Creating a continuum of care : smart technology in patients with cardiovascular disease

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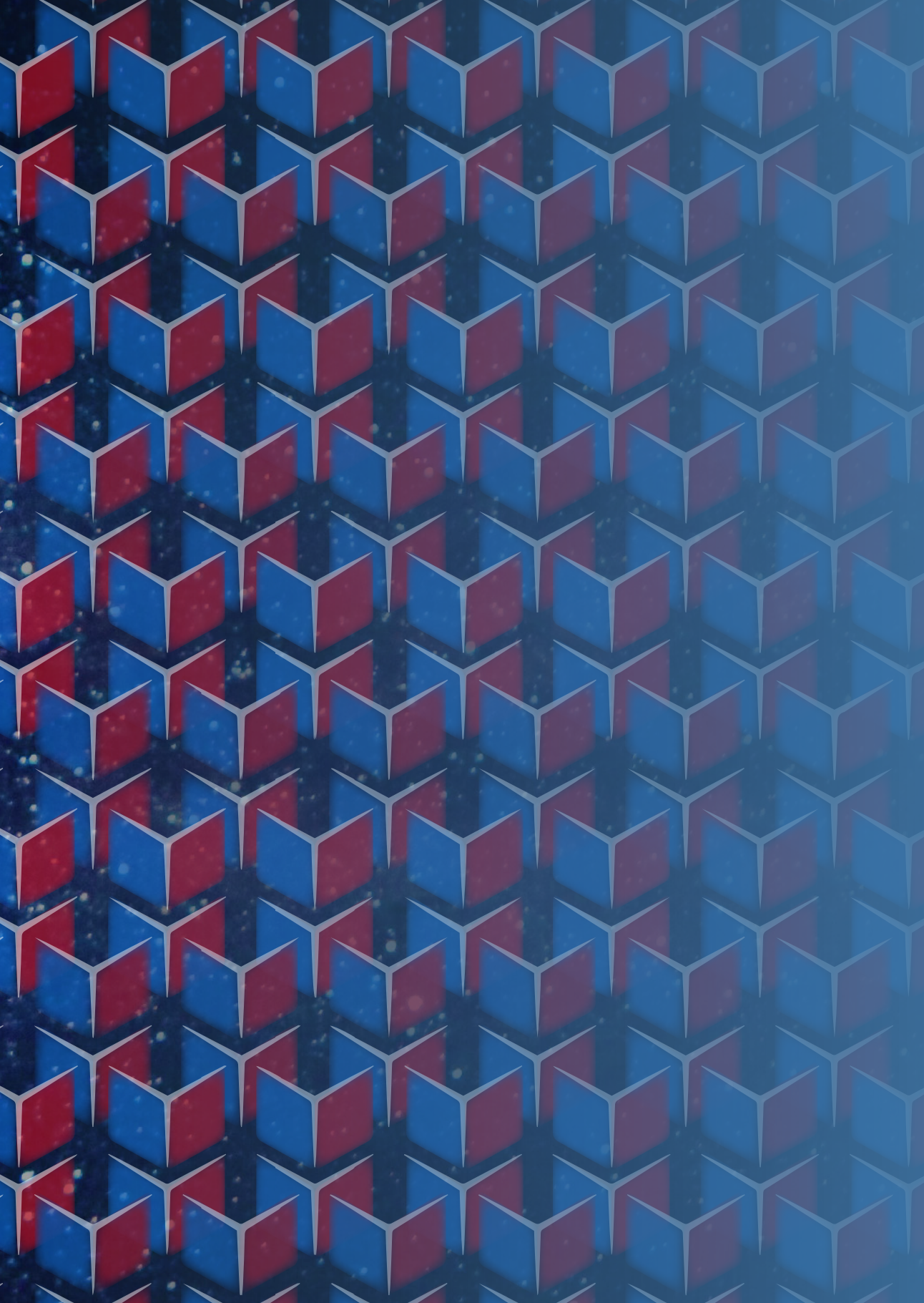

CHAPTER 4

The Box: using smart technology to improve outcome of myocardial infarction patients. Rationale and design of a randomized-controlled trial

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Abstract

Background
Recent evidence suggests that frequent monitoring using smartphone compatible wearables might improve clinical effectiveness and patient satisfaction of care.

Objective
The aim of this study is to investigate the clinical effectiveness and patient satisfaction of a smart technology intervention in patients admitted with a ST elevation myocardial infarction (STEMI) or non ST acute coronary syndrome (NST-ACS).

Methods
In this single center, open, randomized controlled trial (RCT) patients who suffered from STEMI or NST-ACS are 1:1 randomized to an intervention group or control group. Both groups are followed up to 1 year after the index event. The intervention group will take daily measurements with a smartphone compatible electrocardiogram device, BP monitor, weight scale and activity tracker. Furthermore, two out of four outpatient clinic visits are replaced by e-visits (1 and 6 months after index event). The control group will receive regular care, consisting of four outpatient clinic visits (1, 3, 6 and 12 months after index event). All patients will be asked to fill in validated questionnaires about patients satisfaction, quality of life, propensity of medication adherence and physical activity.

Results
Primary outcome of this trial is percentage of patients with controlled blood pressure. Secondary outcomes include patient satisfaction, healthcare utilization, major adverse cardiac events, medication adherence, physical activity, quality of life and percentage of patients in which a sustained arrhythmia is detected.

Conclusion
Smart technology could potentially improve care in post-myocardial infarction patients. This trial will investigate whether usage of smart technology can improve clinical-, and cost-effectiveness of care.

Trial registration
NCT02976376 (clinicaltrials.gov)

Introduction

Current European Society of Cardiology guidelines on secondary prevention in patients with sustained ST-segment elevation myocardial infarction (STEMI) or acute coronary syndrome without persistent ST-segment elevation (NST-ACS) recommend tight blood pressure (BP) control, weight control and adequate physical activity after discharge from the hospital, as well as regular electrocardiograms (ECGs).(1, 2) In current practice, the first year after their initial hospitalization these patients regularly visit the outpatient clinic, where the patient is interviewed, weighed, an ECG is made, BP is measured, lifestyle advices are given and pharmaceutical treatment is evaluated.(3)

In this situation, patients must be physically present at the outpatient clinic.(3) This might pose a burden to the patient, especially in remote areas.(4) Furthermore, it necessitates trained healthcare staff, increasing the workload.

Recent advances in information and communication technology have enabled remote monitoring of vital signs and remote doctor-patient contacts (together part of the broad concept “telemedicine”).(5-9) In recent years, a number of smartphone compatible wearables have received a CE-mark and Food and Drug Administration (FDA) clearance and are available for over-the-counter sale in the European Union and the United States.(10) Some of these smartphone compatible wearables allow for the measurement of (depending on the type of wearable) the number of steps taken per day, BP, weight and the recording of an ECG. The devices are easy-to-use and do not require the assistance of trained healthcare staff. Results of measurements are communicated with smartphone applications (app) tailored to the specific device. Data is uploaded via internet to servers of the manufacturer of the device.(10, 11)

Recent research in various patient populations suggests that telemedicine might improve clinical effectiveness and patient satisfaction of care.(12, 13) Remote and more frequent monitoring with subsequent therapy changes has been shown to improve clinical outcome of patients with uncontrolled hypertension(12) (achieving 18.4% more patients with controlled blood pressure) and with type II diabetes mellitus (a 0.37% reduction in HbA1c, which was statistically significant).(13) Furthermore, remote video contact moments, in which the doctor-patient communicate via a video connection, are potentially time saving for patients.(14, 15) One study found that office visits required an average 50 minutes of a patient’s time, while e-visits only required 22 minutes on average.(15)

We therefore hypothesize that telemedicine improves clinical effectiveness and patient satisfaction of care in the follow-up of STEMI and NST-ACS patients. Thus, the aim of this study is to investigate the clinical effectiveness and patient satisfaction of a smart technology intervention in patients after being admitted with

an STEMI or NST-ACS. In this paper, the rationale and design of this open, single center Randomized Controlled Trial (RCT) are presented.

Methods

Study design (design, randomization and follow-up)

"The Box" is a single-center, open, randomized-controlled trial. It is a parallel group study. The study is conducted at the LUMC, a tertiary care hospital in Leiden, The Netherlands. The trial is registered under clinical trial number NCT02976376 (www.clinicaltrials.gov) and NL56453.058.16(www.toetsingonline.nl). After inclusion, patients are 1:1 randomized to either "The Box" (intervention group) or to regular follow-up (control group). Block randomization per 10 participants is performed. Randomization is stratified per primary diagnosis (STEMI or NST-ACS) and per age (≤50, 51-60, 61-70, 71-80 and >80). A website (www.randomizer.org) is used to generate randomization lists.

Patient population

Patients who are admitted to the cardiology department of the Leiden University Medical Center (LUMC) with STEMI(1) or NST-ACS(2) are eligible for participation. Patients with a STEMI or NST-ACS who match the in-, and exclusion criteria are approached for participation in the protocol within 24 hours after primary percutaneous coronary intervention (PCI). The maximum time between primary PCI and study inclusion is 96 hours. All in-, and exclusion criteria are listed in Table 1.

Regular follow-up

Since 2004, the department has a dedicated care track for patients with STEMI or NST-ACS. Details about this protocol have been described previously by Liem et al.(3) Summarizing, patients with signs and symptoms which are possibly related to myocardial infarction are referred to a percutaneous coronary intervention (PCI) center. Upon arrival, they are immediately transferred to the catheterization department, where primary PCI of the culprit lesion is performed. Before discharge, patients are given written and oral information on the importance of medication adherence and lifestyle advices in accordance with the European Guidelines on cardiovascular disease prevention in clinical practice.(16)

Table 1. Inclusion and exclusion criteria

Inclusion criteria
Patient is admitted with acute myocardial infarction
Patient is able to communicate in English or Dutch at B1 level
Exclusion criteria
Body Mass Index > 35 ($kg \cdot m^{-2}$)
Included in another randomized controlled trial
Does not have wireless internet access at home
Less than 18 years old
Considered an incapacitated adult (this decision is left to the discretion of the responsible cardiologist)
Pregnant
Unwilling to sign the informed consent form

After approximately 48-hours, patients are discharged from the hospital. The standard follow-up during the first year after discharge includes four outpatient clinic visits:

1. Approximately 1 month after STEMI or NST-ACS. This includes a BP measurement, a 10-second, 12-lead ECG, laboratory testing (including kidney function, renal function and lipid spectrum) and an interview with a doctor or nurse practitioner.
2. Approximately 3 months after STEMI or NST-ACS. This includes a BP measurement, a 10-second, 12-lead ECG, stress echo, a 24-hour Holter ECG and an interview with a doctor or nurse practitioner.
3. Approximately 6 months after STEMI or NST-ACS. This includes a BP measurement, a 10-second, 12-lead ECG, 24-hour Holter ECG, laboratory testing (including kidney function, renal function and lipid spectrum), a transthoracic echocardiogram (TTE) and an interview with a doctor or nurse practitioner.
4. Approximately 12 months after STEMI or NST-ACS. This includes a BP measurement, a 10-second, 12-lead ECG, laboratory testing (including kidney function, renal function and lipid spectrum), a TTE and an interview with a doctor or nurse practitioner.

Patients who are randomized to regular follow-up receive the same care as patients who do not participate in the study. A flowchart of regular follow-up is given in Figure 1.

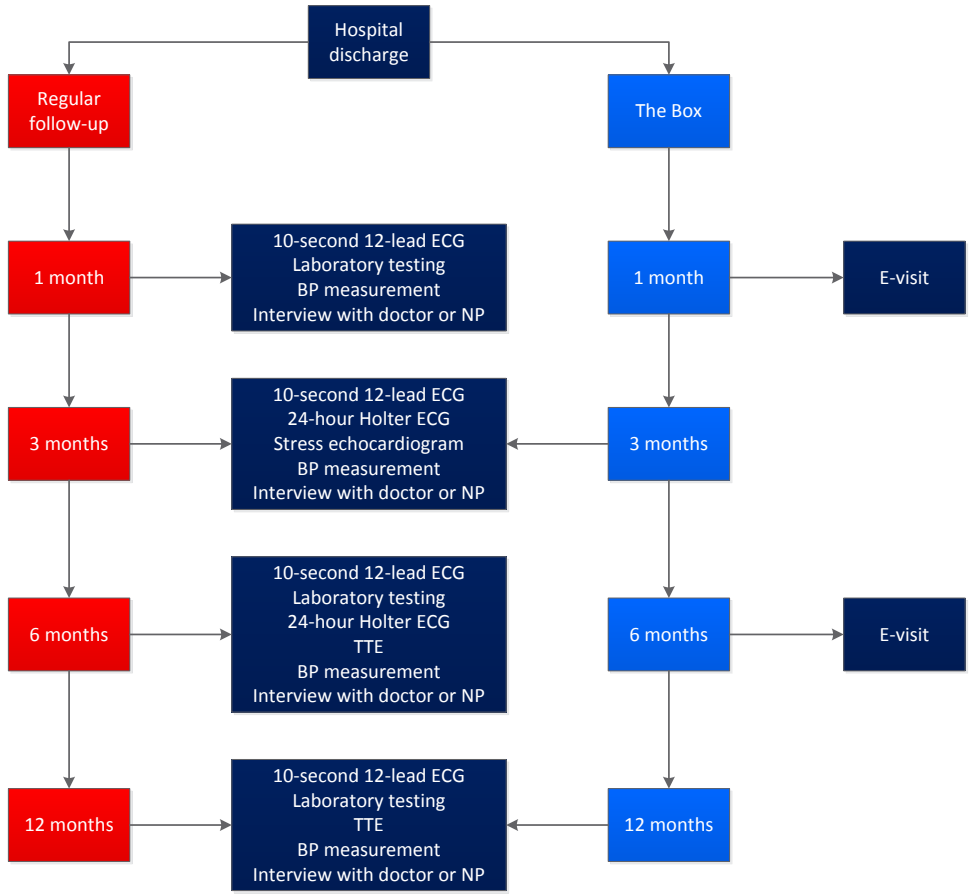

Figure 1. MISSION, follow-up of patients who suffered from STEMI or NST-ACS. BP: blood pressure; ECG: electrocardiogram; NP: nurse practitioner; TTE: transthoracic echocardiogram.

The Box

When randomized to The Box (Figure 2), patients receive a box containing a weight scale, BP monitor, activity tracker and ECG wearable. Patients receive The Box before discharge. They are given the same written and oral information on the importance of medication adherence and lifestyle advices in accordance with the European Guidelines on cardiovascular disease prevention in clinical practice as the control group.(16) The necessary apps are downloaded on the patient's smartphone; necessary accounts are created and the installation of the devices are carried out by a healthcare professional dedicated to the project. Afterwards, patients are given oral instructions on the usage of the devices. They are instructed to measure BP in a sitting position after five minutes of resting. The device should be applied to the left upper arm. Patients are instructed to rest their left under arm

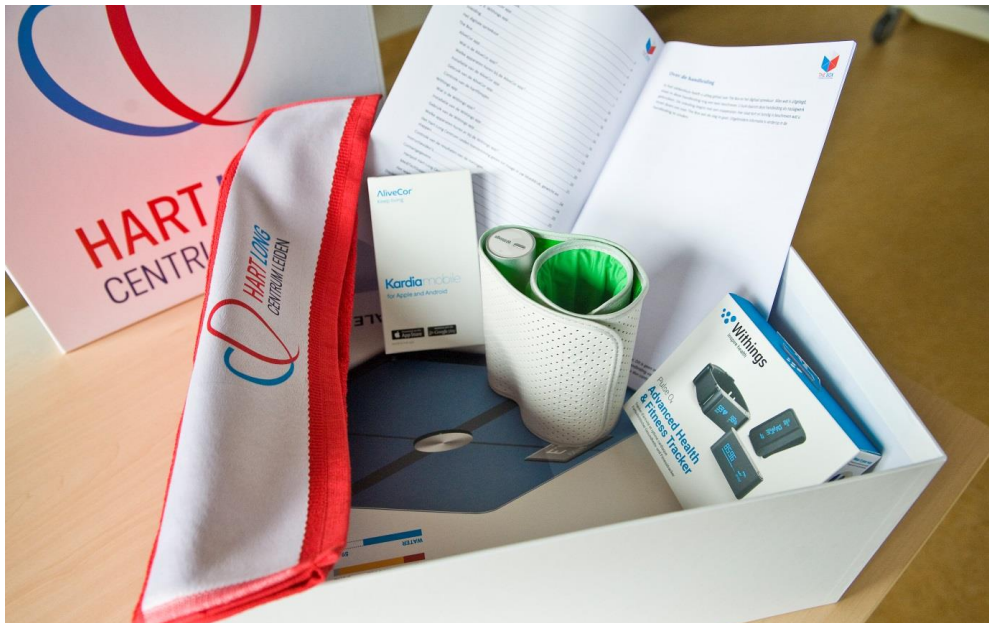

Figure 2. The Box.

on a table. Furthermore, a manual explaining the usage of the below described wearables is handed over with The Box. Also, instruction videos are available on YouTube. Patients who do not own a smartphone or tablet with iOS or Android OS but are willing to participate and randomized to The Box receive a smartphone. Patients are instructed to use their own wireless internet access (e.g. home WiFi network). No mobile data network plan is provided with the smartphone.

Patients are instructed to record a single lead ECG, measure BP and weight daily, preferably at the same moment of the day. Furthermore, they are asked to record a single lead ECG in case of any symptoms of possible cardiac origin (as interpreted by the patient). Lastly, patients are instructed to wear their activity tracker during day to track the daily number of steps and at night to track the duration and quality of sleep. Patients are told that measurements are checked on a daily basis and that they are contacted in case of predefined data irregularities. Patients are explicitly told that they cannot rely on the devices of The Box in emergency situations.

In addition to daily measurements, the 1st and 3rd of the 4 standard outpatient clinic visits are replaced by an e-visit, in which the patient is communicating with the doctor or nurse practitioner via a secured video connection. The content of the interview is comparable to the content of a regular outpatient clinic visit. The same doctors and nurse practitioners are doing the regular outpatient clinic visits and the digital outpatient clinic visits. In the intervention group, the 10-second 12-lead ECG and the laboratory testing one month after the index event is not performed.

Moreover, the 10-second 12-lead ECG, the 24-hour Holter ECG, laboratory testing and the TTE 6 months after the index event is not performed (Figure 1).

Devices

All devices used for this study are non-invasive, battery powered, smartphone compatible devices. They have a CE-mark, are approved by the United States Food and Drug Administration (FDA) and are allowed for over-the-counter sale in the European Union (EU) and the United States of America (USA). The installation and usage of the device is so intuitive that no medical staff needs to assist when the devices are used by the patient.

The usage of the devices requires a smartphone or tablet with Android Operating System (OS) (Google, Mountain View, California, USA) or iOS (Apple Computers, Cupertino, CA, USA). The devices communicate with a dedicated mobile application (app) on the smartphone or tablet, which can be downloaded from the App Store (iOS) or Play Store (Android). The data from the measurements are stored on the smartphone or tablet and uploaded to the app manufacturer's servers (the cloud), which are located in Europe. For synchronization with the cloud, an internet connection (e.g. WiFi, 3G or 4G) is required. Measurements can be done while the smartphone or tablet is offline. In this case, the results of the measurements are stored on the smartphone or tablet, and uploaded to the server when the smartphone is online again.

ECG device

The ECG device (AliveCor, AliveCor Inc., San Francisco, CA, USA) contains two electrodes. The device communicates with the AliveCor app. The ECG device allows the user to record a 30-seconds single lead ECG. To record an ECG, the patient must position two or three fingers of the right hand to one electrode and two or three fingers of the left hand to the other electrode. The device is to be held within approximately 1 to 30 centimetres of the smartphone. An ultrasound signal is sent from the ECG device to the smartphone. This signal is then converted to a live single lead ECG that subsequently is shown on the smartphone screen.(7, 10)

After 30 seconds, an automated algorithm in the app calculates the R-R intervals and formulates a diagnosis, varying from "normal", "possible atrial fibrillation" to "undetermined", on the screen.(10) Then, the patient has the ability to add notes, and is requested to report any symptoms if present before saving the ECG.

Blood pressure monitor

The blood pressure (BP) monitor (Withings S.A., Issy les Moulineaux, France) is a smartphone compatible, battery operated oscillometric blood pressure cuff. It

allows the user to measure systolic BP, diastolic BP and heart rate. The device is applied around the left or right upper arm (depending on the patient's prevalence). Upon pushing the button on the cuff, a connection with the smartphone is made via Bluetooth. The inflation and deflation of the cuff is automated and can be initiated via the dedicated Withings Health Mate app (for iOS and Android) on the smartphone. The average duration of a measurement is approximately 20 seconds. After inflation and deflation, the systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) is shown on the smartphone screen.

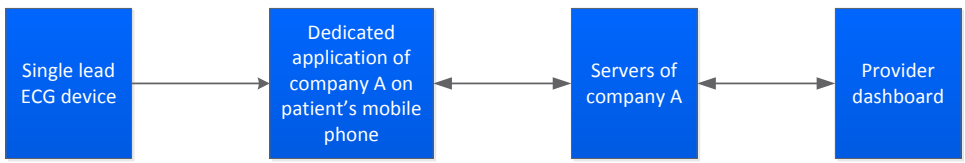

Figure 3. Data integration of single lead ECGs. Legend: company A is the ECG manufacturer. ECG: electrocardiogram.

The weight scale

The weight scale (Withings S.A., Issy les Moulineaux, France) allows the patient to track weight, fat percentage, heart rate and ambient CO_2 parts per million. To measure all four parameters, the patient must stand on the weight scale. While standing on the weight scale, the patient has to select his own account. The results are shown on a screen on the weight scale, and are automatically uploaded via internet to the Withings server.

Activity tracker

The activity tracker (Pulse Ox, Withings S.A., Issy les Moulineaux, France) allows the patient to track the number of steps taken per day. It furthermore allows the patient to track duration and quality of sleep. It has the size of a thumb and can be attached to the wrist or belt. Steps are automatically tracked. The measurement results are sent via Bluetooth to a dedicated smartphone app, compatible with iOS and Android OS.

Storage of the ECGs

Single lead ECGs, made by the single lead ECG device are stored in the cloud. The system offers patients the ability to connect their personal account with a physician's account. The physician then can review the ECGs made by patients linked to his account, including the diagnosis given by the app's algorithm and the symptoms reported by the patient. The automated diagnosis algorithm has a reported sensitivity of 97% and a specificity of 98% for the detection of atrial

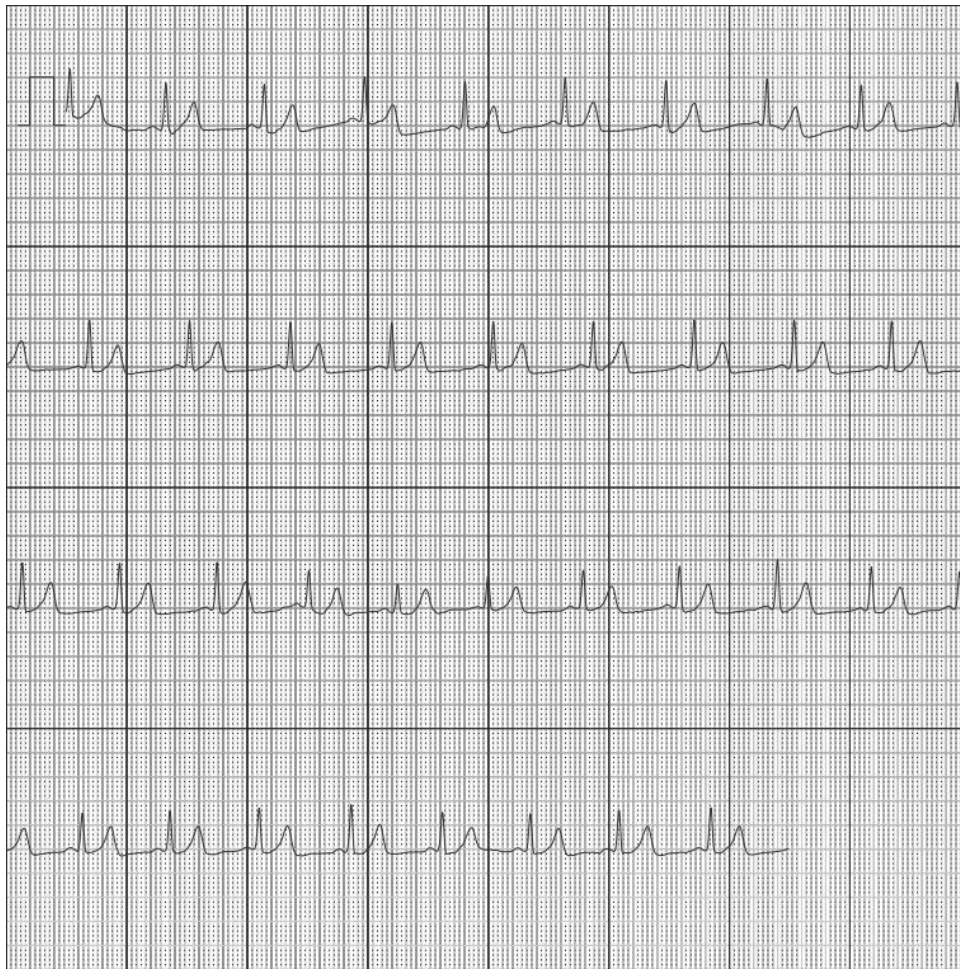

Figure 4. A PDF generated by the ECG device, showing sinus rhythm.

fibrillation.(7) ECGs which are classified by AliveCor as “possible atrial fibrillation” and “undetermined” are subsequently checked by a project dedicated healthcare professional in our department. A patient is contacted if a previously undiagnosed arrhythmia is seen or if a patient repeatedly reported symptoms. A flowchart of the storage of the ECGs is shown in Figure 3. An example of a PDF ECG showing sinus rhythm generated by the ECG device is shown in Figure 4. An example of a PDF ECG showing atrial fibrillation generated by the ECG device is shown in Figure 5.

Data integration in electronic medical record (EMR)

The measurement results from the weight scale, blood pressure monitor and activity tracker are stored on the manufacturer’s server (Withings S.A., Issy les Moulineaux, France). Data are extracted from the Withings server and integrated

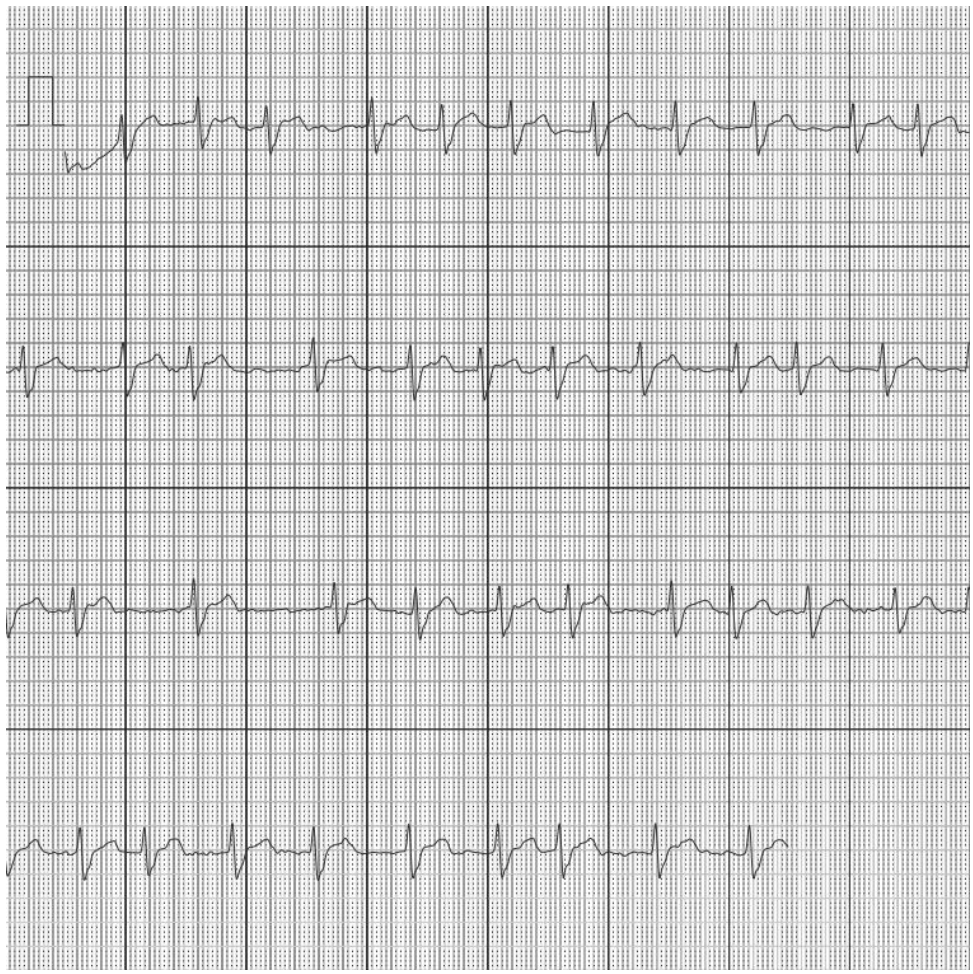

Figure 5. A PDF, generated by the ECG device, showing atrial fibrillation.

in the department's dedicated electronic medical record (EPD-Vision, Department of Cardiology, Leiden University Medical Center, The Netherlands). An automated algorithm searches for predefined irregularities in the data (Table 2). Data can subsequently be displayed in graphic format to facilitate trend analysis. A flowchart of the storage of blood pressure, weight and activity data is given in Figure 6. In case of bugs in this system, a software developer who works at the Department of Cardiology will fix the bug.

Reasons to contact patients

Data are checked daily by a healthcare professional dedicated to the project. When pre-specified irregularities are seen in the data, a patient is contacted within 48 hours by e-mail or phone. These data irregularities are standardized and shown in Table 2.

Table 2. Warnings by the dedicated system

Blood pressure monitor
If a patient has not sent BP for more than 7 consecutive days
If the heart rate is >100 beats per minute
If the systolic BP is >139
If the diastolic BP is > 89
If the systolic BP is 10 mmHg higher than last measurement
If the diastolic BP is 5 mmHg higher than last measurement
If the systolic BP is 10 mmHg higher than 7 measurements before
If the diastolic BP is 5 mmHg higher than 7 measurements before
If the systolic BP is 10 mmHg lower than last measurement
If the diastolic BP is 5 mmHg lower than last measurement
If the systolic BP is 10 mmHg lower than 7 measurements before
If the diastolic BP is 5 mmHg lower than 7 measurements before
Weight scale
If a patient has not sent measurements for more than 7 consecutive days
If the weight is more than 2 kilograms (kg) higher than last measurement
If the weight is more than 3 kilograms (kg) higher than 7 measurements before
If the weight is more than 2 kilograms (kg) lower than last measurement
If the weight is more than 3 kilograms (kg) lower than 7 measurements before
Activity tracker
If a patient has not sent measurements for more than 7 consecutive days

Reasons to adjust therapeutic regimen

Reviewed data are discussed by the data reviewer with the patient's treating physician or nurse practitioner. There are several reasons to contact the patient.

BP monitor: warnings generated by the system on the basis of BP measurements is reviewed by a project dedicated healthcare professional. The reason to change medication is left to the discretion of the treating physician.

Single lead ECG: in case of newly diagnosed arrhythmias lasting at least 30 seconds (atrial fibrillation, atrial flutter, nodal or ventricular escape rhythms, ventricular tachycardias) or at least 4 newly diagnosed asymptomatic premature ventricular contractions (PVC), a 24-Hour Holter ECG is performed. Patients noting chest pain or shortness of breath as symptoms are contacted for an interview by telephone. The decision to change medication or to refer the patient for invasive therapy is left to the discretion of the treating physician.

Weight: weight will not be a primary reason to change therapeutic regimen. Patients can be given lifestyle advices, depending on their height, weight and estimated fat percentage. This is only done at scheduled outpatient clinic visits.

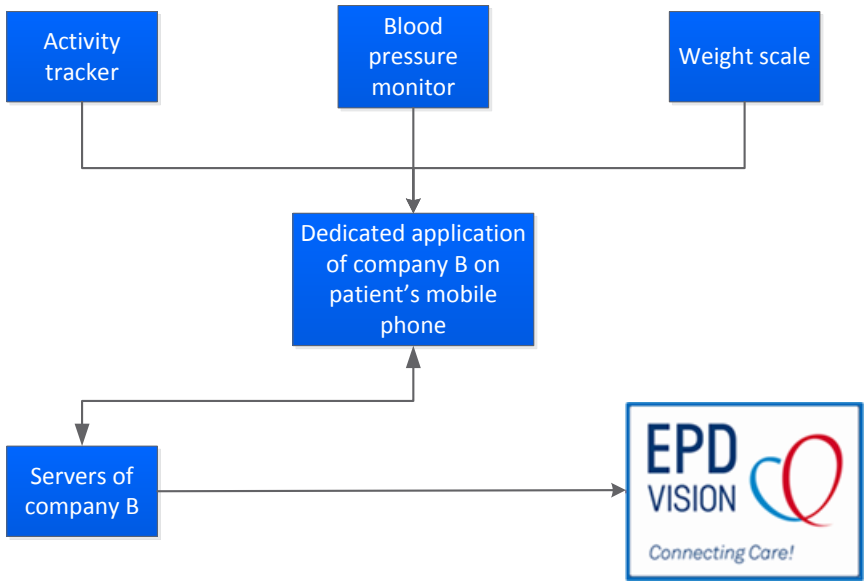

Figure 6. Data integration of the activity tracker, weight scale and BP monitor in the department's Cardiology Information System "EPD-Vision"
Legend: company B is the manufacturer of the activity tracker, blood pressure monitor and weight scale.

Activity: activity tracking data is not a primary reason to change therapeutic regimen. Patients can be advised to exercise more or less, depending on the data. This is only done at scheduled outpatient clinic visits.

Non-adherence

If a patient has not sent measurements from any of his four devices for 21 consecutive days, he is considered non-adherent. A standardized e-mail is sent to the patient, telling that measurements have not been received and that he is urged to contact the hospital in case of any technical difficulties. If no answer is received within 21 days or no measurements are seen within 21 days, the patient is called by telephone. Any technical difficulties or objections by the patient are assessed and solved if possible. If the patient, after this phone call, starts sending measurements, he is considered adherent again. This patient is sent a standardized e-mail in case he becomes non-adherent again. If the patient does not start sending measurements, he is not approached again by e-mail or by telephone to try to affect his non-adherence. However, this patient is not excluded from the trial. This patient is still followed-up according to The Box protocol.

If patients notify the hospital that they want to have regular outpatient clinic visits, they are followed-up according to the regular follow-up protocol.

Questionnaires

All patients, both intervention and control patients, will be asked to fill-in a SF-36 questionnaire,(17) a patient satisfaction questionnaire,(18) a medication adherence questionnaire and an iPAQ questionnaire (to assess the patient's level of physical activity).(19) These questionnaires will be used within one month after myocardial infarction, six months after myocardial infarction and twelve months after myocardial infarction.

Privacy of study participants

To anonymize the data, patients receive an e-mail address consisting of a study code, which they can use to create their Withings and AliveCor accounts. The corresponding names are kept in a separate, password protected database.

Ethical conduct

The study is approved by the Hospital's Medical Ethics Committee (P16.070). It is conducted in accordance to the principles of the Declaration of Helsinki (version 10, October 2013) and in accordance with the Dutch Medical Research Involving Human Subjects Act (WMO) and Good Clinical Practice. Written offline informed consent will be obtained from all participants. The devices used in this study and described above are approved by our Hospital's Instrumentation Department. All devices are CE marked and are available for sale in the European Union. All devices have been bought by our department for this study. No manufacturer has a role in the study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any device manufacturer. All devices are provided to study participants who are randomized to The Box group free of charge.

Study withdrawal

Patients who are randomized from The Box group can be withdrawn from the study if they are either non-adherent (as discussed above) or if they themselves wish to withdraw from the study.
Patients who withdraw from regular follow-up are considered lost to follow-up.

Results

Study outcomes

The primary outcome of this study is the percentage of patients with normalized blood pressure (defined as systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg), as measured at the 12-months outpatient clinic visit.

Secondary outcomes of this study are:

1. The percentage of patients with controlled BP (defined as systolic BP <140 mmHg and diastolic BP <90 mmHg), as measured at the 3-month outpatient clinic visit
2. Patient satisfaction, as assessed by patient satisfaction questionnaire(17)
3. Healthcare utilization, defined as an outpatient clinic visit, emergency care visit or admission for any reason. This will be measured via questionnaires and verified by EMR data
4. Major Adverse Cardiac Events (MACE)
    a. Death of any cause
    b. Cardiac death
    c. Recurrent STEMI
    d. Recurrent NST-ACS
    e. Revascularization
    f. Hospitalization for heart failure
    g. TIA
    h. Ischaemic stroke
5. Propensity of medication adherence, measured by the Morisky MMAS-8 scale(20)
6. Physical activity, as measured by the iPAQ questionnaire(19)
7. Quality of life, measured by the SF-36 questionnaire(18)
8. Percentage of patients in which a previously unknown sustained arrhythmia (≥30 seconds) is detected
9. Cost-effectiveness, expressed as the incremental cost-effectiveness ratio

Economic analysis

To assess cost-effectiveness of the intervention, costs per quality adjusted life year (QALY) will be calculated. The analysis is performed from a societal perspective with a time horizon of one year. Patients receive a healthcare resource use questionnaire at 6-months and 12-months. In this questionnaire, a patient is asked to fill in his total healthcare utilization such as outpatient clinic visits, emergency visits and admissions for any reason and visits to the general practitioner. All outpatient clinic visits, emergency visits and admissions for any reason reported in the questionnaire are verified by EMR data. In the same questionnaire, the patient is asked to fill in total medication use. All health care and medication use are multiplied with standard cost prices to calculate costs.(21) To calculate indirect costs, patients are asked to note absence from paid work and unpaid work as well. Productivity costs are calculated using the friction cost method. Absence is again multiplied against standard cost prices.(21) QALYs are calculated from utility scores from the SF-36 questionnaire, which is administered at baseline, 1 month, 6 months and

12 months.(18, 22) Finally costs and QALYs in both groups are compared. It is our hypothesis that societal costs are lower in the intervention group.

Statistical analysis

A power calculation was done using R (R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.r-project.org). It is based on a comparison of two proportions of patients with controlled blood pressure (defined as a SBP of 139 mmHg or less and a DBP of 89 mmHg or less). We hypothesize that in the "The Box" group 95% of the patients achieves a controlled BP, while in the control group, 75% achieves a controlled BP.(23) For this calculation, an alpha of 0.05, a beta of 0.20 and a margin of 0.07 were chosen, yielding a sample size of 200 patients.

Data are analysed according to the intention-to-treat principle. Causes of missing data are tabulated (Supplement A). The percentage of missing data is expected to be low. Therefore, complete case analysis is done. Analysis is based on the missing-at-random assumption. If the percentage of missing values exceeds 7%, multiple imputation is applied in analysis of the data.

After finishing the study (defined as the last patient's last visit), the proportion of patients with controlled blood pressure will be compared with a Chi-Squared Test. Logistic regression might be done if serious imbalances of baseline variables exist to correct for potential confounding variables.

Percentages of patients with controlled BP at three months (secondary outcome 1) and percentages of patients in which a previously unknown sustained arrhythmia is detected will also be compared with a Chi-Squared Test.

Scores of questionnaires (patient satisfaction questionnaire, Morisky MMAS-8 scale, iPAQ questionnaire and SF-36 questionnaire) and healthcare utilization will be compared using an independent t-test. Major Adverse Cardiac Events (MACE) will only be reported. As the study is underpowered, no statistics will be done on MACE. The numbers will be hypothesis generating.

Discussion

In this paper, we presented the rationale and design of single-center, open, randomized-controlled trial. With this trial, we will evaluate the clinical effectiveness of a smart technology intervention in patients with STEMI and NST-ACS.

Clinical effectiveness

It is expected that with daily monitoring of ECG, blood pressure, weight and steps, data will allow for early detection of high blood pressure and the development of arrhythmias. For this study, percentage of patients with controlled BP at 12 months is chosen as primary outcome. Controlled blood pressure is associated with lower

risk of death, recurrent PCI and stroke in patients who suffered from ACS. Therefore, the European guidelines recommend tight BP control via medication and lifestyle advices.
Percentages of 1-year mortality after STEMI or NST-ACS vary, but have been reported to be under 10%.(24) With a sample size of 200, it is expected that this study is underpowered to detect a significant difference in mortality between the intervention group and control group. It is emphasized that it is not the primary objective of this study to demonstrate a difference in mortality. This study is intended to investigate if regular monitoring of clinical parameters including blood pressure can lead to better control of those parameters, therefore being more guideline compliant.

Patient compliance
All devices used in the intervention group are designed for the consumer market. Patients receive assistance with installation of the devices. After measurements, data is automatically transferred to the hospital. It is expected that this helps accurate and timely transmission, which might enhance patient compliance. To test this hypothesis, all reminders sent to patients for not having measured their data are monitored. “No-shows” at digital outpatient clinic visits as well as at the physical outpatient clinic visits are monitored as well. It is hypothesized that there is no significant difference in the percentage of “no-shows” between the digital outpatient clinic visits and the physical outpatient clinic visit.

Patient satisfaction
During the study, patient satisfaction is monitored via a validated questionnaire. (17) In this study, by design, patients in the intervention group monitor ECG, blood pressure and weight more intensively. This increased frequency of monitoring has potential clinical benefits, such as having early detection of high blood pressure or arrhythmias, as well as allowing patients to see and interpret their own data. This might enhance patient satisfaction of care. On the other hand, daily monitoring might pose a burden to the patient, both physically, as patients have to take time to perform the measurements, as well as mentally, as they might associate monitoring with their illness.

Healthcare utilization
A concern of smart technology interventions is the fear that patients, given their non-medical background and their perceived inability to interpreted medical data correctly, increase the number of contact points with hospitals, leading to more outpatient clinic visits and emergency department visits and therefore to a higher burden on both patients and healthcare staff, without improvement of clinical

outcomes. Scientific evidence describing the relation between increased monitoring frequency and healthcare utilization is however scarce. Patients participating in this study receive clear instructions about the usage of the devices, as well as the reasons for the hospital to contact the patients. It is therefore expected that healthcare utilization is not higher in the intervention group.

Generalizability

Patients with a STEMI or NST-ACS who match the in-, and exclusion criteria are eligible for participation. Patients who do not own a smartphone are not excluded from the RCT, but patients who do not have internet access at home are excluded. This might affect generalizability. However, as 97% of the Dutch population has internet access,(25) it is expected that this exclusion criterion affects generalizability only slightly. The fact that a smartphone is used for remote monitoring might affect generalizability as well. Previous literature has indicated that smartphone literacy decreases with age. Furthermore, patients who do own a smartphone might refuse as well, for various reasons.(26) Thirdly, it is known that patients who participate in RCTs have different demographics than patients who do not.(27) It is therefore expected that generalizability is affected. However, it is emphasized that this might be partly due to the involvement of smartphone technology and partly inherent to the RCT study design in general. As patients are given a smartphone in case they do not own one and technical support is provided, generalizability issues are kept to a minimum.

Conclusion

In summary, the rationale and design of a randomized controlled trial is presented that investigates whether a smart technology intervention can increase clinical effectiveness and patient satisfaction in the follow-up of STEMI or NST-ACS patients.

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