Published in final edited form as:

Heart Fail Rev. 2018 July ; 23(4): 597–607. doi:10.1007/s10741-018-9697-9.

Expanded algorithm for managing patients with acute decompensated heart failure

Joyce N. Njoroge¹, Baljash Cheema¹, Andrew P. Ambrosy², Stephen J. Greene², Sean P. Collins³, Muthiah Vaduganathan⁴, Alexandre Mebazaa^{5,6}, Ovidiu Chioncel⁷, Javed Butler⁸, and Mihai Gheorghiade¹

¹Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

²Duke Clinical Research Institute and Division of Cardiology, Duke University Medical Center, Durham, NC, USA

³Vanderbilt University School of Medicine, Nashville, TN, USA

⁴Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston, MA, USA

⁵Department of Anesthesia and Critical Care, Inserm U942, Hôpitaux Universitaires Saint-Louis-Lariboisière, Paris, France

⁶University Paris Diderot, Paris, France

⁷Institute of Emergency for Cardiovascular Diseases, Bucharest, Romania

⁸Stony Brook University, Stony Brook, NY, USA

Abstract

Heart failure is a complex disease process, the manifestation of various cardiac and noncardiac abnormalities. General treatment approaches for heart failure have remained the same over the past decades despite the advent of novel therapies and monitoring modalities. In the same vein, the readmission rates for heart failure patients remain high and portend a poor prognosis for morbidity and mortality. In this context, development and implementation of improved algorithms for assessing and treating HF patients during hospitalization remains an unmet need. We propose an expanded algorithm for both monitoring and treating patients admitted for acute decompensated heart failure with the goal to improve post-discharge outcomes and decrease rates of rehospitalizations.

Keywords

Heart failure; Acute decompensated heart failure, rehospitalizations; HFrEF

[✉]Joyce N. Njoroge, joyce.njoroge@northwestern.edu.

Introduction

Heart failures not a single disease, but a heterogeneous clinical syndrome that is the manifestation of various cardiac and noncardiac abnormalities. It is commonly seen in individuals 65 years and older and is associated with high rates of morbidity and mortality [1]. Patients hospitalized for heart failure with reduced ejection fraction (HFrEF) have a mortality and read-mission rate as high as 15 and 30%, respectively, at 60–90 days post-discharge which has remained unchanged in the past decade despite the advent of novel therapies and monitoring modalities [2]. Hospitalization and rehospitalizations are strong predictors of negative outcomes such as mortality in patients [3]. In this context, development and implementation of improved algorithms for assessing and treating HF patients during hospitalization remains an unmet need.

In this article, we propose and provide rationale for the use of the following systematic approach during the three phases of hospitalization (initial assessment, inpatient, and post-discharge): (1) adopt a regimented framework for assessing and treating acute decompensated HF, (2) treat beyond clinical congestion, (3) augment use of underused therapies known to improve outcomes, (4) identify and treat noncardiac comorbidities, and (5) emphasize importance of post-discharge follow-up visits. The aim is to utilize tools and strategies for purposes of improving post-discharge clinical outcomes and decreasing rates of rehospitalization.

Adopt a regimented approach to assessing and treating acute decompensated heart failure

The approach to managing acute decompensated HF (ADHF) patients admitted to the hospital has not changed significantly in the past few decades [4–6]. The current treatment algorithm for ADHF focuses on targeting signs and symptoms of congestion with diuretics and vasodilators. However, there are many more factors to consider during the three different phases of admission.

During the initial phase in the emergency department, it is reasonable to use a more focused six-axis assessment model previously described by Gheorghiade et al. by determining de novo vs. chronic HF, clinical severity, precipitants, heart rate and rhythm, blood pressure, and comorbidities [7]. This can guide the triage and initiation of necessary immediate therapies that can be performed in the emergency department before admission.

Once patients are admitted, we propose a transition to a more thorough evaluation using a newly proposed eight-axis model depicted in Fig. 1. This transition is demonstrated in Fig. 2. In the inpatient setting, in addition to treating congestion, there are eight important cardiac and noncardiac entities that have been shown to contribute to the development and exacerbation of HFrEF specifically. These include coronary artery disease, hypertension, myocardial disease, pericardial disease, electrical abnormalities, valvular disease, medical noncompliance, and comorbidities including renal disease, iron deficiency, lung disease, and diabetes. These conditions become equally important in the management of heart failure with preserved ejection fraction (HFpEF) exacerbations as the cardiac pathophysiology is

still poorly understood. Focus on comorbidity management in addition to decongestion is suggested in this cohort as a temporizing measure. As indicated in Fig. 1, determination of ejection fraction is crucial early during the second phase of hospitalization in order to guide assessment and therapies, with the three widely accepted categories being (1) HFrEF if 40%, (2) mid-range EF if between 41 and 49%, and (3) HFpEF if $\geq 50\%$ [8].

A comprehensive cardiovascular assessment can be achieved by further imaging modalities that are more readily available in the second phase of hospitalization. These include echocardiography to determine systolic and diastolic function as well as valvular disease, cardiac MRI to evaluate for pericardial disease (for those without an implantable cardioverter defibrillator or permanent pacemaker), nuclear single-photon emission computed tomography (SPECT) to assess for viable myocardium, and dobutamine stress echocardiography to determine contractile reserve. This information can provide important information for therapies to initiate before discharge. In patients with HFrEF and dysfunctional but viable myocardium, a robust body of evidence supports the potential to improve systolic function with the optimization for guideline-directed medical therapy. For example, the CHRISTMAS (Carvedilol Hibernation Reversible Ischaemia Trial, Marker of Success) study demonstrated that patients with HFrEF and viable myocardium determined by SPECT had an increase in EF when treated with carvedilol [9]. There is also a relationship between the level of myocardial viability and the percent of improvement in EF with carvedilol [10, 11]. Lastly, the inpatient setting allows for easier communication between consulting services to optimize comorbidities.

Each HF patient has varying degrees of the aforementioned conditions contributing to their specific disease process. Occam's Razor—the idea that a singular entity as causal is preferred over multiple contributors—is generally not the appropriate approach in HF patients. Evaluation of all possible components is necessary to develop individualistic treatment plans with multiple therapeutic targets which may confer potential for reversibility of cardiac dysfunction.

Treat beyond clinical congestion

Clinical congestion in HF encompasses the long-recognized signs and symptoms of HF, namely, dyspnea, orthopnea, rales, and peripheral edema. However, much less appreciated is the situation of hemodynamic congestion, defined as elevated left ventricular diastolic pressure despite minimal to absent clinical evidence of HF. The development of clinical and hemodynamic congestion falls on a spectrum of disease severity; as hemodynamic congestion continues to progress, symptoms of clinical congestion start to present themselves up to weeks later [12,13] (Fig. 3). A number of patients lay somewhere on this continuum complaining of dyspnea but not presenting with systemic signs. In one study of 50 patients, the aforementioned signs were absent in 42% of congested patients with proven elevated pulmonary capillary wedge pressure (PCWP) [14]. Many patients may be discharged with improved symptoms but with persistently high left ventricular filling pressures as demonstrated with elevated N-terminal pro-brain-type natriuretic peptide (NT-proBNP), provoked orthopnea, and poor exercise capacity [15]. Outlined below are

additional tools and techniques to increase the sensitivity of evaluation for persistent congestion.

Dyspnea and orthopnea measurement scales

Dyspnea and orthopnea are common presenting symptoms that act as subjective marker for congestion in a patient with ADHF. The current standard assessment of dyspnea is a poor surrogate outcome. In hospital, physician-assessed and patient-reported dyspnea was not independently associated with post-discharge quality of life, survival, or readmissions [16]. Although dyspnea relief remains a goal of therapy for hospitalized patients with heart failure with reduced ejection fraction, this measure may not be a reliable surrogate for long-term patient-centered clinical outcomes with the current assessment approach.

The Likert scale and the visual analogue score (VAS) are tools that minimize subjectivity while assessing the level of orthopnea or dyspnea. Using both scales in conjunction results in an increased strength in sensitivity of evaluation by measuring multiple specific aspects of dyspnea [17]. For example, the provocative dyspnea severity score combines both dyspnea and orthopnea assessments into a single scale [18]. These objective tools represent a patient-centered metric to compare congestion from admission to discharge to ensure symptomatic improvement.

Orthostatic vital signs

In individuals with normal cardiac function and intravascular volume levels, the typical reflex response to positional changes from sitting to standing includes mild reduction in blood pressure and increase in heart rate [19]. However, in decompensated patients with intravascular congestion, these positional changes can have paradoxical effects. Based on the Frank–Starling curve, sarcomeres in congested HF patients are initially overstretched but shrink within ideal range with decreased venous return and resultant decreased preload, causing an improved contractility [20]. Therefore, orthostasis may result in increased cardiac output and improved blood pressures which could indicate intravascular congestion requiring further diuresis. This tool has limitations in utility among patients with hypertrophic cardiomyopathy, aortic stenosis, or atrial fibrillation.

The Valsalva maneuver

In an individual with normal intravascular volume levels, there is a multi-phase response to sustained Valsalva maneuver. Immediately after initiating Valsalva, the increased intrathoracic pressure causes a brief spike in blood pressure followed by decreased venous return and increased systemic vascular resistance causing a drop in blood pressure below baseline. After the strain is released, the reduced intrathoracic pressure causes a further drop in blood pressure followed by increased venous return and decreased vascular resistance (and, therefore, decreased afterload) which allows for a rebound blood pressure elevation [21]. Conversely, in patients with congestion, the release of strain results in a persistently elevated blood pressure due to increased LV diastolic pressure and persistently elevated central pressures [22]. This maneuver has proven to have high correlation with invasively measured ventricular filling pressures demonstrating its utility in monitoring intravascular volume status [23].

The 6-min walk test (6MWT) is a simple tool to elicit symptoms of congestion that may not be present at rest. The ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial found that the 6MWT was one of the most reliable predictors of mortality after hospitalization for worsened HF, alongside PCWP measurements [24]. The 6MWT can be used both in the inpatient setting prior to discharge and for continued monitoring during the third phase of outpatient follow up.

Natriuretic peptide measurement

Comparing the serum level of NT-proBNP on admission and prior to discharge can ensure the correct therapeutic trajectory [25]. NT-proBNP is cleaved from BNP, has more stability in vivo, and has been shown to have higher sensitivity and specificity compared to circulating BNP levels [26]. Patients with persistently elevated NT-proBNP prior to discharge have been found to have significantly higher risk for rehospitalization or death [27]. The utility of monitoring serial NT-proBNP levels in the inpatient setting is challenged by a delay in serum level changes compared to intravascular congestion progression. However, it has been shown that a reduction in NT-proBNP levels by at least 30% from admission is associated with an improvement in post-discharge outcomes [28].

Noninvasive hemodynamic monitoring can be used throughout the three phases of hospitalization for HF. In the emergency department, utilization of ultrasound technology is becoming more convenient with the advent of hand-held devices. Evaluation of inferior vena cava (IVC) compressibility or distension can easily be performed to distinguish between systemic congestion and fluid redistribution [29]. Goonewardena et al. determined that bedside ultrasound of IVC, even with a hand-held device, identified patients with ADHF who would go on to be readmitted for HF exacerbations based on plethoric IVCs with lower collapsibility indexes [30].

Newer imaging modalities, such as bioelectrical impedance vector analysis (BIVA), are being tested as options for intravascular assessment. The use of transthoracic bioelectrical impedance analysis as a marker of fluid accumulation is still gaining traction in the clinical world but it has demonstrated reliability in measuring cardiac output and index when compared to invasive methods [31].

Augment use of underused therapies known to decrease rehospitalizations

Current guideline-directed medical therapy (GDMT) has been well outlined by institutions including the American College of Cardiology (ACC), American Heart Association (AHA), and European Society of Cardiology (ESC) [32]. Despite the well-established body of evidence supporting these guidelines for HFrEF, there remain significant gaps in provision of recommended therapies to patients who qualify for them. This “risk-treatment paradox” and “clinical inertia” may stem from focus on the potential short-term destabilization of clinical status, rather than consideration of the potential long-term benefits of therapy. For example, robust evidence suggests that worsening renal function in the setting of augmented decongestive therapy or initiation of renin–angiotensin–aldosterone system (RAAS) blockade does not negatively impact prognosis, but rather represents a net benefit to the patient [33–36]. Nonetheless, these patients frequently have their ACE inhibitors and

angiotensin receptor blockers (ARBs) stopped without reinitiation prior to discharge. Similarly, in African American patients with stable hemodynamics, less than 25% are discharged on hydralazine and isosorbide dinitrate despite data proving morbidity and mortality benefits in this cohort [37]. Below (and summarized in Table 1) are examples of therapies in HFrEF patients that need to be highlighted for initiation either prior to discharge or during outpatient follow-up in order to further minimize the risk-treatment paradox and promote cardiac dysfunction reversibility.

Digoxin has proven hemodynamic benefits and has been associated with decreased readmission rates. As such, it is endorsed by guidelines to use in appropriate patients with persistent symptoms and rehospitalizations for HFrEF. However, in the last decade, there has been a decrease in prescription rate to only 20–40% from 80% at the peak of its clinical utility [38]. Data suggesting increased mortality with digoxin are uniformly observational and subject to confounding. The DIG trial demonstrated that digoxin, when added to diuretics and ACEi in patients with chronic HFrEF in sinus rhythm, decreased hospitalizations without affecting mortality [39]. This neutral effect on mortality in a large randomized trial is notable amid persistent concerns over the safety of digoxin in routine clinical practice. Moreover, the neutral mortality effect of digoxin in the DIG trial was seen despite the trial protocol calling for aggressive dosing of the agent to achieve serum digoxin concentrations above current guidelines [32]. Evidence suggests that dosing in line with ACC/AHA guidelines further improves the risk-benefit ratio of digoxin therapy.

Mineralocorticoid receptor antagonists

Less than 33% of eligible patients admitted for HF are started on mineralocorticoid receptor antagonists (MRAs) before discharge [40] despite data showing that MRAs significantly reduce early hospitalization rate [41]. In addition to blocking aldosterone's effect on the RAAS, MRAs have been able to prevent aldosterone's promotion of cardiomyocyte fibrosis, oxidative injury, and cardiac remodeling [42]. At higher doses, MRAs can also provide natriuretic benefits and has been used in cirrhotic patients for this effect for years [43]. Importantly, spironolactone is one of the only medications to have a possible role in minimizing the readmission risk in HFpEF patients in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial [44].

Torsemide

The three most commonly used loop diuretic formularies are furosemide, bumetanide, and torsemide. Furosemide historically has been the most frequently used diuretic initially due to cost and early marketing (furosemide being available in the 1960s and torsemide in 1990s) [45]. Although definitive clinical outcome data are lacking, compelling data support torsemide as having distinct advantages over other available loop diuretics [46, 47]. Torsemide has a significantly better bioavailability independent of the presence of gut edema or renal dysfunction [48, 49]. Compared to furosemide's variable bioavailability from 10 to 90% depending on disease state, torsemide's bioavailability is reliably > 80% independent of medical status [50]. An added benefit of torsemide is its longer duration of action (12–18 h) compared to furosemide and bumetanide (6 to 8 h) and its decreased tendency for hypokalemia. The TRANSFORM-HF (Torsemide Comparison with Furosemide for

Management of HF) trial is a large-scale randomized controlled trial currently enrolling approximately 6000 patients hospitalized for HF and will compare the effects of torsemide and furosemide on long-term clinical outcomes (NCT03296813).

Thiazide diuretics

Patients who require chronic diuretic use can frequently develop loop diuretic tolerance due to distal nephron segment hypertrophy and enhanced sodium reabsorption proximal to the diuretic's site of action [51]. Thiazide diuretics can play an important part in potentiating the sodium excretion effects of loop diuretics in these patients [32]. By targeting the distal tubules, thiazides provide a synergistic effect when combined with standard loop diuretics and prevent reabsorption of sodium and water in the ascending loop of Henle and distal convoluted tubules [52]. A current ongoing CLOROTIC (Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure) trial aims to determine utility of combined loop and thiazide diuretic compared to loop diuretic use alone (NCT01647932).

Ivabradine is a chronotropic agent that decreased heart rate and, therefore, cardiac work. It has shown to be beneficial in a specific cohort of chronic HF patients with EF < 35% and heart rate > 70 BPM where it decreased the rate of HF hospitalizations and death from HF³². Initiation in the post-discharge phase should be considered among HFrEF patients already receiving optimal doses of standard GDMT [53]. However, in the stable HF patient admitted for acute decompensation, consideration should be made to initiate prior to discharge. The PRIME-HF (Predischarge Initiation of Ivabradine in the Management of Heart Failure) trial is a randomized prospective study that aims to monitor the rate of continued treatment of ivabradine if started in the predischarge period rather than in clinic (NCT02827500). This information can help guide recommendations for timeline of initiation of therapy.

Angiotensin receptor and neprilysin inhibitors (ARNI) have been shown to improve vasodilation and natriuresis by inhibiting endothelin, vasopressin, sympathetic activity, and the RAAS [54]. The PARADIGM-HF (Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) trial demonstrated better outcomes in HFrEF with treatment with ARNI compared to ACEI [55, 56]. Post hoc analysis of the PARADIGM-HF suggests that these benefits extend to improving clinical outcomes following hospitalization for HF and initiation should be considered during outpatient clinic visits [57]. The ongoing PIONEER-HF (comparison of sacubitril/valsartan versus enalapril on effect on NT-proBNP in patients stabilized from an acute heart failure episode) trial is a large, randomized, double-blind prospective study that aims to assess the effect on congestion by monitoring NT-proBNP levels in the post-discharge setting (NCT02554890).

Ultrafiltration

The interdependence of cardiac and renal function is well recognized, with dysfunction of one organ commonly affecting the other. Balancing cardiac decongestion and renal function is a common struggle that physicians face when treating acute decompensated HF patients [58]. Ultrafiltration offers an option to further decongest HF patients with renal dysfunction.

However, the current data on risk-benefit analysis is inconclusive. The Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) trial tested the effects of ultrafiltration for continued fluid removal in the presence of worsening renal failure but demonstrated an increased association with more adverse events, worsening renal function, and no significant difference in clinical outcomes [59]. Alternatively, the AVOID-HF (Aquapheresis Versus Intravenous Diuretics and Hospitalizations for Heart Failure) trial did not see a difference in adverse events between ultrafiltration and loop diuretic treatment groups [60]. Importantly, there was a longer duration between initial and subsequent HF events within 90 days in the ultrafiltration group compared to diuretic therapy. This study was terminated early for funding reasons but provides incentive to further evaluate its validity as part of an empiric strategy for congestion refractory to aggressive pharmacologic therapy [61–63].

Identify and treat noncardiac comorbidities

Heart failure exacerbations commonly result from the interplay between the underlying cardiac substrate and amplifying mechanisms such as diabetes mellitus, renal failure, and COPD. In patients with HF, a significant number experience rehospitalizations or death secondary to comorbidities rather than heart disease itself. The prognostic significance of noncardiac comorbidities is equally important in HF patients with preserved, mid-range, and reduced ejection fraction [64]. In HFpEF, with potential exception of spironolactone, randomized controlled trials of various therapies have thus far failed to demonstrate improved outcomes. Therefore, there is an increased interest in targeting and optimizing comorbidities as a temporizing measure pending further research for proven therapies. The prevalence and prognostic implications of comorbidities in HFrEF and HFpEF have been previously discussed, but a few specific comorbidities deserve notable mention.

Comorbid diabetes mellitus and heart disease have been shown to have significantly poor overall outcomes. Concurrent diabetes can be seen in up to 44% of HFrEF patients [65] and 32–45% of HFpEF patients [66]. Among patients with diabetes, the most common clinical complication is due to cardiovascular disease, especially HF [67]. However, cumulative data from prior studies suggests that hyperglycemia per se is not a therapeutic target in HF, with multiple glucose-lowering therapies conferring heightened risk for HF events despite added glucose control [68, 69]. In the recent EMPA-REG OUTCOME (Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes) study, empagliflozin, a sodium–glucose cotransporter-2 (SGLT2) inhibitor, demonstrated a positive effect on cardiovascular risk [70]. Specifically, there was a reduction in mortality secondary to cardiovascular etiology as well as a decreased risk of hospitalization for HF compared to placebo (hazards ratio 0.65) [71]. Similar findings were seen with canagliflozin, another SGLT2 inhibitor, in the CANVAS (Canagliflozin Cardiovascular Assessment Study) trial [72]. The mechanism of improved cardiac outcomes is not thought to be due to glycemic control, but the exact pathophysiology is still unknown.

Iron deficiency is a common comorbidity in chronic HF that has been shown to be an indicator of more advanced disease [73] as well as reduced functional capacity and quality of life [74]. Iron deficiency itself has been seen in 33% of CHF patients with or without

anemia and is associated with a reduced event-free survival at 36 months [75]. The deficiency of iron specifically is related to poor outcomes independent of anemia or bone marrow hypoproduction. The RED-HF (Reduction of Events with Darbepoetin Alfa in Heart Failure) trial demonstrated no benefit with treatment with darbepoetin injections in patients with iron-deficiency anemia [76]. The IRONOUT-HF (Iron Repletion Effects on Oxygen Uptake in Heart Failure) trial did not demonstrate benefit in routine oral iron supplementations in HFrEF patients with iron deficiency based on exercise tolerance (6MWT) and peak oxygen uptake [77]. However, studies have shown improved outcomes with intravenous (IV) iron supplementation. The FAIR-HF (Ferinject Assessment in Patients with Iron Deficiency and Chronic Heart Failure) study demonstrated improvement in patient-reported quality of life and exercise capacity with intravenous ferric carboxymaltose (FCM) in iron-deficient patients with and without anemia [78]. The trial also found a significantly lower rate of death due to worsening HF in the FCM arm. Likewise, the CONFIRM-HF (Ferric Carboxymaltose Evaluation on Performance in Patients with Iron Deficiency in Combination with Chronic Heart Failure) trial demonstrated similar results with an improvement in functional capacity measured with 6MWT [79]. In the EFFECT-HF (Effect of Ferric Carboxymaltose on Exercise Capacity in Patients with Heart Failure and Iron Deficiency) trial, the treatment with IV FCM also improved peak oxygen consumption, an objective marker of exercise tolerance [80].

Emphasize post-discharge follow-up visits

There is a period about 2–3 months after discharge known as the vulnerable phase when morbidity and mortality significantly increase compared to any other point in the timeline from admission [81]. This is usually due to short-term worsening of hemodynamics in the setting of suboptimal therapy, medication and diet noncompliance, and other factors. It is becoming increasingly apparent that we must have patients followed up closely in outpatient cardiology clinics early during this period to prevent worsening congestion, renal function, and neurohormonal maladaptations [82].

In order to determine who is at highest risk of poor outcomes during this vulnerable phase, patients can be risk-stratified based on certain prognostic indicators. Hypotension (low systolic blood pressure), ventricular dyssynchrony, anemia, persistently elevated BNP, and hyponatremia have all been found to carry a negative prognosis in patients with AHF [83]. An additional risk-stratifying tool in the peri-discharge period is the Kansas City Cardiomyopathy Questionnaire (KCCQ), a self-reported quality of life report for functional status evaluation. When compared to clinical outcomes, patients with stable chronic HF or New York Heart Association (NYHA) staging consistently had higher KCCQ scores and patients with decompensated HF or NYHA staging had lower scores [84]. Notably, a KCCQ score prior to discharge was associated with a higher 30-day HF readmission rate [85]. The symptoms evaluated by KCCQ tend to be the chief complaints upon re-presentation to the hospital among HF patients. Therefore, KCCQ, as well as the aforementioned clinical signs, has significant utility in a risk prediction model to minimize rehospitalizations when signs of congestion are not present.

Although evidence supporting the exact goals and duties of the early post-discharge visit are lacking, the ACC and AHA mention the goal for immediate post-discharge office centering on reassessment of volume status and renal function, and ensuring current medications are in line with guideline-directed medical therapy (GDMT). For prognostic purposes, repeat biomarker testing can be considered [86]. Additionally, recent research has demonstrated a prognostic rationale for monitoring troponin I levels with an elevated serum level at 1 month predicting increased clinical events at 12 months [87]. Further follow-up must focus on optimizing GDMT, assessing new targets for intervention, and managing comorbid conditions in order to prevent further precipitants and exacerbations [88]. Reflection on other factors such as optimizing macronutrient and micronutrient status must also be considered. Patient coaching is equally crucial to ensure continued follow-up and adherence to medications and diet.

Cardiac rehabilitation is a three-axis program that focuses on improving cardiovascular health, preventing deterioration, and minimizing rehospitalization by counseling patients about healthy lifestyle management, exercise training, and stress reduction. In the HF-ACTION (heart failure: a controlled trial investigating outcomes of exercise training) study, cardiac rehabilitation was found to improve health-related quality of life (self-reported using KCCQ and EQ-5D questionnaires) [89]. However, data indicates that only 10% of eligible patients receive a referral at time of hospital discharge [90]. With the advent of novel access to counseling and cardiac rehab through the internet and mobile phones [91], the barriers to incorporating these non-medical therapeutic measures in daily life are minimized.

Ambulatory invasive hemodynamic monitoring is a novel intervention for continuous assessment in the outpatient setting. The CardioMEMS is an implantable device that measures PCWP to provide early warning of congestion prior to progression requiring inpatient management. Abraham et al. studied its use in NYHA class III HF patients and observed a 30% relative risk reduction at 6 months post-implantation [92]. Although it carries inherent risks during implantation in addition to increased cost compared to standard of care, this device may prove useful for selected patients.

Lastly, patients with severe stage D or NYHA class III-IV HF must be evaluated for invasive devices such as invasive cardiac defibrillators and ventricular assist devices when clinically indicated whether in the inpatient or outpatient setting. Both the ESC and ACC/AHA guidelines elucidate when these invasive devices are indicated, and early identification of candidates is crucial for preventing continued deterioration of cardiac function [8, 32].

Conclusion

The pathophysiology development and exacerbation is multifaceted and, as such, should be assessed more thoroughly. We present an algorithm utilizing a multi-modality assessment of precipitating and aggravating factors and a guideline for improved management of acute decompensated heart failure. This paper highlights the importance of thorough assessment, individualized treatment plans beyond clinical congestion with underutilized therapies, attention to noncardiac comorbidities, and continuing management following

hospitalization. We aim to provide guidance in order to improve overall cardiac function patients.

Acknowledgments

Conflict of interest Dr. Muthiah Vaduganathan is supported by the NHLBI T32 postdoctoral training grant (T32HL007604).

References

1. Gheorghiade M, Vaduganathan M, Fonarow GC, Bonow RO (2013) Rehospitalization for heart failure. *Probl Perspect JACC* 61(4):391–403
2. O'Connor CM, Miller AB, Blair JE et al. (2010) Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction: results from Efficacy of Vasopressin Antagonism in Heart Failure Outcome study with Tolvaptan (EVEREST) program. *Am Heart J* 159: 841–849 [PubMed: 20435194]
3. Solomon SD, Dobson J, Pocock S, Skali H, McMurray JJV, Granger CB, Yusuf S, Swedberg K, Young JB, Michelson EL, Pfeffer MA, for the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) Investigators (2007) Influence of nonfatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. *Circulation* 116(13):1482–1487 [PubMed: 17724259]
4. Ramirez A, Abelman WH (1974) Cardiac decompensation. *NEJM* 290(9):499–501 [PubMed: 4589873]
5. Peacock WF, Braunwald E, Abraham W, Albert N, Burnett J, Christenson R, Collins S, Diercks D, Fonarow G, Hollander J, Kellerman A, Gheorghiade M, Kirk D, Levy P, Maisel A, Massie BM, O'Connor C, Pang P, Shah M, Sopko G, Stevenson L, Storrow A, Teerlink J (2010) National Heart, Lung and Blood Institute working group on emergency department management of acute heart failure: research challenges and opportunities. *JACC*. 56(5): 343–351 [PubMed: 20650354]
6. Hamo CE, Butler J, Gheorghiade M, Chioncel O (2016) The bumpy road to drug development for acute heart failure. *Eur Heart J Supp* 18(Supplement G):G19–G32
7. Gheorghiade M, Braunwald E (2011) A proposed model for initial assessment and management of acute heart failure syndromes. *JAMA* 305:1702–1703 [PubMed: 21521852]
8. Ponikowski P, Voors AA, Anker SD et al. (2016) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association of the ESC. *Eur Heart J* 37(27):2129–2200 [PubMed: 27206819]
9. Cleland JG, Pennell D, Ray S, Murray G, MacFarlane P, Cowley A, Coats A, Lahiri A (1999) The Carvedilol Hibernation Reversible Ischemia Trial: Marker of Success (CHRISTMAS). *Eur J Heart Fail* 1:191–196 [PubMed: 10937930]
10. Cleland JG, Pennell DJ, Ray SG, Coats AJ, Macfarlane PW, Murray GD, Mule JD, Vered Z, Lahiri A, Carvedilol hibernating reversible ischaemia trial: marker of success investigators, On behalf of the CHRISTMAS (Carvedilol Hibernating Reversible Ischaemia Trial: Marker of Success) investigators (2003) Myocardial viability as a determinant of the ejection fraction response to carvedilol in patients with heart failure (CHRISTMAS trial): randomised controlled trial. *Lancet* 362:14–21 [PubMed: 12853194]
11. Greene SJ, Vaduganathan M, Gheorghiade M (2017) Finding the road to recovery: therapeutic and clinical trial implications of dysfunctional viable myocardium in heart failure with reduced ejection fraction. *Eur J Heart Fail* 19(7):870–872 [PubMed: 28464398]
12. Adamsom PB, Magalski A, Braunschweig F et al. (2003) Ongoing right ventricular hemodynamics in heart failure: clinical value of measurements derived from an implantable monitoring system. *J Am Coll Cardiol* 41:565–571 [PubMed: 12598066]
13. Zile MR, Bennett TD, St John Sutton M et al. (2008) Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation* 118(14): 1433–1441 [PubMed: 18794390]

14. Stevenson LW, Perloff JK(1989) The limited reliability of physical signs for estimating hemodynamics in chronic heart failure. *JAMA* 261:884–888 [PubMed: 2913385]
15. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JE, Cleland JG, Dickstein K, Drazner MH, Fonarow GC, Jaarsma T, Jondeau G, Sendon JL, Mebazaa A, Metra M, Nieminen M, Pang PS, Seferovic P, Stevenson LW, van Veldhuisen D, Zannad F, Anker SD, Rhodes A, McMurray J, Filippatos G, European Society of Cardiology, European Society of Intensive Care Medicine (2010) Assessing and grading congestion in acute heart failure. *Eur J Heart Fail* 12(5):423–433 [PubMed: 20354029]
16. Ambrosy AP, Khan H, Udelson JE, Mentz RJ, Chioncel O, Greene SJ, Vaduganathan M, Subacuis HP, Konstam MA, Swedberg K, Zannad F, Maggioni AP, Gheorghiade M, Butler J (2016) Changes in dyspnea status during hospitalization and post-discharge health-related quality of life in hospitalized patients with heart failure: findings from the EVEREST trial. *Circ Heart Fail*. 9: e002458 [PubMed: 27140204]
17. Pang PS, Collins SP, Sauser K, Andrei AC, Storrow AB, Hollander JE, Tavares M, Spinar J, Macarie C, Raev D, Nowak R, Gheorghiade M, Mebazaa A (2014) Assessment of dyspnea early in acute heart failure: patient characteristics and response differences between Likert and visual analog scales. *Acad Emerg Med* 21(6):659–666 [PubMed: 25039550]
18. AbouEzzeddine OF, Lala A, Khazanie PP et al. (2016) Evaluation of a provocative dyspnea severity score in acute heart failure. *Am Heart J* 172:34–41 [PubMed: 26856213]
19. McGee S, Abernethy WB, Simel DL (1999) The rational clinical examination. Is this patient hypovolemic? *JAMA* 281:1022–1029 [PubMed: 10086438]
20. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JE, Cleland JG, Dickstein K, Drazner MH, Fonarow GC, Jaarsma T, Jondeau G, Sendon JL, Mebazaa A, Metra M, Nieminen M, Pang PS, Seferovic P, Stevenson LW, van Veldhuisen D, Zannad F, Anker SD, Rhodes A, McMurray J, Filippatos G, European Society of Cardiology, European Society of Intensive Care Medicine (2010) Assessing and grading congestion in acute heart failure: a scientific statement from the Acute Heart Failure Committee of the Heart Failure Association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. *Eur J Heart Fail* 12:423–433 [PubMed: 20354029]
21. Felker GM, Cuculich PS, Gheorghiade M (2006) The Valsalva maneuver: a bedside ‘biomarker’ for heart failure. *Am J Med* 119: 117–122 [PubMed: 16443410]
22. Knowles JH, Gorlin R, Storey CF (1956) Clinical test for pulmonary congestion with use of the Valsalva maneuver. *JAMA* 160:44–48
23. Weilenmann D, Rickli H, Follath F, Kiowski W, Brunner-la Rocca HP (2002) Noninvasive evaluation of pulmonary capillary wedge pressure by BP response to the Valsalva maneuver. *Chest* 122:140–145 [PubMed: 12114349]
24. Binanay C, Califf RM, Hasselblad V, O’Connor CM, Shah MR, Sopko G, Stevenson LW, Francis GS, Leier CV, Miller LW, ESCAPE Investigators and ESCAPE Study Coordinators (2005) Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA* 294:1625–1633 [PubMed: 16204662]
25. Chioncel O, Collins SP, Greene SJ, Ambrosy AP, Vaduganathan M, Macarie C, Butler J, Gheorghiade M (2016) Natriuretic peptide-guided management in heart failure. *J Cardiovasc Med* 17(8): 556–568
26. Seino Y, Ogawa A, Yamashita T, Fukushima M, Ogata KI, Fukumoto H, Takano T (2004) Application of NT-proBNP and BNP measurements in cardiac care: a more discerning marker for the detection and evaluation of heart failure. *Eur J Heart Fail* 6(3): 295–300 [PubMed: 14987579]
27. Fonarow GC, Peacock WF, Phillips CO, Givertz MM, Lopatin M, ADHERE Scientific Advisory Committee and Investigators (2007) Admission B-type natriuretic peptide levels and in-hospital mortality in acute decompensated heart failure. *JACC*. 49:1943–1950 [PubMed: 17498579]
28. Cohen-Solal A, Logeart D, Huang B, Cai D, Nieminen MS, Mebazaa A (2009) Lowered B-type natriuretic peptide in response to levosimendan or dobutamine treatment is associated with improved survival in patients with severe acutely decompensated heart failure. *JACC* 53(25):2343–2348 [PubMed: 19539144]

29. Ferre RM, Chioncel O, Pang PS, Lang RM, Gheorghiade M, Collins SP (2015) Acute heart failure: the role of focused emergency cardiopulmonary ultrasound in identification and early management. *Eur J Heart Fail* 17:1223–1227 [PubMed: 26467351]
30. Goonewardena SN, Gemignani A, Ronan A, Vasaiwala S, Blair J, Brennan JM, Shah DP, Spencer KT (2008) Comparison of hand-carried ultrasound assessment of the inferior vena cava and N-terminal pro-brain natriuretic peptide for predicting readmission after hospitalization for acute decompensated heart failure. *JACC Cardiovasc Imaging* 1 (5):595–601 [PubMed: 19356487]
31. Van De Water JM, Miller TW (2003) Impedance cardiography: the next vital sign technology? *Chest* 123(6):2028–2033 [PubMed: 12796185]
32. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJV, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Wilson Tang WH, Tsai EJ, Bruce L (2013) Wilkoff. 2013 ACCF/AHA guideline for the management of heart failure. *Circulation* 128:e240–e327 [PubMed: 23741058]
33. Testani JM, Chen J, McCauley BD et al. (2010) Potential effects of aggressive decongestion during the treatment of decompensated heart failure on renal function and survival. *Circulation* 122:265–272 [PubMed: 20606118]
34. Greene SJ, Gheorghiade M, Vaduganathan M, Ambrosy AP, Mentz RJ, Subacius H, Maggioni AP, Nodari S, Konstam MA, Butler J, Filippatos G, on behalf of the EVEREST Trial investigators (2013) EVEREST trial investigators: Haemoconcentration, renal function, and post-discharge outcomes among patients hospitalized for heart failure with reduced ejection fraction: insights from the EVEREST trial. *Eur J Heart Fail* 15:1401–1411 [PubMed: 23845795]
35. Testani JM, Kimmel SE, Dries DL, Coca SG (2011) Prognostic importance of early worsening renal function after initiation of angiotensin-converting enzyme inhibitor therapy in patients with cardiac dysfunction. *Circ Heart Fail* 4(6):685–691 [PubMed: 21903907]
36. Rossignol P, Cleland JG, Bhandari S et al. (2012) Determinants and consequences of renal function variations with aldosterone blocker therapy in heart failure patients after myocardial infarction: insights from the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study. *Circulation* 125:271–279 [PubMed: 22128223]
37. Golwala HB et al. (2013) Use of hydralazineisosorbide dinitrate combination in African American and other race/ethnic group patients with heart failure and reduced left ventricular ejection fraction. *J Am Heart Assoc* 2:e000214 [PubMed: 23966379]
38. Gheorghiade M, Braunwald E (2009) Reconsidering the role for digoxin in the management of acute heart failure syndromes. *JAMA* 302:2146–2147 [PubMed: 19920240]
39. The Digitalis Investigation Group (1997) The effect of digoxin on mortality and morbidity in patients with heart failure. *NEJM* 336: 525–533 [PubMed: 9036306]
40. Albert NM, Yancy CW, Liang L, Zhao X, Hernandez AF, Peterson ED, Cannon CP, Fonarow GC (2009) Use of aldosterone antagonists in heart failure. *JAMA* 302:1658–1665 [PubMed: 19843900]
41. Schrier RW, Gheorghiade M (2011) Challenge of rehospitalizations for heart failure: potential of natriuretic doses of mineralocorticoid receptor antagonists. *Am Heart J* 161:221–223 [PubMed: 21315201]
42. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J (1999) The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *NEJM* 341:709–717 [PubMed: 10471456]
43. Gines P, Schrier RW (2009) Renal failure in cirrhosis. *NEJM* 361: 1279–1290 [PubMed: 19776409]
44. Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, Clausell N, Desai AS, Diaz R, Fleg JL, Gordeev I, Harty B, Heitner JF, Kenwood CT, Lewis EF, O'Meara E, Probstfield JL, Shaburishvili T, Shah SJ, Solomon SD, Sweitzer NK, Yang S, McKinlay S, TOPCAT Investigators (2014) Spironolactone for heart failure with preserved ejection fraction. *NEJM* 370(15): 1383–1392 [PubMed: 24716680]

45. Bikdeli B, Strait KM, Dharmarajan K, Partovian C, Coca SG, Kim N, Li SX, Testani JM, Khan U, Krumholz HM (2013) Dominance of furosemide for loop diuretic therapy in heart failure: time to revisit the alternatives? *JACC* 61(14):1549–1550 [PubMed: 23500272]
46. Müller K, Gamba G, Jaquet F, Hess B (2003) Torasemide vs. furosemide in primary care patients with chronic heart failure NYHA II to IV—efficacy and quality of life. *Eur J Heart Fail* 5(6):793–801 [PubMed: 14675858]
47. Kasama S, Toyama T, Hatori T, Sumino H, Kumakura H, Takayama Y, Ichikawa S, Suzuki T, Kurabayashi M (2006) Effects of torasemide on cardiac sympathetic nerve activity and left ventricular remodelling in patients with congestive heart failure. *Heart* 92(10):1434–1440 [PubMed: 16621879]
48. Vargo DL, Kramer WG, Black PK, Smith WB, Serpas T, Brater DC (1995) Bioavailability, pharmacokinetics, and pharmacodynamics of torsemide and furosemide in patients with congestive heart failure. *Clin Pharmacol Ther* 57(6):601–609 [PubMed: 7781259]
49. Buggey J, Mentz RJ, Pitt B, Eisenstein EL, Anstrom KJ, Velazquez EJ, O'Connor CM (2015) A reappraisal of loop diuretic choice in heart failure patients. *Am Heart J* 169(3):323–333 [PubMed: 25728721]
50. Bleske BE, Welage LS, Kramer WG, Nicklas JM (1998) Pharmacokinetics of torsemide in patients with decompensated and compensated congestive heart failure. *J Clin Pharmacol* 38(8):708–714 [PubMed: 9725546]
51. Elhassan EA, Schrier RW. Disorders of extracellular volume. *Compr Clin Nephrol* (4e). 2010 80–93. Print
52. Ellison DH (1991) The physiologic basis of diuretic synergism: its role in treating diuretic resistance. *Ann Int Med* 114(10):886–894 [PubMed: 2014951]
53. Swedberg K, Komajda M, Bohm M et al. (2010) Ivabradine and outcomes in chronic heart failure (SHIFT): a randomized placebo-controlled study. *Lancet* 376(9744):875–885 [PubMed: 20801500]
54. Segura LM (2011) Dual-acting angiotensin receptor-neprilysin inhibition. *Curr Hypertens Rep* 13:74–78 [PubMed: 21046489]
55. McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR, PARADIGM-HF Investigators and Committees (2014) Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 371:993–1004 [PubMed: 25176015]
56. Xie W, Zheng F, Song X, Zhong B, Yan L (2016) Renin-angiotensin-aldosterone system blockers for heart failure with reduced ejection fraction or left ventricular dysfunction: network meta-analysis. *Int J Cardiol* 205:65–71 [PubMed: 26720043]
57. Desai AS, Claggett BL, Packer M, Zile MR, Rouleau JL, Swedberg K, Shi V, Lefkowitz M, Starling R, Teerlink J, McMurray J, Solomon SD, PARADIGM-HF Investigators (2016) Influence of sacubitril/valsartan (LCZ696) on 30-day readmission after heart failure hospitalization. *J Am Coll Cardiol* 68(3):241–248 [PubMed: 27417000]
58. Li PK, Chow KM, et al (2017) Changes in the worldwide epidemiology of peritoneal dialysis. *Nat Rev Nephrol* 13(2):90–103 [PubMed: 28029154]
59. Bart BA, Goldsmith SR, Lee KL et al. (2012) Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *NEJM* 367:2296–2304 [PubMed: 23131078]
60. Costanzo MR, Negoianu D, Jaski BE, Bart BA, Heywood JT, Anand IS, Smelser JM, Kaneshige AM, Chomsky DB, Adler ED, Haas GJ, Watts JA, Nabut JL, Schollmeyer MP, Fonarow GC (2016) Aquapheresis versus intravenous diuretics and hospitalizations for heart failure. *JACC: Heart Failure* 4(2):95–105 [PubMed: 26519995]
61. Mehrotra R, Kathuria P Place of peritoneal dialysis in the management of treatment-resistant congestive heart failure. *Kidney Int Suppl* 103:S67–S71
62. Cnossen TT, Kooman JP, Konings CJ (2010) Peritoneal dialysis in patients with primary cardiac failure complicated by renal failure. *Blood Purif* 20:146–152
63. Nunez J, Gonazalez M, Minana G et al. (2012) Continuous ambulatory peritoneal dialysis as a therapeutic alternative in patients with advanced congestive heart failure. *Eur J Heart Fail* 14:540–548 [PubMed: 22327061]

64. Chioncel O, Lainscak M, Seferovic PM, Anker SD, Crespo-Leiro MG, Harjola VP, Parissis J, Laroche C, Piepoli MF, Fonseca C, Mebazaa A, Lund L, Ambrosio GA, Coats AJ, Ferrari R, Ruschitzka F, Maggioni AP, Filippatos G (2017) Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC Heart Failure Long-Term Registry. *Eur J Heart Fail* 19:1574–1585. 10.1002/ehf.813 [PubMed: 28386917]
65. Adams JKF, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP (2005) Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J* 149:209–216 [PubMed: 15846257]
66. Ments RJ, Kelly JP, von Lueder TG et al. (2014) Noncardiac comorbidities in heart failure with reduced versus preserved ejection fraction. *JACC*. 64(21):2281–2293 [PubMed: 25456761]
67. Bahrami H, Bluemke DA, Kronmal R, Bertoni AG, Lloyd-Jones DM, Shahar E, Szklo M, Lima JAC (2008) Novel metabolic risk factors for incident heart failure and their relationship with obesity: the MESA (Multi-Ethnic Study of Atherosclerosis) study. *JACC*. 51:1775–1783 [PubMed: 18452784]
68. Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, Jones NP, Komajda M, McMurray JJV (2009) Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicenter, randomized, open-label trial. *Lancet* 373(9681):2125–2135 [PubMed: 19501900]
69. Scirica BM, Bhatt D, Braunwald E et al. (2013) Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus (SAVOR-TIMI 53). *NEJM* 369:1317–1326 [PubMed: 23992601]
70. Grempler R, Thomas L, Eckhardt M, Himmelsbach F, Sauer A, Sharp DE, Bakker RA, Mark M, Klein T, Eickelmann P (2012) Empagliflozin, a novel selective sodium glucose cotransporter-2 (SGLT-2) inhibitor: characterization and comparison with other SGLT-2 inhibitors. *Diabetes Obes Metab* 14:83–90 [PubMed: 21985634]
71. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE, EMPA-REG OUTCOME Investigators (2015) Empagliflozin, cardiovascular outcomes and mortality in type 2 diabetes. *NEJM* 373(22):2117–2128 [PubMed: 26378978]
72. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erond N, Shaw W, Law G, Desai M, Matthews DR, CANVAS Program Collaborative Group (2017) Canagliflozin and cardiovascular and renal events in type 2 diabetes. *NEJM* 377:644–657 [PubMed: 28605608]
73. Groenveld HF, Januzzi JL, Damman K, van Wijngaarden J, Hillege HL, van Veldhuisen DJ, van der Meer P (2008) Anemia and mortality in heart failure patients: a systematic review and meta-analysis. *JACC*. 52:818–827 [PubMed: 18755344]
74. Tang YD, Katz SD (2006) Anemia in chronic heart failure: prevalence, etiology, clinical correlates, and treatment options. *Circ*. 113: 2454–2461
75. Jankowska EA, Rozentryt P, Witkowska A, Nowak J, Hartmann O, Ponikowska B, Borodulin-Nadziejka L, Banasiak W, Polonski L, Filippatos G, McMurray JJV, Anker SD, Ponikowski P (2010) Iron deficiency: an ominous sign in patients with systolic chronic heart failure. *Eur Heart J* 31:1872–1880 [PubMed: 20570952]
76. Swedberg K, Young JB, Anand IS, Cheng S, Desai AS, Diaz R, Maggioni AP, McMurray J, O'Connor C, Pfeffer MA, Solomon SD, Sun Y, Tendera M, van Veldhuisen D, RED-HF Committees, RED-HF Investigators (2013) Treatment of anemia with darbepoietin alfa in systolic heart failure. *NEJM* 368:1210–1219 [PubMed: 23473338]
77. Lewis GD, Malhotra R, Hernandez AF, McNulty SE, Smith A, Felker GM, Tang WHW, LaRue SJ, Redfield MM, Semigran MJ, Givertz MM, van Buren P, Whellan D, Anstrom KJ, Shah MR, Desvigne-Nickens P, Butler J, Braunwald E, for the NHLBI Heart Failure Clinical Research Network (2017) Effects of oral iron repletion on exercise capacity in patients with heart failure with reduced ejection fraction and iron deficiency. *JAMA* 317(19): 1958–1966 [PubMed: 28510680]

78. Gerasimos F, Dimitrios F, Comin C et al. (2013) Intravenous ferric carboxymaltose in iron-deficient chronic heart failure patients with and without anaemia: a subanalysis of the FAIR-HF trial. *Eur J Heart Fail* 15:1267–1276 [PubMed: 23787722]
79. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, McDonagh T, Parkhomenko A, Tavazzi L, Levesque V, Mori C, Roubert B, Filippatos G, Ruschitzka F, Anker SD, for the CONFIRM-HF Investigators (2015) Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. *Eur Heart J* 36(11):657–668 [PubMed: 25176939]
80. van Velhuisen DJ, Ponikowski PI, van der Meer P et al. (2017) Effect of ferric carboxymaltose on exercise capacity in patients with chronic heart failure and iron deficiency. *Circulation*; CIRCULATIONAHA 117:02749
81. Greene SJ, Fonarow GC, Vaduganathan M, Khan SS, Butler J, Gheorghiade M (2015) The vulnerable phase after hospitalization for heart failure. *Nat Rev Cardiol* 12(4):220–229 [PubMed: 25666406]
82. Hernandez AF, Greiner MA, Fonarow GC, Hammill BG, Heidenreich PA, Yancy CW, Peterson ED, Curtis LH (2010) Relationship between early physician follow-up and 30-day readmission among Medicare beneficiaries hospitalized for heart failure. *JAMA* 303:1716–1722 [PubMed: 20442387]
83. Harinstein ME, Flaherty JD, Fonarow GC, Mehra MR, Lang RM, Kim RJ, Cleland JG, Knight BP, Pang PS, Bonow RO, Gheorghiade M (2011) Clinical assessment of acute heart failure syndromes: emergency department through the early post-discharge period. *Heart* 97:1607–1618 [PubMed: 21900586]
84. Green CP, Porter CB, Bresnahan DR, Spertus JA (2000) Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *JACC*. 35(5): 1245–1255 [PubMed: 10758967]
85. Dai S et al. (2016) Kansas City Cardiomyopathy Questionnaire Utility in prediction of 30 day readmission rate in patients with chronic heart failure. *Cardiol Res Pract* 2016(2016):4571201 [PubMed: 27872790]
86. Greene SJ, Maggioni AP, Fonarow GC et al. (2015) Clinical profile and prognostic significance of natriuretic peptide trajectory following hospitalization for worsening chronic heart failure: findings from the ASTRONAUT trial. *Eur J Heart Fail* 17(1):98–108 [PubMed: 25597870]
87. Greene SJ, Butler J, Fonarow GC et al. (2017) Pre-discharge and early post-discharge troponin elevation among patients hospitalized for heart failure with reduced ejection fraction: findings from the ASTRONAUT trial. *Eur J Heart Fail* 20:281–291. 10.1002/ehf.1019 [PubMed: 29044915]
88. Metra M, Gheorghiade M, Bonow RO, Dei Cas L (2010) Postdischarge assessment after a heart failure hospitalization: the next step forward. *Circ* 122:1782–1785
89. Flynn KE, Pina IL, Whellan DJ et al. (2009) Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 301(14):1451–1459 [PubMed: 19351942]
90. Golwala H, Pandey A, Ju C, Butler J, Yancy C, Bhatt DL, Hernandez AF, Fonarow GC (2015) Temporal trends and factors associated with cardiac rehabilitation referral among patients hospitalized with heart failure findings from Get with the Guidelines—Heart Failure Registry. *JACC*. 66(8):917–926 [PubMed: 26293762]
91. Varnfield M, Karunanithi M, Lee CK, Honeyman E, Arnold D, Ding H, Smith C, Walters DL (2014) Smartphone-based home care model improved use of cardiac rehabilitation in postmyocardial infarction patients: results from a randomized controlled trial. *Heart* 100:1770–1779 [PubMed: 24973083]
92. Abraham Wet al (2011) Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomized controlled trial. *Lancet* 377:658–666 [PubMed: 21315441]

Fig. 1.

Eight-axis algorithm for managing ADHF. HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; EF, ejection fraction; HTN, hypertension; CAD, coronary artery disease; CKD, chronic kidney disease; DM2, diabetes mellitus type 2; US, ultrasound; echo, echocardiogram; LHC, left heart catheterization; Dob Echo, dobutamine echocardiography; BIVA, bioelectrical impedance vector analysis; SPECT, single-photon emission computed tomography; ECG, electrocardiogram; EP, electrophysiology; BMP, basic metabolic panel; PFT, pulmonary function test; ACEI, ACE inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; ICD, implantable cardioverter defibrillator; FCM, ferrous carboxymaltose; BP, blood pressure; NPPV, noninvasive positive pressure ventilation; DAPT, dual anti-platelet therapy; PCI, percutaneous intervention; GDMT, guideline-directed medical therapy; Afib, atrial fibrillation; CRT, cardiac resynchronization therapy. Borderline EF (asterisk) is also known as HFmrEF, heart failure with moderately reduced ejection fraction.

Fig. 2. Transition to expanded eight-axis assessment model. ED, emergency department; FU, follow-up; IV, intravenous; GDMT, guideline-directed medical therapy

Fig. 3. Congestion timeline with associated therapeutic recommendations. The spectrum of hemodynamic and clinical congestion requires a thoughtful therapeutic timeline. Hemodynamic congestion typically in the outpatient setting and progresses to clinical congestion possibly requiring admission for management. IV therapies and a thorough multi-modality assessment should be performed as outlined above. Realize that hemodynamic congestion with persistent elevation of LVEDP may be present despite improvement of symptoms. Using the highlighted techniques and tools can further improve hemodynamic congestion before discharge. Post-discharge reassessment is crucial to achieve true euvolemia and prevent re-congestion. Initiation of advanced therapies must be considered on a case by case basis. IV, intravenous; NPs, natriuretic peptides; SBP, systolic blood pressure; HR, heart rate; CRT, cardiac resynchronization therapy; ICD, invasive cardiac defibrillator; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; LVAD, left ventricular assist device; HTX, heart transplant

Table 1

Summary of underutilized heart failure therapies

Therapy	Recommendation	Supporting trials
Digoxin	Use in refractory HFrEF in addition to GDMT to decrease rate of rehospitalization	DIG Trial (1997)
MRAs	HFrEF patients with NYHA III–IV symptoms HFrEF patients with normal renal function	RALES (1999) TOPCAT (2014)
Torsemide	Consideration of torsemide over furosemide as oral loop diuretic therapy in patients with difficult to treat congestion or diuretic resistance	TRANSFORM-HF (current)
Thiazides	Use in combination with loop diuretics in diuretic resistant patients	CLOTOTIC (current)
Ivabradine	HFrEF patients on maximal GDMT with standing HR > 70BPM	SHIFT (2010)
ARNIs	HFrEF patients in place of ACEI	PARADIGM-HF (2014) PIONEER-HF (current)
Ultrafiltration	In ADHF with congestion refractory to medical therapy (level of evidence: C)	RAPID-CHF (2005) CARRESS-HF (2012)

HFrEF heart failure with reduced ejection fraction, *GDMT* guideline-directed medical therapy, *NYHA* New York Heart Association, *HFrEF* heart failure with preserved ejection fraction, *HF* heart failure, *HR* heart rate, *BPM* beats per minute, *ARNI* angiotensin receptor–neprilysin inhibitors, *ACEI* ACE inhibitor, *ADHF* acute decompensated heart failure