EDITORIAL

"HFrEF has now become a chronic condition, and heart failure patients who used to die shortly after the onset of symptoms are nowadays followed up by their physicians for decades. A typical heart failure patient journey is characterized by long periods of stability interrupted by progressive or abrupt episodes of decompensation with worsening of dyspnea, fatigue, and evidence of sodium and water retention and/or of low cardiac output."

Improving heart failure care throughout the patient's journey

by M. Komajda, *France*

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Heart failure is a common condition whose prevalence is increasing across the world and which is associated with poor prognosis and quality of life.[1] The two main subcategories of this syndrome show a remarkable asymmetry regarding treatment strategies: in heart failure with reduced ejection fraction (HFrEF), evidence-based management strategies are available following the positive results of large clinical outcome trials. These strategies include angiotensin-converting enzyme (ACE) inhibitors, β-adrenergic blockers, angiotensin-receptor blockers (ARBs), mineralocorticoid receptor antagonists, ivabradine, and angiotensin receptor/neprilysin inhibitors.[2-7] In addition, nonpharmacological measures such as cardiac resynchronization therapy and implantable cardiac defibrillators have also been shown to reduce mortality in HFrEF with wide QRS duration (cardiac resynchronization therapy) or in HFrEF of ischemic etiology (implantable cardiac defibrillators).[8,9]

The contrast is striking for heart failure with preserved ejection fraction (HFpEF) where no treatment has convincingly been shown to reduce mortality. HFpEF appears to be a heterogeneous condition and the only benefit observed so far is a borderline reduction in heart failure hospitalizations with the ARB candesartan[10] and with spironolactone,[11] though the trial for the latter was criticized for showing considerable geographic heterogeneity in the rate of clinical events.

The secular trends in all-cause and disease-related mortality show a sharp reduction in HFrEF thanks to the available treatment armamentarium: when the landmark trials tested ACE inhibitors in heart failure in the early 90s, the annual mortality rate was between 15% and 20%. However, in the most recent HFrEF trials, the annual rate of fatal events was below 10%. This holds true not only for randomized clinical trials where patients are selected, but also in the general population as suggested by a study performed in several European countries, which demonstrated a uniform reduction in the rate of disease-related deaths.[12]

As a result, HFrEF—which was a condition with high short-term mortality due to pump failure or sudden cardiac death—has now become a chronic condition, and heart failure patients who used to die shortly after the onset of symptoms are nowadays followed up by their physicians for decades. A typical heart failure patient journey is characterized by long periods of stability interrupted by progressive or abrupt episodes of decompensation with worsening of dyspnea, fatigue, and evidence of sodium and water retention and/or of low cardiac output. The current dilemma of HFrEF is therefore about reducing lengthy (10 days on average in Eu-

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rope) and recurrent hospitalizations, which are associated with a very poor quality of life. The heart failure patient's journey is made up of three different phases: the chronic phase, the decompensation phase, and the postdischarge vulnerable phase.

The chronic phase

The chronic phase is characterized by clinical stability in terms of signs, symptoms, and management strategies. During the stable phase, patients do not exhibit any significant change in physical limitation but physicians should, however, regularly look for nonclinical indicators of progressive degradation such as a progressive increase in N-terminal pro-BNP or in Doppler-assessed pulmonary pressure or a reduction in ejection fraction.

This period should also be an opportunity to review the treatment of these "stable" patients. Adherence to guideline-recommended therapies both in terms of class of medication and of dosage is a strong predictor of improved outcomes, including mortality and rehospitalization: in a recent large observational study of HFrEF outpatients conducted in thirty three countries, the rate of prescription of recommended medications was rather satisfactory, but underdosage was widely observed, and when we used a scoring system including both recommended classes and dosage, poor adherence to guidelines was a strong predictor of poor outcomes at six months.[13] The key message to physicians is therefore: *do not rely only on signs and symptoms that have a low sensitivity and regularly review the prescription in order to see if it matches the patient's condition.*

The decompensation phase usually leads to hospitalization

In the majority of cases, decompensation occurs in patients with a known history of heart failure (acute or chronic) whereas de novo heart failure is less common. The recent guidelines of the European Society of Cardiology distinguish three steps in the work up of acute heart failure: (i) identify critical conditions such as cardiogenic shock or respiratory failure that require urgent management; (ii) identify potentially curable underlying causes such as acute coronary syndrome, pulmonary embolism, hypertensive crisis or acute mechanical disorder, all conditions that require urgent specific procedures; (iii) categorize patients based on the presence/absence of congestion (wet/dry) and of preserved/reduced perfusion (warm/cold). The vast majority of patients referred to the hospital for decompensation are "wet." During the hospital phase, acute symptomatic management is the first step based on the clinical profile described above. In most instances congestion improves following the use of high doses of intravenous loop diuretics, and intravenous inotropes can revert reduced peripheral perfusion. However, we are lacking evidence of the benefit of any of these classes of drugs and, in particular, several trials suggest that the use of intravenous inotropes is associated with increased mortality, particularly in heart failure of ischemic origin.[14] Recent attempts with the human recombinant natriuretic peptide nesiritide, ularitide—another natriuretic peptide—and with the vasodilator serelaxin have shown no benefit on postdischarge clinical outcomes and, for some drugs, clinically questionable improvements in dyspnea in hospital.[14-16]

Aside from improving signs and symptoms in critically disabled patients as quickly as possible, two important measures should be taken during the hospital phase:

- Identify precipitating factors—such as poor compliance or failure to adequately follow a low-salt diet—and enroll patients in educational schemes whenever possible. Patient education has been shown to improve long-term outcomes and in particular to reduce rehospitalizations for heart failure. These schemes should include a description of the goal of treatment, of the treatments available with their potential side effects, and of the warning signs of decompensation.
- Initiate evidence-based medications and organize the postdischarge phase: observational studies suggest that this step is not executed optimally in many instances. Patients tend to be discharged with high doses of diuretic agents and low doses of life-saving medications. The coordination of care management with health care professionals downstream of the hospitalization (general practitioners, heart failure nurses, dieticians…) is often poorly organized and leads to *"postdischarge inertia"* resulting in early rehospitalizations.

The postdischarge vulnerable phase

The postdischarge vulnerable phase covers the three to six months that follow a hospitalization for heart failure. It is termed "vulnerable" because it is associated with a high mortality and rehospitalization rate. One of the main causes of this unstable phase is the "postdischarge inertia" mentioned above. If no measure is taken to ensure that a patient discharged from hospital has early appointments with health care professionals in order to reassess his/her condition and uptitrate the recommended drugs, the patient's treatment regimen remains what it was at discharge—ie, high doses of loop diuretics and low doses of disease-modifying drugs. In a survey performed in the departments of cardiology of the greater Paris University, the average time to first postdischarge visit was 45 days, regardless of the type of physician, and in more than 20% of

Selected abbreviations and acronyms

ACE	angiotensin-converting enzyme
ARB	angiotensin receptor blocker
HFpEF	heart failure and preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction

cases no visits were planned.[17] The important message here is that heart failure patients should be carefully followed up after a hospitalization for heart failure and that organizational schemes should be implemented accordingly in order to ensure that optimal therapy is provided and that the rate of early rehospitalizations is reduced. This index is nowadays used in many US hospitals as a quality measure. Specifically, ivabradine has been shown to reduce the incidence of clinical events during the vulnerable phase when administered chronically.[18] This observation suggests that all disease-modifying drugs matching a specific patient's clinical profile should be initiated early during the course of his/her journey.

In summary, significant progress has been made in the management of HFrEF, specifically with regard to mortality. Several challenges remain, including management of HFpEF and of acute heart failure, and reducing early rehospitalizations. The way to reduce the burden of rehospitalizations includes patient education, improved postdischarge organization, and implementation of guidelines-recommended therapies both in terms of classes and dosage. All these measures require proper cooperation and communication between the various professionals who take care of heart failure patients and should lead to a better life for the many patients affected by this condition. ■

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