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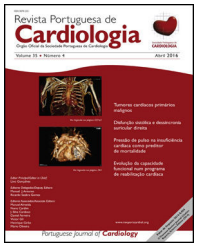

EDITORIAL COMMENT

Remote monitoring of heart failure patients: A complex proximity

Monitorização remota na insuficiência cardíaca: uma proximidade complexa

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Digital technologies are increasingly revolutionizing health care, acting as efficient tools that can contribute to improving access and quality of care, including prevention, diagnosis, treatment, monitoring and management.

Telemonitoring (TM) or remote monitoring refers to the use of telecommunication technologies to monitor the patient's status at a distance. Chronic heart failure (HF) appears to be an ideal condition to potentially benefit from this new concept of care in addition to the traditional HF outpatient care provided by direct ''doctor-patient'' physical contact. Heart failure is highly prevalent among the elderly and is associated with significant mortality and morbidity with recurrent hospitalizations due to episodes of HF decompensation, many of which are potentially preventable.[1] Heart failure-related hospitalizations imply poor quality of life and higher mortality, and are the main factor behind the enormous economic impact of HF on health budgets.[2,3]

The early identification of HF deterioration before the need for urgent hospital admission has been a major focus of interest, and over recent decades, several approaches to TM have been used in an attempt to improve outcomes.[4]

Home TM can involve non-invasive or invasive measuring devices that capture and transfer physiological and disease-related data from the patient to healthcare providers, enabling detection of clinical deterioration and early clinical intervention. Invasive TM uses implantable cardiovascular electronic devices inserted in the patient's body (e.g., cardiac resynchronization therapy devices, cardioverter defibrillators or implantable hemodynamic monitoring) to capture and transmit information about the onset of pulmonary congestion and arrhythmias.

Non-invasive home TM involves periodic self-measurement (usually daily) by the patient of various biodata according to a defined measurement plan (vital signs, weight, electrocardiogram), which are transmitted remotely to health care providers for review.

To be effective, the review of the transferred data must be carried out on the same day, requiring a telemedicine service 24 hours a day, 7 days a week. In case of exceeding the patient's specific cut-off limits, alerts are generated and the medical team intervenes, deciding upon the appropriate management. Usually, non-invasive TM also implies periodic contact between doctor/nurse and the patient, aimed at monitoring symptoms, treatment adherence and providing education to the patients on their HF condition, as well as providing training support on self-management of HF. However, although non-invasive home TM is a very attractive tool and a promising strategy for early clinical intervention and better clinical results, different programs and strategies have led to variable results in clinical tri-

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als. Therefore, its role in the management of patients with HF is still controversial[4] and international guidelines do not recommend the routine use of TM.[5,6]

However, several meta-analyses point to clinical benefits.[7,8] Remote TM with medical support proves to be more effective when compared with conventional healthcare in reducing all-cause hospitalization, HF hospitalization, all-cause mortality, cardiac mortality, and length of stay.[8] The randomized multicentre Telemedical Interventional Management in Heart Failure II (TIM-HF2) trial, included 1571 patients with HF and a HF hospitalisation in the previous 12 months.[9] Patients in the interventional group had a significantly lower percentage of days lost due to unplanned cardiovascular hospitalisation or death of any cause and significantly lower all-cause mortality. However, cardiovascular (CV) mortality was not decreased.[9]

In 2019, a clinical update from the Heart Failure Association of the European Society of Cardiology (ESC) proposed a home telemonitoring model using an approach similar to the one used in TIM-HF2 as part of the medical care for HF patients, to reduce the risk of recurrent CV, HF hospitalizations and CV death.[10] It should be noted, however, that in TIM-HF2, one year after the end of the intervention, the positive effect on mortality and morbidity was no longer observed in a real-world conditions.[11]

In a remote controlled TM environment, different HF populations may eventually show similar beneficial results, although patient fidelity to the program can be a difficult variable to achieve. However, in the context of the real world, this essential factor becomes unmanageable.

Regarding implantable devices for remote patient monitoring, in selected patients the CardioMEMS implantable pulmonary artery pressure (PAP) sensor proved to be effective in significantly reducing the rate of HF hospitalisations, decreasing PAP and improving quality of life in the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes (CHAMPION) trial.[12] The results on the reduction in HF hospitalisation for the intervention group extended during the continuous open-access period with overall 31 months of mean follow-up,[13] and this was recently confirmed in the context of different health systems,[14] as well in a real world setting.[15] In ESC guidelines, the CARDIOMEMS approach was given a Class IIb (level B) indication for symptomatic HF patients with previous HF hospitalization in order to reduce the risk of recurrent HF hospitalizations.[5]

Telemonitoring of a single surrogate parameter of congestion (as intrathoracic impedance) by cardiovascular implantable electronic devices, for early prediction of HF decompensation, was not proven to be beneficial in several trials.[16] But multiparameter TM, integrating pacing parameters with symptoms and signs of HF and structured telephone support was successfully tested in the IN-TIME trial. This showed improved outcomes for HF patients, so much so that this approach was included in the most recent ESC HF guidelines, also with a Class IIb (level B), recommendation.[5]

The fast development of new technologies creates an enormous potential for the increased use of TM for HF patients[4] as a personalized application.

The HeartLogic (Boston Scientific) for CRT-D devices, uses multiple sensors to track physiological trends, combines them into one composite index (consisting of sensing heart sounds, thoracic impedance, respiration rate and its ratio to tidal volume, heart rate and patient activity) and sends a proactive alert of potential worsening HF. This model was tested in the Multisensor Chronic Evaluation in Ambulatory Heart Failure Patients (MultiSENSE) study[17] showing a high sensitivity for detection of HF events, while the median time from alert onset to event occurrence was 34 days, indicating the potential for a very early warning of worsening HF. Further observational studies with this diagnostic tool are ongoing.

Preliminary results of wearables, which incorporate various sensors contributing to an HF alert system, have already shown promising results in the early detection of impending HF rehospitalisation.[18]

The Nanowear Heart Failure Management Multi-sensor Algorithm (NanoSense, NCT03719079) is an ongoing data collection study to develop a multi-sensor algorithm to predict worsening HF. The study device is the SimpleSENSE, a multi-parameter remote diagnostic gender-neutral and size-adjustable undergarment that simultaneously and synchronously monitors and captures more than 100 million data points per patient per day across cardiac, pulmonary, and circulatory biomarkers, including heart rate variability, respiratory rate, impedance cardiography, transthoracic impedance, and sound phonography ('S3' murmur detection). These metrics are continuously transmitted to the Nanowear's platform, where a unique algorithm scores them and alerts physicians to a patient's worsening HF condition. The subjects will be asked to wear the device for approximately 12 hours daily including two hours prior to sleep and two hours after awakening. The NanoSense study will enrol up to 500 subjects to collect data, which includes at least 150 HF hospitalizations. The follow-up period will be 90 days, and the duration of the study is expected to be 2 years.

On the subject of wearable sensors, Martins et al., present, in this issue of the Journal, the design of a new system: MONITORIA (MOnitoring NonInvasively To Overcome mortality Rates of heart Insufficiency on Ambulatory).[19]

MONITORIA is a non-invasive remote multimodal device for home-monitoring of HF patients, which is being developed to capture continuously several vital and electrophysiological variables (heart rate, and heart rate variability, T wave variability, electric conduction abnormalities, atrial and ventricular arrhythmias, respiratory rate and peripheral oxygen saturation), hemodynamic signs (systemic arterial blood pressure, right and left atrial pressures, transthoracic bioimpedance), chemical signs (skin sodium content), and physical activity levels.

Sensors are incorporated into a thoracic vest designed to be comfortable for both genders and body shapes and that must be used 24 hours a day (except for a period of 30 minutes). Measurements are taken continuously, and then transmitted in a raw format to a server on a daily basis. The main objective is to detect promptly early signs of decompensation, act on them and stabilize patients at home, avoiding hospitalizations. Also, in cases of a medical emergency (effective or impending cardiac arrest or suspicion of a myocardial infarction), MONITORIA is designed to have a cardioverter-defibrillator function that can be activated before the arrival of the emergency team.

Transthoracic impedance will be captured using six standard electrocardiogram (ECG) electrodes, and an algorithm will calculate net instantaneous lung impedance and lung fluid status. Impedance will be measured during the nocturnal period, every 30 min, from midnight until 6 am, ensuring that the patient is at supine position, and is not involved in any physical activity. According to the authors, this strict scheme is necessary for a more accurate measurement of lung bioimpedance during the validation phase of the device, but it can also be an obvious limitation for the patient. These impedance electrodes will also enable the assessment of impedance cardiography for blood pressure (BP) determination, as well as cardiac output and the pre-ejection period (by simultaneous recording of the ECG). These parameters can potentially assist the safe and accurate prescription and monitoring of therapies for patients with HF.

Ten additional ECG electrodes (one neutral) will acquire ECG data and monitor not only heart rate and heart rate variability, but also T wave heterogeneity/variability conduction abnormalities, and the occurrence of ECG signs of myocardial ischemia.

Sensors measurements for right atrial and left atrial pressure will be captured every 30 minutes during the night, from midnight to 6 am, and it must be ensured that the patient is supine and makes minimal body movement.

Blood pressure will be measured by integrating data from a photoplethysmography (PPG) sensor system, ECG and bioimpedance data. The algorithm will also be able to integrate data from an accelerometer, not only to identify the most favorable moments for the pulse transit time measurement (a parameter needed to calculate BP), but also to eliminate noise, breathing movements and other artefacts associated with the raw data captured by the ECG, bioimpedance and PPG sensors. An oxygen saturation sensor system, also imbedded into the thoracic vest, will capture the peripheral oxygen saturation.

Skin sodium content measurements will be made using a microfluidic patch (with chemical transducers inside) that absorbs sweat on the surface of the skin. In the validation study, measurements should be taken in a predefined fasting period and two hours after each main meal; a pilot study including normal individuals (as controls) and HF patients will be carried out to determine sodium excretion values through the skin (with control of sodium intake and HF medication).

Activity sensors (a three-axis gyroscope and accelerometer) will allow measurement of body movements, providing the frequency and duration of the patient's physical activity and identifying optimal periods for the other measurements described above.

A software application on the patient's smartphone integrates measurements captured from the wearable device (which is battery driven, changeable every 24h) via Bluetooth, and forwards them to a server solution cloud (integrated in an encrypted and secure network), via the cellular network. Data are stored locally when there is no Bluetooth connection to the patient's mobile application, thus allowing patients to leave the phone behind when going out of the house, without data being lost. When the Bluetooth connection is restored, data is then transferred to the smartphone application, and from there, to the server. A specific application will allow health professionals to integrate remote monitoring into their workflow.

MONITORIA is also prepared to generate alarms for the attending physician via a text message in specific situations, leading to immediate contact and to appropriate action. In addition, in emergency situations, the system will also send an alert to the national emergency medical service. As stated by the authors, in the future, MONITORIA will be able to deliver shocks or functioning as a pacemaker to treat specific arrhythmias, an issue that poses particular problems which the authors commented upon and plan to overcome.

The authors who designed MONITORIA are to be congratulated. However, the next step will be validation. The validation must guarantee, firstly, the effectiveness related to the remote capture and accuracy of the collected data and, secondly, the feasibility of applying the device in clinical practice. In addition, a fundamental issue after ensuring viability will be to define users, patients with HF for whom the device may indeed be clinically relevant. TM interventions need to be designed and adapted according to the characteristics of the target patient population and the implementation context.[20] Even using the best methodology, detecting significant clinical benefits for remote patient monitoring remains complex. In addition, ultimately, the central issue will be how to integrate the data into the existing care systems, improving outcomes and demonstrating that it is cost-effective.

Conflicts of interest

The author has no conflicts of interest to declare.

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