Conflicting past and present of home telemonitoring in Heart Failure: What about the future? //
Widersprüche in Vergangenheit und Gegenwart des Heim-Telemonitorings: Was bringt die Zukunft?

Gonçalves AV, Pereira-da-Silva T
Soares RM, Ferreira RC

ACHTEN SIE AUF DIESE HINWEISE:

**Hypertrophie des linken Ventrikels**

beim Patienten, die typischerweise über 60 Jahre alt sind²

**DIAGNOSE:**

eines Karpaltunnelsyndroms oder einer Lumbalstenose¹³

**ECHOKARDIOGRAPHIE:**

Hypertrophie des linken Ventrikels²

**NERVENSYSTEM:**

Dysfunktion des autonomen Nervensystems einschließlich von gastrointestinalen Beschwerden und unerklärbarem Gewichtsverlust²

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¹ Heart failure with preserved ejection fraction


Conflicting past and present of home telemonitoring in Heart Failure: What about the future?

A.V. Gonçalves, T. Pereira-da-Silva, R. M. Soares, R. C. Ferreira

Introduction

Heart failure (HF) remains the most common cause for hospitalization for people > 65 ys [1]. Projections in the USA show that the prevalence of HF will rise by 46% from 2012 to 2030 [2]. In 2012, the total costs for HF care in the USA was estimated to $30.7 billions. Projections show that by 2030, the total cost of HF care will grow by almost 127% [2]. Furthermore, 25% of those who are hospitalized with HF are readmitted within 30 days [3]. These hospitalizations are a marker of the progression of left ventricular dysfunction and account for up to 70% of the total costs of HF [4].

Clearly, there is a need to predict such episodes and intervene early enough to avoid hospitalization. In 90% of HF hospitalizations, patients present signs and symptoms of pulmonary and systemic congestion [5]. Our standard care for an ambulatory HF patient involves office-based follow-up at least two times a year, supplemented by exams and laboratory tests as needed. Regardless of patients being instructed to monitor their weight and symptoms, signs of volume overload have poor sensitivity for detecting incipient exacerbations, and clinical decompensation starts before these signs and symptoms appear, making hospitalization usually inevitable at this point.

Many strategies have been tested to predict episodes of decompensation as early as possible. Thanks to advances in information communication technology, telemonitoring allowed for physiological data to be transmitted to care providers, with close monitoring of the patient’s clinical status and ensuring detection of HF deterioration earlier, thus preventing HF hospitalization and progression of the disease. Despite all these promises, large randomized controlled trials of varying protocols have reached disparate conclusions regarding the efficacy of disease management.

In this article, the state-of-the-art of telemonitoring is described. It includes an overview of the various strategies tested in order to detect deterioration of HF, trying to understand what is still missing for a better HF management.

Although other reviews have been published on this subject, several of them focussed only on non-invasive telemonitoring or on invasive monitoring devices. This paper provides a global perspective, discussing non-invasive telemonitoring, implantable devices not specifically designed for HF monitoring and implantable devices designed for that purpose. More importantly, relevant results from recent studies have been presented following the publication of other reviews, providing this paper a more contemporary review.

Structured telephone monitoring

A single phone call monitoring strategy can give information about the patients’ symptoms, vital signs, and weight, theoretically reducing the need for office-based visits. If this strategy can improve the outcome of HF patients, is the subject of various published trials.

In the TEN-HMS study, patients with a recent admission for HF and left ventricular ejection fraction (LVEF) < 40% were randomly assigned to home telemonitoring, nurse telephone support and usual care [6]. Home telemonitoring consisted of twice-daily patient self-measurement of weight, blood pressure, heart rate, and rhythm with automatic devices linked to a cardiology centre. The nurse telephone support consisted of specialist nurses who were available to patients by telephone.

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Viele Strategien wurden untersucht, um kardiale Dekompensationen so früh wie möglich zu erkennen. Dank Fortschritten in der Informationstechnologie ermöglicht das Telemonitoring die Übermittlung physiologischer Daten an die Gesundheitsdienstleister. Der klinische Status des Patienten wird genau überwacht und eine frühzeitige Erkennung der HI-Verschlechterung objektiviert. Somit wären Spitalsbehandlungen und Dekompensationen zu verhindern. Trotz allen diesen Prämissewissen haben große randomisierte, kontrollierte Studien mit verschiedenen Protokollen zu unterschiedlichen Schlussfolgerungen hinsichtlich der Wirksamkeit des Krankheitsmanagements geführt.


Schlüsselwörter: Herzinsuffizienz, Heim-Telemonitoring, implantierbare Geräte, implantierbare hämodynamische Sensoren

Abstract: Heart failure (HF) remains the most common cause for hospitalization of people over 65 years of age, with a projection of increased prevalence for the next years. These hospitalizations are a marker of the progression of the disease and account for up to 70% of the total cost of HF.

Many strategies have been tested to predict episodes of decompensation as early as possible. Thanks to advances in information communication technology, telemonitoring allowed for physiological data to be transmitted to care providers, with close monitoring of the patient’s clinical status and ensuring detection of HF deterioration earlier, thus preventing HF hospitalization and progression of the disease. Despite all these promises, large randomized controlled trials of varying protocols have reached disparate conclusions regarding the efficacy of disease management.

This paper reviews what is known about telemonitoring, summarizing the strategies already tried to improve the outcomes of heart failure patients. With these studies in mind, it makes a predictable set of propositions for the changes needed to improve the outcomes of this common disease. J Kardiol 2019; 26 (3–4): 62–7.

Key words: heart failure, home telemonitoring, implantable devices, implantable hemodynamic sensors

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From the Department of Cardiology, Hospital de Santa Marta, Centro Hospitalar de Lisboa Central, Lisbon, Portugal.
Correspondence: António Valentim Gonçalves, MD, Department of Cardiology, Hospital de Santa Marta, Rua de Santa Marta, nº 50, 1169-024, Lisbon, Portugal; e-mail: antonio.a.goncalves.14@gmail.com
The rates of hospital admissions and mortality were similar among patients randomly assigned to nurse telephone support or home telemonitoring, but patients assigned to usual care had higher one-year mortality than patients assigned to receive nurse telephone support or home telemonitoring (45% vs 27% and 29% – p = 0.032).

In the DIAL study, 1518 outpatients in Argentina with stable chronic HF and optimal drug treatment were randomised to telephone intervention with education, counselling, and monitoring by nurses or usual care [7]. The 758 patients in the usual care group were more likely to be admitted for worsening HF or to die than the 760 patients who received the telephone intervention. This benefit was mostly driven by a significant reduction in admissions for HF. Mortality was similar in both groups.

After that, the COACH trial was performed, which was a multicenter, randomized, controlled trial in which 1023 patients were enrolled after hospitalization due to HF [8]. Patients were assigned to one of three groups: a control group (follow-up by a cardiologist) and two intervention groups with additional basic or intensive telephone support by a nurse specialized in management of patients with HF. The combined endpoint of HF-hospitalization and death from any cause was not reduced. All-cause mortality occurred in 29% of patients in the control group, and there was a trend towards lower mortality in the combined intervention groups (hazard ratio, 0.85; 95% confidence interval [CI]: 0.66–1.08; p = 0.18). There were slightly more hospitalizations in the two intervention groups.

Regarding the cost-benefit, a targeted telephone care-management program was successful in reducing medical costs and hospitalizations in a randomized study of 174,120 patients [9].

Overall, the results of different studies addressing a structured telephone monitoring intervention were conflicting. Some of these enrolled a small number of patients or analysed a short follow-up period. A recent meta-analysis with structured telephone support demonstrated a 13% reduction in the risk of all-cause mortality (RR 0.87, 95% CI: 0.77–0.97; participants 9222; studies 22), and a 15% reduction in heart failure related hospitalisations (RR 0.85, 95% CI: 0.77–0.93; participants 7030; studies 16) [10]. Most studies which examined health-related quality of life reported significant improvements.

● Remote monitoring/Telemonitoring

With advances in communication technology, telemonitoring is a particular form of chronic disease management in which patients receive equipment to obtain physiologic data at home. Thereafter, this data is remotely transmitted to care providers on a daily or intermittent basis, allowing close monitoring of the patient's clinical status and promising to detect HF deterioration earlier, allowing for more prompt and effective intervention.

One of the first pieces of evidence regarding the benefits of telemonitoring was shown by the TEN-HMS study. As described before, patients assigned to receive usual care had higher one-year mortality than patients assigned to receive nurse telephone support or home telemonitoring [6].

More trials were necessary to confirm the improving outcome of remote monitoring in patients with HF. The BEAT-HF study evaluated the effectiveness of a care transition intervention using remote patient monitoring in reducing 180-day all-cause readmissions among 1437 older adults hospitalized with HF [11]. Telemonitoring used electronic equipment that collected daily information on blood pressure, heart rate, symptoms, and weight. All-cause readmissions up to 180 days after discharge did not differ between intervention and usual care groups (50.8% and 49.2%, respectively). In secondary analyses, there were no significant differences in 30-day readmission or 180-day mortality, but there was a significant difference in 180-day quality of life favouring the interventional group.

Other important trials included the TEHAF [12], Tele-HF [13], TIM HF [14] and WHARF [15] trials. The TEHAF trial, a multicentre randomized controlled trial, was carried out to test whether telemonitoring reduces HF hospitalizations [12]. With 382 participating patients, mean time to first heart failure-related hospitalization was 161 days for the intervention group and 139 days for the usual-care group, but hospitalizations did not differ between the two groups during one year of follow-up, possibly due to study underpower combined with low event rates in well-treated patients.

The Tele-HF study randomly assigned 1653 patients who had recently been hospitalized for heart failure to undergo either telemonitoring (826 patients) or usual care (827 patients) [13]. Telemonitoring was accomplished by means of a telephone-based interactive voice-response system that collected daily information about symptoms and weight that was reviewed by the patients’ clinicians. The primary endpoint was readmission for any reason or death from any cause within 180 days after enrolment. Secondary endpoints included hospitalization for HF, number of days in the hospital, and number of hospitalizations. The telemonitoring group and the usual-care group did not differ significantly with respect to the primary endpoint, which occurred in 52.3% and 51.5% of patients, respectively (p = 0.75). There were no significant differences between the two groups with respect to the individual components of the primary endpoint or to the secondary endpoints.

The TIM-HF study enrolled 710 stable chronic HF patients in New York Heart Association functional (NYHA) class II or III with a LVEF < 35% and a history of HF decompensation within the previous two years or with a LVEF < 25% [14]. Remote telemedical management used portable devices for electrocardiography monitoring, blood pressure, and body weight measurements connected to a personal digital assistant that sent automated encrypted transmission via cell phones to the telemedical centres. The primary endpoint was death from any cause. The first secondary endpoint was a composite of cardiovascular death and hospitalization for HF. Compared with usual care, remote telemedical management had no significant effect on all-cause mortality (hazard ratio, 0.97; 95% CI: 0.67–1.41; p = 0.87) or on cardiovascular death or HF hospitalization (hazard ratio, 0.89; 95% CI: 0.67–1.19; p = 0.44).

The WHARF trial tested if daily reporting of weight and symptoms in 138 patients with advanced heart failure would reduce rehospitalization and mortality rates despite aggressive
guideline-driven HF care in patients hospitalized with NYHA class III or IV HF and with a LVEF ≤ 35% [15]. The primary endpoint was 6-months hospital readmission. Secondary end points included mortality, HF hospitalization readmission rate, emergency room visitation rate, and quality of life. Despite observing no differences in hospitalization rates, there was a 56.2% relative risk reduction in mortality (p < 0.003) for randomized patients from the remote monitoring group.

Despite the conflicting results in different trials, a recent meta-analysis demonstrated that noninvasive telemonitoring offers statistically and clinically meaningful benefits to people with heart failure, with a 20% reduction in the risk of all-cause mortality (RR 0.80, 95% CI: 0.68–0.94; participants 3740; studies 17), along with a 29% reduction in heart failure related hospitalisations (RR 0.71, 95% CI: 0.60–0.83; participants 2148; studies 8) [10].

The most recent randomized trial (TIM-HF2) was published in 2018 [16]. After a subgroup analysis of the TIM-HF trial [14] suggested that remote patient management has a potential beneficial effect for patients who did not have major depression, the TIM-HF2 trial was designed and performed showing a reduction in time spent in hospital for unplanned cardiovascular events and a reduction in all-cause mortality (hazard ratio 0.70, 95% CI: 0.50–0.96; p = 0.028). In this trial the data was transmitted to the telemedical centre, where physicians and heart failure nurses are available 24 hours a day, then a software (Fontane system) analysed the information and applied predefined algorithms for an individual patient risk profile.

Structured telephone support and non-invasive telemonitoring may therefore reduce the burden of HF hospitalizations, improve quality of life, and possibly reduce mortality in a specific subset of HF patients. Additional benefits of such interventions might be improvements in titration of and adherence to pharmacological therapy, and to reinforce advice about lifestyle [17].

Nevertheless, a major pitfall of non-invasive monitoring is the sensitivity to detect decompensations. Small increases in cardiac filling pressures occur up to 30 days prior to decompensation, and seem to be the first evident physiologic change, even before patients’ weight changes and symptoms develop [18]. This rise in filling pressures likely results from very small increases in intravascular volume due to vascular redistribution and alterations in vascular tone. As the body attempts to maintain homeostasis, autonomic dysregulation ensues, manifested primarily by vagal withdrawal and sympathetic dominance that lead to a decrease in heart rate variability (HRV), which is detectable up to 21 days before hospitalization [19]. The increased filling pressures and autonomic maladaptation can then lead to a more substantial increase in fluid accumulation and/or vascular redistribution that is detectable by intrathoracic impedance measurements as early as 18 days before admission [20]. Finally, overt clinical symptoms and an increase in total body weight may become detectable by the patient around one week prior to admission [21].

Since conventional means of detecting changes in fluid status such as weight and symptom monitoring do not provide sufficient warning, some effort has been made to call attention to implantable devices for the purpose of monitoring HF status. These include devices that have been placed for other indications (permanent pacemakers [PPM], implantable cardioverter-defibrillators [ICD] or cardiac resynchronization therapy [CRT]), and implantable hemodynamic sensors and monitors (IHM) specially designed for measuring mainly intracardiac pressures.

### PPM/ICD/CRT for home monitoring

If indicated, devices are one of the mainstays of treatment for HF patients [22], providing an opportunity to use their potential capabilities to further evaluate the patient. With a capacity to transmit recorded data through an external transmitter to the manufacturer’s central database, information is transferred on a regular basis, and alerts are forwarded to the physician. Some routinely monitored parameters may reflect a patient’s clinical status and predict impending cardiac decompensation [23].

A variety of pathophysiologic changes have been studied in several trials: Adamson et al. showed that heart rate variability (HRV) as an indirect autonomic assessment provides prognostic information when measured over long time periods in patients with heart failure [19]. A total of 397 patients with NYHA class III or IV heart failure were studied. Continuous HRV was measured as the standard deviation of 5-minute median atrial-atrial intervals (SDAAM) sensed by the device. SDAAM < 50 ms when averaged over 4 weeks was associated with increased mortality risk (HR 3.20, p = 0.02) and SDAAM were persistently lower over the entire follow-up period in patients who required hospitalization or died. SDAAM decreased a median of 16 days before hospitalization and returned to baseline after treatment.

As referred earlier, weight gain and symptoms are a late occurrence in the evolution of a decompensation. Other changes were studied, with a lot of enthusiasm created by intrathoracic impedance, that was shown to be inversely correlated with pulmonary capillary wedge pressure and fluid balance and decreased before the onset of patient symptoms and before hospital admission for fluid overload [20].

Several studies tried to demonstrate the clinical benefit of using intrathoracic impedance: In a study with 335 patients with chronic HF who had undergone implantation of an implantable device with a monitoring tool to track changes in intrathoracic impedance (OptiVol) and other diagnostic parameters, patients were randomized to have information available to both physicians and themselves as an audible alert in case of preset threshold crossings (access arm) or usual HF monitoring (control arm) [24]. The primary end point was a composite of all-cause mortality and heart failure hospitalizations. This occurred in 48 patients (29%) in the access arm and in 33 patients (20%) in the control arm (p 0.063; HR, 1.52; 95% CI: 0.97–2.37). This was due mainly to more heart failure hospitalizations (HR, 1.79; 95% CI: 1.08–2.95; p = 0.022), whereas the number of deaths was comparable (19 vs 15; p = 0.54). The number of outpatient visits was higher in the access arm (250 vs 84; p < 0.0001), with more signs of heart failure among control patients during outpatient visits.
More recently, another study evaluated whether early automated fluid status alert notification via telemedicine improves outcome in HF patients [25]. Patients recently implanted with an ICD, with or without CRT therapy, were eligible if one of three conditions was met: prior HF hospitalization, recent diuretic treatment, or recent brain natriuretic peptide increase. 1002 patients were randomized (1:1) to have fluid status alerts automatically transmitted as inaudible text message alerts to the responsible physician or to receive standard care (no alerts). In the intervention arm, following a telemedicine alert, a protocol-specific algorithm with remote review of device data and telephone contact was prescribed to assess symptoms and initiate treatment. The primary endpoint was a composite of all-cause death and cardiovascular hospitalization. The primary endpoint occurred in 227 patients (45.0%) in the intervention arm and 239 patients (48.1%) in the control arm (HR 0.87; 95% CI: 0.72–1.04; p = 0.13). There were 59 (11.7%) deaths in the intervention arm and 63 (12.7%) in the control arm (HR, 0.89; 95% CI: 0.62–1.28; p = 0.52).

Other predictors of clinical decompensation include atrial tachyarrhythmia [5], decreased patient activity level [19] and an increase in the number of both appropriate and inappropriate shocks [26].

Despite the previously described studies having failed to show the clinical benefit of measuring fluid impedance alone, the PARTNERS HF trial was a prospective, multicenter observational study in patients receiving ICD/CRT [27]. A combined HF device diagnostic algorithm was developed on an independent dataset. The algorithm was considered positive if a patient had 2 of the following abnormal criteria during a 1-month period: long atrial fibrillation duration, rapid ventricular rate during atrial fibrillation, high fluid index, low patient activity, abnormal autonamics (high night heart rate or low heart rate variability), or notable device therapy (low CRT pacing or implantable cardioverter-defibrillator shocks), or if they only had a very high (100) fluid index. After analyzing data from 694 patients, those with a positive combined HF device diagnostics had a 5.5-fold increased risk of HF hospitalization with pulmonary signs or symptoms within the next month (hazard ratio: 5.5, 95% CI: 3.4–8.8, p < 0.0001), predicting patients at a higher risk of HF hospitalizations within the subsequent month.

Some studies showed benefit too [28], including one representing our Portuguese reality [29], while others have not been successful [30, 31], including REM-HF which is the largest study, with longest follow-up ever done with remote monitoring on HF, perhaps because only home monitoring with daily verification of transmission has an impact on mortality [32]. The results from the cost-utility analysis demonstrate that it appears to be a cost-effective advantage compared to the conventional method of in-person evaluations [33–35]. Remote monitoring of PPM and ICD data may allow for faster recognition of serious arrhythmias, device problems, or worsening heart failure [36]. Clinic visits could be reduced without compromising safety, while also saving patient, staff and physician time [37]. Given these potential advantages, remote monitoring of implantable devices has been endorsed by recent expert consensus [38].

### Implantable hemodynamic monitors

While alterations in the physiologic parameters measured by ICD/CRT devices can provide useful markers for worsening HF, they do so essentially as surrogates for the elevated ventricular filling pressures. As changes in filling pressures seem to occur earlier than any other measurable parameter during decompensation, they represent an ideal target for earlier intervention [18].

Based on the observation that right ventricular (RV) pressure at the time of pulmonary valve opening is equal to pulmonary artery diastolic pressure, RV pressure at the time of RV maximum change in pressure over time (dP/dt) was considered the pulmonary artery end-diastolic pressure and this correlated with directly measured pulmonary artery diastolic pressures at baseline, during isometric work, and during the Valsalva manoeuvre [39]. This observation was incorporated into an implantable leaded RV pressure monitoring system, which looked similar to a single-lead PPM, to continuously measure RV systolic and diastolic pressures, pulmonary artery end-diastolic pressure, RV dP/dt, heart rate, patient activity level, and temperature. This led to the first randomized controlled trial of implantable hemodynamic monitoring for HF [39]. In total, 274 patients with HF NYHA class III or IV were randomized to a Chronic (Medtronic Inc., Minneapolis, Minnesota) (n = 134) or control (n = 140) group. All patients received optimal medical therapy, but the hemodynamic information from the monitor was used to guide patient management only in the Chronic group. Primary endpoints included freedom from system-related complications, freedom from pressure-sensor failure, and reduction in the rate of HF related events. The two safety endpoints were met with no pressure-sensor failures and system-related complications in only 8% of the 277 patients who underwent implantation. The primary efficacy end point was not met because the Chronic group had a non-significant 21% lower rate of all HF-related events compared with the control group (p = 0.33). The only other major RCT evaluating this technology was recently halted prematurely by the manufacturer due to issues related to lead integrity [40].

Two relatively newer devices have some important advantages when compared to the Chronic system. Their sensors are positioned in a branch of the pulmonary artery (CardioMEMS®, CardioMEMS Inc., Atlanta, GA, USA [41]) or the left atrium (HeartPOD, St. Jude Medical, St. Paul, MN, USA [42]) which not only allows for a more direct measurement of cardiac filling pressures but also avoids subjecting the sensor to the high mechanical and flow-related stresses inherent to the RVOT. Another important difference is that they do not require batteries.

In the HOMESTASIS trial, 40 patients with reduced or preserved left ventricular ejection fraction and a history of New York Heart Association class III or IV heart failure and acute decompensation were implanted with an investigational left atrial pressure monitor, and readings were acquired twice daily [42]. For the first three months, patients and clinicians were blinded to these readings, and treatment continued per usual clinical assessment. Thereafter, left atrial pressure and individualized therapy instructions guided by these pressures were disclosed to the patient. There were improvements in NYHA.
The negative findings of some previous trials highlight the complexity of home monitoring interventions. HF home management involves multiple components, suggesting that telemonitoring in isolation is not likely to be a successful strategy for reducing readmission. Additional features implicate transmission and reception of data with sufficient time to act upon it, a feedback loop to the patient with directions, and sufficient patient empowerment to understand and implement the instructions. Also, although telemonitoring will certainly reduce the need for in-person follow-up, it may actually increase the workload involved [23]. As an example, in the TELE-HF study, while there were only 25 patients per site on average, there were 884 incidents per site requiring responses [13].

Integration of a daily review of remotely collected data into clinical practice is challenging (Fig. 1). Those reviewing data need the appropriate skills and support, as well as the ability to react appropriately. Delays in response, often introduced by multiple layers of review, defeats the purpose of early identification of problems [43].

Identifying which variables are best to monitor requires further study, whether it be patient symptoms, directly recorded data or calculated measurements. Monitoring alone, without adequate follow-up and feedback to the patient, is unlikely to be the solution that prevents HF readmissions or decompensation.

Mobile phone-based remote monitoring systems, along with application-based support of HF patient education and disease management could be relatively inexpensive and convenient tools to improve HF home management. Mobile phones are now widely available and have considerable computational power, while being relatively inexpensive compared to dedicated remote monitoring hardware. These systems are also portable, enabling patients to be monitored anywhere that has mobile phone reception.

Future strategies for monitor HF

Despite all the technologies described previously having offered clinicians an unprecedented wealth of new information in patients with advanced HF, strategies are needed for how to best implement this data into patient disease management. It may be possible in the near future, by providing patients with information and with some kind of alerts, to turn self-monitor and self-manage of HF a reality, similar to the way Diabetes mellitus is treated nowadays [42].

The effect of disease management on outcomes for patients with HF is uncertain due to the heterogeneous nature of the interventions and the poor quality of most of the trials. Large randomized controlled trials of varying protocols have reached disparate conclusions regarding the efficacy of disease management.

While implantable devices and remote monitoring systems will undoubtedly play an important role in a comprehensive approach to outpatient HF management, much of their acceptance is still dependent on further technological refinement, development of infrastructure and systems to facilitate the timely transmission, triage, and integration of the data, and ultimately the demonstration of improved outcomes.

Conflict of Interest

None.
References:


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