

Chapter 6

Heart Failure

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Heat failure is a complex clinical syndrome resulting from a structural or functional abnormality that impairs the ability of the ventricles to fill with or eject blood. Although new-onset heart failure often results from acute pump dysfunction caused by myocardial ischemia or infarction, the development and progression of chronic heart failure is typically mediated by ventricular remodeling and activation of endogenous neurohormonal pathways (e.g., renin-angiotensin-aldosterone system, sympathetic nervous system) that have long-term deleterious effects on the heart and play pivotal roles in the pathophysiology of this disorder.

In patients with chronic heart failure, the left ventricle dilates and/or hypertrophies; this causes the chamber to become more spherical in a process called ventricular remodeling. The geometric changes that affect the left ventricle increase wall stress, depress myocardial performance and activate various neurohormonal compensatory responses that result in salt and water retention despite the presence of excess intravascular volume. In addition to causing peripheral vasoconstriction, elevated levels of circulating neurohormones, such as epinephrine, aldosterone, and angiotensin II, may exert direct toxic effects on cardiac cells by promoting further hypertrophy, stimulating myocardial fibrosis and triggering programmed cell death (apoptosis).

Chronic heart failure represents a broad spectrum of disease ranging from asymptomatic persons with risk factors (Stage A) or structural cardiac abnormalities (Stage B) to patients with overt signs and symptoms of heart failure (Stage C), including those with end-stage disease (Stage D) who may require specialized treatments, palliation, and end-of-life care (Figure 1).

Heart failure, which is predominately a disease of the elderly, represents a major United States public health problem, with a prevalence of over 5 million and an incidence of over 500,000 cases each year. Approximately 80% of patients hospitalized with heart failure are over age 65, making heart failure the most common and most expensive Medicare diagnosis-related group.

Prevention

Longstanding untreated hypertension is associated with the development of both systolic and diastolic heart failure and is an independent risk factor for coronary artery disease. Even modest decreases in systolic blood pressure markedly reduce mortality and the risk of developing heart failure.

Diabetes produces morphologic and functional myocardial abnormalities independent of coronary artery disease and hypertension. Diabetes is associated with left ventricular hypertrophy

and arterial wall stiffening, which may result in impaired left ventricular relaxation and distensibility. Aggressive blood pressure and lipid control appears to provide additional benefits to patients with diabetes above those seen in the general population. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers can prevent the development of heart failure and also provide renal protection in patients with diabetes.

Advise patients to avoid exposure to cardiotoxic substances such as alcohol, tobacco, and illicit drugs, particularly cocaine. Alcohol is a direct myocardial toxin and can cause heart failure. In some patients, abstinence from alcohol can reverse left ventricular dysfunction. Tobacco use significantly increases the risk of coronary artery disease, which in turn can lead to heart failure. Cocaine has direct, as well as indirect, effects on the myocardium that increase the risk of heart failure and sudden cardiac death.

Prolonged tachycardia may be associated with the development of a reversible form of left ventricular dysfunction. Control rapid ventricular responses in patients with atrial fibrillation and other supraventricular tachycardias in order to prevent the development of tachycardia-induced cardiomyopathy. Cardioversion to normal sinus rhythm or improved rate control can restore left ventricular function.

Screening

Because ischemic heart disease is one of the major causes of heart failure in the United States, patients at high-risk for developing coronary artery disease are screened as recommended by national guidelines. Cardiac perfusion imaging at the time of exercise stress testing may establish coronary artery disease as the underlying cause of left ventricular dysfunction. Revascularization may reduce the risk of myocardial infarction and subsequent heart failure. Coronary artery bypass graft surgery in patients with diminished left ventricular function improves ventricular performance and survival compared with medical therapy alone.

Evaluate asymptomatic patients with diastolic, holosystolic, or midsystolic heart murmurs grade ≥ 3 and all patients with a heart murmur accompanied by symptoms of myocardial infarction, syncope, endocarditis, or thromboembolism with an echocardiogram to detect the presence of significant valvular heart disease. Early identification of a significant valvular abnormality may prevent the development of left ventricular dysfunction if the valve can be repaired or replaced.

Look for familial patterns of heart failure by obtaining detailed family histories that focus on episodes of unexplained heart failure, sudden cardiac death, and progressive heart failure in

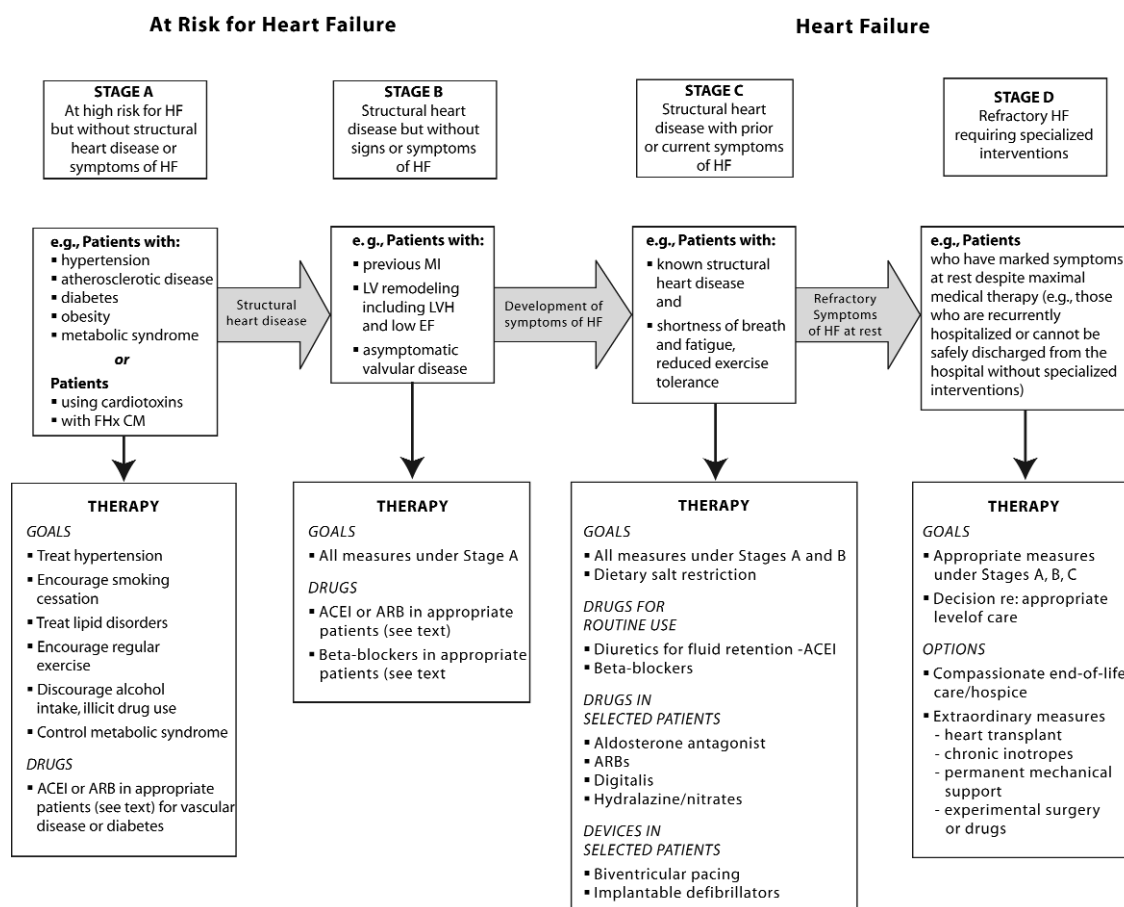


Figure 1 Stages in the development of heart failure and recommended therapy by stage. (ACEI = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; EF = ejection fraction; FHx CM = family history of cardiomyopathy; HF = heart failure; LV = left ventricular; LVH = left ventricular hypertrophy; MI = myocardial infarction.) (From *Circulation*. 2005;112:154-235. Copyright © 2005 by American College of Cardiology Foundation and American Heart Association; with permission.)

young family members. Dilated cardiomyopathies may be familial in a significant percentage of cases. Identification of asymptomatic ventricular dysfunction may allow earlier intervention. A personal or family history of hemochromatosis, Wilson's disease, hypertrophic cardiomyopathy, or amyloidosis may also warrant echocardiographic screening of asymptomatic family members.

Diagnosis

In addition to establishing the diagnosis of heart failure, determine the underlying etiology, differentiate between systolic and diastolic dysfunction, and identify any specific exacerbating or precipitating factors.

The classical manifestations of heart failure include fatigue, dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, and fluid retention. Dyspnea at rest and fatigue may indicate a low cardiac output state. It is important to note that older patients with heart failure often present with nonspecific symptoms such as nocturia, insomnia, irritability, and anorexia that are misdiagnosed as age-related changes or ascribed to age prevalent comorbidities.

The medical history is also used to assess functional capacity, most commonly expressed in terms of the New York Heart

Association (NYHA) classification that describes the effort needed to elicit symptoms:

- *Class I:* Asymptomatic left ventricular dysfunction
- *Class II:* Dyspnea with significant exertion
- *Class III:* Dyspnea with minimal activity including usual activities of daily living
- *Class IV:* Dyspnea at rest

Although the presence of jugular venous distention, abdominal jugular reflux, pulmonary rales, ventricular gallops (S_3 or S_4), any cardiac murmur, and lower extremity edema all increase the likelihood of heart failure, these findings often do not predict the hemodynamic impairment in chronic heart failure. For example, pulmonary rales may reflect the rapidity of onset of heart failure, rather than the degree of volume overload. Elevated jugular venous pressure and an S_3 are each independently associated with adverse outcomes, including progression of heart failure.

Obtain a resting 12-lead electrocardiogram in any patient with new-onset heart failure or an exacerbation of preexisting heart failure to identify the cardiac rhythm and determine the presence of ischemia, prior infarction, left ventricular hypertrophy, and/or conduction system abnormalities.

Common radiographic findings in heart failure patients include cardiomegaly, pulmonary vascular congestion, and pleural effusions, which are often bilateral. Although a chest x-ray may be helpful in determining the cause of a patient's dyspnea, serial chest films are not sensitive to small changes in pulmonary vascular congestion and are not recommended.

Measurement of b-type natriuretic peptide (BNP), a sensitive marker of ventricular pressure and volume overload, should be considered in the evaluation of heart failure when diagnostic uncertainty exists. Higher BNP levels are suggestive of heart failure and may provide additional prognostic information. Conversely, low serum BNP levels are most useful for excluding a diagnosis of heart failure in patients with symptoms of acute dyspnea. In one recent review, a serum BNP level <100 pg/mL was determined to be the most useful test for ruling out heart failure in an emergency department setting, with a negative likelihood ratio of 0.11.

Transthoracic echocardiography is routinely used to determine the underlying etiology of heart failure and is critically important in formulating an effective, individualized treatment plan. Transthoracic echocardiography differentiates between systolic and diastolic dysfunction, and this distinction informs treatment strategies. Systolic dysfunction is usually defined as a left ventricular ejection fraction <40%. The echocardiogram typically shows evidence of ventricular remodeling with an increased left ventricular end diastolic volume and impaired indices of left ventricular contractility. Coronary artery disease, which is the underlying cause of systolic heart failure in about two-thirds of patients, may show echocardiographic evidence of regional wall motion abnormalities and/or post-myocardial infarction ventricular remodeling.

Patients with diastolic dysfunction have ejection fractions >40%. These patients typically have echocardiographic evidence of left ventricular hypertrophy, normal left ventricular end-diastolic volume, and abnormalities of left ventricular diastolic properties, including delayed active relaxation and increased passive stiffness. Because the actual measurement of diastolic function is complex and lacks sensitivity and specificity, the diagnosis of diastolic dysfunction is usually based on the typical symptoms and signs of heart failure associated with normal left ventricular ejection fraction and no valvular abnormalities on echocardiogram. Diastolic heart failure is common, especially in elderly patients, and in conditions causing significant left ventricular hypertrophy, such as hypertension, aortic stenosis, and hypertrophic cardiomyopathy.

Traditional exercise stress tests or pharmacologic stress tests may be useful in selected patients to differentiate heart failure from other conditions, confirm functional capacity, and identify myocardial ischemia. Functional class assessed by stress testing is among the most powerful predictors of survival and outcomes in heart failure.

Therapy

Limiting dietary sodium to 2 g daily and fluid to 2 quarts per day results in fewer hospitalizations for decompensated heart failure.

Patients with more severe heart failure may need more rigorous limitations.

Because exercise may improve both physical and psychological well-being, encourage patients to participate in a long-term aerobic exercise program that is tailored to their functional capacity. Improvement in metabolic and hemodynamic indices occurs in patients with heart failure who undergo exercise conditioning.

All forms of sleep-disordered breathing are common in patients with cardiovascular diseases, especially heart failure and hypertension. Effective therapy of sleep-disordered breathing is associated with significant improvement in blood pressure control, exercise capacity, and quality of life, as well as decreased rates of disease progression and re-hospitalizations for heart failure.

Angiotensin-converting enzyme inhibitors, β -blockers, and, in selected patients, aldosterone antagonists improve survival in heart failure due to systolic dysfunction. Judicious use of digitalis can prevent hospitalization. In one study, the addition of a fixed dose of hydralazine and nitrates increased survival among black patients already taking standard therapy including angiotensin-converting enzyme inhibitors and β -blockers. Drug therapy for patients with systolic dysfunction is summarized in Table 1.

The management of patients with diastolic heart failure is based largely on theoretical concepts and extrapolations from trials in heart failure patients with low ejection fractions. There is general agreement that the approach to such patients includes control of heart rate and blood pressure, maintenance of normal sinus rhythm, and identification and management of myocardial ischemia.

Refer patients with NYHA class III or IV heart failure and a prolonged QRS duration (>120 msec) on electrocardiography for biventricular pacing. Cardiac resynchronization therapy in these patients improves functional capacity, quality of life, and mortality.

Implantation of a cardioverter defibrillator in patients with significant left ventricular systolic dysfunction (ejection fraction \leq 30%-35%) is associated with a reduction in mortality regardless of whether the underlying cardiomyopathy was secondary to an ischemic or nonischemic etiology.

Cardiac transplantation improves survival, functional status, and quality of life in patients with NYHA class III or IV heart failure. Refer patients with severe intractable heart failure despite maximal medical therapy to a cardiac transplantation program for evaluation. Relative contraindications to cardiac transplant include age >65, end-organ damage from diabetes or vascular disease, malignancy, previous stroke, lack of psychosocial support, or active psychiatric illness.

Follow-Up

Once the diagnosis of heart failure and its underlying etiology are established, identify and correct factors responsible for any symptomatic exacerbation. Common reasons for an increase in symptoms or decline in functional status include myocardial ischemia and/or infarction, cardiac arrhythmias (i.e., atrial fibrillation), severe hypertension, worsening renal function, and non-compliance with medications or diet. In general, any condition that causes tachycardia (e.g., fever, infection, anemia, thyrotoxicosis) has the potential to exacerbate heart failure symptoms by

Table 1. Drug Treatment for Heart Failure due to Systolic Dysfunction

Drug	Notes
Angiotensin-converting enzyme inhibitors (enalapril, captopril, lisinopril)	For all classes of heart failure. Inhibits angiotensin-converting enzyme, resulting in decreased conversion of angiotensin I to angiotensin II and decreased metabolism of bradykinin. Improves exercise tolerance, hemodynamic status, and survival. May halt progression and cause regression of HF. Avoid in patients with history of ACE inhibitor-induced angioedema.
β -blockers (carvedilol, metoprolol, bisoprolol)	For all classes of heart failure. Inhibits adrenergic nervous system and improves survival. Reduces sudden death risk and may halt progression and cause regression of HF. Use with caution in patients with NYHA class IV HF. Avoid in patients with significant asthma and high-grade conduction system disease.
Aldosterone antagonists (spironolactone, eplerenone)	Improves survival in patients with NYHA III-IV HF. Improves survival after myocardial infarction with LV dysfunction. Follow potassium level, especially in patients taking ACE inhibitors.
Angiotensin-receptor antagonists (losartan, valsartan, candesartan)	Use in patients who cannot take ACE inhibitors. Inhibits renin-angiotensin system at angiotensin receptor level. Improvement in hemodynamics, symptoms.
Hydralazine and nitrates (isosorbide dinitrate, isosorbide mononitrate)	Reserved for patients intolerant to ACE inhibitors and ARB. Reduces afterload and preload. Improves survival in patients with HF but not so well as ACE inhibitors. May further reduce mortality in black patients when added to ACE inhibitors and β -blockers.
Digitalis glycoside (digoxin)	Positive inotropic agent. Slows heart rate through vagal effects, improves exercise tolerance, and reduces hospitalizations. No survival benefit. Aim for level <2.0 ng/mL. Use lower dose in elderly and in patients with renal insufficiency. Avoid hypokalemia.
Loop diuretics (furosemide, torsemide, bumetanide, ethacrynic acid)	Palliative in patients with congestive symptoms. No survival benefit.
Positive inotropic agents (dobutamine, milrinone)	Used to improve hemodynamics in patients with severe HF and to maintain patients until cardiac transplantation; can also be used continuously at home in nontransplant candidates for palliation. Arrhythmogenic; no survival benefit.

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; HF = heart failure; NYHA = New York Heart Association; LV = left ventricular.

shortening diastole and impairing left ventricular filling. Since polypharmacy is a frequent problem in older patients, be aware that concomitant use of noncardiac medications such as non-steroidal anti-inflammatory drugs and thiazolidinediones may cause significant fluid retention and worsen heart failure.

Serial measurements of a patient's weight will determine clinical stability or the need to adjust diuretic doses. Electrolyte disturbances in heart failure are common due to the effect of medications as well as the pathophysiology of heart failure. Serum sodium ≤ 134 meq/L is an independent risk factor for mortality in heart failure.

Book Enhancement

Go to www.acponline.org/essentials/cardiovascular-section.html to view a chest x-ray showing pulmonary edema and to access tables on the differential diagnosis of heart failure, heart failure

mimics, commonly used tests to evaluate heart failure, and a schema outlining the pathophysiology of heart failure. In *MKSAP for Students 4*, assess yourself with items 33-41 in the **Cardiovascular Medicine** section.

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