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Heart failure and telemedicine: where are we and where are we going? Opportunities and critical issues

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Heart failure (HF) is one of the main causes of morbidity in the world and is responsible for an enormous amount of health costs, mostly due to hospitalizations. The remote control techniques of vital signs and health status have the potential to help prevent factors leading to HF instability by stimulating early therapeutic interventions. The goal of telemedicine is to change the intervention strategy from a 'reactive' type, in which therapy is optimized in response to the worsening of symptoms, to a 'pro-active' type, in which therapeutic changes are undertaken based on changes in the monitored parameters during the sub-clinical phase. This article is aimed at exploring the major results obtained by telemedicine application in HF patients with and without cardiac electronic devices or in those with haemodynamic sensors and to analyse the critical issues and the opportunities of its use.

Introduction

The ageing of the population, the increase in survival from acute diseases, with consequent chronicization of illness and morbidity increase, and recently, the COVID-19 pandemic, have lead to an implementation of telemedicine, that is the development and use of new technologies suitable for the exchange of information for the diagnosis and treatment of disease.[1]

Heart failure (HF) is one of the main causes of morbidity in the world and is responsible for an enormous amount of health costs, mostly due to hospitalization caused by reacutizations. Indeed, HF is currently the first cause of hospital admissions among the older population and accounts for 1–3% of total healthcare economic burden in developed countries.

HF natural course is characterized by periods of clinical stability interrupted by episodes of acute decompensation, that, in turn, are associated with disease progression, increased mortality, and hospital admission. Notably, many HF patients' stages of instability could be avoided if their follow-up was improved both in the vulnerable post-hospital discharge phase and in the medium and long-term phases.

The remote control techniques of vital signs and health status have the potential to help prevent many factors favouring an HF instability (reduced coronary perfusion, uncontrolled hypertension, bradi-tachyarrhythmias, poor compliance with drug therapy) by stimulating early therapeutic interventions and/or appropriate behavioural changes. The goal of telemedicine is to change the intervention strategy from a 'reactive' type in which therapy is optimized in response to the worsening of symptoms, to a 'pro-active' type, in which therapeutic changes are undertaken based on changes in the monitored parameters during the sub-clinical phase, when the patient is still asymptomatic. This article is aimed at exploring the

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major results obtained by telemedicine application in HF patients with and without cardiac electronic devices (CIEDs) or in those with haemodynamic sensors, and to analyse the critical issues and the opportunities of its use.

Telemedicine in heart failure subjects without cardiac electronic devices

Various have been the applications of telemedicine for the management of HF subjects,[2] including:

(1) teleconsultation,
(2) telemonitoring of vital parameters including weight, blood pressure, heart rate (HR), and bioimpedance,
(3) telerehabilitation, both using digital technology (smartphone applications, smart-watches, etc.) and teleconsultations to deliver cardiac rehabilitation from a distance.

Telemonitoring of vital parameters, in turn, has been performed through:

- telephone-based symptoms and sign monitoring,
- videomonitoring of physiological parameters and HF signs,
- mobile-phone monitoring of physiological parameters,
- personal digital assistant devices,
- Home telehealth.

Telemedicine has also been used for the transmissions of information from the healthcare providers to patients, thus allowing their improvement of education, empowerment, self-control of the disease, and adherence to therapy.

Several studies have explored the application of telemedicine for HF management, and many of them have failed to prove its benefit over the standard of care in terms of reduction of HF hospitalizations and cardiovascular mortality.[2] In particular, Chaudhry SI et al.[3] reported data from the largest American experience on the use of telemedicine in 1653 patients discharged after hospitalization for acute HF (mean age: 61 years; 60% in New York Heart Association (NYHA) III–IV class, 70% with a reduced left ventricular (LV) ejection fraction). Patients were enrolled within 30 days of discharge for acute HF end were randomized to be followed in the 'standard of care' arm or in the telemonitoring arm. The latter had to make a free phone call each day and answer guided questions. At the end of the 6-month follow-up (FU), no significant difference between groups was observed both in terms of mortality and hospitalization. A critical aspect of this study that may have certainly influenced the disappointing results is the low adherence of patients to the programme (14% of them did not make any phone calls and only 55% of them were still transmitting data at the end of the 6-month FU). However, many other studies observed benefits from telemonitoring programmes in terms of a reduction in HF-related hospitalizations. An overview of 19 systematic reviews on this topic[2] concluded indeed that telemonitoring and home telehealth appear generally effective in reducing HF rehospitalizations and mortality. A systematic review[4] including 39 trials mostly investigating remote HF management through assessments of symptoms, blood pressure, weight, HR, and heart rhythm, observed a reduction in all-cause mortality of 20% and of HF-related hospitalizations of 37%. Finally, a recent meta-analysis[5] of 16 randomized controlled trials, including 8679 HF patients randomized to remote monitoring (RM) management vs. standard of care, showed no differences in terms of HF-related hospitalizations and cardiovascular mortality between the two groups. However, patients in whom drug treatments were guided by remote management experienced a reduction in all-cause mortality. Subgroup analysis showed that both haemodynamic and arrhythmia telemonitoring-guided management reduced the risk of HF hospitalization too.

Critical issues: *Figure 1* depicts the opportunities and critical points of telemedicine application to HF management. One of the major critical issues is represented by the low adherence of patients to the programmes. This could be improved by enhancing the patients and caregivers education and by involving the general practitioners in the telemonitoring process. This is particularly important when the transmissions of the data for the RM depend on the patient's will, such us in the case of subjects without CIEDs.

Moreover, it is not obvious that a telemedicine centre is efficiently organized, equipped of HF-trained and experienced staff (who knows the characteristics of their patients' disease, their comorbidities, and social welfare problems), and of pre-defined decisional flow-charts for the management of HF patients. Finally, the cost-effectiveness and economic sustainability of telemedicine in HF management of patients without CIEDs is still uncertain.

Opportunities

The opportunities of remote monitoring of HF patients without CIEDs relate to the possibility of continuous monitoring of physiological and clinical parameters of old patients, with physical impairment, often living in remote geographical areas. This seems helpful for an early detection and managing of HF worsening episodes, which in turn leads to an improvement in patients' quality of life and to a potential reduction of HF-related hospitalizations and of cardiovascular mortality. Based on these evidence, the 2021 European Society of Cardiology (ESC) Guidelines for the management of HF[6] suggest that non-invasive telemonitoring may be considered for HF patients in order to reduce the risk of recurrent cardiovascular hospitalizations and death with an IIB class of evidence.

Telemedicine in heart failure patients with haemodynamic sensors

Recently, advanced technologies based on the direct measurement of intracardiac and vascular pressures have been introduced. In the Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure (COMPASS-HF) study,[7] 274 patients in NYHA functional class III–IV, with systolic or diastolic LV dysfunction, with recent hospitalization for HF, in optimized drug therapy, were randomized to underwent implantation of a continuous monitoring device for right ventricular pressure and pulmonary arterial pressure (Chronicle, Medtronic Inc., Minneapolis, MN) or to the standard of care. The device proved to be safe, without implant-related complications: However, no significant

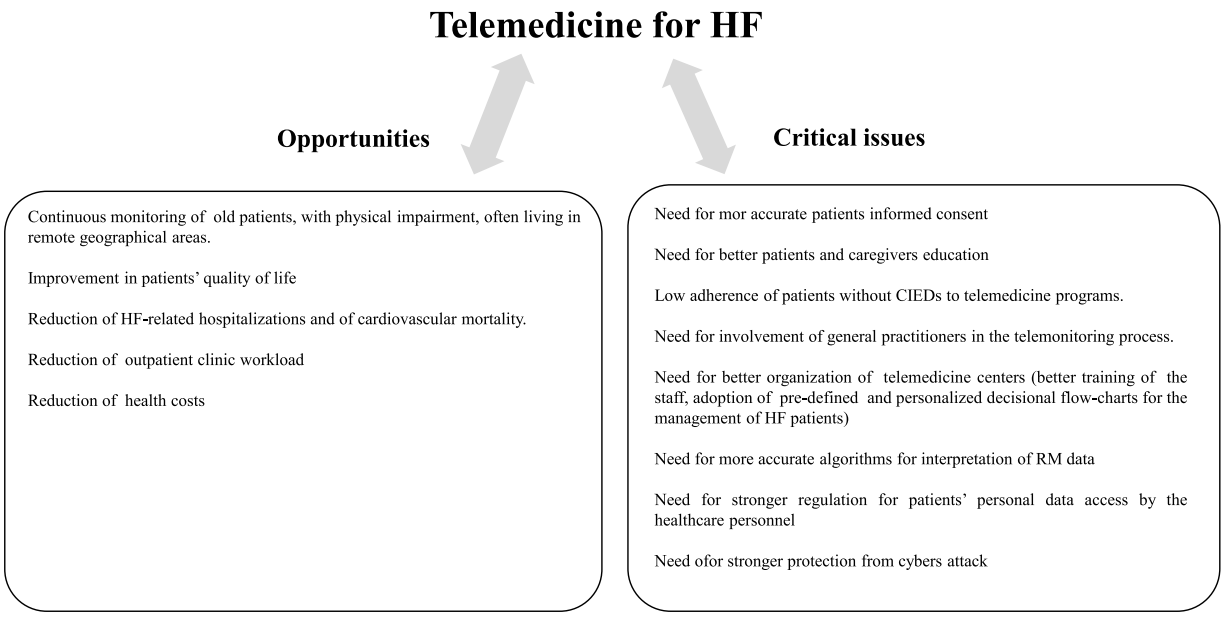

Figure 1 Opportunities and critical issues for telemedicine for HF management. CIEDs, cardiac implanted electronic devices; HF, heart failure; RM, remote monitoring.

difference in HF-related events was observed between groups.

In the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) study, 550 NYHA Class III HF patients were randomized to be followed with RM of pulmonary arterial pressure data measured by an implantable wireless haemodynamic monitor vs. standard of care.[8] The treatment group experienced a 39% reduction in HF-related hospitalizations compared with the control group at 15 months (HR 0·64, 95% CI 0·55–0·75; $P < 0·0001$). Conversely, when the CardioMEMS HF system (Abbott) was adopted to remotely guide pharmacological treatment in HF patients with all ejection fractions (EF), NYHA class II-IV and either a recent HF hospitalization or elevated natriuretic peptides, it showed no benefit in comparison to standard of care.[9]

Critical issues and opportunities

Based on the evidence available today, it is not possible to give unambiguous answers on the reliability, safety, effectiveness, economic sustainability of these devices and on the management changes that could result from their use. The 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic HF suggest that monitoring of pulmonary artery pressure using a wireless haemodynamic monitoring system may be considered in symptomatic patients with HF in order to improve clinical outcomes.[6]

Telemedicine in heart failure patients with cardiac electronic implantable devices

Modern CIEDs, including pacemakers, defibrillators (ICDs), devices for cardiac resynchronization (CRT), loop recorders are able to store an increasing amount of diagnostic information relating to the operations of the device, the incidence of arrhythmias, physiological aspects of the patients' condition and indicators of cardiovascular function. In most patients with CIEDs, outpatient checks are usually performed every 3–12 months depending on the organization of the centre, the complexity of the patient, and the type of device. All the major manufacturers of implantable devices have introduced over the past years, RM systems based on a 'patient unit' capable of interrogating the device and downloading the programmed parameters and diagnostic data. The information is transmitted to a centralized database where the data is decrypted and entered on a secure web portal which can only be accessed by members of the clinical staff who are treating the patient. The currently available systems are based on automatic transmissions that are completely independent from the doctor and the patient, and on transmissions generated by the patient in case of symptoms.

Various RM systems are available, with many common characteristics and substantial differences between them in terms of connectivity, patient involvement, timing of programmed transmissions, and type and programmability of alarms.

Diagnostic parameters

Available diagnostics of CIEDs include measurement of mean, day and night HR, HR variability, patient daily activity, percentage of right ventricular pacing (single and dual chamber devices), percent of biventricular pacing (biventricular devices), thoracic impedance, heart sounds, as well as electronic parameters related to catheter and battery status.

In particular, the average HR over 24 h gives important information for optimizing drug treatment, and, in association with nocturnal HR, HR variability, and data from sensors (activity or accelerometric), provide indirect

information on the patient's activity level and haemodynamic status. The percent of ventricular pacing data can be used to guide device programming and therapy optimization, in order both to limit right ventricular apical pacing with its potential negative consequences on ventricular function and to improve the biventricular pacing rate, when reduced. Remote monitoring of CIEDs is also helpful for an early recognition and treatment of atrial fibrillation (AF) with its related complications (including HF relapses, ischaemic stroke, and inappropriate shocks) and of ventricular arrhythmias, allowing an early optimization of the pharmacological treatment. The intrathoracic impedance detected by the defibrillation electrode is inversely correlated with the capillary wedge pressure and lung water content. A progressive reduction in intrathoracic impedance may predict and precede the onset of clinical signs of HF decompensation. However, algorithms based on the thoracic impedance alone, lack in specificity due to the possibility of false positive related to pulmonary infections or pleural effusions.

Recently, the variation in the heart sounds has been implemented in the diagnostics of some CIEDs. Indeed, in case of impending HF, the third sound (S3) intensity increases due to elevated filling pressures; conversely the first sound (S1) intensity reduces as a marker of left ventricular (LV) contractility impairment, thus resulting in an increased S3/S1 ratio.[10]

Multi-parametric assessment

An improvement in the ability to predict the risk of HF events has resulted from a multi-parametric approach. The PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) study,[11] demonstrated that a multi-parametric score including patient activity, HR, AF burden, intrathoracic impedance variation, percentage of CRT pacing and high ventricular rate proved to be useful in identifying patients at 5.5 higher risk of HF decompensation within the subsequent month. The Multisensor Chronic Evaluation in Ambulatory Heart Failure Patients (MultiSENSE) study,[12] tested a novel index, the HeartLogic ™ (Boston Scientific, St. Paul, Minnesota), combining data from multiple ICD and CRT-D-based sensors including accelerometer-based S1, S3, intrathoracic impedance, respiration rate, the ratio of respiration rate to tidal volume, night HR and patient activity. When used in clinical practice, this index was proved accurate in the identification of subjects at risk of impending HF and effective to prevent events when clinical actions were remotely undertaken in response to its alert.[13]

Recently, a further algorithm[14] combining temporal trend of diurnal and nocturnal HR ventricular extrasystoles, atrial tachyarrhythmia burden, HR variability, physical activity, and thoracic impedance combined with the baseline Seattle HF Model, proved effective in identifying about two-thirds of the first post-implant HF hospitalizations.

Frequency of transmissions

Two main approaches for remote monitoring of subjects with CRTD or AICD are currently in use: systems based on periodic remote FU plus automatic alerts or on continuous monitoring with daily reporting of diagnostic data plus automatic alerts. Previous studies comparing the remote systems, have shown that the high frequency of remote transmissions is not related to a parallel increase of workload for caregivers[15] and that daily transmissions are independently associated with an increased probability of event detection as compared to periodic transmission systems.[16]

Critical issue

A critical issue is represented by the correct understanding of RM management by the patients. Patients' accurate education and collection of the informed consent to RM is crucial. They need to know clearly what to expect from RM, and in particular that it is not meant as an emergency response system. They need to correctly understand how to interface with RM equipment and how to maintain the function of the transceiver and appropriate landline/cellular communication. A further critical issue is represented by the lack of organization of many telemedicine centres. Indeed, although 'smart' technologies able to collect data into sensitive and specific algorithms for the diagnosis of HF relapses is fundamental, a correct and prompt interpretation of information received by RM is also essential, as well as a defined protocol to manage it and to generate appropriate clinical actions. The need of a regulation for data protection, especially in light of the European Union General Data Protection Regulation (GDPR) represents a further critical point. The health employee access to patients' personal data should be regulated and internally controlled. Moreover, the access to patients' personal data stored on servers should be controlled, and remote monitoring system should be protected from unwillingly data disclosing (cyber-attack). Finally, telemedicine services are not reimbursed in many countries, with a consequent lack of resources.

Opportunities

The implementation of RM in the management and care of HF subjects has the potential to reduce outpatient clinic workload and HF hospitalizations and to improve patients quality of life. When a telemedicine centre is well organized and is able to correctly interpret data from RM and to manage alarms (following pre-defined flow-chats), RM seems able to influence patients' outcome too. The 'Influence of Home Monitoring on the Clinical Status of Heart failure patients' (IN-TIME) randomized controlled study[17] demonstrated a significant reduction in mortality among HF patients implanted with ICD or CRT-D followed by daily, multi-parametric telemonitoring as compared with usual care alone. In this study, investigators assumed a proactive behaviour, reacting to significant device-detected observation scheduling an in-person visit or suggesting a patient to be visited by the family doctor.

Remote monitoring of CIEDs has also demonstrated to reduce health costs.[18] A mata-analysis of 11 randomized controlled trials on CIEDs telemonitoring, showed a benefit in terms of reduction of planned hospital visits and monetary costs, despite a modest increase in unplanned hospital and emergency room visits.[19] Based on these evidence, consensus of experts and international guidelines for the management of HF suggest to offer RM of CIEDs to HF patients as part of the standard follow-up.[6,20]

Conclusions

Telemedicine facilitates the control of vital parameters, allows optimization of treatments, improves therapeutic compliance, contributes to the early recognition of HF relapses, helps overcoming logistical-territorial barriers of often elderly patients, enhances the active collaboration between various professional figures making up the multidisciplinary team responsible for home care of HF patients.

Key points for future interventions aiming at developing and implementing the new remote surveillance models could include:

(1) To refine the choice of the ideal patient and the type of telemonitoring programme, by taking into account patients' age, HF severity, comorbidities, patients' self-sufficiency, cognitive responsiveness, and family background.
(2) To personalize remote HF management by educating the patients/caregivers and by creating a pharmacological plan and follow-up monitoring programme.
(3) To refine artificial intelligence-base algorithms that can accurately predict HF relapses
(4) To create a closer collaboration between telemedicine centres, hospitals, specialists, and general practitioners

However, telemedicine alone is not and will not be able to solve the complex clinical and care problems of the HF patient, but is a useful tool to be included in the disease management of HF patients to support the clinic and the patient's socio-health project.

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Data availability

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