Review Article

# How to Change the Medical History of Patients with Heart Failure and Recurrent Hospitalizations?

*Fernanda Almeida Andrade,*[1] *Luana Monferdini,*[2,3] *Jefferson Luís Vieira*[4,5]

*Universidade Federal de São Paulo/UNIFESP,*[1] *São Paulo, SP – Brazil*
*Hospital e Maternidade Celso Pierro – PUC Campinas,*[2] *Campinas, SP – Brazil*
*Hospital das Clínicas Botucatu – Unesp,*[3] *Botucatu, SP – Brazil*
*Hospital de Messejana Dr. Carlos Alberto Studart,*[4] *Fortaleza, CE – Brazil*
*Universidade Federal do Ceará,*[5] *Fortaleza, CE – Brazil*

## Abstract

Heart failure (HF) is a progressive condition, characterized by variable periods of symptomatic stability frequently interrupted by episodes of A worsening condition. These moments of clinical deterioration have been recognized as a distinct phase in the course of HF and indicate a considerably worse prognosis. Preventing readmissions of patients with HF is a growing priority for medical providers, researchers, and healthcare managers. Although evidence-based therapies for treating patients with HF have increased, consistent implementation of these therapies and the development of new strategies to prevent readmissions continue to be areas for continued improvement. In this review, we will discuss some proposals and challenges associated with reducing readmissions due to HF.

## Introduction

Heart failure (HF) is a complex and progressive condition, characterized by variable periods of symptomatic stability, usually interrupted by episodes of decompensation, after which patients rarely return to their initial quality of life (Figure 1). Even during the phase of apparent clinical stability, there is still a significant residual risk of clinical deterioration associated with recurrent readmissions and new cardiovascular events that contribute to the worsening of the disease.[1,2] This course becomes progressively worse until reaching final pump failure and death, or, in rare cases, heart transplantation.

According to the largest database of payment sources for hospital admissions in the United States, the Nationwide Inpatient Sample (NIS), hospitalizations for HF in the country increased from 1,060,540 in 2008 to 1,270,360 in 2018.[3] However, it has become increasingly evident that not all patients with decompensated HF are hospitalized, as many of these patients are treated on an outpatient basis.[4,5] In fact, a significant proportion of patients hospitalized for acutely decompensated HF have recurrent unplanned visits to the doctor's office or to the emergency room before hospital admission. In 2019, more than 1,500,000 emergency consultations with a diagnosis of decompensated HF were recorded in the United States alone.[3] These moments of clinical deterioration have been characterized as a distinct phase in the course of patients with HF, called Worsening Heart Failure (WHF) (Figure 1).[1,6] WHF is defined by the progression of signs and symptoms of HF in patients with chronic ventricular dysfunction despite optimized medical therapy, and involves the need for hospitalization or therapeutic scheduling on an outpatient basis, generally with increased diuretic therapy. This is because the main pathophysiological mechanism of acute HF decompensation is congestion, not low output. According to data from the Brazilian registry of hospitalizations for HF, BREATHE extension, the predominant clinical-hemodynamic profile in admissions for HF in the country between 2011 and 2018 was hot-humid (71.7%), while a small number of patients (12.9%) showed no signs of congestion or poor perfusion;[7] among more than 3,000 evaluated individuals, the main cause of decompensation was low adherence to drug therapy, in 28% of the patients, followed by infections (21%) and arrhythmia (14%). The diversity of readmission triggers highlights the importance of comprehensive care to prevent complications from secondary conditions and patient-specific risk factors (Table 1).

The concept of WHF is evolving, having been mentioned in recent updates to the HF guidelines of the European Society of Cardiology and the AHA/ACC/HFSA[8,9] (Table 2). This phase of the disease marks its degenerative progression and indicates a considerably worse prognosis, whose risk profile is estimated by the progression of the disease and the worsening of the set of symptoms, signs, and/or functional capacity, classifying it as a possible trajectory within stage C.[10]

Approach and treatment of patients with recurrent hospitalizations and WHF

Patients with recurrent hospitalizations and WHF must undergo a thorough evaluation to exclude reversible causes of HF decompensation and ensure optimized treatment based on specific guidelines.[11] Despite the challenges in identifying factors and scenarios that may accelerate readmission, there is a solid underlying rationale for the use of evidence-based medical therapies with an impact on symptomatic relief and hospitalizations in patients with HF, especially those with reduced ejection fraction (HFrEF).[12] In addition to the scheduling of decongestive therapy with diuretics and other emergency measures highlighted in Figure 2, the introduction

## Keywords

Heart Failure; Diuretics; Hospitalization; Mortality.

**Mailing Address: Jefferson Luís Vieira •**
Hospital de Messejana - Unidade de Transplante e Insuficiência Cardíaca - Av. Frei Cirilo, 3480. Postal Code 60864-190, Fortaleza, CE - Brazil
E-mail: jefvieira@yahoo.com.br, jefvieira31@gmail.com
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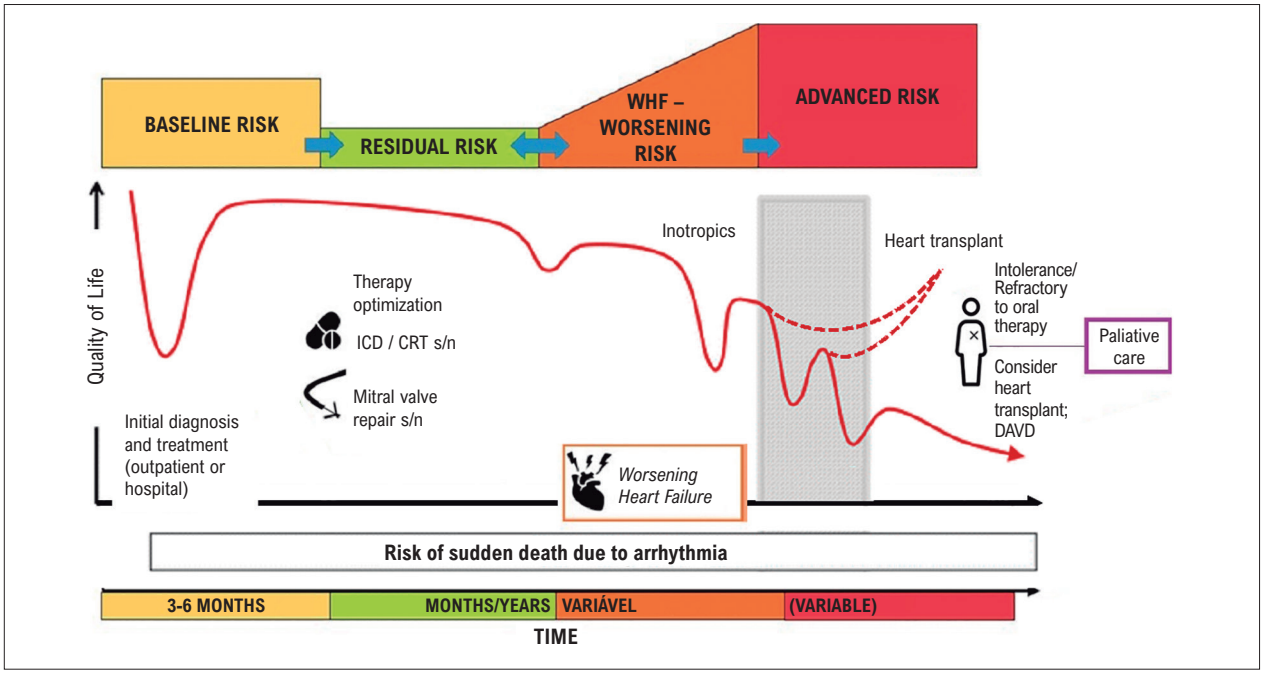


**Figure 1 -** *Journey and risk profiles of patients with heart failure. The diagnosis of HF carries a significant intrinsic clinical risk (baseline risk), which can be reduced through the use of guideline-based medical therapy. Even during the phase of apparent clinical stability, there is still a residual risk of clinical deterioration that may be associated with recurrent readmissions and new cardiovascular events (Worsening Heart Failure). Arrows represent directionality between risk profiles – patients in the worsening phase may respond to optimized therapy and return to a residual risk state or may progress to the advanced risk stage. ICD: implantable cardioverter defibrillator; HF: heart failure; CRT: cardiac resynchronization therapy. Adapted from Greene et al.[1]*

**Table 1 – Causes for worsening heart failure**

| | |
|---|---|
| Low adherence to drug therapy | Failure to follow medication prescriptions as instructed by a healthcare professional can lead to worsening symptoms and a decline in heart function. |
| Increased salt and water intake | Consuming too much salt (sodium) can cause fluid retention, which can worsen heart failure symptoms. Not monitoring your fluid intake and exceeding recommended limits can also be problematic. |
| Cardiac events | Myocardial infarction or other cardiac events can further weaken the heart muscle, leading to aggravated heart failure. |
| Infections | Infections, especially respiratory infections, can overload the heart and worsen symptoms. |
| Arrhythmias | Irregular heart rhythms can reduce the heart's pumping efficiency and contribute to aggravated heart failure. |
| Lifestyle | Smoking, excessive alcohol consumption, and lack of physical activity can worsen heart failure. |
| Other medical conditions | Conditions such as high blood pressure, diabetes, and kidney disease can worsen heart failure if not well controlled. |

(or reintroduction) of medications that constitute the pillars of HF treatment should be initiated in rapid sequence during the care transition phase.[13-15] The additive benefit of these therapies became apparent within a few weeks of use, which is why target or maximum tolerated doses of all drug classes should be sought as quickly as possible. Several medications have been significantly associated with reductions in HFrEF admissions, including digoxin, a combination of hydralazine and nitrate, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, neprilysin and angiotensin receptor (ARNI) inhibitors, antagonists of the mineracolorticoid receptor (ARM), sodium-glucose cotransport-2 inhibitors (iSGLT2), and ivabradine.[16-27] Clinical trials in patients with WHF demonstrated the safety and efficacy of drugs, such as vericiguat, omencativ mecarbil, INRA, and iSGLT2, specifically in this high-risk population.[28-32] In patients with HF with a preserved ejection fraction (HFpEF) and HF with a mildly reduced ejection fraction (HFrEF), who present symptoms and high levels of type B natriuretic peptide (BNP or N-terminal pro- BNP [NT-proBNP]), the use of iSGLT2, and to a lesser extent ARM, has also proven to be effective in reducing hospitalizations due to HF.[33-38]

**Table 2 – Definition of advanced HF defined by SBC, AHA/ACC, ESC, and Heart Failure Society of America guidelines**

| Criterion | SBC | ACC/AHA | ESC | HFSA |
|---|---|---|---|---|
| Severe and persistent symptoms despite optimized therapy | ✔ | ✔ | ✔ | ✔ |
| Important functional limitation (NYHA functional class III or IV) | ✔ | ✔ | ✔ | ✔ |
| Persistent dyspnea with daily living activities | | ✔ | | |
| Recurrent hospitalizations | ✔ | ✔ | ✔ | ✔ |
| Frequent unplanned emergency room visits | ✔ | | ✔ | ✔ |
| Intolerance to maximum therapeutic optimization | ✔ | ✔ | | ✔ |
| Target organ dysfunction | ✔ | ✔ | | ✔ |
| Persistent hyponatremia | ✔ | ✔ | | ✔ |
| Pulmonary or systemic congestion refractory to diuretic therapy | ✔ | ✔ | | ✔ |
| Frequent CDI shocks | ✔ | ✔ | | ✔ |
| Cardiac cachexia | ✔ | ✔ | | ✔ |
| Systolic blood pressure often ≤90 mmHg | | ✔ | | |
| Persistently high BNP or NTproBNP values | ✔ | | ✔ | |
| Severe LV dysfunction, with echocardiographic pattern of pseudonormal or restrictive filling | ✔ | | ✔ | |
| High filling pressures (PCP >16 mmHg +/- PVC >12 mmHg) | | | ✔ | |
| Low capacity in the 6MWT (<300 m) or VO2 peak (<12-14 ml/kg/min), estimated to be of cardiac origin | ✔ | | ✔ | ✔ |
| Severe LV dysfunction with reduced ejection fraction | ✔ | | ✔ | ✔ |
| Dependence on intravenous inotropes | ✔ | | | ✔ |
| Progressive RV dysfunction and secondary PH | ✔ | | | ✔ |

*ACC/AHA: American College of Cardiology/American Heart Association; ICD: implantable cardioverter defibrillator; HF: heart failure; BNP: B-type natriuretic peptide; ESC: European Society of Cardiology; HFSA: Heart Failure Society of America; PH: pulmonary hypertension; NYHA: New York Heart Association; NT-proBNP: N-terminal fraction of type B natriuretic peptide; PCP: pulmonary capillary pressure; CVP: central venous pressure; 6MWT: 6-minute walk test; RV: right ventricle; LV: left ventricle; VO2: oxygen consumption. Adapted from Marcondes-Braga FG, et al.[73]*

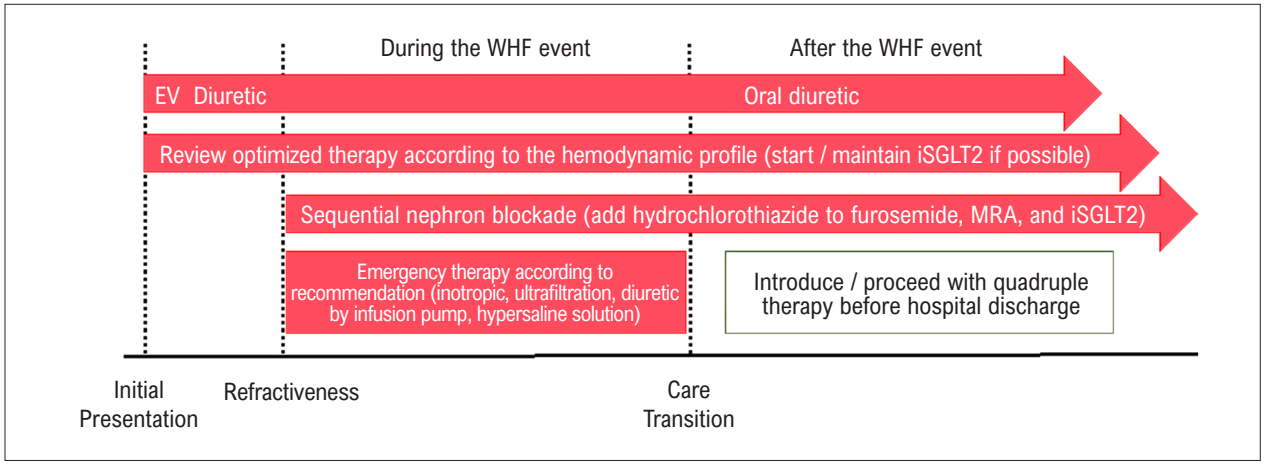


**Figure 2 –** *Decongestive therapy for WHF. Intravenous loop diuretic and sodium-glucose cotransporter-2 (SGLT2) inhibitor are fundamental therapies for decongestion in patients with worsening heart failure (WHF). Other adjuvant therapies may be considered in selected patients. MRA: mineralocorticoid receptor antagonist; IV: intravenous. Adapted from Greene et al.[72]*

Intravenous iron replacement, especially with carboxymaltose or ferric derisomaltose, is also recommended for patients with WHF and an iron deficiency in order to improve the functional status and quality of life, as well as to reduce readmissions.[39-44] Furthermore, for practicality's sake, patients hospitalized due to HF or those receiving outpatient intravenous diuretics already have intravenous access, which can further facilitate the administration of intravenous iron in clinical practice.

Ischemia testing in selected patients, the surgical or percutaneous treatment of heart valve diseases, the management of atrial and ventricular arrhythmias (including a high burden of premature ventricular contractions), resynchronization therapy, and the assessment of situations that may aggravate HF symptoms, such as the use of non-steroidal anti-inflammatory drugs, may also lead to a decrease in readmissions.[45-47] Finally, the consideration of candidates for advanced HF therapies, including heart transplantation and ventricular assist devices, is appropriate for those with symptoms that are refractory to pharmacological therapeutic optimization, be it electrical and/or mechanical.[48,49] Complementary tests, such as the cardiopulmonary exercise test or the 6-minute walk test, in addition to pulmonary artery catheterization, can be useful tools in the evaluation of these patients.

The potential of new technologies to monitor congestion and prevent readmissions is a developing field.[50] To date, the remote monitoring method in patients with HF with the most convincing evidence is CardioMEMS, a device implanted percutaneously in the pulmonary artery, which transmits core blood pressure values to a safe server.[51] CardioMEMS has been shown to be effective and safe in "real-life," cost-effectiveness, and post-marketing studies, and it appears to be a promising strategy with the potential to be added to clinical practices.[52-54] Clinical trials of non-invasive telemonitoring in HF often have conflicting results, due to differences in the populations studied, the health policies of each country, and the monitoring tools adopted.[55-59] The use of natriuretic peptides (BNP or NT-proBNP) as markers of congestion is also part of the assessment and diagnosis of HF, and may be a useful complementary tool for predicting long-term prognosis and readmission.[15,60-62]

## Public health strategies to reduce heart failure readmissions

Identifying public health strategies that can reduce preventable readmissions would be valuable for patients, medical providers, and healthcare managers. Numerous specific interventions have been investigated to try to reduce readmission for HF, including patient education, discharge planning, medication reconciliation, the scheduling of return visits before discharge, early return after discharge, and telemonitoring/follow-up phone calls. However, these studies are typically narrow in scope, focusing on an isolated aspect of patient care and providing a one-size-fits-all approach, with conflicting results in the literature.[59,63-66]

In the United States, the Patient Protection and Affordable Care Act (ACA) was enacted in 2010, seeking to expand opportunities for access to health care and supporting innovative care delivery methods aimed at reducing healthcare costs in general. Among the remuneration models proposed by the ACA is the review of hospital payment methods through the incorporation of care performance indicators, such as hospital readmission. The Hospital Readmissions Reduction Program (HRRP), was created to try to reduce 30-day readmissions by reducing payments to providers with the worst performance, using a methodology adjusted to the profile of the participating institution.[67] The HRRP changed the landscape of hospital readmissions and reimbursement in the United States by imposing substantial Medicare payment penalties on hospitals with higher-than-expected readmission rates.[65] However, although it reduced the readmission rate from 18% to 16% between 2008 and 2016, the HRRP generated controversy for not considering medical complexity and socioeconomic differences between hospitals.[68]

Finally, it is important to mention that a large proportion of patients with HF are admitted for non-cardiovascular conditions, as HF is one of the many comorbidities that can increase the risk of future hospitalizations.[5,69] A proposal for a domain-directed intervention model can be considered during each hospitalization for HF, with guidance for interventions that can reduce risks and

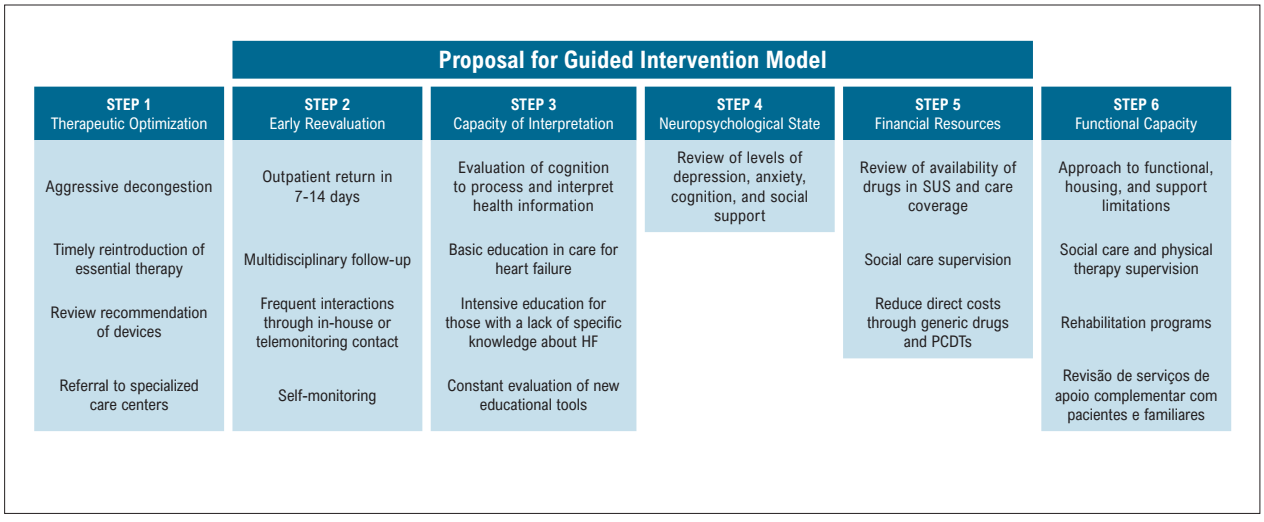


**Figure 3 –** *Proposed targeted intervention model. Patient-centered strategy to reduce readmissions organized into six categories that connect the patient and their disease: therapeutic optimization, early reassessment, interpretability, neuropsychological status, financial resources and functional capacity. By evaluating deficiencies in each of these categories, hospital systems can selectively target interventions more efficiently to reduce readmissions. HF: heart failure; PCDT: Clinical Protocols and Therapeutic Guidelines. Adapted from Sperry et al.*[70]

challenges in the care of patients with HF and recurrent hospitalizations[70] (Figure 3).

### Conclusion and future perspectives

HF continues to be an epidemiological, clinical, and financial challenge for patients, medical service providers, and healthcare managers. Advances in HF therapies have prolonged patient survival, but at the cost of greater clinical complexity and cost of care. Even when clinical treatment is effective in reducing readmissions due to HF, it is not clearly documented whether there is also an improvement in patient survival outcomes.[71]

Although temporary mechanical support has revolutionized the management of cardiogenic shock, the unavailability of prospective data based on robust randomized clinical trials limits our understanding of the risks and benefits of this technology for the patient with recurrent hospitalizations. As experience with long-term support increases, criteria and guidelines for patient selection must be standardized in order to contain the costs of care and improve post-implant outcomes, keeping patients out of the hospital environment and with a quality of life. In transplantation, work to expand the donor pool must continue, while investments in basic and translational research can help improve graft longevity. Research focused on myocardial recovery is urgently needed, as biochemical pathways capable of reversing, if not preventing, HF would radically change our approach to care. Lastly, we must continue to integrate patient-centered and symptom-based palliative care into our advanced HF management paradigm in an attempt to help patients not only live longer, but also live better.

## Author Contributions

Conception and design of the research, Acquisition of data, Writing of the manuscript and Critical revision of the manuscript for content: Andrade FA, Monferdini L, Vieira JL.

### Potential conflict of interest

Dr. Jefferson Vieira reports fee for serving on the adjudication committee of clinical events from the Hospital Israelita Albert Einstein ARO and fees for conferences from AstraZeneca, Boehringer-Ingelheim & Eli Lilly, Novartis, Bayer, Pfizer, Merck and Viatris.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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