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Management of Patients Admitted with Acute Decompensated Heart Failure

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Background: Hospital admission for the treatment of acute decompensated heart failure is an unfortunate certainty in the vast majority of patients with heart failure. Regardless of the etiology, inpatient treatment for acute decompensated heart failure portends a worsening prognosis.

Methods: This review identifies patients with heart failure who need inpatient therapy and provides an overview of recommended therapies and management of these patients in the hospital setting.

Results: Inpatient therapy for patients with acute decompensated heart failure should be directed at decongestion and symptom improvement. Clinicians should also treat possible precipitating events, identify comorbid conditions that may exacerbate heart failure, evaluate and update current guideline-directed medical therapy, and perform risk stratification for all patients. Finally, efforts should be made to educate patients about the importance of restricting salt and fluid, monitoring daily weights, and adhering to a graded exercise program.

Conclusion: Early discharge follow-up and continued optimization of guideline-directed medical therapy are key to preventing future heart failure readmissions.

Keywords: *Disease management, heart failure, inpatients*

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INTRODUCTION

For the vast majority of patients with heart failure, hospital admission for the treatment of acute decompensated heart failure is an unfortunate certainty. Regardless of the etiology, inpatient treatment for acute decompensated heart failure portends a worsening prognosis. Following the seminal event, readmission rates are nearly 50% at 6 months, and 1-year mortality reaches 30%.[1,2] This report identifies patients with heart failure who need inpatient therapy and reviews recommended therapies and management of these patients in the hospital setting. This review focuses on guideline-directed medical therapy in the setting of heart failure with reduced ejection fraction. Advanced heart failure therapies (cardiac transplantation, mechanical circulatory support), including treatment of patients with cardiogenic shock (use of inotropes), are beyond the scope of this review and are not addressed.

CRITERIA FOR INPATIENT HEART FAILURE THERAPY

Identification of patients who require hospitalization is of the upmost importance to relieve symptoms and optimize guideline-directed medical therapy (Table 1). Patients who have progression of heart failure symptoms despite intensification and optimization of outpatient therapies should be considered for admission.[3] The presence of declining renal function at the time of admission is a marker of high mortality in this population, with blood urea nitrogen $\geq$43 mg/dL as the single strongest predictor. Renal failure results in neurohormonal activation and increased congestion that increase adverse outcomes in patients with heart failure.[4]

Several well-validated heart failure risk scores can be used to predict mortality, including the Acute Decompensated Heart Failure National Registry (ADHERE) model, the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) risk score, the Heart Failure Survival Score, and the Seattle Heart Failure Model. The Seattle Heart Failure Model is available as an online application (http://seattleheartfailuremodel.org).

INITIAL EVALUATION

During admission, the clinician should evaluate and treat possible precipitating factors (Table 2), evaluate and update current guideline-directed medical therapy, and perform risk stratification for all patients.

Table 1. Criteria for Inpatient Heart Failure Therapy[3]

Recommend Hospitalization	Consider Hospitalization
Hypotension	Evidence of worsening congestion
	Increased liver function tests suggesting hepatic congestion
	Weight gain
Declining renal function	Electrolyte disturbances
Change in mental status	Comorbid conditions that can worsen heart failure • Pneumonia • Pulmonary embolism • Diabetes • Stroke or transient ischemic attack
Dyspnea at rest	Implantable cardiac defibrillator discharges
Arrhythmia	Newly diagnosed heart failure with signs and symptoms of congestion
Atrial fibrillation	
Ventricular tachycardia	
Acute coronary syndromes	

Patients admitted with previously undiagnosed heart failure should undergo a thorough evaluation for the etiology of heart failure, including ischemic evaluation, electrocardiogram, echocardiogram, cardiac biomarkers, and a thorough review of medical history. Familial syndromes may be present in up to 35% of patients with newly diagnosed idiopathic dilated cardiomyopathy. The precipitating event that results in admission for acute decompensated heart failure can often be elucidated from a thorough review of the patient's lifestyle. Patients and caregivers are often aware of the dietary restrictions but are unclear on the sodium content of many foods. Are patients eating out more often? Are they eating prepared meals labeled as healthy choices that are high in sodium? Many times, patients are unwilling to adhere to the required sodium and fluid restrictions. As patients age, they often become forgetful, and medication doses can be missed or delayed.

INPATIENT PHARMACOLOGIC THERAPIES

Initial therapies during admission for acute decompensated heart failure should be directed at decongestion and symptom improvement.

Diuretics, Vasodilators, and Ultrafiltration

Loop diuretics remain the most commonly used agents among patients admitted for acute decompensated heart failure. These drugs (furosemide, bumetanide, and ethacrynic acid) inhibit the reabsorption of sodium, potassium, and chloride in the ascending loop of Henle. The diuretic effect of these drugs depends on two factors. First, higher doses of loop diuretics may be needed in the setting of severe renal insufficiency or low cardiac output to ensure delivery of sufficient concentrations of the drug to its site of action.[5] Second, the efficacy of loop diuretics also depends on gastrointestinal absorption that can decrease because of bowel wall edema caused by splanchnic congestion in the setting of acute decompensated heart failure. Decreased gastrointestinal absorption and/or insufficient delivery of drug concentrations to the site of action can lead to diuretic resistance. Therefore, appropriate diuretic dosing is vital in maintaining normal volume status among individuals with heart failure.

In the setting of diuretic resistance, increasing the loop diuretic dose will compensate for the pharmacokinetic and pharmacodynamic changes that occur in heart failure and may be an effective strategy.[6] Intravenous (IV) loop diuretics at a dose higher than the outpatient dose or oral loop diuretics with a higher oral bioavailability than furosemide may be used.[7] Current evidence demonstrates no significant difference in patient symptoms or changes in renal function when loop diuretics are administered as a bolus compared to continuous infusion or at a high dose compared to a low dose.[8] Furthermore, no difference appears to exist in the safety and efficacy of bolus injection compared to continuous infusion of loop diuretics.[9]

Despite the lack of evidence to support the use of one loop diuretic over another, IV furosemide remains the most commonly used diuretic in the inpatient setting. Nevertheless, physicians should be familiar with differences in dosing

Table 2. Common Precipitating Factors for Heart Failure Hospital Admission

Nonadherence to guideline-directed medical therapy, diet, and fluid and/or sodium restriction
Accelerated or uncontrolled hypertension
Arrhythmia (most commonly atrial fibrillation)
Acute myocardial infarction
Concurrent infection (pneumonia, viral illness)
Medications – addition of negative inotropes (calcium channel and beta blockers)
Medications that increase sodium retention (steroids, nonsteroidal antiinflammatory drugs, thiazolidinediones)
Pulmonary embolism
Excessive alcohol or illicit drug use
Endocrinologic comorbidities (diabetes mellitus, hypothyroidism, hyperthyroidism)
Acute cardiovascular disease (valvular disease, aortic dissection, myopericarditis, endocarditis)

Table 3. Pharmacokinetics of Loop Diuretics

	Furosemide	Bumetanide	Ethacrynic Acid
Equivalent dosing, mg	20	1	50
Onset of action,[a] min	5	2-3	5
Time to peak effect, min	30	15-30	15-30
Metabolism	50% renal conjugation	50% hepatic	100% hepatic
Dosing frequency	Daily to every 8 hours	Daily to every 12 hours	Daily to every 8 hours

[a]Intravenous route.

between loop diuretics to prevent potential dosing errors (Table 3).

After initiation of IV diuresis, careful hemodynamic monitoring and frequent clinical assessment are required. Although bed rest is recommended during the acute phase of hospitalization to improve diuresis, early ambulation with physical therapy should begin within the first 24 hours of admission. Routine use of Foley catheters is not necessary, but if accurate assessment of urine output is limited because of incontinence or other patient factors, a Foley catheter may be considered. Assessment of volume status should occur at least once per day, including evaluation of peripheral edema (lower extremities, upper extremities, and sacrum), jugular venous pressure, ascites, rales, hepatomegaly, and daily weights. Reevaluation of symptoms of congestion aids in guiding continued management and should focus on the symptoms that prompted hospital admission: dyspnea, orthopnea, nocturnal cough, altered mental status, and fatigue. Close monitoring of vital signs for evidence of diuretic side effects should focus on hypotension, orthostasis, and urine output. While IV diuresis is pursued, careful monitoring of renal function and electrolytes is required to ensure adequate electrolyte replacement and to adjust diuretic dosing as necessary. If large volume diuresis occurs, more frequent laboratory evaluation of renal function and electrolytes may be required.

American College of Cardiology/American Heart Association (ACC/AHA) and Heart Failure Society of America guidelines recommend considering the addition of an IV vasodilator (nitroglycerin/nitroprusside or nesiritide) [Class IIb, Level B] for patients who fail to respond adequately to IV diuresis.[3]

Available data regarding the risks and benefits of nesiritide therapy for acute decompensated heart failure are controversial. Early studies demonstrated improvement in symptoms, acute hemodynamics, weight loss, urine output, renin-angiotensin-aldosterone system activation, and decreased diuretic use without significant neurohormonal stimulation compared to placebo.[10,11] However, these studies found a greater risk of arrhythmia and hypotension. The Vasodilatation in the Management of Acute Congestive Heart Failure (VMAC) study showed that nesiritide provided more rapid hemodynamic improvements and was better tolerated than IV nitroglycerin but found no difference in patient-reported dyspnea scores between the 2 vasodilators.[12] In 2005, a large but controversial metaanalysis reported increased mortality associated with nesiritide use compared to placebo, but methodological concerns called the results of the study into question and raised the call for large randomized clinical trials.[13] Therefore, based on the current available data, routine use of nesiritide for acute decompensated heart failure cannot be recommended. In select patients with adequate blood pressure, intolerance to nitroglycerin or nitroprusside, and significant congestion unresponsive to IV diuresis alone, nesiritide could be considered to improve congestion and acutely reduce symptoms in the early admission period.

In patients with signs of significant volume overload or patients who fail to respond to medical therapy, ultrafiltration may be considered (Class IIb indication).[14] However, based on the results of the recently published Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) trial, routine use of ultrafiltration for the treatment of acute decompensated heart failure cannot be recommended.[15]

Conventional Guideline-Directed Medical Therapy

During admission, all guideline-directed medical therapy should be evaluated and adjusted based on patient presentation. If hypotension is present, holding beta blockers and angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may be beneficial to allow for adequate diuresis and ensure target organ perfusion. However, in the absence of contraindications, guideline-directed medical therapy (beta blockers, ACEIs, aldosterone antagonists) should not be routinely held during admission. Conventional therapies, including beta blockers and ACEIs, have demonstrated morbidity and mortality benefits in heart failure with reduced ejection fraction and are the mainstay of heart failure treatment strategies. ACEI therapy should begin as early as possible during the index hospitalization. In the absence of significant renal dysfunction or hypotension, ACEIs should be initiated at low doses with gradual titration to achieve doses equivalent to those in randomized clinical trials.[16-18]

Angiotensin-Converting Enzyme Inhibitors

Current data support a class effect with ACEIs, but preference should be given to longer-acting ACEIs to reduce the number of pills and ensure consistent neurohormonal blockade. Some caution should be used when considering initiation of ACEIs in patients with hyponatremia because of concerns for hypotension. ACEIs have been shown to have a mortality benefit in early and long-term therapy. ARBs have been shown to be well tolerated and reduce cardiovascular risk in patients who are unable to tolerate ACEIs (cough, hypotension, and renal dysfunction).[4,14]

Beta Blockers

Beta blocker therapy has been shown to reduce morbidity and mortality in all patients with heart failure with reduced

ejection fraction, including those already on ACEIs.[19] Unlike ACEIs, no evidence links beta blockers to a class effect. Only 3 agents in randomized clinical trials have been shown to have favorable effects on survival and disease progression: carvedilol,[19,20] sustained-release metoprolol (succinate),[21] and bisoprolol.[22] Because no direct head-to-head comparison of beta blockers and ACEIs in heart failure exists to date, one agent cannot be recommended over another.[14] As with ACEIs, doses should start low and be titrated to achieve doses similar to those in randomized clinical trials.[14] Beta blockers can be started early in the absence of contraindications such as hypotension or symptomatic bradycardia. Caution should be used when administering beta blockers to patients who have required inotropic therapy during their index hospitalization and to patients with newly diagnosed heart failure.

Mineralocorticoid Receptor Antagonists

For patients with New York Heart Association (NYHA) Class II-IV heart failure symptoms who are already on guideline-directed medical therapy (beta blockers, ACEIs, and diuretics), the addition of mineralocorticoid receptor antagonists (MRAs) has been shown to improve survival rates and reduce heart failure–related hospitalizations. ACC/AHA guidelines recommend MRA therapy (spironolactone, eplerenone) in patients with ejection fraction $\leq$35% in the absence of contraindications.[14] Aldosterone blockade should also be considered in symptomatic patients with left ventricular ejection fraction $\leq$40% after recent myocardial infarction.[23,24]

Caution must be used when administering aldosterone antagonists. They should only be administered to patients with a glomerular filtration rate $>$30 mL/min/1.73 m^2 and serum potassium $<$5.0 mEq/L, and they should not be used in conjunction with other potassium-sparing diuretics. Careful monitoring of renal function, serum potassium, and volume status is necessary after initiation to avoid adverse events from hyperkalemia and renal failure. Spironolactone (a nonselective aldosterone antagonist) carries the risk of painful gynecomastia in male patients who may require switching to the more expensive agent eplerenone (a selective antagonist).[14,23,24]

The addition of isosorbide dinitrate/hydralazine to the treatment regimen for African Americans with NYHA Class II-IV heart failure already on optimal medical therapy (including ACEIs/ARBs) is recommended to reduce morbidity and mortality.[14] Isosorbide dinitrate/hydralazine is also recommended [ACC/AHA Class IIa] for African Americans with Stage C heart failure (current or past symptoms) and reduced ejection fraction who are intolerant of ACEI/ARB therapy.[14] In clinical trials, ACEIs/ARBs have been superior in terms of mortality.[25,26] Therefore, the combination of isosorbide dinitrate/hydralazine should not be used as first-line neurohormonal therapy for patients who have not been trialed on ACEIs/ARBs or aldosterone antagonists.[14] Isosorbide dinitrate/hydralazine should be initiated at low doses (37.5/20 mg, 1 tablet 3 times daily) and titrated to a goal of 2 tablets 3 times daily as tolerated. The high incidence of side effects (headache, gastrointestinal disturbance, and dizziness) has limited adherence to this therapy.

In patients with severe hypervolemic hyponatremia who have or are at risk of active cognitive deficits, arginine vasopressin (AVP) antagonists (conivaptan and tolvaptan) may be considered to aid in the correction of serum sodium and may improve diuresis.[14,27-29] Prior to initiating acute therapy with AVP antagonists, all other possible causes of hyponatremia (syndrome of inappropriate antidiuretic hormone secretion, hypothyroidism, hypoaldosteronism) should be ruled out. Although AVP therapy has been shown to improve serum sodium, no mortality benefit has been shown in patients with heart failure.[14] During AVP antagonist administration, liberalization of sodium restriction, frequent assessment of serum sodium, and discontinuation of therapy once serum sodium is $>$135 mg/dL are important. Long-term use of AVP antagonists is not recommended.[14]

Digoxin

Digoxin and diuretic therapy were once the foundation of heart failure therapy. However, the development of newer, more effective therapies and recent studies evaluating the efficacy of digoxin in the setting of heart failure with reduced ejection fraction have caused the drug to fall out of favor. Digoxin has not been shown to provide any mortality benefit when used in the setting of heart failure with reduced ejection fraction,[30] but digoxin therapy has been shown to decrease hospitalizations for cardiovascular causes—primarily because of a decrease in heart failure hospitalizations.[30] This decrease is most likely because of symptomatic benefits in the setting of heart failure. Important results from the Prospective Randomized study Of Ventricular failure and the Efficacy of Digoxin (PROVED) trial[31] suggest that patients withdrawn from digoxin therapy demonstrated worsening maximal exercise capacity compared to those who were continued on digoxin.[30] Furthermore, in the Randomized Assessment of Digoxin on Inhibitors of the ANgiotensin Converting Enzyme (RADIANCE) study,[32] patients who were switched from digoxin to placebo experienced worsening heart failure, decreased functional capacity, lower quality-of-life scores, decreased ejection fractions, increases in heart rate, and higher body weights compared to patients who continued to receive digoxin therapy.[32] The RADIANCE study suggests that withdrawal of digoxin in patients with heart failure with reduced ejection fraction may result in undesired clinical consequences.

Finally, the narrow therapeutic index of digoxin increases the risk of toxicity and adverse effects. Digoxin is mainly excreted by the kidneys, and as a result, impaired renal function can lead to higher plasma concentrations.[33-35] Chronic heart failure and advanced age can also reduce the volume of distribution of the drug and increase the risk of toxicity. Other causes that can precipitate digoxin toxicity include hypokalemia, hypomagnesemia, hypocalcemia, medication interaction, and hypothyroidism. Current guidelines recommend administering digoxin to patients with heart failure with reduced ejection fraction to decrease heart failure hospitalizations.[14]

Thromboembolism Prophylaxis

Heart failure is a recognized risk factor for thromboembolic events. Venous stasis, hypercoagulability, reduced cardiac output, and decreased ambulation contribute to the

Table 4. Discharge Checklist

✓ Discharge Planning Goals
☐ 1. Guideline-directed medical therapy has been reviewed and patient has been stable for 24 hours.
☐ 2. Potential exacerbating/confounding comorbidities have been addressed.
☐ 3. Exercise tolerance has returned to New York Heart Association Class II.
☐ 4. Volume status has been optimized.
☐ 5. Education has been provided.
☐ 6. Clinic follow-up has been scheduled.

increased risk of thrombosis. When patients are admitted for acute decompensated heart failure, they are often placed on bed rest or confined to a reclining chair, and such patients should receive venous thromboembolism prophylaxis in the absence of contraindications.[14]

MANAGING COMPLICATIONS ASSOCIATED WITH ACUTE DECOMPENSATED HEART FAILURE

As medical therapy for heart failure has progressed, the list of drugs that improve symptoms and reduce mortality has grown. In patients with Stage C heart failure, the list of medications can become daunting, numbering 10 or more (beta blockers, ACEIs, diuretics, isosorbide dinitrate/hydralazine, MRAs, anticoagulants, digoxin), sometimes dosed multiple times per day. The list does not include medications for other comorbid conditions (chronic obstructive pulmonary disease, diabetes mellitus, arthritis). Polypharmacy reduces adherence to medical regimens, increases the risk of drug interactions, and increases the risk of side effects. Hypotension is a common problem faced by clinicians. Multiple antihypertensives, sodium and fluid restriction, autonomic dysfunction, and advancing age predispose patients to orthostatic hypotension and the risk of falls. Declining renal function can also complicate management because many medications worsen renal failure or increase the risk of medication toxicity. In the setting of acute renal failure during hospitalization, diuretics should be reduced or discontinued if renal function continues to decline; reducing or holding the ACEI dose may be necessary. Cardiorenal syndrome, often defined as renal impairment as a result of cardiac dysfunction, can complicate the direction of therapy. The term cardiorenal syndrome has been used to describe acute renal failure in the setting of acute decompensated heart failure and chronic renal failure because of low cardiac output or because of other comorbidities.

DISCHARGE PLANNING

Once the patient's heart failure has been stabilized and medical therapy has achieved appropriate resolution of symptoms, planning for discharge should begin. Discharge planning requires thorough review of the patient's chart including laboratory results, guideline-directed medical therapy, education, and exercise tolerance. A multidisciplinary team including social workers, heart failure nurses, pharmacists, and physicians should coordinate discharge efforts. Education must include the patient, caregivers, and other family members and should focus on lifestyle changes including sodium restriction, fluid restriction, monitoring of daily weights, and a graded exercise program or referral to a cardiac rehabilitation program. Patients and caregivers should be educated on signs and symptoms of heart failure exacerbation and what to do if symptoms worsen.

On the day of discharge, providers should ensure that patients have met goals and complete an appropriate checklist (Table 4).

Table 5. Discharge Performance Measures

1. Left ventricular function was assessed during hospitalization or within the past 6 months.
2. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker therapy was prescribed for patients with heart failure with reduced ejection fraction.
3. Beta blocker therapy was prescribed for patients with heart failure with reduced ejection fraction.
4. Postdischarge appointments have been scheduled.

DISCHARGE PERFORMANCE MEASURES

The ACC recently updated inpatient and outpatient performance measures.[14] The previous measure of comprehensive discharge instructions was retired after analysis suggested that it promoted compliance to core measures often without regard to the quality of care provided. The measures are reported, and local compliance is compared to national benchmarks set by the Centers for Medicare & Medicaid Services. The performance measures reported at discharge are summarized in Table 5.

CONCLUSION

Inpatient therapy for patients with acute decompensated heart failure should be directed at decongestion and symptom improvement. Clinicians should also treat possible precipitating events, identify comorbid conditions that may exacerbate heart failure, evaluate and update current guideline-directed medical therapy, and perform risk stratification for all patients. Finally, effort should be made to educate patients about the importance of restricting sodium and fluid, monitoring daily weights, and adhering to a graded exercise program. Early discharge follow-up and continued optimization of guideline-directed medical therapy are key to preventing future heart failure readmissions.

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