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STATE-OF-THE-ART PAPER

# Rehospitalization for Heart Failure

## Problems and Perspectives

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**With a prevalence of 5.8 million in the United States alone, heart failure (HF) is associated with high morbidity, mortality, and healthcare expenditures. Close to 1 million hospitalizations for heart failure (HHF) occur annually, accounting for over 6.5 million hospital days and a substantial portion of the estimated $37.2 billion that is spent each year on HF in the United States. Although some progress has been made in reducing mortality in patients hospitalized with HF, rates of rehospitalization continue to rise, and approach 30% within 60 to 90 days of discharge. Approximately half of HHF patients have preserved or relatively preserved ejection fraction (EF). Their post-discharge event rate is similar to those with reduced EF. HF readmission is increasingly being used as a quality metric, a basis for hospital reimbursement, and an outcome measure in HF clinical trials. In order to effectively prevent HF readmissions and improve overall outcomes, it is important to have a complete and longitudinal characterization of HHF patients. This paper highlights management strategies that when properly implemented may help reduce HF rehospitalizations and include adopting a mechanistic approach to cardiac abnormalities, treating noncardiac comorbidities, increasing utilization of evidence-based therapies, and improving care transitions, monitoring, and disease management. (J Am Coll Cardiol 2013;61:391–403) © 2013 by the American College of Cardiology Foundation**

Heart failure (HF) is the most common cause of hospitalization in patients over the age of 65, resulting in 6.5 million hospital days in the United States annually (1). In outpatients with chronic HF, a hospitalization is one of the strongest prognostic predictors for increased mortality. Unplanned readmissions also have a heavy associated financial burden and cost Medicare $17.4 billion annually, with HF being the largest contributor (2). Worsening chronic HF resulting in hospitalization may be associated with cardiac and/or renal injury that can contribute to progression of HF.

Heart failure is not a disease, but a manifestation of diverse cardiac and noncardiac abnormalities (3). A distinction should be made between outcomes in outpatients with chronic HF and patients with hospitalization for HF (HHF). In outpatients with HF, prognosis has significantly improved in the last 20 years, given the advent of therapies such as angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs), beta-blockers, mineralocorticoid receptor antagonists (MRAs), and implantable cardioverter-defibrillator (ICD)/cardiac resynchronization therapy devices (CRT). By contrast, patients with HHF continue to have a mortality and readmission rate approaching 15% and 30%, respectively, within 30 to 60 days post-discharge (3). HHF patients have only been characterized in the past decade through registries and trials (4,5), which highlighted the fact that the clinical course and prognosis of these patients differs from that of outpatients with chronic HF.

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## Patient Characterization and Clinical Course

**Definition.** HHF is defined as new-onset or worsening (gradual or rapid) signs and symptoms of HF that require urgent therapy and result in hospitalization (3). HHF comprises patients with: 1) worsening chronic HF (~80%); 2) de novo HF (15%); and 3) advanced or end-stage HF (5%). Traditionally, HHF was not viewed as a distinct entity, but rather a more severe manifestation of chronic HF. However, the majority of HHF patients do not have advanced HF because they respond well to in-hospital therapies. They can be distinguished from patients with

**Abbreviations and Acronyms**

**ACE** = angiotensin-converting enzyme
**ARB** = angiotensin receptor blocker
**CAD** = coronary artery disease
**COPD** = chronic obstructive pulmonary disease
**CRT** = cardiac resynchronization therapy
**ED** = emergency department
**EF** = ejection fraction
**HFpEF** = heart failure with preserved ejection fraction
**HFrEF** = heart failure with reduced ejection fraction
**HHF** = hospitalization for heart failure
**ICD** = implantable cardioverter defibrillator
**LV** = left ventricle/ventricular
**MRA** = mineralocorticoid receptor antagonist

chronic HF by having very abnormal hemodynamic, neurohormonal, and electrolyte abnormalities, often associated with troponin release and rapidly worsening renal function (6). In contrast to outpatients, HHF patients have a very high post-discharge mortality and rehospitalization rate that has not improved in the last 2 decades despite all the available therapies (5,7) (Fig. 1). Unfortunately, trials conducted to date have focused on improving signs and symptoms during hospitalization with short-term therapies, rather than improving post-discharge outcomes (8–10).

**Patient characteristics.** Approximately 50% of HHF patients have preserved or relatively preserved ejection fraction (HFpEF). Table 1 depicts characteristics of patients with HFpEF and with HF with reduced ejection fraction (HFrEF) (4).

The majority of patients are normotensive or hypertensive at presentation (11). Irrespective of ejection fraction (EF), the majority have signs of congestion such as dyspnea, jugular venous distention, and edema. Almost all are initially treated with intravenous diuretics, and few receive intravenous vasodilators or inotropes.

## Outcomes

**Length of stay.** Among HHF patients, the median length of stay is 4.0 days (25th to 75th interquartile range, 3.0 to 7.0 days), and mean length of stay is 6.4 ± 85.2 days in the United States (4).

**Rehospitalization at 30 days.** Among Medicare beneficiaries hospitalized with HF, 27% are rehospitalized within 30 days, and 37% of these rehospitalizations are for HF (2,12,13). In the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) trial, 24% of HHF patients randomized in the United States were readmitted within 30 days of discharge (5) despite the fact that the majority were treated with evidence-based treatments and had early post-discharge visits. In this trial, 48% of all hospitalizations were HF related, 14% were cardiovascular, and 38%, noncardiovascular (Fig. 2). These numbers were considerably different outside of the United States and varied by geographical location (2,14).

**Rehospitalization beyond 30 days.** In the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry, rates of rehospitalization were 30% at 60 to 90 days post-discharge (4). The rates of rehospitalization in patients with HFpEF were similar when compared with those with HFrEF (4,15). Approximately half of the rehospitalizations were not related to HF (5). Table 2 depicts characteristics of patients in the United States rehospitalized within 3 months post-discharge.

**Mortality.** In-hospital mortality for HHF is 2% to 7%, but as high as 20% in patients with severe renal impairment and/or low systolic blood pressure (representing 2% to 5% of all HHF patients). Mortality rates 60 to 90 days post-discharge vary from 5% to 15% (4,5). In the EVEREST trial, 40% of post-discharge deaths were from HF, and 30% were related to sudden cardiac death (5) (Fig. 3). Patients with HFpEF have similar rates of post-discharge mortality compared with those with HFrEF, but the mode of death may differ (4,15).

**Prognostic markers.** Predictors of prognosis include a systolic blood pressure <120 mm Hg at presentation (11,16), presence of coronary artery disease (CAD) (17), hyponatremia (18), renal impairment (6), troponin release (17,19), and ventricular dyssynchrony (QRS duration ≥120 ms) (20). In the early post-discharge period, changes in body weight, signs and symptoms of congestion (21), worsening renal function, and elevation of natriuretic peptides are correlated with readmissions (22) (Table 3). Predictors for readmission are different than those for mortality; systolic blood pressure predicts mortality, whereas an increase in body weight predicts rehospitalization (11,23) (Fig. 4).

Although biomarkers may be useful in helping with diagnosis, prognosis, and management of HHF, their interpretation should account for the presence of cardiac and noncardiac comorbidities such as CAD, atrial fibrillation, chronic obstructive pulmonary disease (COPD), and renal dysfunction (24).

**Precipitants of rehospitalization.** Precipitants for HHF (25) include cardiac factors such as myocardial ischemia, atrial fibrillation, and uncontrolled hypertension; noncardiac factors, such as exacerbation of COPD and infections (Table 4); patient-related factors, such as medication nonadherence, dietary indiscretion, and drug and alcohol abuse; iatrogenic factors, such as use of nonsteroidal anti-inflammatory drugs; and system-related factors, including inadequate access to follow-up care and medications, limited access to low-sodium foods, and poor transitions of care (Table 5).

## Pathophysiology Leading to Rehospitalization

**Congestion.** The main reason for HF readmission is congestion and not low cardiac output (26). However, conges-

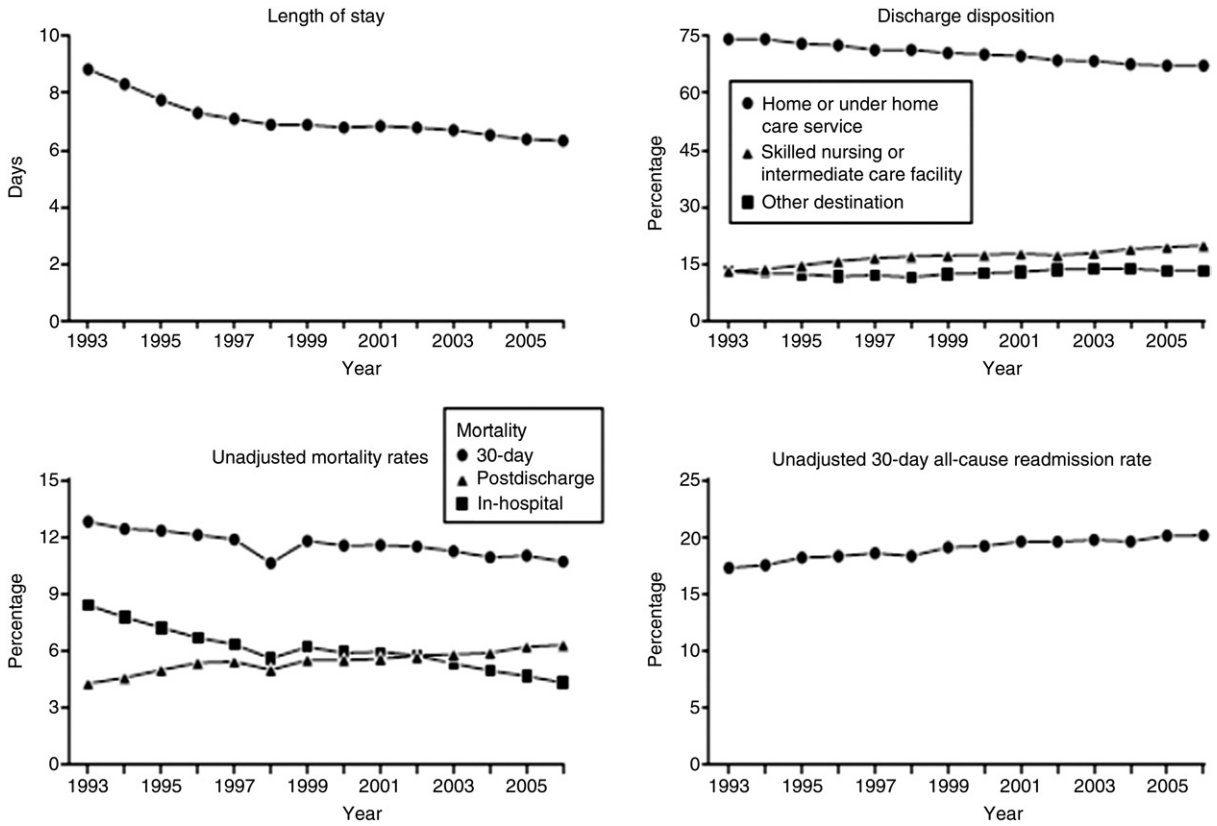


**Figure 1** **Hospitalization for HF in the United States**

Secular trends for length of stay, discharge disposition, unadjusted mortality, and 30-day all-cause readmission rates in Medicare fee-for-service patients hospitalized for heart failure (HF) between 1993 and 2006. Due to their small size, error bars (95% confidence intervals) are included within the size of the data markers. Reproduced, with permission, from Bueno et al. (77).

tion related to high left ventricular (LV) filling pressures may be the result of diverse cardiac abnormalities (e.g., myocardial infarction, valvular disease, arrhythmias). Often, congestion develops gradually before admission. In the outpatient setting, patients may have elevated LV filling pressures in the absence of congestion (dyspnea, jugular venous distention, or edema). This subclinical congestion (26) may precede clinical congestion by days to weeks or be present at discharge (22,27).

Elevated LV filling pressures may contribute to progression of HF by causing subendocardial ischemia/injury (26), altered LV geometry resulting in secondary mitral regurgitation, further activation of the renin-angiotensin-aldosterone system, stimulation of inflammatory mediators, and worsening renal function due to increased venous pressures.

Because congestion is the single most important contributor to readmission, it is important to recognize that many patients after discharge may be "flying under the radar," without clinical congestion, but with elevated LV filling pressures often reflected by the high levels of natriuretic peptides (22).

## Assessment

At presentation, utilizing the 6-axis model (28), patients can be appropriately managed on the basis of limited data. The 6-axis model is a set of easily obtainable parameters (clinical severity, de novo or chronic HF, blood pressure, comorbidities, precipitants, and heart rate/rhythm), each with independent clinical relevance. Severity of HF at the presentation does not correlate with post-discharge outcomes.

Once patients are stabilized, their cardiac structure and function should be evaluated (28). Echocardiography with Doppler should define LV function, left atrial size, presence and severity of mitral regurgitation, pulmonary arterial pressures, and wall motion abnormalities. The extent and severity of CAD should be assessed by invasive and noninvasive testing. Viable, but dysfunctional, myocardium should be assessed, using cardiac magnetic resonance imaging, dobutamine stress echocardiography, single-photon emission computed tomography, or positron emission tomography, and will indicate the potential for myocardial recovery in patients with or without CAD (29,30).

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**Table 1** Baseline Patient Characteristics, HF History, and Findings on Admission by Ventricular Function

| Characteristics at Admission | Patients With LVSD (n = 20,118) | Patients With PSF (n = 21,149) | p Value (LVSD vs. PSF) | Patients With 40% ≤ EF ≤50% (n = 7,321) | Patients With EF >50% (n = 10,072) | p Value (40% ≤ EF ≤50% vs. EF >50%) |
|---|---|---|---|---|---|---|
| Demographics | | | | | | |
| Age, yrs | 70.4 ± 14.3 | 75.1 ± 13.1 | <0.0001 | 74.3 ± 13.0 | 75.6 ± 13.1 | <0.0001 |
| Male | 62 | 38 | <0.0001 | 48 | 32 | <0.0001 |
| Caucasian | 71 | 77 | <0.0001 | 78 | 77 | 0.086 |
| African American | 21 | 15 | <0.0001 | 15 | 15 | 0.88 |
| Medical history | | | | | | |
| Diabetes, insulin-treated | 15 | 17 | <0.0001 | 18 | 16 | 0.013 |
| Diabetes, noninsulin-treated | 24 | 26 | 0.009 | 26 | 25 | 0.418 |
| Hypertension | 66 | 76 | <0.0001 | 74 | 77 | <0.0001 |
| Hyperlipidemia | 34 | 32 | <0.0001 | 35 | 31 | <0.0001 |
| Atrial arrhythmia | 28 | 33 | <0.0001 | 33 | 32 | 0.179 |
| Vital signs on admission | | | | | | |
| Body weight, kg | 78.5 [65.8–94.0] | 78.9 [64.0–97.5] | 0.019 | 79.4 [65.0–97.5] | 78.0 [63.5–97.1] | 0.002 |
| Heart rate, beats/min | 89 ± 22 | 85 ± 21 | <0.0001 | 86 ± 21 | 84 ± 21 | <0.0001 |
| SBP, mm Hg | 135 ± 31 | 149 ± 33 | <0.0001 | 147 ± 33 | 150 ± 33 | <0.0001 |
| DBP, mm Hg | 77 ± 19 | 76 ± 19 | <0.0001 | 77 ± 19 | 75 ± 19 | <0.0001 |
| Etiology | | | | | | |
| Ischemic | 54 | 38 | <0.0001 | 49 | 32 | <0.0001 |
| Hypertensive | 17 | 28 | <0.0001 | 22 | 31 | <0.0001 |
| Idiopathic | 18 | 21 | <0.0001 | 18 | 23 | <0.0001 |
| Findings on admission | | | | | | |
| Acute pulmonary edema | 3 | 2 | 0.27 | 2 | 3 | 0.362 |
| Chest pain | 23 | 24 | 0.512 | 24 | 24 | 0.618 |
| Uncontrolled hypertension | 9 | 12 | <0.0001 | 11 | 12 | 0.075 |
| Dyspnea at rest | 44 | 44 | 0.194 | 46 | 44 | 0.022 |
| Dyspnea on exertion | 63 | 62 | 0.206 | 62 | 62 | 0.719 |
| Rales | 63 | 65 | 0.001 | 67 | 63 | <0.0001 |
| Lower extremity edema | 62 | 68 | <0.0001 | 68 | 68 | 0.211 |
| Jugular venous pulsation | 33 | 26 | <0.0001 | 32 | 29 | 0.0005 |
| Left ventricular EF | 24.3 ± 7.7 | 54.7 ± 10.2 | <0.0001 | 45.0 ± 4.0 | 61.8 ± 7.0 | <0.0001 |
| Laboratory values | | | | | | |
| Serum sodium, mEq/l | 137.7 ± 4.6 | 137.9 ± 4.8 | <0.0001 | 137.9 ± 4.7 | 137.8 ± 4.8 | 0.09 |
| Serum creatinine, mg/dl | 1.4 [1.1–1.9] | 1.3 [1.0–1.8] | <0.0001 | 1.3 [1.0–1.9] | 1.2 [1.0–1.8] | <0.0001 |
| Serum hemoglobin, g/dl | 12.5 ± 2.0 | 11.9 ± 2.0 | <0.0001 | 11.9 ± 2.0 | 11.8 ± 2.0 | 0.0001 |
| BNP, pg/ml | 1,170.0 [603.0–2,280.0] | 601.5 [320.0–1,190.0] | <0.0001 | 757.0 [400.0–1,460.0] | 537.0 [287.0–996.5] | <0.0001 |
| Troponin I, ng/ml | 0.1 [0.1–0.3] | 0.1 [0.0–0.3] | <0.0001 | 0.1 [0.1–0.3] | 0.1 [0.0–0.3] | <0.0001 |
| Medications on admission | | | | | | |
| ACE inhibitor | 45 | 36 | <0.0001 | 38 | 34 | <0.0001 |
| ARB | 11 | 13 | <0.0001 | 12 | 14 | 0.0001 |
| Amlodipine | 5 | 10 | <0.0001 | 9 | 11 | <0.0001 |
| Aldosterone antagonist | 10 | 5 | <0.0001 | 6 | 4 | <0.0001 |
| Beta-blocker | 56 | 52 | <0.0001 | 54 | 50 | <0.0001 |
| Loop diuretic | 63 | 58 | <0.0001 | 59 | 57 | 0.039 |
| Digoxin | 30 | 17 | <0.0001 | 19 | 15 | <0.0001 |
| Aspirin | 42 | 38 | <0.0001 | 41 | 36 | <0.0001 |
| Antiarrhythmic | 13 | 8 | <0.0001 | 10 | 8 | <0.0001 |
| Hydralazine | 3 | 3 | 0.021 | 3 | 3 | 0.346 |
| Nitrate | 22 | 21 | 0.013 | 23 | 20 | <0.0001 |
| Statin* | 40 | 39 | 0.021 | 41 | 37 | <0.0001 |

Values are mean ± SD, %, or median [interquartile range]. Reproduced, with permission, from Fonarow et al. (4). *Statin use among patients with coronary artery disease, cerebrovascular disease/transient ischemic attack, diabetes, hyperlipidemia, or peripheral vascular disease.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BNP = B-type natriuretic peptide; DBP = diastolic blood pressure; EF = ejection fraction; HF = heart failure; LVSD = left ventricular systolic dysfunction; PSF = preserved systolic function; SBP = systolic blood pressure.

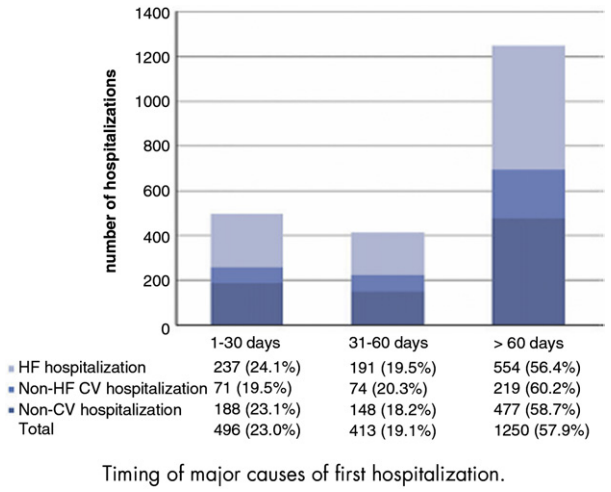


**Figure 2** **Rehospitalization After an Admission for HF**

The number of hospitalizations within 30 days, 31 to 60 days, and more than 60 days after a hospitalization for heart failure (HF) in the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) trial. The reasons for hospitalization are represented in each **bar**. Non-CV hospitalization = noncardiovascular hospitalization; Non-HF CV hospitalization = non-heart failure cardiovascular hospitalization. Figure reproduced, with permission, from O'Connor et al. (5).

Before hospital discharge, signs and symptoms of congestion should be reassessed both at rest and during activity (31), and natriuretic peptide levels measured (32). Patient and family education and assurance that the patient is receiving all evidence-based therapies are essential (1).

## Reducing Readmissions

**Managing congestion.** Prevention of clinical and subclinical congestion is essential to reduce rehospitalization rates. Sodium restriction remains the cornerstone of fluid management, especially in the post-discharge period. Loop diuretic therapy remains the mainstay of congestion management despite the advent of novel and largely untested therapies such as ultrafiltration, vasopressin antagonists, and adenosine-blocking agents (33). Because the goal is to reduce intravascular volume, it is important to consider the mechanism of fluid removal, composition of fluid removed, and whether the reduction is intravascular or extravascular. Although diuretic therapy may worsen renal function during hospitalization, this should not deter aggressive fluid management, as renal impairment may be transient and not represent kidney injury (6). In fact, ACE inhibitors or ARBs may show mortality benefit even though they may also worsen renal function (34).

Most patients experience a significant improvement in clinical congestion during hospitalization, but many have persistent evidence of subclinical congestion. Elevated natriuretic peptide levels at the time of discharge serve as a poor prognostic feature (22) and may warrant further investigation into persistent congestion via dynamic testing (orthopnea, 6-min walk, and so on). Initial and mainte-

**Table 2** **Select Baseline Characteristics for U.S. EVEREST Patients (n = 1,139 [27.6%])**

| Variable | CV Hospitalization <3 Months | CV Hospitalization 3–12 Months | No CV Hospitalization at 1 Year | p Value |
|---|---|---|---|---|
| Patients | 440 (38.6) | 403 (35.4) | 296 (26.0) | |
| Age, yrs | 69 [59–77] | 69 [59–77] | 66 [55.5–77] | 0.101 |
| Male | 323 (73.4) | 308 (76.4) | 218 (73.6) | 0.555 |
| Previous HF hospitalization | 383 (87.2) | 313 (78.1) | 214 (72.5) | <0.001 |
| CAD | 353 (80.2) | 323 (80.3) | 206 (69.8) | 0.001 |
| Previous MI | 257 (58.4) | 233 (58.1) | 133 (44.9) | <0.001 |
| Mitral valve disease | 253 (57.8) | 192 (48.1) | 122 (41.5) | <0.001 |
| Diabetes | 239 (54.3) | 205 (51) | 146 (49.3) | 0.378 |
| Renal insufficiency | 247 (56.3) | 184 (45.8) | 101 (34.1) | <0.001 |
| COPD | 94 (21.4) | 65 (16.2) | 54 (18.2) | 0.151 |
| Orthopnea | 296 (70.5) | 232 (59.3) | 188 (66.2) | 0.004 |
| Supine SBP, mm Hg | 113.5 ± 17.7 | 118.3 ± 19.9 | 119.6 ± 20.5 | <0.001 |
| Supine DBP, mm Hg | 66 ± 12.4 | 67.4 ± 13.2 | 68.9 ± 13.3 | 0.01 |
| LVEF, % | 23.3 ± 8.6 | 24.8 ± 8.5 | 25.6 ± 8.4 | 0.001 |
| QRS, ms | 136.2 ± 37.3 | 133.5 ± 35.9 | 124.2 ± 33.1 | <0.001 |
| Sodium, mEq/l | 138.4 ± 4.5 | 139 ± 4 | 139.4 ± 4.4 | 0.009 |
| BUN, mg/dl | 39.7 ± 22.4 | 34 ± 17.7 | 29.4 ± 15.7 | <0.001 |
| Creatinine, mg/dl | 1.6 ± 0.5 | 1.5 ± 0.5 | 1.4 ± 0.5 | <0.001 |
| Aldosterone, ng/dl | 22.6 ± 30.6 | 14.3 ± 17 | 12.7 ± 13.3 | <0.001 |
| AVP, pg/dl | 2.8 [2.8–6.7] | 2.8 [2.8–6.3] | 2.8 [2.8–5.7] | 0.043 |
| BNP, pg/dl | 1,356.2 [622.5–2,454.6] | 1,059.5 [457.2–2,072.9] | 695.2 [243.7–1,439.2] | <0.001 |
| N-terminal proBNP, pg/dl | 7,170 [3,381–13,507] | 4,962.5 [2,070–11,942] | 3,710 [1,752–6,934] | <0.001 |

Values are n (%), median (interquartile range), or mean ± SD. The baseline characteristics for the U.S. EVEREST patients who were followed for or hospitalized during the first year after randomization are shown by occurrence and time of cardiovascular hospitalization.

AVP = arginine vasopressin; BUN = blood urea nitrogen; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CV = cardiovascular; EVEREST = Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan; LVEF = left ventricular ejection fraction; MI = myocardial infarction; other abbreviations as in Table 1.

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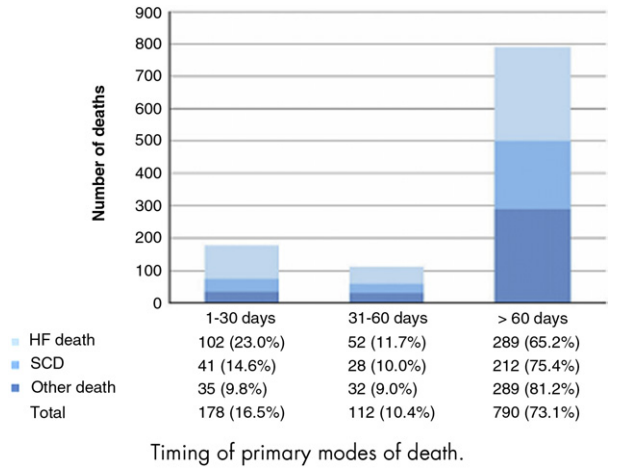


**Figure 3** **Mode of Death After a HHF**

The number of deaths within 30 days, 31 to 60 days, and more than 60 days after a hospitalization for heart failure in the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) trial. Their mode of death is represented in each **bar**. HF death = death from heart failure; SCD = sudden cardiac death. Reproduced, with permission, from O'Connor et al. (5).

nance diuretic dosing strategies (35) should be guided by supine and orthostatic blood pressure measurement and renal function (32,35). Metolazone, a long-acting thiazide-like diuretic, may be used in patients who are unresponsive to initial therapies, but carries a significant risk of hyponatremia. MRAs may be particularly useful, given recent data demonstrating that they significantly reduce the early hospitalization rate (36,37). For patients presenting with hyponatremia, relative hypotension, and/or impaired renal function, tolvaptan, a vasopressin antagonist, should be considered although its long-term effects remain to be determined (38,39).

**Nondiuretic therapies.** Despite improving national trends, a gap persists between cardiovascular guideline recommendations (1) and clinical practice in HF (7). This gap has been the target of current performance measures (40). However, the current performance measures may not be sufficient to improve post-discharge outcome of such a complex condition (40). Patients with HFrEF should receive recommended doses of ACE inhibitors/ARBs, beta-blockers, and MRAs. Data regarding nondiuretic therapies are limited in the setting of hospitalization in patients with HFpEF. Although there is ample evidence of long-term beneficial effects of MRAs on survival and hospitalization rates in HFrEF (41,42), a recent study reported that under one-third of eligible patients who were hospitalized with HF received MRAs at discharge (42). This may be related to the need to monitor serum potassium and renal function in patients receiving these agents.

Hydralazine/nitrate therapy is recommended for African Americans with HFrEF (43). Candidates for revascularization should be identified, and in appropriate patients, discussions regarding device therapies (ICDs and CRT) should occur (1). Although not tested, digoxin possesses many desirable attributes for patients with HHF, given its hemodynamic, neurohormonal, and electrophysiological effects (44). The DIG (Digitalis Investigators Group) trial demonstrated that digoxin, when added to diuretics and ACE inhibitors in patients with chronic HF in sinus rhythm, decreases hospitalizations without adversely affecting survival (45). The DIG ancillary trial assessed the effects of digoxin in patients with HFpEF and showed reduction in HF-related hospitalizations only at 2 years of follow-up (46). It is important to note that data are currently lacking regarding the utility of digoxin in HHF patients. Potentially deleterious agents in HF that are viewed as benign by patients, such as nonsteroidal anti-inflammatory drugs and nasal decongestants, should be avoided.

**A mechanistic approach.** Because HF can be caused by diverse cardiac abnormalities, every attempt should be made to identify specific cardiac abnormalities that contribute to HF (Fig. 5).

**Myocardium.** In patients with HFrEF, the identification of potentially recoverable (viable, but dysfunctional) myocardium is important for prognostic and therapeutic reasons in patients with and without CAD (29,30). Data from a large quality improvement study revealed a third of patients showed an improvement in LVEF from 25% to 46% over a 24-month period after a multidimensional practice-specific treatment approach (47). Clinical decision support tools, chart audits with regular feedback, and other interventions were used to optimize adherence to guideline recommendations in this study. Potential for myocardial recovery was traditionally performed only in patients with CAD to detect stunned or hibernating myocardium to determine utility of revascularization. However, myocardial viability has been shown to predict recovery even in patients without CAD (29,30).

**Coronary arteries.** HHF patients with CAD are at higher risk for mortality and rehospitalization than those without

**Table 3** **Prognostic Value of Individual Elements of the 1-Week Follow-Up Examination**

| 1-Week Follow-Up Components* | IDI Increase (%) | p Value for IDI Increase† |
|---|---|---|
| BNP | 5.5 | <0.001 |
| KCCQ | 3.2 | <0.001 |
| Pedal edema | 2.9 | <0.001 |
| Rales | 2.2 | <0.001 |
| Anemia | 1.5 | <0.001 |
| GFR, ml/min | 1.0 | <0.001 |
| SBP, mm Hg | 0.6 | 0.005 |
| Serum sodium, mmol/l | 0.2 | 0.08 |
| Heart rate, beats/min | 0.03 | 0.48 |

*From highest to lowest IDI increase. †Comparison to model with history (age, sex, race, comorbidities, left ventricular ejection fraction)/discharge medications only. Reproduced, with permission, from Dunlay et al. (21).

GFR = glomerular filtration rate; IDI = integrated discrimination improvement; KCCQ = Kansas City Cardiomyopathy Questionnaire; other abbreviations as in Table 1.

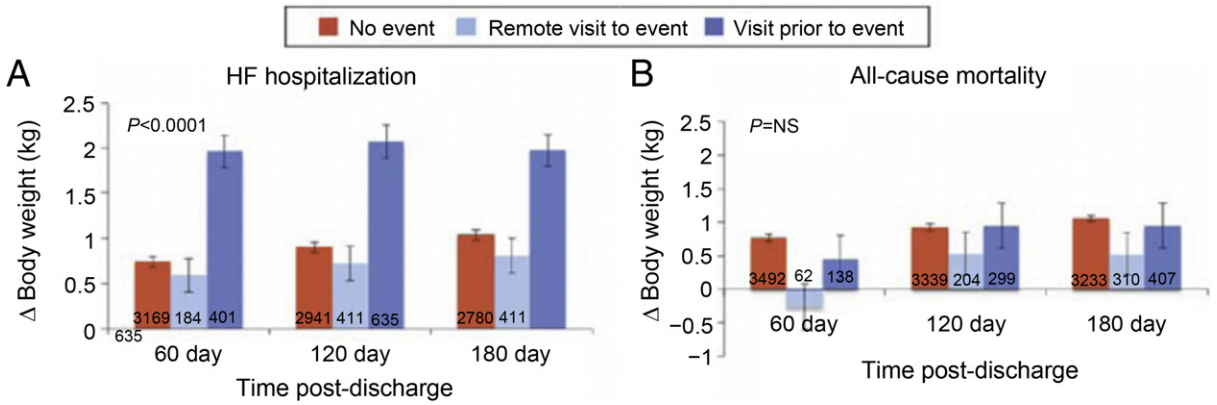


**Figure 4** **Relationship Between Increase in Body Weight and Readmissions**

Body weight (BW) changes and outcomes. Post-discharge changes in BW are plotted as the mean BW in patients without events, at the clinic visit prior to an event, at a remote clinic visit prior to the event in patients with events at 60, 120, and 180 days. Mean values are plotted with standard error from the mean. p Values are for changes in BW in patients with no event and in patients at the visit prior to the event. Reproduced, with permission, from Blair et al. (23).

CAD (17). Although there is a very low rate of clinical ischemic events after discharge (5), progression of CAD may contribute to rehospitalization and mortality. It is plausible that ischemic events may not be clinically recognized due to atypical presentations and significant electrocardiographic abnormalities. Myocardial injury, as evidenced by troponin release during or after discharge (19), may contribute to HF progression and sudden death. Patients with CAD may benefit from HMG-CoA reductase inhibitors, antiplatelet/antithrombotic agents, and revascularization procedures (17,19).

**Electrical system.** Although reducing the heart rate with ivabradine is beneficial in chronic HF (48), the optimal heart rate in HHF has not been determined. Patients with atrial fibrillation should receive anticoagulation and rate control with beta-blockers and digoxin (49). Ventricular dyssynchrony, defined by a wide QRS complex, is common in HHF patients with reduced EF (20,50). Once optimized on medical therapy, this subset of patients may benefit from CRT after hospital discharge. The role of ICD implantation in patients with HHF remains to be determined (51).

**Valves.** Secondary mitral regurgitation from chronic LV dilation is common in HFrEF. It remains unclear whether this is a marker of severity of LV dysfunction or a therapeutic target.

**Systemic hypertension and pulmonary hypertension.** Because systemic hypertension can contribute to progression of HF, strict management with appropriate therapies is warranted. A significant number of HHF patients, particularly those with HFpEF, also have pulmonary venous hypertension. These patients are at higher risk and thus may require closer monitoring (52). Treatment modalities for patients with comorbid pulmonary hypertension remain investigational.

**Noncardiac comorbidities.** A significant number of HHF patients have COPD, diabetes, obstructive sleep apnea, and renal impairment (53–55). Although data are lacking on the treatment of HHF with specific comorbid conditions, addressing these noncardiac comorbidities may serve as an adjunct to current HHF management approaches.

**Heart failure with preserved ejection fraction.** Approximately 50% of HHF patients have HFpEF (15,56). Because evidence-based treatment strategies that are effective in patients with reduced EF have largely been untested in

**Table 4** **Precipitating Factors and Multivariate Risk-Adjusted In-Hospital Clinical Outcomes**

| | | | | In-Hospital Mortality | |
|---|---|---|---|---|---|
| Factor | n | Adjusted LOS Ratio | p Value | Adjusted OR (95% CI) | p Value |
| Ischemia/acute coronary syndrome | 7,155 | 0.99 | 0.22 | 1.20 (1.03–1.40) | 0.02 |
| Arrhythmia | 6,552 | 1.04 | <0.001 | 0.85 (0.71–1.01) | 0.07 |
| Nonadherence to diet | 2,504 | 0.96 | 0.01 | 0.69 (0.48–1.00) | 0.05 |
| Uncontrolled hypertension | 5,220 | 0.96 | <0.001 | 0.74 (0.55–0.99) | 0.04 |
| Nonadherence to medications | 4,309 | 0.96 | <0.001 | 0.88 (0.67–1.17) | 0.39 |
| Pneumonia/respiratory process | 7,426 | 1.08 | <0.001 | 1.60 (1.38–1.85) | <0.001 |
| Worsening renal function | 3,304 | 1.09 | <0.001 | 1.48 (1.23–1.79) | <0.001 |
| Other | 6,171 | 0.99 | 0.23 | 1.15 (0.97–1.36) | 0.10 |

Reproduced, with permission, from Fonarow et al. (25).
CI = confidence interval; LOS = length of stay; OR = odds ratio.

**Table 5** General Considerations Regarding Gaps in Transitions of Care in Heart Failure

| |
|---|
| Physician assessment |
| Failure to recognize worsening clinical status prior to discharge from the hospital |
| Failure to identify or address comorbid conditions (underlying depression, anemia, hypothyroidism, and so on) |
| Medication errors and adverse drug events |
| Failure to recognize worsening clinical status prior to discharge from the hospital |
| No or inadequate provision of education to patient and family/caregiver |
| Failure to clarify whether patient and caregiver understood instructions and plan of care |
| Failure to address prior nonadherence in self-care, diet, medications, therapies, daily weights, follow-up, and testing |
| Providing information on broad themes without details on how to make it work for the individual patient based on lifestyle, economic constraints, social support, and other patient or process factors |
| Handoff communication |
| Lack of communication resulting in primary care provider not knowing patient admitted |
| Poor communication of the care plan to the nursing home team, home healthcare team, primary care physician, or family caregiver |
| Discharge instructions missing, inadequate, incomplete, or illegible |
| Lack of understanding by the healthcare receiver of information regarding heart failure medical and self-care management |
| Hospital to home and discharge planning |
| Medication errors |
| Patient lack of adherence to self-care, e.g., medications, therapies, diet (sodium restriction), and/or daily weights because of poor understanding or confusion about needed care, how to get appointments, or how to access or pay for medications |
| No follow-up appointment or follow-up too long after hospitalization |
| Failure to provide phone number of physician/nurse patient should call if heart failure worsens |

patients with preserved EF, the active management of comorbidities may be even more important in this population (57). Although rehospitalizations due to congestion are frequent in these patients, a significant number of readmissions are related to cardiac and noncardiac comorbidities (57). Optimization of heart rate and blood pressure is important because both can contribute to diastolic abnormalities resulting in pulmonary congestion.

**Transition of care and post-discharge period (vulnerable phase).** The immediate post-discharge period has been termed the "vulnerable phase" of HHF (22). Increased congestion, deteriorating renal function, and worsening neurohormonal abnormalities contribute to early readmission in a subset of patients (22). An early post-discharge visit has been recommended for all patients (40,58), but it is uncertain which subset of patients should be targeted and what should be evaluated/treated during this visit (31). Although the majority of studies have focused on fluid management and intensive monitoring strategies (59–62), a more comprehensive approach is needed.

The early post-discharge visit is part of an ongoing assessment of patient, substrate, and precipitating and amplifying factors (63). Such evaluations may continue after discharge through multiple avenues, including a follow-up phone call, visiting nurses, and an office visit during the vulnerable early-discharge period, telemonitoring, and home weight monitoring (21,31). Office visits should further optimize short-term diuretic strategies, reassess and re-evaluate medication regimens, monitor signs and symptoms of HF including measurement of natriuretic peptides, renal function and body weight, and continue to explore new cardiac and noncardiac targets for intervention (Table 6).

Ambulatory hemodynamic monitoring with implanted sensors has the potential to provide an early warning of decompensation and to facilitate patient management by guiding medication titration based on reliable physiological data (64).

**The role of patient and family.** The patient and patient's family may play a critical role in bridging the transition from hospital to home. Patients and their support network need to understand their disease and the importance of complying with recommended medications, interventions, and lifestyle changes (activity, diet, sodium restriction). The patient is uniquely situated to closely monitor his/her general health status and to detect early signs of worsening HF. Seeking appropriate early medical attention in the outpatient setting may avoid unnecessary readmissions. The patient should be aware that partial or total recovery of LV function is possible and that HF is not always a progressive and fatal condition when properly treated (47). Further data are required to help define the true adjunctive role of support networks in HF management.

**A team-based approach.** The management for each patient is determined by the patient profile including goals of care, socioeconomic circumstances, educational background, and support network. Palliative options should be addressed in those with end-stage HF. The need to provide affordable medications and recommend a feasible diet is important.

The complex medical, social, and economic factors contributing to high readmission rates in HHF necessitate an integrated team approach. The patient, primary care physician, hospital physician, cardiologist, other specialty care physicians (e.g., nephrologist, pulmonologist, and endocrinologist), pharmacist, nurse, family, social worker, and health educator all provide valuable contributions. Rich et al. (65) observed that a nurse-directed, multidisciplinary intervention reduces hospital admissions in elderly patients with HF. Koelling et al. (66) reported that a 1-h, nurse educator–delivered teaching session at the time of discharge resulted in improved clinical outcomes. OPTIMIZE-HF demonstrated that an increase in adherence to guideline-recommended therapies resulted in reduction of a post-discharge rehospitalization. Novel initiatives such as the Hospital to Home program of the American College of Cardiology and Institute for Healthcare Improvement, with a goal to reduce all-cause readmission after HF hospitalization by 20% by 2012, and the Target: Heart Failure program of the American Heart Association may improve the transition from inpatient to outpatient care and catalyze early post-discharge physician contact.

**Avoiding unnecessary admissions.** At present, there are no standard admission criteria. The acuity at presentation

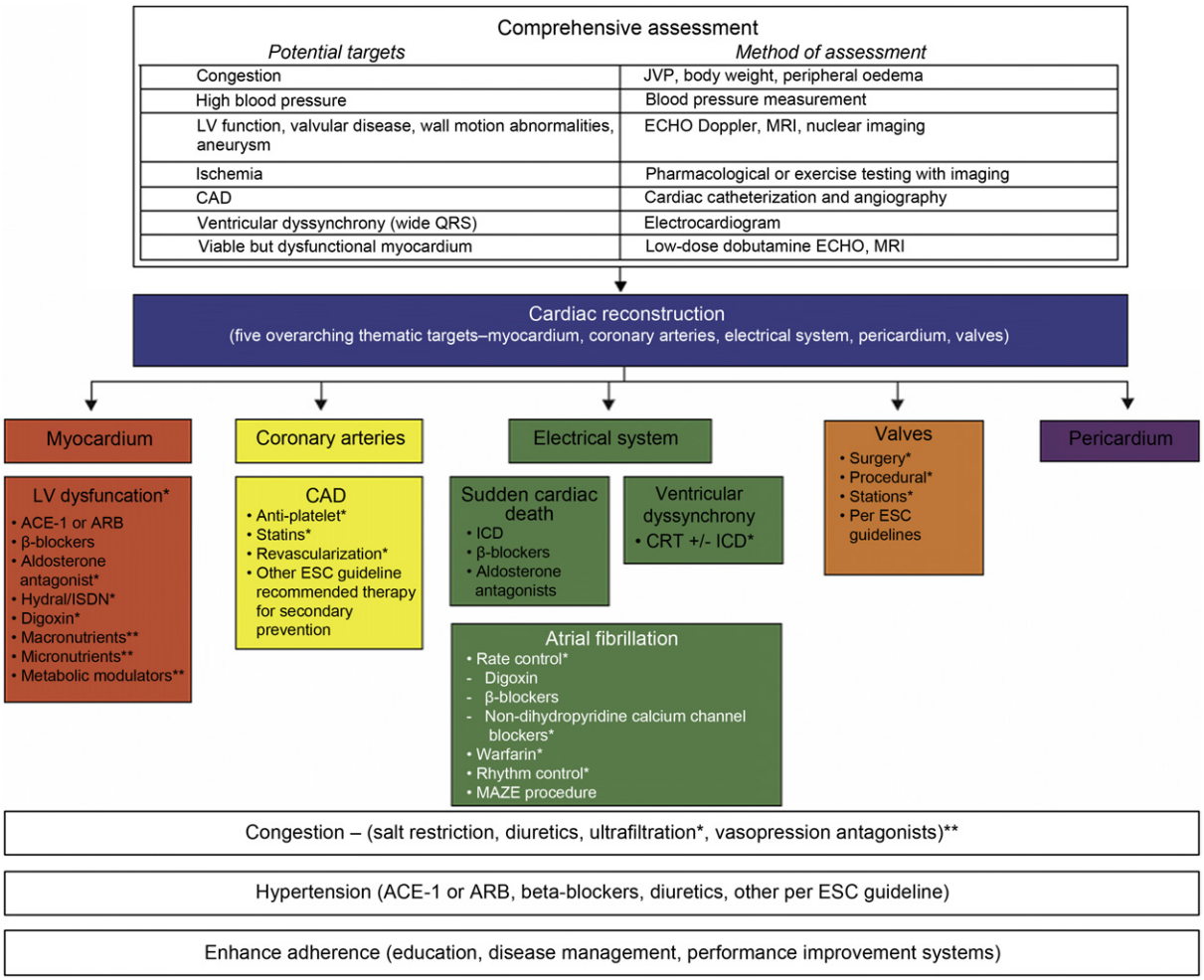


**Figure 5** **A Mechanistic Approach to HHF**

Assessment and targeted implementation of evidence-based therapy in hospitalized patients with heart failure (HHF). *Select patients. **Investigational agents. #Viable but dysfunctional myocardium. ACE-I = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; AHFS = acute heart failure syndrome; ARB = angiotensin receptor blocker; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CRT = chronic resynchronization therapy; ESC = European Society of Cardiology; Hydral = hydralazine; ICD = implantable cardioverter-defibrillator; ISDN = isosorbide dinitrate; JVP = jugular venous pulse; LV = left ventricle; MRI = magnetic resonance imaging. Reproduced, with permission, from Ambrosy et al. J Cardiovasc Med (Hagerstown) 2011;12:258–63.

may have changed in the last decade because the majority of patients with HHF have underlying chronic HF and are receiving evidence-based therapies. In fact, recent registries show that the rate of pulmonary edema and cardiogenic shock is extremely low. It is possible that a significant number of patients presenting to the emergency department (ED) for worsening congestion may be manageable in an observation unit with a planned outpatient visit rather than hospitalization. For these patients, an early follow-up visit can be as beneficial as hospital admission (67,68).

## Performance Measures: Raising the Bar

Although hospitals across the United States are meeting core measures outlined by the Centers for Medicare and Medicaid Services in recent years, the rates of rehospitalization have remained relatively unchanged or only slightly decreased (69). Recent updated American College of Cardiology Foundation/American Heart Association performance measures for HHF patients now include the use of beta-blockers and scheduling the follow-up outpatient visit (40). It remains to be seen whether the implementation of this follow-up visit performance measure will reduce the rehospitalization rate.

## Is 30-Day HF Rehospitalization the "Right" Target?

Current national improvement initiatives and performance measures are focusing on early rehospitalizations for HF. Since July 2009, there has been mandatory reporting of 30-day readmission rates for HF by nongov-

**Table 6 Components of Early Post-Discharge Follow-Up**

| Action | Expected Outcomes | | |
|---|---|---|---|
| | Prevention of Fluid Overload | Improvement in Symptoms | Improvement in Prognosis |
| Education | | | |
| Diet | ++ | ++ | + |
| Exercise | | ++ | + |
| Medications (benefits, side effects) | + | ++ | ++ |
| Weight monitoring | ++ | + | + |
| Detection and treatment of worsening symptoms | ++ | + | + |
| Assessment of compliance | | | |
| Medical therapy | ++ | + | ++ |
| Nonpharmacological prescriptions (diet, exercise, weight monitoring) | ++ | ++ | + |
| Assessment of prognostic variables | | | |
| Clinical | | | |
| Signs of congestion: pulmonary rales, jugular venous congestion, hepatomegaly, peripheral edema | +++ | + | ++ |
| Blood pressure | + | ? | + |
| Heart rate | ? | + ? | + |
| Orthostatic test | + | ? | ? |
| Valsalva maneuver | + | ? | ? |
| ECG | | | |
| QRS duration, indication to CRT | + | ++ | +++ |
| Atrial fibrillation, tachyarrhythmias | + ? | + | ++ |
| Laboratory examinations | | | |
| Myocardial viability* | + | + | ++ ? |
| Natriuretic peptides | ++ | + | + |
| Renal function and electrolytes | + | +/0 | +/++ ? |
| Anemia and/or iron deficiency | ? | ++ | ? |
| Devices for fluid status monitoring | +++ | + | + (++?) |
| Optimization of medical treatment | | | |
| Changes in diuretic doses according to fluid status | +++ | + | + ? |
| Initiation or up-titration of evidence-based therapies (renin-angiotensin-aldosterone antagonists, beta-blockers, digoxin) | + | + | +++ |
| CRT when indicated | + | ++ | +++ |
| ICD when indicated | 0 | 0 | +++ |
| Coronary revascularization when indicated | + | + | + ? |
| Other surgical procedures (e.g., mitral valve surgery) | + | + | ? |

*Viable but potentially salvageable myocardium. Reproduced, with permission, from Metra et al. (31).
CRT = cardiac resynchronization therapy; ECG = electrocardiogram; ICD = implantable cardioverter-defibrillator; ? = lacking definitive data to support effect; 0 = not applicable.

ernmental hospitals (70,71). However, the 30-day readmission may be problematic as a performance measure because risk-adjustment models have poor discrimination and do not take into account the competing risk of mortality. Furthermore, readmission early after hospital discharge may be influenced, not just by quality of care, but by more "fixed" factors, including social support, geographic location, and socioeconomics (72). There is also a potential disconnect between early readmission and short-term post-discharge mortality. Because patients who die early after hospitalization cannot be readmitted, there is a poor correlation between 30-day mortality and 30-day readmission in most hospital centers (73). High or stable rates of 30-day readmission may reflect successful efforts to drive down post-discharge mortality. This hypothesis is supported by data demonstrating different predictors of early readmission and early mortality.

Additionally, even in a well-treated population with a few clinical comorbidities, a substantial number of patients with HF (with reduced EF) are rehospitalized for reasons not directly related to HF (5). Most current post-discharge efforts focus on managing congestion and close hemodynamic monitoring. Although these are important goals, broader strategies to focus on HF-related comorbidities and patient-centered management may be necessary.

Taken together, these findings suggest that 30-day readmission may not be an ideal metric and should not be the only metric for quality. Clearly, not all early rehospitaliza-

tions are "bad," because these provide additional opportunities to implement further therapies, improve patient education, or establish clearer follow-up care strategies (73). Readmission should also not be utilized as a surrogate for mortality.

## Trials in Patients Hospitalized for HF

Trials in HHF patients have been classified into stages A, B, and C (10). Several drug trials have been conducted in HHF patients without much success (8). Negative results could relate to the drug itself, to poor selection of a specific target patient population most likely to benefit, or to trial execution (74). Given the global nature of HHF trials, geographical variations in patient population or standards of care may also have contributed to negative results. However, the main problem with the prior trials is that they have exclusively focused on short-term therapy during hospitalization (stage A and B trials) to improve early symptoms that are already markedly improved by standard therapy (75). Because the primary problem remains high post-discharge event rates, trials should focus on therapies initiated during hospitalization or soon after that are continued post-discharge (76).

## Conclusions

High hospital readmission rates for HF persist despite the major advances in management of chronic HF. It should also be recognized that a significant number of those readmissions occur in patients with HFpEF for which there is no evidence-based therapy. This represents a truly unmet need. Strategies to reduce early readmission rates need to primarily target congestion by reducing keep intravascular volume. Early assessment of clinical deterioration and close monitoring of signs and symptoms of congestion are critical in the post-discharge period. Furthermore, clinicians must strive to treat beyond clinical congestion by addressing comorbidities, precipitating factors, and social circumstances that contribute to worsening HF. This necessitates a mechanistic and comprehensive approach in terms of patient assessment (e.g., substrate and initiating and amplifying factors), time scale of intervention (e.g., ED, inpatient, vulnerable phase assessment, and regular follow-up), and team development (patient, family, hospitalist, primary physician, cardiologist, nurse, pharmacist, social worker, and health educators). It remains to be seen how efforts aimed at reducing 30-day readmission rates will impact long-term outcomes. More registry and trial data with long-term follow-up are necessary to better understand the clinical course of HHF leading to readmission and to investigate interventions that lead to better outcomes. It will also be important to develop alternatives for admissions such as therapies in the ED with early follow-up or in an observation unit. It is realistic to reduce rehospitalization rates, but this will require integration of these efforts on a clinician, hospital, and system level to improve overall outcomes.

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