5882] [Medline: 27302310]
5. Lee S, Riegel B. State of the Science in Heart Failure Symptom Perception Research: An Integrative Review. J Cardiovasc Nurs 2018;33(3):204-210. [doi: 10.1097/JCN.0000000000000445] [Medline: 28858886]
6. Bashi N, Karunanithi M, Fatehi F, Ding H, Walters D. Remote Monitoring of Patients With Heart Failure: An Overview of Systematic Reviews. J Med Internet Res 2017 Jan 20;19(1):e18 [FREE Full text] [doi: 10.2196/jmir.6571] [Medline: 28108430]
7. Athilingam P, Jenkins B. Mobile Phone Apps to Support Heart Failure Self-Care Management: Integrative Review. JMIR Cardio 2018 May 02;2(1):e10057 [FREE Full text] [doi: 10.2196/10057] [Medline: 31758762]
8. Riegel B, Moser DK, Buck HG, Dickson VV, Dunbar SB, Lee CS, American Heart Association Council on CardiovascularStroke Nursing; Council on Peripheral Vascular Disease;Council on Quality of CareOutcomes Research. Self-Care for the Prevention and Management of Cardiovascular Disease and Stroke: A Scientific Statement for Healthcare Professionals From the American Heart Association. J Am Heart Assoc 2017 Aug 31;6(9) [FREE Full text] [doi: 10.1161/JAHA.117.006997] [Medline: 28860232]
9. Carbo A, Gupta M, Tamariz L, Palacio A, Levis S, Nemeth Z, et al. Mobile Technologies for Managing Heart Failure: A Systematic Review and Meta-analysis. Telemed J E Health 2018 Apr 02. [doi: 10.1089/tmj.2017.0269] [Medline: 29608430]
10. Panjrath G, Bostrom L, Witkin L, Katz R. Moving Mobile Health Forward: Combining mHealth with Community Health Workers Bolsters Heart Failure Care. Journal of Cardiac Failure 2018 Aug;24(8):S71. [doi: 10.1016/j.cardfail.2018.07.297]
11. Marcolino MS, Oliveira JAQ, D'Agostino M, Ribeiro AL, Alkmim MBM, Novillo-Ortiz D. The Impact of mHealth Interventions: Systematic Review of Systematic Reviews. JMIR Mhealth Uhealth 2018 Jan 17;6(1):e23 [FREE Full text] [doi: 10.2196/mhealth.8873] [Medline: 29343463]
12. Dickinson MG, Allen LA, Albert NA, DiSalvo T, Ewald GA, Vest AR, et al. Remote Monitoring of Patients With Heart Failure: A White Paper From the Heart Failure Society of America Scientific Statements Committee. J Card Fail 2018 Oct;24(10):682-694. [doi: 10.1016/j.cardfail.2018.08.011] [Medline: 30308242]
13. Snyder CF, Aaronson NK. Use of patient-reported outcomes in clinical practice. Lancet 2009 Aug 01;374(9687):369-370. [doi: 10.1016/S0140-6736(09)61400-8] [Medline: 19647598]
14. Dickman Portz J, Ford K, Bekelman DB, Boxer RS, Kutner JS, Czaja S, et al. "We're Taking Something So Human and Trying to Digitize": Provider Recommendations for mHealth in Palliative Care. J Palliat Med 2020 Feb;23(2):240-247. [doi: 10.1089/jpm.2019.0216] [Medline: 31526220]
15. Starks H, Trinidad SB. Choose your method: a comparison of phenomenology, discourse analysis, and grounded theory. Qual Health Res 2007 Dec;17(10):1372-1380. [doi: 10.1177/1049732307307031] [Medline: 18000076]
16. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007 Dec;19(6):349-357. [doi: 10.1093/intqhc/mzm042] [Medline: 17872937]
17. Creswell J, Poth C. Qualitative inquiry & research design: Choosing among five approaches. Los Angeles: Sage; 2018.

18. Brhel M, Meth H, Maedche A, Werder K. Exploring principles of user-centered agile software development: A literature review. Information and Software Technology 2015 May;61:163-181. [doi: 10.1016/j.infsof.2015.01.004]
19. Carter SM, Little M. Justifying knowledge, justifying method, taking action: epistemologies, methodologies, and methods in qualitative research. Qual Health Res 2007 Dec;17(10):1316-1328. [doi: 10.1177/1049732307306927] [Medline: 18000071]
20. Ando H, Cousins R, Young C. Achieving Saturation in Thematic Analysis: Development and Refinement of a Codebook. Comprehensive Psychology 2014 Feb 20;3. [doi: 10.2466/03.cp.3.4]
21. Seto E, Leonard KJ, Masino C, Cafazzo JA, Barnsley J, Ross HJ. Attitudes of heart failure patients and health care providers towards mobile phone-based remote monitoring. J Med Internet Res 2010 Nov 29;12(4):e55 [FREE Full text] [doi: 10.2196/jmir.1627] [Medline: 21115435]
22. Sarwar CM, Vaduganathan M, Anker SD, Coiro S, Papadimitriou L, Saltz J, et al. Mobile health applications in cardiovascular research. Int J Cardiol 2018 Oct 15;269:265-271. [doi: 10.1016/j.ijcard.2018.06.039] [Medline: 29921516]
23. Turakhia MP, Desai SA, Harrington RA. The Outlook of Digital Health for Cardiovascular Medicine: Challenges but Also Extraordinary Opportunities. JAMA Cardiol 2016 Oct 01;1(7):743-744. [doi: 10.1001/jamacardio.2016.2661] [Medline: 27580275]
24. Dolley S. Big Data's Role in Precision Public Health. Front Public Health 2018;6:68 [FREE Full text] [doi: 10.3389/fpubh.2018.00068] [Medline: 29594091]

Abbreviations

COREQ: Consolidated Criteria for Reporting Qualitative Research
HF: heart failure
mHealth: mobile health

Edited by N Bruining; submitted 03.02.20; peer-reviewed by P Athilingam, H Mufti; comments to author 01.04.20; revised version received 10.04.20; accepted 13.07.20; published 04.09.20.

Please cite as:
Portz JD, Ford KL, Elsbernd K, Knoepke CE, Flint K, Bekelman DB, Boxer RS, Bull S
"I Like the Idea of It…But Probably Wouldn't Use It" - Health Care Provider Perspectives on Heart Failure mHealth: Qualitative Study
JMIR Cardio 2020;4(1):e18101
URL: http://cardio.jmir.org/2020/1/e18101/
doi:10.2196/18101
PMID:32885785

Original Paper

Impact of Remote Titration Combined With Telemonitoring on the Optimization of Guideline-Directed Medical Therapy for Patients With Heart Failure: Internal Pilot of a Randomized Controlled Trial

Veronica Artanian[1], MSc; Heather J Ross[1,2,3,4], MHSc, MD, FRCPC; Valeria E Rac[1,2,5,6], MD, PhD; Mary O'Sullivan[7], BSCN, RN; Darshan H Brahmbhatt[4,7,8], MB, BChir, MRCP; Emily Seto[1,3], PhD, PEng

[1]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

[2]Ted Rogers Centre for Heart Research, Peter Munk Cardiac Centre, University Health Network, Toronto, ON, Canada

[3]Centre for Global eHealth Innovation, Techna Institute, University Health Network, Toronto, ON, Canada

[4]Department of Medicine, University of Toronto, Toronto, ON, Canada

[5]Toronto Health Economics and Technology Assessment Collaborative, University Health Network, Toronto, ON, Canada

[6]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada

[7]Peter Munk Cardiac Centre, Division of Cardiology, University Health Network, Toronto, ON, Canada

[8]National Heart and Lung Institute, Imperial College London, London, United Kingdom

Corresponding Author:
Veronica Artanian, MSc
Institute of Health Policy, Management and Evaluation
Dalla Lana School of Public Health
University of Toronto
155 College St
Toronto, ON, M5T 3M6
Canada
Phone: 1 416 978 4326
Email: art.vt@outlook.com

Abstract

Background: To improve health outcomes in patients with heart failure, guideline-directed medical therapy (GDMT) should be optimized to target doses. However, GDMT remains underutilized, with less than 25% of patients receiving target doses in clinical practice. Telemonitoring could provide reliable and real-time physiological data for clinical decision support to facilitate remote GDMT titration.

Objective: This paper aims to present findings from an internal pilot study regarding the effectiveness of remote titration facilitated by telemonitoring.

Methods: A 2-arm randomized controlled pilot trial comparing remote titration versus standard care in a heart function clinic was conducted. Patients were randomized to undergo remote medication titration facilitated by data from a smartphone-based telemonitoring system or standard titration performed during clinic visits.

Results: A total of 42 patients with new-onset (10/42, 24%) and existing (32/42, 76%) heart failure and a mean age of 55.29 (SD 11.28) years were randomized between January and June 2019. Within 6 months of enrollment, 86% (18/21) of patients in the intervention group achieved optimal doses versus 48% (10/21) of patients in the control group. The median time to dose optimization was 11.0 weeks for the intervention group versus 18.8 weeks for the control group. The number of in-person visits in the intervention group was 54.5% lower than in the control group.

Conclusions: The results of this pilot study suggest that remote titration facilitated by telemonitoring has the potential to increase the proportion of patients who achieve optimal GDMT doses, decrease time to dose optimization, and reduce the number of clinic visits. Remote titration may facilitate optimal and efficient titration of patients with heart failure while reducing the burden for patients to attend in-person clinic visits.

Trial Registration: ClinicalTrials.gov NCT04205513; https://clinicaltrials.gov/ct2/show/NCT04205513

International Registered Report Identifier (IRRID): RR2-10.2196/preprints.19705

(JMIR Cardio 2020;4(1):e21962) doi:10.2196/21962

KEYWORDS

telemonitoring; remote; titration; monitoring; mHealth; heart failure

Introduction

Background

Heart failure (HF) is a progressive condition with periods of stability interrupted by periods of worsening symptoms and instability, often leading to hospitalization [1]. The Canadian Cardiovascular Society distinguishes between HF with preserved ejection fraction (left ventricular ejection fraction [LVEF] ≥50%), HF with midrange ejection fraction (LVEF 41%-49%), and HF with reduced ejection fraction (HFrEF) (LVEF ≤40%) [2]. HFrEF is a distinct group in which large clinical trials have demonstrated the efficacy of neurohumoral inhibition [3].

The recommended therapeutic approach for patients with HFrEF consists of triple therapy with angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or angiotensin receptor–neprilysin inhibitors (ARNIs); β-blockers (BBLs); and mineralocorticoid receptor antagonists (MRAs) [4-6]. These medications have been shown to improve symptoms, reduce hospitalization burden, and provide survival benefit in randomized controlled trials (RCTs) [6-10]. Titration of guideline-directed medical therapy (GDMT) to doses proven effective in clinical trials or maximally tolerated doses is recommended to reduce morbidity and mortality [2]. Expert recommendations suggest that clinicians should aim to achieve target doses within 3 to 6 months of initial HF diagnosis [11].

Despite proven benefits and strong guideline recommendations, large registries confirm that GDMTs are underutilized, and management of HF tends to fall short in respect to dose optimization [12-14]. In clinical practice, evidence from 12,440 patients with HF on the European Society of Cardiology Heart Failure Long-Term Registry showed that about 30% of patients were on target doses of ACEIs and only 18% were on target doses of BBLs [15]. Similarly, the Change the Management of Patients with Heart Failure (CHAMP-HF) registry, which analyzed data from 3518 patients in the United States, revealed that at baseline, only 16.7% of patients were on target doses of ACEIs, ARBs, or ARNIs, 27.5% were on target doses of BBLs, and 76.6% were on target doses of MRA therapy [13].

Evidence-based pharmacotherapies have the greatest potential to improve population-level outcomes, as they are less costly and more easily accessible than devices and surgical procedures available to patients with HF [12]. This reinforces the need to find ways to improve adherence to GDMT. Remote titration of HF medication is a topic that has received little attention despite its potential to contribute to GDMT utilization and optimization.

Previous Research on Remote Titration

Several previous trials have investigated remote titration of HF medication with or without the aid of telemonitoring. Two trials by Steckler et al [16] and Moyer-Knox et al [17] assessed remote medication titration over the phone. Steckler et al [16] found that target doses were achieved in 50% of patients for ACEIs or ARBs and in 41% of patients for BBLs. Moyer-Knox et al [17] found that a total of 71% of patients reached target doses of BBLs within approximately 8 weeks. Two other trials have attempted to use telemonitoring for the purpose of remote titration of HF medication. A study by D'Onofrio et al and Palmisano et al [18,19] found that remote BBL titration allowed 76% of patients in the intervention group to achieve target doses versus only 38% of patients in the control group. Similarly, Spaeder et al [20] also performed a study that focused on rapid titration of BBLs and found no statistical difference in the proportion of patients who reached target doses. However, the time frame required to reach target doses was significantly shorter in the intervention group (33.6 vs 63.7 days; $P<.001$). Lastly, a study by Smeets et al [21] attempted to further automate the titration process by incorporating a clinical decision support component. Patients reported high levels of satisfaction and increased medication adherence. However, many technical issues were encountered, no significant differences were observed in the proportion of patients on target doses of BBLs (50% vs 40%; $P=.69$) or ACEIs (42% vs 40%; $P>.99$), and there was no difference in the time taken to uptitrate to guideline-recommended doses. These trials provided preliminary evidence demonstrating that remote titration can be successful and result in a higher proportion of patients reaching target doses within shorter time frames.

Study Objective

While information and research on remote titration of HF medication is somewhat limited, the results of previous studies have been predominantly positive [16-21]. Building on previous studies of remote titration of BBLs or ACEIs, this study undertakes to investigate remote titration of GDMT triple therapy. An RCT is being conducted with the objective to explore how the combination of remote titration and telemonitoring impacts GDMT optimization compared with standard care. The primary objective of the RCT is to assess the effectiveness of remote titration facilitated by telemonitoring and its impact on the proportion of patients achieving target doses, the time to dose optimization, and the number of visits required to achieve target doses. The secondary objective is to assess the safety of remote titration. This paper reports the findings from an internal pilot [22] of the RCT. As an internal pilot, this study also aims to identify the most suitable primary outcome measure and obtain more accurate data for a sample size calculation.

Methods

Study Design Overview

The internal pilot was part of a 2-arm parallel RCT conducted within a mixed-methods study. A detailed description of the full study protocol was published separately [23]. Patients were randomized into an intervention group that relayed physiological and symptom data via a smartphone-based telemonitoring

platform (remote titration) or a control group that attended regular clinic visits.

This study received approval from the research ethics boards (REB) of the University of Toronto (REB No. 00036655) and the University Health Network (REB No. 18-5351), where patients were recruited and patient data were stored. The study was also registered at ClinicalTrials.gov (NCT04205513).

Participants

Study participants were recruited from the Peter Munk Cardiac Centre (PMCC) Heart Function Clinic (HFC). Patients eligible for enrollment were outpatients not yet at target doses of GDMT (ie, ACEIs, ARBs, BBLs, ARNIs, MRAs, or any combination thereof at suboptimal doses), as determined by their cardiologist. Additional inclusion and exclusion criteria are outlined in Textbox 1 and Textbox 2, respectively. Eligible participants were first identified by their cardiologist during their usual HFC visit and invited to speak to a nurse coordinator regarding participation. They met with the nurse coordinator immediately after their HFC visit and underwent the informed consent process. Patients that agreed to participate in the study were requested to sign a consent form.

Textbox 1. Patient inclusion criteria.

- Able to provide informed consent to participate in the program
- 18 years or older
- Diagnosed with heart failure and followed by a cardiologist at the Peter Munk Cardiac Centre Heart Function Clinic, who has primary responsibility for management of the patient's heart failure
- New York Heart Association class I-III
- Stable heart failure, defined as no hospitalization within 1 month
- Patient was not yet at target doses of guideline-directed medical therapy (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, angiotensin receptor–neprilysin inhibitors, mineralocorticoid receptor antagonists, or any combination thereof at suboptimal doses) and hence qualified for uptitration
- Patient or their informal caregiver spoke and read English adequately to participate in the program and understand the Medly app alerts and prompts
- Ability to comply with using Medly (eg, able to stand on the weight scale, able to answer symptom questions, etc)

Textbox 2. Patient exclusion criteria.

- Active acutely decompensated heart failure
- Already on target doses of guideline-directed medical therapy
- Inability to titrate medications due to adverse events, including:
  - History of angioedema
  - Uncontrolled hypertension
  - Hypotension preventing uptitration
  - Heart rate at rest of <56 beats per minute
- Congenital heart disease
- Previous heart transplant or currently awaiting heart transplant
- Acute coronary syndrome; stroke; transient ischemic attack; cardiac, carotid, or other major cardiovascular surgery; percutaneous coronary intervention; or carotid angioplasty within 6 weeks prior to randomization
- Obstructive or restrictive cardiomyopathy
- Second- or third-degree atrioventricular block without a pacemaker
- Presence of hemodynamically significant mitral or aortic valve disease, except mitral regurgitation
- Presence of other hemodynamically significant obstructive lesions of the left ventricular outflow tract, including aortic and subaortic stenosis, that are not controlled with suitable treatment
- Evidence of hepatic impairment, defined as alanine aminotransferase or aspartate transaminase value more than 3 times the upper normal limit
- Estimated glomerular filtration rate of <30 mL/min/1.73 m^2 at randomization or >35% decline in estimated glomerular filtration rate between visits
- Known stenosis of both renal arteries
- Hyper- or hypothyroidism not controlled by treatment
- Hyperkalemia of >5.5 mmol/L at randomization
- Hyponatremia of <130 mmol/L at randomization
- History of severe asthma or pulmonary disease
- Presence of any other disease that in the clinician's opinion would exclude the patient from the study or result in a life expectancy of <1 year

Medly Telemonitoring Program

Medly, a mobile phone–based telemonitoring program for patients with HF [24,25], was launched at the PMCC HFC in 2016. Medly enables patients to monitor daily weight, blood pressure, heart rate, and symptoms and enter them either manually or via Bluetooth to the Medly app on a mobile phone. The data are then automatically transmitted to a data server. Automated instructions are sent to patients based on a rules-based algorithm that analyzes their measurements and symptoms [26]. Alerts are sent to clinicians and the nurse coordinator in real time if any deterioration is identified. Clinicians can also view alerts and the patients' telemonitoring data through a secure web portal. Since the Medly program is integrated into the PMCC HFC as part of the standard of care, all patients enrolled into the study were monitored through Medly.

Interventions

Patients who met the inclusion criteria were enrolled and randomized 1:1 into one of 2 groups: (1) the control group and (2) the intervention group.

The control group underwent standard titration. Participants attended regular titration visits and were provided with the current standard of care, which included the use of Medly. Medication changes were performed based on data collected through assessments performed during clinic visits.

The intervention group underwent remote titration. Participants were called on the phone every 2 weeks to perform medication changes based on Medly data. Patients received requisitions for blood work to be performed at local labs, if required. Patients in the intervention group could still visit the clinic for assessments and follow-ups at their cardiologist's discretion.

Titration was considered complete when patients reached target GDMT doses specified in the guidelines of the Canadian Cardiovascular Society [4] or maximal tolerated doses, whichever came first.

Outcome Measures

The primary outcome measure was the number of visits required to achieve target doses. This outcome was assessed based on the number of visits, phone calls, and actions performed at each visit or phone call throughout the study.

Secondary outcome measures included the proportion of patients who achieved target doses, assessed based on the medications and dosages taken by patients at baseline and poststudy as well as all changes made in the medication regimen throughout the study, time to dose optimization, assessed based on the mean and median time to dose optimization in weeks and calculated for each study group, and patient safety outcomes, assessed based on any adverse events (AEs) that occurred throughout the study in each study group. In order to differentiate AEs from symptoms frequently encountered by patients during medication titration, AEs were defined as events that caused titration deferral, dose decreases, changes in the type of medication prescribed, titration termination, or an unscheduled visit to the clinic or visit to the emergency department (ED).

Sample Size

The sample size for the pilot was calculated based on the outcome measure of the number of visits required to complete titration by using data obtained from the literature [4,11]. Assuming that regular titration visits take place every 2 weeks over 3 to 6 months and anticipating a relative reduction of at least 35% in the number of visits for the intervention group, the sample size for the internal pilot was calculated to be 42. The calculation was performed assuming 80% power, an α of .05 (2-sided), and an attrition rate of 30%. The sample size of the full RCT was subsequently recalculated based on information obtained from this internal pilot, as described in the "Implications for the Full RCT" section.

Randomization

Patients were randomized 1:1 into control and intervention groups. An online computer-generated randomization tool was used to perform block randomization in blocks of 4 in order to ensure that the treatment groups were as balanced as possible. The generated sequence was used to create randomization envelopes, and the nurse coordinator was provided with the randomly generated treatment allocations within sealed opaque envelopes.

Statistical Methods

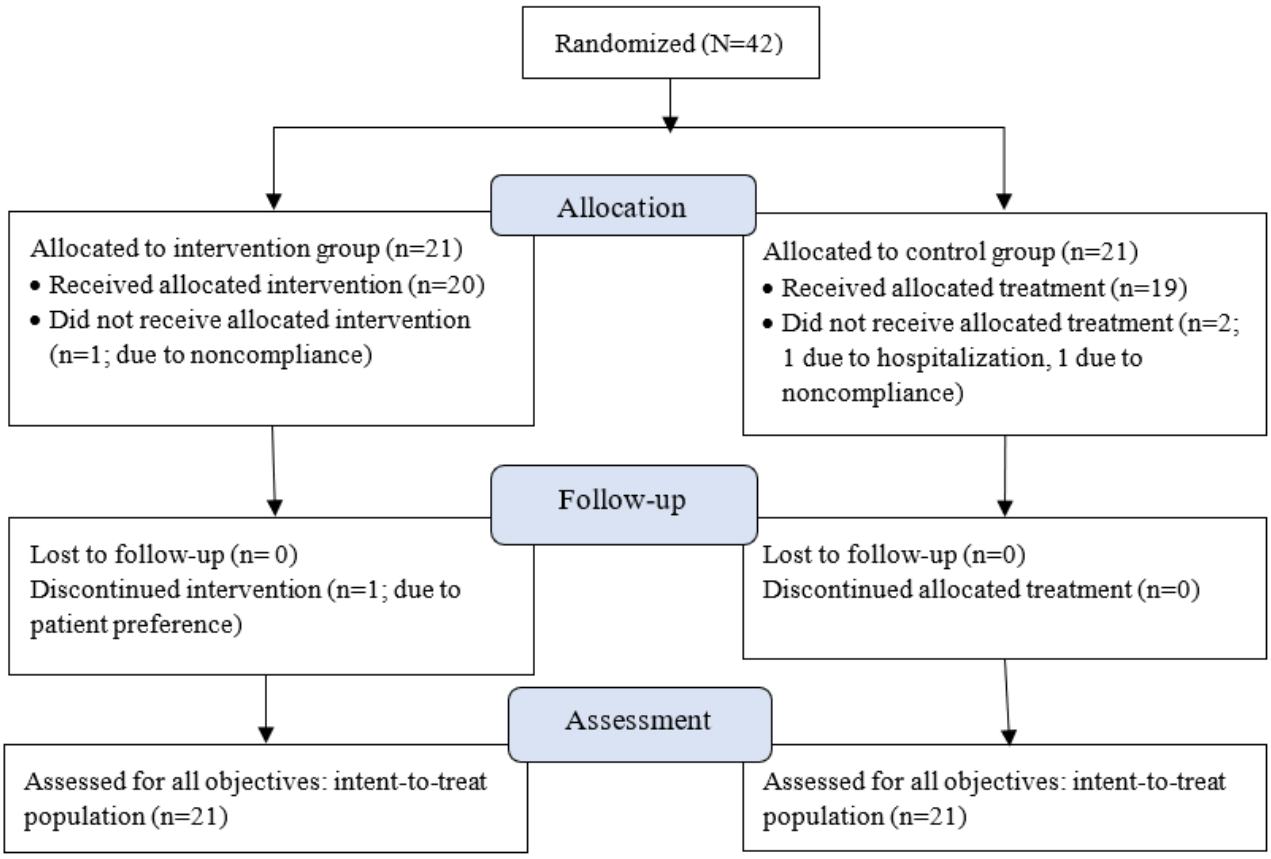
Descriptive, parametric, and nonparametric statistics were performed. McNemar tests were performed on binary baseline and poststudy data, while chi-square tests were performed to compare binary poststudy data between the groups. Independent 2-tailed Student *t* tests and Mann-Whitney tests were performed to compare poststudy data between the groups for normally and nonnormally distributed data, respectively. A *P* value of <.05 was considered significant for all tests. Analysis was performed using the intention-to-treat approach [27] and the IBM SPSS software platform (version 25; IBM Corp).

Results

Recruitment

Figure 1 depicts a CONSORT (Consolidated Standards of Reporting Trials) diagram of the trial participant flow. Patients were enrolled into the study between January and June 2019 and followed between January and December 2019. A total of 42 patients were enrolled into the study at baseline. There were 2 patients in each group who did not complete the trial; however, they were included in the data analysis. Reasons for withdrawal included prolonged illness, noncompliance, and patient preference (patient did not wish to be titrated remotely).

Figure 1. CONSORT diagram of the trial participant flow.



Baseline Data

The baseline demographic and clinical characteristics of the patients are summarized in Table 1. There were more men than women in both groups, which is typical for HFrEF clinics, and the average age of the participants was notably lower than the general HF patient population [28] but was representative of the clinic where the study was conducted. The average age of the patients at the clinic is somewhat younger than the general population of patients with HF because patients are frequently referred to this particular clinic for heart transplant or for mechanical circulatory support device therapy. Therefore, the clinic treats a higher-than-average proportion of severely ill patients compared with other HF clinics, including very young patients with HF. No statistically significant differences were detected between the groups.

Table 1. Characteristics of patient participants in the intervention group and control group.

Variable	Intervention group (n=21)	Control group (n=21)
Age (years), mean (SD)	53.00 (10.04)	57.57 (12.21)
Age range (years), n (%)		
30-59	17 (81%)	11 (52%)
60-79	4 (19%)	10 (48%)
Gender, n (%)		
Male	14 (67%)	16 (76%)
Female	7 (33%)	5 (24%)
NYHA[a] class, n (%)		
I	1 (5%)	3 (14%)
II	13 (62%)	14 (67%)
III	7 (33%)	4 (19%)
LVEF[b], mean (SD)	28.05 (6.65)	27.38 (6.30)
Primary cause of heart failure, n (%)		
Ischemic	9 (43%)	7 (33%)
Idiopathic	6 (29%)	7 (33%)
Other	6 (29%)	7 (33%)
New or existing HF		
New-onset HF[c,d]	6 (29%)	4 (19%)
Existing HF	15 (71%)	17 (81%)
GDMT[e] utilization		
ARNI[f]		
ARNI at any dose	3 (14%)	8 (38%)
ARNI at target dose	1 (5%)	2 (10%)
ACEI[g]		
ACEI at any dose	13 (62%)	8 (38%)
ACEI at target dose	4 (19%)	2 (10%)
ARB[h]		
ARB at any dose	1 (5%)	1 (5%)
ARB at target dose	0 (0%)	0 (0%)
BBL[i]		
BBL at any dose	18 (86%)	18 (86%)
BBL at target dose	5 (24%)	9 (43%)
MRA[j]		
MRA at any dose	13 (62%)	11 (52%)
MRA at target dose	4 (19%)	4 (19%)

[a]NYHA: New York Heart Association.

[b]LVEF: left ventricular ejection fraction.

[c]HF: heart failure.

[d]Diagnosed within 3 months of enrollment.

[e]GDMT: guideline-directed medical therapy.

[f]ARNI: angiotensin receptor–neprilysin inhibitor.

[g]ACEI: angiotensin-converting enzyme inhibitor.

[h]ARB: angiotensin receptor blocker.

[i]BBL: β-blocker.

[j]MRA: mineralocorticoid receptor antagonist.

Both patients with new-onset and existing HF were enrolled into the study. As such, it was important to ensure that there were no significant differences in the starting doses of the patients' GDMT drugs. Table 2 outlines the mean doses of drugs that patients in each of the study groups received at baseline. Drugs prescribed only to 1 patient were not included in the analysis. Mann-Whitney U tests were used to examine differences between the groups whenever possible (n≥5), and no significant differences were identified. Mean starting doses were very similar in both groups for carvedilol and spironolactone, slightly higher in the intervention group for sacubitril-valsartan and ramipril, and slightly higher in the control group for bisoprolol, metoprolol, and perindopril. This variation in starting doses was unlikely to have a substantial impact on study results, particularly since starting doses were more often higher in the control group.

Table 2. Mean doses of GDMT drugs prescribed to patients at baseline.

Medication	Intervention group (n=21)		Control group (n=21)		*P* value
	Participants, n	Dose (mg), mean (SD)	Participants, n	Dose (mg), mean (SD)	
ARNI[a]					
Sacubitril-valsartan	3	116.67 (62.36)	8	100.00 (43.30)	N/A[b]
β-blocker					
Bisoprolol	5	4.50 (3.22)	7	6.25 (3.15)	.19
Carvedilol	9	16.15 (10.82)	9	15.63 (7.22)	.97
Metoprolol	4	40.63 (16.24)	2	56.25 (43.75)	N/A
ACEI[c]					
Ramipril	11	4.55 (2.52)	4	2.92 (1.35)	N/A
Perindopril	2	2.00 (0.00)	4	4.00 (0.00)	N/A
MRA[d]					
Spironolactone	13	19.23 (6.23)	11	21.59 (5.57)	.45

[a]ARNI: angiotensin receptor–neprilysin inhibitor.

[b]N/A: not applicable.

[c]ACEI: angiotensin-converting enzyme inhibitor.

[d]MRA: mineralocorticoid receptor antagonist.

Number of Visits Required to Achieve Target Doses

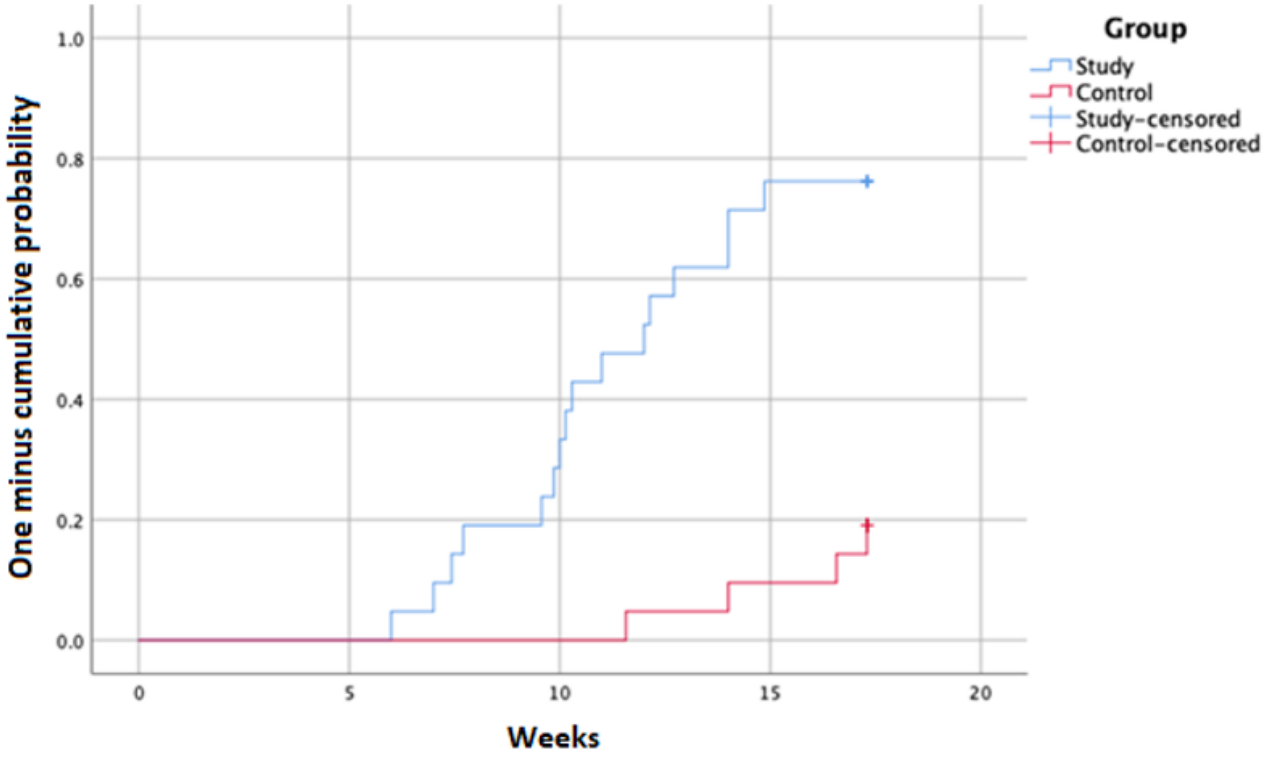
From January to December 2019, the intervention group cumulatively had a total of 20 visits and 99 phone calls for the purposes of titration, while the control group had a total of 44 visits. The number of overall patient-clinician contact points was substantially higher in the intervention group. However, when examining clinic visits alone, there was a 54.5% reduction in the intervention group, as the majority of patient-clinician contact points took place over the phone.

On average, the intervention group had 6.3 (SD 2.1) calls and visits and titrated 2.3 (SD 0.65) drugs, while the control group had 2.3 (SD 1.0) visits and titrated 1.6 (SD 0.9) drugs. These differences were statistically significant, with a *P* value of <.001 for the number of calls and visits and a *P* value of .02 for the number of titrated drugs.

Time to Dose Optimization

The intervention group completed titration within a period of 12.3 (SD 5.0) weeks, with a median of 11.0 weeks, while the control group required 19.0 (SD 4.2) weeks, with a median of 18.8 weeks. A time-to-event analysis was performed to compare titration completion rates between the intervention and control groups over a period of 4 months. Log rank analysis resulted in a *P* value of <.001. The one minus cumulative survival curve was selected to represent the patients that completed titration (Figure 2).

Figure 2. Kaplan-Meier curve of titration completion over a period of 4 months.



Proportion of Patients Who Achieved Target Doses

Table 3 outlines the number and proportion of patients who completed titration in each of the groups within various time frames. Analysis was performed once all participants had been in the study for a minimum of six months. Overall, 19 of the 21 patients (90%) in the intervention group and 11 of the 21 patients (52%) in the control group completed titration at the time of analysis (*P*=.002). In addition, 12 of the 21 patients (57%) in the intervention group and 6 of the 21 patients (29%) in the control group achieved triple therapy at target doses (*P*=.003).

Table 3. Number and proportion of patients who completed titration within various time frames.

Time frame	Intervention group, n (%) (n=21)	Control group, n (%) (n=21)	*P* value
Within 4 months	16 (76%)	4 (19%)	<.001
Within 5 months	18 (86%)	8 (38%)	.001
Within 6 months	18 (86%)	10 (48%)	.004
Over 6 months	19 (90%)	11 (52%)	.002
Total	19 (90%)	11 (52%)	.002

Patient Safety Outcomes

The study was not powered to assess AEs. As such, only descriptive statistics were performed on AE data. AEs occurred in 13 of the 21 patients (62%) in the intervention group and 10 of the 21 patients (48%) in the control group. The most common AEs were hypotension, defined as systolic blood pressure below 90 mmHg (11/38, 29% of all events), and dizziness (10/38, 26%), followed by hyperkalemia, defined as potassium levels above 5.5 mmol/L (6/38, 16%), and fatigue (6/38, 16%). No serious AEs or HF-related hospitalizations occurred during the study. One patient in the control group was removed from the per-protocol population due to a lengthy hospitalization that precluded her from undergoing titration. A total of 4 ED visits took place, 2 in each group. One ED visit in the intervention group was a result of suspected atrial fibrillation, while the other ED visits were not associated with cardiovascular issues. Overall, there were no significant differences between the groups and no indications that the AEs were related to the method of titration (ie, remotely or in clinic).

Discussion

Summary of Findings

In this pilot RCT of telemonitored remote titration versus usual care, remote titration was associated with a larger proportion of patients achieving target doses, shorter time to optimization, and fewer visits required to achieve target doses.

Proportion of Patients That Achieved Target Doses

Remote titration increased the proportion of patients achieving target doses within guideline-recommended timeframes (18/21,

86% in the intervention group vs 10/21, 48% in the control group after 6 months of follow-up). The proportion of patients that achieved target doses in our intervention group was notably higher than the numbers outlined in the literature. The CHAMP-HF registry specified that in the general HF population eligible for GDMT, target doses were prescribed to only 17% of patients for ACEIs or ARBs, 14% for ARNIs, 28% for BBLs, and 77% for MRAs [13]. In comparison, our study found that the intervention group demonstrated achievement of target doses at a rate of 38% (8/21) of patients for ACEIs or ARBs, 38% (8/21) for ARNIs, 86% (18/21) for BBLs, and 67% (14/21) for MRAs. In addition, the CHAMP-HF registry noted that only 1% of patients eligible for all classes of medication were receiving target doses of triple therapy, while in our intervention group, 57% (12/21) of patients achieved optimal triple therapy. Only 29% (6/21) of patients in the control group achieved target doses of triple therapy. The titration rates in the control group were still higher than the numbers outlined in the literature. This can be attributed to the fact that the study was performed in a premier heart function clinic with highly experienced cardiologists, where provider-related barriers, such as knowledge of and comfort with the drug therapy optimization, were mitigated. Remote titration also made it possible to mitigate institutional and patient-related barriers, such as time constraints, transportation limitations, and availability of resources necessary to accommodate visits. This may have enabled the intervention group to complete titration in a much timelier fashion.

Time to Dose Optimization

Our study found that the median time to dose optimization was 11.0 weeks in the intervention group versus 18.8 weeks in the control group, pointing to a nearly 8-week decrease. Similar results were seen in other studies of remote titration. For the time to dose optimization, Steckler et al [16] reported a median time of 54 days, Moyer-Knox et al [17] had a mean time of 42 days, Spaeder et al [20] observed optimal doses with weekly titration over a mean of 33.6 days, and D'Onofrio et al [18] found a mean of 57 days. Overall, our findings fall in line with these studies that primarily examined BBL titration, which comprises about a third of the full GDMT titration process.

Ansari et al [29] noted that in-office, nurse-facilitated medication titration of BBLs achieved 43% titration completion at 12 months. Hickey et al [30] showed that a structured medication titration plan demonstrated a 49% achievement of target doses for ACEIs and ARBs and 46% for BBLs at 6 months. While both of these results were improvements over standard care, they fall short of the results observed in our study, as well as other studies of remote titration.

Time-to-event analysis, presented in Figure 2, outlines the substantial difference in the time to dose optimization between the intervention and control groups. Most patients in the intervention group (16/21, 76%) completed titration within the first 4 months, while only 19% (4/21) of the patients in the control group completed titration within a similar time frame. This is another indicator of the added value that remote titration can introduce into clinical practice. While expert recommendations suggest that clinicians should aim to achieve target doses within 3 to 6 months [11], this timeline is usually quite unfeasible with standard clinic visits [13,14,31,32], and titration may actually take up to 12 months [33]. In contrast, remote titration facilitated by telemonitoring enabled 76% (16/21) of the patients in our intervention group to reach target doses within 4 months and 86% (18/21) within 6 months.

Number of Visits Required to Achieve Target Doses

Experts recommend titrating medication at 1- to 4-week intervals, depending on the individual patient. As a guideline, the dose can usually be doubled every 2 weeks [4]. However, in practice, such frequent visits may prove unfeasible. Patient constraints and institutional limitations often necessitate spacing visits further apart. In our study, patients in the control group had few visits, while patients in the intervention group had regular phone calls for titration every 2 weeks. Analysis revealed a 2.7-fold increase in the overall number of calls plus clinic visits in the intervention group compared with clinic visits in the control group. Remote titration decreased the number of clinic visits required to achieve target doses by 54.5%.

This is a very positive finding, since the difficulty in establishing regular and frequent encounters between clinicians and patients has been noted as a significant barrier to GDMT optimization in many studies [31-34]. Patients have substantial time constraints, transportation limitations, or financial limitations that preclude them from being able to attend frequent appointments. Reducing the number of clinic visits while increasing the number of overall patient-clinician contact points allows for timely optimization of GDMT and substantially reduces the financial burden on patients. Furthermore, from an institutional perspective, the availability of infrastructure and resources necessary to accommodate visits is limited. Remote titration could enable remote optimization of more stable patients and free up clinic space and time for patients that require in-person follow-up, thereby contributing to optimal use of clinic resources. Lastly, the reduction in visits could also contribute to distancing, protecting high-risk patients from potential exposure to pathogens that could deteriorate their condition and predispose them to worse outcomes.

Synthesis of Findings

Guidelines suggest that clinicians should aim to achieve target doses within 3 to 6 months [11]. However, this rapid timeline usually proves unfeasible with standard in-person clinic visits [13,14,31,32]. In practice, optimization of each therapy (ARNIs, ACEIs, or ARBs; BBLs; and MRAs) may require a titration period of 2 to 4 months. With aggressive titration, optimal dosing may be achieved in 6 months; however, in clinical practice it is more likely to take 9 months or potentially up to 12 months [33]. In contrast, remote titration facilitated by telemonitoring enabled 76% (16/21) of patients in our intervention group to reach target doses within 4 months. This points to a significant advantage, especially considering that patients had to attend a minimal number of clinic visits to accomplish this.

The increased proportion of patients who achieved target doses and the shorter timelines observed in this pilot study point to another potential benefit that this intervention could provide to

patients with HF. A meta-analysis conducted in 2017 by Zaman et al [35] assessed data from 32,840 patients and calculated the absolute risk of death associated with deferral of HF medical therapy for 1 year. The analysis showed that a 1-year deferral of treatment could reduce the 1-year survival rate from 90% (if treated) to 78% [35]. Our results suggest that remote titration could prevent detrimental therapy optimization delays that can lead to significant disease progression for patients with HF.

Implications for the Full RCT

As an internal pilot, this study also aimed to inform the choice of the most appropriate primary outcome measure for the full RCT and provide data to contribute to a more accurate sample size calculation. The pilot demonstrated that the initially selected primary outcome measure, the number of clinic visits required to achieve target doses, was strongly influenced by external factors unrelated to the intervention. Furthermore, it did not properly reflect the impact of the intervention on GDMT optimization. The proportion of patients achieving target doses proved to be a central finding that was less susceptible to external factors and served as a good indicator of the utility of remote titration while clearly outlining the differences between the intervention and control groups. Therefore, the new sample size was calculated based on the proportion of patients achieving target doses and determined to be 108 patients [23]. This highlights the importance of internal pilot studies in situations in which there is uncertainty concerning values of such necessary parameters as variances or event rates in the control group [22].

Study Limitations

The results of this study should be interpreted while taking some limitations into account. The sample size, single-center nature of the study, and availability of dedicated staff to support the intervention may impact its external validity.

The small sample size of the study did not allow any adjustment for possible confounders. Therefore, while the study results are promising, the pilot was not designed with the required power to achieve definitive conclusions regarding effectiveness. While a sample size was calculated based on available data, this pilot aimed to obtain data for a more accurate sample size calculation. *P* values should thus be interpreted accordingly.

The patient population enrolled into this study was recruited from a single specialized heart function clinic that had launched the Medly Program in 2016. First, the familiarity of the clinicians involved in this study with telemonitoring, as well as the existing processes for communication of information obtained through Medly, may have mitigated challenges that could have otherwise been encountered. Second, the intervention was supported by a dedicated nurse coordinator, which might not be available at other clinics, limiting the potential generalizability and external validity of the study. Third, as our study investigates process-of-care changes, blinding could not be applied to physicians. The physicians' awareness of the group to which their patients were randomized may have impacted their effort to reach target doses. However, as this applied equally to both study groups, the lack of physician blinding is not expected to have a substantial impact on the outcomes of the study. Lastly, the average age of the participants was notably lower than the general HF patient population. As older populations are generally more technophobic, this could reduce the potential generalizability and external validity of the study. However, a previous study conducted with Medly found that its ease of use and the availability of supporting services led to higher use of the app in older patients. Moreover, patients in older age groups (70 years or older) maintained higher and more consistent adherence rates over time [36].

Analysis was performed once all participants had been in the study for a minimum of six months. At the time of analysis, 7 patients in the control group had not yet completed titration. Therefore, the time to dose optimization and number of visits required to achieve titration in the control group represent estimates that are most likely lower than the final numbers. As such, the differences in these parameters represent a conservative assessment, and the actual impact of remote titration on these factors may be larger than presented here.

Conclusions

A substantial treatment gap exists between guideline-recommended heart failure therapy and the implementation of these guidelines in the clinical care of patients. The results of this pilot study suggest that remote titration facilitated by telemonitoring could be leveraged to garner substantial improvements in GDMT optimization over the standard of care. Remote titration increased the proportion of patients that achieved target doses, decreased the median time to dose optimization, and decreased the number of visits required to achieve target doses. In addition, remote titration may contribute to optimal use of clinic resources by enabling remote therapy optimization for more stable patients while freeing up clinic space and time for patients that require in-person follow-up. Lastly, by facilitating timely optimization of vital therapy for patients with HF and eliminating delays in therapy, remote titration could help reduce preventable disease progression.

Acknowledgments

Funding for this study was provided by the Ted Rogers Centre for Heart Research, the Peter Munk Cardiac Centre site, and through a National Sciences and Engineering Research Council of Canada Discovery grant.

Conflicts of Interest

Members of the research team (ES and HJR) have intellectual property rights of the Medly system. DHB has received travel support from Abbott and Biotronik, and honoraria, travel support, and research funding from Boston Scientific.

Multimedia Appendix 1
CONSORT-EHEALTH checklist (v 1.6.1).
[PDF File (Adobe PDF File), 8751 KB - cardio_v4i1e21962_app1.pdf]

References

1. Cowie MR, Anker SD, Cleland JGF, Felker GM, Filippatos G, Jaarsma T, et al. Improving care for patients with acute heart failure: before, during and after hospitalization. ESC Heart Fail 2014 Dec;1(2):110-145 [FREE Full text] [doi: 10.1002/ehf2.12021] [Medline: 28834628]
2. Howlett JG, Chan M, Ezekowitz JA, Harkness K, Heckman GA, Kouz S, Canadian Cardiovascular Society Heart Failure Guidelines Panels. The Canadian Cardiovascular Society Heart Failure Companion: Bridging Guidelines to Your Practice. Can J Cardiol 2016 Mar;32(3):296-310. [doi: 10.1016/j.cjca.2015.06.019] [Medline: 26391749]
3. Shah SJ, Kitzman DW, Borlaug BA, van Heerebeek L, Zile MR, Kass DA, et al. Phenotype-Specific Treatment of Heart Failure With Preserved Ejection Fraction. Circulation 2016 Jul 05;134(1):73-90. [doi: 10.1161/circulationaha.116.021884]
4. Ezekowitz JA, O'Meara E, McDonald MA, Abrams H, Chan M, Ducharme A, et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure. Can J Cardiol 2017 Nov;33(11):1342-1433. [doi: 10.1016/j.cjca.2017.08.022] [Medline: 29111106]
5. Simpson J, Jhund PS, Silva Cardoso J, Martinez F, Mosterd A, Ramires F, PARADIGM-HF Investigators and Committees. Comparing LCZ696 with enalapril according to baseline risk using the MAGGIC and EMPHASIS-HF risk scores: an analysis of mortality and morbidity in PARADIGM-HF. J Am Coll Cardiol 2015 Nov 10;66(19):2059-2071 [FREE Full text] [doi: 10.1016/j.jacc.2015.08.878] [Medline: 26541915]
6. Jhund PS, McMurray JJV. The neprilysin pathway in heart failure: a review and guide on the use of sacubitril/valsartan. Heart 2016 Sep 01;102(17):1342-1347. [doi: 10.1136/heartjnl-2014-306775] [Medline: 27207980]
7. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2016 Sep 27;68(13):1476-1488 [FREE Full text] [doi: 10.1016/j.jacc.2016.05.011] [Medline: 27216111]
8. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013 Oct 15;62(16):e147-e239 [FREE Full text] [doi: 10.1016/j.jacc.2013.05.019] [Medline: 23747642]
9. Packer M, Bristow MR, Cohn JN, Colucci WS, Fowler MB, Gilbert EM, et al. The Effect of Carvedilol on Morbidity and Mortality in Patients with Chronic Heart Failure. N Engl J Med 1996 May 23;334(21):1349-1355. [doi: 10.1056/nejm199605233342101]
10. McAlister FA, Wiebe N, Ezekowitz JA, Leung AA, Armstrong PW. Meta-analysis: beta-blocker dose, heart rate reduction, and death in patients with heart failure. Ann Intern Med 2009 Jun 02;150(11):784-794. [doi: 10.7326/0003-4819-150-11-200906020-00006] [Medline: 19487713]
11. Yancy CW, Januzzi JL, Allen LA, Butler J, Davis LL, Fonarow GC, et al. 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol 2018 Jan 16;71(2):201-230 [FREE Full text] [doi: 10.1016/j.jacc.2017.11.025] [Medline: 29277252]
12. Jhund PS. Heart failure management: continuing to fail or signs of success? Cardiovasc Drugs Ther 2015 Feb;29(1):5-6. [doi: 10.1007/s10557-015-6574-9] [Medline: 25691249]
13. Greene SJ, Butler J, Albert NM, DeVore AD, Sharma PP, Duffy CI, et al. Medical Therapy for Heart Failure With Reduced Ejection Fraction: The CHAMP-HF Registry. J Am Coll Cardiol 2018 Jul 24;72(4):351-366 [FREE Full text] [doi: 10.1016/j.jacc.2018.04.070] [Medline: 30025570]
14. Marti CN, Fonarow GC, Anker SD, Yancy C, Vaduganathan M, Greene SJ, et al. Medication dosing for heart failure with reduced ejection fraction - opportunities and challenges. Eur J Heart Fail 2019 Mar;21(3):286-296 [FREE Full text] [doi: 10.1002/ejhf.1351] [Medline: 30537163]
15. Maggioni AP, Anker SD, Dahlström U, Filippatos G, Ponikowski P, Zannad F, et al. Are hospitalized or ambulatory patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12,440 patients of the ESC Heart Failure Long-Term Registry. Eur J Heart Fail 2013 Oct;15(10):1173-1184 [FREE Full text] [doi: 10.1093/eurjhf/hft134] [Medline: 23978433]
16. Steckler AE, Bishu K, Wassif H, Sigurdsson G, Wagner J, Jaenicke C, et al. Telephone Titration of Heart Failure Medications. The Journal of Cardiovascular Nursing 2011;26(1):29-36. [doi: 10.1097/jcn.0b013e3181ec1223]
17. Moyer-Knox D, Mueller TM, Vuckovic K, Mischke L, Williams RE. Remote titration of carvedilol for heart failure patients by advanced practice nurses. J Card Fail 2004 Jun;10(3):219-224. [doi: 10.1016/j.cardfail.2003.09.009] [Medline: 15190531]

18. D'Onofrio A, Palmisano P, Rapacciuolo A, Ammendola E, Calò L, Ruocco A, et al. Effectiveness of a management program for outpatient clinic or remote titration of beta-blockers in CRT patients: The RESTORE study. Int J Cardiol 2017 Jun 01;236:290-295. [doi: 10.1016/j.ijcard.2017.02.015] [Medline: 28188000]
19. Palmisano P, Ammendola E, D'Onofrio A, Accogli M, Calò L, Ruocco A, et al. Evaluation of synergistic effects of resynchronization therapy and a β-blocker up-titration strategy based on a predefined patient-management program: the RESTORE study. Clin Cardiol 2015 Jan;38(1):2-7 [FREE Full text] [doi: 10.1002/clc.22352] [Medline: 25580847]
20. Spaeder J, Najjar SS, Gerstenblith G, Hefter G, Kern L, Palmer JG, et al. Rapid titration of carvedilol in patients with congestive heart failure: a randomized trial of automated telemedicine versus frequent outpatient clinic visits. Am Heart J 2006 Apr;151(4):844.e1-844.10. [doi: 10.1016/j.ahj.2005.06.044] [Medline: 16569544]
21. Smeets CJ, Storms V, Vandervoort PM, Dreesen P, Vranken J, Houbrechts M, et al. A Novel Intelligent Two-Way Communication System for Remote Heart Failure Medication Uptitration (the CardioCoach Study): Randomized Controlled Feasibility Trial. JMIR Cardio 2018 Apr 04;2(1):e8 [FREE Full text] [doi: 10.2196/cardio.9153] [Medline: 31758773]
22. Wittes J, Brittain E. The role of internal pilot studies in increasing the efficiency of clinical trials. Stat Med 1990;9(1-2):65-71; discussion 71. [doi: 10.1002/sim.4780090113] [Medline: 2345839]
23. Artanian V, Rac VE, Ross HJ, Seto E. Impact of Remote Titration Combined With Telemonitoring on the Optimization of Guideline-Directed Medical Therapy for Patients With Heart Failure: Protocol for a Randomized Controlled Trial. JMIR Res Protoc 2020 Oct 13;9(10):e19705 [FREE Full text] [doi: 10.2196/19705] [Medline: 33048057]
24. Seto E, Leonard KJ, Cafazzo JA, Barnsley J, Masino C, Ross HJ. Mobile phone-based telemonitoring for heart failure management: a randomized controlled trial. J Med Internet Res 2012 Feb 16;14(1):e31 [FREE Full text] [doi: 10.2196/jmir.1909] [Medline: 22356799]
25. Ware P, Ross HJ, Cafazzo JA, Laporte A, Seto E. Implementation and Evaluation of a Smartphone-Based Telemonitoring Program for Patients With Heart Failure: Mixed-Methods Study Protocol. JMIR Res Protoc 2018 May 03;7(5):e121 [FREE Full text] [doi: 10.2196/resprot.9911] [Medline: 29724704]
26. Seto E, Leonard KJ, Cafazzo JA, Barnsley J, Masino C, Ross HJ. Developing healthcare rule-based expert systems: case study of a heart failure telemonitoring system. Int J Med Inform 2012 Aug;81(8):556-565. [doi: 10.1016/j.ijmedinf.2012.03.001] [Medline: 22465288]
27. Gupta S. Intention-to-treat concept: A review. Perspect Clin Res 2011 Jul;2(3):109-112 [FREE Full text] [doi: 10.4103/2229-3485.83221] [Medline: 21897887]
28. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. Nat Rev Cardiol 2011 Jan;8(1):30-41 [FREE Full text] [doi: 10.1038/nrcardio.2010.165] [Medline: 21060326]
29. Ansari M, Shlipak MG, Heidenreich PA, Van Ostaeyen D, Pohl EC, Browner WS, et al. Improving Guideline Adherence. Circulation 2003 Jun 10;107(22):2799-2804. [doi: 10.1161/01.cir.0000070952.08969.5b]
30. Hickey A, Suna J, Marquart L, Denaro C, Javorsky G, Munns A, et al. Improving medication titration in heart failure by embedding a structured medication titration plan. Int J Cardiol 2016 Dec 01;224:99-106. [doi: 10.1016/j.ijcard.2016.09.001] [Medline: 27643473]
31. Atherton J, Hickey A. Expert Comment: Is Medication Titration in Heart Failure too Complex? Card Fail Rev 2017 Apr;3(1):25-32 [FREE Full text] [doi: 10.15420/cfr.2017:1:2] [Medline: 28785472]
32. Carroll R, Mudge A, Suna J, Denaro C, Atherton J. Prescribing and up-titration in recently hospitalized heart failure patients attending a disease management program. Int J Cardiol 2016 Aug 01;216:121-127. [doi: 10.1016/j.ijcard.2016.04.084] [Medline: 27153136]
33. Gracia E, Hamid A, Butler J. Timely Management of New-Onset Heart Failure. Circulation 2019 Aug 20;140(8):621-623. [doi: 10.1161/circulationaha.118.035452]
34. Gheorghiade M, Albert NM, Curtis AB, Thomas Heywood J, McBride ML, Inge PJ, et al. Medication dosing in outpatients with heart failure after implementation of a practice-based performance improvement intervention: findings from IMPROVE HF. Congest Heart Fail 2012;18(1):9-17 [FREE Full text] [doi: 10.1111/j.1751-7133.2011.00250.x] [Medline: 22277172]
35. Zaman S, Zaman SS, Scholtes T, Shun-Shin MJ, Plymen CM, Francis DP, et al. The mortality risk of deferring optimal medical therapy in heart failure: a systematic comparison against norms for surgical consent and patient information leaflets. Eur J Heart Fail 2017 Nov;19(11):1401-1409 [FREE Full text] [doi: 10.1002/ejhf.838] [Medline: 28597606]
36. Ware P, Dorai M, Ross HJ, Cafazzo JA, Laporte A, Boodoo C, et al. Patient Adherence to a Mobile Phone-Based Heart Failure Telemonitoring Program: A Longitudinal Mixed-Methods Study. JMIR Mhealth Uhealth 2019 Feb 26;7(2):e13259 [FREE Full text] [doi: 10.2196/13259] [Medline: 30806625]

Abbreviations

ACEI: angiotensin-converting enzyme inhibitors
AE: adverse event
ARB: angiotensin receptor blockers
ARNI: angiotensin receptor–neprilysin inhibitors
BBL: β-blockers

CHAMP-HF: Change the Management of Patients with Heart Failure
CONSORT: Consolidated Standards of Reporting Trials
ED: emergency department
GDMT: guideline-directed medical therapy
HF: heart failure
HFC: Heart Function Clinic
HFrEF: heart failure with reduced ejection fraction
LVEF: left ventricular ejection fraction
MRA: mineralocorticoid receptor antagonists
PMCC: Peter Munk Cardiac Centre
RCT: randomized controlled trial

Edited by G Eysenbach; submitted 30.06.20; peer-reviewed by P Essay, C Smeets; comments to author 18.08.20; revised version received 22.09.20; accepted 30.09.20; published 03.11.20.

Please cite as:
Artanian V, Ross HJ, Rac VE, O'Sullivan M, Brahmbhatt DH, Seto E
Impact of Remote Titration Combined With Telemonitoring on the Optimization of Guideline-Directed Medical Therapy for Patients With Heart Failure: Internal Pilot of a Randomized Controlled Trial
JMIR Cardio 2020;4(1):e21962
URL: http://cardio.jmir.org/2020/1/e21962/
doi:10.2196/21962
PMID:33141094

Original Paper

Using an Electronic App to Promote Home-Based Self-Care in Older Patients With Heart Failure: Qualitative Study on Patient and Informal Caregiver Challenges

Sahr Wali[1,2], MSc; Karim Keshavjee[2,3], MSc, MBA, MD, CCFP; Linda Nguyen[4], MSc; Lawrence Mbuagbaw[5], MD, MPH, PhD, FRSPH; Catherine Demers[5,6], MD, MSc, FRCPC

[1]Centre for Global eHealth Innovation, Techna Institute, University Health Network, Toronto, ON, Canada

[2]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

[3]InfoClin, Toronto, ON, Canada

[4]School of Rehabilitation Science, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

[5]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada

[6]Department of Medicine, McMaster University, Hamilton, ON, Canada

Corresponding Author:
Catherine Demers, MD, MSc, FRCPC
Department of Health Research Methods, Evidence and Impact
McMaster University
237 Barton St E
Hamilton, ON, L8L 2X2
Canada
Phone: 1 905 525 9140 ext 73324
Email: demers@hhsc.ca

Related Article:

This is a corrected version. See correction statement: http://cardio.jmir.org/2020/1/e25624/

Abstract

Background: Heart failure (HF) affects many older individuals in North America, with recurrent hospitalizations despite postdischarge strategies to prevent readmission. Proper HF self-care can potentially lead to better clinical outcomes, yet many older patients find self-care challenging. Mobile health (mHealth) apps can provide support to patients with respect to HF self-care. However, many mHealth apps are not designed to consider potential patient barriers, such as literacy, numeracy, and cognitive impairment, leading to challenges for older patients. We previously demonstrated that a paper-based standardized diuretic decision support tool (SDDST) with daily weights and adjustment of diuretic dose led to improved self-care.

Objective: The aim of this study is to better understand the self-care challenges that older patients with HF and their informal care providers (CPs) face on a daily basis, leading to the conversion of the SDDST into a user-centered mHealth app.

Methods: We recruited 14 patients (male: 8/14, 57%) with a confirmed diagnosis of HF, aged ≥60 years, and 7 CPs from the HF clinic and the cardiology ward at the Hamilton General Hospital. Patients were categorized into 3 groups based on the self-care heart failure index: patients with adequate self-care, patients with inadequate self-care without a CP, or patients with inadequate self-care with a CP. We conducted semistructured interviews with patients and their CPs using persona-scenarios. Interviews were transcribed verbatim and analyzed for emerging themes using an inductive approach.

Results: Six themes were identified: usability of technology, communication, app customization, complexity of self-care, usefulness of HF-related information, and long-term use and cost. Many of the challenges patients and CPs reported involved their unfamiliarity with technology and the lack of incentive for its use. However, participants were supportive and more likely to actively use the HF app when informed of the intervention's inclusion of volunteer and nurse assistance.

Conclusions: Patients with varying self-care adequacy levels were willing to use an mHealth app if it was simple in its functionality and user interface. To promote the adoption and usability of these tools, patients confirmed the need for researchers to engage

with end users before developing an app. Findings from this study can be used to help inform the design of an mHealth app to ensure that it is adapted for the needs of older individuals with HF.

(JMIR Cardio 2020;4(1):e15885) doi:10.2196/15885

KEYWORDS

mobile health; mobile apps; heart failure; self-care; mobile phone

Introduction

Burden of Disease

Heart failure (HF) has been defined as a global epidemic affecting 26 million individuals worldwide [1]. With the increasing aging population, HF is the leading cause of hospitalization and mortality in older adults, placing a significant clinical and financial burden on the health care system [2,3]. Patients with HF currently have longer hospital stays, and up to 50% of them are readmitted within 3 months post discharge [3,4]. HF-related readmission is attributed to worsening symptoms and clinical deterioration [5-7]. However, studies have found that the adoption of self-care in patients with HF could lead to a reduction of more than 30% of HF-related hospital readmissions [5,6].

Importance of Self-Care

Self-care is a decision-making process that involves the choice of various behaviors to maintain physiological stability in the face of disease and the appropriate response to symptoms when they occur [7,8]. The process of HF self-care comprises of 3 separate but connected components: (1) self-maintenance, (2) symptom perception, and (3) self-management. Self-maintenance consists of actions associated with treatment adherence [8]. Symptom perception involves individual detection, assurance, and interpretation of physical sensations (ie, body listening and labeling of symptoms). Self-management involves the response to changes in symptoms [8]. Each component of the HF self-care process represents key tasks pivotal to HF stability. Self-management is often inferred as the major area of focus to improve HF outcomes, as it is directly associated with the response to changes in symptoms [8]. However, literature has found that all 3 self-care constructs reflect processes that build on one another and move in sequence to maintain, recognize, and manage physiological stability [8].

Proper HF self-care involves a series of tasks such as daily weight and symptom monitoring and adjusting diuretics based on the patient's symptoms [9-12]. Weight monitoring is identified as a pivotal component of HF self-care, as weight gain is the last common step before worsening clinical outcomes [13]. In the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure randomized control trial (RCT), an increase in body weight after hospitalization was independently associated with a 16% increase (per kg) in the likelihood of 30-day mortality or hospital readmission (hazard ratio per kg increase 1.16; 95% CI 1.09-1.23; $P<.001$) [13]. To effectively manage weight fluctuations and reduce fluid overload, as part of HF self-care, patients should be empowered to manage and adjust their own diuretics in the home setting [11].

Despite the benefits associated with HF self-care, many older adults find the process of self-care challenging [14,15]. Factors such as the absence of an informal care provider (CP; ie, spouse, family member, and friend), poor economic stability, presence of comorbidities, limited knowledge about HF self-care, and the presence of cognitive impairment can potentially limit patients' ability to properly manage their symptoms [9,10,14-17]. Many studies have also reported that patient values are integral to how patients respond to the severity of their symptoms; thus, poor patient adherence could be related to a lack of perceived need or motivation for self-care [17]. Ultimately, to better support patients with their self-care challenges, we must understand the barriers and facilitators they face, to address their unmet needs.

Leveraging Technology to Support Self-Care

With the increasing popularity of mobile phones, the use of mobile health (mHealth) apps can potentially support the process of self-care [2,18,19]. In a systematic review evaluating the state of mHealth apps available for cardiovascular disease, including HF, they found that patients using mHealth apps had greater treatment adherence compared with usual care (odds ratio 4.51, 95% CI 2.38-8.57; $P<.001$) [2]. However, older adults with HF have complex needs, leaving many older adults to not commonly use mHealth apps because of the perception that they are not suited to their needs or capabilities [2,18-20]. Specifically, many older adults with HF have low levels of health and computer literacy, mild cognitive impairment, and visual and hearing challenges, all of which contribute to their poor use of technology [19,21,22]. To improve the adoption of these tools among older adults, mHealth apps should be created using a more user-centered design (UCD) approach to address their needs and limitations [19,23].

We previously conducted a pilot RCT (ClinicalTrials.gov Identifier: NCT01886534) that tested the use of a standardized diuretic decision tool (SDDST; Registered Copyright: 1105713) combined with a talking weight scale, nursing support with home visits, and a literacy and numeracy-sensitive information booklet. The results of this RCT demonstrated that self-management improved significantly in the intervention arm compared with usual care ($P=.005$) [24]. The intervention was safe and feasible. The objective of this study is to better understand the perspectives of patients and care providers (CPs) on their self-care challenges to incorporate their lived context into the design of an HF app (HFApp). Ultimately, the information collected will allow us to convert the SDDST into a user-centered mHealth app to better support HF self-care.

Methods

Study Design

This qualitative descriptive study was guided by the evidence-based UCD framework [25,26]. The study focused on the first phase of the framework to identify end users' needs through a series of semistructured interviews with older patients with HF and their CPs. This approach allowed us to understand the perspectives of patients and CPs, which will inform the design of the electronic version of the HFApp. This study was approved by the Hamilton Integrated Research Ethics Board.

Study Population

A convenience sample of patients at Hamilton General Hospital was invited to participate in the study via telephone (SW). The study population included males and females aged ≥60 years with a primary diagnosis of HF. Both patients admitted to the hospital with a primary diagnosis of HF and patients followed in the HF clinic were considered, as it allowed us to obtain a broad representation of HF diagnoses. The following patients were excluded: (1) those who resided in a long-term care facility, (2) those whose life expectancy was <3 months, (3) those who were referred for cardiovascular surgery before hospital discharge, (4) those who were not on a loop diuretic by mouth, (5) those who were currently on dialysis, or (6) those who were unable to speak English.

Informal caregivers (males and females aged ≥18 years) eligible for recruitment in this study were required to provide the patient with at least 4 hours of ongoing patient support a week (ie, spouse, family member, and friend). CPs were only approached for study participation once patient telephone confirmation was received.

Participant Categorization

We based the UCD framework on the foundation that just as users differ in their technology adequacy levels, patients with HF differ in their levels of self-care adequacy as well [25]. Thus, to ensure that patients from varying self-care adequacy levels were included in this study, we used the validated self-care heart failure index (SCHFI) to appropriately categorize patients [11]. Patients were categorized into 3 different groups according to the presence of a CP and their level of self-care adequacy, where an average score of 70 or higher on the SCHFI was labeled as self-care adequate: (1) adequate self-care with a CP, (2) inadequate self-care without a CP, and (3) inadequate self-care with a CP [11].

All CPs were categorized into one participant group and completed the caregiver contribution self-care heart failure index (CC-SCHFI) [27]. The CC-SCHFI is a modification of the SCHFI, with the same scales for self-care maintenance, self-care management, and self-care confidence. However, the use of the CC-SCHFI allowed for the CPs' contribution to the patients' HF self-care to be measured specific to the 3 main areas of self-care [27]. These scores were also used to evaluate differences in CC-SCHFI scores and CP interview feedback.

Sample Size

We planned to approach a maximum of 20 individuals to participate in the study, consisting of 15 patients with HF (5 within each patient group) and 5 CPs, or until data saturation was reached. We used the guideline of Malterud et al [28] to estimate when data saturation would be reached for both patients and CPs. Due to the study aim and direct participant dialog, a sample size of 20 participants was needed to achieve data saturation.

Patient and Caregiver Interviews

Patients and their CPs participated in one individual semistructured interview. Interviews were held separately for each patient at the Hamilton General Hospital for approximately 2 hours. For patient and CP convenience, interviews were held together with the patient and the CP. Before the start of the interviews, patients and CPs signed an informed consent form. The same individual (SW) conducted all interview sessions using an interview guide script to ensure consistency.

Following participant consent, the interview facilitator (SW) provided a detailed overview of the main components of the interview. Each participant was given a tailored discussion guide containing a summary of the HFApp intervention, a series of mock-ups to visualize the HFApp, and a list of persona-scenarios for discussion (Multimedia Appendices 1 and 2) [29]. Persona-scenarios are documents that have commonly been used in UCD studies to help represent a type of individual that the participant can relate with [30]. A persona describes different types of users, or patients, based on their goals and key behaviors (ie, difficulties adjusting diuretics or using technology). The scenario describes specific situations that the persona may face and subsequently impact their care (ie, forgetting to use the app or visiting relatives). A persona-scenario is commonly used to help provide insight into the patient's needs and expectations, as it allows them to draw on information from another's experience and compare it with their own [7,29].

During the interview, each participant was asked to review one of the listed personas and evaluate whether the HFApp would be an effective tool with respect to the different scenarios. Each participant was also asked to come up with at least one idea on how to improve the intervention. Feedback and suggestions were audio-recorded and transcribed verbatim for analysis.

Data Analysis

Interviews were transcribed verbatim using Microsoft Word and imported into NVivo, Version 10 (QSR International), for data analysis. Braun and Clarke's [31] inductive thematic analysis approach was used to analyze, identify, reflect, and refine emerging themes from the interviews. Two researchers (SW and LN) reviewed the design themes independently (investigator triangulation). The research team was also debriefed about the resultant design themes to ensure that multiple perspectives were incorporated during analysis. The interviewer (SW) was the primary investigator identifying the codes, categories, and themes for the data analysis.

Following thematic analysis, feedback from participant interviews was used to evaluate the changes needed within the HFApp intervention. A series of actions and items corresponding to each theme was developed using Braun and Clarke's [31] methods for qualitative research.

Results

Participant Characteristics

A total of 21 participant interviews were conducted among 14 patients (8/14, 7% male) and 7 CPs (3/7, 43% male). Within the patient groups, there were 6 patients categorized as adequate self-care patients, 4 patients as inadequate self-care patients with a CP, and 4 patients as inadequate self-care patients without a CP. The patients had a mean age of 74 (SD 4) years and a mean left ventricular ejection fraction of 32% (SD 16%). The CPs had an average age of 66 (SD 16) years.

Discussion Sessions

A total of 6 themes were identified: (1) usability of technology, (2) communication, (3) app customization, (4) complexity of self-care, (5) usefulness of HF-related information, and (6) cost and long-term use. The results are summarized in Table 1 and further described in the following section under each design theme. Feedback from each patient with HF is denoted by *P*, whereas each CP is denoted by *C*.

Table 1. Design themes derived from patient and care provider interviews.

Design themes	Factors/design requirement
1. Usability of technology	• Perception that technology will make self-care more challenging • Incentive for technology use needed • Willingness to use technology if kept simple
2. Communication	• Use of direct communication (in person and virtual) with nurse highly desired • Open sharing and access to patient information to improve communication
3. App customization	• Management of medications on one device • Addition of notifications at patient's desired time/manner • Customization of audio and visual format for each patient during setup
4. Complexity of self-care	• Perception that daily management of HF[a] self-care is difficult • Difficulty with diuretic adjustment • Benefits of nursing support
5. Usefulness of HF-related information	• Provision of information from physician and nurses difficult to understand • Interest in information relevant to specific patients
6. Long-term use and costs	• Concerns with potential dependence on the HFApp intervention and future costs • Integration with current device for long-term use and reduce cost

[a]HF: heart failure.

Design Theme 1: Usability of Technology

Perception That Technology Will Make Self-Care More Challenging

Many participants expressed significant resistance regarding the use of technology. When patients and CPs were asked about their current technology usage, they indicated that they either did not use them or specifically did not use any device for HF self-care because of the perception that it would only create more challenges for them:

> *I don't like using any technology, it just makes more problems.* [P, inadequate with CP]

With the consistent negative perception around the use of technology, many patients assumed that the HFApp would become another barrier to their self-care, before the intervention was even fully described. They felt that they were already unfamiliar with technology; therefore, its addition would only further complicate their self-care regimen. Patients and CPs also indicated that they preferred to consult with a real person to manage their HF, as it gave them a sense of comfort and added a *human-touch* to their care. They felt that they already had limited contact with their physicians; thus, the addition of technology would only further isolate their care and contribute to their self-care challenges:

> *I think he would have a lot of difficulty learning how to use it. He barely knows how to use his phone.* [C, adequate]

Lack of Incentive for Technology Use

Both patients and CPs mentioned how they did not view the use of technology as an added benefit to their current treatment regimen, as they would be completing the same tasks with or without it. Due to past difficulties with technology, patients and CPs did not see the need or motivation to use a new device, as they associated the technology as another barrier to their self-care adequacy, rather than a beneficial tool to mitigate some of their self-care challenges:

> *If I'm already writing out my weight everyday and doing fine, I don't see a reason for me to stop what I'm doing and learn something new, like what's the point?* [P, adequate with CP]

Willingness to Use Technology If Kept Simple

After the full HFApp intervention was explained, patients and CPs had a better evaluation of their potential technology usage. They indicated that if the app was simple, as displayed in the mock-ups (Multimedia Appendix 2), they would be willing to learn how to use it. During the persona-scenario discussion, many patients indicated that they shared the same frustrations as the persona *Diane Lambert*, who was unfamiliar with iPads and tablets (Multimedia Appendix 1). They described how learning to use the HFApp would be easier if there were only a few functionalities:

> *I think the app would help Diane (persona), but only if it was really simple. A lot of apps have too many things going on, so I get lost.* [P, adequate with CP]

Design Theme 2: Communication

Use of Direct Communication (In Person and Over Phone) With Nurse Highly Desired

Most patients and CPs articulated how one of their major difficulties involved being able to contact their physician or nurse for support when they were at home. To help resolve this challenge, patients stressed that having a direct source of communication with a member of their care team would be highly beneficial. Specifically, patients and CPs indicated that if the HFApp had nursing support dedicated to answering calls for the intervention, this would help improve both the quality and reliability of the HFApp support as a whole:

> *My doctor even gave me his cell phone number, but I still can't reach him.* [P, inadequate without CP]

During the persona-scenario discussion, patients and CPs also added how being able to receive additional information from a nurse would help them become more confident in their self-care decision making, similar to the persona Christina Williams (Multimedia Appendix 1). They would not have to rely solely on the technology of the HFApp for guidance, which made the use of the entire HF self-care intervention more comforting.

Open Sharing and Access to Patient Information to Improve Communication

Participants emphasized how if the intervention was able to provide nurses and physicians access to their patient's HFApp information, with consent, this would allow for greater accuracy during assessments. This aspect of the HFApp was strongly appealing as patients often felt that there was a gap in their quality of care because their health care provider did not understand their current health condition:

> *The worst is when they think [they are] right, but they don't understand that my symptoms are not the same as before.* [P, adequate with CP]

Patients added that in many cases, they could not remember the depth of their medical history from their last clinic visit, making it difficult for them to reexplain or update the physician or nurse with their health status. They often found it difficult to provide accurate information, as they were not able to remember all of their symptoms and did not always record their weight. Patients and CPs highlighted that by providing physicians and nurses with access to patient information collected by the HFApp, this would help update them during in-person consults and over phone support calls:

> *I try to record my weight, but when my cardiologist asks me questions I don't know what to say...I think having the app track it would be really good for me cause I get lazy.* [P, inadequate with CP]

Information recorded within the HFApp was also deemed beneficial for patients who were able to adequately perform self-care, as they would be able to describe how their HF symptoms worsened even when they were adherent to the process of self-care.

Design Theme 3: App Customization

When participants were asked about using the HFApp, the concept of customization was a major factor that influenced their decision to use the app for self-care. Patients mentioned how the ability to tailor the tool to their needs would increase the overall appeal and usability of the app, as older adults with HF have varying needs and capabilities.

Management of Medications on One Device

Patients were disappointed with the inability to manage multiple medications within the design of the current HFApp. Some patients stressed that they would become reliant on the technology and would need one common system to manage all their medications. As patients with HF are often required to take many medications, they believed that being able to track all of them in one place would make their self-care easier:

> *I have diabetes too, so why wouldn't I be able to manage both? I could have like a separate space for it...I think it would be really helpful.* [P, adequate with CP]

Addition of Notifications at Patient's Desired Time/Manner

Patients and CPs began to acknowledge the benefits of using the HFApp; however, they stressed that there was a need for notifications and reminders to be integrated within the HFApp to obtain its optimal functionality. They stated that it is often difficult to maintain their treatment routine because of a number of factors (eg, tiring, confusing, and limited mobility) but mainly because they are forgetful. To combat this issue, creating a reminder system within the HFApp and setting them according to the patient's daily routine would help promote treatment adherence:

> *I always forget to do it. If you don't tell me I won't do it. So, if you want me to use this thing, you better buzz me until I do it...For me, I would make sure it kept buzzing me until I got onto that scale.* [P, inadequate without CP]

Customization of Audio and Visual Format for Each Individual Patient During Setup

Many older adults with HF may have visual or hearing impairment. To optimize the app potential, participants suggested that visual and hearing preferences should be adjustable to help accommodate various patient needs and

capabilities. Specifically, participants highlighted that during the on-boarding and setup of the HFApp, these customizations can be discussed and assorted with the assistance of a nurse:

> *I know my dad's vision is getting worse. He's too stubborn to admit it, but I think maybe if the app could repeat each thing out loud when you click it that would really help. Or just use really big fonts and bright colors.* [C, adequate]

Design Theme 4: Complexity of Self-Care

Perception That Daily Management of HF Self-Care Is Difficult

During the persona-scenario discussions, participants had varying attitudes (positive and negative) regarding HF self-care; however, the majority of patients with HF agreed that they found the process to be difficult. They specifically indicated that the daily management was overwhelming, especially when patients had multiple comorbidities:

> *There's too many things to remember and I have diabetes, so I mix those up too.* [P, inadequate with CP]

They viewed the management of HF as a burden for their daily routine. Patients even indicated that they consciously decided not to perform self-care tasks because they felt if they were unable to adequately perform all the tasks, these tasks would not make a difference on their health. In reflection to this, according to the patient SCHFI scores recorded, only 50% (7/14) of the patients interviewed indicated that they weighed themselves on a regular basis.

Difficulty With Diuretic Adjustment

Patients reported that they often had difficulty with adjusting their diuretic dosing. Both patients and CPs expressed their fear in changing the dosage incorrectly and potentially worsening their symptoms. They acknowledged the importance of correct diuretic dosing, but their limited self-efficacy highlighted the potential for the HFApp to improve their confidence in completing this task:

> *My wife asks me to help her, but I don't know if I'm doing it right either. Every morning I hope her weight is the same, so I don't have to think about it again.* [C, adequate]

Benefits of Nursing Support

Participants had preestablished views on the complexity of self-care and their difficulty in managing their symptoms. When the inclusion of the nurse home visits, as part of the HFApp intervention, was explained, both patients with and without earlier experience with nurse home visits agreed on the benefits of their presence. The significance of the nursing support varied among patients with inadequate and adequate self-care scores, where patients with inadequate scores felt a stronger need for them compared with patients with adequate self-care scores:

> *Yeah, I would love that. Just to come and make sure I'm alright...This beats having to wait for an appointment.* [P, inadequate with CP]

Design Theme 5: Usefulness of HF-Related Information

Provision of Information From Physicians and Nurses Difficult to Understand

Participants expressed the lack of clarity in the information provided to them by both nurses and physicians. Patients specifically expressed how they either did not understand or would simply forget about the information after their appointment:

> *They keep talking and repeating stuff, but I don't understand...I just nod my head because I don't want to disappoint them.* [P, inadequate with CP]

Interest in Information Relevant to Specific Patient

Both CPs and patients felt that they were consistently given generic information regarding their HF self-care. CPs were concerned about this issue, as they felt that the advice from their physician should be held at a higher degree and tailored to their individual case:

> *My husband is good with managing his weight. He still gets short of breath. I don't know how to you know help, but I told his doctor, and they don't seem to get him either.* [C, adequate]

When CPs and patients reviewed the persona-scenario of *Christina Williams* (Multimedia Appendix 1), a few adequate self-care patients connected with her situation. They agreed on the frustration of following their regimen but still experiencing worsening symptoms. Nonetheless, they identified that if the HFApp could provide specific information relevant to the patient, their physician could use this information as a reference point of discussion during their appointments:

> *I'm like Christina (persona)… what if I could have my doctor use this info on the app when he talks to me. So he has a better idea of what's going on.* [P, adequate with CP]

Design Theme 6: Long-Term Use and Costs

Concerns With Potential Dependence on HFApp Intervention and Future Costs

Following the HFApp explanation, participants were intrigued with the intervention's implementation; however, they also had concerns about the longevity and sustainability of its use. The HFApp was described as a service free of charge for the patient; however, patients and CPs expressed their fear of potentially becoming dependent on its use and then having to pay for the use of the app later:

> *I think we need something to tell us that hey you won't be charged later, and if you are you get a refund or something.* [P, inadequate with CP]

Integration With Current Device for Long-Term Use and Reduce Cost

Some participants recommended integrating the app on current devices (tablet, smartphone, and iPad). They felt that this could reduce the cost for the stakeholder/funder and could improve

the usability of the app, as it would allow for a seamless integration with the devices they are currently using:

> *I already have one of those iPad things, so I don't really need another one. I can just put your app on my iPad. This way you don't have to pay or I don't have to pay now or later, whatever you decide...Either way more bang for your buck.* [P, inadequate with CP]

Identifying What's Next—Summarized Actions and Items

To determine the changes needed for the HFApp intervention, a table outlining each design theme factor with the corresponding action and item was created (Multimedia Appendix 3). The specifics relating to each design theme and the resultant action and item are further described in Multimedia Appendix 3.

Discussion

Principal Findings

Our study demonstrates that older adults with HF and their CPs are willing to use an mHealth app to assist them with their self-care. We identified 6 major design themes that provided insight into the challenges associated with patient self-care and the implications it may have for the HFApp. These findings can be translated into app design specifications to improve the usability of the HFApp intervention, as aligned with our study objective. However, older adults have varying complex needs, which will require additional mechanisms of customization within the HFApp to ensure that it is simple, effective, and usable (Multimedia Appendix 3).

Through this study, it became evident that participants had varying experiences with using technology, but patients and CPs commonly felt that it would create more challenges than benefits. Their unfamiliarity with technology made it clear that there was a lack of incentive for using the HFApp intervention, as any source of technology was seen as burdensome. We found this challenge to be common among many older adult populations, as a systematic review of mHealth-based HF interventions similarly found that over 20% of patients failed to even start the use of the mHealth tool because of difficulties with using their mobile phone [32]. They also reported that they had a 60% attrition rate mainly because of patient-reported technical difficulties (ie, complex language and poor user interface) [32]. To combat this issue, participants indicated that the mHealth tool would need to be simple, and they would need to be provided with proper support to ensure that they are comfortable with its use. To facilitate these design requirements, we outlined the following key items to improve the usability of the HFApp: (1) simple instruction manual on HFApp, (2) summary on the benefits of HFApp specific to self-care challenges, (3) refined user interface for older adult needs, and (4) volunteer support for technical issues (Multimedia Appendix 3). These action items were chosen on the basis that the nursing and volunteer technical support were the components that patients and CPs indicated would improve their comfort and confidence with the HFApp [33,34]. This feedback is consistent with other studies that have incorporated the use of nursing or trained volunteer support [35]. In an RCT (n=316) evaluating the use of trained community volunteers to facilitate the uptake of a mHealth intervention (TAPApp) to support self-care in patients aged >70 years, patients indicated that the trained volunteers played a significant role in promoting continued self-care at home [35]. Older adults with HF already face challenges when using technology; thus, it is not enough to simplify the user interface of the tool, but the technology must be equipped with the proper support channels to meet their needs [36].

One of the key challenges identified by the patients and CPs involved their inability to contact their physician or nurse to help manage their HF symptoms. The inability to communicate with a health care professional led participants to suggest the HFApp to become a source for direct communication to increase their comfort in using the technology and confidence in making self-care decisions. However, as some patients preferred to speak solely to their physician, this became a topic of concern because of barriers associated with physician time constraints [37]. Several studies have found that physicians are less willing to use mHealth tools because of the concern that it will increase their already heavy workload [38]. Assistive technologies, such as mHealth, were initially designed to reduce physician workload; however, if these tools require additional physician involvement, this could threaten the feasibility of the overall intervention [37,39]. In addition, reliance on consistent communication could also become burdensome to patient care, as they have already emphasized their difficulties in adjusting their diuretics with confidence, and any further direct support would decrease their potential to independently make self-care decisions [39]. To prevent an increase in physician workload and patient dependence on provider guidance, we informed patients that physicians and nurses could have access to their HFApp information. Most patients and CPs wanted their physician to be up to date with their condition, as they would not be able to recall all their self-care information during appointments. In reflection of this feedback, we added action items in Multimedia Appendix 3 that would provide mechanisms for voluntary nurse and physician access to patient data and scheduled visits. With this approach, physicians would not be obliged to review their patient data but could access this additional information during appointments. Thus, while recognizing the physician and patient-focused concerns for mHealth tools raised in previous literature, this approach to the HFApp provides an app design that would promote independent self-care and would not limit physicians' ongoing responsibilities.

As patients and CPs became more comfortable with the idea of using technology for HF self-care, they began to outline specific features they would like to add to customize the app according to their personal preferences and needs. Patients wanted to be able to manage multiple medications for their HF on the HFApp. However, because diuretics are the only medication patients can adjust that have an impact on their weight, we did not include multiple medication management options [40,41]. Other medications for HF management need to be adjusted solely by physicians, advanced practice nurses, or physician assistants as

the risk of incorrect dosing can lead to hypotension, bradycardia, or electrolyte imbalances [40,41]. Nevertheless, despite these barriers to patient-led medication adjustments, we found that a recent study has begun to evaluate whether the use of mHealth-enabled telemonitoring program and connected real-time physiological data for clinical decision support and patient self-management can be used to facilitate remote mediation titration (ClinicalTrials.gov Identifier: NCT04205513) [42]. This RCT is currently ongoing; however, its study design highlights the need for further investigation into this topic, to determine the potential opportunity or need to incorporate medication titration within the HFApp [42].

To promote technology use, patients strongly desired the use of notifications. In this context, notifications would be similar to a *nudge* to guide patient behavior. The nudge theory, developed by American economist Richard Thaler, discusses this concept where the nudge serves as a mode of reinforcement or indirect suggestion to promote positive decision making [43,44]. Patients may fail to take their medication or weigh themselves simply because they forget. However, as patients have different schedules and preferences, notifications would need to be tailored to each of the patient's preferences to increase its effectiveness and prevent the possibility of *nudge fatigue* [44,45]. Consistent with previous studies that have used notifications or reminder systems, it has been reported that alerts or reminders are the most common and effective mode to promote patient self-care behaviors [46,47]. Thus, given that patients used our paper-based SDDST effectively, integrating notifications with adjustable settings within the HFApp should be considered to improve the continued use of the intervention (Multimedia Appendix 3).

Both patients and CPs expressed that the information provided by physicians or nurses was often not understood or not applicable to their condition. The current standard of care involves nurses providing general HF self-care education to patients and CPs during clinic visits and patients being provided standardized HF booklets, based on national guidelines, to take home. However, for patients and CPs to gain the benefits associated with HF education, the information must be simple to understand and specific to the patient [33,48]. Past studies have indicated that individualized education is key to help patients gain the skills needed for adequate self-care, as it accommodates their learning style and level of health literacy [33,49]. In an RCT (n=223) evaluating the effect of a teaching session with a nurse educator, patients were reported to have increased self-care adherence (P=.001) and lower risk of rehospitalization (P=.02) compared with standard care [50]. In reflection of patient feedback and literature findings, we aim to incorporate a simple and literacy- and numeracy-sensitive HF summary for nurses to educate patients (Multimedia Appendix 3). Building on the theme of usefulness of HF information, a patient also proposed having their electronic medical record (EMR) information connected to the HFApp. This feature or approach would help both patients and physicians, as it would increase the accuracy of their diuretic dosage at home and their diagnosis in the clinic. Nevertheless, as many hospitals utilize various EMR platforms, the compatibility of patient data to the app may be difficult to resolve and the approval for its use may be challenging to obtain. One approach to help mitigate this challenge involves partnering with various health systems or hospitals. Recently, Apple has announced that patients will be able to access their EMR data on their iPhone or iPad because of their partnership with 12 national health systems [51]. They have also partnered with health care software companies such as Epic and Cerner to facilitate interoperability with the app [52]. Thus, with these innovative announcements, the potential for mHealth apps, such as the HFApp, to be seamlessly integrated with EMR systems is becoming more probable.

Toward the end of the persona-scenario discussion, participants had a growing concern regarding the cost of the intervention. They highlighted that continued use of the HFApp could lead to a source of dependency for the intervention, which could jeopardize their health condition if the technology was not covered through health insurance plans. Therefore, a source of long-term funding is needed to confirm patient support. We suggest that by prescribing the HFApp intervention as a treatment or standard of care, we would potentially be able to cover the associated costs through public or private insurance plans [53]. In a qualitative study on oncology providers' attitude on prescribing mHealth apps, they found that providers were open to recommending or prescribing apps as part of patient care, provided that they have been properly evaluated [54]. Building on this idea, a mixed methods study evaluating the effectiveness of an HF telemonitoring program found that their intervention improved patient self-care and used these results to establish the intervention as part of standard of care at a specialist heart function clinic [55]. The paper-based SDDST has only been evaluated in a pilot study and is not currently being used within standard care; thus, the effectiveness, use, and costs of the HFApp would need to be further investigated to develop the foundational results to support its prescription as standard of care (Multimedia Appendix 3).

Some older adults with HF suggested the integration of the HFApp on their own personal devices (eg, tablet, smartphone, and iPad). They claimed that this could reduce any upfront costs associated with the tool and improve the convenience of the intervention. The HFApp is designed to be used on one device solely for HF self-care, as there is concern that integrating the HFApp on personal devices will potentially complicate the tool and reduce its overall usability [56]. Studies have reported that the additional functions on personal devices create a higher possibility for error or misuse [56]. Thus, it is recommended that for older adults, it may be more beneficial to have one device for one purpose [56].

Limitations

We aimed to recruit patients with varying self-care adequacy levels to prevent the occurrence of selection bias in our evaluation and to ensure that we would obtain feedback from a range of patients. However, all participants were recruited from the Hamilton General Hospital, which may have created some sampling bias. Throughout the persona-scenario discussion sessions, patients and CPs were also limited in their ability to interact with the HFApp, as we did not have a developed prototype. The focus of this study was to obtain feedback on patient self-care challenges based on the mock-ups and

intervention description to inform the design of the HFApp prototype. However, once the HFApp prototype is fully developed, further testing would need to be conducted.

Future Research

Currently, patients and CPs have reported that one of the greatest issues impeding technology use for HF self-care involves their complex design. Considering this, future studies should look to involve patients with HF and their CPs to inform the design of their intervention. Furthermore, as many other facilitators for mHealth usage involve logistical considerations with nurses and physicians (ie, communication and costs), further investigation into the perspectives of CPs should be completed to evaluate the feasibility of specific tool features.

Conclusions

To our knowledge, this is the first study that has collected feedback regarding the design of an mHealth app from patients with varying HF self-care adequacy levels. We found that patients with HF were willing to adopt an electronic health app if it was easy to use and customizable to their preferences. Technology has displayed its potential to improve clinical outcomes; however, there is a need to better understand how to improve their adoption among the growing population of older adults. The usability of these tools is strongly dependent on its design; thus, it is important to consult with patients and CPs regarding their needs, challenges, and capabilities to help guide the development of their app.

Acknowledgments

This work was completed at McMaster University.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Patient and informal caregiver persona-scenarios.
[PDF File (Adobe PDF File), 12017 KB - cardio_v4i1e15885_app1.pdf]

Multimedia Appendix 2
Discussion session mock-up designs.
[PDF File (Adobe PDF File), 830 KB - cardio_v4i1e15885_app2.pdf]

Multimedia Appendix 3
Design theme analysis outlining actions and items to improve the HFApp intervention.
[DOCX File , 23 KB - cardio_v4i1e15885_app3.docx]

References

1. Savarese GL. Global public health burden of heart failure. Card Fail Rev 2017;3(1):7-11. [doi: 10.15420/cfr.2016:25:2]
2. Gandhi S, Chen S, Hong L, Sun K, Gong E, Li C, et al. Effect of mobile health interventions on the secondary prevention of cardiovascular disease: systematic review and meta-analysis. Can J Cardiol 2017 Feb;33(2):219-231. [doi: 10.1016/j.cjca.2016.08.017] [Medline: 27956043]
3. Community Management of Heart Failure. Cardiac Care Network. 2014. URL: https://www.ccs.ca/eguidelines/Content/Topics/HeartFailure/8%20Community%20Management%20of%20Heart%20Failure.htm [accessed 2020-10-29]
4. Vaartjes I, Hoes A, Reitsma J, de Bruin A, Grobbee D, Mosterd A, et al. Age- and gender-specific risk of death after first hospitalization for heart failure. BMC Public Health 2010 Oct 22;10:637 [FREE Full text] [doi: 10.1186/1471-2458-10-637] [Medline: 20969758]
5. Annema C, Luttik M, Jaarsma T. Reasons for readmission in heart failure: perspectives of patients, caregivers, cardiologists, and heart failure nurses. Heart Lung 2009;38(5):427-434. [doi: 10.1016/j.hrtlng.2008.12.002] [Medline: 19755193]
6. Platz E, Jhund PS, Claggett BL, Pfeffer MA, Swedberg K, Granger CB, et al. Prevalence and prognostic importance of precipitating factors leading to heart failure hospitalization: recurrent hospitalizations and mortality. Eur J Heart Fail 2018 Feb;20(2):295-303. [doi: 10.1002/ejhf.901] [Medline: 28872259]
7. O'Connor CM. High heart failure readmission rates: is it the health system's fault? JACC Heart Fail 2017 May;5(5):393 [FREE Full text] [doi: 10.1016/j.jchf.2017.03.011] [Medline: 28449800]
8. Riegel B, Dickson VV, Faulkner KM. The situation-specific theory of heart failure self-care. J Cardiovasc Nurs 2016;31(3):226-235. [doi: 10.1097/JCN.0000000000000244] [Medline: 25774844]
9. Blair JE, Huffman M, Shah SJ. Heart failure in North America. Curr Cardiol Rev 2013 May;9(2):128-146. [doi: 10.2174/1573403x11309020006] [Medline: 23597296]

10. Ditewig JB, Blok H, Havers J, van Veenendaal H. Effectiveness of self-management interventions on mortality, hospital readmissions, chronic heart failure hospitalization rate and quality of life in patients with chronic heart failure: a systematic review. Patient Educ Couns 2010 Mar;78(3):297-315. [doi: 10.1016/j.pec.2010.01.016] [Medline: 20202778]
11. Riegel B, Moser DK, Anker SD, Appel LJ, Dunbar SB, Grady KL, American Heart Association Council on Cardiovascular Nursing, American Heart Association Council on Cardiovascular Nursing, American Heart Association Council on Clinical Cardiology, American Heart Association Council on Nutrition, Physical Activity,Metabolism, American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research. State of the science: promoting self-care in persons with heart failure: a scientific statement from the American Heart Association. Circulation 2009 Sep 22;120(12):1141-1163. [doi: 10.1161/CIRCULATIONAHA.109.192628] [Medline: 19720935]
12. Toback M, Clark N. Strategies to improve self-management in heart failure patients. Contemp Nurse 2017 Feb;53(1):105-120. [doi: 10.1080/10376178.2017.1290537] [Medline: 28151071]
13. Ambrosy AP, Cerbin LP, Armstrong PW, Butler J, Coles A, DeVore AD, et al. Body weight change during and after hospitalization for acute heart failure: patient characteristics, markers of congestion, and outcomes: findings from the ascend-HF trial. JACC Heart Fail 2017 Jan;5(1):1-13 [FREE Full text] [doi: 10.1016/j.jchf.2016.09.012] [Medline: 28034373]
14. Spaling MA, Currie K, Strachan PH, Harkness K, Clark AM. Improving support for heart failure patients: a systematic review to understand patients' perspectives on self-care. J Adv Nurs 2015 Nov;71(11):2478-2489. [doi: 10.1111/jan.12712] [Medline: 26084885]
15. Jaarsma T, Strömberg A, Ben Gal T, Cameron J, Driscoll A, Duengen H, et al. Comparison of self-care behaviors of heart failure patients in 15 countries worldwide. Patient Educ Couns 2013 Jul;92(1):114-120. [doi: 10.1016/j.pec.2013.02.017] [Medline: 23579040]
16. Cannon JA, Moffitt P, Perez-Moreno AC, Walters MR, Broomfield NM, McMurray JJ, et al. Cognitive impairment and heart failure: systematic review and meta-analysis. J Card Fail 2017 Jun;23(6):464-475. [doi: 10.1016/j.cardfail.2017.04.007] [Medline: 28433667]
17. Jaarsma T, Cameron J, Riegel B, Stromberg A. Factors related to self-care in heart failure patients according to the middle-range theory of self-care of chronic illness: a literature update. Curr Heart Fail Rep 2017 Apr;14(2):71-77 [FREE Full text] [doi: 10.1007/s11897-017-0324-1] [Medline: 28213768]
18. App Developer Economics. Research2guidance. 2018. URL: http://research2guidance.com/r2g/r2g--App-Developer-Economics-2015.pdf [accessed 2017-07-20]
19. Cajita M, Hodgson N, Budhathoki C, Han HR. Intention to use mhealth in older adults with heart failure. J Cardiovasc Nurs 2017;32(6):E1-E7 [FREE Full text] [doi: 10.1097/JCN.0000000000000401] [Medline: 28248747]
20. Kuerbis A, Mulliken A, Muench F, Moore A, Gardner D. Older adults and mobile technology: factors that enhance and inhibit utilization in the context of behavioral health. Ment Health Addict Res 2017;2(2):-. [doi: 10.15761/mhar.1000136]
21. Harman D. The aging process. Proc Natl Acad Sci U S A 1981 Nov;78(11):7124-7128. [doi: 10.1073/pnas.78.11.7124] [Medline: 6947277]
22. Sneha S, Varshney U. Enabling ubiquitous patient monitoring: model, decision protocols, opportunities and challenges. Decis Support Syst 2009 Feb;46(3):606-619. [doi: 10.1016/j.dss.2008.11.014]
23. Lloyd T, Buck H, Foy A, Black S, Pinter A, Pogash R, et al. The Penn state heart assistant: a pilot study of a web-based intervention to improve self-care of heart failure patients. Health Informatics J 2019 Jun;25(2):292-303. [doi: 10.1177/1460458217704247] [Medline: 28504048]
24. Demers C. A simple multi-component intervention improves self-management in heart failure. Can J Cardiol 2014;30:S201 [FREE Full text]
25. McCurdie T, Taneva S, Casselman M, Yeung M, McDaniel C, Ho W, et al. mHealth consumer apps: the case for user-centered design. Biomed Instrum Technol 2012;Suppl:49-56. [doi: 10.2345/0899-8205-46.s2.49] [Medline: 23039777]
26. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health 2000 Aug;23(4):334-340. [doi: 10.1002/1098-240x(200008)23:4<334::aid-nur9>3.0.co;2-g]
27. Vellone E, Barbaranelli C, Pucciarelli G, Zeffiro V, Alvaro R, Riegel B. Validity and reliability of the caregiver contribution to self-care of heart failure index version 2. J Cardiovasc Nurs 2020;35(3):280-290. [doi: 10.1097/JCN.0000000000000655] [Medline: 32084084]
28. Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. Qual Health Res 2016 Nov;26(13):1753-1760. [doi: 10.1177/1049732315617444] [Medline: 26613970]
29. Holden RJ, Joshi P, Rao K, Varrier A, Daley CN, Bolchini D, et al. Modeling Personas for Older Adults with Heart Failure. In: Proceedings of the Human Factors and Ergonomics Society Annual Meeting. 2018 Sep 27 Presented at: HFES; September 2-6, 2018; New York, USA. [doi: 10.1177/1541931218621246]
30. Kneale L, Mikles S, Choi YK, Thompson H, Demiris G. Using scenarios and personas to enhance the effectiveness of heuristic usability evaluations for older adults and their care team. J Biomed Inform 2017 Sep;73:43-50 [FREE Full text] [doi: 10.1016/j.jbi.2017.07.008] [Medline: 28867476]
31. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]

32. Cajita MI, Gleason KT, Han H. A systematic review of mhealth-based heart failure interventions. J Cardiovasc Nurs 2016;31(3):E10-E22 [FREE Full text] [doi: 10.1097/JCN.0000000000000305] [Medline: 26544175]
33. Cajita MI, Cajita TR, Han H. Health literacy and heart failure: a systematic review. J Cardiovasc Nurs 2016;31(2):121-130 [FREE Full text] [doi: 10.1097/JCN.0000000000000229] [Medline: 25569150]
34. Ware P, Bartlett SJ, Paré G, Symeonidis I, Tannenbaum C, Bartlett G, et al. Using ehealth technologies: interests, preferences, and concerns of older adults. Interact J Med Res 2017 Mar 23;6(1):e3 [FREE Full text] [doi: 10.2196/ijmr.4447] [Medline: 28336506]
35. Dolovich L, Oliver D, Lamarche L, Agarwal G, Carr T, Chan D, et al. A protocol for a pragmatic randomized controlled trial using the health teams advancing patient experience: strengthening quality (health tapestry) platform approach to promote person-focused primary healthcare for older adults. Implement Sci 2016 Apr 5;11:49 [FREE Full text] [doi: 10.1186/s13012-016-0407-5] [Medline: 27044360]
36. Fleuren M, Wiefferink K, Paulussen T. Determinants of innovation within health care organizations: literature review and Delphi study. Int J Qual Health Care 2004 Apr;16(2):107-123. [doi: 10.1093/intqhc/mzh030] [Medline: 15051705]
37. Sezgin E, Özkan-Yildirim S, Yildirim S. Investigation of physicians' awareness and use of mHealth apps: a mixed method study. Health Policy Technol 2017 Sep;6(3):251-267. [doi: 10.1016/j.hlpt.2017.07.007]
38. de Grood C, Raissi A, Kwon Y, Santana M. Adoption of e-health technology by physicians: a scoping review. J Multidiscip Healthc 2016;9:335-344 [FREE Full text] [doi: 10.2147/JMDH.S103881] [Medline: 27536128]
39. Logan AG, Jassal SV. Building a stronger care loop through mhealth technology. JAMA Intern Med 2018 Jun 1;178(6):809-811. [doi: 10.1001/jamainternmed.2018.1168] [Medline: 29710104]
40. Palazzuoli A, Ruocco G, Ronco C, McCullough PA. Loop diuretics in acute heart failure: beyond the decongestive relief for the kidney. Crit Care 2015 Sep 3;19:296 [FREE Full text] [doi: 10.1186/s13054-015-1017-3] [Medline: 26335137]
41. Cooper HA, Dries DL, Davis CE, Shen YL, Domanski MJ. Diuretics and risk of arrhythmic death in patients with left ventricular dysfunction. Circulation 1999 Sep 21;100(12):1311-1315. [doi: 10.1161/01.cir.100.12.1311] [Medline: 10491376]
42. Kirk V. Use of Telemonitoring to Facilitate Heart Failure Medication Titration. Ehealth Virtual Library. URL: https://library.e-healthconference.com/search-speaker?search_speaker=48430 [accessed 2017-09-12]
43. Arno A, Thomas S. The efficacy of nudge theory strategies in influencing adult dietary behaviour: a systematic review and meta-analysis. BMC Public Health 2016 Jul 30;16:676 [FREE Full text] [doi: 10.1186/s12889-016-3272-x] [Medline: 27475752]
44. Gatwood J, Hohmeier KC, Brooks IM. Beyond the reminder: the next steps in pharmacist-driven, mHealth patient engagement. J Am Pharm Assoc (2003) 2019;59(2S):S21-S24. [doi: 10.1016/j.japh.2018.10.003] [Medline: 30448025]
45. Chang LL, DeVore AD, Granger BB, Eapen ZJ, Ariely D, Hernandez AF. Leveraging behavioral economics to improve heart failure care and outcomes. Circulation 2017 Aug 22;136(8):765-772. [doi: 10.1161/CIRCULATIONAHA.117.028380] [Medline: 28827221]
46. Woods LS, Duff J, Roehrer E, Walker K, Cummings E. Patients' experiences of using a consumer mhealth app for self-management of heart failure: mixed-methods study. JMIR Hum Factors 2019 May 2;6(2):e13009 [FREE Full text] [doi: 10.2196/13009] [Medline: 31045504]
47. Wali S, Demers C, Shah H, Wali H, Lim D, Naik N, et al. Evaluation of heart failure apps to promote self-care: systematic app search. JMIR Mhealth Uhealth 2019 Nov 11;7(11):e13173 [FREE Full text] [doi: 10.2196/13173] [Medline: 31710298]
48. Chindalo P, Keshavjee K, Karim A, Brahmbhatt RN. Health apps by design: a reference architecture for mobile engagement. Int J Handheld Comput Res 2016;7(2):-. [doi: 10.4018/ijhcr.2016040103]
49. Westlake C, Sethares K. Learning style, health literacy, and 90-day health care utilization in heart failure patients. J Cardiac Fail 2015 Aug;21(8):S77. [doi: 10.1016/j.cardfail.2015.06.241]
50. Koelling TM, Johnson ML, Cody RJ, Aaronson KD. Discharge education improves clinical outcomes in patients with chronic heart failure. Circulation 2005 Jan 18;111(2):179-185. [doi: 10.1161/01.CIR.0000151811.53450.B8] [Medline: 15642765]
51. Ventola C. Mobile devices and apps for health care professionals: uses and benefits. P T 2014 May;39(5):356-364 [FREE Full text] [Medline: 24883008]
52. Wicklund E. Apple Unveils Mhealth Integration With EMR Data Through Health App. mHealth Intelligence. URL: https://mhealthintelligence.com/news/apple-unveils-mhealth-integration-with-emr-data-through-health-app [accessed 2018-10-20]
53. Lopez Segui F, Pratdepadua Bufill C, Abdon Gimenez N, Martinez Roldan J, Garcia Cuyas F. The prescription of mobile apps by primary care teams: a pilot project in Catalonia. JMIR Mhealth Uhealth 2018 Jun 21;6(6):e10701 [FREE Full text] [doi: 10.2196/10701] [Medline: 29929948]
54. Berkowitz CM, Zullig LL, Koontz BF, Smith SK. Prescribing an app? Oncology providers' views on mobile health apps for cancer care. JCO Clin Cancer Inform 2017 Nov;1:1-7. [doi: 10.1200/CCI.17.00107] [Medline: 30657404]
55. Ware P, Ross HJ, Cafazzo JA, Laporte A, Seto E. Implementation and evaluation of a smartphone-based telemonitoring program for patients with heart failure: mixed-methods study protocol. JMIR Res Protoc 2018 May 3;7(5):e121 [FREE Full text] [doi: 10.2196/resprot.9911] [Medline: 29724704]

56. Arnhold M, Quade M, Kirch W. Mobile applications for diabetics: a systematic review and expert-based usability evaluation considering the special requirements of diabetes patients age 50 years or older. J Med Internet Res 2014 Apr 9;16(4):e104 [FREE Full text] [doi: 10.2196/jmir.2968] [Medline: 24718852]

Abbreviations

CC-SCHFI: caregiver contribution self-care heart failure index
CP: care provider
EMR: electronic medical record
HF: heart failure
mHealth: mobile health
RCT: randomized control trial
SCHFI: self-care heart failure index
SDDST: standardized diuretic decision support tool
UCD: user-centered design

Edited by G Eysenbach; submitted 14.08.19; peer-reviewed by C Yu, H Mehdizadeh, F Nunes, M Li; comments to author 21.10.19; revised version received 06.01.20; accepted 19.10.20; published 09.11.20.

Please cite as:
Wali S, Keshavjee K, Nguyen L, Mbuagbaw L, Demers C
Using an Electronic App to Promote Home-Based Self-Care in Older Patients With Heart Failure: Qualitative Study on Patient and Informal Caregiver Challenges
JMIR Cardio 2020;4(1):e15885
URL: http://cardio.jmir.org/2020/1/e15885/
doi:10.2196/15885
PMID:33164901

Original Paper

Assisting Home-Based Resistance Training for Normotensive and Prehypertensive Individuals Using Ambient Lighting and Sonification Feedback: Sensor-Based System Evaluation

Mustafa Radha[1,2*], MSc; Niels den Boer[2*], MSc; Martijn C Willemsen[2], PhD; Thom Paardekooper[3], BSc; Wijnand A IJsselsteijn[2], PhD; Francesco Sartor[1,4*], PhD

[1]Royal Philips, Eindhoven, Netherlands

[2]Eindhoven University of Technology, Eindhoven, Netherlands

[3]The Hague University of Applied Sciences, The Hague, Netherlands

[4]Bangor University, Bangor, United Kingdom

[*]these authors contributed equally

Corresponding Author:
Francesco Sartor, PhD
Royal Philips
High Tech Campus 34
Eindhoven, 5656 AE
Netherlands
Phone: 31 681497376
Email: francesco.sartor@philips.com

Abstract

Background: Physical exercise is an effective lifestyle intervention to improve blood pressure. Although aerobic sports can be performed anywhere, resistance exercises are traditionally performed at the gym; extending the latter to the home setting may promote an increase in the number of practitioners.

Objective: This study aims to evaluate a sensor-based system that guides resistance exercises through ambient lighting and sonification (A/S) feedback in a home setting in 34 study participants who were normotensive and prehypertensive.

Methods: Participants took part in a 1.5-hour exercise session in which they experienced the A/S feedback (ie, experimental condition) as well as a control condition (ie, no feedback) and a reference condition (ie, verbal feedback through a human remote coach). The system was evaluated for improving exercise form (range of motion, timing, and breathing patterns) as well as psychophysiological experience (perceived exertion, attentional focus, competence, and motivation).

Results: A/S feedback was significantly better than the control for concentric (mean 2.48, SD 0.75 seconds; $P<.001$) and eccentric (mean 2.92, SD 1.05 seconds; $P<.001$) contraction times, concentric range of motion consistency (mean 15.64, SD 8.31 cm vs mean 17.94, SD 9.75 cm; $P<.001$), and perceived exertion (mean 3.37, SD 0.78 vs mean 3.64, SD 0.76; $P<.001$). However, A/S feedback did not outperform verbal feedback on any of these measures. The breathing technique was best in the control condition (ie, without any feedback). Participants did not show more positive changes in perceived competence with A/S feedback or verbal feedback.

Conclusions: The system seemed to improve resistance exercise execution and perception in comparison with the control, but did not outperform a human tele-coach. Further research is warranted to improve the breathing technique.

(JMIR Cardio 2020;4(1):e16354) doi:10.2196/16354

KEYWORDS

hypertension; sonification; respiratory guidance; intrinsic motivation; physical exertion

Introduction

Background

Hypertension, or high blood pressure (BP), is a key risk factor for cardiovascular diseases [1]. Effective hypertension management is therefore a major theme in public health. Besides BP medication, nonpharmacological lifestyle interventions have been proven to be successful in the management of hypertension [2]. Appropriate lifestyle modifications may not only lower or control BP in patients with hypertension but also effectively delay or prevent hypertension in nonhypertensives [3]. The European Societies of Hypertension and Cardiology endorse a wide variety of lifestyle interventions for the reduction of BP: salt restriction; moderation of alcohol consumption; a diet rich in vegetables, fruits, and low-fat dairy products; weight reduction; regular exercise; and smoking cessation [3,4].

Physical exercise is a particularly effective intervention to combat hypertension [2]. Dynamic resistance training is often recommended as a supplement to aerobic exercise as several meta-analyses have concluded that it reduces BP by 2 to 3 mm Hg among people with hypertension [5]. Although such an exercise prescription can result in a positive effect on BP postexercise, during the activity itself, there is an acute heightened BP response. Sorace et al [6] identified several factors that influence the acute BP response during resistance training. It was found that the amount of cardiovascular stress is a function of load, number of sets and repetitions, contraction time, rest periods, and whether one performs the Valsalva maneuver (ie, attempt to exhale while the airway is blocked). In accordance with these findings, the American College of Sports Medicine (ACSM) guidelines on resistance exercise states that such exercises should be executed with proper form and technique to ensure optimal health benefits and reduce the risk of injuries. Movements should be rhythmic, performed at a moderate repetition duration (3 seconds concentric and 3 seconds eccentric), with a full range of motion and a normal breathing pattern without breath-holding [7]. These recommendations may be difficult to follow for inexperienced exercisers.

In addition, people who have hypertension find it hard to adhere to exercise recommendations in general [8]. Adopting a more active lifestyle often requires a difficult behavior change. Numerous barriers exist that may influence participation in physical activity [9]. Whereas aerobic activities can be performed anywhere, resistance training is traditionally performed at the gym, which a considerable number of patients with hypertension are known not to attend [10]. Encouraging people to perform resistance training at home could eliminate this barrier. Thus, tools to assist in home-based exercise could also reduce the barriers that patients with hypertension face when changing their behavior.

Research in the field of sonification has shown that movements in physical activity can be improved by providing auditory nonspeech feedback based on sensor data. Sonification, a subtype of auditory displays, covers the technique of rendering sound in response to data and interactions [11]. Kramer et al [12] defined sonification as the transformation of data relations into perceived relations in an acoustic signal for the purpose of facilitating communication or interpretation. Applications of sonification in physical activity often used the parameter mapping approach, where movement kinematics are mapped to sound parameters to inform people about their performance. Real-time sonic feedback then aims to correct and optimize one's technique during a specific exercise. For example, Schaffert and Effenberg [13] created a sonification feedback system called Sofirow for elite rowers to enhance their perception of movement execution. Furthermore, Smith and Claveau [14] investigated how sonification can support a student in imitating the complex motion of an instructor, increasing both spatial and temporal accuracy. Yang and Hunt [15] developed a real-time sonification system to support people performing a bicep curl. They used Microsoft Kinect to track the vertical position of the hand.

Furthermore, literature in the domain of paced breathing suggests that visual stimuli can be used to guide people's respiration [16,17], which could potentially be used to obtain a proper breathing technique during exercise. This could potentially prevent the BP–elevating Valsalva maneuver [18], which for the most part consists of holding one's breath. Correct breathing during resistance exercise is not always intuitive to people, as some are inclined to hold their breath when lifting weight. Therefore, it is important to search for a way in which people can be supported with a proper breathing technique without breath-holding during home-based resistance training.

Objectives

In this study, we aimed to understand whether a combination of ambient lighting and sonification (A/S) feedback could help people in need of resistance exercise in performing such exercises in a safe and effective manner. An A/S feedback system was developed for this purpose and was tested by a group of volunteers who were prehypertensive and normotensive. The effects of the system were measured using metrics of proper exercise performance as well as self-reported psychophysiological measures. These end points were compared with a control condition in which the system was not used as well as to a reference condition where a human provided tele-coaching, representing an upper bound of exercise guidance.

Methods

Conditions

Ambient Lighting and Sonification Feedback Condition

The A/S feedback system was developed such that the ambient light and sonification feedback could be delivered automatically based on recorded movement features (described in the *Movement Features* section). At the start of this condition, participants were given a short trial where they could experience how the sound changed based on their movement. Both verbal instructions and sounds of the ambient light sonification feedback were delivered through headphones.

Sonification

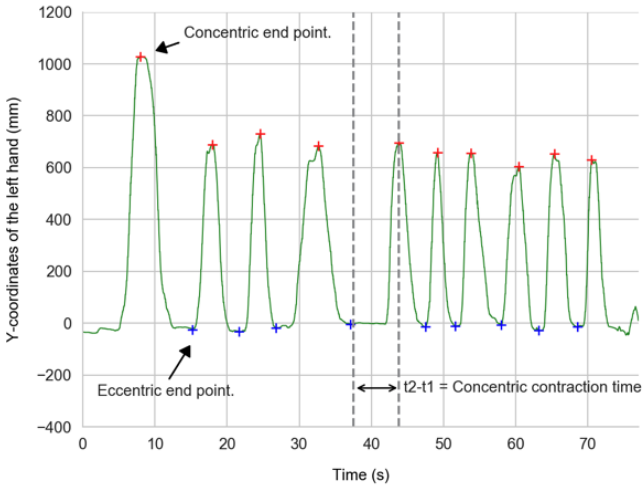
The sonification system used a change in the sound pitch to convey information about whether the user's pace was correct,

too fast, or too slow. This perceptual dimension of sound corresponds to the physical dimension known as frequency. The repetitive movement of resistance training closely resembles a sine wave. The optimal reference sine wave was calculated based on ideal contraction time lengths (3 seconds concentric and 3 seconds eccentric), and its phase was aligned with the measured movements of the participants. In this way, when a user makes a correction in his or her pace, this was almost immediately reflected in the sound pitch. The difference in movement velocity between the sinusoidal model and the measured motion was mapped to perceivable sonic frequencies. A piano sample was looped that comprised a melody in the frequency range of 185 to 247 Hz. If the obtained difference exceeded the predefined bounds, it was scaled linearly to control the transpose dial to go up or down one octave at most. This corresponds to a range with a minimum frequency of 92 Hz and a maximum frequency of 494 Hz. On reaching the concentric or eccentric end points, the time difference between the ideal end point time and actual end point time was calculated. Earcons were used to provide feedback, which are brief sounds that represent specific events or convey specific information (ie, the auditory counterpart of an icon). A *success* earcon was triggered in the case of a correct movement, and a *corrective* earcon was played to inform the user they went too far. If the participant does not reach the ideal end point, no sound is played. The earcons had a higher pitch for concentric end points compared with the eccentric earcons. In addition to assisting with a proper range of motion, an additional earcon was used that signaled the 10 repetitions mark. Before the beginning of the study, participants were familiarized with the auditory cues to ensure that the equipment was functioning properly and that they were able to hear the auditory cues.

Ambient Light

Three Philips hue lights were used to provide respiratory guidance (Figure 1). The lights were programmed to switch from minimal brightness to maximum brightness in 3 seconds, and vice versa. When no respiration was measured through the microphone for 6 seconds, the lights were turned off to signal the participant to resume breathing, as a means to counteract the Valsalva maneuver.

Figure 1. Left: example of the experimental setting while performing frontal shoulder raises showing the Kinect placement, the ambient lights (green light on the table, and a spot light on the roof, not visible), and the white panel behind which the coaching experimenter is sitting. In the verbal and A/S condition, the participant wears headphones to add the auditory feedback. Right: recording of the bicep curl with the Kinect in Max 7, showing how the concentric and eccentric contraction times and endpoints are derived. A/S: ambient light and sonification.



Control Condition: No Feedback

In the control condition, exercise performance was measured without giving feedback to participants about their performance. This meant that participants were left on their own to carry out the exercise in line with previous instructions on contraction time, range of motion, and breathing technique. In addition, they also had to count the repetitions themselves to ensure that they performed 10 repetitions as they did not receive any notification in this condition when they finished a set.

Reference Condition: Verbal Feedback

In the verbal condition, an experimenter was designated as the coach. The coaching experimenter first calibrated the system according to the actual range of motion of the participants. During the exercise itself, an opaque screen was placed between the coaching experimenter and the participant, simulating a tele-coach setting (Figure 1). Feedback was provided through verbal prompts, such as “Try not to hold your breath,” “Next time you may go a little higher,” “Highest point is correct,” “Try to move a bit slower,” and “The pace is good.” The experimenter made use of the metrics displayed at the maximum interface to determine what type of feedback to give.

Study Design and Participants

Recruitment and Exclusion

The experiment was ethically approved by the Internal Committee for Biomedical Experiments of Philips Research in conformity with the Declaration of Helsinki. A total of 37 participants were recruited by an external recruitment agency that identified eligible volunteers based on the following inclusion criteria: (1) men and women who were normotensive, prehypertensive, or regulated stage 1 hypertensive (ie, normal BP because of medications); (2) sedentary lifestyle; (3) physically capable of exercising with the upper limbs at a

moderate intensity (ie, no injuries or movement impairments); and (4) aged between 40 and 60 years and BMI<30. Furthermore, people who had chronic conditions other than regulated stage 1 hypertension, took medication other than BP–lowering medication for stage 1 hypertension, were pregnant, or had a hearing impairment were excluded. Technical difficulties on the first day of testing resulted in data loss of the first 3 participants, leaving us with data from 34 participants altogether, comprising 16 men and 18 women.

Study Design

A within-subjects design was used for this experiment. Participants performed 3 exercises corresponding to the 3 different conditions: control (ie, no feedback), verbal feedback, or A/S feedback. The order of feedback type, as well as the order of exercise type, were counterbalanced to cancel out fatigue, practice, and carryover effects. On the basis of the 3 conditions and 3 kinds of exercise (bicep curls, frontal shoulder raises, and inclined pectoral flies), 9 randomization blocks (3×3) were created, and the 34 participants were split into groups of 4 per block (Multimedia Appendix 1). The main dependent variables that were measured included variables related to exercise performance (ie, concentric and eccentric contraction time, concentric and eccentric end points, and respiration) and several psychological variables (ie, perceived competence, interest and enjoyment, attention, and rate of perceived exertion).

Of the 37 participants who volunteered to take place in this study, 23 participants were prehypertensive: people with baseline BP>120/80 mm Hg, of whom 17 had baseline BP>130/90 mm Hg. The rest (n=14) were normotensive (baseline BP<120/80 mm Hg). Regarding educational level, 8 participants completed secondary school, 9 secondary vocational education, 16 higher professional education, and 4 university education. Participants' anthropometric and physiological characteristics are shown in Table 1.

Table 1. Characteristics of the participants after excluding 3 participants.

Characteristics	Values (N=34[a]; 16 men and 18 women), mean (SD)
Age (years)	51.11 (5.75)
Height (m)	1.75 (0.08)
Weight (kg)	76.95 (13.28)
BMI (kg/m^2)	25.06 (3.21)
Resting systolic blood pressure (mm Hg)	129.52 (11.56)
Resting diastolic blood pressure (mm Hg)	81.85 (8.36)
Resting heart rate (bpm[b])	70.97 (9.69)

[a]21 prehypertensive and 13 normotensive.

[b]bpm: beats per minute.

Power

A priori sample size calculation with the G*Power software indicated for a repeated measures design that a sample size of 36 was required to be 90% certain of detecting a medium effect size (Cohen *f*=0.25) in the concentric or eccentric contraction times (further details in the *Movement Features* section), with an alpha error of *P*<.05. Owing to double scheduling, 1 extra participant was tested. This resulted in a total sample size of 37, comprising 16 men and 21 women, with an average age of 50.97 (SD 5.77) years. However, after excluding the first 3 participants because of technical difficulties with the setup, only 34 remained.

Measures

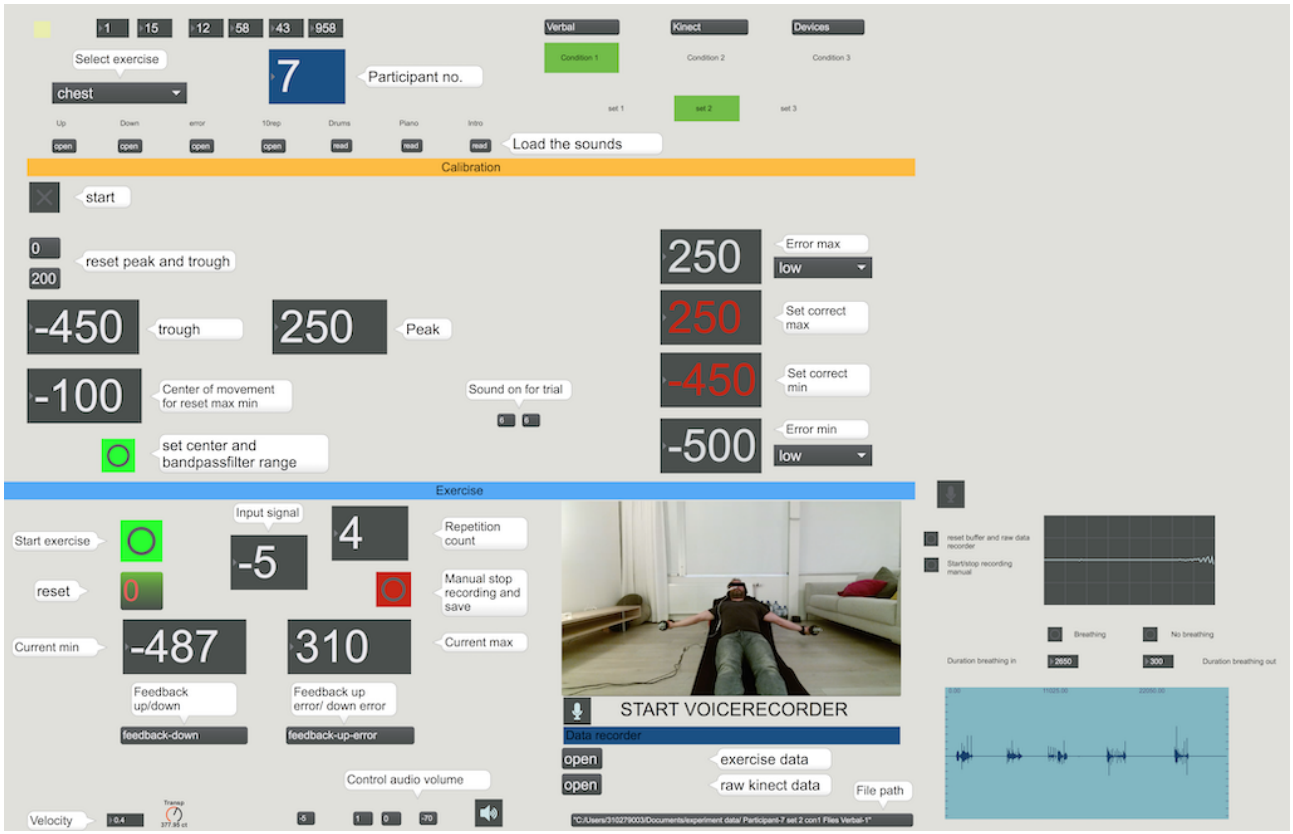
Movement Features

Spatial and temporal kinematic exercise information was captured with a depth camera, Microsoft Kinect version 2.0 (Microsoft Corporation). The camera stream was captured in Max 7 software (Cycling '74), a visual programming language for prototyping interactive multimedia applications. The Max plug-in dp.kinect2 was used [19], with which the 3D coordinates of the limb's joints can be extracted. As the resistance training exercises in this study all involved congruent arm movements, only the y-coordinates of the left hand were used. These coordinates were recorded at 30 frames per second. To deal with measurement errors and noise in the signal, the coordinate signal was smoothed with the dp.kinect smoothing filter (dp.kinect2 @smoothing 0.5 0.8 0.3 0.01 0.01). The main interface was created to facilitate nonautomated interaction between the experimenter and the system, such as setting the condition and a set number for an exercise session. Finally, exercise quality–related metrics were visualized to help the researcher (who was acting as a tele-coach) to assess participants' performance during the verbal feedback condition (Figure 2).

The turning points from the lifting phase to the lowering phase, and vice versa, represented the concentric and eccentric end points, which were used to assess whether participants were able to exercise with a range of motion that corresponded to what was instructed (Figure 1). In the case of bicep curls and frontal shoulder raises, the distance of the hand, measured in millimeters, was taken relative to the person's center of mass. For the pectoral flies, the person's head was taken as the origin, as this was the only stable reference point Kinect could detect while laying down in an inclined position. Each repetition was divided into a lifting phase (ie, concentric contraction time) and a lowering phase (ie, eccentric contraction time) to determine if participants were able to maintain the instructed exercise pace,

either with or against gravity (Figure 1). Concentric and eccentric contraction times were defined as the time change (delta) between a concentric and an eccentric end point. In line with the ACSM guidelines for resistance training and in consultation with a fitness coach, participants were instructed to exercise at a pace of 3 seconds up and 3 seconds down. The participants were instructed to perform exactly 10 repetitions. In both the verbal and A/S conditions, people were informed when they reached that number, but in the control condition, participants had to count by themselves.

Figure 2. Max 7 dashboard to control experimental conditions, calibrate performance measures, and monitor exercise performance.



Physiological Features

The breathing rate was measured using a microphone attached to a headset that recorded the exhalations of the participants in a Waveform Audio File Format. To assess whether participants were able to breathe with a proper breathing technique during the exercise, the audio signal was visually inspected to count the number of exhalations. As it is generally advised to breathe in line with the movement, 10 exhalations were considered a perfect breathing rhythm. Continuous heart rate was monitored by means of a chest strap (RS800CX, Polar Electro) throughout the whole experiment. BP (Mobilograph) was monitored at the end of each set.

Self-Reported Features

Perceived Exertion

The Borg 0-10 category ratio scale (Borg CR-10) was used to assess the amount of perceived physical exertion in the participants [20]. The scale has been validated for use in resistance exercise [21]. The linear scale ranges from *nothing at all* to *hard* to *very very hard (maximal)*. For this study, a Dutch translation of the scale was used. After each set, participants were asked to rate their overall effort by choosing any number on the scale, allowing ratings in between numbers as well. In addition, the subjective comments of participants were gathered to evaluate the potential of technology-enabled feedback and possible implications for future use. After the exercise session was completed, a semistructured interview was conducted, including questions about participants' experience regarding the type of feedback received during the 3 resistance training exercises.

Focus of Attention

The focus of attention of the participants was measured using a 10-point scale, ranging from 0 complete dissociation (external thoughts, daydreaming, environment, and singing songs) to 10 complete association (internal thoughts, how body feels, breathing, and muscles soreness). This one-item scale proved to be a valid and effective measure of attention strategies during effortful physical activity in previous research [22].

Motivation

Two subscales of the intrinsic motivation inventory (IMI) scale, perceived competence and interest/enjoyment, were used as measures of motivation. The other 4 subscales (effort, value/usefulness, felt pressure and tension, and perceived control/choice) were not used as they were deemed redundant with other measures of this study or not applicable. The interest/enjoyment and perceived competence subscale included 7 and 5 items, respectively. Responses were given on a 7-item Likert-type rating scale ranging from *not at all true* to *very true*. Negatively phrased questions were reversed for analysis. Item

questions were translated to Dutch to increase the understandability of the questionnaire. A reliability analysis was carried out on the items of both subscales. Cronbach alpha showed the questionnaire to reach acceptable reliability (α=.871 for interest/enjoyment and α=.937 for perceived competence). Dropping any item would reduce alpha, so all items were retained. The IMI has also been previously validated in a sports setting by McAuley et al [23].

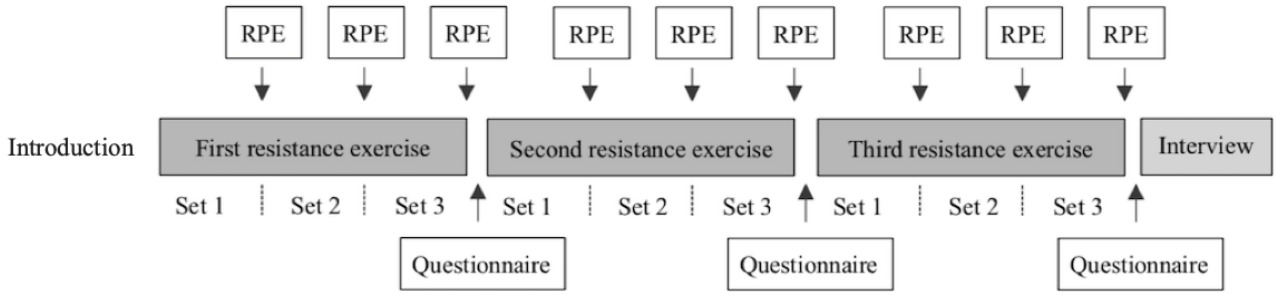
Procedure

The study laboratory closely resembled a living room environment, which benefits the external validity of the study. Before continuing with the study, participants' BP was checked to ensure that it was safe to proceed. As caffeine, nicotine, alcohol, or recreational drugs may influence BP, it was communicated to participants upfront to refrain from them for at least two hours before the test. Baseline BP levels were measured, and participants who did not exceed the upper limit for prehypertension (<139/89 mm Hg) could continue.

At the beginning of each exercise, a human kinetic technologist demonstrated proper execution. Subsequently, participants were asked to evaluate different weights using a Borg-scale in 3 repetitions. This was done until a weight was found, which participants rated as a 3 on the scale, which is considered a moderate intensity load. Then, the participants stood in front of the Kinect and put on a headset with the microphone. During the experiment, participants were asked to perform 3 different resistance exercises, where each exercise consisted of 3 sets of 10 repetitions, each exercise using a different feedback condition. Participants were instructed to indicate if the load was too high to adjust it and were also informed of their freedom to withdraw from the study at any time.

After each set, participants were instructed to take place on a couch, where they were asked to indicate their rating of perceived exertion (RPE) for the set that was just completed. In addition, their BP was measured to ensure that it stayed within safe bounds. According to the ACSM, exercise should be stopped when BP exceeds 200 mm Hg systolic or 110 mm Hg diastolic, but as an additional precaution, the safety bound was set to <180/105 mm Hg. None of the participants reached this bound. After the exercise was completed (ie, after 3 sets), they were asked to fill out a questionnaire about their perceived competence, interest/enjoyment, and attention regarding the just finished exercise while a cup of water was served. Finally, after completion of the entire exercise session, the subjective experience of the participants was measured using a semistructured interview (Figure 3).

Figure 3. Study procedure. RPE: rating of perceived exertion.



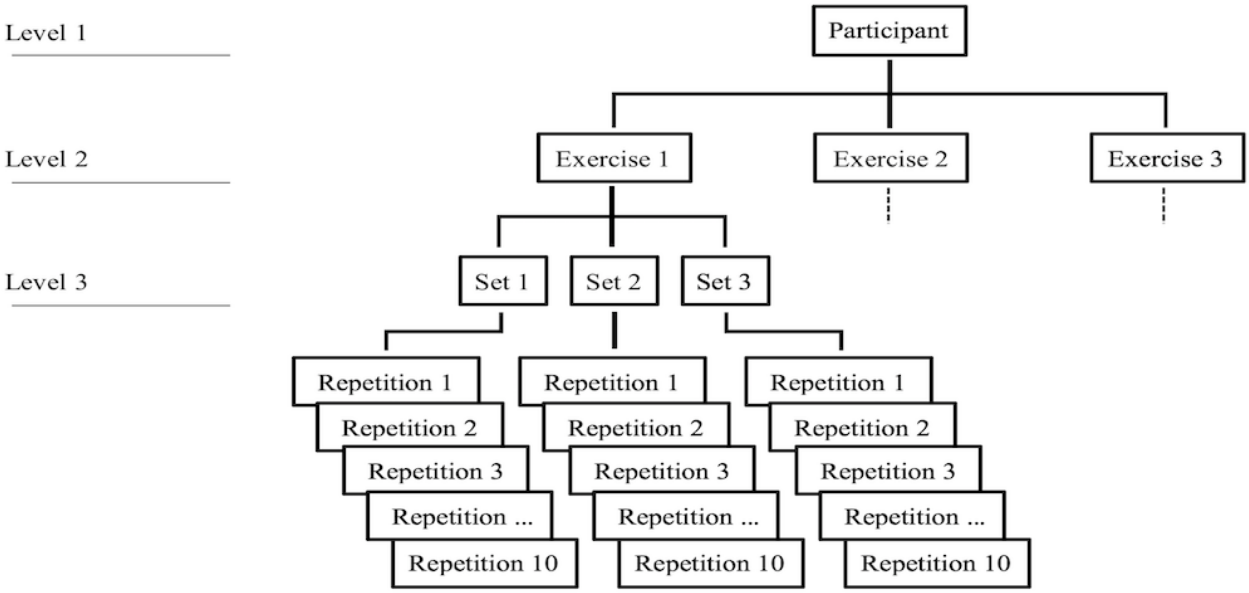
Statistical Analysis

To compare feedback and control conditions on measures of exercise performance and perceptions of exertion, a linear mixed effects regression (LMER) model was used for analysis, as observations on individuals were nested within higher-level groups (Figure 4). Compared with a more traditional approach with repeated-measures analysis of variance (ANOVA) analysis, LMER allows controlling for the variance associated with random factors without data aggregation.

Concentric/eccentric contraction times were compared on the repetition level, whereas concentric/eccentric end points, as well as respiration and RPE, were studied at the set level. To deal with nonindependence, the levels *participant* and *exercise type* were added as random factors. The software package LMER in R [24] was used to conduct the linear mixed effects analysis, where *P* values for the regression coefficients beta verbal, (β_V), beta A/S ($\beta_{A/S}$), beta repetition (β_{rep}), and beta ambient light/sonification ($\beta_{set*A/S}$) were obtained with the LMER test package [25].

Furthermore, to examine differences between feedback conditions on measures of attention, perceived competence, and intrinsic motivation, either a 1-way repeated-measures ANOVA test (in case the normality assumption was satisfied) or a nonparametric Friedman test (in case the normality assumption was violated) was used for analysis.

Figure 4. Hierarchical model.



Results

Descriptive statistics of the contraction times and contraction end points are presented in Table 2. Visual inspection of residual plots revealed a deviation from homoscedasticity and normality for both concentric and eccentric repetition times; therefore, a log10 transformation was applied to the dependent variable before analysis. To investigate whether there was a learning effect over the number of sets and repetitions for each of the feedback conditions, interaction effects with sets and repetitions were included.

Table 2. Descriptive statistics of all behavioral measures for each feedback type.

Contraction metrics	Control, mean (SD)	Verbal, mean (SD)	Ambient lighting and sonification, mean (SD)
Concentric contraction time (second)	2.17 (0.72)	2.76 (0.66)	2.48 (0.75)
Eccentric contraction time (second)	2.69 (0.91)	3.09 (0.75)	2.92 (1.05)
Concentric endpoint variation (mm)	17.93 (9.75)	19.66 (13.74)	15.64 (8.31)
Eccentric endpoint variation (mm)	10.70 (6.89)	12.94 (12.05)	12.77 (8.07)

Concentric Contraction Time

Violin plots of the concentric contraction time for each feedback condition are shown in Figure 5. To examine the effects of feedback on concentric contraction time, a series of linear mixed effects models was fitted using maximum likelihood estimation on log-transformed concentric contraction times. The model for concentric contraction time is shown in Table 3. Compared with the control condition (mean 2.17, SD 0.72), concentric contraction times were significantly higher and closer to the target of 3 seconds in the verbal feedback (mean 2.76, SD 0.66; β_V=.124; *P*<.001) and A/S feedback condition (mean 2.48, SD 0.75; $\beta_{A/S}$=.066; *P*<.001). Subsequent *sets* were performed a little slower (β_{set}=.011, *P*<.001), and within a set, the pace of concentric contractions increased (β_{rep}=−.005; *P*<.001; Figure 5). However, in the case of A/S feedback, concentric contraction times actually decreased from set 1 to set 3 ($\beta_{set*A/S}$=−.029; *P*<.001; Figure 5).

Figure 5. Distributions of concentric (top) and eccentric (bottom) contraction times, colored by condition, and reported per set. A/S: ambient light and sonification.

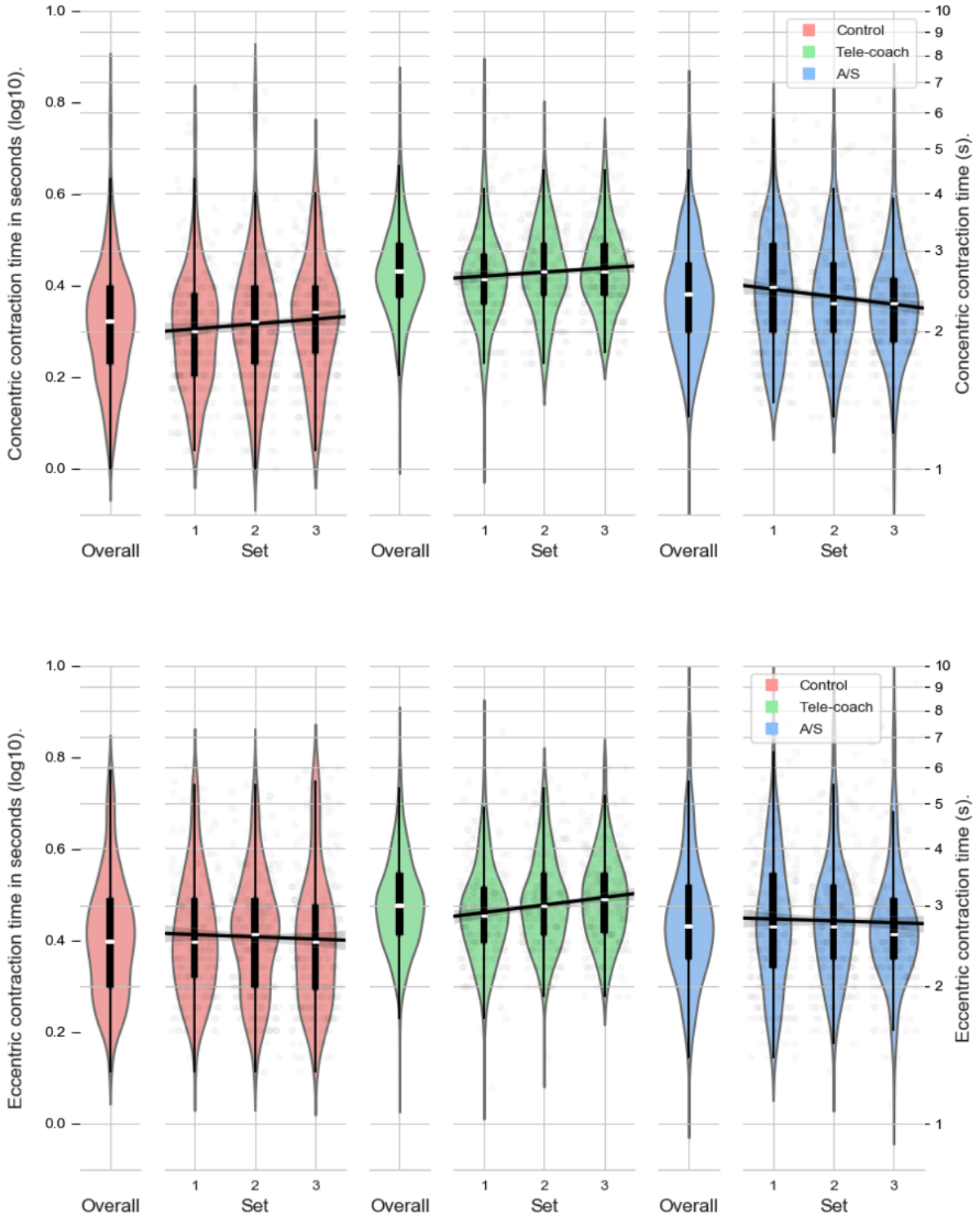


Table 3. Multi-level mixed model parameters.

Modeled parameter[a] and key characteristics of modeled parameter	Beta	SE (beta)	*t* test value
Concentric contractions			
Intercept	.315	.023	14.02[b]
Verbal	.124	.005	25.45[b]
A/S[c]	.066	.005	13.95[b]
Set	.011	.004	2.87[d]
Rep	−.005	.001	−4.53[b]
Set x[e] verbal	−.001	.006	−0.25
Set x A/S	−.029	.006	−5.12[b]
Rep x verbal	−.001	.002	−0.77
Rep x A/S	−.000	.002	−0.53
Eccentric contractions			
Intercept	.408	.033	12.52[b]
Verbal	.082	.005	17.42[b]
A/S	.038	.005	8.33[b]
Set	−.005	.004	−1.25
Rep	−.002	.001	−1.93
Set x Verbal	.020	.005	3.66[b]
Set x A/S	−.001	.005	−0.19
Concentric end points			
Intercept	17.41	2.53	6.87[d]
Verbal	1.73	.40	4.31[b]
A/S	−1.99	.39	−5.07[b]
Set	−1.35	.33	−4.03[b]
Set x Verbal	−3.19	.48	−6.72[b]
Eccentric end points			
Intercept	10.78	3.98	2.71
Verbal	3.89	.29	13.54[b]
A/S	2.02	.28	7.19[b]
Set	−0.75	.24	−3.17[d]
Set x Verbal	1.28	.34	3.76[b]
Set x AS	−0.13	.34	−0.38
Respiration			
Intercept	11.10	.54	20.42[b]
Verbal	1.86	.13	14.22[b]
A/S	3.51	.13	27.03[b]
Set	−.04	.11	−0.36
Set x Verbal	−.46	.16	−2.93[d]

Modeled parameter[a] and key characteristics of modeled parameter	Beta	SE (beta)	*t* test value
Set x AS	−.65	.16	−4.20[b]
Perceived exertion			
Intercept	3.65	.24	14.95[b]
Verbal	.04	.03	1.37
A/S	−.31	.03	−11.72[b]
Set	.15	.02	6.43[b]
Set x Verbal	.02	.03	0.72
Set x AS	−.01	.03	−0.45

[a]For each of the conditions (verbal, A/S, and intercept representing the control condition), slope estimates (beta), their variation across participants (SE), and the *t* test value are given.

[b]*P*<.001.

[c]A/S: ambient lighting and sonification.

[d]*P*<.01.

[e]x: interactions between effects.

Eccentric Contraction Time

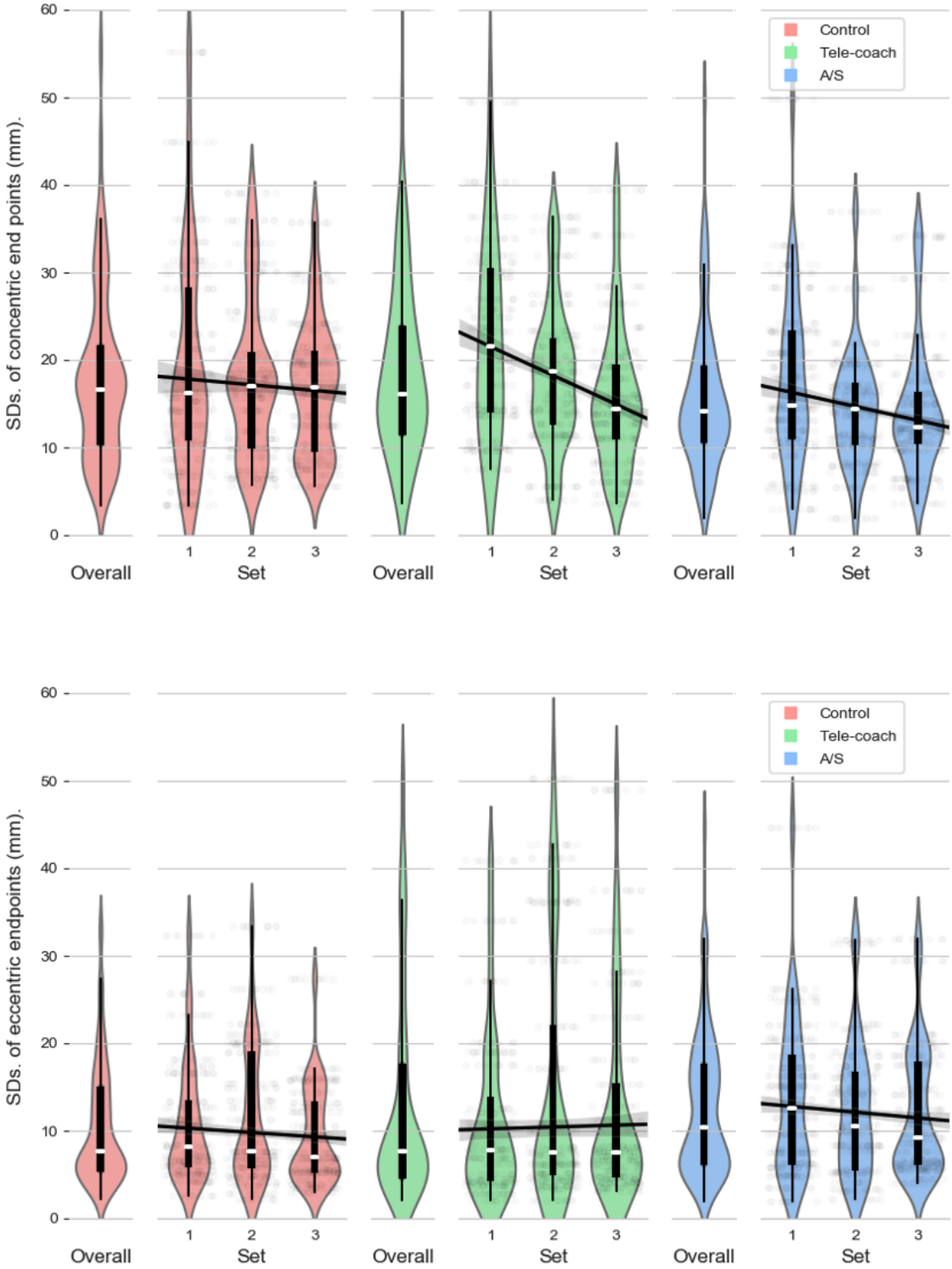
As shown in Figure 5, eccentric contraction times were relative to the control condition (mean 2.69, SD 0.91), significantly higher and closer to the target of 3 seconds in the verbal feedback condition (mean 3.09, SD 0.75; β_V=.082; *P*<.001) and A/S condition (mean 2.92, SD 1.05; $\beta_{A/S}$=.038, *P*<.001). In the case of verbal feedback, later *sets* were performed a little slower (β_V=.020; *P*<.001), but in the control (β_{set}=−.005; *P*=.39) and A/S feedback ($\alpha_{set*A/S}$=−.001, *P*=.85), the pace of eccentric contractions between sets remained constant (Figure 5). Furthermore, an effect of repetitions was found (β_{rep}=−.002; *P*<.001), eccentric contraction times were consistent within each set, as can be seen in Figure 5.

The V (ie, verbal) versus A/S model revealed that eccentric contraction times were significantly lower in the A/S feedback condition (mean 2.92, SD 1.05) compared with the verbal feedback condition (mean 3.09, SD 0.75; $\beta_{V\ vs\ A/S}$=−.044; *P*<.001). However, from Figure 5, it can be tentatively concluded that both feedback types resulted in comparable support in reaching eccentric contraction times close to the instructed pace of 3 seconds.

Concentric End Point Variations

The model for concentric end point variations is shown in Table 3. As can be seen in Figure 6, compared with the control condition (mean 17.94, SD 9.75), the spread of concentric end points per set was significantly higher in the verbal feedback condition (mean 19.66, SD 13.74; β_V=1.73, *P*<.001) but lower in the A/S feedback condition (mean 15.64, SD 8.31; $\beta_{A/S}$=−1.99, *P*<.001). Although on average, participants performed best in the A/S feedback condition over time (Figure 6), there was a stronger decrease in concentric end point variation in the verbal feedback condition (β_{set*V}=−3.19; *P*<.001) compared with the other 2 conditions (β_{set}=−1.35, *P*<.001 and $\beta_{set*A/S}$=−.22, *P*=.64).

Figure 6. Distributions of the variations (standard deviation) in concentric (top) and eccentric (bottom) contraction endpoints colored by condition and reported per set. A/S: ambient light and sonification.



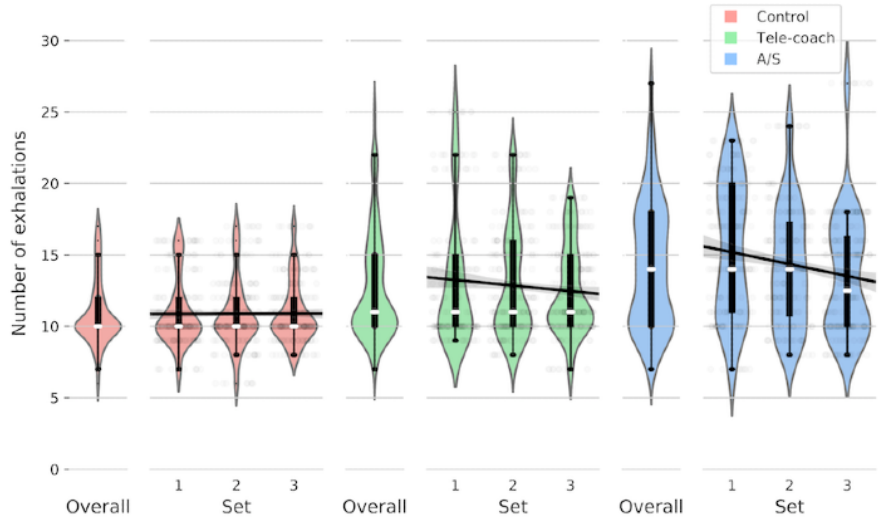
Eccentric End Point Variations

Table 3 shows the results of the linear mixed effects analysis for eccentric end points. Relative to the control condition (mean 10.60, SD 6.89), as shown in Figure 6, variations of eccentric end points per set were significantly higher in the verbal feedback condition (mean 12.94, SD 12.05; β_V=3.89; *P*<.001) and A/S feedback condition (mean 12.77, SD 8.07; $\beta_{A/S}$=2.02; *P*<.001). Eccentric end point variation decreased for every next set in the control and to a similar extent in the A/S feedback condition (β_{set}=−.75, β_{set*V}=−.13; *P*=.70). However, in the case of verbal feedback, the variation in eccentric end points actually increased from set 1 to set 3 (β_V=1.28; *P*<.001), as can also be seen in Figure 6.

Respiration

The results of the linear mixed effects analysis for respiration are displayed in Table 3. As Figure 7 shows, the number of participants' exhalations significantly increased from the control condition (mean 10.88, SD 2.28 exhalations per set) to the verbal feedback condition (mean 12.83, SD 3.86 exhalations per set; β_V=1.86; *P*<.001) as well as to the A/S feedback condition (mean 14.29, SD 4.46 exhalations per set; $\beta_{A/S}$ =3.51; *P*<.001). Furthermore, from Figure 7, it can be tentatively concluded that the number of attempts of Valsalva maneuver did not differ among feedback conditions. Participants did improve over time (Figure 7), showing a decrease in respiration rate with later sets in both the verbal feedback condition (β_{set*V}=−.46; *P*<.001) and A/S feedback condition ($\beta_{set*A/S}$=−.65; *P*<.001). As there was no main effect of the *set*, the rate of respiration remained constant in the control condition (β_{set}=−.04; *P*=.72).

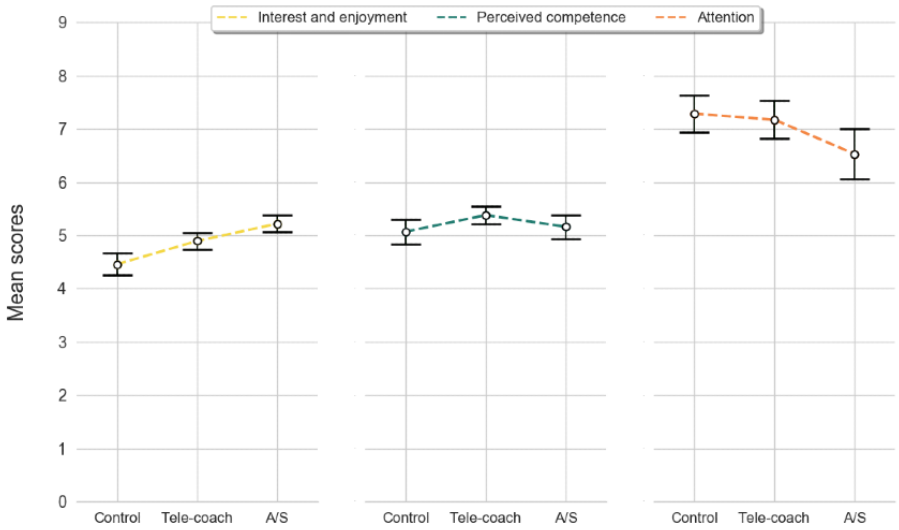
Figure 7. Distribution of total number of exhalations recorded over a set, colored by the condition. A/S: ambient light and sonification.



Perceived Competence

The perceived competence scores are shown in Figure 8. The sonification condition was not normally distributed; therefore, a nonparametric Friedman test was used to investigate intervention effects. There was no significant difference in perceived competence between feedback conditions (χ^2_2=0.6; *P*=.75).

Figure 8. Distributions (mean and SE bars) of scores for psychophysiological measures from left to right: interest/enjoyment, perceived competence, and attention, reported per set. A/S: ambient light and sonification.



Interest/Enjoyment

Interest and enjoyment are shown per condition in Figure 8. A 1-way repeated-measures ANOVA was used to examine whether there was a significant difference in interest/enjoyment among feedback conditions. The Mauchly test of sphericity indicated that the assumption of sphericity was violated (χ^2_2=9.74; *P*=.01); hence, the Huyhn-Feldt Epsilon correction was used. A significant effect of feedback type on interest/enjoyment was

found ($F_{1.666,58.310}$=12.380; P<.001; partial η^2=0.261). Post-hoc pairwise comparisons using the Bonferroni correction revealed that verbal feedback elicited an increase in interest/enjoyment compared with no feedback (mean 4.89, SD 0.95 vs mean 4.46, SD 1.25, respectively), which was significant (P=.03). Exercising with A/S feedback increased interest/enjoyment the most (mean 5.22, SD 0.93), which was significantly different from no feedback (P<.001) and verbal feedback (P=.05).

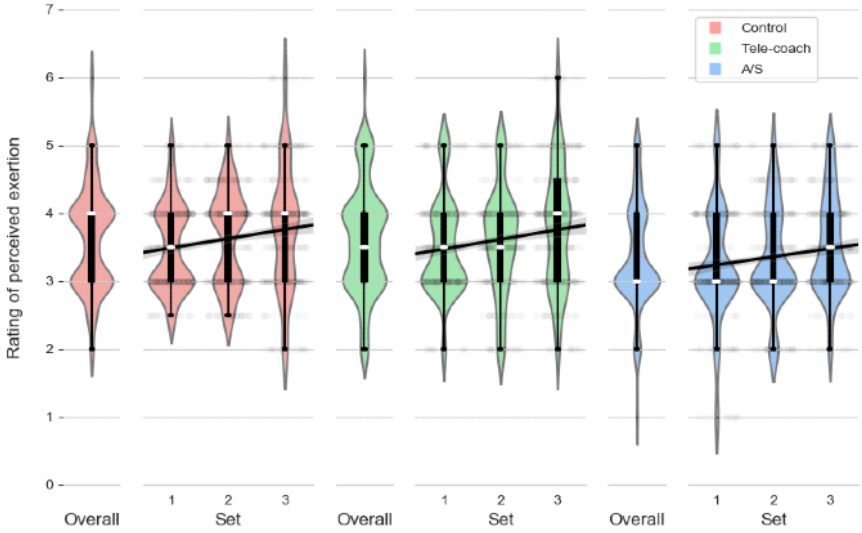
Focus of Attention

The focus of attention is shown in Figure 8. On average, the attention of the participants was more diverted in the A/S feedback condition (mean 6.53, SD 2.81) than in the control (mean 7.29, SD 2.05) and verbal feedback condition (mean 7.17, SD 2.11). However, a Friedman test (the normality assumption was violated for all feedback types) indicated that attention scores were not statistically different among feedback conditions (χ^2_2=0.698; P=.71).

Rating of Perceived Exertion

Results of the linear mixed effects analysis for RPE are presented in Table 3. As can be seen in Figure 9, participants rated their perceived level of exertion to be significantly lower when the exercise was accompanied by A/S feedback (mean 3.37, SD 0.78; $\beta_{A/S}$=−.31; P<.001) compared with the control (mean 3.64, SD 0.76) and verbal feedback (mean 3.64, SD 0.82; $\beta_{V\ vs\ A/S}$=−.36; P<.001). As shown in Figure 9, perceptions of effort increased from set 1 to set 3 (β_{set}=.15; P<.001), and this increase was the same in all conditions (β_{set*V}=.02, P=.47 and $\beta_{set*A/S}$=−.01, P=.65).

Figure 9. RPE per set, colored for each of the 3 conditions. A/S: ambient light and sonification; RPE: rating of perceived exertion.



User Experience

Of the 34 participants, 16 indicated that they preferred the verbal condition, 15 favored the ambient light sonification feedback, and 3 participants indicated they preferred to exercise without the addition of feedback. One participant did not make a clear statement regarding the condition preference.

Discussion

Previous Research

Previous research has used sonification to improve movement in physical activity [26,27]. However, its research base remains scarce, and its application in resistance training is limited. Therefore, this study aimed to investigate its potential as a feedback intervention in the home environment to improve resistance training performance. A feedback system was developed in which the left-hand movement of participants was analyzed and sonified for the purpose of improving exercise performance and compared with a control condition where no feedback is provided and a verbal condition that represents human verbal feedback.

Effect of Ambient Lighting and Sonification Feedback on Exercise Performance

It was found that, in line with our hypothesis, A/S feedback resulted in more consistent concentric and eccentric contraction times with what had been instructed compared with the control. However, compared with the verbal condition, A/S feedback offered less support for concentric contraction times, but to a similar extent for eccentric contraction times. Thus, when people exercised without feedback, they were inclined to go faster than what was instructed, but with the support of verbal feedback as well as A/S feedback, their exercise pace could be corrected. When inspecting the results at the set level, it can be noticed that A/S feedback becomes significantly less effective in providing support for concentric contraction times over the 3 sets. Interview results revealed that about one-third of participants stated that they disliked the sonification used, such as the change in pitch, melody, and corrective earcon, which might explain the decline in performance over sets in this condition. Subsequent research may look into how the sound aesthetics of sonification can be improved and/or personalized to individual preferences.

It was also hypothesized that A/S feedback would support participants with a proper range of motion. The results are mixed, showing more consistent concentric contraction times in this condition, but less consistency for eccentric end points compared with verbal and control conditions. However, the magnitude of the differences between feedback conditions was small, suggesting that people generally have no difficulty in finding the right range of motion.

Moraveji et al [28] demonstrated that people can also adapt their breathing to a visual stimulus without requiring their full attention. However, whether pulsating light can also be effective without requiring people's full attention was not known. The results did not provide evidence for this because the respiration rates of the participants were higher in both feedback conditions than in the control condition, in which their breathing technique adhered most to exercise recommendations. Increased arousal during exercise may reduce the attention allocated to background lighting. The majority of participants mentioned that they found the ambient light unsupportive or did not notice them, where some even mentioned that their breathing technique seemed to worsen because of the light. The results of this study further showed that the respiration rates of the participants were especially high for the first set but started to decrease with subsequent sets. This might indicate a habituation effect to the A/S feedback system that was not accounted for in their first interaction with the system.

Effect of Ambient Lighting and Sonification Feedback on Perceived Competence and Intrinsic Motivation

Past research suggests that fostering people's perception of competence can result in higher quality motivations, which in turn have been found to positively predict exercise adaptation and maintenance [29,30]. It is further suggested that this can be achieved by providing positive and corrective (verbal) feedback [31,32]. However, whether this can also be accomplished through positive and corrective nonspeech feedback (ie, A/S feedback), in a resistance training situation, has not yet been investigated. In contrast with our hypothesis, the results showed that neither verbal nor A/S feedback conditions had a significant effect on perceived competence. Thus, after 3 sets of resistance training with verbal or A/S feedback conditions, participants did not feel more competent than the control in performing the exercise correctly. It was found that participants on average had high scores on perceived competence, regardless of the feedback they received. A possible reason for this is that the 3 exercises selected for this research were easy to carry out or that the weight used to exercise with was not challenging enough. According to Deci et al [33], such feedback promotes competence when the activity provides an optimal challenge. The interview results supported this as the exercises were generally considered to be easy. A more speculative explanation would be that feedback was perceived as negative, which may hamper the positive effects on competence. It might have been that to build confidence, participants needed more time with the A/S feedback system.

The results indicate that people reported to be significantly more intrinsically motivated for the verbal and A/S feedback condition compared with the control, and the A/S feedback condition had a larger effect size than the verbal condition.

Effect of Ambient Lighting and Sonification Feedback on Attentional Focus and Rating of Perceived Exertion

Previous research suggested that auditory and visual stimuli, often in the form of music or video, can be effective dissociative strategies to distract people's attention from internal sensations that may also reduce perceptions of effort [22,34]. There is a clear trend that people in the A/S condition have a more dissociative focus than in the verbal and control conditions. Furthermore, the results indicated that when participants were presented with feedback in both sensory modalities, they reported a significantly lower RPE when compared with the other conditions, even though the initial load was comparable. Thus, it appears that when feedback is presented in both the auditory and visual sensory modality, participants may be more distracted from internal stimuli and, at the same time, report a lower RPE. These results are in line with the effects of music and video on effort [34]. Further research is warranted to examine whether lowering perceived exertion during resistance training in response to dissociative attentional stimuli (ie, feedback) has implications for resistance training adherence.

Comparison to Related Work

In the sonification workshop of Schaffert and Effenberg [13], it was observed that rowing athletes cared primarily about the functional aspect of the sound, and not necessarily its esthetics. This is not in line with the findings in this work, where a considerable subgroup did not enjoy the sonification. This could possibly be because athletes care more about the performance quality of exercises and thus are willing to listen to unrefined sounds if these can aid them in performing better. Both findings were obtained through interviews. A quantitative comparison between sound esthetics might be more conclusive. Yang and Hunt [15] used sonification to guide the movements of bicep curls and achieved similar results as in this study, showing that the feedback has a positive effect on the pacing of the movement. They also showed a higher enjoyment when the feedback system was used in comparison with the control, similar to the increased enjoyment measured with the IMI in this study.

As for ambient light as a mechanism to guide the pace of breathing, previous studies have shown that people are able to synchronize their breathing to visual cues, such as during radiotherapy [16], to reduce people's motion. This is not what was observed in this study. However, most of these studies were set up so that the full attention of the participants was focused on the visual cue. Findings by Brandt [35] showed that participants do not synchronize their pace of breathing well to the ambient light when not explicitly instructed to do so. The increase in arousal during exercise in this study might have also limited the attention pool available to focus on the ambient light and thus resulted in a similar effect, where people did not respond to the ambient light.

Limitations and Future Research

There are limitations to this study. It could be that participants may have mixed up the ambient light and sonification feedback,

trying to align breathing to sonic feedback instead of visual stimuli, and vice versa. Interview results suggest that this was unlikely, as most participants clearly noted that the visual stimuli were not supportive for breathing, suggesting that participants knew how to interpret the stimuli, but future research is warranted to investigate the stimuli separately. Next, the limited challenge associated with the light weights might have influenced the measure of perceived competence, and future research should study how the measures are affected under different intensity levels. Finally, the study was limited in duration and may have been sufficient to account for habituation effects to the system, and longitudinal aspects of a resistance exercise intervention are unknown, both of which provide opportunities for future study.

Conclusions

An ambient lighting/sonification (A/S) feedback system was evaluated for its ability to support individuals in performing resistance exercise according to guidelines in a home setting. It was contrasted against a control condition in which participants did not receive feedback and a reference condition in which a human verbally provided feedback. Although the verbal condition was best at enhancing concentric contraction times, the developed concept of A/S feedback also succeeded in improving participants' contraction times compared with the control. Furthermore, it improved the range of motion, where it improved concentric contraction end points more than verbal and control, and eccentric contraction end points more than control only. Ambient light turned out to be unsupportive of a proper breathing technique during resistance exercise. With respect to psychological determinants of physical activity, both A/S feedback and verbal conditions failed to promote perceptions of competence. Participants did, however, report higher levels of intrinsic motivation for A/S compared with both verbal and control conditions. Finally, it was found that the A/S feedback resulted in a trend where participants reported having a more dissociative focus while also reporting a significantly lower perception of effort. It would be interesting to test in future studies whether a combination of auditory and visual feedback may be used during resistance training to lower perceptions of effort, which could potentially increase exercise adherence. In this study, A/S feedback assistance seemed to improve exercise execution and psychosocial attitude of individuals who were normotensive and prehypertensive when performing a single session of home-based resistance exercise in comparison to using no feedback at all, but there was no clear advantage over a human tele-coach providing verbal feedback.

Conflicts of Interest

MR and FS work for Royal Philips Electronics. NB and TP were conducting their internships at Philips Research when the study was performed. All other authors have no conflicts of interest.

Multimedia Appendix 1
Permutations diagram.
[PNG File , 122 KB - cardio_v4i1e16354_app1.png]

References

1. World Health Organization. 2013. A Global Brief on Hypertension: Silent Killer, Global Public Health Crisis URL: https://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/ [accessed 2020-05-21]
2. Dickinson HO, Mason JM, Nicolson DJ, Campbell F, Beyer FR, Cook JV, et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. J Hypertens 2006 Feb;24(2):215-233. [doi: 10.1097/01.hjh.0000199800.72563.26] [Medline: 16508562]
3. Task Force for the Management of Arterial Hypertension of the European Society of Hypertension, Task Force for the Management of Arterial Hypertension of the European Society of Cardiology. 2013 ESH/ESC guidelines for the management of arterial hypertension. Blood Press 2013 Aug;22(4):193-278. [doi: 10.3109/08037051.2013.812549] [Medline: 23777479]
4. Radha M, Willemsen MC, Boerhof M, IJsselsteijn WA. Lifestyle Recommendations for Hypertension through Rasch-Based Feasibility Modeling. In: Proceedings of the 2016 Conference on User Modeling Adaptation and Personalization. 2016 Presented at: UMAP'16; July 13-17, 2016; Halifax, Canada. [doi: 10.1145/2930238.2930251]
5. Pescatello LS. Exercise and hypertension: recent advances in exercise prescription. Curr Hypertens Rep 2005 Aug;7(4):281-286. [doi: 10.1007/s11906-005-0026-z] [Medline: 16061047]
6. Sorace P, Churilla JR, Magyari PM. Resistance training for hypertension. ACSM Health Fit J 2012;16(1):13-18. [doi: 10.1249/fit.0b013e31823d0079]
7. ACSM's Guidelines for Exercise Testing and Prescription. Baltimore, MA: Lippincott Williams & Wilkins; 2013.
8. Uzun S, Kara B, Yokuşoğlu M, Arslan F, Yilmaz MB, Karaeren H. The assessment of adherence of hypertensive individuals to treatment and lifestyle change recommendations. Anadolu Kardiyol Derg 2009 Apr;9(2):102-109 [FREE Full text] [Medline: 19357051]
9. Biddle SJ, Mutrie N. Psychology of Physical Activity: Determinants, Well-Being and Interventions. Abingdon, United Kingdom: Routledge; 2007.

10. Tobi P, Estacio EV, Yu G, Renton A, Foster N. Who stays, who drops out? Biosocial predictors of longer-term adherence in participants attending an exercise referral scheme in the UK. BMC Public Health 2012 May 11;12:347 [FREE Full text] [doi: 10.1186/1471-2458-12-347] [Medline: 22578185]
11. Hermann T, Hunt A, Neuhoff JG. The Sonification Handbook. Berlin, Germany: Logos Verlag Berlin; 2011.
12. Kramer G. Auditory Display: Sonification, Audification, And Auditory Interfaces. New York, USA: CRC Press; 1995.
13. Schaffert N, Mattes K, Effenberg AO. SMARTech - Georgia Tech. 2011. The sound of Rowing Stroke Cycles as Acoustic Feedback URL: https://smartech.gatech.edu/handle/1853/51919 [accessed 2020-05-21]
14. Smith KM, Claveau D. SMARTech - Georgia Tech. 2014. The Sonification and Learning of Human Motion URL: https://smartech.gatech.edu/handle/1853/52049 [accessed 2020-04-21]
15. Yang J, Hunt A. SMARTech - Georgia Tech. 2015. Real-time sonification of biceps curl exercise using muscular activity and kinematics URL: https://smartech.gatech.edu/handle/1853/54152 [accessed 2020-05-21]
16. George R, Chung TD, Vedam SS, Ramakrishnan V, Mohan R, Weiss E, et al. Audio-visual biofeedback for respiratory-gated radiotherapy: impact of audio instruction and audio-visual biofeedback on respiratory-gated radiotherapy. Int J Radiat Oncol Biol Phys 2006 Jul 1;65(3):924-933. [doi: 10.1016/j.ijrobp.2006.02.035] [Medline: 16751075]
17. Rambaudi LR, Rossi E, Mántaras MC, Perrone MS, Siri LN. Visual aided pacing in respiratory maneuvers. J Phys: Conf Ser 2007 Dec 6;90:012034. [doi: 10.1088/1742-6596/90/1/012034]
18. Linsenbardt ST, Thomas TR, Madsen RW. Effect of breathing techniques on blood pressure response to resistance exercise. Br J Sports Med 1992 Jun;26(2):97-100 [FREE Full text] [doi: 10.1136/bjsm.26.2.97] [Medline: 1623367]
19. Dale Phurrough. 2017. dp.kinect2 extension for Cycling ’74 Max (Version 1.1) URL: https://hidale.com/shop/dp-kinect2/ [accessed 2020-05-21]
20. Borg G. Borg's Perceived Exertion and Pain Scales. Champaign, Illinois: Human Kinetics; 1998.
21. Day ML, McGuigan MR, Brice G, Foster C. Monitoring exercise intensity during resistance training using the session RPE scale. J Strength Cond Res 2004 May;18(2):353-358. [doi: 10.1519/R-13113.1] [Medline: 15142026]
22. Razon S, Basevitch I, Land W, Thompson B, Tenenbaum G. Perception of exertion and attention allocation as a function of visual and auditory conditions. Psychol Sport Exerc 2009 Nov;10(6):636-643. [doi: 10.1016/j.psychsport.2009.03.007]
23. McAuley E, Duncan T, Tammen VV. Psychometric properties of the intrinsic motivation inventory in a competitive sport setting: a confirmatory factor analysis. Res Q Exerc Sport 1989 Mar;60(1):48-58. [doi: 10.1080/02701367.1989.10607413] [Medline: 2489825]
24. Gałecki A, Burzykowski T. Linear Mixed-Effects Models Using R: A Step-by-Step Approach. New York, USA: Springer Publications; 2010.
25. Kuznetsova A, Brockhoff P, Christensen RH, Brockhoff PB, Christensen RH, Kuznetsova TA, et al. Science Open. 2014. Lmertest: Tests for Random and Fixed Effects for Linear Mixed Effect Models (Lmer Objects of Lme4 Package) URL: https://www.scienceopen.com/document?vid=2824d3b1-0469-424c-8ae3-d06688168d2b [accessed 2020-05-21]
26. Cesarini D, Hermann T, Ungerechts BE. An Interactive Sonification System for Swimming Evaluated by Users. In: Proceedings of the Conference on Sonification of Health and Environmental Data. 2014 Presented at: SoniHED'19; August 15, 2014; York, UK. [doi: 10.13140/2.1.4665.9845]
27. Yang J, Hunt A. Sonic Trainer: Real-time Sonification of Muscular Activity and Limb Positions in General Physical Exercise. In: Proceedings of the 4th Interactive Sonification Workshop. 2013 Presented at: ISW'13; December 10, 20132013; Erlangen, Germany URL: https://tinyurl.com/ydftlfu5
28. Moraveji N, Olson B, Nguyen T, Saadat M, Khalighi Y, Pea R, et al. Peripheral Paced Respiration: Influencing User Physiology During Information Work. In: Proceedings of the 24th Annual ACM Symposium on User Interface Software and Technology. 2011 Presented at: UIST'11; October 16-19, 2011; Santa Barbara, CA. [doi: 10.1145/2047196.2047250]
29. Markland D. Self-determination moderates the effects of perceived competence on intrinsic motivation in an exercise setting. J Sport Exercise Psy 1999;21(4):351-361. [doi: 10.1123/jsep.21.4.351]
30. Vallerand RJ, Reid G. On the causal effects of perceived competence on intrinsic motivation: a test of cognitive evaluation theory. J Sport Psychol 1984;6(1):94-102. [doi: 10.1123/jsp.6.1.94]
31. Amorose AJ, Horn TS. Intrinsic motivation: relationships with collegiate athletes' gender, scholarship status, and perceptions of their coaches' behavior. J Sport Exercise Psy 2000;22:63-84. [doi: 10.1123/jsep.22.1.63]
32. Black SJ, Weiss MR. The relationship among perceived coaching behaviors, perceptions of ability, and motivation in competitive age-group swimmers. J Sport Exercise Psy 1992;14(3):309-325. [doi: 10.1123/jsep.14.3.309]
33. Deci EL, Ryan R. Intrinsic Motivation and Self-Determination in Human Behavior. New York, USA: Springer; 1985.
34. Yamashita S, Iwai K, Akimoto T, Sugawara J, Kono I. Effects of music during exercise on RPE, heart rate and the autonomic nervous system. J Sports Med Phys Fitness 2006 Sep;46(3):425-430. [Medline: 16998447]
35. Brandt I. SematicScholar. 2010. The Influence of Rhythmic Changes in Lighting on Breathing Rhythm and Relaxation URL: https://www.semanticscholar.org/paper/The-influence-of-rhythmic-changes-in-lighting-on-Brandt/abe788ed07054ff0699ba81a14af25cd0edaf732 [accessed 2020-05-21]

Abbreviations

A/S: ambient light and sonification
ACSM: American College of Sports Medicine
ANOVA: analysis of variance
BP: blood pressure
IMI: intrinsic motivation inventory
LMER: linear mixed effects regression
RPE: rating of perceived exertion

Edited by G Eysenbach; submitted 21.09.19; peer-reviewed by J Edwards, E Bellei; comments to author 09.12.19; revised version received 21.01.20; accepted 06.02.20; published 29.06.20.

Please cite as:
Radha M, den Boer N, Willemsen MC, Paardekooper T, IJsselsteijn WA, Sartor F
Assisting Home-Based Resistance Training for Normotensive and Prehypertensive Individuals Using Ambient Lighting and Sonification Feedback: Sensor-Based System Evaluation
JMIR Cardio 2020;4(1):e16354
URL: https://cardio.jmir.org/2020/1/e16354
doi:10.2196/16354
PMID:32597789

Original Paper

Minimal Patient Clinical Variables to Accurately Predict Stress Echocardiography Outcome: Validation Study Using Machine Learning Techniques

Mohamed Bennasar[1], BSc, MSc, PhD; Duncan Banks[2], BSc, PhD; Blaine A Price[1], MSc; Attila Kardos[3], MD, PhD

[1]School of Computing and Comms, The Open University, Milton Keynes, United Kingdom

[2]School of Life, Health and Chemical Sciences, The Open University, Milton Keynes, United Kingdom

[3]Department of Cardiology, Milton Keynes University Hospital NHS Foundation Trust, Milton Keynes, United Kingdom

Corresponding Author:
Duncan Banks, BSc, PhD
School of Life, Health and Chemical Sciences
The Open University
Walton Hall
Milton Keynes,
United Kingdom
Phone: 44 190 865 9198
Email: Duncan.Banks@open.ac.uk

Abstract

Background: Stress echocardiography is a well-established diagnostic tool for suspected coronary artery disease (CAD). Cardiovascular risk factors are used in the assessment of the probability of CAD. The link between the outcome of stress echocardiography and patients' variables including risk factors, current medication, and anthropometric variables has not been widely investigated.

Objective: This study aimed to use machine learning to predict significant CAD defined by positive stress echocardiography results in patients with chest pain based on anthropometrics, cardiovascular risk factors, and medication as variables. This could allow clinical prioritization of patients with likely prediction of CAD, thus saving clinician time and improving outcomes.

Methods: A machine learning framework was proposed to automate the prediction of stress echocardiography results. The framework consisted of four stages: feature extraction, preprocessing, feature selection, and classification stage. A mutual information–based feature selection method was used to investigate the amount of information that each feature carried to define the positive outcome of stress echocardiography. Two classification algorithms, support vector machine (SVM) and random forest classifiers, have been deployed. Data from 529 patients were used to train and validate the framework. Patient mean age was 61 (SD 12) years. The data consists of anthropological data and cardiovascular risk factors such as gender, age, weight, family history, diabetes, smoking history, hypertension, hypercholesterolemia, prior diagnosis of CAD, and prescribed medications at the time of the test. There were 82 positive (abnormal) and 447 negative (normal) stress echocardiography results. The framework was evaluated using the whole dataset including cases with prior diagnosis of CAD. Five-fold cross-validation was used to validate the performance of the framework. We also investigated the model in the subset of patients with no prior CAD.

Results: The feature selection methods showed that prior diagnosis of CAD, sex, and prescribed medications such as angiotensin-converting enzyme inhibitor/angiotensin receptor blocker were the features that shared the most information about the outcome of stress echocardiography. SVM classifiers showed the best trade-off between sensitivity and specificity and was achieved with three features. Using only these three features, we achieved an accuracy of 67.63% with sensitivity and specificity 72.87% and 66.67% respectively. However, for patients with no prior diagnosis of CAD, only two features (sex and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use) were needed to achieve accuracy of 70.32% with sensitivity and specificity at 70.24%.

Conclusions: This study shows that machine learning can predict the outcome of stress echocardiography based on only a few features: patient prior cardiac history, gender, and prescribed medication. Further research recruiting higher number of patients who underwent stress echocardiography could further improve the performance of the proposed algorithm with the potential of facilitating patient selection for early treatment/intervention avoiding unnecessary downstream testing.

(JMIR Cardio 2020;4(1):e16975) doi:10.2196/16975

KEYWORDS

stress echocardiography; coronary heart disease; risk factors; machine learning; feature selection; risk prediction

Introduction

Cardiovascular disease (CVD) is the leading cause of death in Western societies [1]. In the United Kingdom, 7.4 million people are living with CVD, which is more than twice the number of people who suffer from cancer and Alzheimer disease. More than 43,000 people under the age of 75 die each year due to CVD costing national health services in the United Kingdom about £9 billion (US $11 billion) [2]. Coronary artery disease (CAD) is the most common form of CVD and may lead to sudden death [3].

Diagnosing CAD early can save lives and reduce risk of myocardial infarction and stroke. Diagnostic procedures are typically performed in specialized cardiac centers to diagnose CAD and risk stratify patients using tests such as a stress echocardiogram. Stress echocardiography is a diagnostic tool to assess the functionality of the heart and blood delivery under stress, such as treadmill or bicycle exercise test or following administration of a drug such as dobutamine. Dobutamine is a pharmacological agent administered intravenously to increase the heart rate in a similar way that would occur during physical exercise. During dobutamine stress echocardiography, incremental doses of dobutamine in 3-minute stages are administered until the termination of the test criteria is achieved. The principle of stress echocardiography is to increase the myocardial oxygen uptake/demand; if the supply is insufficient due to blocked heart arteries, echocardiographic features of this mismatch can be detected by identifying regional wall motion abnormalities in the underperfused heart muscle region during the test. Echocardiographic images are acquired at rest, during the intermediate stage, peak stress, and in recovery. The classical criteria were used as a termination of the test (ie, target heart rate achieved, development of typical chest pain symptoms with or without regional wall motion abnormalities, hemodynamically significant arrhythmias, or development of symptomatic hypotension). Positive or abnormal stress echocardiography is defined as developments of new regional wall motion abnormalities. Wall motion abnormalities were defined as hypokinesia if the wall thickness was maintained and the endocardial excursion was between 5 and 2 mm, akinesia if the wall thickness was reduced and the endocardial excursion was less than 2 mm, and dyskinesia if the wall thickness was reduced and the endocardial excursion was outward moving in systole. Dobutamine stress echocardiography has a sensitivity and specificity of 83% and 86%, respectively [4]. A computer-based algorithm in image analysis and interpretation can play a significant role in the early diagnosis of CAD. Many machine learning–based methods have been devolved for image analysis to aid diagnosis and prognostic monitoring of CAD [5].

Machine learning is a term used to define computer algorithms that can be trained to learn the patterns in training data. These algorithms are then effectively able to make predictions on unseen data. The ability of machine learning techniques to learn from experience without any explicit guidelines for the program or following any predefined rules is making these techniques increasingly popular in many domains [6]. Machine learning in health care has enormous potential in supporting health care practitioners in decision making, enhancing diagnostic accuracy, and reducing health care cost [7]. Machine learning can be used as part of a computer-aided clinician decision support system to assimilate patterns and act as an appropriate source of knowledge.

Several frameworks that employ machine learning for CAD prediction have been proposed [8]. These techniques are used either for predicting the outcome of observations or discovering the hidden pattern and structure in the data not readily recognizable to humans. The data often used for this kind of research include patient anthropometric data, blood test results, and data obtained from various investigation modalities used in the diagnosis of CAD such as electrocardiography, computed tomography angiography, and transthoracic echocardiography [8].

Clinical data have been used to predict coronary events: Voss et al [9] used 10 years of follow-up data from 5159 middle-age men with a 6.3% incidence of coronary events during that period of time. Multilayer perceptron was used to build their model. The study involved 57 clinical and laboratory variables to train the multilayer perceptron. The reported results showed that the area under the curve was 0.89. Gharehchopogh and Khalifelu [10] employed deep learning as a learning algorithm for building a prediction model; the learning algorithm was trained using data from 40 participants that included age, sex, hypertension, and smoking. The reported classification accuracy was 0.85 for heart failure cases.

Another study employed machine learning on clinical and laboratory data of 378,256 patients to predict the first CVD event [11]. The data used consisted of 30 attributes including risk factors, laboratory data, medications, and information about history of CVD and other chronic diseases such as poor mental health, chronic obstructive pulmonary disease, kidney disease, and rheumatoid arthritis. The authors applied four machine learning algorithms: random forest, logistic regression, gradient boosting, and neural networks. The reported results showed that the best performance was achieved by the neural network algorithm with a sensitivity of 67.5% and specificity of 70.7%.

In this pilot study, we aimed to investigate the performance of a machine learning algorithm in predicting the stress echocardiography outcome in patients investigated for suspected CAD. Unlike previous research, we are testing a sophisticated feature selection method to investigate the significance of cardiovascular risk factors, current medication, and anthropometric data in this prediction.

Methods

Population and Data Sources

The cohort of patients was derived from the Cardiology Department at Milton Keynes University Hospital in the United Kingdom. Anonymized clinical data had been extracted from patients' electronic records, predominantly based on the very detailed stress echocardiography reports introduced prospectively by one author (AK), a senior cardiologist, at the time of the development of stress echocardiography services in the hospital. We included all patients (n=563) examined using dobutamine stress echocardiography between 2002 and 2004 with available data. However, we excluded 34 patients who had incomplete clinical data about their risk factors, leaving 529 for this study.

This study used real patient data, which can raise some ethical concerns such as the patient's permission to use their data and any confidential information that may exposed because of this research. This was resolved by having hospital staff, the direct clinical care provider, anonymize the records before they were sent for analysis. This study was registered by the institutional clinical governance department, Milton Keynes University Hospital (clinical governance project reference number: 33).

Table 1 summarizes patient characteristics for the whole population and separately for the two groups with positive and negative stress echocardiography results. All of these patients had a complete dataset for the anthropometric variables; risk factors such as gender, age, weight, family history (defined as having a first-degree relative who had a myocardial infarction or died suddenly below the age of 60 years), diabetes, smoking status, hypertension, hypercholesterolemia, and prior history of CAD; prescribed medication related to CAD including beta receptor blockers, calcium channel blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACE-I/ARB), antiplatelets, nitrates, statins, and diuretics; and the stress echocardiography results. The features in the table describe the number of patients who have that risk factor positive, for example; 306 of the total 529 participants had hypertension, and 313 of them had abnormal serum cholesterol level.

Table 1. Characteristics of patients and their stress echocardiography outcome.

Characteristic	Total (n=529)	SE[a] positive (n=82)	SE negative (n=447)
Risk factor			
Sex, male, n (%)	249 (47.1)	61 (74.4)	188 (42.1)
Age in years, mean (SD)	61.23 (11.83)	62.92 (10.56)	60.93 (12.06)
Weight (kg), mean (SD)	80.82 (17.25)	83.06 (15.88)	80.45 (17.49)
Hypertension, n (%)	306 (57.8)	42 (51.2)	264 (59.0)
Hypercholesterolemia, n (%)	313 (59.2)	50 (61.0)	263 (58.8)
Smoking, n (%)			
Ex-smoker	107 (20.2)	24 (29.3)	83 (18.5)
Nonsmoker	330 (62.4)	40 (48.8)	290 (64.8)
Smoker	92 (17.4)	18 (22.0)	74 (16.5)
Diabetes mellitus, n (%)	99 (18.7)	19 (23.2)	80 (17.8)
Family history, n (%)	223 (42.2)	35 (42.7)	188 (42.0)
Prior history of CAD[a], n (%)	123 (23.3)	40 (48.8)	83 (18.5)
Medication, n (%)			
Beta receptor blocker	281 (53.1)	58 (70.7)	223 (49.8)
Calcium channel blocker	137 (25.9)	22 (26.8)	115 (25.7)
ACE-I/ARB[a]	258 (48.8)	59 (72.0)	199 (44.5)
Antiplatelet therapy	344 (65.0)	64 (78.0)	280 (62.3)
Nitrate	159 (30.1)	36 (43.9)	123 (27.5)
Statin	314 (59.4)	59 (72.0)	255 (57.0)
Diurectic	129 (24.4)	23 (28.0)	106 (23.7)

[a]SE: stress echocardiography

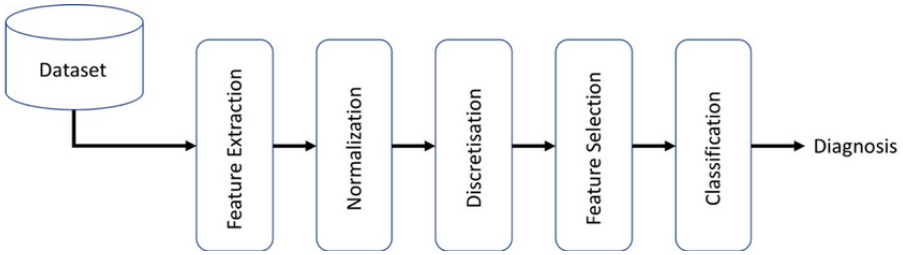
[a]CAD: coronary artery disease.

[a]ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker.

Proposed Framework

The collected data were used to predict the outcome of the stress test based on the patient's clinical information. Figure 1 shows the architecture of the framework that was used to study the risk factors and medication (referred to as features in this article); we then used these features to investigate the prediction power of this clinical data. Raw data were received as a mixture of text and numerical values. Therefore, the first stage in the proposed framework was the preprocessing stage where natural language processing was used to extract and quantify the needed information from the text, including sex, age, weight, risk factors, medications, and the final outcome of the stress test (positive/negative). The criteria shown in Table 1 were used to convert the text into numerical values.

Figure 1. Experiment framework.



Feature normalization is the second stage used for continuous features (age and weight), which are normalized using the following equation for normalizing continuous features: .

Two normalized features were then discretized using the equal width discretization method: , where N is the number of bins [12]. In this method, the value of these features is allocated to one of the decimal numbers between 1 and 10. This method divides the range of the feature values into 10 bins of equal width.

Each feature value is assigned to a bin based on the range into which it falls. The reason for the discretization stage is that most of the machine learning algorithms perform better with discretized data [13]. Due the bias of the feature selection stage on the continuous features [14], the discretization stage is also needed to discretize these features before they were submitted to the feature selection stage.

Feature selection, the fourth stage in this framework, is a set of techniques used to measure the significance of each feature for predicting the class label (outcome of the stress test). In this study, the joint mutual information maximization (JMIM) filter feature selection method [15] is used to rank the features according to the amount of information the feature adds to the selected subset. The method measures the amount of information that each feature shares with the class. At the end of this stage, all features (sex, age, weight, risk factors, and medications) will be ranked based on their significance in predicting the class label. This method has been developed based on information theory [16], and the mechanism of the method is explained below.

The value of mutual information between any two variables can be calculated using entropy. It is the amount of uncertainty about a random variable. Suppose $F = \{f_1,f_2,....f_N\}$ is a discrete variable and $C = \{c,c,....c_N\}$ is a class label; the probability density function is .

The mutual information equation between F and C is as follows:

The JMIM method employs the maximum of the minimum criterion. The feature selected by the JMIM method is the one that maximizes the goal function, shown below, where $I(f_i,f_s;C)$ is the joint mutual information between the candidate feature and the features already selected in the previous iteration. The method employs the forward greedy search algorithm, seen below the equation.

The method does not rank the features based on their individual discriminative power, it selects the features that provide the most information as a subgroup; the interaction information between the features is important in selecting the next significant feature. Therefore, if the list of submitted features is changed, the rank order may be different. The whole dataset was submitted to the JMIM method to identify the significant subset of features (clinical variables). Smialowski et al [17] reported that the feature selection stage should be included within folds-cross validation. However, that can cause instability to the results of the feature selection as submitting data with different instances may lead to different values of probability density function which consequently may lead to changes in the order of the significant features. This paper aims to define the clinical variables that can best predict the outcome of stress echocardiography in the diagnosis of CAD. Therefore, the whole dataset was used at the feature selection stage to take advantage of each valuable instance in the data.

The outcome of the stress test was predicted in the classification stage. Two alternative classifiers were tested at this stage: support vector machine (SVM) [18] and random forest classifiers [19]. The performance of each classifier was evaluated using 5-fold cross-validation. The dataset is imbalanced; there are more than 4 times the negative stress echocardiograms in the data than positive stress echocardiography cases. To overcome this problem, more weight was given to the minority class, and a ratio of 4:1 has been used with SVM; this means giving the minority class 4 times the weight that is given to the majority class. Due to this skewness in the number of classes, classification accuracy will not be a

good measure for the performance, as it will be affected mainly by the ability of the classifier to recognize the majority of classes correctly. Therefore, sensitivity and specificity were used to provide a measure for the performance of the classifier in correctly classifying each class.

The data were randomly divided into 5 folds, with 4 of them used to train the classifier and 1 for testing, and then this process was repeated 4 more times, at each time 4 folds were used for training and 4 of the folds that had never been used for testing before was used to test the classifier. At each time, the accuracy, sensitivity, and specificity were calculated. The overall accuracy, sensitivity, and specificity are the average of the 5.

To find the subset of features that produces the best prediction performance, the classifier is trained and tested after adding every feature according to its rank identified at the feature selection stage.

Results

The proposed framework was used to study the whole dataset including the risk factors and medications, and it was also used to study a subset of the dataset that excluded the cases with prior CAD to investigate the influence of this variable on the performance of the model. Table 2 shows the characteristics of this subset of patients referred to in the rest of this paper as the subdataset.

The prevalence of abnormal stress echocardiography was 15.5%. A total of 447 patients had negative stress echocardiography results (84.5%). There were fewer women than men within the positive group, and the opposite was true with the negative stress echocardiography results. Mean age was 62.92 (SD 10.56) years and 60.93 (SD 12) years in the positive and negative groups, respectively (Table 1).

The feature selection stage was used to rank the features (clinical variables) in the whole dataset, and the significant features for the whole dataset are depicted by Table 3. The table shows that for the whole cohort of patients, CAD is the most significant feature for predicting stress echocardiography outcome, followed by sex, ACE-I/ARB use, and smoking status.

The results showed that prior CAD has the strongest power to distinguish between positive and negative stress echocardiography results. Sex appeared second because most of the positive cases were male, and most of the negative were female. ACE-I/ARB use was the only applied medication among the five most significant features. On the other hand, age, family history, and diabetes appeared the least contributory features in this model.

Table 2. Characteristics of patients and their stress echocardiography outcome in those with no prior ischemic heart disease.

Characteristic	SE[a] positive (n=42)	SE negative (n=364)
Risk factor		
Sex, male, n (%)	33 (78.6)	147 (40.4)
Age in years, mean (SD)	64.28 (9.80)	60.96 (12.20)
Weight (kg), mean (SD)	80.31 (13.18)	80.46 (17.37)
Hypertension, n (%)	25 (59.5)	216 (59.3)
Hypercholesterolemia, n (%)	33 (78.6)	219 (60.1)
Smoking, n (%)		
Ex-smoker	13 (31.0)	13 (3.5)
Nonsmoker	17 (40.5)	227 (62.3)
Smoker	12 (28.6)	65 (17.8)
Diabetes mellitus, n (%)	6 (14.3)	67 (18.4)
Family history, n (%)	17 (40.5)	132 (36.2)
Medication, n (%)		
Beta receptor blocker	28 (66.7)	166 (45.6)
Calcium channel blocker	9 (21.4)	89 (24.4)
ACE-I/ARB[a]	32 (76.2)	148 (40.6)
Antiplatelet therapy	34 (81.0)	216 (59.3)
Nitrate	24 (57.1)	95 (26.1)
Statin	29 (69.0)	201 (55.2)
Diurectic	12 (28.6)	87 (23.9)

[a]SE: stress echocardiography.

[a]ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

Table 3. Feature rankings.

No	Feature
1	Prior diagnosis of coronary artery disease
2	Sex
3	ACE-I/ARB[a]
4	Weight
5	Smoking status
6	Beta receptor blocker
7	Hypercholesterolemia
8	Antiplatelet therapy
9	Statin
10	Nitrate
11	Hypertension
12	Calcium channel blocker
13	Diuretic
14	Diabetes mellitus
15	Family history
16	Age

[a]ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker.

Feature selection has been also applied on the subdataset. The order of the features was slightly different as the prior CAD feature was excluded from the data. Table 4 depicts the order of the features, and it shows that sex, ACE-I/ARB, cholesterol, nitrates, and smoking status are the five most significant features. The only difference from the previous results when the whole dataset was used is the swap between serum cholesterol and smoking status. Serum cholesterol status became the third most significant feature followed by nitrates medication, which was not among the most important.

Table 4. Feature ranking in the model for patients with no prior ischemic heart disease.

No	Feature
1	Sex
2	ACE-I/ARB[a]
3	Hypercholesterolaemia
4	Nitrate
5	Smoking status
6	Statin
7	Weight
8	Beta receptor blocker
9	Antiplatelet therapy
10	Hypertension
11	Diuretic
12	Calcium channel blocker
13	Diabetes mellitus
14	Family history
15	Age

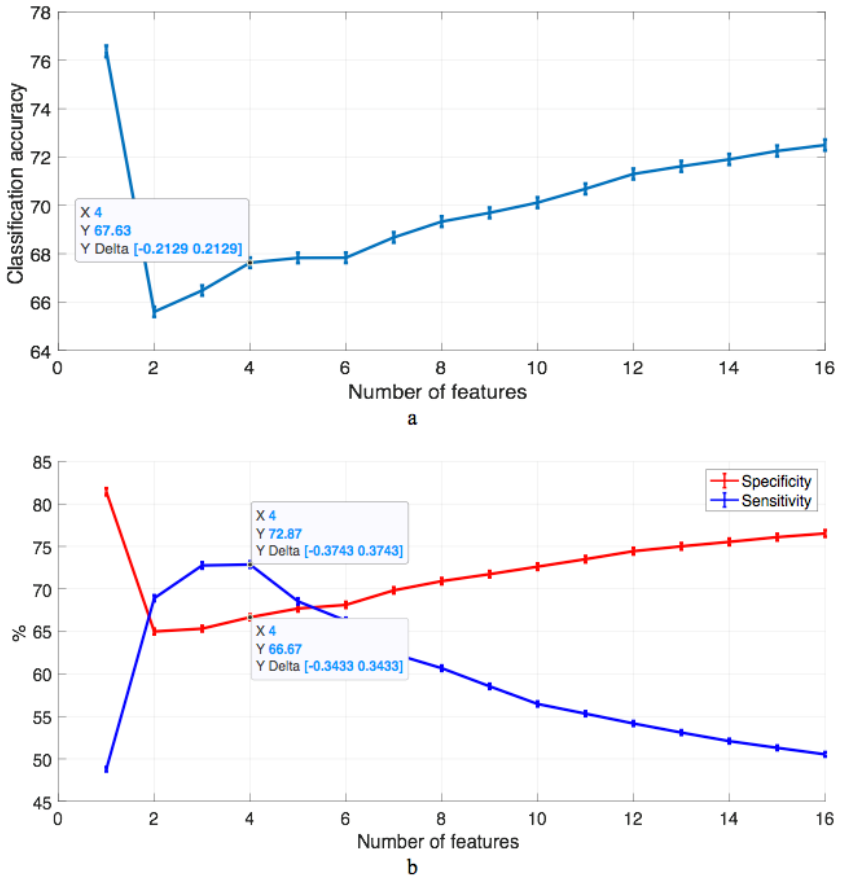
[a]ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker.

As mentioned earlier, two classification algorithms were used in this study: SVM and random forest. The results showed that the performances of the two classifiers were close to each other. However, the SVM slightly outperformed the random forest

classifier. In this paper, only results produced by the SVM are presented.

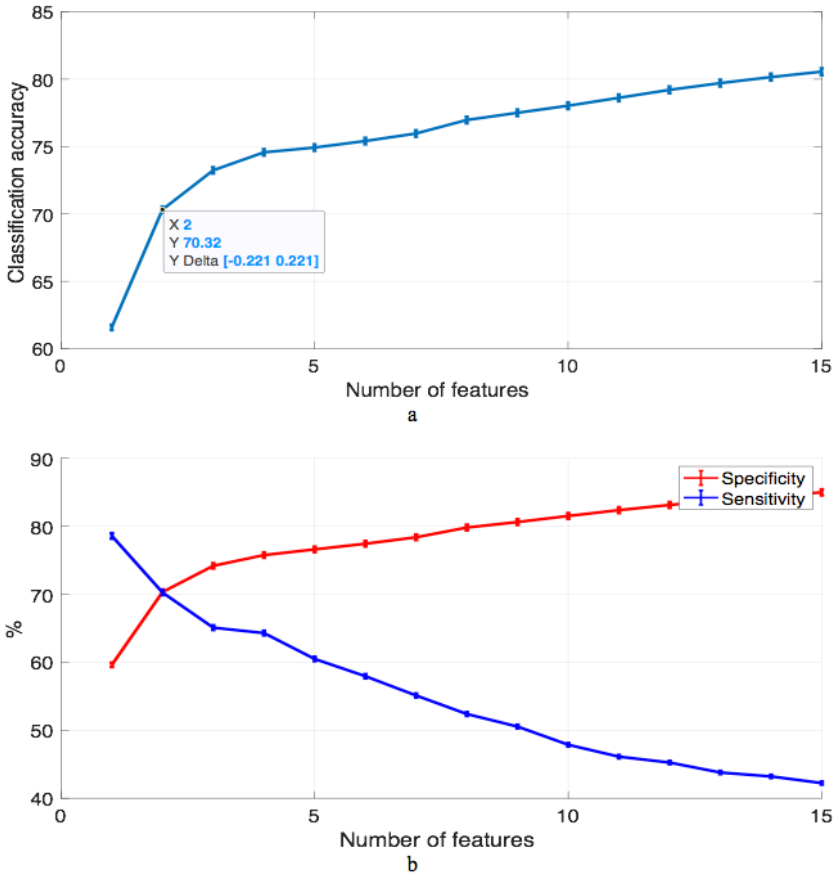
Figure 2 shows that the best trade-off between sensitivity and specificity, 72.87% and 66.67%, respectively, was achieved by the subset of the most significant four features (prior CAD, sex, weight, and ACE-I/ARB use). The classification accuracy was 67.63%. The figure also showed that when more features were added, sensitivity started to decrease and specificity started to increase; therefore accuracy is correlated more with sensitivity due to this skewness in the number of classes. This drop in sensitivity means that the rest of the features are either redundant or irrelevant for recognizing positive cases. When whole features were used only about 50% of the positive cases were classified correctly. On the other hand, random forest showed a slightly lower performance when the value of sensitivity, specificity, and classification accuracy were all the same (69.2%); this figure has been achieved with the most significant four features.

Figure 2. Performance of support vector machine classifier: (a) classification accuracy ± standard error and (b) sensitivity and specificity ± standard error.



The experiment was repeated on data from patients with no known prior CAD. The performance of the classification stage is depicted in Figure 3. The sensitivity was slightly affected by excluding patients with CAD as a feature from the data, however, the specificity increased. The classifier produced the best trade-off between sensitivity and specificity, both 70.24%, with only using two features (sex and ACE-I/ARB use). The accuracy also increased to 70.32% due to the increase of the specificity figure.

Figure 3. Performance of support vector machine classifier for subdataset: (a) classification accuracy ± standard error and (b) sensitivity and specificity ± standard error.



To test the robustness of the proposed framework, the experiment was repeated again and the model trained without sex features. The results showed that the best performance was achieved with the best four features (prior CAD, ACE-I/ARB, beta receptor blocker, and smoking status): 72.87% and 60.23%, respectively. The accuracy decreased to 62.19%.

Discussion

Principal Findings

Feature selection is used as part of the proposed framework; these techniques have the capability to investigate the multidimensional relation between features and class label. In previous research [11], classifiers were used to evaluate the significance of the features based on their importance for the classification algorithm. The selected features are very specific to the classifier. This study employed the classifier independent feature selection method (JMIM) to investigate the relation between features of clinical data and class label (test outcome) in the context of the features that were selected in the previous iterations. This means that once we have selected the features, they can be used with any classifier. SVM and random forest classifiers were tested in this study, and SVM slightly outperformed random forest in our dataset.

The results of the feature selection and classification stages showed that prior CAD is the most important risk factor for distinguishing between positive and negative cases. Sex, weight, and smoking status are among the group of most significant five features, and the only current medication that is within this group is ACE-I/ARB. Hypertension, diabetes, and positive family history are shown as the least significant features for the discrimination task. Only four features were needed to achieve the best performance (prior CAD, sex, weight, and ACE-I/ARB use), which means by knowing only this information about patients, the proposed framework is able to classify 72.87% of the positive cases and 66.67% of the negative cases correctly, outperforming the previous study [11]. ACE-I/ARB is used for several cardiovascular conditions and secondary prevention after an acute coronary event. This feature carries information about these conditions, and that is why it is the most powerful predictor of stress echocardiography outcome. For patients with no prior history of CAD, knowing the sex and whether the patient is taking ACE-I/ARB is sufficient to predict stress echocardiography outcome in the majority of cases.

To study the robustness of the framework, performance was tested without any information about prior diagnosis of CAD. Once this was tested, the order of the feature changed; cholesterol and nitrate medication became among the most significant of the five features. The feature weight was less significant in this model. This change in the order of the features can be attributable to the information interaction between them.

Because prior diagnosis of CAD is such a powerful predictor of a positive stress echocardiogram, the other features contribute so little information by comparison, and it is hard to see their value. However, once these patients are removed from the

dataset, we can see the predictive power of the other features for patients with no previous history of CAD.

Features like age, diabetes, and family history are shown to be less significant for discriminating between positive and negative cases. It also showed that information about medications added significant value and could enhance the discrimination power of the clinical data. It also showed that interaction between features is important and can affect the order of the selected subset. Moreover, increasing the granularity of the value of the risk factors may improve their discriminative power by using continuous instead of categorial variables.

Strengths

To our knowledge, this is the first study that has investigated applying machine learning techniques to a simple dataset of patient anthropometrics, cardiovascular risk factor profiles, and cardioactive medications to predict positive or abnormal stress echocardiography results. The study also investigated the performance of different machine learning techniques and employed a sophisticated feature selection method to study the significance of the clinical attributes. This method considers the interaction between clinical variables when analyzing their significance and the class label. The proposed framework outperforms the other tools that have been proposed in the literature [11] in predicting CAD by more than 9%. The proposed framework can also be employed on data collected using other cardiovascular stress tests aimed to detect inducible ischemia.

Limitations and Future Work

In this paper, we report preliminary results using only 529 patients. The data includes only anthropometric and clinical data that has been collected during the patient's hospital visit. Including more data from patient medical records could enhance the generic behavior of any proposed model and improve the performance of the developed model. As we have a large dataset going back nearly 20 years, the model could be extended to predict mortality due to a cardiovascular event.

Conclusions

Machine learning techniques can offer the very promising prospect of faster and more accurate diagnosis (especially for high-risk groups), prioritizing higher risk patients and increasing the capacity of clinicians. However, it is well known that most machine learning techniques are considered to be black boxes, where the model produces results that are difficult to interpret. Despite the black box nature of various machine learning approaches, feature selection techniques can improve understanding of the relationship between the diagnosis and clinical attributes. Data visualization methods can improve understanding of the produced model and interpretation of the output.

None of the clinical information detailing the results of the positive stress test such as wall motion score index were included with the clinical data. Inclusion may further differentiate between high- and low-risk patients.

Acknowledgments

This research was partly funded by UK Engineering and Physical Sciences Research Council grants EP/P01013X/1 (STRETCH) to BP and MB, EP/R013144/1 (SAUSE) to BP, and an Open University Priority Research Area grant to DB.

Conflicts of Interest

None declared.

References

1. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015 Jan 10;385(9963):117-171 [FREE Full text] [doi: 10.1016/S0140-6736(14)61682-2] [Medline: 25530442]
2. British Heart Foundation. 2020 Jan. UK factsheet URL: https://www.bhf.org.uk/-/media/files/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf?la=en [accessed 2020-05-17]
3. Patidar S, Pachori RB, Rajendra Acharya U. Automated diagnosis of coronary artery disease using tunable-Q wavelet transform applied on heart rate signals. Knowl Based Syst 2015 Jul;82:1-10. [doi: 10.1016/j.knosys.2015.02.011]
4. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, ESC Committee for Practice Guidelines, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013 Oct;34(38):2949-3003. [doi: 10.1093/eurheartj/eht296] [Medline: 23996286]
5. Safdar S, Zafar S, Zafar N, Khan NF. Machine learning based decision support systems (DSS) for heart disease diagnosis: a review. Artif Intell Rev 2017 Mar 25;50(4):597-623. [doi: 10.1007/s10462-017-9552-8]
6. Singh G, Al'Aref SJ, Van Assen M, Kim TS, van Rosendael A, Kolli KK, et al. Machine learning in cardiac CT: basic concepts and contemporary data. J Cardiovasc Comput Tomogr 2018;12(3):192-201. [doi: 10.1016/j.jcct.2018.04.010] [Medline: 29754806]
7. Mastoi Q, Wah T, Gopal Raj R, Iqbal U. Automated diagnosis of coronary artery disease: a review and workflow. Cardiol Res Pract 2018;2018:2016282 [FREE Full text] [doi: 10.1155/2018/2016282] [Medline: 29507812]

8. Johnson KW, Torres Soto J, Glicksberg BS, Shameer K, Miotto R, Ali M, et al. Artificial intelligence in cardiology. J Am Coll Cardiol 2018 Jun 12;71(23):2668-2679 [FREE Full text] [doi: 10.1016/j.jacc.2018.03.521] [Medline: 29880128]
9. Voss R, Cullen P, Schulte H, Assmann G. Prediction of risk of coronary events in middle-aged men in the Prospective Cardiovascular Münster Study (PROCAM) using neural networks. Int J Epidemiol 2002 Dec;31(6):1253-1262. [doi: 10.1093/ije/31.6.1253] [Medline: 12540731]
10. Gharehchopogh F, Khalifelu Z. Neural network application in diagnosis of patient: a case study. 2011 Presented at: Int Conf Comput Netw Inf Technol; 2011; Abbottabad p. 245-249.
11. Weng SF, Reps J, Kai J, Garibaldi JM, Qureshi N. Can machine-learning improve cardiovascular risk prediction using routine clinical data? PLoS One 2017 Apr;12(4):e0174944 [FREE Full text] [doi: 10.1371/journal.pone.0174944] [Medline: 28376093]
12. Dougherty J, Kohavi R, Sahami M. Supervised and unsupervised discretization of continuous features. 1995 Presented at: Proceedings of the Twelfth International Conference on Machine Learning; 1995; Tahoe City p. 194-202. [doi: 10.1016/b978-1-55860-377-6.50032-3]
13. Bennasar M, Setchi R, Hicks Y. Unsupervised discretization method based on adjustable intervals. Front Artif Intell Appl 2012;79:87. [doi: 10.3233/978-1-61499-105-2-79]
14. Bennasar M, Setchi R, Hicks Y. Feature interaction maximisation. Pattern Recognit Lett 2013 Oct;34(14):1630-1635. [doi: 10.1016/j.patrec.2013.04.002]
15. Bennasar M, Hicks Y, Setchi R. Feature selection using joint mutual information maximisation. Expert Syst Appl 2015 Dec;42(22):8520-8532. [doi: 10.1016/j.eswa.2015.07.007]
16. Cover T, Thomas J. Elements of Information Theory. 2nd Edition. Hoboken: Wiley-Interscience; 2006.
17. Smialowski P, Frishman D, Kramer S. Pitfalls of supervised feature selection. Bioinformatics 2010 Feb 01;26(3):440-443 [FREE Full text] [doi: 10.1093/bioinformatics/btp621] [Medline: 19880370]
18. Saunders C, Stitson M, Weston J. Support vector machine reference manual. London: University of London; 1998. URL: https://eprints.soton.ac.uk/258959/1/SVM_Reference.pdf [accessed 2020-05-18]
19. Breiman L. Random forests. Mach Learn 2001;45(1):5-32. [doi: 10.1023/A:1010933404324]

Abbreviations

ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker
CAD: coronary artery disease
CVD: cardiovascular disease
JMIM: joint mutual information maximization
SVM: support vector machine

Edited by G Eysenbach; submitted 08.11.19; peer-reviewed by HC Lee, M Alsharqi ; comments to author 12.12.19; revised version received 23.12.19; accepted 18.03.20; published 29.05.20.

Please cite as:
Bennasar M, Banks D, Price BA, Kardos A
Minimal Patient Clinical Variables to Accurately Predict Stress Echocardiography Outcome: Validation Study Using Machine Learning Techniques
JMIR Cardio 2020;4(1):e16975
URL: http://cardio.jmir.org/2020/1/e16975/
doi:10.2196/16975
PMID:32469316

Original Paper

Google Trends Insights Into Reduced Acute Coronary Syndrome Admissions During the COVID-19 Pandemic: Infodemiology Study

Conor Senecal[1], MD; Rajiv Gulati[1], MD, PhD; Amir Lerman[1], MD

Mayo Clinic, Rochester, MN, United States

Corresponding Author:
Amir Lerman, MD
Mayo Clinic
200 1st St SW
Rochester, MN, 55905
United States
Phone: 1 507 255 1622
Email: Lerman.amir@mayo.edu

Abstract

Background: During the coronavirus disease (COVID-19) pandemic, a reduction in the presentation of acute coronary syndrome (ACS) has been noted in several countries. However, whether these trends reflect a reduction in ACS incidence or a decrease in emergency room visits is unknown. Using Google Trends, queries for chest pain that have previously been shown to closely correlate with coronary heart disease were compared with searches for myocardial infarction and COVID-19 symptoms.

Objective: The current study evaluates if search terms (or topics) pertaining to chest pain symptoms correlate with the reported decrease in presentations of ACS.

Methods: Google Trends data for search terms “chest pain,” “myocardial infarction,” “cough,” and “fever” were obtained from June 1, 2019, to May 31, 2020. Related queries were evaluated for a relationship to coronary heart disease.

Results: Following the onset of the COVID-19 pandemic, chest pain searches increased in all countries studied by at least 34% (USA *P*=.003, Spain *P*=.007, UK *P*=.001, Italy *P*=.002), while searches for myocardial infarction dropped or remained unchanged. Rising searches for chest pain included “coronavirus chest pain,” “home remedies for chest pain,” and “natural remedies for chest pain.” Searches on COVID-19 symptoms (eg, cough, fever) rose initially but returned to baseline while chest pain–related searches remained elevated throughout May.

Conclusions: Search engine queries for chest pain have risen during the pandemic as have related searches with alternative attribution for chest pain or home care for chest pain, suggesting that recent drops in ACS presentations may be due to patients avoiding the emergency room and potential treatment in the midst of the COVID-19 pandemic.

(JMIR Cardio 2020;4(1):e20426) doi:10.2196/20426

KEYWORDS

Google Trends; acute coronary syndrome; coronary heart disease; online search; internet; trend; COVID-19; heart; cardiovascular

Introduction

Amid the coronavirus disease (COVID-19) pandemic, a reduction in ST-elevation myocardial infarction (STEMI) activations and presentation to the emergency room across the United States has been noted [1]. In a large diverse community setting in California, acute coronary syndrome (ACS) admissions fell by nearly half [2]. Similarly, in the United Kingdom, there has been a sharp decline in emergency department (ED) visits for myocardial ischemia [3], and in Italy, ACS admissions were noted to fall dramatically [4]. The extent to which these observations are due to a true reduction in ACS incidence or avoidance of hospitals remains unknown. Even in the setting of a pandemic, delays in diagnosis and treatment for ACS is associated with increased mortality [5]. Our previous work has shown a consistent correlation between search engine queries for chest pain and similar symptoms with the prevalence of coronary artery disease [6]. COVID-19–related changes in search patterns pertaining to health care have already been reported [7,8]. Given that chest pain is not a common symptom of COVID-19, this relationship would be expected to be consistent during a pandemic [9]. We investigated changes in chest pain search frequency before and after the onset of the COVID-19 pandemic and compared this to myocardial infarction

search frequency, as well as changes in search frequency for symptoms of COVID-19.

Methods

The use of Google Trends search data in health research has been previously described [10]. Results provided by this service are reported as relative search volume (RSV). Each data point is divided by the total searches pertaining to the geographic area and time range it represents to compare relative popularity. The resulting numbers are then scaled on a range of 0 to 100 based on a topic's proportion to all searches on all topics. Different regions or time frames that show the same RSV for a term do not always have the same total search volumes. For example, a given RSV for "chest pain" in the United States is only directly comparable to an RSV for Italy if the searches were performed together, and even in this circumstance the frequency represents the popularity of a search per the total volume of searches in the geographic area as opposed to absolute search volume. Due to this limitation, comparisons of RSV were only made within single queries (ie, searched together). Since RSV is reported based on an adjusted 0-100 scale for each query, comparisons of RSV from separate queries are not useful. Therefore, statistical comparisons used in this analysis were carried out between data from single queries (Table 1). Search topics were used in this analysis as they encompass synonyms, similar terms, and results from multiple languages for the topic searched as opposed to search terms, which only returns results on the exact term used. For example, the topic "myocardial infarction" includes the terms "heart attack," "symptoms of heart attack," or "infarto de miocardio." More information about Google Trends search results is available online [11]. The URL for each query made in Google Trends has been included in Table 1 to provide the exact search terminology used.

We queried "chest pain" and "myocardial infarction" separately as topics from June 1, 2019, to May 31, 2020, in the following search regions: the United States, the United Kingdom, Spain, and Italy. As only five queries are simultaneously allowed, we then created a search with the "chest pain" topic and the "myocardial infarction" topic for the United States during the same time frame to allow for a direct comparison. We defined the pre–COVID-19 and post–COVID-19 time frames as before and after March 1, the day following the first confirmed US death from COVID-19. Additionally, we separately searched "cough" and "fever" symptoms associated with COVID-19 for the United States during the same time frame. Pre– and post–COVID-19 mean RSVs were compared using paired *t* tests with an alpha of .05 and 95% CIs.

Google Trends also provides "related queries" to searches made by the same users and separates these into those that have increased the most compared to a previous time period ("rising") and those most commonly searched ("top"). These search terms were evaluated for any relationship to reduced ACS presentations. Queries were made for "chest pain," "chest pain – corona," and "chest pain – COVID" from March 15 to April 15, the month-long period with the highest searches for chest pain in the post–COVID-19 analysis, with the latter two queries made in an attempt to isolate searches unrelated to COVID-19. For these searches, search terms were used as opposed to topics to allow for the removal of COVID-19–associated terminology.

Table 1. Google Trends queries used for data acquisition.

Search terms	Duration	Geography	URL
Chest pain (topic)	June 1, 2019 - May 30, 2020	United States, Spain, Italy, United Kingdom	https://bit.ly/3dPisGi
Myocardial infarction (topic)	June 1, 2019 - May 30, 2020	United States, Spain, Italy, United Kingdom	https://bit.ly/3dV5EOO
Fever (topic) + cough (topic)	June 1, 2019 - May 30, 2020	United States	https://rb.gy/wnbvci
Chest pain (topic) + myocardial infarction (topic)	June 1, 2019 - May 30, 2020	United States	https://bit.ly/37mL8E5
Chest pain (topic), chest pain – COVID (term), chest pain – corona (term)	March 15, 2020 - April 15, 2020	United States	https://bit.ly/30LdiHy

Results

Search frequency for chest pain and myocardial infarction topics from June 1, 2019, to May 31, 2020, in the United States, Spain, United Kingdom, and Italy are shown in Figure 1. From June 1, 2019 to March 1, 2020, search frequency for chest pain varied between the four countries evaluated but showed little variation. From March 1 to May 31, 2020, all four countries evaluated saw a rise in searches for chest pain compared to the period prior to March 1, 2020 (USA *P*=.003, Spain *P*=.007, UK *P*=.001, Italy *P*=.002). All countries had at least a 34% rise in searches, with Spain seeing the largest increase at 84%. RSV for the topic myocardial infarction also varied in the four countries. The United States and Italy exhibited a significant drop in searches related to myocardial infarction from baseline, of 9% (57% to 52%, *P*=.001) and 10% (33% to 29%, *P*=.008), respectively, between March 1 to May 31, 2020. Similarly, searches for myocardial infarction fell in the United Kingdom and Spain but did not reach statistical significance. In the United States, the topic myocardial infarction was searched 1.4x as often as the topic chest pain before March 1, 2020; after that date it was searched 0.91x as often. "Chest pain – COVID" and "chest pain – corona" both showed an increase in search volume from pre–COVID-19 to post–COVID-19 time frames as well.

Rising searches associated with chest pain searches are shown in Table 2 and included "is chest pain a symptom of COVID" and "is chest pain a sign of coronavirus." Rising searches unrelated to COVID-19 included "home remedies for chest pain" and "natural remedies for chest pain," which both had a

>41x increase, along with "persistent pain or pressure in the chest," which had a 6x increase. Top related queries for all three queries were similar, with top two being "pain in chest" and "coronavirus chest pain."

The RSV of "chest pain" was compared to "common symptoms of COVID-19," and this is displayed in Figure 2 from January 1, 2020, to May 31, 2020. All searches had increased in RSV from the period before March 1 to the period after (fever: RSV=30 to 48, *P*=.02; cough: RSV=40 to 44, *P*=.59; chest pain: RSV=43 to 57, *P*=.003); however, throughout March and early April searches for COVID-19 symptoms declined and returned to the previous baseline at an accelerated rate compared to chest pain searches. The search volume for "cough" returned to the pre–COVID-19 baseline on April 12, 2020, while the search volume for "fever" returned to baseline by May 3, 2020. In contrast, the search volume for "chest pain" did not return to its pre–COVID-19 baseline average until May 31, 2020.

Figure 1. Relative daily search frequency of chest pain (top) and myocardial infarction (bottom) from June 1, 2020, to May 31, 2020, in the United States, United Kingdom, Spain, and Italy.

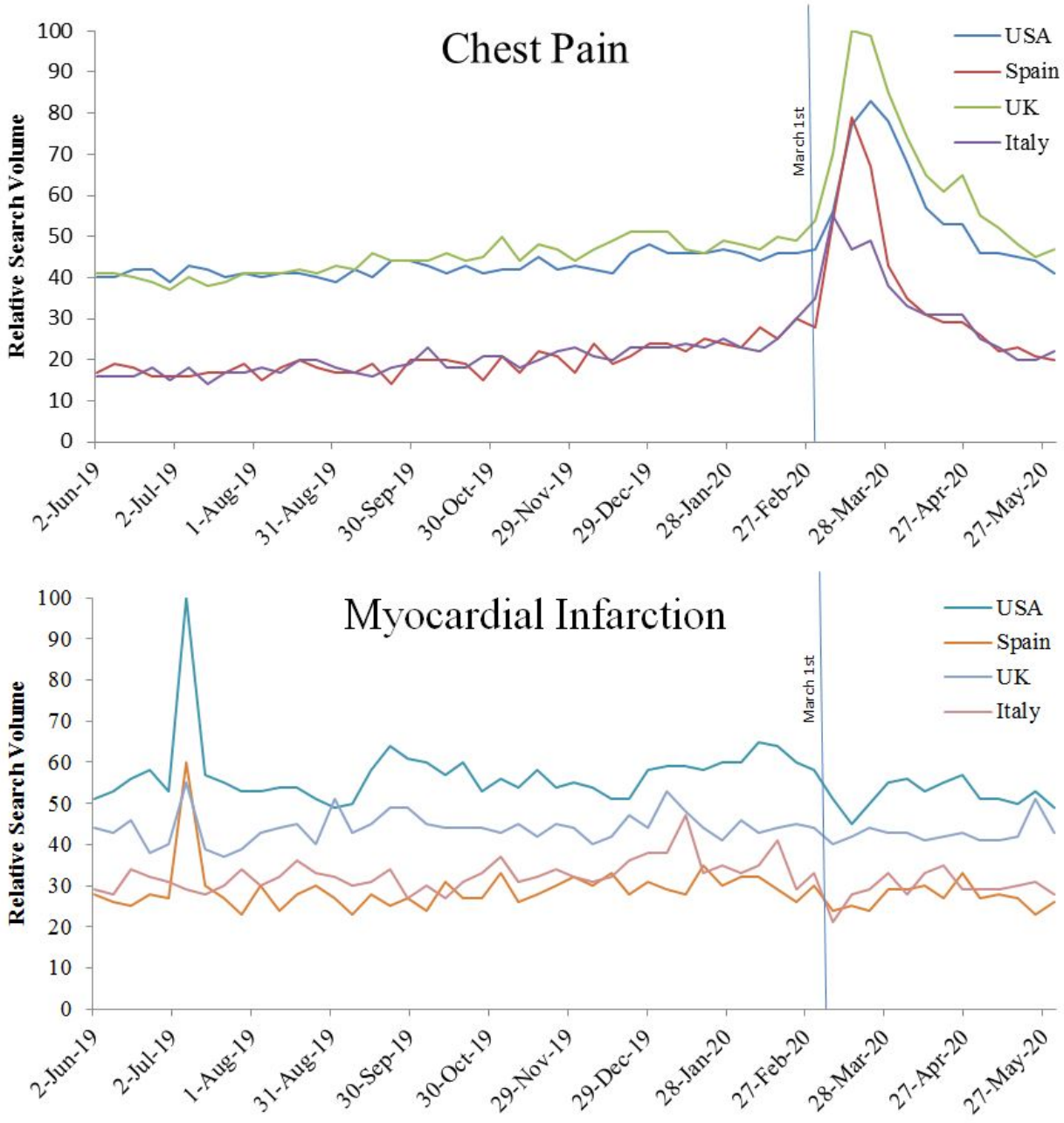
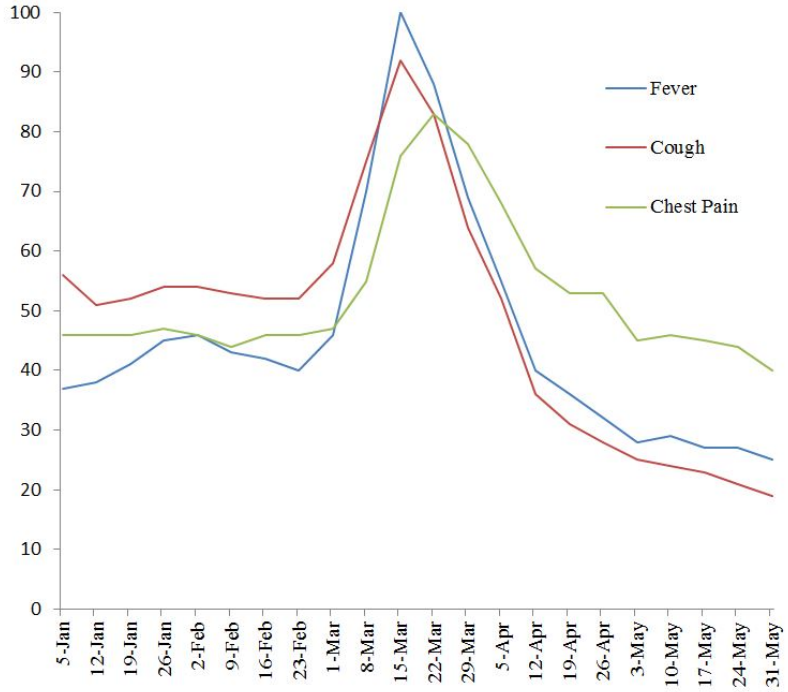


Table 2. Rising chest pain–related queries from March 15, 2020, to April 15, 2020, United States.

Term	RSV[a] increase (%)
"Chest pain"	
"covid19 chest pain"	Breakout
"is chest pain a symptom of COVID-19"	Breakout
"home remedies for chest pain"	Breakout
"is chest pain a symptom of the coronavirus"	Breakout
"natural remedies for chest pain"	Breakout
"is chest pain a symptom of allergies"	4150
"COVID chest pain"	1400
"Chest pain – COVID"	
"is chest pain a sign of coronavirus"	Breakout
"can bad posture cause chest pain"	Breakout
"persistent pain or pressure in the chest"	Breakout
"chest pain coronavirus symptom"	600
"corona chest pain"	550
"corona virus and chest pain"	450
"chest pain symptom of coronavirus"	450
"Chest pain – corona"	
"is chest pain a symptom of COVID-19"	Breakout
"is chest pain a sign of coronavirus"	Breakout
"chest pain COVID"	1950
"COVID symptoms"	1450
"COVID-19 symptoms"	1400
"chest pain with coronavirus"	1200
"COVID-19 chest pain"	1200

[a]RSV: relative search volume.

Figure 2. Relative daily search volume of "chest pain," "cough," and "shortness of breath" (January 1, 2020, to May 31, 2020).



Discussion

The major finding of our study is the marked increase in search frequency of terms and topics related to chest pain that began at the onset of the COVID-19 pandemic in the four countries studied. The discordance between the rise in chest pain searches and the documented reduction in hospital-recorded ACS admissions and ED presentations raises the possibility that patients chose to avoid presentation to health care facilities despite experiencing concerning cardiac symptoms or attributed such symptoms to another etiology.

During the period of study, searches for chest pain and myocardial infarction occurred with steady frequency until COVID-19 began spreading in the United States. After that time, searches for chest pain increased substantially as may be expected given the known increase in ACS events with other viral illnesses and the social and economic stress presented by the pandemic [12]. However, during the same period, myocardial infarction searches declined. Possibilities for the fall in myocardial infarction searches include a reduced public awareness of myocardial infarction in the context of heightened awareness for COVID-19 [13]. Increased chest pain searches could be due to coronary heart disease or noncardiac causes including COVID-19. The increased frequency in searches such as “is chest pain a symptom of COVID-19” and “coronavirus chest pain” likely indicated some of the increase is from greater interest in COVID-19. However, we evaluated chest pain searches that excluded COVID-19 or corona terms to limit this effect and still found an increase in chest pain search volume supporting a rise in non–COVID-19–related chest pain searches. Several rising related searches seem to reflect people trying to manage symptoms without health care intervention such as “home remedies for chest pain” and natural “remedies for chest pain.”

The rise in the search for COVID-19 symptoms at the onset of the pandemic in the United States is expected; however, these search volumes declined below their baseline averages by early May as opposed to actual infections, which have dramatically increased during that time frame [2]. Chest pain search volume has not declined at the same pace as symptoms for COVID-19 and has remained elevated from baseline through April until the last week of May. If rises in chest pain search volume were solely due to COVID-19–related searches, then its search volume should have mirrored that of publicized symptoms for COVID-19. Interestingly, May represents a month when strict stay-at-home orders were slowly relaxed throughout the country [14]. This could represent a fall in chest pain searches that closely mirrors an increase in people’s ability to seek care.

While there are inherent limitations to infodemiology using Google Trends data, it remains a valuable tool for providing nearly real-time data with extensive search volumes. Once accurate public reporting of ACS admissions incidence is available, it would be useful to compare the changes in search volume seen. Patient survey data regarding their management of chest pain during the epidemic may also provide a useful mechanism to help understand patient decisions. Chest pain has not been reported as a common symptom of COVID-19; however, given the short experience with this pathogen it is possible this could be currently underreported.

Overall, the data provided support for an increase in the burden of chest pain and potentially ACS during the COVID-19 pandemic, a time when multiple reports have shown a drop in ED presentation and admission for ACS. It also provides some insights into strategies patients are using to avoid health care interaction. Public health officials should emphasize and potentially utilize online access to inform the public about the need to seek medical care for potentially life-threatening symptoms even in the midst of the COVID-19 pandemic.

Conflicts of Interest

None declared.

References

1. Garcia S, Albaghdadi MS, Meraj PM, Schmidt C, Garberich R, Jaffer FA, et al. Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States During COVID-19 Pandemic. J Am Coll Cardiol 2020 Jun 09;75(22):2871-2872 [FREE Full text] [doi: 10.1016/j.jacc.2020.04.011] [Medline: 32283124]
2. Solomon MD, McNulty EJ, Rana JS, Leong TK, Lee C, Sung S, et al. The Covid-19 Pandemic and the Incidence of Acute Myocardial Infarction. N Engl J Med 2020 Aug 13;383(7):691-693. [doi: 10.1056/nejmc2015630]
3. Bakker J. Lives at risk due to 50% drop in heart attack A&E attendances. BHF. 2020 Apr. URL: https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2020/april/drop-in-heart-attack-patients-amidst-coronavirus-outbreak [accessed 2020-08-06]
4. De Filippo O, D'Ascenzo F, Angelini F, Bocchino PP, Conrotto F, Saglietto A, et al. Reduced Rate of Hospital Admissions for ACS during Covid-19 Outbreak in Northern Italy. N Engl J Med 2020 Jul 02;383(1):88-89. [doi: 10.1056/nejmc2009166]
5. Terkelsen CJ. System Delay and Mortality Among Patients With STEMI Treated With Primary Percutaneous Coronary Intervention. JAMA 2010 Aug 18;304(7):763. [doi: 10.1001/jama.2010.1139]
6. Senecal C, Widmer RJ, Lerman LO, Lerman A. Association of Search Engine Queries for Chest Pain With Coronary Heart Disease Epidemiology. JAMA Cardiol 2018 Dec 01;3(12):1218-1221 [FREE Full text] [doi: 10.1001/jamacardio.2018.3459] [Medline: 30422176]
7. Jacobson NC, Lekkas D, Price G, Heinz MV, Song M, O'Malley AJ, et al. Flattening the Mental Health Curve: COVID-19 Stay-at-Home Orders Are Associated With Alterations in Mental Health Search Behavior in the United States. JMIR Ment Health 2020 Jun 1;7(6):e19347. [doi: 10.2196/19347]
8. Higgins T, Wu A, Sharma D, Illing E, Rubel K, Ting J, Snot Force Alliance. Correlations of Online Search Engine Trends With Coronavirus Disease (COVID-19) Incidence: Infodemiology Study. JMIR Public Health Surveill 2020 May 21;6(2):e19702 [FREE Full text] [doi: 10.2196/19702] [Medline: 32401211]
9. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 2020 Feb;395(10223):497-506. [doi: 10.1016/s0140-6736(20)30183-5]
10. Mavragani A, Ochoa G, Tsagarakis KP. Assessing the Methods, Tools, and Statistical Approaches in Google Trends Research: Systematic Review. J Med Internet Res 2018 Nov 06;20(11):e270 [FREE Full text] [doi: 10.2196/jmir.9366] [Medline: 30401664]
11. Google Trends. URL: http://trends.google.com [accessed 2020-06-08]
12. Kwong JC, Schwartz KL, Campitelli MA, Chung H, Crowcroft NS, Karnauchow T, et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med 2018 Jan 25;378(4):345-353. [doi: 10.1056/NEJMoa1702090] [Medline: 29365305]
13. Brigo F, Igwe SC, Ausserer H, Nardone R, Tezzon F, Bongiovanni LG, et al. Why do people Google epilepsy? An infodemiological study of online behavior for epilepsy-related search terms. Epilepsy Behav 2014 Feb;31:67-70. [doi: 10.1016/j.yebeh.2013.11.020] [Medline: 24361764]
14. Elassar A. This is where each state is during its phased reopening. CNN. 2020. URL: https://www.cnn.com/interactive/2020/us/states-reopen-coronavirus-trnd/ [accessed 2020-06-08]

Abbreviations

ACS: acute coronary syndrome
COVID-19: coronavirus disease
ED: emergency department
RSV: relative search volume
STEMI: ST-elevation myocardial infarction

Edited by G Eysenbach; submitted 18.05.20; peer-reviewed by R Widmer, J Van den Eynde, M K.; comments to author 02.06.20; revised version received 17.06.20; accepted 23.07.20; published 24.08.20.

Please cite as:
Senecal C, Gulati R, Lerman A
Google Trends Insights Into Reduced Acute Coronary Syndrome Admissions During the COVID-19 Pandemic: Infodemiology Study
JMIR Cardio 2020;4(1):e20426
URL: http://cardio.jmir.org/2020/1/e20426/
doi:10.2196/20426
PMID:32831186

Original Paper

Using Mobile Health Tools to Assess Physical Activity Guideline Adherence and Smoking Urges: Secondary Analysis of mActive-Smoke

Rongzi Shan[1,2], BSc; Lisa R Yanek[3], MPH; Luke G Silverman-Lloyd[1,4], BA; Sina Kianoush[1,5], MD, MPH; Michael J Blaha[1], MD, MPH; Charles A German[6], MD; Garth N Graham[7], MD, MPH; Seth S Martin[1], MD, MHS

[1]Ciccarone Center for the Prevention of Cardiovascular Disease, Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States

[2]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, United States

[3]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States

[4]University of California, Berkeley-University of California, San Francisco Joint Medical Program, Berkeley, CA, United States

[5]Yale New Haven Medical Center - Waterbury Hospital, Waterbury, CT, United States

[6]Heart and Vascular Center of Excellence, Wake Forest Baptist Health, Winston-Salem, NC, United States

[7]Aetna Foundation, Hartford, CT, United States

Corresponding Author:
Seth S Martin, MD, MHS
Ciccarone Center for the Prevention of Cardiovascular Disease
Division of Cardiology, Department of Medicine
Johns Hopkins University School of Medicine
600 N Wolfe Street
Carnegie 591
Baltimore, MD, 21287
United States
Phone: 1 4105020469
Email: smart100@jhmi.edu

Abstract

Background: Rates of cigarette smoking are decreasing because of public health initiatives, pharmacological aids, and clinician focus on smoking cessation. However, a sedentary lifestyle increases cardiovascular risk, and therefore, inactive smokers have a particularly enhanced risk of cardiovascular disease.

Objective: In this secondary analysis of mActive-Smoke, a 12-week observational study, we investigated adherence to guideline-recommended moderate-to-vigorous physical activity (MVPA) in smokers and its association with the urge to smoke.

Methods: We enrolled 60 active smokers (≥3 cigarettes per day) and recorded continuous step counts with the Fitbit Charge HR. MVPA was defined as a cadence of greater than or equal to 100 steps per minute. Participants were prompted to report instantaneous smoking urges via text message 3 times a day on a Likert scale from 1 to 9. We used a mixed effects linear model for repeated measures, controlling for demographics and baseline activity level, to investigate the association between MVPA and urge.

Results: A total of 53 participants (mean age 40 [SD 12] years, 57% [30/53] women, 49% [26/53] nonwhite, and 38% [20/53] obese) recorded 6 to 12 weeks of data. Data from 3633 person-days were analyzed, with a mean of 69 days per participant. Among all participants, median daily MVPA was 6 min (IQR 2-13), which differed by sex (12 min [IQR 3-20] for men vs 3.5 min [IQR 1-9] for women; *P*=.004) and BMI (2.5 min [IQR 1-8.3] for obese vs 10 min [IQR 3-15] for nonobese; *P*=.04). The median total MVPA minutes per week was 80 (IQR 31-162). Only 10% (5/51; 95% CI 4% to 22%) of participants met national guidelines of 150 min per week of MVPA on at least 50% of weeks. Adjusted models showed no association between the number of MVPA minutes per day and mean daily smoking urge (*P*=.72).

Conclusions: The prevalence of MVPA was low in adult smokers who rarely met national guidelines for MVPA. Given the poor physical activity attainment in smokers, more work is required to enhance physical activity in this population.

(JMIR Cardio 2020;4(1):e14963) doi:10.2196/14963

KEYWORDS

physical activity; smoking; mHealth; fitness trackers; short message service

Introduction

Background

Smoking cessation and physical activity both lead to significant improvements in health [1]. Although smoking rates are decreasing because of regulation and taxation, behavioral counseling, and pharmacotherapy [1], an individual's attempts to quit smoking are still challenging [2]. Furthermore, because a sedentary lifestyle increases cardiovascular risk [3], inactive smokers have a particularly enhanced risk of cardiovascular disease. The 2018 US Physical Activity Guidelines recommend greater than or equal to 150 min per week moderate activity or greater than or equal to 75 min per week vigorous physical activity (VPA), accumulated over bouts of any duration [4]. However, the prevalence of meeting these activity guidelines in the general adult population is unsatisfactory, with half of the US adults attaining fewer than 150 min of moderate-to-vigorous physical activity (MVPA) during leisure time per week, by self-report [4]. Moreover, 2 studies in young adults [5] and youth aged 14 to 18 years [6] found that self-reported attainment of physical activity guidelines was positively associated with noncigarette forms of tobacco use (eg, electronic cigarettes) but inversely associated with cigarette smoking, suggesting that physical inactivity and cigarette smoking may be compounding risk factors.

Physical activity has been suggested as an aid for smoking cessation, potentially through moderation of cravings and prevention of weight gain [7,8], but evidence is conflicting. Although there is insufficient evidence to recommend exercise as an aid for smoking cessation [7,9], previous meta-analyses suggested that acute bouts of exercise decrease urges, with activities at moderate to vigorous intensity having the greatest effect [10,11]. In addition, a study on active smokers found that a higher level of habitual MVPA was significantly associated with lower smoking urges [12]. However, this study used 7-day physical activity recall for assessing the levels of MVPA, leading to potential recall bias.

Methodological limitations such as recall bias and poor ecological validity are common in prior studies of exercise and smoking. Self-report for physical activity has been shown to poorly correlate with accelerometer data in accurately measuring MVPA and sedentary time, whereas ecological momentary assessment using mobile health (mHealth) tools, designed to sample real-time behaviors and experiences in the natural environment, performed better [13].

Objectives

The goal of mActive-Smoke, a 12-week prospective observational study, was to assess the day-level association between objectively measured physical activity and concurrent smoking urges. Previously reported primary results [14] demonstrate that acute bouts of physical activity (ie, number of steps accumulated in a 30-min period before urge reporting), but not total daily steps, were associated with a modest decrease in smoking urges. Although we previously found a temporal association between acute bouts of activity and decreased urge, it is unclear whether the intensity of daily activity is associated with daily urge. In addition, despite well-established contributions of physical inactivity [3] and smoking on cardiovascular risk, there is limited research describing adherence to physical activity guidelines in adult smokers, with prior research mostly reliant on self-reported data. Thus, in this secondary analysis, we used prospective, objective measures to investigate adherence to guideline-recommended MVPA and the association between the intensity of physical activity and the urge to smoke.

Methods

Study Aim and Design

The aims of this secondary analysis were to report adherence to physical activity guidelines among smokers in the mActive-Smoke study population and to investigate the relationship between the intensity of physical activity and the urge to smoke. The methods for this 12-week prospective observational study have been previously reported [14], and a summary is provided below (Recruitment and Measurement of Baseline Variables and Data Collection). This study was approved by the Johns Hopkins School of Medicine Institutional Review Board.

Recruitment and Measurement of Baseline Variables

We recruited 60 participants from April 7, 2016, to September 2, 2016, using on-site advertisements, social media, and physician referrals. Participants met inclusion criteria if they were aged 18 years or older, smoked at least 3 cigarettes per day on average, owned a smartphone, and were able to perform normal physical activity. Participants were screened for eligibility via email. At an initial meeting with a study coordinator, participants completed an enrollment questionnaire to record demographic characteristics, self-reported BMI (weight [kg]/height [m^2]), physical activity, and smoking behavior. Baseline physical activity was assessed by the International Physical Activity Questionnaire (IPAQ)-short form, a questionnaire assessing walking time, sedentary time, and MVPA time in the past 7 days [15]. A *high* IPAQ score is defined as the equivalent of either VPA on 3 days or more per week at greater than or equal to 1500 metabolic equivalent of task (MET) minutes per week or 5 days or more per week of any combination of MVPA meeting greater than or equal to 3000 MET minutes per week [16]. Baseline smoking behavior was assessed with the Arizona Smoking Assessment Questionnaire [17].

Data Collection

For the measurement of physical activity, participants used the Fitbit Charge HR (Fitbit Inc), a wrist-worn triaxial digital

accelerometer allowing continuous monitoring of activity and heart rate. Patients were not instructed to alter their physical activity, but they could access step counts via the Fitbit mobile app (Fitbit Inc). Data from the Fitbit, including steps and the Fitbit-generated intensity level, were compiled in Fitabase, a secure research platform that collects real-time data from activity tracking devices [18]. Day-level and minute-level data were downloaded from Fitabase for each participant.

To measure smoking urges, an automated messaging service sent SMS text messages to participants 3 times per day, requesting that they respond with their instantaneous urge to smoke on a 9-point Likert scale from low to high. These messages were sent at participant-defined times, corresponding roughly to waking up, lunchtime, and returning home at the end of a day.

Participants were asked to complete a Web-based end-of-study survey regarding the study experience and their perceptions on physical activity and smoking urges. Survey questions and results were previously reported [14].

Statistical Analysis

Baseline characteristics were summarized using descriptive statistics, frequency for categorical data and mean (SD) and median (IQR) for continuous data. Spearman and Pearson correlation coefficients were used for associations between variables.

As participants were not required to wear Fitbits during sleep, we defined nonwear time as 90 consecutive minutes of missing heart rate data between the hours of 10 am and 10 pm. Days with 2 or more 90-min nonwear periods and wear time of fewer than 6 hours within the target time window were excluded [19]. At least 6 total weeks of recorded data were required for inclusion. For the calculation of the prevalence of meeting weekly MVPA goals, we included weeks for which participants contributed 4 or more days of complete data [20].

Fitbit assigns minute-level activity into 4 intensity levels (0: *sedentary*, 1: *light*, 2: *moderate*, and 3: *vigorous*) [18]. We eschewed this measure of intensity given the proprietary algorithms and concern about accuracy [21,22] and used cadence as a surrogate measure of intensity. We elected to not include heart rate because of concerns about the accuracy of Fitbit's heart rate measurement, particularly at vigorous intensities [23]. However, to explore the nature of Fitbit's intensity variable, we compare daily MVPA minutes by Fitbit intensity levels (number of minutes spent at intensity level 2 or 3) with daily MVPA minutes by cadence threshold.

Cadence (steps per minute) is associated with objectively measured speed and intensity under controlled experimental conditions [24]. A threshold of 100 steps per minute is an evidence-based value generally associated with moderate intensity or greater than or equal to 3 METs and is best described as brisk walking, whereas a threshold of 130 steps per minute is associated with vigorous intensity or greater than or equal to 6 METs [25]. We created 4 cadence categories defined as 0 steps per minute (*no movement*), 1 to 59 steps per minute (*incidental movement to purposeful steps*), 60 to 99 steps per minute (*slow to medium walking*), and greater than or equal to 100 steps per minute (*brisk walking and faster*), whereas VPA was defined as cadence of greater than or equal to 130 steps per minute [25]. Daily minutes of MVPA were calculated by summing the minutes spent at cadence of greater than or equal to 100 steps per minute, and daily minutes of VPA was calculated by summing the minutes spent at cadence of greater than or equal to 130 steps per minute. We also calculated moderate+2×VPA, which weights moderate activity as 1 min and vigorous activity as 2 min, in accordance with physical activity guidelines [20], but as the results remained similar, we reported only MVPA and VPA.

Given the positively skewed data, we described MVPA minutes using median (IQR) and used the Wilcoxon rank sum test for comparing between-group differences. We reported the within-person and between-person prevalence of physical activity guideline adherence. We also estimated the prevalence of adherence with obtaining at least 150 min of MVPA or 75 min of VPA per week on greater than or equal to 50% of the study weeks. Although the physical activity guidelines were developed based on self-report, we opted to apply the physical activity guidelines to cadence measurements to provide a clinical context for the objective data. Daily urge to smoke was described using mean (SD) of the 3 to 4 urge messages sent each day. The mean daily urge was normally distributed and was treated as a continuous variable.

A repeated measures multivariable mixed effects linear model, accounting for autoregression and heteroscedasticity, was used to evaluate the relationship between daily MVPA minutes and daily urge. We adjusted for age, sex, race, education, BMI, baseline cigarettes per day, and baseline physical activity, which were selected a priori. Baseline physical activity was defined as a high level of activity or not by IPAQ. We explored interactions between age, sex, obesity status, baseline physical activity, and baseline cigarettes per day with daily MVPA minutes, with $P<.10$ considered evidence of interaction. The analysis was conducted using Stata (version 15·1; StataCorp).

Results

Study Flow and Baseline Characteristics

The study flow diagram, baseline characteristics, and survey results have been previously reported [14]. In brief, 60 participants were enrolled, and 53 participants recorded at least 6 weeks of data and were thus included in this analysis. In addition, 45 participants recorded 12 weeks of data, and 8 participants recorded 6 to 12 weeks of data. Of all participant-weeks, 80.1% (144/723) of weeks included at least 4 days of complete data. Participants sent a mean of 290 (SD 62) SMS text messages quantifying the urge to smoke. Moreover, 49 participants completed the Web-based exit survey. After excluding days using nonwear criteria, data from 3633 days were analyzed, with a mean of 69 days of data contributed by each participant. The mean age was 40 (SD 12) years, with 57% (30/53) women, 49% (26/53) nonwhite participants, and 30% (16/53) with a bachelor's degree or higher. In addition, 40% (21/53) of participants were overweight, 38% (20/53) were obese, and 53% (28/53) had a high level of baseline activity as assessed by IPAQ (Table 1).

Table 1. Baseline characteristics of mActive-Smoke participants (N=53).

Characteristic	Participants, n (%)
Sex	
Men	23 (43)
Women	30 (57)
Age (years)	
22-29	11 (21)
30-39	16 (30)
40-49	15 (28)
50-59	7 (13)
60-65	4 (8)
Race	
White	27 (51)
Nonwhite	26 (49)
Education	
High school diploma or less	8 (15)
Associate degree or some college	29 (55)
Bachelor's degree or higher	16 (30)
BMI (kg/m^2)	
<25.0 (normal or underweight)	12 (23)
25.0-29.9 (overweight)	21 (40)
≥30.0 (obese)	20 (38)
International Physical Activity Questionnaire[a]	
Low	6 (11)
Moderate	19 (36)
High	28 (53)
Cigarettes smoked per day	
≤10	34 (64)
>10	19 (36)

[a]Categories defined by International Physical Activity Questionnaire guidelines.

Patterns of Physical Activity

Participants accumulated a median of 7807 steps per day (IQR 5383-10,824). Of 53 participants, 31 (58%) met the recommended 30 min per day of MVPA on 1 or more days over the study duration. Of these 31 participants, the 30 min per day MVPA goal was met on a mean of 19% of days. Prevalence of adherence to national physical activity guidelines, defined as the proportion of participants who obtained at least 150 min per week of MVPA on at least 50% of total weeks, was 10% (5/51; 95% CI 4% to 21%). No participants attained at least 75 min per week of VPA on at least 50% of total weeks. Of the 53 participants, only 15 (28%) met 150 min per week of MVPA at least once throughout the study, and those 15 participants met that goal on a mean of 36% of weeks.

Overall, the median total MVPA minutes per week was 80 (IQR 31-162). Among all participants, median daily MVPA (more than 100 steps per min) was 6 min (IQR 2-13), whereas median daily minutes spent in lighter activity (60-99 steps per min) was 23 min (IQR 17-24). The median number of minutes spent in MVPA was significantly higher among men (12 min, IQR 3-20) than women (3.5 min, IQR 1-9; P=.004). The median number of minutes spent in lighter activity was also significantly higher among men (34 min, IQR 26-52) than women (18 min, IQR 15-23; P<.001). When comparing obese and nonobese participants, only MVPA minutes were significantly different, with median of 10 min (IQR 3-15) in participants with BMI less than 30 kg/m^2 versus median of 2.5 min (IQR 1-8.3) in participants with BMI greater than or equal to 30 kg/m^2 (P=.04; Table 2). There was poor correlation between the median daily MVPA minutes and baseline activity level (low, moderate, or high) as assessed by IPAQ (Spearman coefficient=−0.162; P=.25).

Table 2. Daily minutes spent at cadence bands by demographic characteristics over the study duration.

Characteristic	60 to 99 steps per minute, median (IQR)	More than 100 steps per minute, median (IQR)
Sex		
Men	34 (26-52)[a]	12 (3-20)[a]
Women	18 (15-23)[a]	3.5 (1-9)[a]
Age (years)		
<40	28.5 (17-44.3)	6.25 (2-15.5)
≥40	22.5 (18-29)	5 (2-12)
BMI (kg/m^2)		
<30	29 (18-44.5)	10 (3-15)[b]
≥30	21 (15.5-28)	2.5 (1-8.3)[b]

[a]*P*<.01, two-sample Wilcoxon rank sum test.

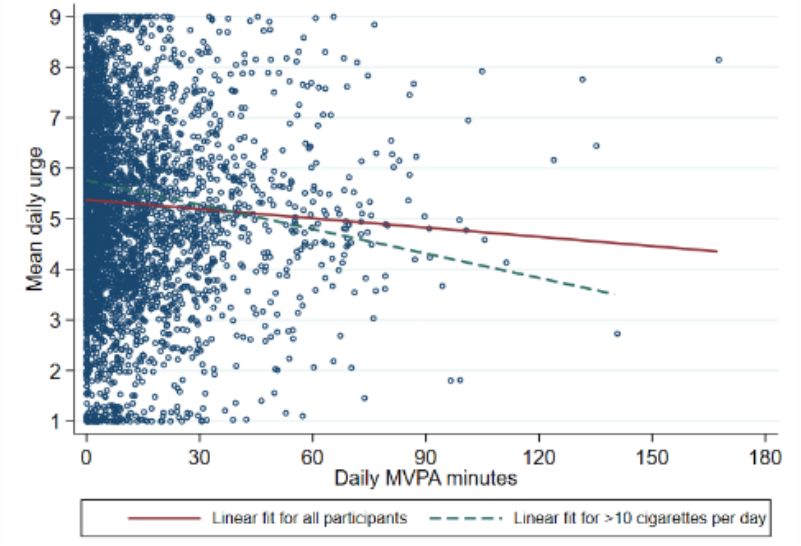
[b]*P*<.05, two-sample Wilcoxon rank sum test.

Association Between Day-Level Intensity and Urge

The number of daily MVPA minutes was positively skewed, with no clear association with urge upon inspection (Figure 1). Furthermore, logarithmic transformation of the MVPA variable did not reveal any clear relation with mean daily urge. There was no significant association between daily MVPA minutes and mean daily urge to smoke in either the unadjusted model (*P*=.74) or the adjusted model (*P*=.72).

We explored the interaction of daily MVPA minutes with binary demographic factors, defined as age greater than or equal to 40 years, sex, BMI greater than or equal to 30 kg/m^2, and baseline high activity based on IPAQ. The *P* values for interaction are as follows: .41 for age, .15 for sex, .90 for BMI, and .32 for high activity. Thus, no interaction terms were included in the adjusted models.

Figure 1. Mean daily smoking urge plotted against daily minutes of moderate-to-vigorous physical activity for all participants (N=53; 3633 person-days). MVPA: moderate-to-vigorous physical activity.



Sensitivity Analysis

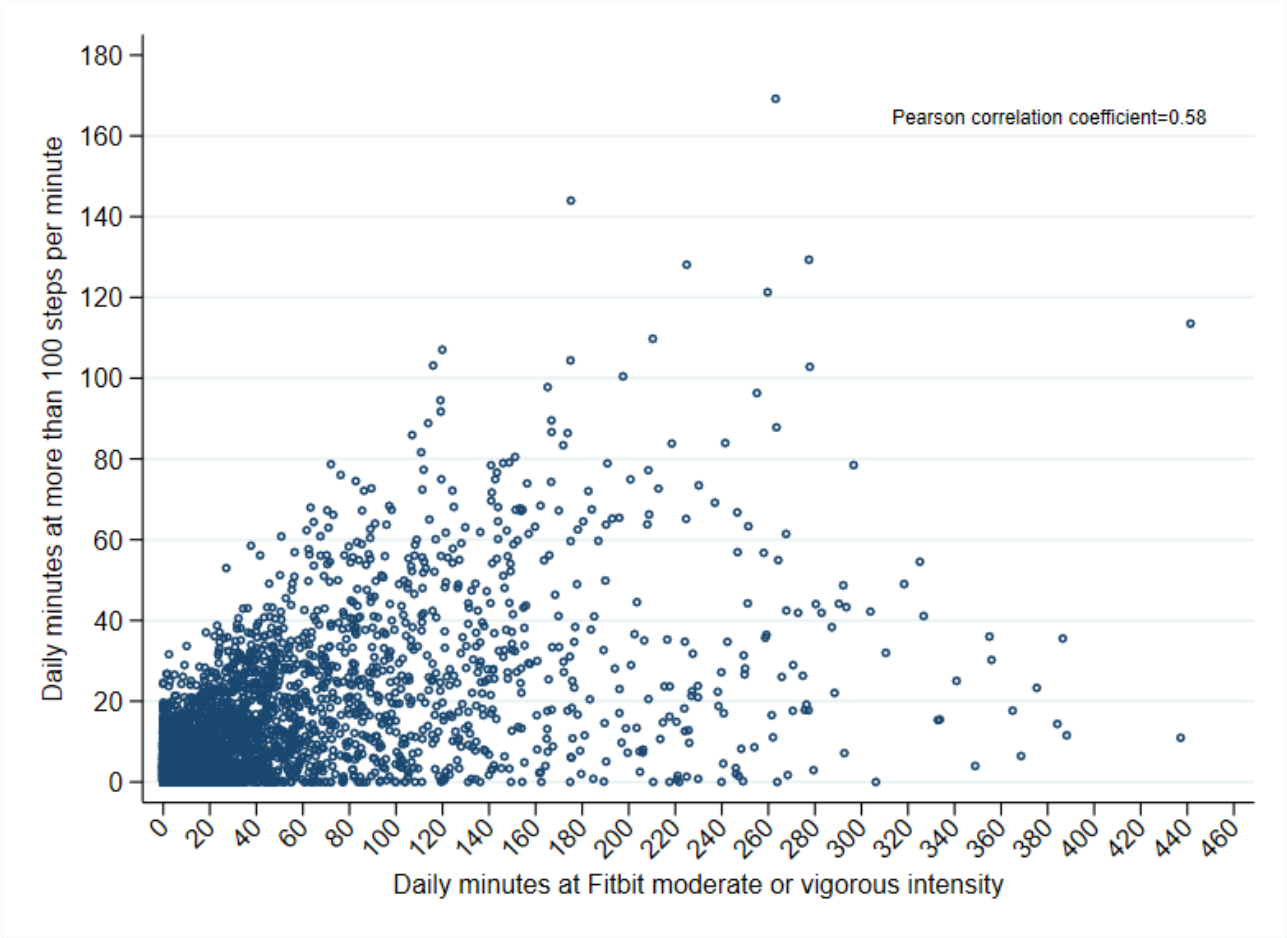
Given that our prior work validating the urge to smoke revealed a positive association between mean urge over the course of the study and the number of cigarettes per day reported at the end of the study [14], we explored associations by baseline cigarette consumption. When stratifying by baseline cigarettes per day, those who smoked more than 10 cigarettes per day (n=19; 1333 person-days) had 0.293 lower daily urge per 30 min per day of MVPA (*P*=.03; 95% CI −0.563 to −0.023; Figure 1), but this was not significant on stratifying by greater than equal to 15 (n=16; 1100 person-days; *P*=.80) or greater than equal to 20 cigarettes per day (n=11; 809 person-days; *P*=.88).

Comparison of Cadence Versus Fitbit's Intensity Levels

To elucidate the nature of Fitbit's intensity variable, we compared the distribution of daily MVPA minutes calculated using the definition of cadence greater than or equal to 100 steps per minute with the distribution of daily MVPA minutes as defined by the number of minutes spent at *moderate*- or *vigorous*-intensity levels as defined by Fitbit's algorithm (Figure

2). Although there was some correlation between daily MVPA minutes by cadence and daily MVPA minutes by Fitbit intensity (Pearson coefficient=0.58), the minutes categorized by Fitbit as MVPA tended to have lower cadences than the threshold of 100 steps per minute. The minutes that Fitbit categorized as *moderate* intensity had a median of 41 steps accumulated within that minute (IQR 14-67, range 0-138), whereas minutes categorized as *vigorous* intensity had a median of 95 steps accumulated (IQR 57-106, range 0-215). This led to a wider spread of daily MVPA minutes by Fitbit intensity (range 0-451 min) than by cadence (range 0-167 min).

Figure 2. Daily moderate-to-vigorous physical activity (MVPA) minutes calculated using cadence thresholds versus daily MVPA minutes calculated using Fitbit's intensity levels.



Discussion

Principal Findings

In this secondary analysis of data from mActive-Smoke, we described intensity of physical activity in free-living adult smokers and found that the prevalence of MVPA was low, with 10% (5/51) of participants attaining greater than or equal to 150 min of MVPA on at least 50% of study weeks and no participants attaining greater than or equal to 75 min of VPA on at least 50% of study weeks. Overall, the median daily MVPA was 6 min, and this differed by sex and BMI. Most participants achieved at least 30 min per day of light-intensity activity (60-99 steps per minute) over the study duration. In regression analyses, there was no association between daily MVPA minutes and mean daily smoking urges among all participants. In addition, this study provides exploratory insights on using Fitbit's intensity level to determine MVPA, compared with accepted cadence thresholds, which is a simpler marker of intensity available across measurement devices.

Comparison With Prior Work

This study highlights the low prevalence of MVPA in adult smokers in a free-living environment and poor adherence to the 2018 US Physical Activity Guidelines of greater than or equal to 150 min per week of MVPA. Our results corroborate observations by prior analyses of accelerometer data from the National Health and Nutrition Examination Survey (NHANES), which are representative of the general US population. Using 2005 to 2006 NHANES data, Tucker et al [20] found that 59.6% of adults met the 2008 US Physical Activity Guidelines by self-report, whereas 8.6% of adults met the guidelines by accelerometer measurement, using the goal of greater than or equal to 150 min per week of MVPA in the 10-min bout. In the 2018 US Physical Activity Guidelines, the 10-min bout requirement was removed; thus, we did not include bouts in the calculation of MVPA minutes. Doing so would likely further reduce the estimated attainment of recommended physical activity levels and, as such, would not impact the conclusion of low levels of physical activity guideline adherence.

Another analysis of 2005 to 2006 NHANES data found that US adults accumulated only about 7 min per day of self-selected activity at a cadence of greater than or equal to 100 steps per minute (generally defined as MVPA), but the participants did accumulate, on average, about 30 min per day of activity at cadences of more than 60 steps per minute [26]. The NHANES dataset from these prior studies included accelerometer data over 1 to 7 days, whereas our data were obtained over 6 to 12 weeks [20,26], thus suggesting that low levels of physical activity may persist over time. These results highlight a need for further work in promoting physical activity in smokers to mitigate the compounding cardiovascular risk factors of inactivity and smoking.

Although there was no intervention to increase physical activity, 82% (40/49) of participants reported in the exit survey that they believed the study helped increase their physical activity [14], affirming the potential of mHealth tools and self-monitoring in promoting behavioral change. Furthermore, the 2018 Physical Activity Guidelines recommend information technology and mHealth interventions as a future direction for tracking and promoting physical activity [4].

This study also addresses the recall bias in prior studies on physical activity and smoking urges. For example, Haasova et al [12] showed that more habitual MVPA minutes based on 7-day activity recall significantly correlated with decreased urge over the past 7 days in 98 smokers. The difference between results from this 7-day recall study and our analysis suggests that the prevalence of MVPA and granularity of data are important factors to consider in studies on physical activity and smoking urge. Specifically, median daily MVPA based on 7-day recall was 45 min (IQR 17-77) in the study by Hassova et al [12], whereas we measured median daily MVPA over 12 weeks to be 6 min (IQR 2-13) using minute-level and day-level granularity of data. This is unsurprising given that this analysis and prior studies [13] found poor correlation between self-reported intensity via IPAQ and accelerometer-measured intensity.

This study analyzed intensity on a day level by quantifying the total daily minutes of MVPA for each person-day, which builds on prior studies showing that short bouts of MVPA acutely decrease cigarette cravings in a controlled laboratory setting [11]. In addition, we build on our primary analysis of mActive-Smoke, which showed that increased rate of step accumulation within 15-, 30-, or 60-min time windows before urge reporting was associated with decreased urge. When comparing our results with these prior studies on acute effects, we conclude that although MVPA may modestly decrease the urge to smoke immediately after physical activity, the effect of MVPA on the urge to smoke does not appear to persist throughout the day.

Limitations

We acknowledge that this was a relatively small, single-center study, not generalizable to smokers everywhere. Despite the low prevalence of MVPA, the participants in this study had fairly high total daily step counts, suggesting that these participants may be active throughout the day at lighter intensities. This confers cardiovascular health benefits over a more sedentary lifestyle but may not be enough to affect smoking urges [4]. In addition, there is inherent selection bias, as participants who enrolled in this study were more likely to have an interest in behavior change, and step counts and urge reporting may be subject to the Hawthorne effect. However, it is important to note that even as part of a research study, the physical activity observed was low and similar to prior studies of the general population.

As this was a post hoc analysis, the sample size was not powered to test correlations between intensity and smoking urge. Although the total number of observations was high, the number of participants in this pilot study was relatively small, especially in the stratified models. However, we did account for repeated measures and autoregression in the model, and our smallest stratified group contained 809 person-days.

In addition, mActive-Smoke participants were lighter smokers, with 36% (19/53) reporting more than 10 cigarettes per day at baseline. Prior studies generally used a minimum of 10 cigarettes per day as the threshold for study inclusion [9,12]. We did not collect data on the time since the last cigarette to avoid overburdening participants with text messages; thus, we could not adjust for the potential confounding effect of recent smoking on urge. These factors may have generated a flooring effect, as physical activity may be less able to further reduce smoking urge when the urge is already low, either from a recent cigarette or because of lighter smokers having lower urges. We previously validated the urge scale and found that self-reported urges correlated well with daily cigarette consumption.

Cadence is an imprecise marker of intensity, correlating well with caloric expenditure, but does not account for types of activity other than walking or running, leading to possible underestimation of MVPA. In addition, the cadence thresholds used in these analyses were not adjusted for stride length variation among participants. Bias from lack of stride length adjustment is likely to be minimal, as overestimation of MVPA in participants with shorter stride is partially offset by underestimation of MVPA in participants with longer stride. Although the Fitbit Charge HR reports minute-level intensity levels, METs, and heart rate, we opted for cadence as the measure of intensity, as it is less dependent on other factors such as resting heart rate, comorbidities, and medications. Furthermore, validation studies have raised concerns about the accuracy of Fitbit's reporting of heart rate [23], intensity, and energy expenditure, although step count was generally accurate [21,27].

Despite the advantages of objective activity measures, it is important to note that physical activity guidelines were developed based on self-reported data, and there are currently no guidelines based on accelerometer data. Linking objective measures with physical activity guideline attainment to provide clinical context has been done previously [20], but this method requires further validation in future studies. More work is needed to develop guidelines based on objective metrics of physical activity. Future directions include devising the optimal method of incorporating heart rate data into measurement of MVPA while accounting for medications and clinical characteristics. Finally, Fitbit provides other information about health behaviors,

such as sleep, which could impact both physical activity and smoking urge and warrants further exploration.

Conclusions

In this 12-week observational study of adult smokers using mHealth tools for real-time assessment of physical activity and smoking urge, the prevalence of MVPA was low, and participants rarely met national guidelines for physical activity. We found no day-averaged association between intensity of activity and smoking urges. On the basis of the known benefits of physical activity and the low levels observed in this study, more work is needed to address physical activity promotion in smokers.

Acknowledgments

The Aetna Foundation funded the study through a grant to Johns Hopkins University and had no role in the study design, data collection, or statistical analysis. One writing team member from the Aetna Foundation participated in manuscript editing. The corresponding author had full access to all data and final responsibility for the decision to submit for publication.

Authors' Contributions

RS drafted the manuscript. RS, LRY, and LGSL analyzed the data. SK and LGSL collected the data. MJB, SSM, SK, and LGSL designed the study and developed the protocol. All authors edited the manuscript and approved the final version.

Conflicts of Interest

RS and LGSL report grants from the Aetna Foundation during the conduct of the study. LRY, SK, CAG, and GNG have nothing to disclose. MJB reports grants from the Aetna Foundation during the conduct of the study, grants from the National Institutes of Health, grants and personal fees from the US Food and Drug Administration, grants from the American Heart Association, grants from the American College of Cardiology, grants and personal fees from Amgen, personal fees from Novartis, personal fees from Sanofi, personal fees from Novo Nordisk, personal fees from Bayer, and personal fees from Medicure, outside the submitted work. SSM reports grants from the Aetna Foundation during the conduct of the study; personal fees from Amgen, Sanofi, Regeneron, Esperion, Novo Nordisk, Quest Diagnostics, and Akcea Therapeutics; and research support from Apple, Google, iHealth, Nokia, the Maryland Innovation Initiative, American Heart Association, PJ Schafer Memorial Fund, and David and June Trone Family Foundation, outside the submitted work. In addition, SSM has a pending patent on a System of low-density lipoprotein cholesterol estimation.

References

1. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation 2018 Mar 20;137(12):e67-492. [doi: 10.1161/CIR.0000000000000558] [Medline: 29386200]
2. Hughes J, Keely J, Naud S. Shape of the relapse curve and long-term abstinence among untreated smokers. Addiction 2004 Jan;99(1):29-38. [doi: 10.1111/j.1360-0443.2004.00540.x] [Medline: 14678060]
3. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, Lancet Physical Activity Series 2 Executive Committe, Lancet Sedentary Behaviour Working Group. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet 2016 Sep 24;388(10051):1302-1310. [doi: 10.1016/S0140-6736(16)30370-1] [Medline: 27475271]
4. Office of Disease Prevention and Health Promotion. 2018. 2018 Physical Activity Guidelines Advisory Committee Scientific Report URL: https://health.gov/paguidelines/second-edition/report/pdf/PAG_Advisory_Committee_Report.pdf [accessed 2019-01-29]
5. Walker A, Langdon J, Johnson K. Relationships among meeting physical-activity guidelines and health risk behaviors. J Phys Act Health 2015 Jun;12(6):776-781. [doi: 10.1123/jpah.2014-0079] [Medline: 25110985]
6. Milicic S, Piérard E, DeCicca P, Leatherdale ST. Examining the association between physical activity, sedentary behavior and sport participation with e-cigarette use and smoking status in a large sample of Canadian youth. Nicotine Tob Res 2019 Feb 18;21(3):285-292 [FREE Full text] [doi: 10.1093/ntr/ntx238] [Medline: 29099946]
7. Ussher MH, Taylor AH, Faulkner GE. Exercise interventions for smoking cessation. Cochrane Database Syst Rev 2014 Aug 29(8):CD002295. [doi: 10.1002/14651858.CD002295.pub5] [Medline: 25170798]
8. Thompson TP, Greaves CJ, Ayres R, Aveyard P, Warren FC, Byng R, et al. An exploratory analysis of the smoking and physical activity outcomes from a pilot randomized controlled trial of an exercise assisted reduction to stop smoking intervention in disadvantaged groups. Nicotine Tob Res 2016 Mar;18(3):289-297. [doi: 10.1093/ntr/ntv099] [Medline: 25969453]
9. Klinsophon T, Thaveeratitham P, Sitthipornvorakul E, Janwantanakul P. Effect of exercise type on smoking cessation: a meta-analysis of randomized controlled trials. BMC Res Notes 2017 Sep 6;10(1):442 [FREE Full text] [doi: 10.1186/s13104-017-2762-y] [Medline: 28874175]

10. Haasova M, Warren F, Ussher M, van Rensburg KJ, Faulkner G, Cropley M, et al. The acute effects of physical activity on cigarette cravings: systematic review and meta-analysis with individual participant data. Addiction 2013 Jan;108(1):26-37. [doi: 10.1111/j.1360-0443.2012.04034.x] [Medline: 22861822]
11. Haasova M, Warren FC, Ussher M, van Rensburg KJ, Faulkner G, Cropley M, et al. The acute effects of physical activity on cigarette cravings: exploration of potential moderators, mediators and physical activity attributes using individual participant data (IPD) meta-analyses. Psychopharmacology (Berl) 2014 Apr;231(7):1267-1275. [doi: 10.1007/s00213-014-3450-4] [Medline: 24522330]
12. Haasova M, Warren FC, Thompson T, Ussher M, Taylor AH. The association between habitual physical activity and cigarette cravings, and influence of smokers' characteristics in disadvantaged smokers not ready to quit. Psychopharmacology (Berl) 2016 Jul;233(14):2765-2774 [FREE Full text] [doi: 10.1007/s00213-016-4326-6] [Medline: 27256353]
13. Knell G, Gabriel K, Businelle M, Shuval K, Wetter D, Kendzor D. Ecological momentary assessment of physical activity: validation study. J Med Internet Res 2017 Jul 18;19(7):e253 [FREE Full text] [doi: 10.2196/jmir.7602] [Medline: 28720556]
14. Silverman-Lloyd LG, Kianoush S, Blaha MJ, Sabina AB, Graham GN, Martin SS. mActive-Smoke: a prospective observational study using mobile health tools to assess the association of physical activity with smoking urges. JMIR Mhealth Uhealth 2018 May 11;6(5):e121 [FREE Full text] [doi: 10.2196/mhealth.9292] [Medline: 29752250]
15. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
16. Bauman A, Bull F, Chey T, Craig C, Ainsworth B, Sallis J, et al. The International Prevalence Study on Physical Activity: results from 20 countries. Int J Behav Nutr Phys Act 2009 Mar 31;6:21 [FREE Full text] [doi: 10.1186/1479-5868-6-21] [Medline: 19335883]
17. The University of Arizona Cancer Center. Behavior Measurement and Interventions URL: https://cancercenter.arizona.edu/researchers/shared-resources/behavioral-measurement-and-interventions [accessed 2019-06-05] [WebCite Cache ID 78uCl7Pho]
18. Fitabase. 2018. Fitabase Data Dictionary URL: https://www.fitabase.com/media/1748/fitabasedatadictionary.pdf [accessed 2019-06-06] [WebCite Cache ID 78w1eBN4d]
19. Schrack JA, Cooper R, Koster A, Shiroma EJ, Murabito JM, Rejeski WJ, et al. Assessing daily physical activity in older adults: unraveling the complexity of monitors, measures, and methods. J Gerontol A Biol Sci Med Sci 2016 Aug;71(8):1039-1048 [FREE Full text] [doi: 10.1093/gerona/glw026] [Medline: 26957472]
20. Tucker JM, Welk GJ, Beyler NK. Physical activity in US: adults compliance with the Physical Activity Guidelines for Americans. Am J Prev Med 2011 Apr;40(4):454-461. [doi: 10.1016/j.amepre.2010.12.016] [Medline: 21406280]
21. Dominick GM, Winfree KN, Pohlig RT, Papas MA. Physical activity assessment between consumer- and research-grade accelerometers: a comparative study in free-living conditions. JMIR Mhealth Uhealth 2016 Sep 19;4(3):e110 [FREE Full text] [doi: 10.2196/mhealth.6281] [Medline: 27644334]
22. Evenson KR, Goto MM, Furberg RD. Systematic review of the validity and reliability of consumer-wearable activity trackers. Int J Behav Nutr Phys Act 2015 Dec 18;12:159 [FREE Full text] [doi: 10.1186/s12966-015-0314-1] [Medline: 26684758]
23. Wang R, Blackburn G, Desai M, Phelan D, Gillinov L, Houghtaling P, et al. Accuracy of wrist-worn heart rate monitors. JAMA Cardiol 2017 Jan 1;2(1):104-106. [doi: 10.1001/jamacardio.2016.3340] [Medline: 27732703]
24. Tudor-Locke C, Han H, Aguiar E, Barreira TV, Schuna JM, Kang M, et al. How fast is fast enough? Walking cadence (steps/min) as a practical estimate of intensity in adults: a narrative review. Br J Sports Med 2018 Jun;52(12):776-788 [FREE Full text] [doi: 10.1136/bjsports-2017-097628] [Medline: 29858465]
25. Tudor-Locke C, Craig CL, Brown WJ, Clemes SA, de Cocker K, Giles-Corti B, et al. How many steps/day are enough? For adults. Int J Behav Nutr Phys Act 2011 Jul 28;8:79 [FREE Full text] [doi: 10.1186/1479-5868-8-79] [Medline: 21798015]
26. Tudor-Locke C, Camhi SM, Leonardi C, Johnson WD, Katzmarzyk PT, Earnest CP, et al. Patterns of adult stepping cadence in the 2005-2006 NHANES. Prev Med 2011 Sep;53(3):178-181. [doi: 10.1016/j.ypmed.2011.06.004] [Medline: 21708187]
27. Alharbi M, Bauman A, Neubeck L, Gallagher R. Validation of Fitbit-Flex as a measure of free-living physical activity in a community-based phase III cardiac rehabilitation population. Eur J Prev Cardiol 2016 Sep;23(14):1476-1485. [doi: 10.1177/2047487316634883] [Medline: 26907794]

Abbreviations

IPAQ: International Physical Activity Questionnaire
MET: metabolic equivalent of task
mHealth: mobile health
MVPA: moderate-to-vigorous physical activity
NHANES: National Health and Nutrition Examination Survey
VPA: vigorous physical activity

Edited by N Bruining; submitted 11.06.19; peer-reviewed by G Knell, M Andrews, K Winfree; comments to author 14.08.19; revised version received 30.09.19; accepted 01.11.19; published 06.01.20.

Please cite as:
Shan R, Yanek LR, Silverman-Lloyd LG, Kianoush S, Blaha MJ, German CA, Graham GN, Martin SS
Using Mobile Health Tools to Assess Physical Activity Guideline Adherence and Smoking Urges: Secondary Analysis of mActive-Smoke
JMIR Cardio 2020;4(1):e14963
URL: https://cardio.jmir.org/2020/1/e14963
doi:10.2196/14963
PMID:31904575

Corrigenda and Addenda

Correction: Using an Electronic App to Promote Home-Based Self-Care in Older Patients With Heart Failure: Qualitative Study on Patient and Informal Caregiver Challenges

Sahr Wali[1,2], MSc; Karim Keshavjee[2,3], MSc, MBA, MD, CCFP; Linda Nguyen[4], MSc; Lawrence Mbuagbaw[5], MD, MPH, PhD, FRSPH; Catherine Demers[5,6], MD, MSc, FRCPC

[1]Centre for Global eHealth Innovation, Techna Institute, University Health Network, Toronto, ON, Canada

[2]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

[3]InfoClin, Toronto, ON, Canada

[4]School of Rehabilitation Science, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

[5]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada

[6]Department of Medicine, McMaster University, Hamilton, ON, Canada

Corresponding Author:
Catherine Demers, MD, MSc, FRCPC
Department of Health Research Methods, Evidence and Impact
McMaster University
237 Barton St E
Hamilton, ON, L8L 2X2
Canada
Phone: 1 905 525 9140 ext 73324
Email: demers@hhsc.ca

Related Article:

Correction of: https://cardio.jmir.org/2020/1/e15885/

(JMIR Cardio 2020;4(1):e25624) doi:10.2196/25624

In "Using an Electronic App to Promote Home-Based Self-Care in Older Patients With Heart Failure: Qualitative Study on Patient and Informal Caregiver Challenges" (JMIR Cardio 2020;4(1):e15885) the authors noted two errors.

In the originally published article, Sahr Wali was listed as the Corresponding Author. The Corresponding Author address was listed as:

Institute of Health Policy, Management and Evaluation
Dalla Lana School of Public Health
University of Toronto
155 College St
Toronto, ON, M5T 3M6
Canada
Phone: 1 416 978 4326
Email: sahr.wali@mail.utoronto.ca

In the corrected version, the Corresponding Author has been changed to Catherine Demers, with the Corresponding Author address:

Department of Health Research Methods, Evidence and Impact
McMaster University
237 Barton St E
Hamilton, ON, L8L 2X2
Canada
Phone: 1 905 525 9140 ext 73324
Email: demers@hhsc.ca

An Acknowledgements section has also been added to the original paper with the following text:

This work was completed at McMaster University.

The correction will appear in the online version of the paper on the JMIR Publications website on November 11, 2020, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Submitted 09.11.20; this is a non–peer-reviewed article;accepted 10.11.20; published 11.11.20.

Please cite as:
Wali S, Keshavjee K, Nguyen L, Mbuagbaw L, Demers C
Correction: Using an Electronic App to Promote Home-Based Self-Care in Older Patients With Heart Failure: Qualitative Study on Patient and Informal Caregiver Challenges
JMIR Cardio 2020;4(1):e25624
URL: http://cardio.jmir.org/2020/1/e25624/
doi:10.2196/25624
PMID:33175695

Original Paper

The Atrial Fibrillation Health Literacy Information Technology Trial: Pilot Trial of a Mobile Health App for Atrial Fibrillation

Emily Guhl[1], BA, MD; Andrew D Althouse[2], PhD; Alexandra M Pusateri[3], BSc; Everlyne Kimani[4], BSc; Michael K Paasche-Orlow[5], MPH, MA, MD; Timothy W Bickmore[4], PhD; Jared W Magnani[1,2], MSc, MD

[1]Heart and Vascular Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, United States

[2]Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, United States

[3]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States

[4]College of Computer and Information Science, Northeastern University, Boston, MA, United States

[5]Section of General Internal Medicine, Department of Medicine, Boston University, Boston, MA, United States

Corresponding Author:
Emily Guhl, BA, MD
Heart and Vascular Institute
University of Pittsburgh Medical Center
200 Lothrop St
Pittsburgh, PA, 15213
United States
Phone: 1 4126473429
Email: guhlen@upmc.edu

Abstract

Background: Atrial fibrillation (AF) is a common arrhythmia that adversely affects health-related quality of life (HRQoL). We conducted a pilot trial of individuals with AF using a smartphone to provide a relational agent as well as rhythm monitoring. We employed our pilot to measure acceptability and adherence and to assess its effectiveness in improving HRQoL and adherence.

Objective: This study aims to measure acceptability and adherence and to assess its effectiveness to improve HRQoL and adherence.

Methods: Participants were recruited from ambulatory clinics and randomized to a 30-day intervention or usual care. We collected baseline characteristics and conducted baseline and 30-day assessments of HRQoL using the Atrial Fibrillation Effect on Quality of Life (AFEQT) measure and self-reported adherence to anticoagulation. The intervention consisted of a smartphone-based relational agent, which simulates face-to-face counseling and delivered content on AF education, adherence, and symptom monitoring with prompted rhythm monitoring. We compared differences in AFEQT and adherence at 30 days, adjusted for baseline values. We quantified participants' use and acceptability of the intervention.

Results: A total of 120 participants were recruited and randomized (59 to control and 61 to intervention) to the pilot trial (mean age 72.1 years, SD 9.10; 62/120, 51.7% women). The control group had a 95% follow-up, and the intervention group had a 93% follow-up. The intervention group demonstrated significantly higher improvement in total AFEQT scores (adjusted mean difference 4.5; 95% CI 0.6-8.3; *P*=.03) and in daily activity (adjusted mean difference 7.1; 95% CI 1.8-12.4; *P*=.009) compared with the control between baseline and 30 days. The intervention group showed significantly improved self-reported adherence to anticoagulation therapy at 30 days (intervention 3.5%; control 23.2%; adjusted difference 16.6%; 95% CI 2.8%-30.4%; *P*<.001). Qualitative assessments of acceptability identified that participants found the relational agent useful, informative, and trustworthy.

Conclusions: Individuals randomized to a 30-day smartphone intervention with a relational agent and rhythm monitoring showed significant improvement in HRQoL and adherence. Participants had favorable acceptability of the intervention with both objective use and qualitative assessments of acceptability.

(JMIR Cardio 2020;4(1):e17162) doi:10.2196/17162

KEYWORDS

atrial fibrillation; health-related quality of life; medication adherence; health literacy; mobile phone

Introduction

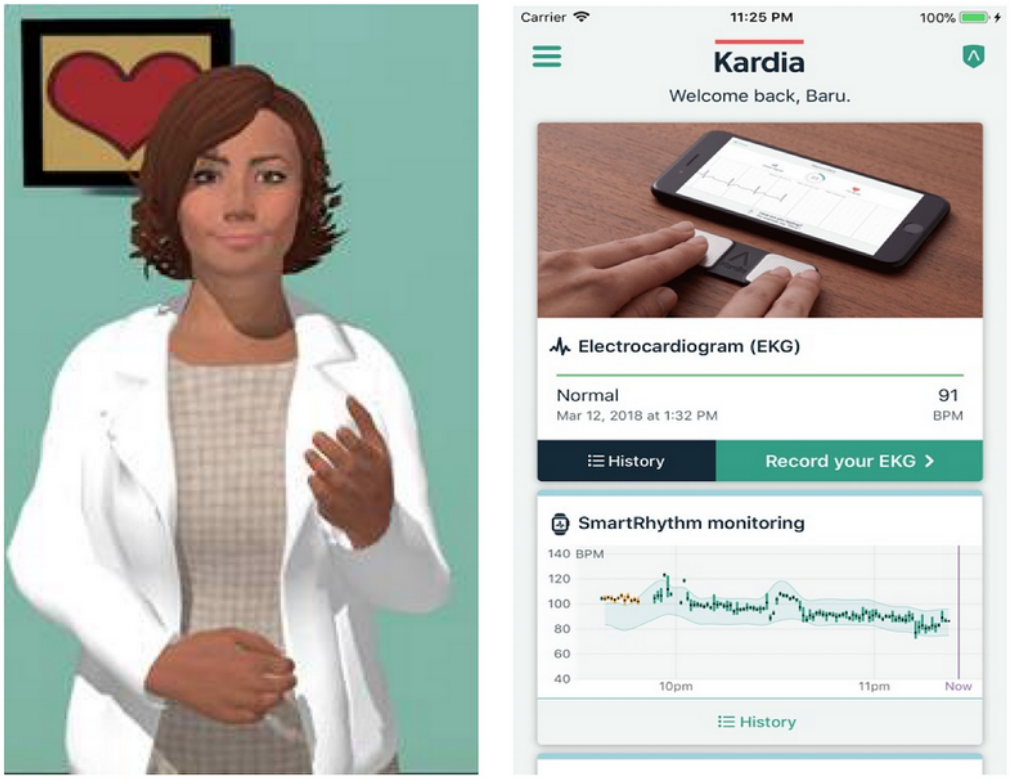
Background

Atrial fibrillation (AF) is a highly prevalent cardiac arrhythmia. AF is challenging for patients because it typically requires long-term adherence to anticoagulation for stroke prevention, symptom assessment, symptom monitoring, and navigating subspecialty care [1]. AF is an important cause of stroke, heart failure, and death. In addition, the symptoms, treatment burden, prognostic uncertainty, and adverse effects on general health and functional status associated with AF may worsen health-related quality of life (HRQoL) in patients with the condition [2]. The effect of AF on HRQoL may be amplified by limited health literacy [3], which can exacerbate the challenges patients face in negotiating a chronic and complex disease such as AF. Individuals with limited health literacy are particularly vulnerable to AF as the condition requires education, decision-making, and long-term adherence. Previous work looking at one-time educational sessions in those with limited health literacy and AF did not improve outcomes in AF [3]. In a population where limited health literacy has an impact on patient-centered outcomes, an intervention that allows for ongoing intervention, such as a mobile app, may improve outcomes.

Objectives

We have developed a mobile health technology intervention using a relational agent with the goal of improving patient-centered care in AF [4]. The agent functions by simulating a face-to-face conversation with a health counselor using synthetic speech and an animated counselor that uses nonverbal conversational behaviors such as hand gestures and facial displays (Figure 1). In each interaction, the relational agent dialogue is tailored with the patient using their name and personal information as well as responding to their conversational inputs from the current and prior conversations. Our team has used relational agents in multiple health contexts with the goal of fostering a therapeutic alliance and assisting self-care in individuals with chronic medical conditions, particularly those with limited health literacy [5-9]. We have implemented relational agents to improve self-care and health outcomes such as increasing physical activity in older adults, improving communication at hospital discharge to prevent readmission rates, and educate patients for shared decision-making [5,10-12]. Relational agents provide an interactive resource for longitudinal patient engagement that contrasts with traditional media for patient education, such as web-based videos or literature. Relational agents have the further advantage of expressing empathy during interactions in addition to the opportunities to conduct didactic interventions, repeated assessments, and monitoring.

Figure 1. Relational agent as presented by a smartphone to individuals randomized to the intervention (left); Kardia app as presented by a smartphone (right).



This pilot trial implemented a limited relational agent designed to improve adherence and HRQoL in individuals with AF. In conjunction with the relational agent, we used AliveCor's Kardia mobile heart rate and rhythm monitor (Kardia), a validated and Food and Drug Administration–approved instrument for smartphone-based heart monitoring [13]. Our relational agent curriculum taught patients how to use and interpret the Kardia and guided Kardia use when they reported symptoms. We expect that the real-time feedback of the Kardia-recorded rhythm, particularly when individuals are experiencing symptoms, will

enhance patient understanding of the disease. We hypothesized that our intervention would result in better AF-specific HRQoL and adherence when compared with usual care in a pilot cohort of 120 participants.

Methods

Trial Design and Recruitment

We conducted a single-center, parallel arm pilot trial, termed the Atrial Fibrillation Health Literacy Information Technology Trial, registered at ClinicalTrials.gov (NCT030935558). Our trial was conducted according to the CONSORT (Consolidated Standards of Reporting Trials) statement and guidelines for pilot and feasibility trials. Our primary outcome for this study was HRQoL measured with the Atrial Fibrillation Effect on Quality of Life (AFEQT) measure (range 0-100, higher scores associated with superior HRQoL). Our secondary outcomes included self-reported adherence to anticoagulation and assessment of intervention acceptability by qualitative and quantitative measurements.

Study participants were recruited while receiving care at ambulatory facilities at the University of Pittsburgh Medical Center, a large regional health care system spanning multiple sites in Pittsburgh, Pennsylvania. Participants were identified by reviewing the electronic medical record, referral to the study using the University of Pittsburgh's Center for Assistance in Research eRecord protocol, referral by clinical providers, or participant-initiated self-referral. Inclusion criteria were (1) age ≥18 years, (2) history of chronic AF, (3) prescribed oral anticoagulation for stroke prevention secondary to AF, and (4) English-speaking sufficient to use a smartphone-based relational agent as ascertained by the study screener. Participants were excluded from this pilot trial if they had AF deemed attributable to a non-cardiac cause, had undergone cardiothoracic or thoracic surgery within 30 days of evaluation, were unable to use the smartphone apps after training, had a life expectancy of <12 months as identified by a concurrent diagnosis (such as malignancy), or by determination of the research team for not being able to participate in the informed consent process. Prior experience with a smartphone was not a criterion for participation. Individuals without a smartphone randomized to the intervention arm were provided with one for their general use during the 30-day study period. Participants in the intervention were also given the Kardia device. Intervention participants received a training session on how to use the smartphone, relational agent, and Kardia apps. Participants randomized to the intervention were provided with instructions on how to access the relational agent and the Kardia. They were provided with a comprehensive orientation to the phone and the intervention apps. Participants were provided with instructions until they demonstrated adequate familiarity with the instruments. All participants recorded an electrocardiogram with the Kardia under study personnel supervision. The orientation session was concluded when participants were able to demonstrate how to turn the phone on, charge it, and access and use the apps. The study protocol and informed consent were reviewed and approved by the University of Pittsburgh Institutional Review Board.

Patient and Public Involvement

Content for the relational agent was informed by interviewing individual patients about their experience of AF. During the interviews, patients identified the principal challenges of AF and self-management. Patients described obstacles to understanding the disease, its causes, chronicity, and potential outcomes; adherence to anticoagulation, including both intentional (eg, forgetting and electing to forego) and nonintentional (eg, transportation to pharmacy) adherence to anticoagulation; symptom recognition and how to respond to symptoms; self-care approaches to AF, such as monitoring symptoms; and preparation for the clinical encounter.

Relational Agent Development and Content

The intervention arm includes a smartphone-based relational agent named *Tanya* (Figure 1) that simulates a face-to-face conversation with a health coach using synthetic speech and accompanying animated behavior such as hand gestures. *Tanya* functions to augment patient-centered health care by providing health education, monitoring, and problem-solving for users. The content is tailored for individual use by using the user's name and appropriate time context (eg, "Good Afternoon"). As the user goes through the relational agent's content, she is given the choice to select from a menu of responses, which then prompts the relational agent's response. In addition, the relational agent can be programmed to refer to prior content areas and obtain repeated assessments to follow for the resolution of reported problems. The content for the relational agent was developed by a review of patient-centered domains, review of the literature, and qualitative interviews with patients. Prior work has demonstrated that relational agents provide health education and counseling that are accessible to individuals with limited health and computer literacy and diverse socioeconomic backgrounds [5-9]. We developed a dialogue for this relational agent by reviewing patient-centered domains, literature, and qualitative interviews with patients with AF. The dialogue content was organized as modules that focused on 3 different domains: AF education, symptoms, and adherence. Relational agent dialogue referred to the Kardia regularly to reinforce its use, provide instruction on the use of the device, and direct users to check rhythm concomitant with reporting symptoms. We monitored the modular content accessed and frequency and duration of relational agent usage.

Participant Assessments

Assessments were obtained at clinical sites following the administration of informed consent. Participant age, sex, race, and ethnicity were obtained from electronic medical records. Smoking status, educational attainment, and annual income were self-reported. BMI was extracted from the medical records. Clinical history, including hypertension, diabetes, cardiovascular disease, heart failure, and prior stroke or transient ischemic attack, was obtained from the medical records, as were medications (ie, anticoagulants, antiarrhythmics, and rate control agents) and treatments (ie, cardioversion and pulmonary vein isolation) relevant to AF. For the measure of health literacy, we used the Short-Test Of Functional Health Literacy in Adults, which is a 36-item measure that is scored from 1 to 36, with higher scores indicating superior health literacy and scores of

23 indicating limited health literacy [14]. Depression was measured using the Patient Health Questionnaire-9, a validated 9-item questionnaire scored from 0 to 27, with scores >10 correlating with the presence of depression and increasing scores correlating with increasing depression severity [15].

We assessed HRQoL and self-reported anticoagulant adherence at baseline and at 30 days. The AFEQT is a validated 20-item instrument measuring self-reported HRQoL specific to AF (range 0-100, higher scores associated with superior HRQoL) [16]. In addition to providing a global measure of AF-specific HRQoL, the AFEQT measures the impact of AF on HRQoL across the 4 domains of symptoms, daily activities, treatment concerns, and treatment satisfaction. The overall AFEQT score is calculated using a composite of the first 3 domains: symptoms, daily activities, and treatment concerns. The domain scores are calculated using the sum of the responses of the answers for each specific category. Both composite and domain AFEQT scores range from 0 to 100, with higher scores representing superior HRQoL. Medication adherence was measured at enrollment and follow-up by asking participants about their specific agent for anticoagulation. Participants were asked (1) "Do you sometimes forget to take [name of prescribed anticoagulant medication]?" and (2) "Over the past two weeks, were there days that you did not take [name of prescribed anticoagulant medication]?" Participants randomized to the intervention arm completed assessments and interviews at 30 days to report and describe their response to the relational agent. Qualitative assessment of relational agents was performed by administering patient questionnaires with free-text responses to those in the intervention arm. Examples of questions included in the acceptability assessment were "What did you like least about the application?," "What were your overall impressions of Tanya?," or "How did you feel about having Tanya with you all of the time?." Responses were recorded and assessed for representative quotations.

Randomization and Data Collection

Individuals eligible for participation in the study were approached by the study team. After agreeing to participate and undergoing informed consent, they were randomized, with allocation concealed, 1:1 to receive the intervention or usual care using a computer-generated randomization scheme with the Research Electronic Data Capture hosted at the University of Pittsburgh [17]. Randomization was not blinded as individuals receiving the intervention underwent installation of the relational agent and Kardia apps on their smartphones or received a study smartphone with these apps for temporary use. Individuals in the intervention arm were instructed to use the apps daily. Study staff, outcome assessors, and data analysts were not blinded to the allocation as the intervention group had additional assessments of the app.

Statistical Analysis

For our sample size calculation, we assumed an SD in the AFEQT score ranging from 16 to 24 units, consistent with prior literature and a smaller-sized, single-arm demonstration of our intervention [4,18,19]. With an estimated population mean difference of 12 points between the intervention and control arms and an SD of 22 points, a total sample size of 120 participants would have 85% power to show a difference between the intervention and control groups. Continuous variables were summarized by their mean and SD and categorical variables by their frequency and percentage. ANCOVA (analysis of covariance) was used to compare differences in follow-up AFEQT scores between the intervention and control arms adjusting for baseline scores [20]. A 2-tailed alpha value of .05 was deemed statistically significant. All analyses were conducted as intention-to-treat, with no participants excluded from analyses, regardless of their adherence to the intervention. As this study was a pilot trial, no adjustments were made for multiple comparisons. Statistical analyses were performed using SAS (version 9.4; SAS Institute).

Results

Baseline Characteristics

Multimedia Appendix 1 describes the enrollments and follow-up of the study. From July 2017 to April 2018, a total of 527 individuals eligible for participation were identified as attending scheduled clinic visits. Of these, the study team was able to approach 236, of whom 129 agreed to participate. The first available 120 individuals were then consented for enrollment and randomized (59 to the control group and 61 to the intervention group). Table 1 describes the characteristics of the 120 enrolled participants by the study arm. Participants were aged 72.1 (SD 9.1) years, and 51.7% (62/120) participants were women. Age and sex distributions were similar in the 2 arms, although control arm participants were more likely to have heart failure and diabetes than those in the intervention arm. The cohort was well educated, with 60.8% (73/120) having a bachelor's degree or higher. Of the total cohort, 35.0% (42/120) reported an annual household income of <US $50,000. Of the 61 participants randomized to receive the intervention, 93.4% (57/61) completed the 30-day follow-up and 4 decided to leave the study. There were 59 individuals randomized to the control, of whom 94.9% (56/59) completed the 30-day follow-up, with the remaining leaving the study for unknown reasons.

Table 1. Characteristics of pilot trial participants by treatment arm.

Characteristics[a]	All participants (n=120)	Control (n=59)	Intervention (n=61)
Age (years), mean (SD)	72.1 (9.10)	72.6 (7.28)	71.7 (10.6)
Female gender, n (%)	62 (51.7)	30 (50.8)	32 (52.5)
White race, n (%)	111 (92.5)	54 (91.5)	57 (93.4)
BMI (m/kg^2), mean (SD)	30.9 (6.79)	31.0 (5.92)	30.8 (7.61)
Smoking history, n (%)			
Never	63 (52.5)	30 (50.8)	33 (54.1)
Former	53 (44.1)	25 (42.4)	28 (45.9)
Current	4 (3.3)	4 (6.8)	0 (0.0)
Heart failure, n (%)	24 (20.0)	14 (23.7)	10 (16.4)
Preserved, n (%)	15 (12.5)	9 (15.3)	6 (9.8)
Reduced, n (%)	9 (7.5)	5 (8.5)	4 (6.6)
Hypertension, n (%)	105 (87.5)	50 (84.7)	55 (90.2)
Diabetes, n (%)	29 (24.2)	17 (28.8)	12 (19.7)
Stroke/TIA[b], n (%)	1 (0.8)	1 (1.7)	0 (0.0)
Vascular disease, n (%)	30 (25.0)	15 (25.4)	15 (24.6)
Education, n (%)			
High school/vocational	34 (28.3)	21 (35.6)	13 (21.3)
Some college	13 (10.8)	6 (10.2)	7 (11.5)
Bachelor's degree	33 (27.5)	17 (28.8)	16 (26.2)
Graduate	40 (33.3)	15 (25.4)	25 (41.0)
Income (US $), n (%)			
<19,999	10 (8.3)	6 (10.2)	4 (6.6)
20,000-49,999	32 (26.7)	17 (28.8)	15 (24.6)
50,000-99,999	30 (25.0)	13 (22.0)	17 (27.9)
>100,000	25 (20.8)	11 (18.6)	14 (23.0)
S-TOFHLA[c], mean (SD)	30.1 (4.5)	30.3 (4.0)	30.0 (4.9)
S-TOFHLA ≤23, n (%)	10 (8.3)	4 (6.8)	6 (9.8)
PHQ-9[d] score, (units)	3 (1-4)	3 (1-6)	3 (1-4)

[a]Continuous variables are presented as mean (SD), and categorical variables are presented as number (percentage).

[b]TIA: transient ischemic attack.

[c]S-TOFHLA: Short-Test Of Functional Health Literacy in Adults.

[d]PHQ-9: Patient Health Questionnaire-9.

AFEQT scores

Multimedia Appendix 2 graphically displays the AFEQT scores of the control and interventional arms at baseline and 30-day follow-up. Table 2 reports the between-group contrast in 30-day AFEQT scores by total score and individual domains with covariate adjustment for baseline scores. Intervention participants had better scores in total AFEQT (adjusted mean difference 4.5; 95% CI 0.6-8.3; *P*=.03) and daily activity domain (adjusted mean difference 7.1; 95% CI 1.8-12.4; *P*=.009) scores compared with the control with adjustment for baseline. Anticoagulant adherence data are presented in Table 3, which shows significantly greater improvement in the interventional group compared with the control group for both self-report anticoagulant adherence items.

Table 2. Atrial Fibrillation Effect on Quality of Life scores, baseline and 30-day follow-up, by treatment arm.

Scores and subscores	Control, mean (SD)		Intervention, mean (SD)		Adjusted mean difference	
	Baseline	Follow-up	Baseline	Follow-up	Adjusted mean difference (95% CI)[a]	*P* value[b]
AFEQT[c] symptom	83.7 (19.7)	82.8 (21.2)	85.9 (14.5)	87.6 (15.2)	3.1 (−1.3 to 9.6)	.26
AFEQT daily activity	69.6 (23.8)	69.5 (22.3)	77.6 (19.9)	82.6 (18.6)	7.1 (1.8 to 12.4)	.009
AFEQT treatment	79.4 (20.1)	80.4 (21.2)	83.8 (15.7)	87.1 (14.8)	2.9 (−1.9 to 7.8)	.24
AFEQT satisfaction	79.3 (22.9)	79.3 (19.3)	78.5 (23.1)	83.3 (20.9)	4.3 (−2.6 to 11.3)	.22
AFEQT total	76.0 (17.6)	76.1 (16.7)	81.5 (14.2)	85.2 (14.1)	4.5 (0.6 to 8.3)	.03

[a]Estimate of the adjusted mean difference (95% CI) between follow-up AFEQT score in intervention group versus control group from analysis of covariance model with follow-up AFEQT score as outcome variable, adjusting for baseline score as covariate.

[b]*P* value from analysis of covariance model comparing follow-up AFEQT score between intervention group versus control group with adjustment for baseline score.

[c]AFEQT: Atrial Fibrillation Effect on Quality of Life.

Table 3. Self-reported adherence to anticoagulation by treatment arm.

Adherence questions	Control, n (%)		Intervention, n (%)			
	Baseline (n=59)	Follow-up (n=56)	Baseline (n=61)	Follow-up (n=57)	Adjusted % difference (95% CI)[a]	*P* value[b]
Do you sometimes forget to take (name of anticoagulant medication)?[c]	13 (22)	13 (23.2)	17 (27.9)	2 (3.5)	16.6 (2.8 to 30.4)	<.001
Over the past 2 weeks, were there any days you did not take (name of anticoagulant medication)?[c]	4 (6.8)	6 (10.7)	11 (18)	2 (3.5)	7.9 (−1.5 to 17.2)	.09

[a]Estimate of the adjusted percentage difference (95% CI) of follow-up adherence in the intervention group versus control group from logistic regression model with follow-up adherence as outcome variable, adjusting for baseline adherence as covariate.

[b]*P* value from logistic regression model comparing follow-up adherence between intervention group versus control group with adjustment for baseline adherence.

[c]Numbers and percentages reflect the number of participants answering “yes” to each item.

Adherence

We observed moderate adherence to the intervention. Participants in the intervention had a median of 18 (interquartile range 19) conversations with the relational agent over 30 days and used the agent for a median of 15 (interquartile range 13) days. The mean total duration of interactions with the relational agents was 40.7 (SD 24.3) min over the 30-day period, averaging 2.1 (SD 1.0) min per conversation. Of the 61 participants in the intervention group, 48 (79%) completed the AF education module and 43 (70%) completed the medication adherence counseling module (Textbox 1). The number of symptoms reported to the relational agent ranged from 0 to 14 (mean 1.3, SD 2.3). The median number of days of Kardia use was 25 over the 30-day intervention with a range of 1 to 30 days of usage.

Textbox 1. Summary of relational agent domain content.

Education

- Causes of atrial fibrillation
- Atrial fibrillation treatment strategies
- Stroke prevention in atrial fibrillation
- AliveCor Kardia use, troubleshooting

Symptoms

- Overview of common symptoms
- Chest pain and chest pressure
- Heart racing or palpitations
- Dyspnea and shortness of breath
- Fatigue

Adherence

- Overview of adherence
- Adherence to medications
- Adherence barriers
- Strategies to address barriers

Patient activation

- Goals for self-management
- Preparing for the medical encounter

Acceptability

Multimedia Appendices 3 and 4 present representative examples of conversations that intervention participants had with the relational agent. Multimedia Appendix 3 presents an exchange that a user had describing a symptom and the use of the AliveCor Kardia heart rate and rhythm monitor to correlate symptomatic palpitations with cardiac rhythm assessment. Multimedia Appendix 4 illustrates the relational agent teaching a user about the relevance and utility of using the Kardia. Our qualitative assessments of acceptability informed us that most intervention participants found the relational agent useful, informative, and trustworthy. On a range from 1 (“not at all”) to 7 (“very satisfied”), intervention participants indicated a median score of 6 (response range 1 to 7), which indicated that they were satisfied working with the relational agent. Likewise, participants indicated that they found talking with the agent easy (median 1, response range 1 [“easy”] to 7 [“difficult”]). Participants reported that the content was repetitive with a median score of 5 (response range 1 to 7), with 1 indicating “not at all” and 7 indicating “very repetitious.” Direct quotes from intervention participants are that the relational agent “made it easier to accept the information” and that the app provided “control to do something simple daily to take care of myself in this stressful situation.” We summarize the selected quotes in Textbox 2.

Textbox 2. Representative responses of pilot trial participants randomized to the intervention arm.

What were your overall impressions of the atrial fibrillation app?

- "You can bring up information on Afib on the internet and read most of the same stuff on your own, but with Tanya you have a structured presentation that you're led through, so you end up getting the information you should be getting."

What were your overall impressions of Tanya?

- "I liked the fact that she didn't seem to make me afraid or say very drastic things."
- "She made it easy to accept the information."
- "I had good impressions."
- "It's like going to the doctor's office every day to learn about A fib."

What did you like most about the app?

- "EKG is helping me figure out if I am in Afib and matching up the symptoms that I'm feeling with what that says can be helpful."
- "You're going through what I'm going through, and you're stressed out and depressed. At least each day I got a sense that I was trying to make myself better and do something for myself by talking to Tanya."

How did you feel about having Tanya with you all of the time?

- "Feeling like I had control to do something simple daily to take care of myself in this stressful situation."

What did you like least about the app?

- "Tanya was artificial, she wasn't real. But she was fun."
- "It was hard for me to think of her as a real person."
- "It was repetitive, nothing new after a while."

Discussion

Principal Findings

In this pilot trial of 120 individuals with chronic AF, we implemented a novel intervention that combined a relational agent with the Kardia heart rate and rhythm monitor for smartphones. After 30 days, intervention participants reported significantly better HRQoL as measured by the AF-specific AFEQT measure than control participants, as well as better self-reported adherence to anticoagulation. Our results support that a relational agent in combination with the Kardia may have the potential to improve patient-reported outcomes in AF. These results extend our previous work, which has demonstrated that relational agents are an appropriate vehicle for patient education, monitoring, and problem-solving.

In this pilot trial, we focused on HRQoL and adherence to anticoagulation because of their importance for long-term success with this chronic condition. HRQoL is a central benchmark in AF management, as recognized by the United States and international professional society guidelines [1,21]. As a patient-centered outcome, HRQoL provides a meaningful gauge for how patients experience a chronic disease. Individuals with AF may have extensive symptoms and experience the burden of long-term treatment with increased risk for multiple adverse outcomes, all of which adversely affect HRQoL. We consider the AFEQT as an appropriate measure to evaluate HRQoL because of its specificity to AF and relevant domains (symptoms, daily activities, treatment concern, and treatment satisfaction). Adherence to anticoagulation is vital for the prevention of long-term cardioembolic stroke. Evidence suggests the challenges that patients have with maintaining adherence to anticoagulation therapy with either warfarin or direct-acting oral anticoagulants [22-24].

Participants receiving the intervention in this pilot trial had better AFEQT scores than those receiving the control after 30 days. The minimally important difference for change in the AFEQT score has been suggested as 12 units in a moderate-sized, 3-month study of patients undergoing electrophysiologic interventions for control of AF [25]. We used this quantity to determine the statistical power for this pilot trial. Although statistically significant, the magnitude of improvement for the total AFEQT score did not meet this threshold. However, we did observe that control participant scores were essentially unchanged between the baseline and 30-day assessments. Therefore, we conclude that the pilot was effective in demonstrating that a relational agent can improve HRQoL in individuals with AF. We are particularly encouraged by the improvement in adherence reported by the intervention participants, given the essential role of anticoagulation in stroke prevention and AF pharmacologic management. HRQoL warrants continued attention as a patient-reported outcome in AF. Most evaluation of HRQoL in AF is related to treatment pharmacologic and invasive therapies for the condition. We expect that enhanced patient education, symptom monitoring, and development of self-care skills—all appropriate for a relational agent curriculum—may improve the patient experience with AF and concomitantly enhance HRQoL and medication adherence.

In our pilot study, the limited improvement in AFEQT may have stemmed from multiple factors. First, the duration of the

intervention was only 30 days, which we considered adequate for a pilot trial with limited relational agent content. We expect that a longer duration of use could bolster the effect of the relational agent on HRQoL. Second, more extensive relational agent content, both in terms of scope as well as the depth of exchanges, would improve the value of the relational agent to patients. Our content here—focused on education, anticoagulant adherence, and symptom identification—was of limited scope. Although we had good engagement, we expect that enhanced content has the potential to bolster sustained, longer-term use. A more expansive content may extend participant engagement and provide avenues for greater depth of self-care tasks, such as monitoring and responding to symptoms and adherence challenges. We surmise that both the duration and the content as employed in this pilot study were likely not adequate to result in a more meaningful improvement in HRQoL. Likewise, we encouraged participants to use the Kardia after reporting symptoms. However, we did not link relational agent content to those results to enhance the correlation of symptoms with rate and rhythm recordings. Finally, we did not link the intervention to avenues for the modification of patient care in this pilot study. The relational agent delivered via smartphones has the potential to monitor symptoms coupled with the Kardia results. Such monitoring may, in turn, provide important clinical information to support the adjustment of therapies for AF. For mobile health app content to have sustained impact, it must provide results to the hub of clinical care. We intend to address the deficits described here in subsequent apps of a relational agent for AF. Our objective is to develop a more extensive relational agent with a better interface with the Kardia results. In addition, we intend to build mechanisms for reporting the unique data obtained by the interventions to clinicians, thereby facilitating improvement to patient care.

Strengths and Limitations

We successfully combined our smartphone relational agent and Kardia technologies and showed that this approach was highly acceptable and enhanced patient self-care for patients with AF. We found significant improvements in HRQoL and self-reported anticoagulant adherence in the intervention arm. Our results provide substantive data to guide an enhanced relational agent for a larger-sized trial and encourage the development of a more extensive relational agent.

Our study has several important limitations. First, the limited time frame and content may have reduced engagement with the intervention. Second, we did not assess the sustainability of the intervention effect. Third, this pilot cohort was predominantly White and relatively well educated. We have designed the relation agent to be accessible for people with limited health literacy; however, an examination of potential differential treatment effects will require a more diverse cohort. Fourth, we measured adherence using self-reported measures rather than an objective measure of adherence; the self-reported measure is subject to reporting and response-shift bias. Fifth, we did not have an active control group. As such, we are not able to distinguish the mechanism for improvements in our outcomes in the intervention arm of our pilot trial. Such improvements may be attributable to specific effects of the intervention's content, the increased attention provided by receiving a relational agent, or the novelty of providing a smartphone and app. It is also possible that engagement with the agent was enhanced by participants' awareness of use being monitored. Next, we also recognize that our study had a selection bias. We were only able to approach 236 of 527 eligible participants, noting that many who were eligible were not accessible to us (ie, did not attend clinic appointments where the study team was conducting recruitment). Additionally, given loss to follow-up, missing data, and study withdrawal, we did not achieve our calculated estimated sample size of n=120, which limits our power. We acknowledge this as a limitation because the final sample size was short of the planned 120 in our power calculation. Sixth, relational agent content was informed by interviewing patients about their challenges with AF. Although we did not conduct this assessment in a systematic manner, we considered the content for this pilot trial adequately informed by patient input. Finally, participant assessments were not conducted by blinded assessors, which may have introduced biases in responding to questions such as self-reported adherence.

This pilot trial provides the foundation for a larger clinical trial guided by these preliminary efficacy and acceptability results. Although we saw promising results in the pilot trial, our results reflect the effect of a small number of participants, particularly when evaluating adherence; a larger clinical trial will further evaluate and confirm this effect. We expect that the relational agent coupled with the Kardia has the potential to improve patient-centered care in AF and provide a low-cost, effective means of reducing the social and medical morbidity associated with this chronic disease.

Conclusions

In this pilot trial (n=120) evaluating a novel, AF-focused relational agent in concert with the Kardia heart rhythm monitor, we found that individuals receiving the intervention had significantly greater improvement in AF-specific HRQoL and self-reported anticoagulant adherence. In addition, the relational agent demonstrated favorable acceptability with adequate usage in the intervention group and positive qualitative assessments of the app.

Acknowledgments

This work was supported by the Doris Duke Charitable Foundation Award 2015084 and the National Heart, Lung, and Blood Institute (R01 HL143010).

Authors' Contributions

EG and JWM contributed to the study concept and design, results interpretation, drafting, and revision of the manuscript. ADA contributed to statistical analysis, results interpretation, and drafting and revision of the manuscript. EK, AMP, MKPO, and TWB contributed to the study concept, design, and revision of the manuscript. All authors have read and approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Flow diagram of progress through trial.
[PNG File , 101 KB - cardio_v4i1e17162_app1.png]

Multimedia Appendix 2
Comparison of Atrial Fibrillation Effect on Quality of Life scores, by study arm, at baseline and 30-day follow-up.
[PNG File , 77 KB - cardio_v4i1e17162_app2.png]

Multimedia Appendix 3
Naomi.
[PNG File , 271 KB - cardio_v4i1e17162_app3.png]

Multimedia Appendix 4
Frank.
[PNG File , 267 KB - cardio_v4i1e17162_app4.png]

References

1. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American college of cardiology/American heart association task force on practice guidelines and the heart rhythm society. Circulation 2014 Dec 2;130(23):2071-2104. [doi: 10.1161/CIR.0000000000000040] [Medline: 24682348]
2. Dudink EA, Erküner O, Berg J, Nieuwlaat R, CB CB, Weijs B, et al. The influence of progression of atrial fibrillation on quality of life: a report from the Euro heart survey. Europace 2018 Jun 1;20(6):929-934. [doi: 10.1093/europace/eux217] [Medline: 29016989]
3. Magnani JW, Mujahid MS, Aronow HD, Cené CW, Dickson VV, Havranek E, American Heart Association Council on Epidemiology and Prevention; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research;Stroke Council. Health literacy and cardiovascular disease: fundamental relevance to primary and secondary prevention: a scientific statement from the American Heart Association. Circulation 2018 Jul 10;138(2):e48-e74 [FREE Full text] [doi: 10.1161/CIR.0000000000000579] [Medline: 29866648]
4. Magnani JW, Schlusser CL, Kimani E, Rollman BL, Paasche-Orlow MK, Bickmore TW. The atrial fibrillation health literacy information technology system: pilot assessment. JMIR Cardio 2017;1(2):e7 [FREE Full text] [doi: 10.2196/cardio.8543] [Medline: 29473644]
5. Bickmore TW, Silliman RA, Nelson K, Cheng DM, Winter M, Henault L, et al. A randomized controlled trial of an automated exercise coach for older adults. J Am Geriatr Soc 2013 Oct;61(10):1676-1683. [doi: 10.1111/jgs.12449] [Medline: 24001030]
6. Utami D, Bickmore TW, Barry B, Paasche-Orlow MK. Health literacy and usability of clinical trial search engines. J Health Commun 2014;19(Suppl 2):190-204. [doi: 10.1080/10810730.2014.938842] [Medline: 25315593]
7. Bickmore TW, Utami D, Matsuyama R, Paasche-Orlow MK. Improving access to online health information with conversational agents: a randomized controlled experiment. J Med Internet Res 2016 Jan 4;18(1):e1 [FREE Full text] [doi: 10.2196/jmir.5239] [Medline: 26728964]
8. Gwynn KB, Winter MR, Cabral HJ, Wolf MS, Hanchate AD, Henault L, et al. Racial disparities in patient activation: evaluating the mediating role of health literacy with path analyses. Patient Educ Couns 2016 Jun;99(6):1033-1037 [FREE Full text] [doi: 10.1016/j.pec.2015.12.020] [Medline: 26809936]
9. Zhang Z, Bickmore TW, Paasche-Orlow MK. Perceived organizational affiliation and its effects on patient trust: role modeling with embodied conversational agents. Patient Educ Couns 2017 Sep;100(9):1730-1737. [doi: 10.1016/j.pec.2017.03.017] [Medline: 28381330]

10. King AC, Bickmore T, Campero I, Pruitt L, Yin L. Employing virtual advisors in preventive care for underserved communities: results from the COMPASS study. J Health Commun 2013;18(12):1449-1464 [FREE Full text] [doi: 10.1080/10810730.2013.798374] [Medline: 23941610]
11. Bickmore TW, Pfeifer LM, Paasche-Orlow MK. Using computer agents to explain medical documents to patients with low health literacy. Patient Educ Couns 2009 Jun;75(3):315-320 [FREE Full text] [doi: 10.1016/j.pec.2009.02.007] [Medline: 19297116]
12. Ehrenfeld J, Sandberg W, Kwo J, Bickmore T. Use of a Computer Agent to Explain Anesthesia Concepts to Patients. Relational Agents Group. 2010. URL: http://relationalagents.com/publications/asa10.pdf [accessed 2020-08-12]
13. Halcox JP, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, et al. Assessment of remote heart rhythm sampling using the Alivecor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. Circulation 2017 Nov 7;136(19):1784-1794. [doi: 10.1161/CIRCULATIONAHA.117.030583] [Medline: 28851729]
14. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. Patient Educ Couns 1999 Sep;38(1):33-42. [doi: 10.1016/s0738-3991(98)00116-5] [Medline: 14528569]
15. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [doi: 10.1046/j.1525-1497.2001.016009606.x] [Medline: 11556941]
16. Spertus J, Dorian P, Bubien R, Lewis S, Godejohn D, Reynolds MR, et al. Development and validation of the atrial fibrillation effect on quality-of-life (AFEQT) questionnaire in patients with atrial fibrillation. Circ Arrhythm Electrophysiol 2011 Feb;4(1):15-25. [doi: 10.1161/CIRCEP.110.958033] [Medline: 21160035]
17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
18. Kotecha D, Ahmed A, Calvert M, Lencioni M, Terwee CB, Lane DA. Patient-reported outcomes for quality of life assessment in atrial fibrillation: a systematic review of measurement properties. PLoS One 2016;11(11):e0165790 [FREE Full text] [doi: 10.1371/journal.pone.0165790] [Medline: 27802324]
19. Randolph TC, Simon DN, Thomas L, Allen LA, Fonarow GC, Gersh BJ, ORBIT AF Investigators and Patients. Patient factors associated with quality of life in atrial fibrillation. Am Heart J 2016 Dec;182:135-143 [FREE Full text] [doi: 10.1016/j.ahj.2016.08.003] [Medline: 27914493]
20. Harrell Jr FJ, Slaughter J. Biostatistics for Biomedical Research. University School of Medicine Nashville. 2001. URL: https://hbiostat.org/doc/bbr.pdf [accessed 2020-08-12]
21. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur J Cardiothorac Surg 2016 Nov;50(5):e1-88. [doi: 10.1093/ejcts/ezw313] [Medline: 27663299]
22. Brown JD, Shewale AR, Talbert JC. Adherence to rivaroxaban, dabigatran, and apixaban for stroke prevention in incident, treatment-naïve nonvalvular atrial fibrillation. J Manag Care Spec Pharm 2016 Nov;22(11):1319-1329 [FREE Full text] [doi: 10.18553/jmcp.2016.22.11.1319] [Medline: 27783556]
23. Beyer-Westendorf J, Ehlken B, Evers T. Real-world persistence and adherence to oral anticoagulation for stroke risk reduction in patients with atrial fibrillation. Europace 2016 Aug;18(8):1150-1157. [doi: 10.1093/europace/euv421] [Medline: 26830891]
24. Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, et al. Warfarin discontinuation after starting warfarin for atrial fibrillation. Circ Cardiovasc Qual Outcomes 2010 Nov;3(6):624-631 [FREE Full text] [doi: 10.1161/CIRCOUTCOMES.110.937680] [Medline: 20959565]
25. Dorian P, Burk C, Mullin CM, Bubien R, Godejohn D, Reynolds MR, et al. Interpreting changes in quality of life in atrial fibrillation: how much change is meaningful? Am Heart J 2013 Aug;166(2):381-7.e8. [doi: 10.1016/j.ahj.2013.04.015] [Medline: 23895823]

Abbreviations

AF: atrial fibrillation
AFEQT: Atrial Fibrillation Effect on Quality of Life
HRQoL: health-related quality of life

Edited by N Bruining; submitted 23.11.19; peer-reviewed by E Grekin, J Martínez-Miranda, J Wienert; comments to author 07.02.20; revised version received 01.03.20; accepted 13.07.20; published 04.09.20.

Please cite as:
Guhl E, Althouse AD, Pusateri AM, Kimani E, Paasche-Orlow MK, Bickmore TW, Magnani JW
The Atrial Fibrillation Health Literacy Information Technology Trial: Pilot Trial of a Mobile Health App for Atrial Fibrillation
JMIR Cardio 2020;4(1):e17162
URL: http://cardio.jmir.org/2020/1/e17162/
doi:10.2196/17162
PMID:32886070

Original Paper

A Novel Virtual Reality Medical Image Display System for Group Discussions of Congenital Heart Disease: Development and Usability Testing

Byeol Kim[1], MSc; Yue-Hin Loke[2], MD; Paige Mass[2], BSc; Matthew R Irwin[3], MAS; Conrad Capeland[3], BFA; Laura Olivieri[2], MD; Axel Krieger[1], PhD

[1]University of Maryland, College Park, MD, United States

[2]Children's National Hospital, Washington, DC, United States

[3]Indicated LLC, New York City, NY, United States

Corresponding Author:
Byeol Kim, MSc
University of Maryland
2181 Glenn L Martin Hall
University of Maryland
College Park, MD, 20742
United States
Phone: 1 516 428 3217
Email: star@umd.edu

Abstract

Background: The complex 3-dimensional (3D) nature of anatomical abnormalities in congenital heart disease (CHD) necessitates multidisciplinary group discussions centered around the review of medical images such as magnetic resonance imaging. Currently, group viewings of medical images are constrained to 2-dimensional (2D) cross-sectional displays of 3D scans. However, 2D display methods could introduce additional challenges since they require physicians to accurately reconstruct the images mentally into 3D anatomies for diagnosis, staging, and planning of surgery or other therapies. Virtual reality (VR) software may enhance diagnosis and care of CHD via 3D visualization of medical images. Yet, present-day VR developments for medicine lack the emphasis on multiuser collaborative environments, and the effect of displays and level of immersion for diagnosing CHDs have not been studied.

Objective: The objective of the study was to evaluate and compare the diagnostic accuracies and preferences of various display systems, including the conventional 2D display and a novel group VR software, in group discussions of CHD.

Methods: A total of 22 medical trainees consisting of 1 first-year, 10 second-year, 4 third-year, and 1 fourth-year residents and 6 medical students, who volunteered for the study, were formed into groups of 4 to 5 participants. Each group discussed three diagnostic cases of CHD with varying structural complexity using conventional 2D display and group VR software. A group VR software, Cardiac Review 3D, was developed by our team using the Unity engine. By using different display hardware, VR was classified into nonimmersive and full-immersive settings. The discussion time, diagnostic accuracy score, and peer assessment were collected to capture the group and individual diagnostic performances. The diagnostic accuracies for each participant were scored by two experienced cardiologists following a predetermined answer rubric. At the end of the study, all participants were provided a survey to rank their preferences of the display systems for performing group medical discussions.

Results: Diagnostic accuracies were highest when groups used the full-immersive VR compared with the conventional and nonimmersive VR (χ^2_2=9.0, P=.01) displays. Differences between the display systems were more prominent with increasing case complexity (χ^2_2=14.1, P<.001) where full-immersive VR had accuracy scores that were 54.49% and 146.82% higher than conventional and nonimmersive VR, respectively. The diagnostic accuracies provided by the two cardiologists for each participant did not statistically differ from each other (t=–1.01, P=.31). The full-immersive VR was ranked as the most preferred display for performing group CHD discussions by 68% of the participants.

Conclusions: The most preferred display system among medical trainees for visualizing medical images during group diagnostic discussions is full-immersive VR, with a trend toward improved diagnostic accuracy in complex anatomical abnormalities. Immersion is a crucial feature of displays of medical images for diagnostic accuracy in collaborative discussions.

(JMIR Cardio 2020;4(1):e20633) doi:10.2196/20633

KEYWORDS

virtual reality; cardiac diagnostics; usability study; congenital heart disease; group collaboration

Introduction

Congenital heart disease (CHD) is the most common birth defect, occurring in 8/1000 neonates [1]. Management of CHD depends largely on anatomy [2], making detailed cardiac imaging (eg, echocardiogram and cardiac magnetic resonance imaging [MRI]) a necessity for accurate detection and preoperative planning of CHD. For preoperative planning of CHD, group multidisciplinary meetings are held between pediatric cardiologists, pediatric cardiac intensivists, and cardiac surgeons with cardiac imaging displayed in a conference-style room for review and discussion [3,4]. Cardiac imaging is typically displayed with visualization software geared toward Digital Imaging and Communications in Medicine (DICOM) formats, across a screen projector as either 2-dimensional (2D) images, cross-sections of 3-dimensional (3D) scans, or 3D volume renderings [5]. Despite the advancements in interactive 3D displays, the interpretation of cardiac imaging often relies on individual physicians to use 2D images and mentally reconstructing 3D objects.

Advances in medical imaging and additive technologies now allow for 3D printing of CHD anatomies [6]. 3D printing can use a variety of materials and colors to build customized and personalized anatomical models [7,8]. The printed models are useful for preoperative planning of CHD repair [6] as well as medical and surgical training [9-11]. However, 3D printing is cost- and time-intensive [7,12,13] and physically constraining, making a free-form visualization such as magnification or cropping challenging.

Virtual reality (VR) is an alternative 3D displaying modality with relatively lower costs and time use that provides free-form visualization. Although the physical models do not exist, realism is boosted through simulated physics [14,15] and implemented tools to deliver touch, auditory, and olfactory senses [16-18]. These attributes make VR one of the popular methods for training medical professionals [19-22], planning surgeries [23-26], and delivering therapies and rehabilitation [27-29]. Several commercial VR software programs are available for clinical decision making and surgical planning. Surgical Theater (Surgical Theater Inc) provides a platform allowing surgeons to virtually walk inside the patient anatomy to analyze neurological conditions and plan surgeries accordingly. Anatomy Viewer (The Body VR) converts DICOM images into 3D volume models that can be scaled, rotated, and cropped for identifying tumors and lesions. ImmersiveView Surgical Planning (ImmersiveTouch Inc) uses tactile haptic feedback and medical images for surgeons to visualize and rehearse surgeries. These commercial VR software programs all have functionality to visualize DICOM formatted data in 3D with multiple features assisting the diagnosing and surgical planning process.

Despite the advancements of VR in medicine, VR has been receiving criticism on its ability to facilitate collaboration, and the efficacy of VR has not been evaluated in group-based collaborative medical discussions, which is the bedrock of the clinical profession. VR necessitates full immersion for users to have bolstered sensation of the real world in VR [30]. However, full immersion also removes the face-to-face communication that contributes significantly to team productivity [31], moderation of team empowerment [32], knowledge transfer [33], and promotion of innovative solutions [34,35]. With limited knowledge existing on the influence of VR in collaboration, current VR development for medicine lacks emphasis on multiuser collaborative environments. Additional interaction features are essential for users to collaborate in VR. Furthermore, the multiuser environment needs to be optimized to balance network needs and avoid frame rate losses or lag. We developed a novel cardiac display software, Cardiac Review 3D, to address these shortcomings with the following design goals:

- Interactive display of medical anatomy: provide features to easily scrutinize the abnormalities of anatomies
- Knowledge sharing: enable storage of the virtual notes taken during the discussion for future access
- View sharing: establish an environment where multiple users can view the 3D medical images and provide feedback concurrently
- User experience: optimize the network and frame rates for a smooth user experience

Cardiac Review 3D was built with two levels of immersion. Full immersion is accomplished by using a head-mounted display (HMD), and nonimmersive VR uses a tablet. A conventional 2D display and the two extensions of Cardiac Review 3D were compared to identify the best display system for collaborative medical discussions. We hypothesized that VR, regardless of the level of immersion, better conveys the anatomical abnormalities of CHDs, bolstering diagnostic accuracy compared with the conventional display. This study was designed to imitate cardiac group diagnostic meetings where one physician controls the display systems presented to multiple medical providers who collaboratively identify the cardiac conditions related to CHD. Additionally, the study explored individual preferences of the display systems for group discussion.

Methods

Recruitment

This study was conducted under institutional review board approval. Medical trainees from Children's National Hospital in Washington, DC, were recruited for the study (N=22). Of the participants, there were 1 first-year, 10 second-year, 4 third-year, and 1 fourth-year residents and 6 medical students. The participants were split into groups of 4 or 5 to maintain

small group discussions. All participants gave informed consent prior to their participation. A minimum of 20 participants were recruited to achieve a power of 80% and a level of significance of 5% (2-sided) for detecting an effect size of 0.7 between pairs.

Moderator

An experienced pediatric cardiologist from Children's National Hospital acted as a moderator in the study. The moderator's role and responsibilities were to give lectures on three chosen cases of CHD, provide instructions on how to interact with the display systems, and present answers to the diagnostic questions. The moderator's interaction with the participants strictly followed a prewritten script.

Medical Image Selection and Acquisition

Selection of Congenital Heart Disease Cases

The discussion topics included three cases of CHD: atrial septal defect (ASD), coarctation of aorta (CoA), and tetralogy of Fallot with pulmonary atresia and major aortopulmonary collateral artery (MAPCA). The selected cases each entail a spectrum of CHD in terms of surgical complexity and perioperative mortality risk, established by the Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery's STS-EACTS Congential Heart Surgery Mortality Categories (STAT Mortality Categories) [36]. Under the STAT Category, procedures are grouped from 1 to 5 (lowest to highest) based on estimated mortality risk and surgical difficulty. Under this classification, ASDs are classified under STAT Category 1 (estimated mortality risk of 0.3%), extended end-to-end repair of CoA is under STAT Category 2 (estimated mortality risk of 1.7%), and MAPCA is under STAT Category 4 (estimated mortality risk of 10.2%) [36].

Each case of CHD requires complex cardiovascular imaging for accurate diagnosis. ASDs, one of the most common forms of CHD, are typically well recognized on 2D echocardiography [37]. CoA, a discrete obstruction across the aortic isthmus, can also be identified by echocardiography; however, visualization of complex arch configurations (particularly after surgical repair) benefit from cross-sectional imaging such as cardiac MRI [38]. MAPCA is a very specific form of cyanotic CHD that results in loss of the pulmonary vessels, which are now directly connected to the aorta. Diagnostic imaging of MAPCA has been traditionally challenging and currently serves as a prime application for use of 3D imaging and 3D printing in cardiac surgical planning [39]. The mental workflow required for analysis of these defects is also intended to correlate with diagnostic complexity, as demonstrated in Table 1.

Table 1. Mental workflow for diagnosing three cases of congenital heart disease.

CHD[a] case	Designed tasks	Mental workflow
ASD[b]	Recognition of primum-type ASD vs secundum-type ASD	1. Recognize atrial septal defect. 2. Recognize location of atrioventricular valves. 3. Identify primum ASD that is immediately superior to atrioventricular valves OR secundum ASD that is central to atrial septum.
CoA[c]	Recognition of unrepaired CoA vs repaired CoA with gothic arch	1. Recognize aortic arch regions: ascending aorta, transverse arch, descending aorta. 2. Recognize normal head vessel anatomy and area immediately distal to left subclavian artery (aortic isthmus). 3. Identify the pathological narrowing of aortic isthmus as CoA OR identify gothic arch shape in repaired CoA, which has a larger height to transverse ratio (taller height than width).
MAPCA[d]	Identify number of aortopulmonary collaterals and their respective takeoff points	1. Recognize aortic arch regions: ascending aorta, transverse arch, descending aorta. 2. Recognize normal head vessel anatomy. 3. Identify pathological aortopulmonary collateral. 4. Identify the origin of each respective aortopulmonary collateral with respect to arch region throughout the heart.

[a]CHD: congenital heart disease.

[b]ASD: atrial septal defect.

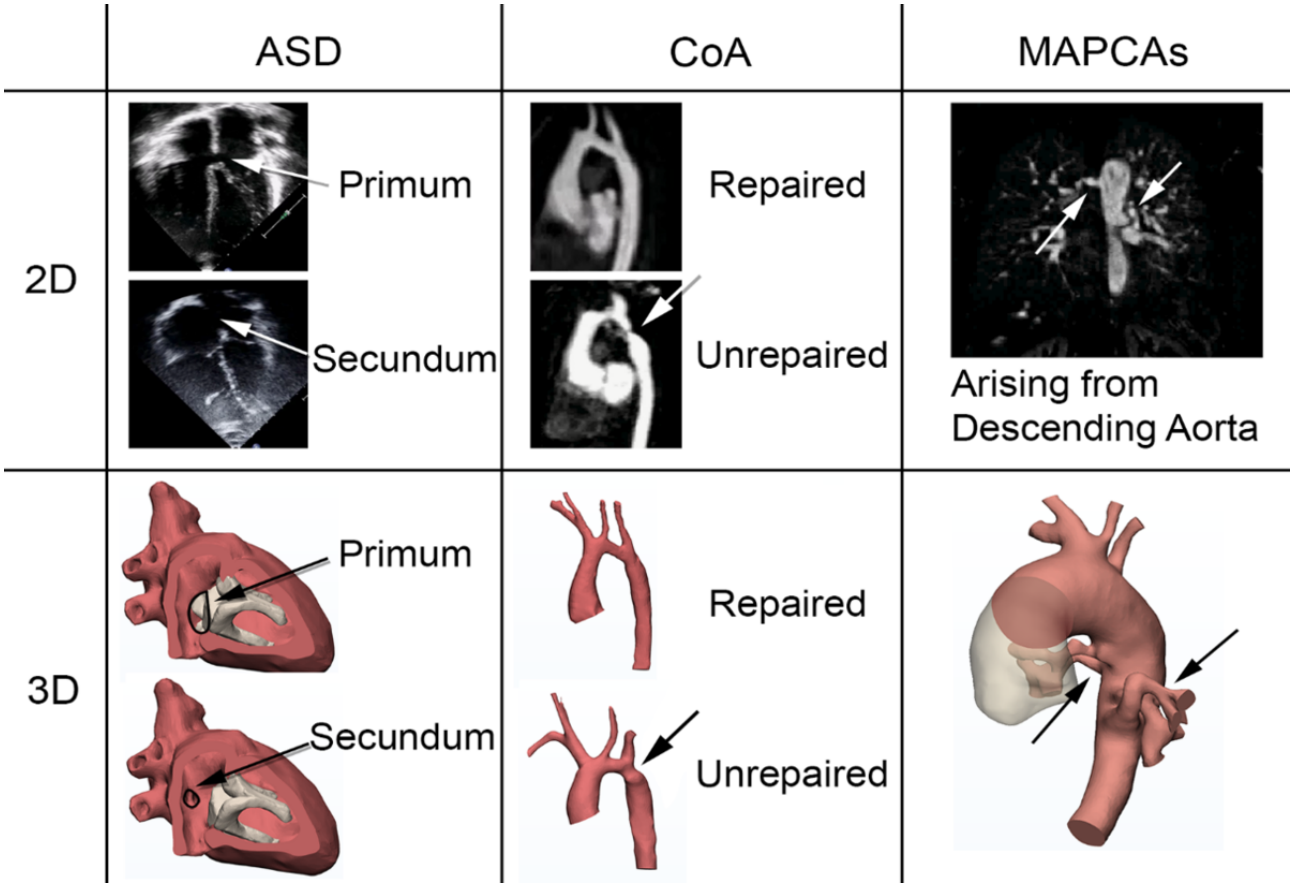
[c]CoA: coarctation of aorta.

[d]MAPCA: major aortopulmonary collateral artery.

Medical Image Acquisition

Imaging datasets, acquired by standard-of-care imaging methods (MRI), were anonymized and exported as DICOM files. The DICOM files were manually segmented using thresholding and semiautomatic edge detection segmentation techniques in Mimics (Materialise) to create a 3D model, which was exported as a stereolithography file (see bottom 3D row in Figure 1) to be loaded into the Cardiac Review 3D software for group display.

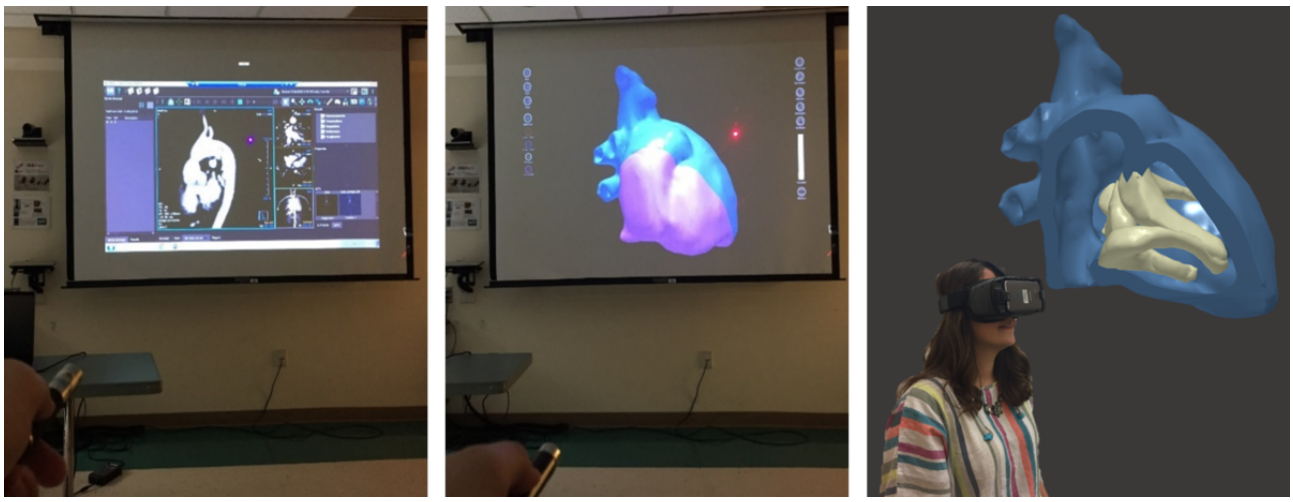
Figure 1. Medical images of the congenital heart disease cases: 2D (top) and 3D (bottom). Arrows represent the anatomical regions to scrutinize for correct diagnosis. ASD: atrial septal defect; CoA: coarctation of aorta; MAPCA: major aortopulmonary collateral artery.



Medical Image Display Systems

The study evaluated three medical imaging display systems—conventional, nonimmersive VR, and full-immersive VR (Figure 2)—for group diagnostic discussions of the CHDs. The conventional display system visualized 2D medical images on a projector screen. The nonimmersive VR system projected 3D medical images visualized in Surface Pro tablet (Microsoft Corp) onto a shared screen. A mobile HMD, Gear VR (Samsung Electronics Co Ltd), was provided to each participant for the full-immersive VR system, where 3D medical images were visualized in a virtual world.

Figure 2. The setup of the conventional (left), nonimmersive virtual reality (middle), and full-immersive virtual reality (right) display systems in the study.

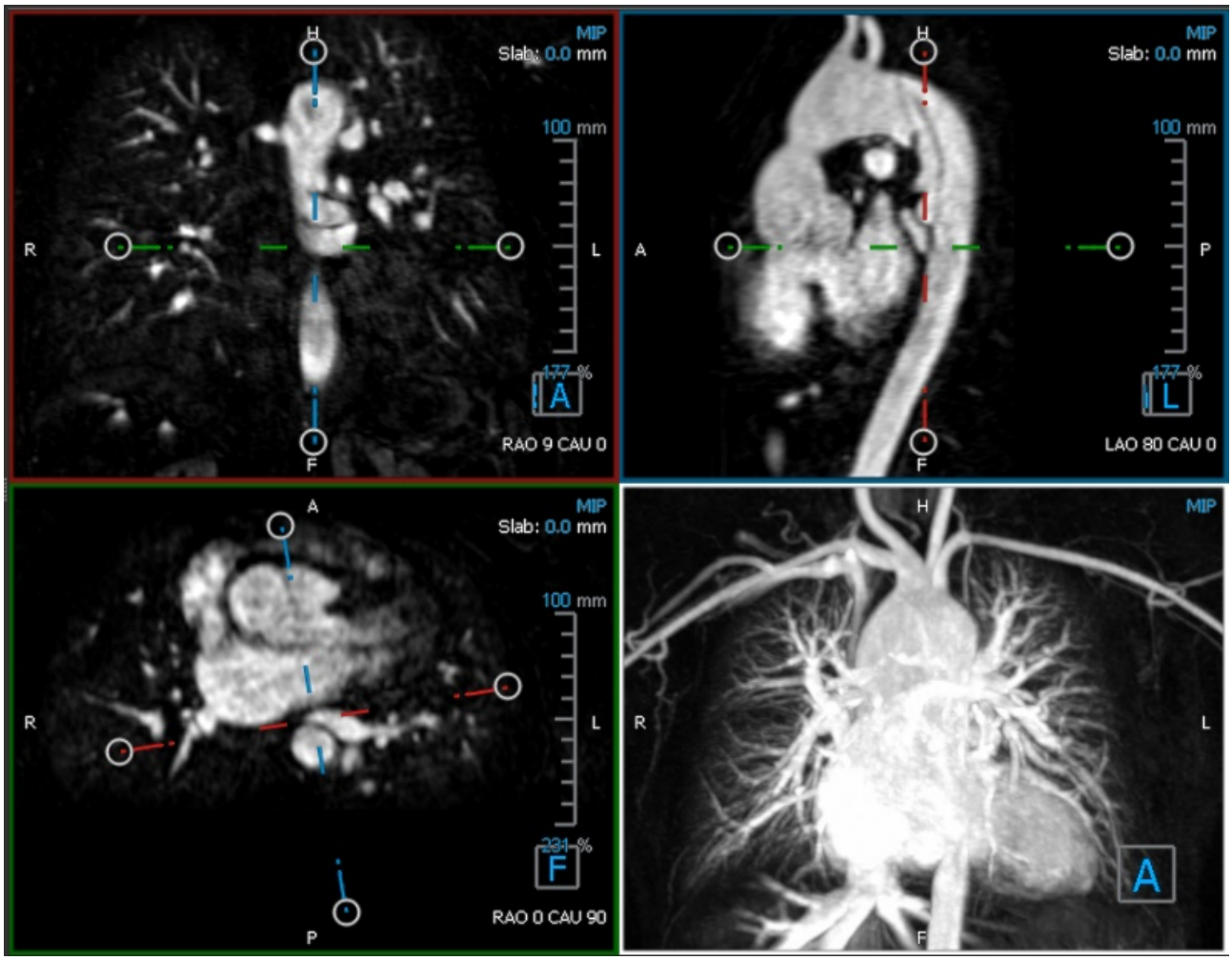


Conventional Display System

The conventional display system (CDS) used commercial cardiovascular imaging software running on a laptop that was duplicated on a projection screen (49×87 inch) located in front of the participants. For echocardiographic visualization of ASD, the 2D echo image of a standard 4-chamber apical view was exported from Xcelera (Philips Healthcare) in AVI format and presented via PowerPoint (Microsoft Corp) as a looped video.

Cardiac MRI visualization of CoA and MAPCA was performed directly via Medis Suite MR (Medis Medical Imaging). Specifically, the 3D View suite was used to visualize cross-sectional anatomy through multiplanar reformatting technique, providing 2D cross-sectional images of the cardiac anatomy (Figure 3).

Figure 3. 2D cross-sectional images of the repaired coarctation of aorta.



Each participant was provided with a unique color of laser pointer to pinpoint the images from a distance during the discussion phase using the CDS. While the discussion was in progress, the moderator was only responsible for complying with participants' verbal directions for translating and rotating the 2D multiplanar reformatting view. The moderator did not provide any guidance toward the designated task.

Nonimmersive Virtual Reality Display System

Cardiac Review 3D was developed with the Unity engine (Unity Technologies) based on the four design goals: medical features, knowledge sharing, view sharing, and user experience. For medical features, a multitouch gesture interface with one finger to rotate, a 2-finger pinch gesture to zoom, and a 2-finger touch-and-drag gesture to pan were implemented. When loading multiple 3D models concurrently, each model was assigned a different color to ease the differentiation process. Interior (or back) faces of the 3D models were rendered with a desaturated color relative to exterior faces to accentuate the differences between inner and outer surfaces when clipping into the 3D model.

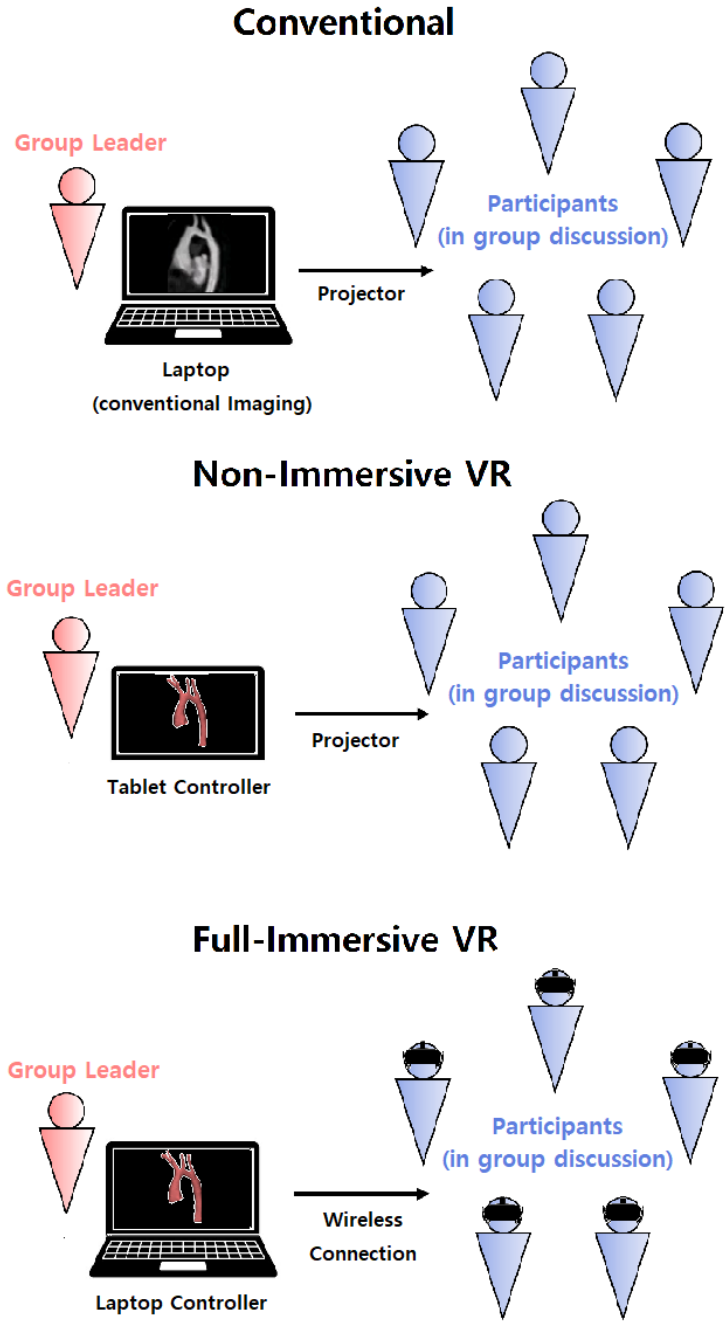
Knowledge sharing was accomplished through cloud-based storage of the cardiac datasets and associated annotated reports. The reports incorporated text labeling of 3D surface points, linear measurements, screenshots, and general annotations. Considering potential difficulty in estimating the true size of cardiac anatomies, two 3D marking points could be placed onto the 3D models to measure the lengths. The software provided options to export all markups and screenshots from the discussion into a PDF file to facilitate future review as well as a custom project file export to enable editing of 3D models and associated markups.

A tablet was chosen as the nonimmersive virtual reality display system (NIV) platform to support portability in surgical conferences, operating rooms, and intensive care unit settings. The view sharing of the tablet was achieved by a projection screen with laser pointers (Figure 2) and verbal requests for manipulating the anatomies, mimicking the CDS setup. Again, the moderator was only responsible for manipulating the 3D models as requested by the participants.

Full-Immersive Virtual Reality Display System

The full-immersive virtual reality display system (FIV) incorporated the same medical review and knowledge-sharing features as the tablet platform of the Cardiac Review 3D (Figure 4). Loading and manipulating the 3D models, including zoom, rotation, and clipping, was controlled for all users by the moderator using a laptop running the Cardiac Review 3D in a server mode. The same interaction level and method were required between the participants and the moderator as the CDS and NIV. However, the view-sharing approach (ie, laser pointer) needed modifications since HMDs were worn by all patients, obstructing face-to-face communication. The server laptop and HMDs were connected via Wi-Fi to a wireless router to form a local network. Then the user datagram protocol was implemented to facilitate the network data transfer used to synchronize the 3D model manipulations from the laptop server to each client HMD.

Figure 4. Diagram of group discussion format for each display system (from the top: conventional, nonimmersive virtual reality, and full-immersive virtual reality displays). VR: virtual reality.



This allowed for each HMD user to freely turn their heads to look around without translational components and to place a virtual pointer on the 3D surface model during the discussion, with their view of the virtual environment updating at 60 frames per second. For easy distinction, a unique pointer color was assigned to each HMD. The virtual pointer could be dropped anywhere on the 3D surface model by tapping on the touchpad located on the right side of the headset device. Selecting the location of this pointer placement was achieved by using the built-in gyroscope sensor of the Gear VR to determine the gaze

vector of the users' view relative to the 3D surface model at the time the touchpad was tapped. The gaze vector was then tested against the 3D surface to determine if the vector intersected the surface, and if so, the users' unique colored virtual pointer was placed at that point by the software. The pointers placed by a participant were visible by all participants, facilitating discussion around specific 3D features visible on the inner or outer surfaces of the 3D models.

Experimental Tasks and Procedure

A group orientation was provided at the beginning of the study. After the participants gave informed consent, the demographic survey was distributed and the moderator introduced himself and requested that participants greet each other and introduce themselves. The study was organized into 3 cases of CHD, each with 3 separate phases: lecture, group discussion, and postdiscussion survey. To avoid order bias, the 3 cases of CHD were randomly coupled with 3 display systems and provided in random order (Table 2). These selections were accomplished by running a MATLAB (The MathWorks Inc) script that generated random discussion combinations and orders.

Table 2. Discussion orders (congenital heart disease variation; display system) of each group.

Group	Discussion 1	Discussion 2	Discussion 3
1	CoA[a]; NIV[b]	MAPCA[c]; FIV[d]	ASD[e]; CDS[f]
2	ASD; FIV	CoA; CDS	MAPCA; NIV
3	ASD; NIV	CoA; FIV	MAPCA; CDS
4	MAPCA; CDS	ASD; FIV	CoA; NIV
5	CoA; CDS	MAPCA; FIV	ASD; NIV

[a]CoA: coarctation of aorta.

[b]NIV: nonimmersive virtual reality display system.

[c]MAPCA: major aortopulmonary collateral artery.

[d]FIV: full-immersive virtual reality display system.

[e]ASD: atrial septal defect.

[f]CDS: conventional display system.

For the lecture phase, the moderator prepared PowerPoint slides with a brief summary of each CHD case. The moderator explained the deviations from the norm presented for each CHD case under discussion and its standard diagnostic approach. The group discussion phase was solely held by the participants, who were not permitted to ask the moderator any questions that could be a hint at the CHD diagnosis. Discussions were limited to 10 minutes but could adjourn early if consensus were made within a group. All discussions were audio recorded for measuring the time duration for each group to reach a consensus.

The postdiscussion survey was provided to be answered individually, based on the possibility of individual learning variance from group discussions [40]. The discussion that used FIV included an additional survey about the experience of wearing the HMD. A comparison survey was given to each participant at the end of the study.

Survey Design

Demographic Survey

The demographic survey consisted of 5 questions regarding the participant's gender, year in residency, prior experience in VR, and impression of VR. Those who reported having prior experience in VR were requested to list the specific VR applications they tried. All participants were asked to score their impression of VR, which was categorized into negative, neutral, and positive. The strength of the negative and positive impression of VR was noted by increase in the magnitude of the value, from 1 to 5.

Postdiscussion Survey

The post discussion survey consisted of the diagnostics and peer assessment questionnaires. The diagnostics questionnaires were designed to measure the accuracy of the diagnosis made for each case of CHD using the different display systems. The ASD diagnostics questionnaire inquired about identifying the primum and secundum type of ASD. The CoA questionnaire prompted the participant to distinguish between the normal versus gothic arch. The MAPCA diagnostic questionnaire asked about identifying the number of MAPCAs and the respective origins of each MAPCA at the aortic arch. To further evaluate the confidence and depth of the diagnostics, participants were requested to back their statements with explanations. These responses were graded by two experienced cardiologists from Children's National Hospital with a predetermined answer rubric after the completion of the study (Table 3). The grading was performed individually.

Table 3. Grading rubric of the diagnostic questionnaires used in the study.

CHD[a]	Answer (max +2)	Explanation (max +2)
ASD[b]	Case 1 is secundum ASD and case 2 is primum ASD (+2)	• ASD in case 1 is central to atrial septum OR ASD in case 2 is above the atrioventricular valve (+2) • If atrial septum or atrioventricular valves not specifically mentioned, only partial credit (+1)
CoA[c]	Arch 1 is gothic arch and arch 2 is normal arch (+2)	• Arch 1 has larger height-to-transverse ratio (taller height than width) OR arch 2 has narrowing distal to the left subclavian artery (+2) • If height-to-transverse ratio (taller height than width) OR narrowing distal to left subclavian/narrowing of isthmus not specifically mentioned, only partial credit (+ 1)
MAPCA[d]	Total = 4 MAPCAs	• Two from transverse arch (+1); only partial credit if transverse arch not specifically named (+0.5) • Two from descending aorta (+1); only partial credit if descending aorta not specifically named (+0.5)

[a]CHD: congenital heart disease.

[b]ASD: atrial septal defect.

[c]CoA: coarctation of aorta.

[d]MAPCA: major aortopulmonary collateral artery.

The peer assessment was provided for evaluating the ease of collaboration with their peers as a result of the display system used. The questionnaires included Q1: organization of the meeting; Q2: concentration; Q3: listening attentiveness; Q4: individual participation; Q5: knowledge exchange; Q6: perceived emotion; and Q7: perceived boredom [32-34]. All questionnaires were formatted into a 5-point Likert scale.

Comparison Survey

The comparison survey included the participants' preferences and perspectives on the ease of the display systems for performing group diagnostic discussion. Both components were measured using a ranking system with 1 being the most preferred or easiest use and 3 being the least preferred and most difficult use of display system in group diagnostic discussions. The reasons and thought processes behind the ranking choices were noted.

Virtual Reality Usability Survey

The VR usability survey prompted participants to report any physical discomfort or motion sickness experienced when wearing the HMD. Eyeglass wearers were asked whether they wore their glasses with the HMD or took them off; they were also asked about their visual experience and physical comfort level regarding eyeglass and HMD interaction.

Statistical Analysis

Kruskal-Wallis and Dunn tests were performed to confirm the level of medical experience matched between the assigned groups (n=5). Additionally, an analysis of variance test was performed to test whether diagnostic accuracies varied between the groups. The Kruskal-Wallis test followed by the Dunn test were also used in comparing the changes in diagnostic accuracy between the display systems in each CHD variation. Friedman and Wilcoxon signed-rank tests were used in peer assessment and the comparison survey to determine whether responses differed between display systems. A Fisher exact test was performed to determine the influence of usability of HMD (ie, motion sickness and physical discomfort) on the postdiscussion survey and comparison survey responses. The Kruskal-Wallis test was performed to explore any influence of impression of VR before experiment on preference rating. All statistical analysis was performed on R 64-bit version 3.5.3 software (R Foundation for Statistical Computing) with significance being .05 or lower in *P* values.

Results

Demographic Survey

Two participants claimed to have prior experience with using immersive VR from playing VR games and exploring real estate property in VR. Both participants had moderately positive impressions of VR (ie, 1 and 2 points on a scale between –5 and +5) compared with the group of 20 participants without prior experience with VR (2.6 [SD 1.96]). The Kruskal-Wallis test showed that the results on VR impression did not show any difference in the choice of display preference (CDS χ^2=4.1, *P*=.53; NIV χ^2=4.5, *P*=.49; FIV χ^2=1.3, *P*=.93). Due to the small sample size of those with prior VR experience, we could not directly test if VR experience influenced the choice of the most preferred display.

Group Assignment

Between 4 to 5 participants were assigned to each of 5 groups according to participant availability. The Kruskal-Wallis test (χ^2_4=10.7, *P*=.03) was used to gauge differences in medical experience levels between the groups (Table 4). Further investigation with the Dunn test using the Benjamini-Hochberg method showed that group 3 had more medically experienced participants than group 5 (*z*=–2.19, *P*=.048). However, the diagnostic accuracy performance in CHD cases between the 5 groups did not show any statistical difference based on analysis of variance.

Table 4. Dunn test results comparing participants' years of medical experience between the groups.

Years of medical experience	Groups Z-score (*P* value)				
	1	2	3	4	5
1	N/A[a]	–2.32 (.05)	0.35 (.41)	–0.52 (.38)	–1.96 (.06)
2	–2.32 (.05)	N/A	2.54 (.06)	1.67 (.09)	0.23 (.41)
3	0.35 (.41)	2.54 (.06)	N/A	–0.82 (.30)	–2.19 (.048)
4	–0.52 (.38)	1.67 (.09)	–0.82 (.30)	N/A	–1.37 (.14)
5	–1.96 (.06)	0.23 (.41)	–2.19 (.048)	–1.37 (.14)	N/A

[a]N/A: not applicable.

Discussion Time

The discussion times of each group (n=5) and CHD variation are shown in Table 5. Despite being classified as the least complex CHD case in the study, the averaged discussion times for ASD (172 seconds) were slightly longer than for CoA (159 seconds). The trend was visible in all groups except for group 3. All groups spent the longest discussion time on the MAPCA case. The averaged discussion time for MAPCA was 382 seconds, more than twice the time for the ASD and CoA discussions.

Table 5. Discussion times of the congenital heart disease variations for all groups and on average.

Discussion time	ASD[a]		CoA[b]		MAPCA[c]	
Group	Display system	Time (s)	Display system	Time (s)	Display system	Time (s)
1	CDS[d]	279	NIV[e]	262	FIV[f]	367
2	FIV	373	CDS	293	NIV	585
3	NIV	80	FIV	144	CDS	501
4	FIV	71	NIV	64	CDS	294
5	NIV	58	CDS	34	FIV	165
Average	N/A[g]	172	N/A	159	N/A	382

[a]ASD: atrial septal defect.

[b]CoA: coarctation of aorta.

[c]MAPCA: major aortopulmonary collateral artery.

[d]CDS: conventional display system.

[e]NIV: nonimmersive virtual reality display system.

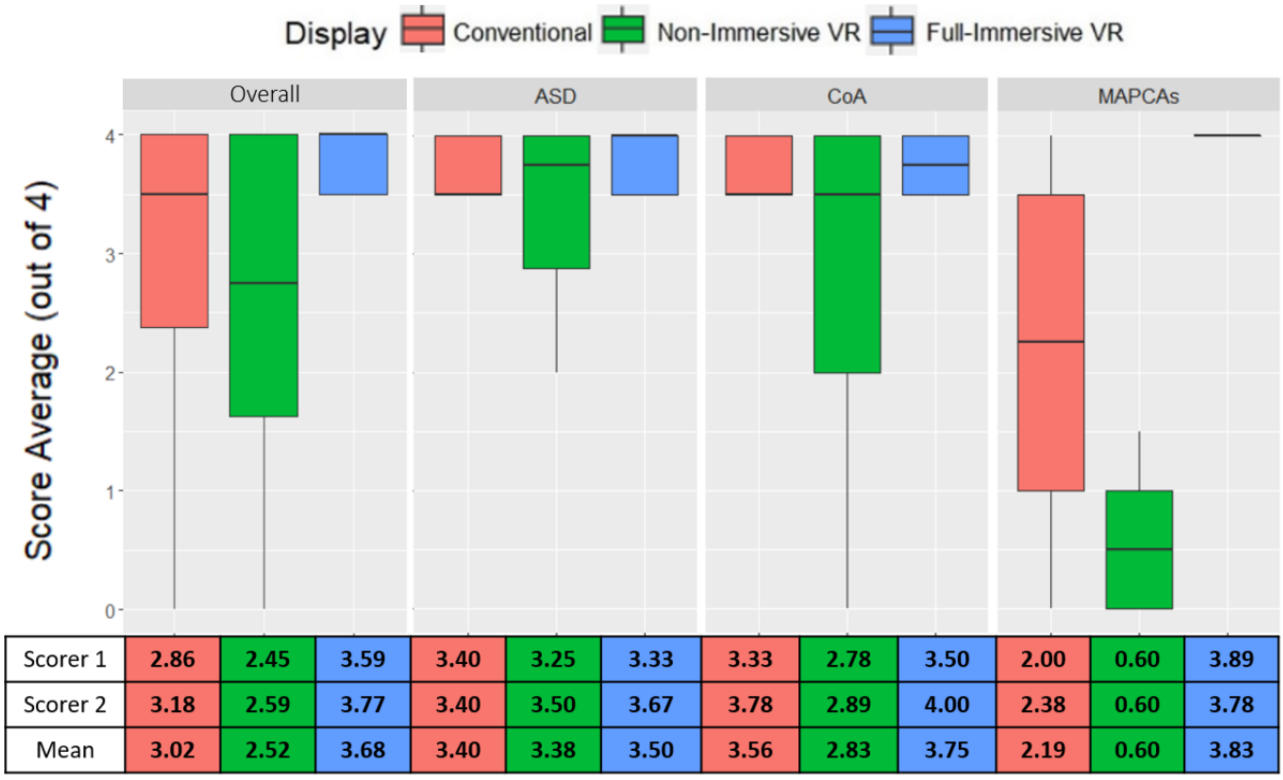
[f]FIV: full-immersive virtual reality display system.

[g]N/A: not applicable.

Postdiscussion Survey

Each participant received a diagnostic accuracy score ranging between 0 and 4 for each of the CHD cases. Two cardiologists individually graded the participants' diagnostic performance according to the rubric (Table 3). The diagnostic accuracy scores were compared for each display system and CHD variation and broken down by cardiologist (Figure 5). No statistical differences were found between the grades of the two scorers (t=–1.01, P=.31).

Figure 5. Diagnostic accuracy scores by type of congenital heart disease and display system (top) and by cardiologist (bottom). VR: virtual reality; ASD: atrial septal defect; CoA: coarctation of aorta; MAPCA: major aortopulmonary collateral artery.



Scorer 1	2.86	2.45	3.59	3.40	3.25	3.33	3.33	2.78	3.50	2.00	0.60	3.89
Scorer 2	3.18	2.59	3.77	3.40	3.50	3.67	3.78	2.89	4.00	2.38	0.60	3.78
Mean	3.02	2.52	3.68	3.40	3.38	3.50	3.56	2.83	3.75	2.19	0.60	3.83

The overall diagnostic accuracy difference between the display systems was statistically significant (χ^2_2=9.0, *P*=.01) where FIV had the highest averaged accuracy (Table 6). Differences became even more prominent with increasing case complexity (χ^2_2=14.1, *P*<.001; Table 6). For MAPCA, the average score percentage differences between the groups that used FIV to CDS and NIV were 54.49% and 146.82%, respectively. With the rise of CHD complexity, decreases in average scores of 35.59% and 82.86% were observed in CDS and NIV, respectively. Indeed, the Dunn test indicated that the averaged diagnostic accuracy of MAPCA for the FIV groups were significantly higher compared with the NIV groups (*z*=3.57, *P*=.001; Table 6).

Table 6. Kruskal-Wallis and Dunn test results on the overall congenital heart disease cases and broken down by type between the display systems on diagnostic accuracies.

Diagnostic accuracies	Kruskal-Wallis χ^2 (*P* value)	Dunn Z-score (adj. *P* value)		
	Between display systems	CDS[a] vs NIV[b]	CDS vs FIV[c]	NIV vs FIV
Overall	9.0 (.01)	0.65 (.51)	–2.21 (.04)	2.86 (.01)
ASD[d]	0.2 (.91)	–0.11 (.91)	–0.41 (>.99)	0.33 (>.99)
CoA[e]	1.0 (.62)	0.74 (.69)	–0.30 (.77)	0.88 (>.99)
MAPCA[f]	14.1 (<.001)	1.33 (.18)	–2.53 (.02)	3.57 (.001)

[a]CDS: conventional display system.

[b]NIV: nonimmersive virtual reality display system.

[c]FIV: full-immersive virtual reality display system.

[d]ASD: atrial septal defect.

[e]CoA: coarctation of aorta.

[f]MAPCA: major aortopulmonary collateral artery.

No significant difference between the display systems for each peer assessment questionnaire was found using the Friedman test (Q1 χ^2=0.4, *P*=.82; Q2 χ^2=3.4, *P*=.18; Q3 χ^2=0.4, *P*=.82; Q4 χ^2=1.3, *P*=.53; Q5 χ^2=1.8, *P*=.42; Q6 χ^2=0.2, *P*=.934; Q7 χ^2=3.4, *P*=.19).

Comparison Survey

Approximately two-thirds of the participants (15/22, 68%) ranked the FIV as the most preferred display system for performing group diagnostic discussions, and the rest of the participants (7/22, 33%) chose the NIV. The preference ranking ratings of the display systems were statistically significantly

different based on the outcome of the Friedman test (χ^2_2=31.6, *P*<.001). Further testing with Wilcoxon signed-rank tests indicated that the median ranking rating of the FIV was statistically significantly higher than the median ranking rating of the NIV (*z*=3.33, *P*<.001) and CDS (*z*=4.10, *P*<.001). The NIV (10/22, 46%) and the FIV (8/22, 36%) received a similar number of votes for the easiest display system to use in group discussions or roughly twice as many as the number of the votes for CDS (4/22, 18%). The Friedman test revealed that a statistically significant difference between the display systems existed on the display system ease ranking (χ^2_2=20.6, *P*<.001). The median CDS ranking rating on ease of use were found to be statistically significantly lower than that of FIV (*z*=1.93, *P*=.047) and NIV (*z*=2.39, *P*=.01; Table 7) using the Wilcoxon signed-rank test.

Table 7. Friedman test and Wilcoxon signed-rank test results on the comparison survey between the display systems.

Comparison survey	Friedman test χ^2 (*P* value)	Wilcoxon signed-rank test z-score (*P* value)		
	Between display systems	CDS[a] vs NIV[b]	CDS vs FIV[c]	FIV vs FIV
Preference	31.5 (<.001)	3.33 (<.001)	4.11 (<.001)	1.83 (.049)
Easiness	20.6 (<.001)	2.39 (.01)	1.93 (.047)	–0.80 (.63)

[a]CDS: conventional display system.

[b]NIV: nonimmersive virtual reality display system.

[c]FIV: full-immersive virtual reality display system

Virtual Reality Usability Survey

A total of 27% (6/22) of participant reported motion sickness from wearing the HMD. These participants were more likely to provide lower scores on concentration (*P*=.009) and knowledge exchange (*P*=.046) of the discussion using the FIV. Almost half (10/22, 45%) of participants experienced some level of physical discomfort especially around their noses from the heaviness of the HMD. Of the participants wearing glasses, 40% (2/5) removed them while using the HMD due to physical discomfort. However, no statistical differences were found between the groups that did or did not report physical discomfort and wore or did not wear glasses on all surveys (Table 8 and 9) and diagnostic performance using FIV (Table 8).

Table 8. Preference and ease of use ratings and diagnostic accuracy using the full-immersive virtual reality display system between the groups with and without physical discomfort, motion sickness, and eyeglass use.

Impact of usability on preference and diagnostic accuracies	Fisher exact test *P* value						
	Preference			Ease of use			FIV[a] diagnostic accuracy
	CDS[b]	NIV[c]	FIV	CDS	NIV	FIV	Score
Physical discomfort	.57	.17	.85	.20	>.99	>.99	.77
Motion sickness	.15	.34	.43	.67	.29	.58	>.99
Glasses	>.99	>.99	>.99	.48	.51	>.99	>.99

[a]FIV: full-immersive virtual reality display system.

[b]CDS: conventional display system.

[c]NIV: nonimmersivevirtual reality display system.

Table 9. Peer assessment scores using the full-immersive virtual reality display system between the groups with and without physical discomfort, motion sickness, and eyeglass use.

Impact of usability on peer assessment	Fisher exact test *P* value						
	Q1	Q2	Q3	Q4	Q5	Q6	Q7
Physical discomfort	.57	.77	>.99	.55	.29	.48	.59
Motion sickness	>.99	.009	.07	.59	.046	.07	>.99
Glasses	>.99	.64	>.99	>.99	.54	>.99	.25

Discussion

Principal Findings

The FIV involved wearing HMD, which caused some physical discomfort and motion sickness and required training. These experiences could result in negative emotions, which are shown to be negatively related to team performances [41]. However, the FIV was rated as the most preferred medical image display system. The survey responses revealed that the realistic and interactive visualization ability such as interior viewing, rotating, and zooming in/out of the 3D anatomical models were the reasons for the better rating. CDS required succinct and accurate verbal directions for adjusting the sagittal, coronal, and frontal planes to orient the cross-sectional viewing and then processing them into the volumetric anatomy. The higher demand of mental conceptualization made the CDS the most difficult display system to use.

FIV has been facing criticism for the absence of face-to-face communication, which is related to reduced group collaboration quality [42-44]. Some studies emphasized the use of avatars as a remedy to improve social presence and communication in VR [45,46]. Although face-to-face communication was not featured in our clinical viewing software, providing shared perspective of anatomies and a mechanism for concurrent feedback was sufficient for enhanced group diagnostic performance. FIV showed strong diagnostic accuracy regardless of the CHD complexity unlike the other display systems, which showed worsened accuracy with increasing complexity.

Limitations

To investigate the group diagnostic performances, an active discussion environment with experienced physicians across multiple disciplines was desirable. However, the recruitment process was challenged by a limited pool of trained physicians and their busy schedules. The study, therefore, recruited medical trainees who varied in years of medical experiences. A larger number of participants would increase the power of statistical results, but there was limited availability of pediatric residents (40 residents per class, with competing clinical demands), making 22 participants a realistic recruitment achievement. Due to the small data size, high standard deviations were observed in CDS and NIV, which increases the range of true diagnostic accuracy value. However, since the probability of false positive is lower with a smaller data sample size [47], the probability of falsely rejecting the differences in MAPCA diagnostic accuracy between display system is small. Nevertheless, we plan to narrow the spectrum of CHD cases down to the STAT categories of 4 and 5 in a future study to further evaluate the impact of displays on complex CHD cases.

Gender difference was disregarded in the study since the ratio of women to men was 19 to 3. Groups were formed based on participant availability. We confirmed through the Dunn test using the Benjamini-Hochberg method that except for groups 3 and 5 (P=.048), years of medical experience (eg, residency standing) did not vary between the groups. Since there was no statistical diagnostic performance difference found between the groups, we conclude that the participants' years of experience were not an influential factor for performing tasks provided in the study.

The exact reason behind FIV being more preferred than the NIV could not be identified through the comparison survey results. Since the features of FIV and NIV are identical except for the immersion aspect, we suspect the perceived novelty of the VR experience could have impacted the choice in preferred displays. There were 20 participants who had never experienced VR prior to the experiments. To them, everything about FIV was novel, therefore they could have experienced increased perceived reward and individual preference toward the VR [48], leading them to prefer the FIV for CHD diagnosis tasks. To test the hypothesis, a future study will include a survey on novelty and compare its result on the preference rating.

The Cardiac Review 3D currently uses DICOM images that are 3D reconstructed and segmented into stereolithography file-formatted data. Since 3D reconstruction is not a routinely performed task in medicine, stereolithography is not stored in DICOM or part of the electronic patient records. To be compatible with the existing medical workflow, the logistics of storing 3D reconstructed data in DICOM is being identified.

Conclusions

The Cardiac Review 3D is unique clinical viewing software with multiuser access and interaction. The software allows for visualization and manipulations of 3D anatomical models through zooming, rotating, panning, linear measurement, and adjustable clipping plane features. The text annotations, screenshots, and report features allow for taking notes in text and image forms for future access and archiving. User datagram protocol was implemented with virtual pointer for multiuser access and participation.

This study evaluated the group diagnostic discussion performances of the CDS, NIV, and FIV. Despite the lack of face-to-face communication and reduced concentration from motion sickness, the group discussions that used FIV demonstrated the best diagnostic accuracy overall and particularly for the most complex form of CHD. It also was the only display system that showed improving trend of diagnostic accuracy with increasing CHD complexity. The FIV relied on bulky hardware associated with physical discomfort, motion sickness, and increased learning process; however, it was still the most preferred display system for performing group diagnostic discussions.

The application of FIV has successfully supported improved diagnostic accuracy in CHD group discussions. FIV has the potential to bolster collaborative performance in discussion of other anatomies, medical education, and surgical planning. Expanding the significance of our findings, we believe that nonmedical fields such as computer-aided design, architecture, urban design, search and rescue, and military training that necessitate understanding of complex 3D structures may benefit from the use of FIV in collaborative discussions.

The Cardiac Review 3D provides features for medical doctors to visualize and interact with the patient anatomies in 3D in a group setting. Implementation of this technology could potentially bolster the diagnosis and preoperative planning of

CHD, especially for complex cases (eg, MAPCA) by reducing the mental workload and capability of converting 2D cross-sectional images of anatomies into 3D and easily maneuvering around the anatomies.

Acknowledgments

This study was supported by a Children's National Board of Visitors Grant.

Authors' Contributions

BK, YL, LO, and AK designed the study under institutional review board approval at the Children's National Hospital. BK created the surveys provided to the participants. With the approval, BK, YL, and PM ran experiments and collected data. The collected data were statistically analyzed and graphed by BK. YL created tables 1 and 3 and figures 1, 3, and 4. PM created figure 2. BK wrote the majority of the manuscript and created the rest of the tables and figures. YL wrote the medical image selection and acquisition section. AK, LO, MI, and CC conceived of and created the virtual reality medical image display system. LO and AK managed the team as coadvisors of this study. All authors reviewed and edited the final manuscript.

Conflicts of Interest

None declared.

References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation 2015 Jan 27;131(4):e29-e322. [doi: 10.1161/CIR.0000000000000152] [Medline: 25520374]
2. Sun R, Liu M, Lu L, Zheng Y, Zhang P. Congenital heart disease: causes, diagnosis, symptoms, and treatments. Cell Biochem Biophys 2015 Jul;72(3):857-860. [doi: 10.1007/s12013-015-0551-6] [Medline: 25638345]
3. Grant EK, Olivieri LJ. The role of 3-D heart models in planning and executing interventional procedures. Can J Cardiol 2017 Sep;33(9):1074-1081. [doi: 10.1016/j.cjca.2017.02.009] [Medline: 28624249]
4. Ong CS, Loke Y, Opfermann J, Olivieri L, Vricella L, Krieger A, et al. Virtual surgery for conduit reconstruction of the right ventricular outflow tract. World J Pediatr Congenit Heart Surg 2017 May;8(3):391-393 [FREE Full text] [doi: 10.1177/2150135117692777] [Medline: 28520540]
5. Haak D, Page C, Deserno TM. A survey of DICOM viewer software to integrate clinical research and medical imaging. J Digit Imaging 2016 Apr;29(2):206-215 [FREE Full text] [doi: 10.1007/s10278-015-9833-1] [Medline: 26482912]
6. Farooqi KM, Mahmood F. Innovations in preoperative planning: insights into another dimension using 3D printing for cardiac disease. J Cardiothorac Vasc Anesth 2018 Aug;32(4):1937-1945. [doi: 10.1053/j.jvca.2017.11.037] [Medline: 29277300]
7. Chen X, Possel JK, Wacongne C, van Ham AF, Klink PC, Roelfsema PR. 3D printing and modelling of customized implants and surgical guides for non-human primates. J Neurosci Methods 2017 Jul 15;286:38-55 [FREE Full text] [doi: 10.1016/j.jneumeth.2017.05.013] [Medline: 28512008]
8. Ventola CL. Medical applications for 3D printing: current and projected uses. Pharm Ther 2014 Oct;39(10):704-711 [FREE Full text] [Medline: 25336867]
9. Loke Y, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. BMC Med Educ 2017 Mar 11;17(1):54 [FREE Full text] [doi: 10.1186/s12909-017-0889-0] [Medline: 28284205]
10. Olivieri LJ, Zurakowski D, Ramakrishnan K, Su L, Alfares FA, Irwin MR, et al. Novel, 3D display of heart models in the postoperative care setting improves CICU caregiver confidence. World J Pediatr Congenit Heart Surg 2018 Mar;9(2):206-213. [doi: 10.1177/2150135117745005] [Medline: 29544410]
11. Shuhaiber JH. Augmented reality in surgery. Arch Surg 2004 Feb;139(2):170-174. [doi: 10.1001/archsurg.139.2.170] [Medline: 14769575]
12. Martelli N, Serrano C, van den Brink H, Pineau J, Prognon P, Borget I, et al. Advantages and disadvantages of 3-dimensional printing in surgery: a systematic review. Surgery 2016 Jun;159(6):1485-1500. [doi: 10.1016/j.surg.2015.12.017] [Medline: 26832986]
13. Mitsouras D, Liacouras P, Imanzadeh A, Giannopoulos AA, Cai T, Kumamaru KK, et al. Medical 3D printing for the radiologist. Radiographics 2015;35(7):1965-1988 [FREE Full text] [doi: 10.1148/rg.2015140320] [Medline: 26562233]
14. Choi K, Sun H, Heng P. An efficient and scalable deformable model for virtual reality-based medical applications. Artif Intell Med 2004 Sep;32(1):51-69. [doi: 10.1016/j.artmed.2004.01.013] [Medline: 15350624]
15. Seymour NE, Røtnes JS. Challenges to the development of complex virtual reality surgical simulations. Surg Endosc 2006 Nov;20(11):1774-1777. [doi: 10.1007/s00464-006-0107-3] [Medline: 16960667]
16. Hoekstra A. 3D Audio for Virtual Reality Exposure Therapy [Thesis]. Delft: Delft University of Technology; 2013.

17. Ku J, Mraz R, Baker N, Zakzanis KK, Lee JH, Kim IY, et al. A data glove with tactile feedback for FMRI of virtual reality experiments. Cyberpsychol Behav 2003 Oct;6(5):497-508. [doi: 10.1089/109493103769710523] [Medline: 14583125]
18. Munyan BG, Neer SM, Beidel DC, Jentsch F. Olfactory stimuli increase presence in virtual environments. PLoS One 2016;11(6):e0157568 [FREE Full text] [doi: 10.1371/journal.pone.0157568] [Medline: 27310253]
19. Khalifa YM, Bogorad D, Gibson V, Peifer J, Nussbaum J. Virtual reality in ophthalmology training. Surv Ophthalmol 2006;51(3):259-273. [doi: 10.1016/j.survophthal.2006.02.005] [Medline: 16644366]
20. LeBlanc F, Champagne BJ, Augestad KM, Neary PC, Senagore AJ, Ellis CN, Colorectal Surgery Training Group. A comparison of human cadaver and augmented reality simulator models for straight laparoscopic colorectal skills acquisition training. J Am Coll Surg 2010 Aug;211(2):250-255. [doi: 10.1016/j.jamcollsurg.2010.04.002] [Medline: 20670864]
21. Moody L, Waterworth A, McCarthy AD, Harley PJ, Smallwood RH. The feasibility of a mixed reality surgical training environment. Virtual Reality 2007 Aug 23;12(2):77-86. [doi: 10.1007/s10055-007-0080-8]
22. Vera AM, Russo M, Mohsin A, Tsuda S. Augmented reality telementoring (ART) platform: a randomized controlled trial to assess the efficacy of a new surgical education technology. Surg Endosc 2014 Dec;28(12):3467-3472. [doi: 10.1007/s00464-014-3625-4] [Medline: 24962856]
23. Foo J, Lobe T, Winer E. A virtual reality environment for patient data visualization and endoscopic surgical planning. J Laparoendosc Adv Surg Tech A 2009 Apr;19 Suppl 1:S211-S217. [doi: 10.1089/lap.2008.0159.supp] [Medline: 18999974]
24. Robiony M, Salvo I, Costa F, Zerman N, Bazzocchi M, Toso F, et al. Virtual reality surgical planning for maxillofacial distraction osteogenesis: the role of reverse engineering rapid prototyping and cooperative work. J Oral Maxillofac Surg 2007 Jun;65(6):1198-1208. [doi: 10.1016/j.joms.2005.12.080] [Medline: 17517306]
25. Tang R, Ma L, Rong Z, Li M, Zeng J, Wang X, et al. Augmented reality technology for preoperative planning and intraoperative navigation during hepatobiliary surgery: a review of current methods. Hepatobiliary Pancreat Dis Int 2018 Apr;17(2):101-112. [doi: 10.1016/j.hbpd.2018.02.002] [Medline: 29567047]
26. Vávra P, Roman J, Zonča P, Ihnát P, Němec M, Kumar J, et al. Recent development of augmented reality in surgery: a review. J Healthc Eng 2017;2017:4574172 [FREE Full text] [doi: 10.1155/2017/4574172] [Medline: 29065604]
27. Dunn J, Yeo E, Moghaddampour P, Chau B, Humbert S. Virtual and augmented reality in the treatment of phantom limb pain: a literature review. NeuroRehabilitation 2017;40(4):595-601. [doi: 10.3233/NRE-171447] [Medline: 28211829]
28. Mousavi Hondori H, Khademi M, Dodakian L, Cramer SC, Lopes CV. A spatial augmented Reality rehab system for post-stroke hand rehabilitation. Stud Health Technol Inform 2013;184:279-285. [Medline: 23400171]
29. Powers MB, Rothbaum BO. Recent advances in virtual reality therapy for anxiety and related disorders: introduction to the special issue. J Anxiety Disord 2019 Jan;61:1-2. [doi: 10.1016/j.janxdis.2018.08.007] [Medline: 30181011]
30. Cooper N, Milella F, Pinto C, Cant I, White M, Meyer G. The effects of substitute multisensory feedback on task performance and the sense of presence in a virtual reality environment. PLoS One 2018;13(2):e0191846 [FREE Full text] [doi: 10.1371/journal.pone.0191846] [Medline: 29390023]
31. Salis S, Williams A. Knowledge sharing through face-to-face communication and labour productivity: evidence from British workplaces. Brit J Industrial Relations 2010;48(2):436-459. [doi: 10.1111/j.1467-8543.2009.00762.x]
32. Kirkman BL, Rosen B, Tesluk PE, Gibson CB. The impact of team empowerment on virtual team performance: the moderating role of face-to-face interaction. Acad Manag J 2004 Apr 01;47(2):175-192. [doi: 10.2307/20159571]
33. Joshi K, Sarker SA, Sarker SU. Knowledge transfer among face-to-face information systems development team members: examining the role of knowledge, source, and relational context. 2044 Presented at: Proceedings of the 37th Hawaii International Conference on System Sciences; 2004; Big Island. [doi: 10.1109/hicss.2004.1265596]
34. Gera S. Virtual teams versus face to face teams: a review of literature. IOSR J Bus Manag 2013;11(2):1-4. [doi: 10.9790/487x-1120104]
35. Teasley S, Covi L, Krishnan M, Olson J. How does radical collocation help a team succeed? 2000 Presented at: Proceedings of the 2000 ACM Conference on Computer Supported Cooperative Work; 2000; Philadelphia p. 339-346. [doi: 10.1145/358916.359005]
36. O'Brien SM, Clarke DR, Jacobs JP, Jacobs ML, Lacour-Gayet FG, Pizarro C, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. J Thorac Cardiovasc Surg 2009 Nov;138(5):1139-1153 [FREE Full text] [doi: 10.1016/j.jtcvs.2009.03.071] [Medline: 19837218]
37. Prakash A, Powell AJ, Geva T. Multimodality noninvasive imaging for assessment of congenital heart disease. Circ Cardiovasc Imaging 2010 Jan;3(1):112-125. [doi: 10.1161/CIRCIMAGING.109.875021] [Medline: 20086225]
38. Dijkema EJ, Leiner T, Grotenhuis HB. Diagnosis, imaging and clinical management of aortic coarctation. Heart 2017 Aug;103(15):1148-1155. [doi: 10.1136/heartjnl-2017-311173] [Medline: 28377475]
39. Anwar S, Rockefeller T, Raptis DA, Woodard PK, Eghtesady P. 3D printing provides a precise approach in the treatment of tetralogy of fallot, pulmonary atresia with major aortopulmonary collateral arteries. Curr Treat Options Cardiovasc Med 2018 Feb 03;20(1):5. [doi: 10.1007/s11936-018-0594-2] [Medline: 29397465]
40. Stenlund T, Jönsson FU, Jonsson B. Group discussions and test-enhanced learning: individual learning outcomes and personality characteristics. Educ Psychol (Lond) 2017 Feb 07;37(2):145-156 [FREE Full text] [doi: 10.1080/01443410.2016.1143087] [Medline: 28392609]

41. Jordan PJ, Lawrence SA, Troth AC. The impact of negative mood on team performance. J Manag Org 2015 Feb 02;12(2):131-145. [doi: 10.5172/jmo.2006.12.2.131]
42. Boughzala I, Vreede G, Limayem M. Team collaboration in virtual worlds: editorial to the special issue. J Assoc Inf Syst 2012 Oct;13(10):714-734. [doi: 10.17705/1jais.00313]
43. Davis A, Murphy J, Owens D, Khazanchi D, Zigurs I. Avatars, people, and virtual worlds: foundations for research in metaverses. J Assoc Inf Syst 2009 Feb;10(2):90-117. [doi: 10.17705/1jais.00183]
44. Kahai SS, Carroll E, Jestice R. Team collaboration in virtual worlds. SIGMIS Database 2007 Oct 28;38(4):61-68. [doi: 10.1145/1314234.1314246]
45. Pan Y, Steed A. The impact of self-avatars on trust and collaboration in shared virtual environments. PLoS One 2017;12(12):e0189078 [FREE Full text] [doi: 10.1371/journal.pone.0189078] [Medline: 29240837]
46. Smith H, Neff M. Communication behavior in embodied virtual reality. 2018 Presented at: Proceedings of the 2018 CHI Conference on Human Factors in Computing Systems; 2018; Montreal p. 1-12. [doi: 10.1145/3173574.3173863]
47. Krousel-Wood MA, Chambers RB, Muntner P. Clinicians' guide to statistics for medical practice and research: Part II. Ochsner J 2007;7(1):3-7 [FREE Full text] [Medline: 21603472]
48. Khattri S, Kumbargere Nagraj S, Arora A, Eachempati P, Kusum C, Bhat K, et al. Adjunctive systemic antimicrobials for the non-surgical treatment of periodontitis. Cochrane Database Syst Rev 2020 Nov 16;11:CD012568. [doi: 10.1002/14651858.CD012568.pub2] [Medline: 33197289]

Abbreviations

2D: 2-dimensional
3D: 3-dimensional
ASD: atrial septal defect
CDS: conventional display system
CHD: congenital heart disease
CoA: coarctation of aorta
DICOM: Digital Imaging and Communications in Medicine
FIV: full-immersive virtual reality display system
HMD: head-mounted display
MAPCA: major aortopulmonary collateral artery
MRI: magnetic resonance imaging
NIV: nonimmersive virtual reality display system
STAT Mortality Categories: STS-EACTS Congential Heart Surgery Mortality Categories
STS-EACTS: Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery
VR: virtual reality

Edited by G Eysenbach; submitted 31.05.20; peer-reviewed by M Schuuring, J Salisbury; comments to author 18.08.20; revised version received 12.10.20; accepted 24.10.20; published 08.12.20.

Please cite as:
Kim B, Loke YH, Mass P, Irwin MR, Capeland C, Olivieri L, Krieger A
A Novel Virtual Reality Medical Image Display System for Group Discussions of Congenital Heart Disease: Development and Usability Testing
JMIR Cardio 2020;4(1):e20633
URL: http://cardio.jmir.org/2020/1/e20633/
doi:10.2196/20633
PMID:33289675

Publisher:
JMIR Publications
130 Queens Quay East.
Toronto, ON, M5A 3Y5
Phone: (+1) 416-583-2040
Email: support@jmir.org