

Integrated Management and Risk Dynamics During the Vulnerable Phase of Heart Failure: Insights from Recent Evidence

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Abstract

Heart failure remains a significant challenge for healthcare systems globally, associated with high hospitalization and mortality rates. Episodes of acute decompensation require immediate evaluation and hospital treatment; however, the greatest risk for adverse events occurs after discharge from the hospital. The first 3 months after discharge, known as the "vulnerable phase," are characterized by a high incidence of rehospitalization and mortality, making it a critical period for therapeutic intervention. This narrative review was based on a structured literature search in the PubMed/MEDLINE databases, focusing on European Society of Cardiology (ESC) guidelines and recently published clinical trials, with the aim of

identifying consensus on the management of the vulnerable phase and analyzing its applicability in our clinical practice.

This article summarizes the latest evidence on the importance of optimizing guideline-directed medical therapy, not only during the acute phase, but also in the period before and immediately after hospital discharge. Beyond the traditional focus on short-term acute stabilization, the pre-discharge phase is a key window for hemodynamic stabilization, decongestion, management of comorbidities, and titration of oral therapy. In parallel, early post-discharge follow-up based on clinical assessment, multidisciplinary coordination, patient education, and laboratory biomarkers improves risk

stratification. Implementation of this integrated approach shifts the focus from isolated short-term management to strategies that significantly reduce adverse events during this transitional period.

Keywords: Heart failure, vulnerable phase, decongestion, GDMT

INTRODUCTION

The Vulnerable Phase Paradigm

The high number of hospitalizations, mortality, and significant health costs make heart failure (HF) a major global challenge (1).

According to the 2021 European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic HF, the management of patients hospitalized for acute decompensation can be divided into three phases, each of which has different therapeutic approaches: pre-hospital phase/early hospital phase (immediate), intra-hospital phase (intermediate), and pre-discharge phase/vulnerable phase (2). The focus of the first two phases is primarily on diagnosis, etiology, hemodynamic stabilization of the patient, including congestion and/or hypoperfusion, and the initiation of evidence-based therapies. Meanwhile, strategies related to the pre-discharge period and early post-discharge follow-up are still under development and evaluation in clinical studies, while their implementation in daily practice presents more challenges (2, 3).

Despite recent advances in the treatment of chronic heart failure, the vulnerable phase remains the period with the highest risk for rehospitalization and mortality. Because of these adverse outcomes, the first three months after discharge from the hospital are considered the “vulnerable phase” (4). This period begins immediately after an acute episode and lasts up to 90 days, being divided into three subphases: very early (first month), early (up to 60 days), and late

(60–90 days). About 30% of patients hospitalized for heart failure return to the hospital within 3 months of discharge, while mortality during this period can reach approximately 10%. (5). Several studies show that rehospitalizations are more frequent in patients with heart failure with reduced ejection fraction (HFrEF) compared with heart failure with preserved ejection fraction (HFpEF). However, during the vulnerable phase, trends in hospital readmissions are similar in both groups, suggesting a greater role of comorbidities, especially in HFpEF (6, 7). Also, a significant proportion of rehospitalizations within 30 days occur for non-cardiac causes (8).

In addition to the pathophysiological mechanisms of the disease and the presence of comorbidities, several factors related to our heart failure management strategies contribute to the vulnerable phase being the most critical period for these patients. One of the most important is discharge from the hospital with residual congestion, which is associated with a more unfavorable prognosis. Also, post-discharge follow-up is often inadequate or not well structured, increasing the risk of clinical deterioration and rehospitalization. Another important problem remains the use of suboptimal doses of the main heart failure therapies, which limits the maximum benefit from treatment and negatively affects the course of the disease (9).

Furthermore, an essential element in this period is the coordination of care between hospital and outpatient services, which often results in fragmentation and is associated with limited

access to follow-up programs. Early post-discharge visits and patient and caregiver education, along with initiation of cardiac rehabilitation, represent important interventions for improving prognosis. On the other hand, subclinical hemodynamic changes may precede the appearance of clinical symptoms of congestion, emphasizing the need for early and structured monitoring after hospital discharge. However, despite the use of biomarkers and clinical parameters for risk stratification, a reliable and standardized model for identifying patients at high risk for rehospitalization is still lacking (10).

METHODOLOGY

This narrative review summarizes contemporary scientific literature on the management of heart failure (HF) throughout the vulnerable phase. The literature was selected through a structured search of the PubMed database by using the keywords "heart failure," "vulnerable phase," "decongestion," and "GDMT", focusing mainly on the ESC 2021 Guidelines and scientific publications from recent years. This review is designed to present a clear synthesis of the latest clinical evidence and consensus.

By analyzing international management strategies, we aim to assess their relevance and applicability to clinical practice in Albania, with particular reference to the "Mother Teresa" University Hospital Center. This review is particularly relevant in the context of our healthcare system, where several gaps continue to

affect the management of patients with heart failure. These include fragmented follow-up between the cardiologist and internist in tertiary centers and the family doctor in primary care, as well as the difficulty of rapid and optimal titration of guideline-directed medical therapy (GDMT) or incomplete decongestion at the time of discharge from the hospital. The absence of structured cardiac rehabilitation programs and difficulties in outpatient monitoring of biomarkers (such as NT-proBNP) after hospital discharge increase the risk of rehospitalization. Through this article, we aim to offer a practical guide to improve the management of these patients in real conditions.

Risk Stratification Using Clinical Assessment, Biomarkers, and Imaging Modalities

Identification of high-risk patients is essential for personalized management of heart failure. The literature highlights the importance of several key indicators, including clinical assessment, biomarkers, laboratory parameters, and imaging for risk stratification.

Clinical Assessment

Clinical assessment, although routinely used to identify congestion in our patients, has a low accuracy rate for identifying subclinical congestion, which is also the main cause of rehospitalization. Signs of congestion and hypoperfusion are associated with worse prognosis. The proposed "congestion scores" include symptoms such as dyspnea, orthopnea, and fatigue, as well as signs such as rales,

peripheral edema, jugular venous distension, and hepatomegaly (11). Additionally, assessment of body weight and NYHA functional class should be integrated into the pre-discharge assessment. Measurement of blood pressure and heart rate is an important factor for prognostic stratification and individualization of guideline-directed medical therapy (GDMT), as hypotension may limit tolerance to ACEi/ARB, especially ARNI, while the presence of congestion may delay the initiation of beta-blocker therapy (9).

An analysis of the ESC-EORP-HFA registry showed that 30.9% of patients are discharged from hospital with residual congestion after an episode of acute cardiac decompensation, highlighting the importance of accurately identifying the degree of congestion in the pre-discharge period, not only based on clinical examination (4).

Laboratory Biomarkers

Natriuretic peptides (BNP/NT-proBNP) are the most powerful predictors of risk after discharge (2). An increasing trajectory of NT-proBNP is directly associated with cardiovascular mortality and rehospitalizations. Absolute values and reduction of NT-proBNP at discharge have significant prognostic value, with higher levels and insufficient reduction being associated with increased 180-day mortality (12). ESC guidelines recommend measuring them both on admission and before discharge (9). These data help identify high-risk patients and guide more intensive management after discharge.

In addition to them, other biomarkers such as CA125 and adrenomedullin may have a complementary role in the future (13).

Hemoconcentration, which reflects a relative decrease in plasma volume, is associated with a better prognosis (14) while natriuresis and diuresis, used to assess the response to diuretics, determines the early efficacy of decongestant therapy (2).

Among the monitoring markers of organ damage, including renal, hepatic parameters, and cardiac troponin, pre-discharge renal function parameters are of particular importance, as they are crucial for the use of Renin-Angiotensin-Aldosterone system inhibitor therapies (2).

Imaging Evaluation

In the pre-discharge phase, comprehensive imaging plays an important role in identifying residual congestion. Chest radiography can help detect pulmonary congestion and pleural effusions, as well as assess response to treatment, while the main methods for assessing congestion include echocardiography, lung ultrasound (LUS), and inferior vena cava (IVC) assessment (15).

Parameters such as E/e', mitral valve velocities, and left atrial volume are used to estimate left ventricular filling pressures, but in acute practice, they have more limited sensitivity (2). Likewise, the severity of mitral regurgitation and the velocity of tricuspid regurgitation may aid in a multiparametric approach to assessing response to treatment and residual congestion.

LUS and IVC are simple bedside methods that quickly reflect volume status; dilated IVC with low collapsibility is associated with a higher risk of rehospitalization (16). The number of B-lines correlates with the degree of pulmonary congestion and is strongly associated with prognosis, with ≥ 15 B-lines at discharge being associated with a more than fivefold increase in the risk of rehospitalization or death (16).

The importance of using a multimodal approach based on clinical, laboratory, and imaging evaluation to identify subclinical congestion is particularly important, as this form of congestion is not identified by physical examination of the patient alone (9).

Optimization of Pharmacological Therapy *Towards an Intensive and Rapid Strategy*

Hospitalization represents a window of opportunity for GDMT optimization, with early initiation of the four therapeutic pillars once clinical stability is achieved, with particular emphasis on SGLT2 inhibitors due to their safety and ease of use. The high-intensity strategy, supported by the STRONG-HF study, recommends rapid dose titration in the first weeks after discharge, avoiding clinical inertia associated with worse outcomes. This process requires close and structured monitoring, while slight changes in renal function or blood pressure should not lead to unnecessary interruption of therapy (9).

Advances in Emerging Therapies for Heart Failure

Recent evidence has significantly expanded therapeutic options for patients with heart failure across the entire ejection fraction spectrum, including both HFrEF and HFpEF. This has led to a more unified treatment approach, with several drug classes showing benefits in reducing mortality and rehospitalizations regardless of disease phenotype, reinforcing the importance of a comprehensive and personalized management strategy.

• SGLT2 inhibitors and new MRAs

SGLT2 inhibitors (dapagliflozin and empagliflozin) are now standard therapy in heart failure regardless of ejection fraction and are associated with reductions in mortality and rehospitalizations. Their benefits are related not only to the diuretic effect, but also to more complex mechanisms such as metabolic modulation, anti-inflammatory effects, and improvement of cardiac and renal hemodynamics (17, 18). An important innovation is the use of Finerenone in patients with HF with preserved EF, with a 16% reduction in mortality, offering a safer profile regarding hyperkalemia compared to spironolactone (19).

• Incretin Therapies for the Obese Phenotype

Obesity is a key driver of HFpEF development, playing an important role in both pathogenesis and worsening of clinical course. It contributes through complex mechanisms that include chronic systemic inflammation, endothelial dysfunction, increased circulating volume and hemodynamic load, and the development of

ventricular hypertrophy and rigidity. Also, obesity is often associated with other comorbidities such as hypertension, diabetes, and metabolic syndrome, which further amplify the risk for HFpEF and make its management more difficult clinically. Recent studies (STEP-HFpEF) have shown that semaglutide and tirzepatide significantly improve quality of life, reduce body weight, and reduce the risk of death or rehospitalization by 38% in obese patients with HF (20).

• *Other Therapies and Glycosides*

Vericiguat, a guanylate cyclase stimulator, is recommended for patients with HFrEF who have had a recent exacerbation (21).

The DIGIT-HF study has shown that digitoxin reduces mortality and rehospitalizations by 18% in patients with HFrEF already receiving standard treatment (22).

Treatment of iron deficiency with ferric carboxymaltose remains a key recommendation to improve functional capacity and reduce rehospitalizations (23).

Technological Innovations and Device Interventions

Technology has revolutionized monitoring during the vulnerable phase. The CardioMEMS system, which measures pulmonary artery pressure remotely, has proven effective in reducing rehospitalization and improving quality of life in real-world settings (24).

Also, transcatheter valvular interventions (TEER) for mitral and tricuspid regurgitation

have shown consistent benefits in survival and symptom reduction (25).

Cardiac rehabilitation remains a cornerstone, which can now also be provided through telemonitoring, increasing access for frail patients (10).

CONCLUSIONS

Successful management of the vulnerable phase requires a paradigm shift: from isolated treatment of symptoms to an integrated strategy that includes thorough decongestion, early initiation of the four pillars of GDMT, and rigorous multidisciplinary follow-up.

The integration of new drugs (finerenone, incretin) and remote monitoring technologies offers new hope for breaking the cycle of repeated hospitalizations and improving the long-term prognosis for patients with heart failure. The main challenge remains the implementation of this evidence in our daily practice, where close coordination between the hospital physician, the family physician, and ongoing patient education is key to the success of this critical transition.

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