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Chapter 37: Acute Decompensated Heart Failure

Brent N. Reed; Stormi E. Gale; Zachary L. Cox

CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 9, Heart Failure.

KEY CONCEPTS

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1. Patients presenting to the hospital with acute decompensated heart failure (ADHF) can be categorized into four hemodynamic subsets based on volume status (euvolemic or "dry" vs volume overloaded or "wet") and cardiac output (adequate cardiac output or "warm" vs hypoperfusion or "cold"). Patients may be warm and dry, warm and wet, cold and dry, or cold and wet.

2. While invasive hemodynamic monitoring using a pulmonary artery (PA) catheter does not alter outcomes in a broad population of ADHF patients, it may be considered in those who are refractory to initial therapy, in those whose hemodynamic status is unclear, or in those with clinically significant hypotension (ie, systolic blood pressure <80 mm Hg) or worsening renal function despite standard therapy.

3. Key hemodynamic parameters monitored with a PA catheter include pulmonary capillary wedge pressure (PCWP; reflecting fluid status or "preload"), cardiac output or cardiac index (CI; often used to reflect the innate contractility of the heart), and systemic vascular resistance (SVR; reflecting vascular tone or "afterload"). Although a normal PCWP (6-12 mm Hg) is desirable in healthy patients, higher ventricular filling pressures (15-18 mm Hg) are often necessary for patients with heart failure (HF).

4. Treatment goals for ADHF include relief of congestive symptoms, restoration of systemic tissue perfusion via improved cardiac output, and minimization of further cardiac damage and other adverse drug reactions.

5. Optimizing oral chronic HF therapy in the setting of ADHF may assist with improving cardiac output, relieving congestion, and preventing hospital readmission.

6. Pharmacologic therapies used in the management of ADHF can be broadly classified according to whether they improve volume overload and/or low cardiac output. No therapy studied to date has conclusively been shown to reduce mortality, and some may worsen outcomes.

7. Intravenous (IV) loop diuretics are considered first-line therapy for the management of ADHF associated with volume overload. Administration as a bolus or continuous infusion appears to be equally effective and safe when selected as initial therapy, although high-dose loop diuretic therapy (ie, 2.5 times the oral regimen prior to admission) is associated with greater volume removal. The addition of a thiazide-type diuretic may be considered in patients with diuretic resistance. If patients continue to be refractory to, or experience worsening of renal function with, diuretic therapy, placement of a PA catheter may help guide therapies such as IV vasodilators and/or inotropes.

8. Ultrafiltration may be considered in patients with diuretic resistance or those with worsening renal impairment despite IV vasodilator and/or inotrope therapy.

9. Intravenous vasodilators may be added to diuretics for rapid resolution of congestive symptoms, especially in patients with acute pulmonary edema or severe hypertension. Such therapy may also be considered in patients who fail to respond to aggressive treatment with

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diuretics. In the absence of hypotension (systolic blood pressure <90 mm Hg or symptomatic hypotension) or reduced left ventricular filling pressures, IV vasodilators should also be considered prior to IV inotropes in patients with ADHF and evidence of low cardiac output. Frequent blood pressure monitoring is necessary to ensure their safe use.

10 Intravenous inotropes are recommended for maintaining systemic perfusion and end-organ function in hypotensive patients with evidence of severe left ventricular dysfunction and low cardiac output. Inotropic therapy may also be considered in patients who do not tolerate or respond to IV vasodilators or in patients with worsening renal function despite standard therapy. Patients receiving IV inotropes should be monitored continuously for arrhythmias.

11 Temporary mechanical circulatory support (MCS) is indicated in select patients with severe ADHF or those with advanced HF who are refractory to pharmacologic therapy. The intra-aortic balloon pump (IABP) is the most common type of temporary MCS but provides the least amount of hemodynamic support. Other types of temporary MCS include temporary ventricular assist devices (VADs) and extracorporeal membrane oxygenation (ECMO).

12 Cardiac transplantation remains the only definitive therapy for advanced HF. Given the extended wait time for identifying suitable donors, implantation of a durable VAD may be considered for patients who are eligible for cardiac transplantation (ie, “bridge to transplant”) or in whom transplantation is not an option (ie, “destination therapy”).

BEYOND THE BOOK

BEYOND THE BOOK

Pair up with a classmate and create a series of flashcards, in which you describe and list several characteristics of a patient in one of the four hemodynamic subsets on one side (ie, signs, symptoms, physical examination findings, laboratory values) and the appropriate classification and treatment approach on the other side. Present your partner with the case, and ask them to recommend an initial treatment and monitoring plan. Ensure that at least one of each of the four hemodynamic subsets is represented in your stack of cards, but also try varying the complexity and severity of each case/list. For example, start with a simple case/list of characteristics consistent with fluid overload (ie, subset II or “warm and wet”), and ask your partner to recommend an intravenous diuretic regimen based on the patient’s home diuretic dose. Later, progress to patient scenarios/cards representing subset III (“cold and dry”) and IV (“cold and wet”). For each case/card, ask your partner to list patient-specific factors that might influence the treatment approach (eg, hypotension when deciding between a vasodilator and inotrope) as well as monitoring parameters for the therapies selected. For an extra challenge, add in some cases/cards where you provide values from a pulmonary artery catheter or include a patient who develops diuretic resistance. Compare and contrast your partner’s recommendations with those you wrote on the back of the card.

INTRODUCTION

The clinical course of heart failure (HF) manifests as periods of relative stability with increasingly frequent episodes of decompensation as the disease progresses.[1] Several terms have been used to characterize worsening HF requiring hospitalization. Patients with persistent symptoms requiring specialized interventions despite guideline-directed medical therapy (GDMT) are classified as having advanced HF or Stage D, according to the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) system.[2] Due to the presence of HF symptoms with minimal activity or at rest, these patients are also typically classified as New York Heart Association (NYHA) class III or IV, respectively. The terms *acute decompensated heart failure* (ADHF) and *exacerbation of heart failure* refer to those patients with new or worsening signs or symptoms of HF (often as a result of volume overload and/or low cardiac output [CO]) requiring medical intervention such as an emergency department visit or hospitalization. The term *acute heart failure* may be misleading as it more often refers to patients with a sudden onset of HF signs or symptoms following previously normal cardiac function (eg, following myocardial infarction [MI]). This chapter focuses on the management of patients with ADHF, which may include those with heart failure with reduced ejection fraction (HFrEF) or heart failure with preserved ejection fraction (HFpEF).

Despite the considerable morbidity and mortality associated with ADHF, few randomized controlled trials have been conducted in this patient

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population. For those studies that have been published, the heterogeneity of patients enrolled often limits clinical application. Nonetheless, clinical practice guidelines for HF issued by ACCF/AHA include sections specifically focused on the management of advanced HF and ADHF; these and other consensus-based recommendations will be referenced where relevant throughout this chapter.[2,3]

EPIDEMIOLOGY

An estimated 6 million American adults have HF, and projections indicate that prevalence is likely to increase nearly 50% by 2030.[4] The growing number of patients living with HF has led to substantial increases in hospitalization rates for ADHF. Recent data indicate that over 1 million patients are hospitalized for HF annually, contributing to significant increases in morbidity and mortality and adding substantial burden to the healthcare system.[4,5] Hospitalization for HF has been independently associated with increases in subsequent hospitalization as well as decreased survival, which may explain why the mortality rate at 5 years remains high (42.3%).[4,6] The cost of HF is projected to approach $70 billion by 2030, an increase thought to be driven primarily by the costs of acute care.[4]

ETIOLOGY AND PATHOPHYSIOLOGY

The underlying etiology of ADHF varies and is often multifactorial. De novo HF may occur due to left ventricular dysfunction following a large MI or sudden elevation in blood pressure; such cases represent approximately 25% of admissions.[6] However, most hospitalizations for ADHF (70%) comprise patients experiencing an acute worsening of chronic HF[7]; readers are referred to Chapter 36, "Chronic Heart Failure," for a more detailed discussion of the etiology and pathophysiology of chronic HF including precipitating factors. Patients can become refractory to oral therapies and decompensate after even a relatively mild insult (eg, dietary indiscretion, nonsteroidal anti-inflammatory drug use), medication nonadherence, or concurrent noncardiac illness (eg, infection). New or worsening cardiac processes, such as MI, atrial or ventricular arrhythmias, hypertensive crises, myocarditis, or acute valvular insufficiency, may also produce ADHF in an otherwise stable patient. Exacerbations of chronic HFrEF and HFpEF occur in approximately equal numbers.[2] A minority of patients (5%) present with gradual, progressive worsening of CO and refractoriness to therapy due to advanced left ventricular systolic dysfunction.[7]

Several studies have provided a better understanding of the prognostic factors associated with ADHF. Blood urea nitrogen (BUN) is the best individual predictor of in-hospital mortality, followed by low systolic blood pressure and elevated serum creatinine.[7] Hyponatremia, elevations in troponin I, ischemic etiology, and poor functional capacity are also negative prognostic factors.[6,8] Use of GDMT at discharge and coronary angiography or implantable cardioverter-defibrillator placement during hospitalization are associated with improved prognosis, suggesting that optimal management during hospitalization can yield beneficial effects on subsequent prognosis.[8]

CLINICAL PRESENTATION

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CLINICAL PRESENTATION: Acute Decompensated Heart Failure

General

- Patients with ADHF typically present in one of four hemodynamic subsets (Fig. 37-1) based on the presence of volume overload (ie, congestion) and/or low cardiac output (ie, tissue hypoperfusion).
- Hemodynamic status can be ascertained in most patients based on their history and physical examination; some may require invasive hemodynamic monitoring.

Symptoms

- Volume overload: dyspnea, orthopnea, paroxysmal nocturnal dyspnea, ascites, gastrointestinal symptoms (poor appetite, nausea, early satiety), peripheral edema, weight gain.
- Low output: altered mental status, fatigue, gastrointestinal symptoms (similar to volume overload), decreased urine output.

Signs

- Volume overload: pulmonary crackles (or rales), elevated jugular venous pressure, abdominojugular reflux, S3 gallop, peripheral edema.
- Low output: tachycardia, hypotension (more commonly) or hypertension, narrow pulse pressure, cool extremities, pallor, cachexia.

Laboratory Values

- Volume overload: B-type natriuretic peptide <100 pg/mL (ng/L; 29 pmol/L) and N-terminal B-type natriuretic peptide <300 pg/mL (ng/L; 35 pmol/L) are negatively predictive for congestive ADHF; serum sodium concentration <130 mEq/L (mmol/L); elevated alkaline phosphatase; elevated gamma-glutamyl transferase.
- Low cardiac output: evidence of end-organ injury due to impaired perfusion, such as elevated liver transaminases and serum creatinine; mixed venous oxygen concentration <60% (0.60); elevated serum lactate.

Hemodynamic Monitoring

- Volume overload: pulmonary capillary wedge pressure >18 mm Hg; other volumetric pressures (eg, right atrial pressure, pulmonary artery diastolic pressure) are also commonly elevated.
- Low cardiac output: cardiac index <2.2 L/min/m^2 (0.037 L/s/m^2), with or without systemic vascular resistance >1,400 dyne·sec·cm^{-5} (18 Wood units; 140 MPa·s/m^3).

1 A careful history and physical examination are key components of an ADHF diagnosis. The history should focus on potential etiologies of ADHF; the presence of precipitating factors; the onset, duration, and severity of symptoms; and a careful medication history. Hemodynamic status should also be ascertained to guide initial therapy. Patients presenting with ADHF may be categorized into one of four hemodynamic subsets based on volume status (euvolemic or “dry” vs volume overloaded or “wet”) and CO (adequate CO or “warm” vs hypoperfusion or “cold”). The corresponding subsets are warm and dry (subset I), warm and wet (subset II), cold and dry (subset III), or cold and wet (subset IV; Fig. 37-1). The term *cardiogenic shock* may also be used to describe patients in subsets III and IV who present with low blood pressure and evidence of tissue hypoperfusion. In addition to guiding therapeutic decision making, these four hemodynamic profiles are also predictive of clinical outcomes. Compared to dry-warm patients, patients in the wet-warm and wet-cold subsets have a 2-fold and 2.5-fold greater risk of death at 1 year, respectively.[7]

FIGURE 37-1

General management algorithm for ADHF based on clinical presentation. Patients may be categorized into a hemodynamic subset based on signs and

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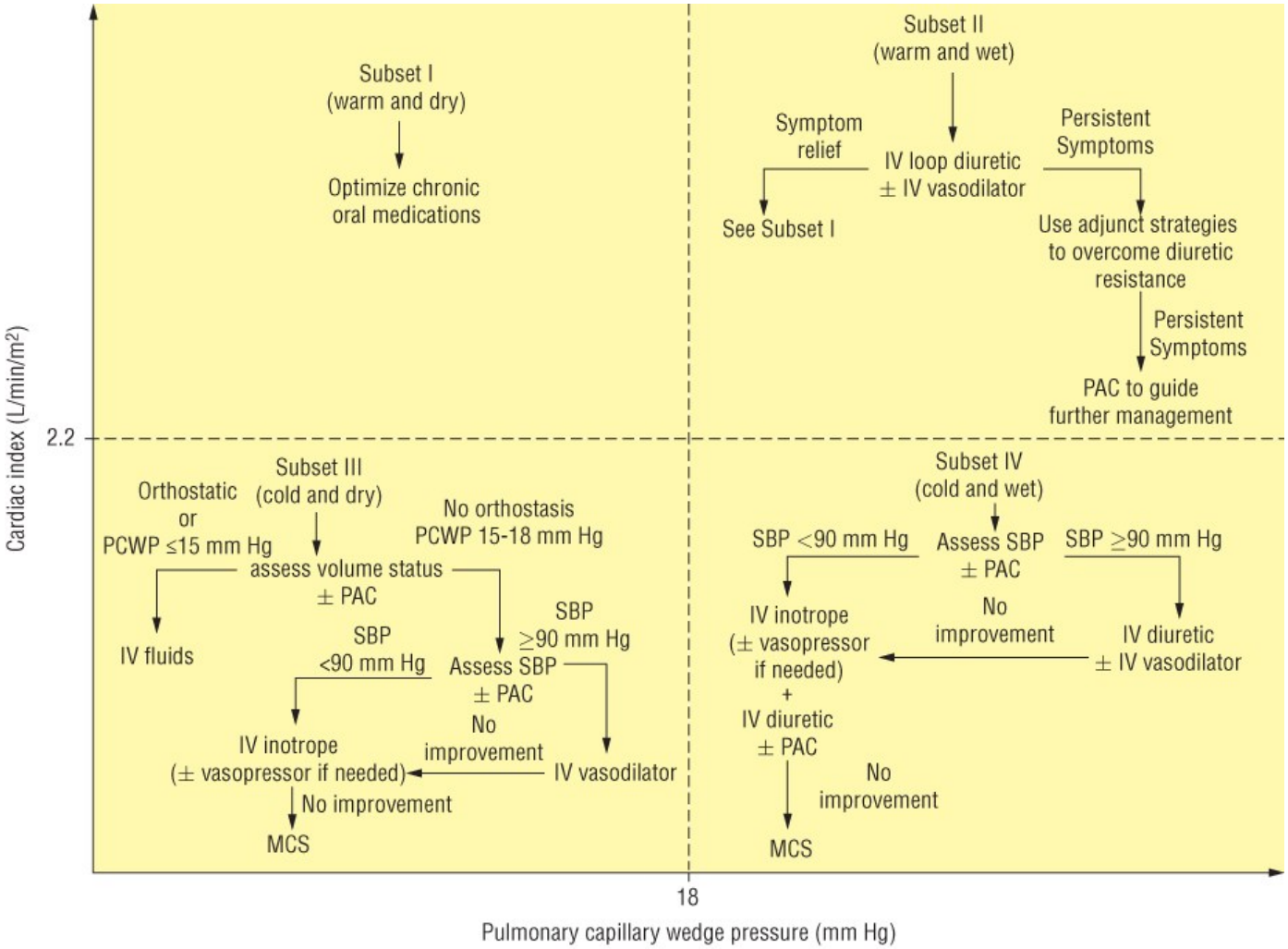
symptoms or invasive hemodynamic monitoring. Adjunct strategies for overcoming diuretic resistance include increasing the dose of loop diuretic; switching to a continuous infusion; adding a diuretic with an alternative mechanism of action, an IV vasodilator, or an IV inotrope; and in select patients, adding MCS. (IV, intravenous; MCS, mechanical circulatory support; PAC, pulmonary artery catheter; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure.)



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Although hemodynamic status can be determined in most patients based on signs and symptoms, a small subset of patients may require invasive hemodynamic monitoring to guide therapy. In this latter population, measurement of the pulmonary capillary wedge pressure (PCWP) and cardiac index (CI) may be used to categorize patients by volume status and CO, respectively. A PCWP greater than 18 mm Hg often reflects volume overload and is generally used to distinguish "wet" from "dry" subsets, whereas a CI less than 2.2 L/min/m^2 (0.037 L/s/m^2) is often used to distinguish "cold" from "warm" subsets; use of these invasive hemodynamic parameters will be discussed in further detail later in this chapter.

Hospitalization for ADHF should be considered based on the clinical findings listed in Table 37-1. Most patients do not require admission to an intensive care unit and may be admitted to a monitored unit or general medical floor. If a patient experiences hemodynamic instability necessitating frequent monitoring of vital signs, invasive hemodynamic monitoring, or rapid titration of IV medications (with concurrent monitoring), admission to an intensive care unit may be required to ensure optimal outcomes.

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TABLE 37-1

Indications for Hospitalization in Patients Presenting with ADHF

Presenting Features	Clinical Findings
Evidence of fluid overload	• Weight gain >10 kg (consider if >5 kg) • Symptoms of congestion (eg, dyspnea on exertion or at rest, orthopnea, PND, and early satiety[a]) • Signs of congestion (eg, tachypnea with oxygen saturation <90% [0.90], JVD, crackles, hepatomegaly, and lower extremity edema)
Evidence of low cardiac output	• Extreme fatigue • Hypotension, narrow pulse pressure • Cool extremities
Evidence of organ hypoperfusion	• Worsening renal or hepatic function • Altered mental status
Concomitant cardiovascular diseases that could compromise hemodynamic status	• Uncontrolled hypertension • Myocardial ischemia or infarction • Valvular disease • Arrhythmia (eg, atrial fibrillation with rapid ventricular response, ventricular tachycardia, and repeated ICD shocks)
Other conditions that could compromise hemodynamic status	• Severe electrolyte deficiency (potassium and magnesium) • Acute exacerbation of pulmonary disease (eg, asthma, COPD, or pulmonary embolus) • Infection such as pneumonia or urosepsis • Symptomatic hypothyroidism or hyperthyroidism • Use of medications with negative inotropic effects (eg, nondihydropyridine calcium antagonists)

COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter defibrillator; JVD, jugular venous distension; PND, paroxysmal nocturnal dyspnea.

[a]Early satiety may also be a symptom of low cardiac output.

Signs and Symptoms

Important elements of the physical examination include assessment of vital signs and weight, cardiac auscultation for heart sounds and murmurs, pulmonary auscultation for crackles, presence and severity of peripheral edema, and evidence of end-organ dysfunction. The most common presentation of ADHF is severe volume overload. Symptoms consistent with pulmonary congestion include orthopnea and dyspnea with minimal exertion, and those associated with systemic congestion include gastrointestinal (GI) discomfort, ascites, and peripheral edema. Orthopnea is the symptom that best correlates with elevated pulmonary pressure, whereas jugular venous pressure is the most reliable sign of volume status, warranting evaluation at admission as well as throughout hospitalization as an indicator of diuretic efficacy.[7] An S3 gallop, suggestive of increased volume in the left ventricle, has high diagnostic specificity for ADHF.[7] Other physical findings, such as pulmonary crackles and lower extremity edema,

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have low specificity and sensitivity for the diagnosis of ADHF.

Signs and symptoms of low CO are often nonspecific and may include generalized fatigue, cool extremities, and pallor. Manifestations of impaired end-organ perfusion may also be present, such as altered mental status (decreased perfusion to the central nervous system) or decreased urine output (decreased renal perfusion). Hypotension and narrow pulse pressure may also suggest low CO. Gastrointestinal symptoms such as poor appetite, nausea, and early satiety may be a sign of poor perfusion to the GI tract, abdominal congestion, or both. Many patients will present with signs and symptoms of both wet and cold subsets; in these patients, symptoms of low CO may not be obvious until the congestion has been optimally treated.

Laboratory Findings

Plasma B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) concentrations are positively correlated with the degree of left ventricular dysfunction and HF, and are now frequently used to assist in the differential diagnosis of dyspnea (HF vs pulmonary disorders). A low BNP concentration, often defined as less than 100 pg/mL (ng/L; 29 pmol/L), is highly predictive for excluding HF as an underlying etiology for dyspnea.[7] An NT-proBNP concentration of less than 300 pg/mL (ng/L; 35 pmol/L) is similarly predictive for excluding HF. In addition, an elevated BNP concentration prior to discharge is associated with an increased risk of poor long-term outcomes. However, some limitations exist. For example, any disease process that increases right heart pressures will elevate BNP, such as pulmonary emboli, chronic obstructive lung disease, and pulmonary arterial hypertension. In addition, BNP concentrations may be mildly increased with advanced age, female gender, renal dysfunction, and use of sacubitril/valsartan, and may be lower in the setting of obesity. Although the role of BNP in HF remains an area of ongoing research, guidelines recommend obtaining a BNP or NT-proBNP in order to assist with clinical decision making when the diagnosis of ADHF is uncertain and for determining the prognosis or severity of disease.[2]

A number of other laboratory tests should also be obtained to identify precipitating factors for ADHF (eg, thyroid function tests, complete blood count to assess for infection). In particular, cardiac enzymes (eg, troponin) should be obtained to exclude the presence of myocardial ischemia. Routine serum chemistries (eg, serum creatinine, liver function tests) should also be obtained to assess end-organ perfusion. Ferritin, serum iron, and transferrin iron-binding capacity should be obtained to screen for iron deficiency, even in patients without anemia. Profound volume overload may also contribute to aberrations in serum markers of end-organ function due to venous congestion. Other helpful laboratory tests include markers of peripheral tissue perfusion, such as venous oxygenation saturation and serum lactate concentrations.

Invasive Hemodynamic Monitoring

2 Invasive hemodynamic monitoring is usually performed with a flow-directed pulmonary artery (PA) catheter (also known as Swan-Ganz catheter) placed percutaneously into a central vein and advanced through the right side of the heart and into the PA. This process may also be referred to as right heart catheterization (in contrast to left heart catheterization, which is often used to visualize the coronary arteries). Because routine use of a PA catheter in patients with ADHF does not improve survival, invasive hemodynamic monitoring should be reserved for select patients with ADHF.[9] For example, it often provides important information in patients whose clinical status is unclear or complicated (eg, cardiogenic shock), or as a guide for titrating rapidly acting medications (eg, IV vasodilators).[3] As a consequence, invasive hemodynamic monitoring should be considered in patients who are refractory to initial therapy, whose volume status is unclear, or who have clinically significant hypotension (eg, systolic blood pressure <80 mm Hg) or worsening renal function (WRF) despite appropriate initial therapy.[10] Hemodynamic assessment is also required in patients being evaluated for mechanical circulatory support (MCS) or cardiac transplantation. Finally, documentation of an adequate hemodynamic response to IV inotropic therapy is often necessary in order to obtain approval for reimbursement for chronic outpatient inotropic therapy.[2]

3 Several important hemodynamic parameters can be obtained from a PA catheter. Inflation of a balloon proximal to the end port allows the catheter to be “wedged” inside a pulmonary capillary, yielding the PCWP. In the absence of an intracardiac shunt, mitral valve disease, or severe pulmonary disease, the PCWP may be used to estimate left ventricular end-diastolic pressure, or “preload.” Preload refers to the stretch incurred by cardiac myocytes in response to increased volumetric pressure. Thus, PCWP can be a useful marker of volume status; elevated PCWP is often indicative of volume overload, whereas reduced PCWP indicates dehydration or inadequate ventricular filling pressure. The relationship between preload (or PCWP) and CO is described by the Frank-Starling mechanism, which is depicted in Fig. 37-2. Due to the much flatter curve observed in patients with HF, increases in preload do not confer the same improvements in CO observed in patients with normal cardiac function. Consequently, higher pressures (ie, 15-18 mm Hg, compared to a normal range of 6-12 mm Hg) are often required in patients with HF in order to optimize CO. Excess preload (PCWP >18 mm Hg) manifests as signs and symptoms of congestion. Fortunately, PCWP can be lowered to 15 to 18 mm Hg with relatively little decrease in CO due

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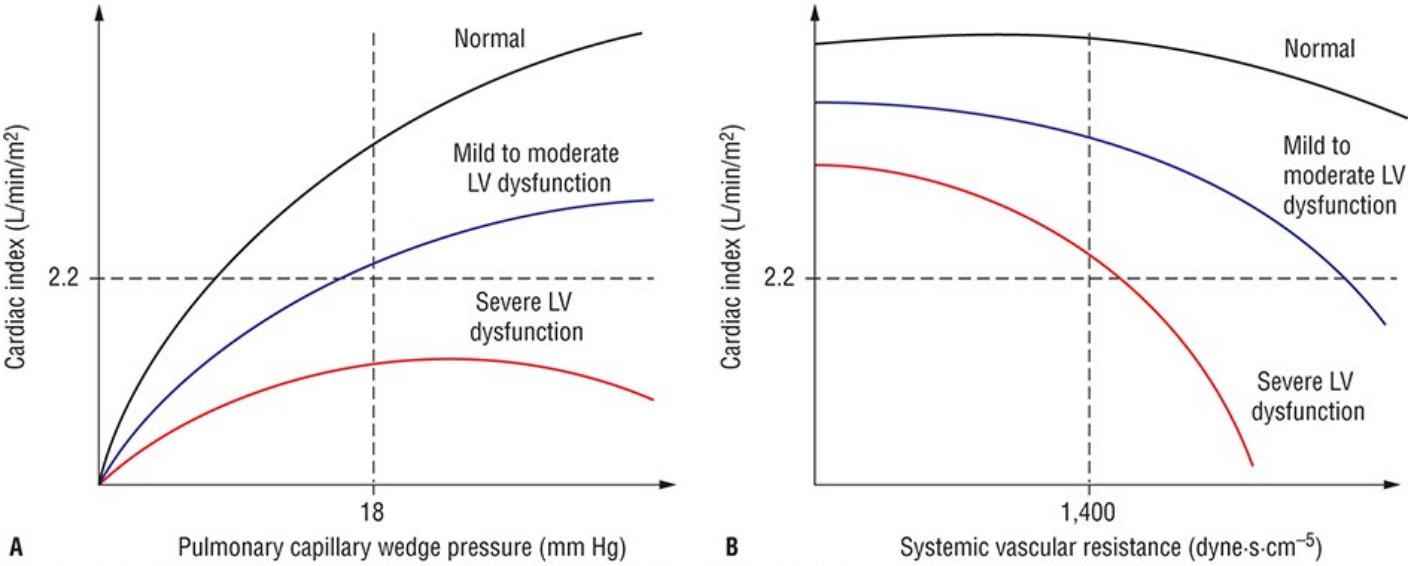
to the flatter shape of the Frank–Starling curve in HF. Extreme elevations in PCWP (representing profound volume overload) are also thought to worsen cardiac function, although a precise mechanism for this phenomenon is unknown. Of the parameters that can be obtained via PA catheterization, an elevated PCWP is most consistently associated with a worse prognosis.[11]

FIGURE 37-2

Hemodynamic alterations in HF. (A) An illustration of the relationship between cardiac output (displayed as cardiac index, which is cardiac output normalized for body surface area) and preload (displayed as pulmonary capillary wedge pressure) according to the severity of left ventricular function. (B) An illustration of the corresponding relationship between cardiac output and afterload (displayed as systemic vascular resistance). (LV, left ventricular.)



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A PA catheter may also be used to determine CO or the volume of blood being pumped by the heart (particularly by the left ventricle) over a unit of time. CO is often normalized for body surface area to yield CI, which allows measurements to be made without considering the body size. Using parameters derived from the PA catheter, CO is calculated based on one of two methods. The thermodilution method for determining CO is performed by releasing cooled fluid from a proximal port on the PA catheter and measuring the resulting change in temperature at a downstream thermistor over a period of time. In the Fick method, blood flow is calculated using the difference between arterial and venous oxygen concentration, the oxygen-carrying capacity of hemoglobin, and a population constant for oxygen consumption over time. The preferred method for determining CO varies by clinician, although the presence of certain comorbid conditions (eg, valvular abnormalities and pulmonary disease) may make one method more or less accurate in an individual patient. However, because the determination of CO by the Fick method depends on a set of assumptions (eg, rate of oxygen consumption according to gender and body size), the thermodilution method is generally thought to be a more reliable predictor of outcomes in critically ill patients.[12,13]

The systemic vascular resistance (SVR) can also be calculated using parameters measured by the PA catheter, including CO, mean arterial pressure (MAP), and central venous pressure (CVP). Also referred to as total peripheral resistance or arterial impedance, SVR reflects "afterload," or the total sum of forces impeding the ejection of blood from the left ventricle. Vasoconstriction (ie, decreased diameter of arterial vessel lumen) increases vascular resistance, whereas vasodilation decreases it. Although SVR is inversely related to CO, patients with normal left ventricular function can often withstand relatively high elevations in SVR, as shown in Fig. 37-2. However, in patients with HF, even a moderately elevated SVR can compromise left ventricular performance. Elevated SVR is common in untreated HF and generally responsive to oral or IV vasodilators. Conversely, a reduction in resistance is consistent with vasodilatory shock (eg, sepsis) and is routinely managed with IV vasopressor therapy (see Chapter e42, "Shock Syndromes").

When the heart rate is held constant, CO reflects stroke volume, or the volume of blood being pumped by the heart (particularly by the left ventricle)

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with each beat. Although stroke volume is in part determined by cardiac contractility, it is also influenced by preload and afterload, and alterations in CO (or CI) should therefore be interpreted in the context of PCWP and SVR. For example, a low CI (<2.2 L/min/m^2[0.037 L/s/m^2]) in the setting of a low PCWP (<6 mm Hg) may represent decreased preload due to hypovolemia rather than impaired contractility (Fig. 37-2). Similarly, a low CI in the setting of high SVR (>1,400 dyne·sec·cm^{-5} [18 Wood units; 140 MPa·s/m^3]) may represent impaired left ventricular performance due to excess afterload (Fig. 37-2). In both of these cases, CI could be increased directly (via inotropic therapy, for example), but a more optimal strategy would be to first address the aberrations in PCWP or SVR contributing to low CI.

A PA catheter can also be used to measure pulmonary vascular resistance (PVR), which represents the impedance of blood flow from the right ventricle to the pulmonary circulation. Pulmonary hypertension and pulmonary edema are two common causes of elevated PVR. Just as SVR is calculated using MAP, PVR is calculated using the mean PA pressure, which incorporates the PA systolic and diastolic pressures. The PA diastolic pressure may also be useful if the PA catheter fails to wedge (making it impossible to obtain PCWP). If the PCWP and PA diastolic pressure have been correlated prior to the failure to wedge, then the PA diastolic pressure may be followed as a surrogate marker of volume status. Normal values for these hemodynamic parameters are listed in Table 37-2.

TABLE 37-2

Normal Hemodynamic Values

Central Venous (Right Atrial) Pressure, mean, CVP	<5 mm Hg
Right Ventricular Pressure (Systolic/Diastolic)	25/0 mm Hg
Pulmonary Artery Pressure (Systolic/Diastolic), PAS/PAD	25/10 mm Hg
Pulmonary Arterial Pressure, mean, PAP	<18 mm Hg
Pulmonary Capillary Wedge Pressure, PCWP	<12 mm Hg[a]
Systemic Arterial Pressure (Systolic/Diastolic), SBP/DBP	120/80 mm Hg
Mean Arterial Pressure, MAP = (DBP+[1/3 (SBP-DBP])	70-110 mm Hg
Cardiac Output, CO	4-6 L/min
Cardiac Index, CI = CO/BSA	2.8-4.2 L/min/m^2 (0.047-0.070 L/s/m^2)
Systemic Vascular Resistance, SVR = ([MAP–CVP]*80)/(CO)	800-1,400 dyne·sec·cm^{-5} (10-18 Wood units; 80 - 140 MPa·s/m^3)
Pulmonary Vascular Resistance, PVR = ([PAP–CVP]*80)/(CO)	100-200 dyne·sec·cm^{-5} (1.25-2.5 Wood units; 10 - 20 MPa·s/m^3)
Arterial Oxygen Saturation	90%-94% (0.90-0.94)
Mixed Venous Oxygen Saturation	60%-80% (0.60-0.80)

BSA, body surface area.

[a]A higher than normal pulmonary capillary wedge pressure (ie, 15-18 mm Hg) is often accepted in patients with HF. See text for details.

PATIENT CARE PROCESS

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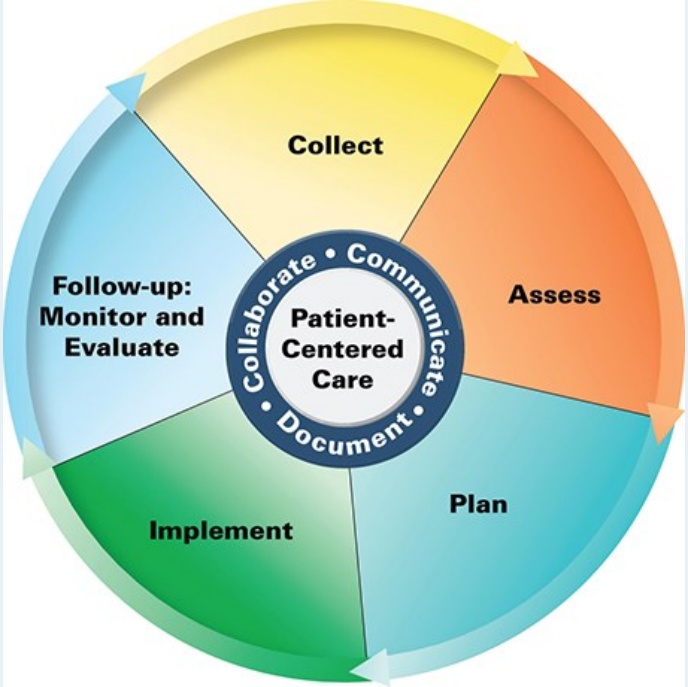
Patient Care Process for Acute Decompensated Heart Failure (ADHF)



Collect (see Tables 37-1 and 37-6)

- Patient characteristics (eg, age, sex, genetic ancestry, pregnancy status)
- Patient medical history (personal and family)
- Social history (eg, tobacco, ethanol, illicit drug use) and dietary habits, including fluid intake and sodium intake
- Current medications, including over-the-counter (OTC) medications (especially nonsteroidal anti-inflammatory drug [NSAID] and decongestant use), herbal products, and dietary supplements
- Subjective data
  - Signs/symptoms of fluid overload (eg, weight changes, dyspnea on exertion or at rest, orthopnea, paroxysmal nocturnal dyspnea, abdominal fullness, lower extremity edema, early satiety)
  - Signs/symptoms of low cardiac output (eg, fatigue, dyspnea on exertion, early satiety)
  - Signs/symptoms associated with precipitating factors (eg, chest pain, palpitations, presyncope, and syncope)
  - Ability to complete activities of daily living
  - Adherence to medications and dietary restrictions
- Objective data
  - Weight on admission and daily throughout hospital stay (standing weight preferred if not bedridden)
  - Blood pressure (BP), heart rate (HR), respiratory rate (RR), and arterial oxygen saturation every 1 to 6 hours depending on the severity of illness
  - Continuous telemetry monitoring, especially if administering intravenous inotropes or if concerned for arrhythmias

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- Pertinent laboratory values, especially sodium, potassium, serum creatinine, blood urea nitrogen (BUN), liver function tests, B-type natriuretic peptide
- Various diagnostic tests depending on presumed etiology of acute decompensation, the severity of illness, and drug therapy selection

Assess (see Table 37-1; Figs. 37-1 and 37-2)

- Potential etiologies of decompensation
- Volume status (eg, increase in weight, signs/symptoms of fluid overload)
- Perfusion status (eg, complaints of fatigue, objective data consistent with low cardiac output)
- Ability/willingness to pay for newer guideline-directed medical therapies for heart failure (eg, sacubitril/valsartan, sodium-glucose co-transporter-2 inhibitors)
- Ability/willingness to obtain laboratory monitoring tests
- Emotional status (eg, presence of anxiety, depression)

Plan (see Tables 37-3 to 37-6; Figs. 37-1, 37-3, and 37-4)*

- Drug therapy regimen, including guideline-directed medical therapies for heart failure as well as dose, route, frequency, and duration
- Monitoring parameters for efficacy (eg, weight to maintain euvolemia, surrogate markers of end-organ function) and safety (eg, orthostasis); frequency and timing of follow-up
- Patient education (eg, purpose of treatment, dietary and lifestyle modification, drug-specific)
- Referrals to other providers when appropriate

Implement (see Table 37-6)*

- Provide patient education regarding all elements of the treatment plan (eg, self-monitoring of weight, sodium and fluid dietary restriction, self-titration of diuretic dose in select patients)
- Use motivational interviewing and coaching strategies to maximize adherence
- Schedule follow-up in 3 to 8 days following hospital discharge

Follow-up: Monitor and Evaluate (see Tables 37-1 and 37-6)

- Resolution of symptoms of fluid overload or low cardiac output
- Presence of adverse drug reactions (eg, orthostasis due to over-diuresis or excess vasodilation)
- Obtain relevant laboratory monitoring data (eg, potassium, magnesium, BUN/serum creatinine [diuretics]; BP [eg, sacubitril/valsartan, ACE inhibitor, ARB, β-blocker]; and HR [eg, β-blocker])
- Patient adherence to treatment plan
- Reevaluate need for escalation of guideline-directed medical therapy (up-titration or initiation of additional therapies) or referral for nonpharmacologic therapies (eg, ICD, CRT, mitral valve repair) or advanced therapies (eg, ventricular assist device, transplant)

**In collaboration with the patient, caregivers, and other healthcare professionals.*

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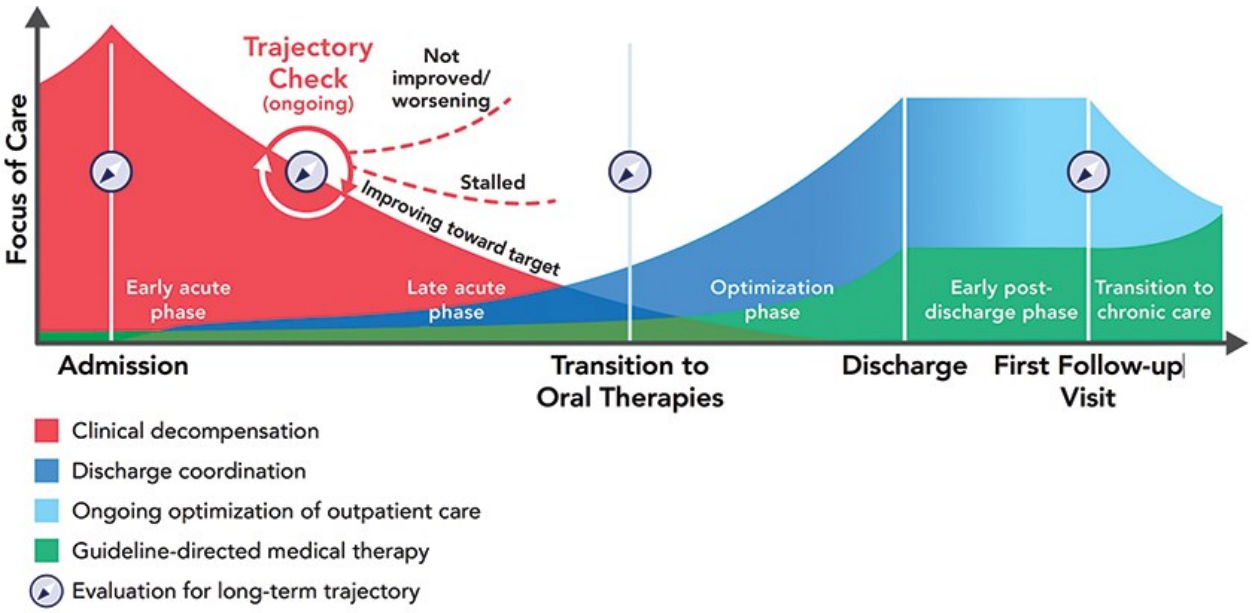
TREATMENT

Desired Outcomes

4 The overall goals of therapy in ADHF evolve over the course of a hospitalization (Fig. 37-3).[3] During the acute phase, the goals are to relieve symptoms, improve hemodynamic stability (ie, restore end-organ perfusion if compromised), and reduce short-term mortality, and address precipitating factors (eg, arrhythmias, hypertension, myocardial ischemia, medication or dietary nonadherence). Other key considerations include evaluating medications (including noncardiac medications) that may worsen cardiac function. Although IV diuretic, vasodilator, and inotropic therapy can be very effective at achieving these short-term goals, their efficacy must be balanced against the potential for serious adverse drug reactions. Decongestion should be prioritized even if it is accompanied by mild to moderate WRF, as failure to relieve congestion prior to discharge increases the risk of rehospitalization and mortality.[13-15] Patients should be routinely evaluated for their progress toward these goals as care may need to be escalated for those whose progress stalls or worsens despite routine therapy. For patients whose course improves with therapy, the focus of care shifts to the optimization of GDMT, patient education, and coordination of care, all of which are critical to preventing rehospitalization and improving survival. When available and appropriate, patients should be referred to an HF disease management program.[2]

FIGURE 37-3

Clinical course of HF hospitalization. Graphic depiction of HF hospitalization, showing the degree of focus on clinical decompensation (red), discharge coordination (blue), ongoing coordination of outpatient care (light blue), and optimization of guideline-directed medical therapy (green), with ongoing assessment of the clinical course (circle with arrows), and key time points for review and revision of the long-term disease trajectory for the HF journey (compass signs). *(Reproduced, with permission, from Hollenberg SM, Warner Stevenson L, Ahmad T, et al. 2019 ACC Expert Consensus Decision Pathway on Risk Assessment, Management, and Clinical Trajectory of Patients Hospitalized With Heart Failure: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2019;74(15):1966-2011.)*



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General Approach to Treatment

5 An important step in the management of ADHF is to assess medications being taken prior to admission and determine whether adjustment or discontinuation is required. Medications that may cause or contribute to ADHF due to negative inotropic effects (eg, nondihydropyridine calcium channel blockers) or by promoting fluid retention (eg, NSAIDs, mineralocorticoids, thiazolidinediones) should be discontinued. If fluid retention is

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evident on physical examination, aggressive diuresis should be pursued. The use of IV diuretics is recommended over increased doses of oral diuretics, and the regimen being taken prior to admission should be used to guide initial IV diuretic dosing.[2] In the absence of cardiogenic shock or symptomatic hypotension, every effort should be made to continue all GDMT for HF. β-Blocker therapy may be temporarily held or dose-reduced if recent initiation or up-titration is responsible for acute decompensation. Otherwise, β-blocker discontinuation is discouraged as it worsens outcomes in patients with ADHF.[16,17] Appropriateness of initiating β-blockers prior to discharge will be discussed later in this chapter.

Select GDMT may also need to be temporarily held in the setting of renal dysfunction, especially if oliguria or hyperkalemia is present (eg, ACE inhibitors, angiotensin receptor blockers, angiotensin receptor-neprilysin inhibitors, aldosterone antagonists). Therapies that may cause WRF (eg, ACE inhibitors, angiotensin receptor blockers, angiotensin receptor-neprilysin inhibitors) should only be initiated or up-titrated cautiously during aggressive volume removal with IV diuretic therapy. In addition, serum potassium concentrations should be monitored closely as IV diuretic therapy is transitioned to oral diuretic therapy, especially if an aldosterone antagonist has been initiated during the hospital stay; this ensures therapy can be tolerated on the intended oral diuretic dose prescribed at discharge. Most patients may continue to receive digoxin at doses targeting a trough serum concentration of 0.5 to 0.9 ng/mL (mcg/L; 0.6-1.2 nmol/L).[2] Discontinuation of digoxin is generally discouraged as withdrawal of therapy can worsen HF.[18,19] Digoxin should only be discontinued if serum concentrations cannot be safely maintained within the desirable range (eg, fluctuating renal function) or if patients demonstrate evidence of toxicity.

6 The acute management of ADHF is based primarily on hemodynamic status.[2] Patients with underlying HFrEF may present in any of the four hemodynamic subsets, whereas those with HFpEF usually present in subset II. Two general approaches exist for determining hemodynamic status. One is to use simple clinical parameters (eg, signs and symptoms, blood pressure, and organ function), and the other is to use these in conjunction with invasive hemodynamic monitoring. A management algorithm based on the hemodynamic subset is depicted in Fig. 37-1. The hemodynamic effects exerted by pharmacologic therapies used in the management of ADHF are illustrated in Fig. 37-4.

FIGURE 37-4

Hemodynamic effects of pharmacologic therapy in ADHF. Pharmacologic agents used in the management of ADHF exert important effects on cardiovascular hemodynamics. Although diuretics and venodilators reduce preload, this does not substantially reduce cardiac output in patients with heart failure and adequate filling pressures due to a flatter Frank–Starling curve. Arterial vasodilators reduce afterload, producing an increase in cardiac output as a consequence of improved left ventricular performance in patients with reduced ejection fraction. Vasodilators with effects on both venous and arterial tissue may reduce both preload and afterload. Inotropes improve contractility directly, although some agents (eg, milrinone) may exert salutary effects on afterload via vasodilation.

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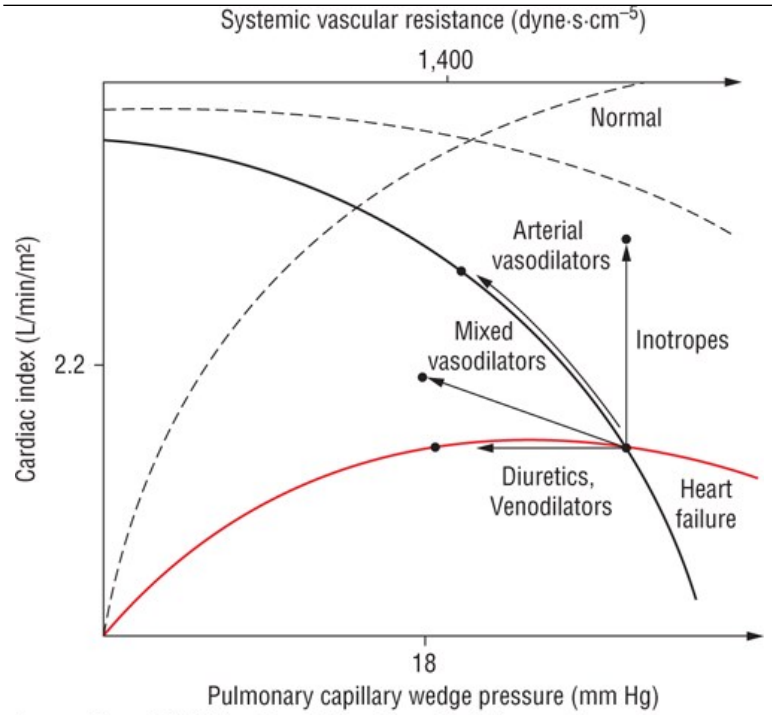

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Subset I (Warm and Dry)

Patients in subset I generally do not have signs and symptoms of volume overload or hypoperfusion and usually have CI and PCWP values within appropriate ranges. Patients in this subset have the lowest risk of mortality and do not require immediate intervention other than optimization of GDMT for HF.

Subset II (Warm and Wet)

Patients in subset II are likely to present with signs and symptoms of congestion (eg, orthopnea and peripheral edema) due to increased hydrostatic pressure in the pulmonary and systemic circulation, but without evidence of peripheral hypoperfusion. As a consequence, they often have adequate CO but a PCWP greater than 18 mm Hg. The primary goal of therapy in these patients is to relieve symptoms of congestion by lowering PCWP to an acceptable range (ie, 15-18 mm Hg). Considerably greater reductions should generally be avoided, as these could compromise CO, increase heart rate, or provoke neurohormonal activation.

Intravenous agents that reduce preload via diuresis and/or direct venodilation (eg, loop diuretics) are the most appropriate initial therapy for patients presenting in subset II. Although symptomatic improvement may occur within minutes of IV loop diuretic administration, significant relief of congestive symptoms may require several hours in select patients. Resistance to loop diuretics may occur, requiring dose escalation or addition of thiazide-type diuretics. IV vasodilators with effects on primarily the venous vasculature (eg, nitroglycerin) may be used for rapid venodilation (see Fig. 37-4), which can aid in acutely improving dyspnea. IV vasodilators do not improve outcomes in ADHF beyond dyspnea relief and should therefore be reserved for patients with acute pulmonary edema with respiratory distress or severe hypertension and avoided in patients with low blood pressure. Failure to respond to these therapies may indicate the presence of impaired CO and should prompt a reevaluation of perfusion status (with or without PA catheter insertion).

Patients in subset II should also be placed on a sodium restriction (2-3 g daily). In patients with moderate hyponatremia (<130 mEq/L [mmol/L]) or excess fluid intake that limits effective decongestion, fluid restriction (<2 L daily) should be considered. In patients with worsening or severe hyponatremia (<125 mEq/L [mmol/L]), a stricter fluid restriction may be necessary and an arginine vasopressin (AVP) antagonist may be considered in patients who develop neurologic symptoms.[2] Finally, supplemental oxygen should be administered as needed for hypoxemia (arterial oxygen

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saturation <90% [0.90]).

Subset III (Cold and Dry)

Patients in subset III present with evidence of peripheral hypoperfusion (eg, weakness, decreased urine output, and weak pulses) but no signs or symptoms of congestion. They often present with a CI of less than 2.2 L/min/m^2 (0.037 L/s/m^2) but no abnormal elevation in PCWP. The mortality rate of patients in subset III is higher than that of patients with adequate perfusion.[20] Although the treatment goal is to alleviate signs and symptoms of hypoperfusion by increasing CI and perfusion to essential organs, therapy may differ based on initial presentation. If evidence of hypovolemia exists (eg, orthostatic hypotension) or PCWP is below 15 mm Hg, IV fluids should be cautiously administered to provide a more optimal left ventricular filling pressure (ie, 15-18 mm Hg), consequently improving CI (see Fig. 37-1). As this presentation most often occurs in the setting of overly aggressive diuresis, diuretic therapy should be withheld and fluid restriction liberalized; these interventions alone may obviate the need for IV fluids.

In patients whose CI remains low despite restoration of optimal left ventricular filling pressures, IV positive inotropic agents (eg, dobutamine and milrinone) and/or IV arterial vasodilators (eg, nitroprusside) may be necessary to achieve adequate CI (see Fig. 37-4). IV inotropes should also be avoided in patients with low left ventricular filling pressure and generally reserved for patients with evidence of severely low CO who are not candidates for IV vasodilators (ie, hypotension). They may also be used to "bridge" patients to MCS or heart transplantation, or as palliative therapy to improve functional status and quality of life in patients who are ineligible for definitive therapies.

Subset IV (Cold and Wet)

Patients in subset IV present with signs and symptoms of both volume overload and peripheral hypoperfusion, and often have a PCWP exceeding 18 mm Hg and a CI of less than 2.2 L/min/m^2 (0.037 L/s/m^2). This subset is characterized by the worst prognosis of all four and represents the most common hemodynamic profile for patients with end-stage HF. Given the severity of HF, patients in subset IV cannot maintain adequate CI despite elevated left ventricular filling pressure and increased myocardial fiber stretch. Treatment goals for these patients include alleviation of signs and symptoms of congestion and hypoperfusion by increasing CI to above 2.2 L/min/m^2 (0.037 L/s/m^2) and reducing PCWP to 15 to 18 mm Hg while maintaining adequate MAP. Therapy often involves a combination of agents used in subsets II and III (ie, a combination of IV diuretic plus vasodilator or inotrope). These targets may be difficult to achieve and often necessitate careful monitoring and individualization of drug therapy. In the presence of significant hypotension and low MAP (and SVR is low to normal or unknown), vasodilators should be avoided. In some cases, even the vasodilating effects of inotropic therapy may compromise MAP, requiring that combined inotrope and vasopressor therapy (eg, dobutamine plus norepinephrine) or an inotrope with vasopressor activity (eg, dopamine) be used to achieve adequate end-organ perfusion. Once end-organ perfusion and hemodynamic stability have been restored, therapy can then be adjusted to obtain the desired clinical response (see Fig. 37-1).

Pharmacologic Therapy

Despite advances in the care of patients with HF, none of the therapies used in the treatment of ADHF confer long-term improvements in morbidity and mortality, and some may cause harm when used indiscriminately (eg, IV inotropes). Therefore, the primary role of pharmacologic therapy in ADHF is to relieve acute symptoms and stabilize patients so that GDMT may be safely initiated or titrated.

Loop Diuretics

The IV loop diuretics furosemide and bumetanide are the mainstay of therapy for relieving congestion in the setting of ADHF (Table 37-3); furosemide remains the most widely studied and used in this setting.[21] Bolus administration reduces preload within 5 to 15 minutes by functional venodilation and later (>20 minutes) via sodium and water excretion, thereby improving pulmonary congestion. Although patients with HFrEF can tolerate significant reductions in preload without compromising stroke volume, excessive diuresis (ie, PCWP <12 mm Hg or CVP <3 mm Hg) can lead to a decline in CO (see Fig. 37-4). Excessive or rapid reductions in preload may also compromise CO in patients with preload-dependent conditions (eg, aortic stenosis, hypertrophic obstructive cardiomyopathy, restrictive or constrictive cardiomyopathies, right ventricular failure, or severe diastolic dysfunction) or if diuresis exceeds the rate at which fluid can migrate from the interstitial space back into the systemic vasculature (ie, transcapillary refill rate). One scenario in which the latter may occur is with reduced oncotic pressure resulting from hypoalbuminemia, which is common in patients with advanced HF who become malnourished due to early satiety (as a consequence of abdominal edema and/or reduced perfusion to the GI tract). Patients with these conditions often require less aggressive decongestion goals (eg, net negative 1 L per day, or an amount of urine output that is

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approximately 1 L more than all of the fluid taken in over the course of a day).

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TABLE 37-3

Diuretics Commonly Used for the Management of ADHF

Loop Diuretics			
Characteristic	**Furosemide**	**Bumetanide**	
Oral bioavailability	10-100% (mean 50%)	80-90%	
Dose equivalence (IV)[a]	20-40 mg	1 mg	
Usual intermittent bolus dose (maximum)[b]	40-160 mg (200-300 mg)	1-4 mg (6-8 mg)	
Usual infusion rate (maximum)[b]	10-20 mg/hr (40-80 mg/hr)	0.5 mg/hr (2-4 mg/hr)	
Duration of action	4-6 hours	4-6 hours	
Thiazide-Type Diuretics			
Characteristic	**Metolazone**	**Chlorothiazide**	**Hydrochlorothiazide**
Usual dose (maximum)[b]	2.5-5 mg orally once daily (20 mg/day)	500 mg IV twice daily (2,000 mg/day)	50 mg orally once daily (200 mg/day)
Duration of action	12-24 hours	6-12 hours	5-15 hours
Other considerations	Oral absorption is erratic and delayed. No evidence of superiority to other thiazides but is most commonly used.	Oral formulations have poor absorption and should not be used. More costly but no evidence of superiority over other thiazides.	Higher doses than those used for hypertension are typically required to facilitate diuresis.

IV, intravenous.

[a]Torsemide is currently unavailable in an intravenous formulation, but its IV dose equivalence is 20 mg.

[b]Some institutions have published experience with higher doses; the ranges and maximum doses listed may be exceeded if the benefits justify the risks.

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Unlike arterial vasodilators and positive inotropic agents, diuretics do not cause an upward shift in the Frank–Starling curve or significantly increase CO in most patients (see Fig. 37-4). In some cases, patients with severe congestion may experience improvements in CO as PCWP approaches the normal range (see Fig. 37-4), which may explain why renal function occasionally improves in the setting of diuresis. Alternatively, improvements in renal function may reflect the relief of congestive nephropathy.

IV loop diuretics are recommended as first-line therapy for patients with ADHF and volume overload.[2] Although the oral bioavailability of loop diuretics is relatively unchanged in patients with HF who have adequate GI perfusion, the rate of absorption is prolonged by approximately twofold and peak concentrations are reduced by approximately half. Because loop diuretics have a sigmoidal-shaped concentration–response curve, prolonged absorption may result in concentrations that fail to reach the threshold necessary for producing diuresis, necessitating the use of IV therapy.

Low doses (ie, doses equivalent to IV furosemide 20-40 mg) once to twice daily should initially be selected in patients with ADHF who are naïve to loop diuretics. For patients taking loop diuretics prior to admission, a total daily dose of 1 to 2.5 times their home dose is recommended.[2,21] Higher doses are associated with more rapid relief of congestive symptoms but may also mildly increase the risk of transient worsening of renal function (WRF).[21,22]

Once an initial total daily dose is determined from the home diuretic regimen, doses may be administered as either an IV bolus (ie, divided every 12 hours) or continuous IV infusion.[2] Although major differences in relief of congestive symptoms, weight loss, or long-term outcomes have not been observed between these two methods of administration, a greater natriuretic effect may occur when the same total daily dose is administered as a continuous infusion rather than an IV bolus.[21-23] Given limitations in the designs of published trials, the appropriate method of administration for loop diuretic therapy in ADHF remains an area of controversy.[24,25]

Subsequent doses of loop diuretic therapy should be adjusted to patient response, as determined by urine output, weight loss, or urine sodium concentrations (goal >70 mEq/L [mmol/L]). Most patients tolerate at least a 2-L per day net negative diuresis (or a 2-kg weight loss), but diuretic therapy must be highly individualized in order to obtain the desired improvement in congestive symptoms while avoiding a reduction in CO, symptomatic hypotension, or WRF. Importantly, WRF alone should not be interpreted as evidence of euvolemia or as a reason to discontinue diuretics, as at least mild to moderate WRF occurs in approximately half of patients with ADHF.[21,26] The prognostic significance of WRF is strongly associated with the etiology of injury and among patients achieving decongestion with diuresis, WRF is not indicative of renal tubular injury or a worsened prognosis.[15,26,27] Therefore, careful evaluation of the patient's volume status and clinical context should guide decisions about diuretic therapy and GDMT (eg, ACE inhibitors, angiotensin receptor blockers, sacubitril/valsartan). Invasive hemodynamic monitoring can also be used to confirm volume status when the appropriate next steps are unclear based on changes to physical examination or laboratory findings. Finally, electrolyte depletion (eg, potassium, magnesium) should also be monitored daily at minimum and more frequently when high doses or combination diuretic therapy is used.

Strategies to Overcome Diuretic Resistance

Occasionally, patients respond inadequately to appropriate doses of loop diuretics, a phenomenon subjectively referred to as diuretic resistance. Unfortunately, attempts to define diuretic resistance in quantitative terms have not resulted in clinically applicable measures, and the mechanisms responsible for diuretic resistance are diverse.[28] However, the predominant mechanisms of diuretic resistance are intra-renal, specifically diminished diuretic response in the loop of Henle, and compensatory sodium reabsorption in the distal convoluted tubule.[28] Over time, the distal tubule may also undergo hypertrophy, thereby enhancing its ability to reabsorb sodium. Impaired CO resulting in reduced renal perfusion is an infrequent contributor to diuretic resistance, thus IV inotropic therapy should only be used to treat diuretic resistance if patients are in hemodynamic subset IV (ie, cold and wet).

Diuretic resistance is primarily treated by increasing the doses of loop diuretics or augmenting them by adding a diuretic with an alternative mechanism of action (eg, thiazide-type diuretics).[2] Although an escalation of loop diuretics should be prioritized due to an increased risk of adverse events with combination diuretic therapy, no consensus exists regarding the dose at which alternative diuretics should be added.[28,29] Given the sigmoidal dose–response curve of loop diuretics, a doubling of the dose is required to improve diuresis. Bolus doses should be increased if an inadequate response is not observed within six hours and the frequency of dosing should be increased if a response is observed but patients still fail to meet overall diuresis goals. Transitioning to continuous infusion loop diuretics may also be considered provided it is accompanied by a substantial increase in the total daily dose, although studies comparing this approach to IV bolus administration in patients with diuretic resistance have not been performed.

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For patients with refractory congestion despite increased doses of loop diuretics, adding a distal tubule blocker such as oral metolazone, oral hydrochlorothiazide, or IV chlorothiazide (Table 37-3) can produce a synergistic diuretic effect.[2] Inhibition of sodium reabsorption in the loop of Henle increases sodium delivery to (and reabsorption in) the distal convoluted tubule, which can be subsequently blocked by a thiazide-type diuretic. When added to loop diuretics, IV chlorothiazide and oral metolazone are similarly efficacious and safe, as the higher potency and longer duration of metolazone likely compensate for its erratic absorption and delayed onset of action.[30] Sequential nephron blockade with a loop and thiazide-type diuretic should generally be reserved for hospitalized patients, as profound diuresis with severe electrolyte and intravascular volume depletion may occur. Patients should also receive close follow-up (eg, weight, vital signs, serum potassium, and assessment for orthostatic hypotension) to avoid serious adverse events.

Several other pharmacologic strategies have been investigated for relieving congestion or overcoming diuretic resistance in ADHF.[31] Studies are currently underway to investigate the addition of acetazolamide, a carbonic anhydrase inhibitor, to loop diuretics in patients with ADHF. On the basis of their benefits in patients with chronic HFrEF, sodium-glucose cotransporter-2 (SGLT2) inhibitors are also being explored for their diuretic and natriuretic effects in patients with ADHF. One strategy for enhancing diuresis that has fallen out of favor is the administration of low doses of dopamine (ie, 2-5 mcg/kg/min), as this approach does not consistently improve congestive symptoms or diuresis and it increases the risk of tachyarrhythmias.[32,33] Given the evidence of β-mediated effects at lower infusion rates, dopamine likely does not provide any advantages over a traditional inotrope when used in this setting.

Vasopressin Antagonists

Vasopressin receptor antagonists have been extensively studied in ADHF, particularly when complicated by severe hyponatremia, which is commonly defined as a serum sodium concentration of less than 125 mEq/L (mmol/L). Heart failure is most commonly associated with hypervolemic hyponatremia and is often characterized by inappropriately elevated concentrations of AVP or antidiuretic hormone. In the setting of HF, reduced CO leads to excess stimulation of arterial baroreceptors, which in turn enhances AVP secretion and consequently, stimulation of vasopressin receptors. Of particular importance in ADHF are V_2 receptors, which are located in the renal tubules, where stimulation by AVP results in net water reabsorption.

Although the prevalence of hyponatremia in patients with HF varies by the serum sodium threshold used, as many as one in five patients hospitalized with ADHF present with serum sodium concentrations less than 136 mEq/L (mmol/L).[34] Furthermore, the presence of hyponatremia has been associated with increased mortality in this population.[35]

Most cases of hyponatremia are mild, asymptomatic, and self-limited, but prompt diagnosis and management is critical for the less common but life-threatening presentation, which may include lethargy, confusion, respiratory arrest, cerebral edema, seizures, coma, or death. Because vasopressin antagonists have failed to improve outcomes in ADHF beyond increases in serum sodium concentrations and marginal improvements in urine output and congestive symptoms, their role is limited to the treatment of severe hyponatremia.[2,36,37]

The two currently available vasopressin receptor antagonists are tolvaptan and conivaptan. Tolvaptan selectively binds to and inhibits the V_2 receptor, whereas conivaptan nonselectively inhibits both V_{1A} and V_2 receptors. Stimulation of V_{1A} receptors in vascular smooth muscle and myocardium results in vasoconstriction, myocyte hypertrophy, and positive inotropic effects, but the clinical consequences of inhibiting these effects with conivaptan are unknown. Conivaptan is an IV agent indicated for hypervolemic and euvolemic hyponatremia resulting from a variety of causes, but because it is not indicated in patients with ADHF, its use will not be discussed in further detail here.

Tolvaptan is orally bioavailable and indicated for the management of hypervolemic and euvolemic hyponatremia in patients with SIADH, cirrhosis, or HF. It is typically initiated at 15 mg daily and then titrated to 30 mg or 60 mg as needed for resolution of hyponatremia (ie, typically no longer than several days to a week). Importantly, tolvaptan is a substrate of cytochrome P450 3A4 and is contraindicated with potent inhibitors of this enzyme. Patients receiving vasopressin antagonists must be monitored closely to avoid an overly rapid rise in serum sodium (>12 mEq/L [mmol/L] per 24 hours); fluid restrictions should be liberalized to reduce this risk.

Vasodilators

Current guidelines focus on the role of IV vasodilators as an adjunct treatment for refractory congestive symptoms,[2] but they may also be helpful

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for restoring tissue perfusion in select patients with low CO. Vasodilators are commonly classified according to their most prominent site of action (ie, arterial or venous circulation). As described in the section on patients in subset II, venodilators act as preload reducers by increasing venous capacitance, thus reducing symptoms of pulmonary congestion in patients with high ventricular filling pressures. Arterial vasodilators exert their beneficial effects by counteracting the peripheral vasoconstriction and impaired CO that can result from the activation of the sympathetic nervous system, renin–angiotensin–aldosterone system, and other neurohormonal mediators in both acute and chronic HF. In these patients, arterial vasodilators act as impedance-reducing agents, reducing afterload and causing a reflexive improvement in left ventricular performance and thus an increase in CO. Mixed vasodilators act on both resistance and capacitance vessels, reducing congestive symptoms while increasing CO.

Intravenous vasodilators should, therefore, be considered prior to positive inotropic therapy in patients with low CO and elevated SVR (or elevated blood pressure in those without a PA catheter). For patients in whom blood pressure or SVR is already low, including those receiving GDMT with vasodilating effects (eg, ACE inhibitors) or those with advanced HF, hypotension may preclude the use of IV vasodilators. In patients with advanced HF and limited contractile reserve, increases in left ventricular performance may not fully compensate for reductions in afterload, leading to worsening hypotension. In addition, IV vasodilators have not been extensively studied in patients with HFpEF, where a sudden drop in preload may compromise existing defects in ventricular filling, leading to decreased CO.[38]

The most commonly used IV vasodilators in ADHF are nitroglycerin and sodium nitroprusside, which differ according to their effects on arterial and venous circulation (Table 37-4). Nitroglycerin is primarily a venodilator (except at high doses), whereas sodium nitroprusside is a mixed venous and arterial vasodilator. Once stabilized on IV therapies, transitioning to oral vasodilators (eg, nitrates/hydralazine, ACE inhibitors) should be considered.

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TABLE 37-4

Vasodilators Commonly Utilized for the Management of ADHF[a]

Drug (Vasodilatory Effect)	Onset, Half-life	Elimination	Dose	HR	MAP	PCWP	CO[b]	SVR
Nitroglycerin (venous > arterial)	Immediate, <4 mins	Inactive metabolites in urine	10-20 mcg/min and titrate 10-20 mcg/min q10–20 mins, max 200 mcg/kg/min	0/↑	0/↓	↓	0/↑	0/↓
Nitroprusside (venous = arterial)	Immediate, 2 mins	Cyanide (hepatic), thiocyanate (renal)	0.1-0.2 mcg/kg/min, titrate 0.1-0.2 mcg/kg/min q10-20 mins, max 3 mcg/kg/min	0/↑	0/↓	↓	↑	↓
Furosemide (venous only)	1 hr (PO)/5 mins (IV), 2 hrs	Urine	Variable[c]	0	0/↓	↓	0	0
Isosorbide dinitrate (venous only)	1 hr, 2-5 hrs for active metabolites	Hepatic	10-60 mg q8h	0/↑	0	↓	0	0
Hydralazine (arterial only)	1-2 hrs (PO), 3-7 hrs	Hepatic	12.5-100 mg q6–8h	0/↑	0/↓	0	↑	↓
Captopril (arterial > venous)	<15 mins, 2-4 hrs	Urine	6.25-50 mg q8h	0	0/↓	↓	↑	↓

[a]See text for a more detailed description of the interpatient variability in response.

[b]Indirect effects due to decreased arterial impedance.

[c]Intravenous bolus administered <0.4 mg/min.

↑, increase; ↓, decrease; 0, no change; HR, heart rate; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; CI, continuous infusion; CO, cardiac output; IVB, intravenous bolus; SVR, systemic vascular resistance.

Nitroglycerin

Intravenous nitroglycerin is often preferred for preload reduction in patients with ADHF, especially those requiring urgent relief of dyspnea (ie, acute pulmonary congestion). Because of its short half-life (1-3 minutes), IV nitroglycerin is administered by continuous infusion. Its major hemodynamic effects are reductions in preload and PCWP via functional venodilation and mild arterial vasodilation that is particularly evident in patients with HF and elevated SVR or when given in doses exceeding 100 mcg/min (see Table 37-4).[39] At higher doses, nitroglycerin displays potent coronary vasodilating properties, exerting beneficial effects on myocardial oxygen demand and supply and making it the vasodilator of choice for patients with severe HF and ischemic heart disease.

Nitroglycerin should be initiated at a dose of 5 to 10 mcg/min (0.1 mcg/kg/min) and increased every 5 to 10 minutes as tolerated. Hypotension and an excessive decrease in PCWP are important dose-limiting adverse drug reactions. Maintenance doses usually vary from 35 to 200 mcg/min (0.5-3 mcg/kg/min). While tolerance to the hemodynamic effects of nitroglycerin may develop within hours of continuous administration, some patients

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experience a sustained response; this variability in response to nitroglycerin requires that patients be continuously monitored (eg, symptoms, hemodynamic parameters) to guide adjustments to therapy. Nitroglycerin should not be used in the presence of elevated intracranial pressure because it may worsen cerebral edema in this setting.

Sodium Nitroprusside

As a result of its balanced effects in arterial and venous tissue, sodium nitroprusside increases CI to a similar degree as dobutamine and milrinone despite having no direct inotropic activity; however, greater decreases in PCWP, SVR, and blood pressure are generally observed. MAP may remain fairly constant due to reflexive improvements in stroke volume and CO but can decrease based on the extent of arterial smooth muscle relaxation. Patients with normal left ventricular function do not experience an increase in stroke volume when SVR falls because the normal ventricle is fairly insensitive to changes in afterload. Consequently, these patients may experience a significant decrease in blood pressure in response to arterial vasodilators. These differences explain why sodium nitroprusside is a potent antihypertensive agent in patients without HF but causes less hypotension and reflex tachycardia in the presence of left ventricular dysfunction (see Fig. 37-2). Nonetheless, hypotension remains an important dose-limiting effect of sodium nitroprusside, and its use should be primarily reserved for patients with elevated SVR. Close monitoring of therapy is warranted, as even modest increases in heart rate can have adverse consequences in patients with underlying ischemic heart disease and/or resting tachycardia.

Sodium nitroprusside is an effective strategy for the short-term management of patients with acute HF across a variety of settings (eg, acute MI, valvular regurgitation, postcoronary bypass surgery, and ADHF). Generally, sodium nitroprusside does not worsen, and may even improve, the balance between myocardial oxygen demand and supply by lowering both left ventricular wall tension (thus reducing oxygen demand) and end-diastolic pressure (thereby increasing subendocardial blood flow). However, an excessive decrease in systemic arterial pressure may reduce coronary perfusion and worsen ischemia due to coronary steal. Consequently, therapy should be avoided in patients with recent MI in the absence of persistent congestive symptoms or elevated ventricular filling pressures.[40] In ADHF specifically, sodium nitroprusside improves low CO and may support the initiation and titration of GDMT, even among patients with lower MAP (<85 mm Hg).[41]

Sodium nitroprusside has a rapid onset of action, but its effects last less than 10 minutes, necessitating administration by continuous IV infusion. Its short duration of action also allows precise dose-titration based on clinical and hemodynamic response. As with nitroglycerin, sodium nitroprusside should be initiated at low doses (0.1-0.2 mcg/kg/min) to avoid excessive hypotension and increased by small increments (0.1-0.2 mcg/kg/min) every 5 to 10 minutes as tolerated. Effective doses usually range from 0.5 to 3 mcg/kg/min. A rebound phenomenon, which may be due to reflex neurohormonal activation during sodium nitroprusside therapy, has been reported following abrupt withdrawal in patients with HF. Therefore, therapy should be tapered slowly when transitioning patients to oral medications. As with nitroglycerin, sodium nitroprusside should be avoided in the presence of elevated intracranial pressure as it may worsen cerebral edema in this setting.

Following IV administration, sodium nitroprusside interacts with hemoglobin to release cyanide, which undergoes hepatic conversion to thiocyanate before it is eliminated renally. As a consequence, sodium nitroprusside can cause cyanide and thiocyanate toxicity, but these effects are unlikely when doses less than 3 mcg/kg/min are administered for less than 3 days, except in patients with significant renal impairment (ie, serum creatinine concentration >3 mg/dL (265 µmol/L). Closer monitoring for signs and symptoms of toxicity (eg, altered mental status, nausea or vomiting, metabolic acidosis) should be considered in patients with renal impairment or when higher doses or prolonged durations of sodium nitroprusside must be used.

Inotropes

10 Patients in subsets III and IV ("cold" subsets) require prompt correction of low CO in order to restore peripheral tissue perfusion and preserve end-organ function. Although IV inotropes can improve peripheral hypoperfusion by directly enhancing cardiac contractility, their association with adverse outcomes (eg, arrhythmias, in-hospital mortality) necessitates that they are reserved for select patients with refractory ADHF, particularly those unable to tolerate vasodilators due to hypotension.[42] Inotrope therapy should be considered only as a temporizing measure for maintaining end-organ perfusion in patients with cardiogenic shock or evidence of severely depressed CO and low systolic blood pressure (ie, ineligible for IV vasodilators) until definitive therapy can be initiated, as a "bridge" for those with advanced HF who are eligible for MCS or cardiac transplantation, or for palliation of symptoms in patients with advanced HF who are not eligible for MCS or cardiac transplantation.[2]

Patients in these latter two groups may require placement of an indwelling IV catheter for continuous outpatient administration of inotropic therapy.

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Palliative use of IV inotropes should only be considered after multiple unsuccessful attempts have been made to wean therapy and maximize GDMT, as the risk of mortality is likely increased with IV inotrope use.

Importantly, IV inotropes rarely, if ever, produce a single cardiovascular action. Even when intended for a specific purpose (eg, positive inotropic effects), other cardiovascular effects (tachycardia, vasodilation, or vasoconstriction) may either add to the therapeutic effect of the drug or cause adverse drug reactions that negate or even outweigh its intended therapeutic benefit. How an individual patient will respond to an intervention is often difficult to anticipate. For this reason, hemodynamic monitoring with a PA catheter may be useful.

The two IV inotropic agents most commonly used for the management of ADHF are dobutamine and milrinone. Although both drugs increase intracellular concentrations of cAMP, they do so by different mechanisms. Dobutamine activates adenylate cyclase through direct stimulation of β-adrenergic receptors, thus catalyzing the conversion of adenosine triphosphate to cAMP, whereas milrinone reduces degradation of cAMP by inhibiting phosphodiesterase type 3. Increased intracellular cAMP enhances phospholipase (and subsequently phosphorylase) activity, increasing the rate and extent of calcium influx during systole and thus enhancing contractility. In addition, cAMP enhances the reuptake of calcium by the sarcoplasmic reticulum during diastole, improving active relaxation (ie, positive lusitropic effects). Comparisons between dobutamine and milrinone indicate that the two agents generally produce similar hemodynamic effects, although dobutamine is usually associated with more pronounced increases in heart rate and milrinone is associated with greater relaxation in arterial smooth muscle. Differences in the pharmacologic effects of the two agents may confer advantages or disadvantages in an individual patient; these and other clinical considerations for their use in the management of ADHF will be reviewed in the sections to follow.

Digoxin rarely has a role in hemodynamically unstable patients due to its limited inotropic effects. In patients who take digoxin as chronic therapy, discontinuation or dose-adjustment during an acute decompensation is generally unnecessary unless changes in renal function increase the risk of toxicity. As discussed previously in this chapter, discontinuation should be discouraged in the absence of toxicity, given the potential for digoxin withdrawal.[18,19]

Dobutamine

The receptor activities of dobutamine and other adrenergic agonists are summarized in Table 37-5. Dobutamine, a synthetic catecholamine, is a β_1- and β_2-receptor agonist with some α_1-agonist effects. Because dobutamine does not cause the release of norepinephrine from nerve terminals, its positive inotropic effects are attributed to its action on β_1-receptors. Stimulation of cardiac β_1-receptors by dobutamine does not generally produce a significant change in heart rate, thus explaining its modest chronotropic effects. Modest peripheral β_2-receptor-mediated vasodilation tends to offset minor α_1-receptor-mediated vasoconstriction. In addition, the increase in CO often results in a reflexive decline in SVR. As a consequence, the net hemodynamic effect of dobutamine, particularly at low doses, is usually vasodilation.

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TABLE 37-5

Inotropes Commonly Used for the Management of ADHF[a]

Drug	Onset, Half-life	Dose	Receptor Affinity ($\alpha_1/\beta_1/\beta_2$)	HR	MAP	PCWP	CO	SVR
Dobutamine	<10 mins, 2 mins	1-2 mcg/kg/min, titrate 1-2 mcg/kg/min q10–20 mins, max 20 mcg/kg/min	↑/↑↑↑↑/↑↑	0/↑	0	↓	↑	0/↓
Milrinone	5-15 mins, 1-4 hrs, (prolonged if renal dysfunction)	0.1-0.2 mcg/kg/min, titrate 0.1 mcg/kg/min q4–16 hrs (titrate slowly in renal dysfunction), max 0.75 mcg/kg/min (IVB dose generally avoided)	Phosphodiesterase inhibition	0/↑	0/↓	↓	↑	↓

[a]See text for a more detailed description of the dose-dependent hemodynamic effects.

The effects of dobutamine are observed within minutes, but its peak effects may take up to 10 minutes to occur. Initial doses of 2.5 to 5 mcg/kg/min may be adjusted based on clinical and hemodynamic responses. Although doses of up to 20 mcg/kg/min are occasionally used, most patients are maintained at doses of 7.5 mcg/kg/min or less. The cardiac index is increased due to inotropic stimulation, arterial vasodilation, and a variable increase in heart rate. Because of offsetting changes in arteriolar resistance and CI, dobutamine usually causes relatively little change in MAP, unlike the more consistent increases observed with vasopressors. Although its impact on heart rate is variable, the major adverse drug reactions of dobutamine are tachycardia and ventricular arrhythmias. Potentially detrimental increases in oxygen consumption have also been observed. While concerns exist regarding the attenuation of its effects during prolonged administration, changes in receptor expression require that dobutamine be slowly tapered rather than abruptly discontinued.

Milrinone

Milrinone is a bipyridine derivative that inhibits phosphodiesterase 3, an enzyme responsible for the breakdown of cAMP to adenosine monophosphate (AMP). Because both inotropic and vasodilating effects contribute to its therapeutic effects in ADHF, milrinone is often referred to as an inodilator. The relative balance of these pharmacologic effects may vary with dose and underlying cardiovascular pathology.

During IV administration, milrinone produces an increase in stroke volume (and therefore CO) with minimal change in heart rate (see Table 37-5). Despite an increase in CI, MAP may remain constant due to a concomitant decrease in arteriolar resistance. However, the vasodilating effects of milrinone may predominate, leading to a decrease in blood pressure and reflex tachycardia. As such, milrinone should be used cautiously in severely hypotensive patients because it does not increase, and may even decrease, arterial blood pressure.

The half-life of milrinone is about one hour but may be as long as 3 to 6 hours in patients with renal dysfunction. The longer elimination half-life of milrinone presents several disadvantages in patients with ADHF, including the inability to perform minute-to-minute titrations based on hemodynamic changes and persistence of adverse drug reactions (eg, arrhythmias or hypotension) following drug discontinuation. Although a loading dose is still listed in the product labeling for milrinone (50 mcg/kg administered over 10 minutes), this practice is uncommon due to an increased risk of hypotension.[43] Most patients are started on a maintenance infusion of 0.1 to 0.3 mcg/kg/min (up to 0.75 mcg/kg/min). Milrinone is excreted unchanged in the urine, and thus its infusion rate should be decreased by 50% to 70% in patients with significant renal impairment.

The most notable adverse drug reactions associated with milrinone are arrhythmia, hypotension, and thrombocytopenia. Although the incidence of thrombocytopenia is rare, patients should still have platelet counts measured before and during therapy.

Inotrope Selection

Although outcomes are similar between dobutamine and milrinone in patients with cardiogenic shock, certain characteristics may make one agent

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more ideal in an individual patient.[44] Dobutamine should be considered when a significant decrease in MAP might further compromise hemodynamic function, as this is more common with the initiation of milrinone. The selection of an inotropic drug should also consider whether patients are receiving chronic β-blocker therapy and whether a β_1-selective agent (eg, metoprolol succinate) or mixed α, β-blocking agent (eg, carvedilol) is used. Traditionally, milrinone has been advocated in patients who are receiving chronic β-blocker therapy because its inotropic effects do not involve β-receptor stimulation. However, the hemodynamic effects of dobutamine may persist in the presence of β-blocker therapy, particularly with β_1-selective agents as a result of β-receptor upregulation or selective activation of β_2-receptors by dobutamine.[45] Similar effects are not observed in the presence of carvedilol, which may inhibit the hemodynamic benefits of dobutamine entirely. Concomitant carvedilol therapy may augment the hemodynamic effects of milrinone based on studies with a structurally similar phosphodiesterase inhibitor, enoximone.[45]

The combination of dobutamine and milrinone is likely to produce additive effects on CO and PCWP, suggesting that this regimen may be considered in patients who have dose-limiting adverse drug reactions with either drug class. However, whether this combination provides a therapeutic advantage over the combined use of a positive inotrope and a traditional vasodilator (eg, sodium nitroprusside) is unclear.

Agents with Combined Inotropic and Vasopressor Activity

Although therapies that can increase SVR are generally avoided in ADHF, agents with combined inotropic and vasopressor activity, such as norepinephrine or dopamine, may be required in select scenarios where marked systemic hypotension may preclude the use of traditional IV inotropes (eg, mixed shock, refractory cardiogenic shock). Alternatively, these agents may be used in combination with traditional inotropes so that adjustments can be made to each agent independently to achieve the desired hemodynamic response. Although these strategies are common in clinical practice, minimal data exist to support their use.

Norepinephrine is an endogenous catecholamine that exerts its hemodynamic effects via direct stimulation of α_1- and β_1-adrenergic receptors. Its effects on β_1-adrenergic receptors in myocardial tissue are thought to confer improvements in CO because of increases in heart rate and cardiac contractility. However, despite having a similar affinity for α_1- and β_1-adrenergic receptors, enhanced vasoconstriction via activation of peripheral α_1-receptors appears to be the predominant hemodynamic effect observed clinically. The limited impact of norepinephrine on CO may be due to its lack of affinity for β_2-receptors, which would both enhance cardiac contractility and balance its effects on α_1-receptors in vascular smooth muscle. The affinity of norepinephrine for adrenergic receptors does not appreciably differ based on dose.

Dopamine is an endogenous precursor of norepinephrine and exerts its effects by directly stimulating adrenergic receptors as well as causing the release of norepinephrine from adrenergic nerve terminals. In contrast with norepinephrine, dopamine produces dose-dependent hemodynamic effects because of its relative affinity for α_1-, β_1-, β_2-, and D_1- (vascular dopaminergic) receptors (see Table 37-5). The positive inotropic effects of dopamine are mediated primarily by β_1-receptors and become more prominent at doses of 2 to 5 mcg/kg/min. The cardiac index is increased because of an increase in stroke volume and a variable increase in heart rate, which is also partially dose-dependent. Minimal changes in SVR occur, presumably because neither vasodilation (D_1- and β_2-receptor-mediated) nor vasoconstriction (α_1-receptor-mediated) predominates. However, at doses between 5 and 10 mcg/kg/min, chronotropy and α1-receptor-mediated vasoconstriction become more prominent. MAP is usually raised because of increases in both CI and SVR (see Table 37-5).

Epinephrine is also an endogenous catecholamine that exerts its hemodynamic effects via direct stimulation of α_1-, α_2-, and β_1-adrenergic receptors. Similar to dopamine, epinephrine exerts dose-dependent hemodynamic effects, including increased selectivity for β_1-adrenergic receptors at lower doses (ie, 0.01-0.05 mcg/kg/min) whereas increased α-adrenergic activity is seen at higher doses (ie, >0.5 mcg/kg/min).

The vasoconstriction observed with higher doses of norepinephrine and dopamine may limit improvements in CI by concomitantly increasing afterload and preload. Consequently, they should generally be reserved for patients with low CO and low systolic blood pressure despite adequate ventricular filling pressures, or as an adjunct to inotrope therapy when hypotension precludes the use of inotrope therapy alone. At higher doses, agents with vasopressor activity may alter several parameters that increase myocardial oxygen demand (eg, increased heart rate, contractility, and systolic pressure) and potentially decrease myocardial blood flow (eg, coronary vasoconstriction and increased wall tension), which may worsen ischemia in patients with coronary artery disease. As with dobutamine and milrinone, arrhythmogenesis is also more common at higher doses, although this risk appears to be greater with dopamine than with norepinephrine.[46]

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Nonpharmacologic Therapy

Several nonpharmacologic therapies are routinely used in ADHF. All patients with congestive symptoms should be placed on a sodium restriction. Given a complex relationship between sodium restriction and ADHF outcomes, no consensus exists on an appropriate sodium limit. For example, intense targets (<0.8 g/day) do not improve outcomes in ADHF, and higher levels of sodium intake (including the administration of hypertonic saline) may counterintuitively improve diuresis in select patients.[47,48] Based on these uncertainties, a general range of <2-3 g daily is recommended for most patients with ADHF.[2] Fluid restriction should also be considered for those with refractory symptoms. Noninvasive ventilation may be considered in patients with respiratory distress due to acute pulmonary edema, particularly those at risk for intubation. Although most patients with limited mobility should receive pharmacologic thromboprophylaxis with unfractionated heparin or low-molecular-weight heparin, mechanical thromboprophylaxis with intermittent pneumatic compression devices may be considered in patients at high risk for bleeding complications.

Most of the nonpharmacologic therapies used in ADHF are primarily reserved for patients who have failed pharmacologic therapy. Ultrafiltration and wireless invasive hemodynamic monitoring (W-IHM) may be used in the management of congestive symptoms, whereas MCS (temporary or durable devices) and cardiac transplantation may be considered in those with advanced disease.[2]

Ultrafiltration

8 Renal impairment is common among patients with ADHF, and advanced forms may warrant the use of renal replacement therapy (eg, hemodialysis, ultrafiltration). Ultrafiltration involves the circulation of blood through a high-pressure circuit, where plasma water is removed from whole blood via a semipermeable membrane. Hemodialysis also involves the use of a semipermeable membrane, but water and solutes (eg, electrolytes, toxins) are removed via diffusion as a result of concentration differences between blood and dialysate (a fluid mixture that runs countercurrent to blood flow on the other side of the membrane). As a result of its mechanism of action, ultrafiltration reduces PCWP without adversely affecting hemodynamics or serum electrolyte concentrations.

Ultrafiltration has emerged as an effective strategy for fluid removal in patients with ADHF (up to 500 mL/h), but it is not superior to adequate doses of diuretic therapy and also increases the risk of adverse events.[49-51] Complications of ultrafiltration include those associated with central venous access (eg, infection), adverse effects from the use of IV heparin (to prevent thrombosis of the access line), and intravascular volume depletion, which increases the risk of WRF. Taken altogether, ultrafiltration should generally be reserved for patients demonstrating diuretic resistance despite optimal diuretic therapy, severe renal impairment following diuretic administration, or continued renal impairment despite inotropic therapy.

Wireless Implantable Hemodynamic Monitoring

Increases in cardiac filling pressures often precede the development of congestive symptoms, and W-IHM has recently emerged as a strategy for using early hemodynamic changes to adjust therapy and thus prevent ADHF in high-risk patients.[52] The CardioMEMS Heart Failure System (Abbott; Lake Bluff, IL) consists of a wireless sensor implanted into the PA during a right heart catheterization and an electronic capturing system that collects information on PA systolic, diastolic, and mean pressures. In addition to guiding therapy adjustments during acute hospitalization, W-IHM can also be telemonitored after patients are discharged from the hospital, permitting further titration of diuretic therapy and GDMT. Despite decreasing the risk of HF hospitalization, widespread use of W-IHM has been limited due to concerns regarding the long-term durability and cost-effectiveness of the device.

Temporary MCS

11 For patients with refractory ADHF, temporary MCS may be considered for hemodynamic stabilization until the underlying etiology of cardiac dysfunction resolves or has been corrected (“bridge to recovery”) or until evaluation for definitive therapy (eg, durable MCS or cardiac transplantation) can be completed (“bridge to decision”).[2] Due to the invasive nature of MCS and its potential complications, therapy should be reserved for patients who are refractory to maximally tolerated pharmacologic therapy. Intravenous vasodilators and inotropic agents may also be used in conjunction with temporary MCS to maximize hemodynamic and clinical benefits or to facilitate device removal. Regardless of the modality selected, systemic anticoagulation with intravenous therapies (eg, unfractionated heparin) is required to prevent device thrombosis. Temporary MCS should generally be avoided in patients with irreversible advanced HF and no plan for definitive management, those with contraindications to anticoagulation therapy, and those with comorbid conditions or anatomical abnormalities that preclude device implantation. The three most common modalities of temporary MCS

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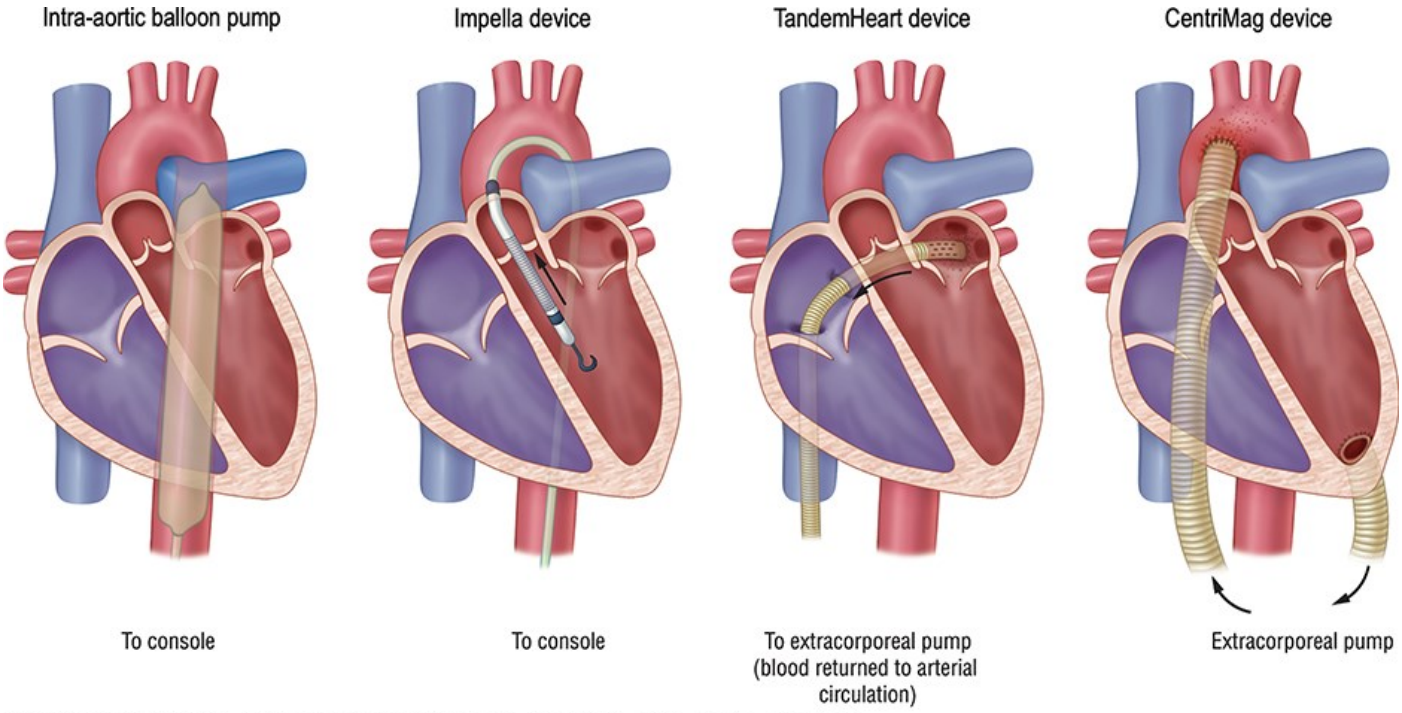
are the IABP, VAD, and extracorporeal membrane oxygenation (ECMO) (Fig. 37-5). Unique features, contraindications, and complications of each type of device will be discussed in the sections to follow.

FIGURE 37-5

Common types of temporary MCS. An intra-aortic balloon pump (IABP) is advanced into the descending aorta where it inflates during diastole (shown), displacing blood and improving coronary filling. During systole (not shown), the IABP deflates, producing a vacuum-like effect that reduces peripheral resistance. An example of a percutaneous VAD is the Impella device, which is advanced through the aortic valve, where blood is transferred from the left ventricle to the aorta by an axial flow pump. The TandemHeart VAD is also a device inserted percutaneously into a large peripheral vein and advanced across the intra-atrial septum. Blood is removed from the left atrium and propelled by an extracorporeal centrifugal flow pump back into the systemic circulation (not shown). The CentriMag VAD uses an inflow cannula that is surgically inserted into the apex of the left ventricle, where blood is transferred to an extracorporeal centrifugal flow pump (not shown), where it is returned to the systemic circulation via an outflow cannula surgically inserted into the aorta. In extracorporeal membrane oxygenation (ECMO) (not shown), the inflow and outflow cannula are inserted into peripheral vessels.



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Intra-aortic Balloon Pump

An IABP consists of a polyethylene balloon mounted on a catheter that is inserted percutaneously into the femoral artery and advanced into the descending thoracic aorta (see Fig. 37-5). During counterpulsation, the balloon is synchronized with the electrocardiogram (or alternatively, changes in pressure) so that it inflates during diastole and displaces blood to the proximal aorta, thus increasing diastolic pressure and coronary perfusion. The balloon deflates just prior to the opening of the aortic valve during systole, which causes a sudden "vacuum-like" decrease in aortic pressure, allowing the left ventricle to pump against reduced arterial impedance. Although the IABP is the most commonly employed modality of temporary MCS due to its ease of use, it only provides an estimated 1.0 L/min of CO. As a consequence, the primary benefits of an IABP are enhanced coronary perfusion, increased myocardial oxygen supply, and reduced myocardial oxygen demand. It may be particularly useful for patients with myocardial ischemia complicated by cardiogenic shock, although it has not been shown to improve mortality in this setting.[53] Systemic anticoagulation is generally recommended, although cases of IABP use without anticoagulation have been reported and practices vary across institutions.[54] Complications of the IABP include vascular injury, thrombocytopenia, and renal impairment due to obstruction of the splanchnic circulation by balloon malposition. Use

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should be avoided in patients with severe peripheral vascular disease or significant aortic regurgitation (eg, aortic insufficiency).

Ventricular Assist Devices

A VAD provides hemodynamic support by assisting and, in some cases, replacing the pumping functions of the right and/or left ventricles. Compared to an IABP, temporary VADs confer greater hemodynamic improvements but no differences in long-term survival.[55] A left ventricular assist device (LVAD) propels blood from the left ventricle or left atrium to the ascending aorta, whereas a right VAD propels blood from the right ventricle or right atrium to the PA. A right VAD may be used alone or in conjunction with an LVAD; this latter configuration is known as a biventricular assist device. All VADs are preload-dependent, meaning that adequate intra-ventricular filling pressure (ie, volume) is required to optimize blood flow. As with the native ventricle in HF, VADs are also afterload-sensitive, meaning that excess peripheral resistance can impair blood flow. Complications of VAD implantation include bleeding, infections, stroke, and risks associated with the specific implantation technique. In addition, the devices can cause thrombosis, renal and hepatic dysfunction, and arrhythmias. Right ventricular failure is a unique complication of LVAD implantation as a result of increased venous return, persistently elevated pulmonary pressures, and changes in right ventricular geometry.

Percutaneous VADs include the Impella series (Abiomed, Danvers, MA) and TandemHeart (CardiacAssist, Pittsburgh, PA). Most Impella devices are inserted percutaneously into a large peripheral artery and advanced in a retrograde fashion across the aortic valve, where blood is advanced from the left ventricle to the ascending aorta via axial flow (see Fig. 37-5). The amount of CO augmented by the Impella device depends on the model used; for example, the Impella 2.5 and 5.0 models supply 2.5 L and 5.0 L/min of flow, respectively. Hemolysis is a common complication of Impella use due to the axial flow facilitated by the device. The TandemHeart device consists of an inflow cannula placed percutaneously into a large peripheral vein and advanced transseptally into the left atrium (see Fig. 37-5). Blood is withdrawn from the left atrium by an extracorporeal pump and propelled via an outflow cannula placed percutaneously into a large artery. Up to 5.0 L/min of flow can be provided by the TandemHeart. Due to its placement across the intra-atrial septum, perforation and shunt formation are potential complications with this device.

The most common surgically implanted temporary VAD is the CentriMag (Thoractec Corp., Pleasanton, CA), which can provide right, left, or biventricular support and up to 10 L/min of CO. The CentriMag device consists of a centrifugal flow extracorporeal pump and surgically placed inflow and outflow cannula supporting the affected ventricle (see Fig. 37-5). Given the surgical technique required for placement of the CentriMag device, tissue injury is its most common complication.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation may be venoarterial or venovenous in nature. In venoarterial ECMO, deoxygenated blood is transported from the venous circulation to an extracorporeal oxygenator and centrifugal flow pump and returned as oxygenated blood to the arterial circulation. In contrast, venovenous ECMO consists of only extracorporeal oxygenation; hemodynamic support is provided by native cardiac function. As a consequence, venoarterial ECMO is more common in the management of refractory ADHF, where up to 8 L/min of cardiac support can be provided. Complications of ECMO include bleeding, infections, and organ dysfunction. Serum drug concentrations can also be significantly impacted as a result of an increased volume of distribution, decreased elimination due to hepatic and/or renal impairment, and sequestration of drugs in the ECMO circuit.

Advanced Therapies

No consensus definition exists for advanced HF or the stage at which patients should be considered for definitive therapies such as durable MCS and heart transplantation. Nonetheless, evaluation for these advanced therapies is commonly initiated during an admission for ADHF, particularly if hospitalization is accompanied by severe symptoms at rest, intolerance of GDMT, decline in organ function, refractory arrhythmias, or an inability to be successfully weaned from inotropic or temporary MCS support. Because of the complexity of care, potential risks, and resource implications of durable MCS and heart transplantation, patients with advanced HF must undergo a rigorous interdisciplinary evaluation before becoming eligible candidates. Components of this evaluation commonly include past medical, surgical, and psychosocial history, medication and adverse event history, adherence to medications and medical care, comorbid conditions, risks for postoperative complications, and health insurance coverage. Relative contraindications to the use of advanced therapies include excess perioperative risk, irreversible pulmonary hypertension, inability to manage postoperative care (eg, medication therapy, monitoring), and concurrent survival-limiting diseases (eg, malignancy).

Durable MCS

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The most common indications for durable MCS are temporary device implantation in patients awaiting heart transplantation who are unlikely to survive the duration of time required for identifying a suitable donor ("bridge to transplantation") and permanent device implantation in patients who are ineligible for heart transplantation due to advanced age or comorbid conditions ("destination therapy"). Although far less common than with temporary MCS, durable VADs may be implanted in patients who are likely to become eligible transplant candidates ("bridge to decision") but the evaluation is incomplete or has been delayed until certain requirements can be satisfied (eg, smoking cessation). Durable MCS is almost exclusively comprised of LVAD implantation, although select patients may remain hospitalized with right VAD or biventricular support while awaiting transplantation.

Durable LVADs are implanted by inserting an inflow cannula into the apex of the left ventricle, which is connected to an intracorporeal pumping unit; blood is returned to the systemic circulation via an outflow cannula inserted into the aorta. Whereas previous devices provided hemodynamic support via pulsatile flow, newer-generation devices utilize a continuous flow mechanism, allowing them to be smaller in size, less subject to deterioration over time, and conferring an improvement in event-free survival.[56] Prolonged unloading of the left ventricle with an LVAD in combination with drug therapy can produce sustained recovery in LV function, amelioration of symptoms, and in some cases, device explantation.[57] The three continuous flow LVADs currently approved for use in the United States are the axial flow HeartMate II LVAD (Abbott; Lake Bluff, IL) and centrifugal flow HeartMate 3 LVAD (Abbott) and HeartWare Ventricular Assist Device (HVAD) (HeartWare, Inc; Framingham, MA). All three devices are capable of providing up to 10 L/min of CO. For complete heart replacement therapy, total artificial heart systems continue to be investigated, although their size and embolic complications limit widespread use.

Complications following durable LVAD placement are similar to those described for temporary devices. Device malfunction may occur with long-term use but has become rare with advances in technology. The most perplexing challenge in the care of LVAD patients remains identifying a chronic antithrombotic regimen that balances the risk of device thrombosis and bleeding. Antithrombotic regimens most often include a vitamin K antagonist and antiplatelet agent, although the goal international normalized ratio (INR) range and antiplatelet agents selected (eg, aspirin, dipyridamole, clopidogrel) may vary significantly by the center. The efficacy and safety of direct oral anticoagulants in LVAD recipients have yet to be established. Suspected pump thrombosis should be promptly evaluated, although no consensus exists on an appropriate treatment strategy (eg, enhanced antiplatelet or anticoagulant therapy, thrombolysis, or pump exchange).[58]

Heart Transplantation

12 Orthotopic heart transplantation remains the optimal management strategy for patients with irreversible advanced HF, as 10-year survival rates approach 60% among patients transplanted after 2001.[59] Unfortunately, the shortage of acceptable donor hearts has prolonged waiting times and many patients succumb to their disease prior to transplantation. Another significant percentage of patients are deemed ineligible for heart transplantation because of age, concurrent illnesses, psychosocial factors, or other reasons. The shortage of donor hearts has prompted the development of new surgical strategies, including ventricular aneurysm resection, mitral valve repair, and myocardial cell transplantation, which have resulted in variable degrees of improvement. Further development of these and other techniques may offer additional options in patients who are not eligible for VAD implantation or heart transplantation. For a more detailed discussion of heart transplantation, see Chapter 109 "Solid Organ Transplantation."

EVALUATION OF THERAPEUTIC OUTCOMES

Daily monitoring to assess the efficacy of drug therapy is critical to assuring optimal outcomes and should include weight, strict measurement of fluid intake and output, and HF signs and symptoms (Table 37-6). Foley catheter placement is not recommended unless close monitoring of urine output is not otherwise possible. Safety endpoints such as monitoring for electrolyte depletion, symptomatic hypotension, and renal dysfunction should be assessed frequently. While many safety parameters can be monitored daily, some will need to be monitored more frequently based on the patient's clinical status. Vital signs should be assessed multiple times throughout the day at a frequency that is appropriate for the patient's degree of stability. Orthostatic blood pressure should be assessed at least once daily.

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TABLE 37-6

Monitoring Recommendations for Patients Hospitalized with ADHF

Parameter	Frequency	Notes
Weight	Daily	Assess after voiding in the morning
		Use the same scale each day, standing weight if possible
		Account for increase or decrease in food intake
Fluid balance	Daily[a]	Strict intake and output
Vital signs	More than daily	Blood pressure and heart rate, including signs/symptoms of orthostatic hypotension, rhythm (continuous)
Signs of congestion and/or low output	Daily[a]	Jugular venous distension, crackles, hepatomegaly, splenomegaly, hepatojugular reflux, ascites, lower extremity edema, hypotension, narrow pulse pressures, cool extremities, altered mental status, worsening renal or hepatic function
Symptoms of congestion and/or low output	Daily[a]	Dyspnea on exertion or at rest, orthopnea, paroxysmal nocturnal dyspnea, nausea/vomiting, early satiety, fatigue, lightheadedness, chest pain, palpitations
Electrolytes	Daily[a]	Potassium, magnesium, sodium
Renal function	Daily[a]	Blood urea nitrogen and serum creatinine including ratio to assess volume status (ie, over-diuresis)
Hepatic function	Variable[a]	Alk Phos and GGT primarily for fluid overload, AST and ALT primarily for hypoperfusion
BNP, NT-proBNP	Admission, discharge	Admission for diagnosis, discharge for prognosis
Other	Variable	Troponin and other cardiac enzymes if myocardial strain
		Arterial blood gas if hypoxic
		Lactate, if hypoperfusion present
		Iron panel, regardless of hemoglobin concentrations

Alk Phos, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BNP, B-type natriuretic peptide; GGT, gamma-glutamyltransferase; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

[a]Daily unless a change in clinical status warrants more frequent assessment (eg, high-dose, continuous infusion, and/or combination diuretic therapy; rapidly changing clinical status).

Patients with ADHF may have critically reduced CO, usually with low arterial blood pressure and systemic hypoperfusion resulting in organ system dysfunction (ie, cardiogenic shock). They may also have pulmonary edema with hypoxemia, respiratory acidosis, and markedly increased work of

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breathing. With cardiopulmonary support, response to interventions should be assessed promptly to allow for timely adjustments in treatment. Continuous telemetry monitoring, continuous pulse oximetry, urine flow, and automated blood pressure recordings are standards of care for critically ill patients with cardiopulmonary decompensation. Peripheral or femoral arterial catheters may be used for continuous and accurate assessment of arterial pressure.

Preparing for Discharge

Patients should not be discharged until optimal volume status is achieved and they have been successfully transitioned from an IV to an oral diuretic regimen and IV inotropes and vasodilators have been discontinued for at least 24 hours. Given the known benefits of discharging patients on GDMT, hospitalization for ADHF represents an ideal opportunity to optimize these therapies. As such, efforts should be made to initiate (or reinitiate if held earlier in the admission) GDMT in hemodynamically stable patients without contraindications.[3] For example, low-dose β-blocker therapy may be safely initiated at discharge without increasing the risk of readmission,[60] and transitioning eligible patients to the angiotensin receptor neprilysin inhibitor (ARNI) sacubitril/valsartan should also be considered.[61] Patients who are hemodynamically stable and have been successfully transitioned to oral diuretics should be considered for SGTL2 inhibitor therapy given reductions in the risk of cardiovascular death and rehospitalization when these therapies are initiated prior to or shortly after discharge.[62] In patients with iron deficiency (ie, serum ferritin <100 ng/mL [mcg/L] or 100 to 299 ng/mL [mcg/L] with transferrin saturation <20%), IV iron repletion should be considered prior to or shortly after discharge to improve symptoms and quality of life and potentially reduce the risk of HF rehospitalization.[63] If relevant, smoking cessation must be addressed to avoid delay in consideration for advanced therapies. In patients with reduced LVEF, use of GDMT or intolerance to such should be documented in the medical record.[64]

Prior to discharge, patients and caregivers should be counseled on dietary sodium restriction as well as monitoring body weight daily and parameters for when to titrate diuretics or call a healthcare provider for further instruction (eg, 3-lb [1.4 kg] weight gain in 24 hours). Medication changes (initiation, discontinuation, dose change) should be clearly conveyed verbally and in writing and financial coverage for all medication assured. The importance of dietary and medication adherence should be emphasized. Appropriate follow-up should be scheduled, including an appointment within 7 days post-discharge and a nurse visit or phone call at 3 days for select patients. Pertinent follow-up labs (eg, potassium, serum creatinine) should also be scheduled, including other medication-related labs (eg, INR for warfarin, serum digoxin concentration). All patients should be considered for referral to a multidisciplinary disease management program.[65,66]

CONCLUSION

Several recent clinical trials have addressed many controversies in the management of ADHF, including the appropriate dosing of diuretics and the use of vasoactive therapies in patients with volume overload. Still, many unanswered questions remain, including optimal use of GDMT in the setting of ADHF. Many advances in MCS have extended the lives of patients awaiting a transplant; however, limited evidence exists to guide the management of this patient population, including how to avoid and manage complications associated with these devices. Finally, ideal management of patients with ADHF includes optimization of GDMT, optimal communication with patients, caregivers, and other healthcare providers with each care transition, and outpatient follow-up with a collaborative, multidisciplinary team.

ABBREVIATIONS

ACCF	American College of Cardiology Foundation
ACE	angiotensin-converting enzyme
ADHF	acute decompensated heart failure
AHA	American Heart Association
AMP	adenosine monophosphate

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AVP	arginine vasopressin
BNP	B-type natriuretic peptide
BUN	blood urea nitrogen
cAMP	cyclic adenosine monophosphate
cGMP	cyclic guanosine monophosphate
CI	cardiac index
CO	cardiac output
CVP	central venous pressure
DT	destination therapy
ECMO	extracorporeal membrane oxygenation
GDMT	guideline-directed medical therapy
GI	gastrointestinal
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HVAD	HeartWare Ventricular Assist Device
IABP	intra-aortic balloon pump
INR	international normalized ratio
IV	intravenous
JVD	jugular venous distension
LVAD	left ventricular assist device
MAP	mean arterial pressure
MCS	mechanical circulatory support
MI	myocardial infarction
NYHA	New York Heart Association
PA	pulmonary artery

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PCWP	pulmonary capillary wedge pressure
PVR	pulmonary vascular resistance
SIADH	syndrome of inappropriate diuretic hormone
SVR	systemic vascular resistance
VAD	ventricular assist device
W-IHM	wireless invasive hemodynamic monitoring
WRF	worsening renal function

REFERENCES

1. McIlvennan Colleen K, Allen Larry A. Palliative care in patients with heart failure. *BMJ.* 2016;353:i1010. 10.1136/bmj.i1010.

2. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;62(16):e147–e239. [PubMed: 23747642]

3. Hollenberg SM, Warner Stevenson L, Ahmad T, et al. 2019 ACC expert consensus decision pathway on risk assessment, management, and clinical trajectory of patients hospitalized with heart failure: A report of the American College of Cardiology solution set oversight committee. *J Am Coll Cardiol.* 2019;74(15):1966–2011. 10.1016/j.jacc.2019.08.001
[PubMed: 31526538] .

4. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics-2021 update: A report from the American Heart Association. *Circulation*. 2021;143(8):e254–e743. 10.1161/CIR.0000000000000950
[PubMed: 33501848] .

5. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: Lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol.* 2014;63(12):1123–1133. [PubMed: 24491689]

6. Kurmani S, Squire I. Acute heart failure: Definition, classification and epidemiology. *Curr Heart Fail Rep.* 2017;14(5):385–392. 10.1007/s11897-017-0351-y
[PubMed: 28785969] .

7. Fonarow GC, Adams KF, Abraham WT, et al. Risk stratification for in-hospital mortality in acutely decompensated heart failure: Classification and regression tree analysis. *JAMA.* 2005;293(5):572–580. [PubMed: 15687312]

8. O'Connor CM, Abraham WT, Albert NM, et al. Predictors of mortality after discharge in patients hospitalized with heart failure: An analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). *Am Heart J.* 2008;156(4):662–673.
[PubMed: 18926148]

9. Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: The ESCAPE trial. *JAMA.* 2005;294(13):1625–1633. [PubMed: 16204662]

10. Garan AR, Kanwar M, Thayer KL, et al. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. *J Am Coll Cardiol Heart Fail.* 2020;8(11):903–913. 10.1016/j.jchf.2020.08.012

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[PubMed: 33121702] .

11. Opotowsky AR, Hess E, Maron BA, et al. Thermodilution vs estimated fick cardiac output measurement in clinical practice: An analysis of mortality from the veterans affairs clinical assessment, reporting, and tracking (VA CART) program and vanderbilt university. *JAMA Cardiol.* 2017;2(10):1090–1099. 10.1001/jamacardio.2017.2945
[PubMed: 28877293] .

12. Aalders M, Kok W. Comparison of hemodynamic factors predicting prognosis in heart failure: A systematic review. *J Clin Med.* 2019;8(10):1757. 10.3390/jcm8101757
[PubMed: 31652650] .

13. Chioncel O, Mebazaa A, Maggioni AP, et al. Acute heart failure congestion and perfusion status: Impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA Heart Failure Long-Term Registry. *Eur J Heart Fail.* 2019;21(11):1338–1352. 10.1002/ejhf.1492
[PubMed: 31127678] .

14. Testani JM, Chen J, McCauley BD, et al. Potential effects of aggressive decongestion during the treatment of decompensated heart failure on renal function and survival. *Circulation*. 2010;122(3):265–72. 10.1161/CIRCULATIONAHA.109.933275
[PubMed: 20606118] .

15. Damman K, Testani JM. The kidney in heart failure: An update. *Eur Heart J.* 2015;36(23):1437–1444. 10.1093/eurheartj/ehv010
[PubMed: 25838436] .

16. Fonarow GC, Abraham WT, Albert NM, et al. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure: Findings from the OPTIMIZE-HF program. *J Am Coll Cardiol.* 2008;52(3):90–199.

17. Jondeau G, Neuder Y, Eicher J-C, et al. B-CONVINCED: Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalizED for a decompensation episode. *Eur Heart J.* 2009;30(18):2186–2192. [PubMed: 19717851]

18. Packer M, Gheorghiade M, Young JB, et al. Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting-enzyme inhibitors. RADIANCE Study. *N Engl J Med.* 1993;329(1):1–7. [PubMed: 8505940]

19. Uretsky BF, Young JB, Shahidi FE, Yellen LG, Harrison MC, Jolly MK. Randomized study assessing the effect of digoxin withdrawal in patients with mild to moderate chronic congestive heart failure: Results of the PROVED trial. PROVED Investigative Group. *J Am Coll Cardiol.* 1993;22(4):955–962.
[PubMed: 8409069]

20. Forrester JS, Diamond G, Chatterjee K, Swan HJ. Medical therapy of acute myocardial infarction by application of hemodynamic subsets (first of two parts). *N Engl J Med.* 1976;295(24):1356–1362. [PubMed: 790191]

21. Felker GM, Lee KL, Bull DA, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med.* 2011;364(9):797–805.
[PubMed: 21366472]

22. Dormans TP, van Meyel JJ, Gerlag PG, Tan Y, Russel FG, Smits P. Diuretic efficacy of high dose furosemide in severe heart failure: Bolus injection versus continuous infusion. *J Am Coll Cardiol.* 1996;28(2):376–382. [PubMed: 8800113]

23. Thomson MR, Nappi JM, Dunn SP, Hollis IB, Rodgers JE, Van Bakel AB. Continuous versus intermittent infusion of furosemide in acute decompensated heart failure. *J Card Fail.* 2010;16(3):88–193.

24. Sharma K, Vasihnav J, Kalathiya R, et al. Randomized evaluation of heart failure with preserved ejection fraction patients with acute heart failure and dopamine: The ROPA-DOP trial. *JACC Heart Fail.* 2018;6(10):859–870. [PubMed: 30098962]

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25. Reed BN, Gottlieb SS. Diuretic strategies and renal dysfunction in heart failure with preserved ejection fraction. *JACC Heart Fail.* 2018;6(12):1049–1050. [PubMed: 30497646]

26. Mullens W, Damman K, Testani JM, et al. Evaluation of kidney function throughout the heart failure trajectory: A position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2020;22(4):584–603. 10.1002/ejhf.1697 [PubMed: 31908120] .

27. Ahmad T, Jackson K, Rao VS, et al. Worsening renal function in patients with acute heart failure undergoing aggressive diuresis is not associated with tubular injury. *Circulation*. 2018;137(19):2016–2028. 10.1161/CIRCULATIONAHA.117.030112 [PubMed: 29352071] .

28. Felker GM, Ellison DH, Mullens W, et al. Diuretic therapy for patients with heart failure: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020;75(10):1178–1195. 10.1016/j.jacc.2019.12.059 [PubMed: 32164892] .

29. Mullens W, Damman K, Harjola VP, et al. The use of diuretics in heart failure with congestion: A position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2019;21(2):137–155. 10.1002/ejhf.1369 [PubMed: 30600580] .

30. Cox ZL, Hung R, Lenihan DJ, et al. Diuretic strategies for loop diuretic resistance in acute heart failure: The 3T Trial. *J Am Coll Cardiol Heart Fail.* 2020;8(3):157–168. 10.1016/j.jchf.2019.09.012 [PubMed: 31838029] .

31. Butler J, Anstrom KJ, Felker GM, et al. Efficacy and safety of spironolactone in acute heart failure: The ATHENA-HF randomized clinical Trial. *JAMA Cardiol.* 2017;2(9):950–958. 10.1001/jamacardio.2017.2198 [PubMed: 28700781] .

32. Giamouzis G, Butler J, Starling RC, et al. Impact of dopamine infusion on renal function in hospitalized heart failure patients: Results of the Dopamine in Acute Decompensated Heart Failure (DAD-HF) Trial. *J Card Fail.* 2010;16(12):922–930. [PubMed: 21111980]

33. Chen HH, Anstrom KJ, Givertz MM, et al. Low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: The ROSE acute heart failure randomized trial. *JAMA.* 2013;310(23):2533–2543. [PubMed: 24247300]

34. Gheorghiade M, Gattis WA, O'Connor CM, et al. Effects of tolvaptan, a vasopressin antagonist, in patients hospitalized with worsening heart failure: A randomized controlled trial. *JAMA.* 2004;291(16):1963–1971. [PubMed: 15113814]

35. Lee WH, Packer M. Prognostic importance of serum sodium concentration and its modification by converting-enzyme inhibition in patients with severe chronic heart failure. *Circulation*. 1986;73(2):257–267. [PubMed: 3002660]

36. Gheorghiade M, Konstam MA, Burnett JC, et al. Short-term clinical effects of tolvaptan, an oral vasopressin antagonist, in patients hospitalized for heart failure: The EVEREST Clinical Status Trials. *JAMA.* 2007;297(12):1332–1343. [PubMed: 17384438]

37. Felker GM, Mentz RJ, Cole RT, et al. Efficacy and safety of tolvaptan in patients hospitalized with acute heart failure. *J Am Coll Cardiol.* 2017;69(11):1399–1406. [PubMed: 27654854]

38. Schwartzenberg S, Redfield MM, From AM, Sorajja P, Nishimura RA, Borlaug BA. Effects of vasodilation in heart failure with preserved or reduced ejection fraction implications of distinct pathophysiologies on response to therapy. *J Am Coll Cardiol.* 2012;59(5):442–451. [PubMed: 22281246]

39. Publication Committee for the VMAC Investigators (Vasodilatation in the Management of Acute CHF). Intravenous nesiritide vs nitroglycerin for treatment of decompensated congestive heart failure: A randomized controlled trial. *JAMA.* 2002;287(12):1531–1540. [PubMed: 11911755]

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40. Cohn JN, Franciosa JA, Francis GS, et al. Effect of short-term infusion of sodium nitroprusside on mortality rate in acute myocardial infarction complicated by left ventricular failure: results of a Veterans Administration cooperative study. *N Engl J Med.* 1982;306:1129–1135. doi: 10.1056/NEJM198205133061902.

41. Mullens W, Abrahams Z, Francis GS, et al. Sodium nitroprusside for advanced low-output heart failure. *J Am Coll Cardiol.* 2008;52(3):200–207. [PubMed: 18617068]

42. Abraham WT, Adams KF, Fonarow GC, et al. In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: An analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). *J Am Coll Cardiol.* 2005;46(1):57–64. [PubMed: 15992636]

43. Cuffe MS, Califf RM, Adams KF, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: A randomized controlled trial. *JAMA.* 2002;287(12):1541–1547. [PubMed: 11911756]

44. Mathew R, Di Santo P, Jung RG, et al. Milrinone as compared with dobutamine in the treatment of cardiogenic shock. *N Engl J Med.* 2021;385(6):516–525. 10.1056/NEJMoa2026845
[PubMed: 34347952] .

45. Metra M, Nodari S, D'Aloia A, et al. Beta-blocker therapy influences the hemodynamic response to inotropic agents in patients with heart failure: A randomized comparison of dobutamine and enoximone before and after chronic treatment with metoprolol or carvedilol. *J Am Coll Cardiol.* 2002;40(7):1248–1258. [PubMed: 12383572]

46. De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med.* 2010;362(9):779–789. [PubMed: 20200382]

47. Aliti GB, Rabelo ER, Clausell N, et al. Aggressive fluid and sodium restriction in acute decompensated heart failure: A randomized clinical trial. *JAMA Intern Med.* 2013;173(12):1058–1064. 10.1001/jamainternmed.2013.552
[PubMed: 23689381] .

48. Griffin M, Soufer A, Goljo E, et al. Real world use of hypertonic saline in refractory acute decompensated heart failure: A U.S. center's 2xperience. *J Am Coll Cardiol Heart Fail.* 2020;8(3):199–208. 10.1016/j.jchf.2019.10.012
[PubMed: 32035891] .

49. Costanzo MR, Guglin ME, Saltzberg MT, et al. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol.* 2007;49(6):675–683. [PubMed: 17291932]

50. Bart BA, Goldsmith SR, Lee KL, et al. Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *N Engl J Med.* 2012;367(24):2296–2304. [PubMed: 23131078]

51. Costanzo MR, Negoianu D, Jaski BE, et al. Aquapheresis versus intravenous diuretics and hospitalizations for heart failure. *J Am Coll Cardiol Heart Fail.* 2016;4(2):95–105. 10.1016/j.jchf.2015.08.005
[PubMed: 26519995] .

52. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: A randomised controlled trial. *Lancet*. 2011;377(9766):658–696. [PubMed: 21315441]

53. Thiele H, Zeymer U, Neumann F-J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med.* 2012;367(14):1287–1296. [PubMed: 22920912]

54. Pucher PH, Cummings IG, Shipolini AR, McCormack DJ. Is heparin needed for patients with an intra-aortic balloon pump? *Interact Cardiovasc Thorac Surg.* 2012;15(1):36–139. [PubMed: 22723541]

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55. Cheng JM, den Uil CA, Hoeks SE, et al. Percutaneous left ventricular assist devices vs. intra-aortic balloon pump counterpulsation for treatment of cardiogenic shock: A meta-analysis of controlled trials. *Eur Heart J.* 2009;30(17):2102–2108. [PubMed: 19617601]

56. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med.* 2009;361(23):2241–2251. [PubMed: 19920051]

57. Birks EJ, Tansley PD, Hardy J, et al. Left ventricular assist device and drug therapy for the reversal of heart failure. *N Engl J Med.* 2006;355(18):1873–1884. [PubMed: 17079761]

58. Goldstein DJ, John R, Salerno C, et al. Algorithm for the diagnosis and management of suspected pump thrombus. *J Heart Lung Transplant.* 2013;32(7):667–670. [PubMed: 23796150]

59. Khush KK, Cherikh WS, Chambers DC, et al. The international thoracic organ transplant registry of the International Society for Heart and Lung Transplantation: Thirty-sixth adult heart transplantation report - 2019; focus theme: donor and recipient size match. *J Heart Lung Transplant.* 2019;38(10):1056–1066. 10.1016/j.healun.2019.08.004
[PubMed: 31548031] .

60. Gattis WA1, O'Connor CM, Gallup DS, Hasselblad V, Gheorghiade M; IMPACT-HF Investigators and Coordinators. Predischarge initiation of carvedilol in patients hospitalized for decompensated heart failure: Results of the Initiation Management Predischarge: Process for Assessment of Carvedilol Therapy in Heart Failure (IMPACT-HF) trial. *J Am Coll Cardiol.* 2004;43(9):1534–1541. [PubMed: 15120808]

61. Velazquez Eric J, Morrow David A, DeVore Adam D, et al. Angiotensin–neprilysin inhibition in acute decompensated heart failure. *N Engl J Med.* 2019;380:539–548. 10.1056/nejmoa1812851.

62. Bhatt DL, Szarek M, Steg PG, et al. Sotagliflozin in patients with diabetes and recent worsening heart failure. *N Engl J Med.* 2021;384(2):117–128. 10.1056/NEJMoa2030183
[PubMed: 33200892] .

63. Ponikowski P, Kirwan BA, Anker SD, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: A multicentre, double-blind, randomised, controlled trial. *Lancet*. 2020;396(10266):1895–1904. 10.1016/S0140-6736(20)32339-4
[PubMed: 33197395] .

64. Heidenreich PA, Fonarow GC, Breathett K, et al. 2020 ACC/AHA clinical performance and quality measures for adults with heart failure: A report of the American College of Cardiology/American Heart Association task force on performance measures. *J Am Coll Cardiol.* 2020;76:2527–2564. doi: 10.1016/j.jacc.2020.07.023

65. Milfred-LaForest SK, Chow SL, DiDomenico RJ, et al. Clinical pharmacy services in heart failure: An opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. *Pharmacotherapy.* 2013;33(5):529–548. [PubMed: 23649813]

66. Albert NM, Barnason S, Deswal A, et al. Transitions of care in heart failure: A scientific statement from the American Heart Association. *Circ Heart Fail.* 2015;8(2):384–409. [PubMed: 25604605]

SELF-ASSESSMENT QUESTIONS

A 58-year-old male with a history of ischemic cardiomyopathy presents to clinic with orthopnea, dyspnea with minimal exertion, 3+ pitting edema, fatigue, anorexia, nausea, and early satiety.

1. These signs and symptoms are consistent with:

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A. Volume overload only

B. Low cardiac output only

C. Both volume overload and low cardiac output

D. Neither volume overload or low cardiac output

2. A 62-year-old female is admitted to the hospital with acute decompensated heart failure and a pulmonary artery catheter is placed. The pulmonary capillary wedge pressure is 28 mm Hg and the cardiac index is 1.8 L/min/m^2 (0.03 L/s/m^2). These hemodynamic values are consistent with which one of the following hemodynamic subsets?

A. I (warm and dry)

B. II (warm and wet)

C. III (cold and dry)

D. IV (cold and wet)

3. All of the following strategies would be reasonable for overcoming diuretic resistance in a patient currently receiving furosemide 120 mg IV twice daily, *EXCEPT*:

A. Adding spironolactone 25 mg orally once daily

B. Increasing the dose of furosemide to 240 mg IV twice daily

C. Increasing the frequency of furosemide to 120 mg IV three times daily

D. Adding metolazone 2.5 mg orally once daily

4. Which of the following laboratory values should be monitored to assess the safety of furosemide? Select all that apply.

A. Brain natriuretic peptide

B. Serum creatinine

C. Potassium

D. Liver transaminases

5. A patient is admitted with acute decompensated heart failure and evidence of low cardiac output. The patient's current medications include sacubitril/valsartan 49/51 mg twice daily, furosemide 40 mg twice daily, metoprolol succinate (CR/XL) 200 mg daily, and digoxin 0.125 mg daily. The patient has been stable on these doses for the previous 4 months. The team decides that inotropic therapy is indicated. Which of the following would be an appropriate agent to initiate at this time?

A. Dopamine

B. Dobutamine

C. Milrinone

D. Either B or C

Questions 6 through 8 refer to the following case:

A 57-year-old African American patient with ischemic cardiomyopathy (ejection fraction 25% [0.25]) presents to the emergency department (ED) with

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acute decompensated heart failure. His vital signs include blood pressure 103/77 mm Hg (negative for orthostasis), heart rate 92 bpm, respiratory rate 23 rpm, and oxygen saturation 91% [0.91] on 4 L by nasal cannula. Physical examination reveals jugular venous distension, crackles at the bases bilaterally, ascites, and trace bilateral lower extremity edema. The patient reports to a 10 lb (4.5 kg) weight gain in the past 2 weeks since his metoprolol dose was increased despite strict adherence to both dietary restrictions and medications. In the ED, he already received furosemide 160 mg IV once with minimal response in urine output. Pertinent labs include potassium 5.1 mEq/L (mmol/L), B-type natriuretic peptide 950 pg/mL (ng/L; 275 pmol/L), blood urea nitrogen 32 mg/dL (11.4 mmol/L), and serum creatinine 2.2 mg/dL (194 µmol/L) (baseline). The patient's medications on admission include lisinopril 10 mg daily, metoprolol succinate (CR/XL) 150 mg daily, and furosemide 120 mg twice daily.

6. How should the patient's β-blocker be managed at this time?

   A. Continue at the current dose

   B. Discontinue immediately

   C. Reduce to the last tolerated dose

   D. Change to atenolol

7. Which of the following would be appropriate for managing this patient's volume overload?

   A. Initiate furosemide 160 mg IV twice daily

   B. Change to bumetanide mg IV twice daily

   C. Initiate furosemide 20 mg/h IV continuous infusion plus metolazone 5 mg by mouth daily

   D. Initiate furosemide 5 mg/h IV continuous infusion

8. Which of the following guideline-directed medical therapies would be appropriate to initiate prior to this patient's discharge? (Assume discharge laboratory values are identical to the admission values provided above.)

   A. Spironolactone 25 mg by mouth once daily

   B. Digoxin 0.125 mg by mouth once daily

   C. Candesartan 4 mg by mouth once daily

   D. Isosorbide dinitrate 20 mg and hydralazine 37.5 mg by mouth three times daily

Questions 9 through 11 refer to the following case:

A 63-year-old female with hypertensive cardiomyopathy (ejection fraction 30%–35% [0.30-0.35]) presents with a chief complaint of "always feeling tired." Her daughter reports that the patient's exercise tolerance has significantly declined recently despite strict adherence to a low-sodium diet and medications that include sacubitril/valsartan 24/26 mg twice daily, carvedilol 12.5 mg twice daily, furosemide 80 mg twice daily, and digoxin 0.125 mg daily. Vital signs include blood pressure 92/57 mm Hg (mild orthostasis), heart rate 95 bpm, and respiratory rate 16 rpm. On physical examination, she has no findings consistent with volume overload. Laboratory analysis reveals sodium 135 mEq/L (mmol/L), potassium 4.9 mEq/L (mmol/L), blood urea nitrogen (BUN) 45 mg/dL (16.1 mmol/L), and serum creatinine (SCr) 2.2 mg/dL (194 µmol/L) (baseline BUN 27 mg/dL [9.6 mmol/L] / SCr 1.1 mg/dL [97 µmol/L]). Upon further questioning, the patient admits to occasional dizziness.

9. In which of the following hemodynamic subsets should this patient be placed?

   A. Subset I (warm and dry)

   B. Subset II (warm and wet)

   C. Subset III (cold and dry)

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D. Subset IV (cold and wet)

10. Which of the following laboratory parameters would assist in confirming the volume status of this patient?

A. C-reactive protein

B. B-type natriuretic peptide

C. Serum albumin

D. Hemoglobin

11. Which of the following would be the optimal initial intervention for this patient?

A. Change furosemide to 80 mg IV twice daily

B. Hold furosemide and initiate cautious hydration with IV fluids

C. Hold carvedilol and initiate dobutamine at 2 mcg/kg/min IV

D. Increase carvedilol to 25 mg by mouth twice daily

12. Compared to dobutamine, which of the following is true regarding milrinone?

A. Lower risk of hypotension

B. Greater dependence on hepatic clearance

C. Longer elimination half-life

D. Increased risk of arrhythmias

Questions 13 and 14 refer to the following case:

An 84-year-old white male with ischemic cardiomyopathy (ejection fraction 20%-25% [0.20-0.25]) presents to the hospital with acute decompensated heart failure. Vital signs include blood pressure 89/55 mm Hg, heart rate 93 bpm (no orthostasis present), and respiratory rate 20 rpm. Physical examination reveals jugular venous distention, positive S3 sound, bilateral crackles throughout on lung auscultation, and 3+ bilateral edema to the thighs. Chest radiograph reveals pulmonary edema and pleural effusions. Hemodynamic measurements obtained by pulmonary artery catheter include pulmonary capillary wedge pressure 28 mm Hg, cardiac index 1.7 L/min/m^2 (0.028 L/s/m^2), and systemic vascular resistance 1,000 dyne·s·cm^{-5} (12.5 Wood units; 100 MPa·s/m^3). The patient's laboratory values are all normal, except blood urea nitrogen (BUN) 34 mg/dL (12.1 mmol/L), and serum creatinine (SCr) 1.5 mg/dL (133 µmol/L) (baseline BUN 32 mg/dL [11.4 mmol/L] and 0.9 mg/dL [80 µmol/L]). Medications on admission include lisinopril 10 mg daily, bisoprolol 10 mg daily, bumetanide 2 mg twice daily, atorvastatin 40 mg daily, and aspirin 81 mg daily.

13. Which of the following would be an appropriate initial strategy for managing this patient's volume overload?

A. Furosemide 80 mg IV twice daily

B. Furosemide 80 mg IV twice daily plus metolazone 10 mg by mouth once daily

C. Furosemide 20 mg/h IV continuous infusion

D. Nitroglycerin 25 mcg/min IV continuous infusion

14. Which of the following therapies would be appropriate for managing this patient's low output?

A. Sodium nitroprusside 0.1 mcg/kg/min IV continuous infusion

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B. Nitroglycerin 25 mcg/min IV continuous infusion

C. Dopamine 10 mcg/kg/min IV continuous infusion

D. Dobutamine 2 mcg/kg/min IV continuous infusion

15. Which of the following modalities of temporary mechanical circulatory support provides the least amount of hemodynamic support?

A. Intra-aortic Balloon Pump

B. Percutaneous VAD (eg, Impella Device)

C. Surgical VAD (eg, Centrimag)

D. Extracorporal Membrane Oxygenation (ECMO)

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** The patient is exhibiting signs and symptoms of volume overload (orthopnea, dyspnea, nausea, 3+ pitting edema). In addition, the patient is exhibiting symptoms of low cardiac output (fatigue, early satiety). Early satiety may be a symptom of either volume overload due to fluid accumulation around the stomach (ie, abdominal edema) or low cardiac output due to reduced blood flow to the stomach. (See Clinical Presentation; Table 37-1)

2. **D.** The patient's elevated PCWP of 28 mm Hg indicates volume overload (wet) and the decreased cardiac index of 1.8 L/min/m^2 (0.03 L/s/m^2) indicates low cardiac output (cold). Consequently, the patient would fall into subset IV of cold and wet (making all of the remaining combinations incorrect). (See Invasive Hemodynamic Monitoring; Fig. 37-1)

3. **A.** At a dose of 25 mg daily, spironolactone produces only minimal diuretic effects and would be unlikely to overcome diuretic resistance, even when combined with a loop diuretic. Lower doses of spironolactone inhibit myocardial fibrosis and pathologic remodeling in chronic heart failure, but much higher doses are required to reliably augment diuresis. Increasing the dose of furosemide will shift drug concentrations toward the top of the concentration-response curve and improve diuresis, so answer choice B is incorrect. Changing to furosemide 120 mg IV three times daily would increase the daily dose and may be effective if the patient is making urine in response to 120 mg but is not achieving overall diuresis goals, so answer choice C is incorrect. Adding metolazone, a thiazide-type diuretic, would produce a synergistic diuretic effect due to sequential nephron blockade, so answer choice D is incorrect. (See Strategies to Overcome Diuretic Resistance)

4. **B** and **C**. Furosemide and other loop diuretics can cause acute kidney injury when diuresis is too rapid, which is why serum creatinine should be routinely monitored (Answer B). Additionally, loop diuretics can cause several electrolyte abnormalities, with hypokalemia and hypomagnesemia being the perturbations observed most frequently (Answer C). Elevations in brain natriuretic peptide reflect stretch-mediated injury in the myocardium (ie, due to excess volume) and would not indicate furosemide toxicity, making answer choice A incorrect. Finally, liver transaminases such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) can be a reflection of low cardiac output (ie, cardiogenic shock), but they are not used to monitor the safety of furosemide, making answer choice D incorrect. (See Loop Diuretics; Table 37-5)

5. **D.** Either dobutamine or milrinone would be a reasonable option for this patient, as both agents have been shown to produce similar hemodynamic effects in patients receiving metoprolol (making answer choices B and C incorrect). Traditionally, milrinone has been advocated in patients receiving chronic β-blocker therapy because its inotropic effects do not involve β-receptor stimulation. However, research has shown that the hemodynamic effects of dobutamine may persist in the presence of chronic β-blocker therapy, particularly with β_1-selective agents. Since the patient is not presenting in a mixed shock state (eg, cardiogenic and vasodilatory shock), dopamine would not be an appropriate choice (answer A), given its variable inotropic and vasopressor effects. (See Inotropes, Inotrope Selection)

6. **C.** The patient's metoprolol dose was recently increased and may be responsible for his acute decompensation due to its negative inotropic effects. As such, the dose of metoprolol should be reduced back down to the patient's last tolerated dose. Metoprolol should not be discontinued in the absence of evidence of low output as stopping a patient's β-blocker during an acute decompensation has been associated with worse outcomes, making answer choice B incorrect. Changing metoprolol to atenolol would not be helpful as atenolol has not been shown to improve outcomes in

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heart failure, making answer choice D incorrect. Continuing the current dose (answer A) would only be warranted if the dose had been stable for a reasonable period (ie, several weeks) prior to the acute decompensation. (See General Approach to Treatment)

7. **C.** Initiating a furosemide regimen at up to 2.5 times the patient's home dose (a 20 mg/h infusion would be 480 mg/day or twice that of her home regimen), plus adding metolazone, a thiazide-type diuretic with an alternative mechanism of action, would produce a synergistic diuretic effect due to sequential nephron blockade. Since the patient had a minimal response to furosemide 160 mg IV, it is unlikely that the threshold for diuresis has been reached; scheduling this dose more frequently would therefore be unlikely to elicit a diuretic response, making answer choice A incorrect. Changing to bumetanide 2 mg IV twice daily would represent a decrease from the dose she received in the ED (as the equipotency of IV bumetanide to IV furosemide is approximately 1 to 20-40), making answer choice B incorrect. Administering a continuous infusion of furosemide at 5 mg/h would also be an overall dose decrease (ie, an equivalent of furosemide 120 mg IV over a 24-hour period), so answer choice D is incorrect. (See Loop Diuretics; Strategies to Overcome Diuretic Resistance)

8. **D.** In self-identified African American patients with New York Heart Association class III-IV symptoms, the combination of isosorbide dinitrate and hydralazine has been shown to reduce mortality and hospitalizations when added to a background of ACE inhibitor and β-blocker therapy. Answer choice A would be incorrect since the patient's potassium is 5.1 mEq/L (mmol/L) and adding spironolactone would likely exacerbate hyperkalemia, especially given baseline renal dysfunction. Whereasdigoxin may improve the patient's symptoms and reduce the risk of rehospitalization, it is usually reserved for patients with advanced disease who have already been optimized on therapies associated with improvements in survival. Notably, renal dysfunction would not be a contraindication to digoxin as long as serum concentrations could be maintained within the appropriate range. Answer choice C is incorrect since the patient is already on lisinopril and candesartan would likely worsen the patient's renal function and hyperkalemia. (See Preparing for Discharge)

9. **C.** The patient does not have any signs of fluid overload as evidenced by physical exam, making answer choices B and D incorrect. Instead, she presents with signs and symptoms of both hypoperfusion (answer A is incorrect) and being volume-depleted—complaining of fatigue, having a blood pressure of 92/57 mmHg with mild orthostasis and an elevated BUN and SCr, and endorsing occasional dizziness. (See Clinical Presentation; Table 37-1)

10. **B.** B-type natriuretic peptide (BNP) is a counterregulatory neurohormone released in response to increased filling pressures. A BNP concentration that is not increased from baseline would have a strong negative predictive value for ruling out the presence of volume overload. C-reactive protein is a marker of inflammation and would not be helpful for confirming the patient's volume status, so answer choice A is incorrect. Serum albumin is primarily a marker of nutritional status, so answer choice C is incorrect. Hemoglobin is primarily a marker of anemia, so answer choice D is incorrect. (See Laboratory Findings)

11. **B.** Since the patient is volume depleted, her furosemide should be held and cautious hydration with IV fluids should be administered. Changing furosemide to 80 mg IV twice daily would further worsen dehydration and kidney dysfunction, so answer choice B is incorrect. Although the patient has evidence of hypoperfusion, this is likely due to lack of volume (ie, low end of the Frank–Starling curve) and inotropic support should not be considered until a euvolemic state has been achieved. Hence, holding carvedilol and initiating dobutamine would not be appropriate at this time, making answer choice C incorrect. Answer choice D is incorrect, given the potential negative inotropic effects associated with higher β-blocker doses; carvedilol should be maintained at its current dose until evidence of hypoperfusion has resolved. (See General Approach to Treatment; Loop Diuretics; Fig. 37-1)

12. **C.** Although outcomes between dobutamine and milrinone are generally similar in patients with cardiogenic shock, some pharmacologic differences may make one of the two therapies more optimal in a given patient. One of the disadvantages of milrinone is its longer elimination half-life compared to dobutamine (Answer C), which prevents minute-to-minute titrations in hemodynamically labile patients. Answer choice A is incorrect because milrinone has a higher, not lower, risk of hypotension due to its vasodilating effects in vascular smooth muscle. Answer choice B is incorrect because milrinone is primarily dependent on renal rather than hepatic clearance. Finally, the risk of arrhythmias is similar between dobutamine and milrinone, making answer choice D incorrect. (See Inotropes)

13. **A.** The patient is presenting with volume overload requiring aggressive diuresis. Furosemide 80 mg IV twice daily would be a reasonable initial dose given the patient's low blood pressure and acutely elevated serum creatinine. Notably, if these signs of hypoperfusion were not present, a more aggressive dose (eg, up to 2.5 times the oral home dose administered intravenously) would be appropriate, as high doses have been associated with more rapid relief of congestive symptoms. Combination diuretic therapy (ie, addition of a thiazide-type diuretic such as metolazone) may be

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considered in patients with refractory congestive symptoms, but this approach is usually reserved for patients who have failed an adequate trial of loop diuretics, making answer choice B incorrect. Answer choice C is incorrect since a continuous infusion of furosemide at 20 mg/h would be equivalent to furosemide 480 mg IV over a 24-hour period and would exceed the initial dose increases shown to be safe in patients with acute decompensated heart failure. Vasodilators may be considered for the treatment of refractory congestive symptoms, but such therapy should be avoided in patients with hypotension, making answer choice D incorrect. (See Loop Diuretics; Strategies to Overcome Diuretic Resistance)

14. **D.** Since the patient's cardiac index is low and systemic vascular resistance is normal, positive inotropic therapy should be considered. Answer choices B, C, and D are incorrect since these medications are strictly vasodilators and are contraindicated in patients with low blood pressure in the absence of elevated systemic vascular resistance. Finally, answer choice C would be incorrect because dopamine exerts unpredictable effects and its inotropic action at 10 mcg/kg/min would be accompanied by vasoconstriction, which may further worsen left ventricular dysfunction. (See General Approach to Treatment; Vasodilators; Inotropes; Fig. 37-1).

15. **A.** Despite its frequent use, intra-aortic balloon pump counterpulsation provides the least amount of hemodynamic support (approximately 1 L/min of cardiac output) among the options listed. The remaining modalities all provide considerably greater levels of hemodynamic support, with augmentation in cardiac output ranging from 2.5 with select percutaneous ventricular assist devices (eg, Impella 2.5) to 10 L/min with surgical ventricular assist devices (eg, CentriMag). (See Temporary Mechanical Circulatory Support)

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