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**ACC/AHA Pocket Guideline**

**Based on the ACC/AHA 2005  
Guideline Update**



# **Diagnosis and Management of Chronic Heart Failure in the Adult**

**August 2005**

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# Diagnosis and Management of Chronic Heart Failure in the Adult

**August 2005**

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## I. Introduction

Heart failure (HF) is a major and growing public health problem in the United States. Approximately 5 million patients in this country have HF, and more than 550,000 patients are diagnosed with HF for the first time each year. The disorder is the primary reason for 12 to 15 million office visits and 6.5 million hospital days each year. From 1990 to 1999, the annual number of hospitalizations has increased from approximately 810,000 to more than 1 million for HF as a primary diagnosis and from 2.4 to 3.6 million for HF as a primary or secondary diagnosis. In 2001, nearly 53,000 patients died of HF as a primary cause. The number of HF deaths has increased steadily despite advances in treatment, in part because better treatment and “salvage” of patients with acute myocardial infarctions (MIs) earlier in life have resulted in a greater number of patients with HF.

Heart failure is primarily a condition of the elderly, and thus the widely recognized “aging of the population” also contributes to the increasing incidence of HF. The incidence of HF approaches 10 per 1,000 people after age 65, and approximately 80% of patients hospitalized with HF are more than 65 years old. Heart failure is the most common Medicare diagnosis-related group (i.e., hospital discharge diagnosis), and more Medicare dollars are spent for the diagnosis and treatment of HF than for any other diagnosis. The total estimated direct and indirect costs for HF in 2004 were approximately \$27.9 billion. In the United States, approximately \$2.9 billion annually is spent on drugs for the treatment of HF.



The American College of Cardiology (ACC) and the American Heart Association (AHA) first published guidelines for the evaluation and management of HF in 1995 and published revised guidelines in 2001. Since that time, a great deal of progress has been made in the development of both pharmacological and nonpharmacological approaches to treatment for this common, costly, disabling, and potentially fatal disorder. Available treatments have increased, but this increase has rendered clinical decision making far more complex. The timing and sequence of initiating treatments and the appropriateness of prescribing them in combination are uncertain. The increasing recognition of the existence of clinical HF in patients with a normal ejection fraction (EF) has also led to heightened awareness of the limitations of evidence-based therapy for this important group of patients. For these reasons, the two organizations believed that it was appropriate to reassess and update these guidelines, fully recognizing that the optimal therapy of HF remains a work in progress and that future advances will require that the guideline be updated again.

In formulating the 2001 document, the writing committee decided to take a new approach to the classification of HF, one that emphasized both the development and progression of the disease. In doing so, the 2001 document identified four stages involved in the development of the HF syndrome. The first two stages (A and B) are clearly not HF but are an attempt to help healthcare providers identify patients early who are at risk for developing HF. Stages A and B patients are best defined as

those with risk factors that clearly predispose toward the development of HF. For example, patients with coronary artery disease, hypertension, or diabetes mellitus who do not yet demonstrate impaired left ventricular (LV) function, hypertrophy, or geometric chamber distortion would be considered Stage A, whereas patients who are asymptomatic but demonstrate LV hypertrophy and/or impaired LV function would be designated as Stage B. Stage C then denotes patients with current or past symptoms of HF associated with underlying structural heart disease (the bulk of patients with HF), and Stage D designates patients with truly refractory HF who might be eligible for specialized, advanced treatment strategies, such as mechanical circulatory support, procedures to facilitate fluid removal, continuous inotropic infusions, or cardiac transplantation or other innovative or experimental surgical procedures, or for end-of-life care, such as hospice.

A classification of recommendation and level of evidence have been assigned to each recommendation. Classification of recommendations and levels of evidence are expressed in the ACC/AHA format as follows and described in more detail in *Table 1*.

### **Classification of Recommendations**

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**Class I**      Conditions for which there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful, and/or effective.

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**Class II** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

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**Class IIa** Weight of evidence/opinion is in favor of usefulness/efficacy.

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**Class IIb** Usefulness/efficacy is less well established by evidence/opinion.

---

**Class III** Conditions for which there is evidence and/or general agreement that a procedure/therapy is not useful/effective and in some cases may be harmful.

---

### **Level of Evidence**

- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B: Data derived from a single randomized trial, or nonrandomized studies.
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.

Recommendations relevant to a class of drugs specify the use of the drugs shown to be effective in clinical trials unless there is reason to believe that such drugs have a broad class effect.

**Table 1. Applying Classification of Recommendations and Level of Evidence in ACC/AHA Format**

		SIZE OF TREATMENT EFFECT	
		CLASS I <i>Benefit &gt;&gt;&gt; Risk</i> Procedure/Treatment <b>SHOULD</b> be performed/ administered	CLASS IIa <i>Benefit &gt;&gt; Risk</i> <i>Additional studies with focused objectives needed</i> <b>IT IS REASONABLE</b> to perform procedure/administer treatment
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	LEVEL A Multiple (3-5) population risk strata evaluated* General consistency of direction and magnitude of effect	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>
	LEVEL B Limited (2-3) population risk strata evaluated*	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Limited evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>
	LEVEL C Very limited (1-2) population risk strata evaluated*	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Only expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation in favor of treatment or procedure being useful/effective</li> <li>■ Only diverging expert opinion, case studies, or standard-of-care</li> </ul>
Suggested phrases for writing recommendations		should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated

\*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use.



<p><b>CLASS IIb</b>  <i>Benefit <math>\geq</math> Risk</i>  <i>Additional studies with broad objectives needed; additional registry data would be helpful</i>            Procedure/Treatment <b>MAY BE CONSIDERED</b></p>	<p><b>CLASS III</b>  <i>Risk <math>\geq</math> Benefit</i>  <i>No additional studies needed</i>            Procedure/Treatment should <b>NOT</b> be performed/administered <b>SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</b></p>
<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Greater conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>
<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Greater conflicting evidence from single randomized trial or nonrandomized studies</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Limited evidence from single randomized trial or nonrandomized studies</li> </ul>
<ul style="list-style-type: none"> <li>■ Recommendation's usefulness/efficacy less well established</li> <li>■ Only diverging expert opinion, case studies, or standard-of-care</li> </ul>	<ul style="list-style-type: none"> <li>■ Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>■ Only expert opinion, case studies, or standard-of-care</li> </ul>

may/might be considered  
 may/might be reasonable  
 usefulness/effectiveness is  
 unknown/unclear/uncertain  
 or not well established

is not recommended  
 is not indicated  
 should not  
 is not useful/effective/beneficial  
 may be harmful



## II. Characterization of HF as a Clinical Syndrome

### A. Definition of HF

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema. Both abnormalities can impair the functional capacity and quality of life of affected individuals, but they do not necessarily dominate the clinical picture at the same time. Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema and report few symptoms of dyspnea or fatigue. Because not all patients have volume overload at the time of initial or subsequent evaluation, the term “heart failure” is preferred over the older term “congestive heart failure.”

The clinical syndrome of HF may result from disorders of the pericardium, myocardium, endocardium, or great vessels, but the majority of patients with HF have symptoms due to an impairment of LV myocardial function. Heart failure may be associated with a wide spectrum of LV functional abnormalities, which may range from patients with normal LV size and preserved EF to those with severe dilatation and/or markedly reduced EF. In most patients, abnormalities of systolic and diastolic dysfunction coexist, regardless of EF. Patients with normal EF may have a different natural history and may require different treatment strategies than patients with reduced EF, although such differences remain controversial.

Coronary artery disease, hypertension, and dilated cardiomyopathy are the causes of HF in a substantial proportion of patients in the Western world. As many as 30% of patients with dilated cardiomyopathy may have a genetic cause. Valvular heart disease is still a common cause of HF. In fact, nearly any form of heart disease may ultimately lead to the HF syndrome.

It should be emphasized that HF is not equivalent to cardiomyopathy or to LV dysfunction; these latter terms describe possible structural or functional reasons for the development of HF. Instead, HF is defined as a clinical syndrome that is characterized by specific symptoms (dyspnea and fatigue) in the medical history and signs (edema, rales) on the physical examination. There is no single diagnostic test for HF because it is largely a clinical diagnosis that is based on a careful history and physical examination.

### **B. Heart Failure as a Symptomatic Disorder**

The approach that is most commonly used to quantify the degree of functional limitation imposed by HF is one first developed by the New York Heart Association. This system assigns patients to one of four functional classes, depending on the degree of effort needed to elicit symptoms: patients may have symptoms of HF at rest (class IV), on less-than-ordinary exertion (class III), on ordinary exertion

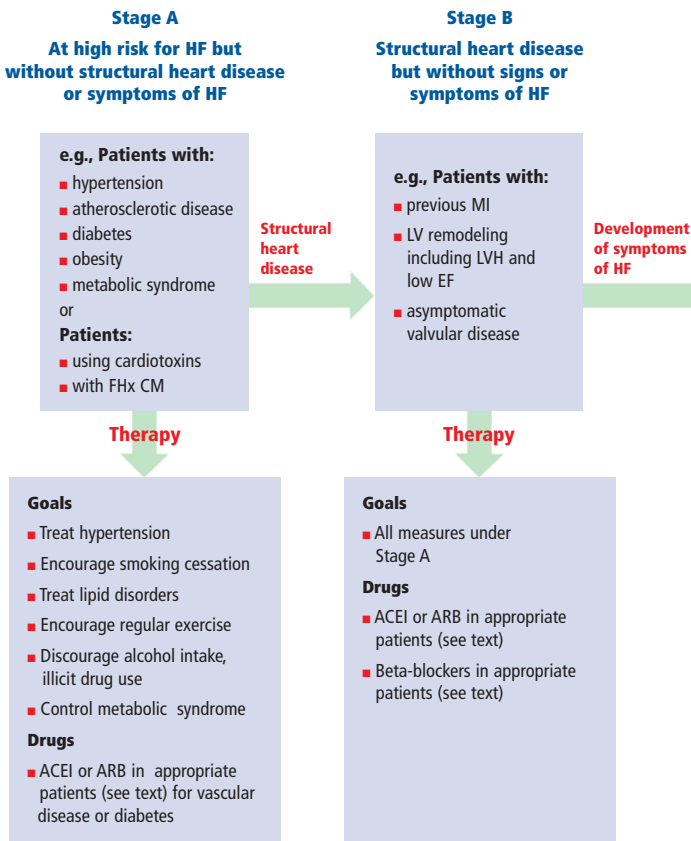
(class II), or only at levels of exertion that would limit normal individuals (class I). Although the functional class tends to deteriorate over periods of time, most patients with HF do not typically show an uninterrupted and inexorable worsening of symptoms. Instead, the severity of symptoms characteristically fluctuates even in the absence of changes in medications, and changes in medications and diet can have either favorable or adverse effects on functional capacity in the absence of measurable changes in ventricular function. Some patients may demonstrate remarkable recovery, sometimes associated with improvement in structural and functional abnormalities. Usually, sustained improvement is associated with drug therapy, and that therapy should be continued indefinitely.



**Figure 1. Stages in the development of heart failure/ recommended therapy by stage.**

**At Risk for Heart Failure**

Characterization



FHx CM = family history of cardiomyopathy; ACEI = angiotensin converting enzyme inhibitors; and ARB = angiotensin receptor blocker.

## Heart Failure

### Stage C Structural heart disease with prior or current symptoms of HF

#### e.g., Patients with:

- known structural heart disease and
- shortness of breath and fatigue, reduced exercise tolerance

Refractory  
symptoms  
of HF at rest

### Stage D Refractory HF requiring specialized interventions

#### e.g., Patients

who have marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

Therapy

#### Goals

- All measures under Stages A and B
- Dietary salt restriction

#### Drugs for Routine Use

- Diuretics for fluid retention
- ACEI
- Beta-blockers

#### Drugs in Selected Patients

- Aldosterone antagonist
- ARBs
- Digitalis
- Hydralazine/nitrates

#### Devices in Selected Patients

- Biventricular pacing
- Implantable defibrillators

Therapy

#### Goals

- Appropriate measures under Stages A, B, C
- Decision re: appropriate level of care

#### Options

- Compassionate end-of-life care/hospice
- Extraordinary measures
  - heart transplant
  - chronic inotropes
  - permanent mechanical support
  - experimental surgery or drugs

### C. Heart Failure as a Progressive Disorder

Left ventricular dysfunction begins with some injury to, or stress on, the myocardium and is generally a progressive process, even in the absence of a new identifiable insult to the heart. The principal manifestation of such progression is a change in the geometry and structure of the LV, such that the chamber dilates and/or hypertrophies and becomes more spherical—a process referred to as cardiac remodeling. Although several factors can accelerate the process of LV remodeling, there is substantial evidence that the activation of endogenous neurohormonal systems plays an important role in cardiac remodeling and thereby in the progression of HF. Patients with HF have elevated circulating or tissue levels of norepinephrine, angiotensin II, aldosterone, endothelin, vasopressin, and cytokines, which can act (alone or in concert) to adversely affect the structure and function of the heart. These neurohormonal factors not only increase the hemodynamic stresses on the ventricle by causing sodium retention and peripheral vasoconstriction but may also exert direct toxic effects on cardiac cells and stimulate myocardial fibrosis, which can further alter the architecture and impair the performance of the failing heart. Neurohormonal activation also has direct deleterious effects on the myocytes and interstitium, altering the performance and phenotype of these cells.



### III. Assessment of Patients

#### Recommendations for the Initial Clinical Assessment of Patients Presenting With HF

---

#### Class I

1. A thorough history and physical examination should be obtained/performed in patients presenting with HF to identify cardiac and noncardiac disorders or behaviors that might cause or accelerate the development or progression of HF. *(Level of Evidence: C)*
2. A careful history of current and past use of alcohol, illicit drugs, current or past standard or “alternative therapies,” and chemotherapy drugs should be obtained from patients presenting with HF. *(Level of Evidence: C)*
3. In patients presenting with HF, initial assessment should be made of the patient's ability to perform routine and desired activities of daily living. *(Level of Evidence: C)*
4. Initial examination of patients presenting with HF should include assessment of the patient's volume status, orthostatic blood pressure changes, measurement of weight and height, and calculation of body mass index. *(Level of Evidence: C)*
5. Initial laboratory evaluation of patients presenting with HF should include complete blood count, urinalysis, serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum

creatinine, fasting blood glucose (glycohemoglobin), lipid profile, liver function tests, and thyroid-stimulating hormone. *(Level of Evidence: C)*

6. Twelve-lead electrocardiogram and chest radiograph (PA and lateral) should be performed initially in all patients presenting with HF.

*(Level of Evidence: C)*

7. Two-dimensional echocardiography with Doppler should be performed during initial evaluation of patients presenting with HF to assess LVEF, LV size, wall thickness, and valve function. Radionuclide ventriculography can be performed to assess LVEF and volumes. *(Level of Evidence: C)*

8. Coronary arteriography should be performed in patients presenting with HF who have angina or significant ischemia unless the patient is not eligible for revascularization of any kind. *(Level of Evidence: B)*

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**Class IIa**

1. Coronary arteriography is reasonable for patients presenting with HF who have chest pain that may or may not be of cardiac origin who have not had evaluation of their coronary anatomy and who have no contraindications to coronary revascularization. *(Level of Evidence: C)*

2. Coronary arteriography is reasonable for patients presenting with HF who have known or suspected coronary artery disease but who do not have angina unless the patient is not eligible for revascularization of any kind. *(Level of Evidence: C)*

3. Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with HF who have known coronary artery disease and no angina unless the patient is not eligible for revascularization of any kind. *(Level of Evidence: B)*
4. Maximal exercise testing with or without measurement of respiratory gas exchange and/or blood oxygen saturation is reasonable in patients presenting with HF to help determine whether HF is the cause of exercise limitation when the contribution of HF is uncertain. *(Level of Evidence: C)*
5. Maximal exercise testing with measurement of respiratory gas exchange is reasonable to identify high-risk patients presenting with HF who are candidates for cardiac transplantation or other advanced treatments. *(Level of Evidence: B)*
6. Screening for hemochromatosis, sleep-disturbed breathing, or human immunodeficiency virus is reasonable in selected patients who present with HF. *(Level of Evidence: C)*
7. Diagnostic tests for rheumatologic diseases, amyloidosis, or pheochromocytoma are reasonable in patients presenting with HF in whom there is a clinical suspicion of these diseases. *(Level of Evidence: C)*
8. Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy. *(Level of Evidence: C)*

9. Measurement of B-type natriuretic peptide can be useful in the evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of HF is uncertain. *(Level of Evidence: A)*

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### **Class IIb**

1. Noninvasive imaging may be considered to define the likelihood of coronary artery disease in patients with HF and LV dysfunction. *(Level of Evidence: C)*

2. Maximal exercise testing with or without measurement of respiratory gas exchange may be considered to facilitate prescription of an appropriate exercise program for patients presenting with HF. *(Level of Evidence: C)*

3. Holter monitoring might be considered in patients presenting with HF who have a history of MI and are being considered for electrophysiologic study to document VT inducibility. *(Level of Evidence: C)*

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### **Class III**

1. Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF. *(Level of Evidence: C)*

2. Routine use of signal-averaged electrocardiography is not recommended for the evaluation of patients presenting with HF. *(Level of Evidence: C)*

3. Routine measurement of circulating levels of neurohormones (e.g., norepinephrine or endothelin) is not recommended for patients presenting with HF. *(Level of Evidence: C)*

## Recommendations for Serial Clinical Assessment of Patients Presenting With HF

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- Class I**
1. Assessment should be made at each visit of the ability of a patient with HF to perform routine and desired activities of daily living. *(Level of Evidence: C)*
  2. Assessment should be made at each visit of volume status and weight of a patient with HF. *(Level of Evidence: C)*
  3. Careful history of current use of alcohol, tobacco, illicit drugs, “alternative therapies,” and chemotherapy drugs, as well as diet and sodium intake, should be obtained at each visit of a patient with HF. *(Level of Evidence: C)*
- 

- Class IIa**
1. Repeat measurement of EF and the severity of structural remodeling can provide useful information in patients with HF who have had a change in clinical status or who have experienced or recovered from a clinical event or received treatment that might have had a significant effect on cardiac function. *(Level of Evidence: C)*
- 

- Class IIb**
1. The value of serial measurements of B-type natriuretic peptide to guide therapy for patients with HF is not well established. *(Level of Evidence: C)*

## A. Initial Evaluation of Patients

### 1. Identification of Patients

In general, patients with LV dysfunction or HF present to the physician in one of three ways: (1) With a syndrome of decreased exercise tolerance. Most patients with HF seek medical attention with complaints of a reduction in their effort tolerance due to dyspnea and/or fatigue. (2) With a syndrome of fluid retention. Patients may present with complaints of leg or abdominal swelling as their primary (or only) symptom. (3) With no symptoms or symptoms of another cardiac or noncardiac disorder. During their evaluation for a disorder other than HF (e.g., abnormal heart sounds or abnormal electrocardiogram or chest X-ray, hypertension or hypotension, diabetes mellitus, an acute MI, an arrhythmia, or a pulmonary or systemic thromboembolic event), patients may be found to have evidence of cardiac enlargement or dysfunction.

### 2. Identification of a Structural and Functional Abnormality

A complete history and physical examination are the first steps in evaluating the structural abnormality or cause responsible for the development of HF. The single most useful diagnostic test in the evaluation of patients with HF is the comprehensive 2-dimensional echocardiogram coupled with

Doppler flow studies to determine whether abnormalities of myocardium, heart valves, or pericardium are present and which chambers are involved. Three fundamental questions must be addressed: (1) is the LVEF preserved or reduced, (2) is the structure of the LV normal or abnormal, and (3) are there other structural abnormalities such as valvular, pericardial, or right ventricular abnormalities that could account for the clinical presentation? This information should be quantified with a numerical estimate of EF, measurement of ventricular dimensions and/or volumes, measurement of wall thickness, and evaluation of chamber geometry and regional wall motion.

Other tests may be used to provide information regarding the nature and severity of the cardiac abnormality. However, because of their low sensitivity and specificity, neither the chest radiograph nor the electrocardiogram should form the primary basis for determining the specific cardiac abnormality responsible for the development of HF.

### **3. Evaluation of Cause of HF**

Identification of the condition responsible for the cardiac structural and/or functional abnormalities may be important, because some conditions that lead to LV dysfunction are potentially treatable and/or reversible.

**Table 2. Evaluation of the Cause of Heart Failure: The History**

**History to include inquiry regarding:**

- Hypertension
- Diabetes
- Dyslipidemia
- Valvular heart disease
- Coronary or peripheral vascular disease
- Myopathy
- Rheumatic fever
- Mediastinal irradiation
- History or symptoms of sleep-disordered breathing
- Exposure to cardiotoxic agents
- Current and past alcohol consumption
- Smoking
- Collagen vascular disease
- Exposure to sexually transmitted diseases
- Thyroid disorder
- Pheochromocytoma
- Obesity

**Family history to include inquiry regarding:**

- Predisposition to atherosclerotic disease (Hx of MIs, strokes, PAD)
- Sudden cardiac death
- Myopathy
- Conduction system disease (need for pacemaker)
- Tachyarrhythmias
- Cardiomyopathy (unexplained HF)
- Skeletal myopathies

HF = heart failure; HX = history;

MI = myocardial infarction; and PAD = peripheral arterial disease.

#### 4. Laboratory Testing

Laboratory testing may reveal the presence of disorders or conditions that can lead to or exacerbate HF. The initial evaluation of patients with HF should include a complete blood count, urinalysis, serum electrolytes (including calcium and magnesium), glycohemoglobin, and blood lipids, as well as tests of both renal and hepatic function, a chest radiograph, and a 12-lead electrocardiogram. Thyroid-function tests (especially thyroid-stimulating hormone) should be measured, because both hyperthyroidism and hypothyroidism can be a primary or contributory cause of HF.

Several recent assays have been developed for B-type (formerly known as brain) natriuretic peptide and related peptides. Several of the natriuretic peptides are synthesized by and released from the heart. Elevated plasma B-type natriuretic peptide levels have been associated with reduced LVEF, LV hypertrophy, elevated LV filling pressures, and acute MI and ischemia, although they can occur in other settings, such as pulmonary embolism and chronic obstructive pulmonary disease. They are sensitive to other biological factors, such as age, sex, weight, and renal function. Elevated levels lend support to a diagnosis of abnormal ventricular function or hemodynamics causing symptomatic HF.

## **5. Evaluation of the Possibility of Coronary Artery Disease**

Coronary artery disease is believed to be the underlying cause in approximately two thirds of patients with HF and low EF and also contributes to the progression of HF through mechanisms that include endothelial dysfunction, ischemia, and infarction. Recent cohort studies suggest that there is less often a history of prior MI in patients with HF and preserved EF, although coronary artery disease is often evident on angiography or at autopsy.

### **B. Ongoing Evaluation of Patients**

Once the nature and cause of the structural abnormalities leading to the development of HF have been defined, healthcare providers should focus on the clinical assessment of patients, both during the initial presentation and during subsequent visits. This clinical assessment should identify symptoms and their functional consequences and should evaluate the short- and long-term risks of disease progression and death whenever appropriate. This ongoing review of the patient's clinical status is critical to the appropriate selection and monitoring of treatments.

During the initial and subsequent visits, healthcare providers should inquire about the type, severity, and duration of symptoms that occur during daily living and that may impair the patient's functional capacity. It is critically important for healthcare providers to evaluate the fluid or volume status of patients with HF during the initial visit and each follow-up examination. This assessment plays a pivotal role in determining the need for diuretic therapy and in detecting sodium excesses or deficiencies that may limit efficacy and decrease the tolerability of drugs used to treat HF.



#### **IV. Therapy**

*Table 3* describes cardiovascular medications useful for treatment of various stages of HF (see *Figure 1* for an explanation of the stages of HF).

**Table 3. Cardiovascular Medications Useful for Treatment of Various Stages\* of Heart Failure**

Drug	Stage A	Stage B	Stage C
<b>ACE Inhibitors</b>			
Benazepril	H	—	—
Captopril	H, DN	Post MI	HF
Enalapril	H, DN	HF	HF
Fosinopril	H	—	HF
Lisinopril	H, DN	Post MI	HF
Moexipril	H	—	—
Perindopril	H, CV Risk	—	—
Quinapril	H	—	HF
Ramipril	H, CV Risk	Post MI	Post MI
Trandolapril	H	Post MI	Post MI
<b>Angiotensin Receptor Blockers</b>			
Candesartan	H	—	HF
Eprosartan	H	—	—
Irbesartan	H, DN	—	—
Losartan	H, DN	CV Risk	—
Olmesartan	H	—	—
Telmisartan	H	—	—
Valsartan	H, DN	Post MI	Post MI, HF
<b>Aldosterone Blockers</b>			
Eplerenone	H	Post MI	Post MI
Spirolactone	H	—	HF
<b>Beta Blockers</b>			
Acebutolol	H	—	—
Atenolol	H	Post MI	—
Betaxolol	H	—	—
Bisoprolol	H	—	HF
Carteolol	H	—	—
Carvedilol	H	Post MI	HF, Post MI
Labetalol	H	—	—
Metoprolol succinate	H	—	HF
Metoprolol tartrate	H	Post MI	—
Nadolol	H	—	—
Penbutolol	H	—	—
Pindolol	H	—	—
Propranolol	H	Post MI	—
Timolol	H	Post MI	—
<b>Digoxin</b>	—	—	HF

\*See Figure 1 for explanation of stages of heart failure.

**CV Risk** = reduction in future cardiovascular events; **DN** = diabetic nephropathy; **H** = hypertension; **HF** = heart failure and asymptomatic left ventricular dysfunction; **Post MI** = reduction in heart failure or other cardiac events following myocardial infarction.

## A. Patients at High Risk for Developing HF (Stage A)

Many conditions or behaviors that are associated with an increased risk of structural heart disease can be identified before patients show any evidence of structural abnormalities. Because early modification of many of these factors can reduce the risk of HF, the recommendation of appropriate medical interventions to patients with these risk factors provides the earliest opportunity to reduce the impact of HF on public and individual health.

### Recommendations

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- Class I**
1. In patients at high risk for developing HF, systolic and diastolic hypertension should be controlled in accordance with contemporary guidelines. *(Level of Evidence: A)*
  2. In patients at high risk for developing HF, lipid disorders should be treated in accordance with contemporary guidelines. *(Level of Evidence: A)*
  3. For patients with diabetes mellitus (who are all at high risk for developing HF), blood sugar should be controlled in accordance with contemporary guidelines. *(Level of Evidence: C)*
  4. Patients at high risk for developing HF should be counseled to avoid behaviors that may increase the risk of HF (e.g., smoking, excessive alcohol consumption, and illicit drug use). *(Level of Evidence: C)*

5. Ventricular rate should be controlled or sinus rhythm restored in patients with supraventricular tachyarrhythmias who are at high risk for developing HF. *(Level of Evidence: B)*
  6. Thyroid disorders should be treated in accordance with contemporary guidelines in patients at high risk for developing HF. *(Level of Evidence: C)*
  7. Healthcare providers should perform periodic evaluation for signs and symptoms of HF in patients at high risk for developing HF. *(Level of Evidence: C)*
  8. In patients at high risk for developing HF who have known atherosclerotic vascular disease, healthcare providers should follow current guidelines for secondary prevention. *(Level of Evidence: C)*
  9. Healthcare providers should perform a noninvasive evaluation of LV function (i.e., LVEF) in patients with a strong family history of cardiomyopathy or in those receiving cardiotoxic interventions. *(Level of Evidence: C)*
- 

- Class IIa**
1. Angiotensin converting enzyme inhibitors or beta-blockers can be useful to prevent HF in patients at high risk for developing HF who have a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension with associated cardiovascular risk factors. *(Level of Evidence: A)*
  2. Angiotensin II receptor blockers can be useful to prevent HF in patients at high risk for developing HF who have a history of atherosclerotic vascular

disease, diabetes mellitus, or hypertension with associated cardiovascular risk factors. *(Level of Evidence: C)*

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- Class III** 1. Routine use of nutritional supplements solely to prevent the development of structural heart disease should not be recommended for patients at high risk for developing HF. *(Level of Evidence: C)*
- 

## **B. Patients With Cardiac Structural Abnormalities or Remodeling Who Have Not Developed HF Symptoms (Stage B)**

Patients without HF symptoms but who have had an MI or have evidence of LV remodeling are at considerable risk of developing HF. In such patients, the incidence of HF can be decreased by reducing the risk of additional injury and by retarding the evolution and progression of LV remodeling. Initial appropriate measures include those listed as Class I recommendations for patients in Stage A (also see Section V).

### **Recommendations**

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- Class I** 1. All Class I recommendations for Stage A should apply to patients with cardiac structural abnormalities who have not developed HF. *(Levels of Evidence: A, B, and C as appropriate)*
2. Beta-blockers and angiotensin converting enzyme inhibitors should be used in all patients with a recent or remote history of MI regardless of EF or presence of HF (see Table 3). *(Level of Evidence: A)*

3. Beta-blockers are indicated in all patients without a history of MI who have a reduced LVEF with no HF symptoms (see Table 3 and text). *(Level of Evidence: C)*
4. Angiotensin converting enzyme inhibitors should be used in patients with a reduced EF and no symptoms of HF, even if they have not experienced MI. *(Level of Evidence: A)*
5. An angiotensin II receptor blocker should be administered to post-MI patients without HF who are intolerant of angiotensin converting enzyme inhibitors and have a low LVEF. *(Level of Evidence: B)*
6. Patients who have not developed HF symptoms should be treated according to contemporary guidelines after an acute MI. *(Level of Evidence: C)*
7. Coronary revascularization should be recommended in appropriate patients without symptoms of HF in accordance with contemporary guidelines (see *ACC/AHA Guidelines for the Management of Patients With Chronic Stable Angina*). *(Level of Evidence: A)*
8. Valve replacement or repair should be recommended for patients with hemodynamically significant valvular stenosis or regurgitation and no symptoms of HF in accordance with contemporary guidelines. *(Level of Evidence: B)*

- 
- Class IIa**
1. Angiotensin converting enzyme inhibitors or angiotensin II receptor blockers can be beneficial in patients with hypertension and LV hypertrophy and no symptoms of HF. *(Level of Evidence B)*
  2. Angiotensin II receptor blockers can be beneficial in patients with low EF and no symptoms of HF who are intolerant of angiotensin converting enzyme inhibitors. *(Level of Evidence: C)*
  3. Placement of an ICD is reasonable in patients with ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF of 30% or less, are NYHA functional class I on chronic optimal medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year. *(Level of Evidence: B)*
- 

- Class IIb**
1. Placement of an implantable cardioverter-defibrillator might be considered in patients without HF who have nonischemic cardiomyopathy and an LVEF less than or equal to 30% who are in New York Heart Association functional class I with chronic optimal medical therapy and who have a reasonable expectation of survival with good functional status for more than one year. *(Level of Evidence: C)*
- 

- Class III**
1. Digoxin should not be used in patients with low EF, sinus rhythm, and no history of HF symptoms, because in this population, the risk of harm is not balanced by any known benefit. *(Level of Evidence: C)*

2. Use of nutritional supplements to treat structural heart disease or to prevent the development of symptoms of HF is not recommended. (*Level of Evidence: C*)

3. Calcium channel blockers with negative inotropic effects may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI (see text in Stage C). (*Level of Evidence: C*)

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## **C. Patients With Current or Prior Symptoms of HF (Stage C)**

### **1. Patients With Reduced LVEF**

Measures listed as Class I recommendations for patients in stages A or B are also appropriate for patients with current or prior symptoms of HF (also see Section V). In addition, moderate sodium restriction, along with daily measurement of weight, is indicated to permit effective use of lower and safer doses of diuretic drugs, even if overt sodium retention can be controlled by the use of diuretics. Immunization with influenza and pneumococcal vaccines may reduce the risk of a respiratory infection. Although most patients should not participate in heavy labor or exhaustive sports, physical activity should be encouraged (except during periods of acute exacerbation of the signs and symptoms of HF or in patients with suspected myocarditis), because restriction of activity promotes physical deconditioning, which may adversely affect clinical status and contribute to the exercise intolerance of patients with HF.

## Recommendations

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### Class I

1. Measures listed as Class I recommendations for patients in stages A and B are also appropriate for patients in Stage C. (*Levels of Evidence: A, B, and C as appropriate*)
2. Diuretics and salt restriction are indicated in patients with current or prior symptoms of HF and reduced LVEF who have evidence of fluid retention (see Table 4). (*Level of Evidence: C*)
3. Angiotensin converting enzyme inhibitors are recommended for all patients with current or prior symptoms of HF and reduced LVEF, unless contraindicated (see Table 3 and text). (*Level of Evidence: A*)
4. Beta-blockers (using one of the three proven to reduce mortality, ie. bisoprolol, carvedilol, and sustained release metoprolol succinate) are recommended for all stable patients with current or prior symptoms of HF and reduced LVEF, unless contraindicated (see Table 3 and text). (*Level of Evidence: A*)
5. Angiotensin II receptor blockers approved for the treatment of HF (see Table 3) are recommended in patients with current or prior symptoms of HF and reduced LVEF who are intolerant of angiotensin converting enzyme inhibitors (see text for information regarding patients with angioedema). (*Level of Evidence: A*)

6. Drugs known to adversely affect the clinical status of patients with current or prior symptoms of HF and reduced LVEF should be avoided or withdrawn whenever possible (e.g., nonsteroidal anti-inflammatory drugs, most antiarrhythmic drugs, and most calcium channel blocking drugs; see text). *(Level of Evidence: B)*

7. Exercise training is beneficial as an adjunctive approach to improve clinical status in ambulatory patients with current or prior symptoms of HF and reduced LVEF. *(Level of Evidence: B)*

8. An implantable cardioverter-defibrillator is recommended as secondary prevention to prolong survival in patients with current or prior symptoms of HF and reduced LVEF who have a history of cardiac arrest, ventricular fibrillation, or hemo-dynamically destabilizing ventricular tachycardia. *(Level of Evidence: A)*

9. Implantable cardioverter-defibrillator therapy is recommended for primary prevention to reduce total mortality by a reduction in sudden cardiac death in patients with ischemic heart disease who are at least 40 days post-MI, have an LVEF less than or equal to 30%, with New York Heart Association functional class II or III symptoms, while undergoing chronic optimal medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year. *(Level of Evidence: A)*

10. Implantable cardioverter-defibrillator therapy is recommended for primary prevention to reduce total mortality by a reduction in sudden cardiac death in

patients with nonischemic cardiomyopathy who have an LVEF less than or equal to 30%, with New York Heart Association functional class II or III symptoms while undergoing chronic optimal medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year. (*Level of Evidence: B*)

11. Patients with LVEFs less than or equal to 35%, sinus rhythm, and New York Heart Association functional class III or ambulatory class IV symptoms despite recommended, optimal medical therapy and who have cardiac dyssynchrony, which is currently defined as a QRS duration greater than 0.12 ms, should receive cardiac resynchronization therapy unless contraindicated. (*Level of Evidence: A*)

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**Class IIa**

1. Angiotensin II receptor blockers are reasonable to use as alternatives to angiotensin converting enzyme inhibitors as first-line therapy for patients with mild to moderate HF and reduced LVEF, especially for patients already taking angiotensin II receptor blockers for other indications. (*Level of Evidence: A*)

2. Digitalis can be beneficial in patients with current or prior symptoms of HF and reduced LVEF to decrease hospitalizations for HF. (*Level of Evidence: B*)

3. The addition of a combination of hydralazine and a nitrate is reasonable for patients with reduced LVEF who are already taking an

angiotensin converting enzyme inhibitor and beta-blocker for symptomatic HF and who have persistent symptoms. *(Level of Evidence: A)*

4. Addition of an aldosterone antagonist is reasonable in selected patients with moderately severe to severe symptoms of HF and reduced LVEF who can be carefully monitored for preserved renal function and normal potassium concentration. Creatinine should be less than or equal to 2.5 mg/dL in men or less than or equal to 2.0 mg/dL in women and potassium should be less than 5.0 mEq/l.

*(Level of Evidence: B)*

5. Placement of an implantable cardioverter-defibrillator is reasonable in patients with LVEF of 30% to 35% of any origin with New York Heart Association functional class II or III symptoms who are taking chronic optimal medical therapy and who have reasonable expectation of survival with good functional status of more than 1 year.

*(Level of Evidence: B)*

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**Class IIb** 1. A combination of hydralazine and a nitrate might be reasonable in patients with current or prior symptoms of HF and reduced LVEF who cannot be given an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker because of drug intolerance, hypotension, or renal insufficiency.

*(Level of Evidence: C)*

2. The addition of an angiotensin II receptor blocker may be considered in persistently symptomatic patients with reduced LVEF who are already being treated with conventional therapy.

*(Level of Evidence: B)*

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### **Class III**

1. Routine combined use of an angiotensin converting enzyme inhibitor, an angiotensin II receptor blocker, and an aldosterone antagonist is not recommended for patients with current or prior symptoms of HF and reduced LVEF. *(Level of Evidence: C)*

2. Calcium channel blocking drugs are not indicated as routine treatment for HF in patients with current or prior symptoms of HF and reduced LVEF.

*(Level of Evidence: A)*

3. Long-term use of an infusion of a positive inotropic drug may be harmful and is not recommended for patients with current or prior symptoms of HF and reduced LVEF, except as palliation for patients with end-stage disease who cannot be stabilized with standard medical treatment (see recommendations for Stage D). *(Level of Evidence: C)*

4. Use of nutritional supplements as treatment for HF is not indicated in patients with current or prior symptoms of HF and reduced LVEF. *(Level of Evidence: C)*

5. Hormonal therapies other than to replete deficiencies are not recommended and may be harmful to patients with current or prior symptoms of HF and reduced LVEF. *(Level of Evidence: C)*

**Table 4. Oral Diuretics Recommended for Use in the Treatment of Chronic Heart Failure**

<b>Drug</b>	<b>Initial Daily Dose(s)</b>	<b>Maximum Total Daily Dose</b>	<b>Duration of Action</b>
<b>Loop diuretics</b>			
Bumetanide	0.5 to 1.0 mg once or twice	10 mg	4 to 6 hours
Furosemide	20 to 40 mg once or twice	600 mg	6 to 8 hours
Torsemide	10 to 20 mg once	200 mg	12 to 16 hours
<b>Thiazide diuretics</b>			
Chlorothiazide	250 to 500 mg once or twice	1000 mg	6 to 12 hours
Chlorthalidone	12.5 to 25 mg once	100 mg	24 to 72 hours
Hydrochlorothiazide	25 mg once or twice	200 mg	6 to 12 hours
Indapamide	2.5 once	5 mg	36 hours
Metolazone	2.5 mg once	20 mg	12 to 24 hours
<b>Potassium-sparing diuretics</b>			
Amiloride	5 mg once	20 mg	24 hours
Spironolactone	12.5 to 25 mg once	50 mg*	2 to 3 days
Triamterene	50 to 75 mg twice	200 mg	7 to 9 hours
<b>Sequential nephron blockade</b>			
Metolazone	2.5 to 10 mg once plus loop diuretic	—	—
Hydrochlorothiazide	25 to 100 mg once or twice plus loop diuretic	—	—
Chlorothiazide (IV)	500 to 1000 mg once plus loop diuretic	—	—

mg = milligrams; IV = intravenous.

\*Higher doses may occasionally be used with close monitoring.

**Table 5. Intravenous Diuretic Medications Useful for the Treatment of Severe Heart Failure**

<b>Drug</b>	<b>Initial Dose</b>	<b>Maximum Single Dose</b>
<b>Loop diuretics</b>		
Bumetanide	1.0 mg	4 to 8 mg
Furosemide	40 mg	160 to 200 mg
Torsemide	10 mg	100 to 200 mg
<b>Thiazide diuretics</b>		
Chlorothiazide	500 mg	1000 mg
<b>Sequential nephron blockade</b>	Chlorothiazide 500 to 1000 mg IV once or twice plus loop diuretics once; multiple doses per day Metolazone (as Zaroxolyn or Diulo) 2.5 to 5 mg PO once or twice daily with loop diuretic	
<b>Intravenous infusions</b>		
Bumetanide	1-mg IV load, then 0.5 to 2 mg per hour infusion	
Furosemide	40-mg IV load, then 10 to 40 mg per hour infusion	
Torsemide	20-mg IV load, then 5 to 20 mg per hour infusion	

IV = intravenous; mg = milligrams; and PO = by mouth.

**Table 6. Inhibitors of the Renin-Angiotensin-Aldosterone System and Beta-Blockers Commonly Used for the Treatment of Patients With Heart Failure With Low Ejection Fraction**

<b>Drug</b>	<b>Initial Daily Dose(s)</b>	<b>Maximum Doses(s)</b>
<b>ACE inhibitors</b>		
Captopril	6.25 mg 3 times	50 mg 3 times
Enalapril	2.5 mg twice	10 to 20 mg twice
Fosinopril	5 to 10 mg once	40 mg once
Lisinopril	2.5 to 5 mg once	20 to 40 mg once
Perindopril	2 mg once	8 to 16 mg once
Quinapril	5 mg twice	20 mg twice
Ramipril	1.25 to 2.5 mg once	10 mg once
Trandolapril	1 mg once	4 mg once
<b>Angiotensin receptor blockers</b>		
Candesartan	4 to 8 mg once	32 mg once
Losartan	25 to 50 mg once	50 to 100 mg once
Valsartan	20 to 40 mg twice	160 mg twice
<b>Aldosterone antagonists</b>		
Spironolactone	12.5 to 25 mg once	25 mg once or twice
Eplerenone	25 mg once	50 mg once
<b>Beta-blockers</b>		
Bisoprolol	1.25 mg once	10 mg once
Carvedilol	3.125 mg twice	25 mg twice 50 mg twice for patients > 85 kg
Metoprolol succinate extended release (metoprolol CR/XL)	12.5 to 25 mg once	200 mg once

ACE = angiotensin converting enzyme; mg = milligrams; and kg = kilograms.

## **Table 7. Guidelines for Minimizing the Risk of Hyperkalemia in Patients Treated With Aldosterone Antagonists**

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1. Impaired renal function is a risk factor for hyperkalemia during treatment with aldosterone antagonists. The risk of hyperkalemia increases progressively when serum creatinine exceeds 1.6 mg per dl.\* In elderly patients or others with low muscle mass in whom serum creatinine does not accurately reflect glomerular filtration rate, determination that glomerular filtration rate or creatinine clearance exceeds 30 ml per min is recommended.
2. Aldosterone antagonists should not be administered to patients with baseline serum potassium in excess of 5.0 mEq per liter.
3. An initial dose of spironolactone 12.5 mg or eplerenone 25 mg is recommended, after which the dose may be increased to spironolactone 25 mg or eplerenone 50 mg if appropriate.
4. The risk of hyperkalemia is increased with concomitant use of higher doses of ACE inhibitors (captopril greater than or equal to 75 mg daily; enalapril or lisinopril greater than or equal to 10 mg daily).
5. Non-steroidal anti-inflammatory drugs and cyclo-oxygenase-2 inhibitors should be avoided.
6. Potassium supplements should be discontinued or reduced.
7. Close monitoring of serum potassium is required; potassium levels and renal function should be checked in 3 days and at 1 week after initiation of therapy and at least monthly for the first 3 months.
8. Diarrhea or other causes of dehydration should be addressed emergently.

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ACE = angiotensin converting enzyme.

\*Although the entry criteria for the trials of aldosterone antagonists included creatinine greater than 2.5 mg per dl, the majority of patients had creatinine much lower; in 1 trial, 95% of patients had creatinine less than or equal to 1.7 mg per dl.

## **Ventricular Arrhythmias and Prevention of Sudden Death**

Patients with LV dilation and reduced EF frequently manifest ventricular tachyarrhythmias, both non-sustained ventricular tachycardia and sustained ventricular tachycardia. The cardiac mortality of patients with all types of ventricular tachyarrhythmias is high. The high mortality results from non-sudden (e.g., progressive) HF, as well as sudden death. Sudden death is often equated with a primary arrhythmic event, but multiple causes of sudden death have been documented and include ischemic events such as acute MI, electrolyte disturbances, pulmonary or systemic emboli, or other vascular events. Although ventricular tachyarrhythmias are the most common rhythms associated with unexpected sudden death, bradycardia and other pulseless supraventricular rhythms are common in patients with advanced HF.

## **Cardiac Resynchronization Therapy**

Approximately one third of patients with low EF and class III to IV symptoms of HF manifest a QRS duration greater than 120 ms. This electrocardiographic representation of abnormal cardiac conduction has been used to identify patients with ventricular dyssynchrony. The mechanical consequences of dyssynchrony include suboptimal ventricular filling,

a reduction in LV  $dP/dt$  (rate of rise of ventricular contractile force or pressure), prolonged duration (and therefore greater severity) of mitral regurgitation, and paradoxical septal wall motion. Ventricular dyssynchrony has also been associated with increased mortality in HF patients. Such dyssynchronous contraction can be addressed by electrically activating the right ventricle and LV in a synchronized manner with a biventricular pacemaker device. This approach to HF therapy, commonly called cardiac resynchronization therapy (CRT), may enhance ventricular contraction and reduce the degree of secondary mitral regurgitation. In addition, the short-term use of CRT has been associated with improvements in cardiac function and hemodynamics without an accompanying increase in oxygen utilization, as well as adaptive changes in the biochemistry of the failing heart.

Cardiac resynchronization therapy, when added to optimal medical therapy in persistently symptomatic patients, has resulted in significant improvements in quality of life, functional class, exercise capacity (by peak oxygen uptake) and exercise distance during a 6-minute walk test, and EF in patients randomized to CRT or to the combination of CRT and an implantable cardioverter-defibrillator. There is strong evidence to support the use of CRT to improve symptoms, exercise capacity, quality of life, LVEF, and survival and to decrease hospitalizations in patients with persistently symptomatic HF undergoing optimal medical therapy who have cardiac dyssynchrony (as evidenced by a prolonged QRS duration); the use of an implantable cardioverter-

defibrillator in combination with CRT should be based on the indications for implantable cardioverter-defibrillator therapy.

## **Exercise Training**

Several controlled trials have shown that exercise training can lessen symptoms, increase exercise capacity, and improve the quality of life of patients with chronic HF. The improvement was comparable to that achieved with pharmacological interventions and was in addition to the benefits of angiotensin converting enzyme inhibitors and beta-blockers.

## **2. Patients With HF and Normal LVEF**

In the absence of other controlled clinical trials, the management of these patients is based on the control of physiological factors (blood pressure, heart rate, blood volume, and myocardial ischemia) that are known to exert important effects on ventricular relaxation. Recommendations regarding the use of anticoagulation and antiarrhythmic agents apply to all patients with HF, irrespective of LVEF.

### **Recommendations**

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- Class I** 1. Physicians should control systolic and diastolic hypertension in patients with HF and normal LVEF, in accordance with published guidelines.  
*(Level of Evidence: A)*

2. Physicians should control ventricular rate in patients with HF and normal LVEF and atrial fibrillation. *(Level of Evidence: C)*

3. Physicians should use diuretics to control pulmonary congestion and peripheral edema in patients with HF and normal LVEF. *(Level of Evidence: C)*

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**Class IIa** 1. Coronary revascularization is reasonable in patients with HF and normal LVEF and coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to be having an adverse effect on cardiac function. *(Level of Evidence: C)*

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**Class IIb** 1. Restoration and maintenance of sinus rhythm in patients with atrial fibrillation and HF and normal LVEF might be useful to improve symptoms. *(Level of Evidence: C)*

2. The use of beta-adrenergic blocking agents, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, or calcium antagonists in patients with HF and normal LVEF and controlled hypertension might be effective to minimize symptoms of HF. *(Level of Evidence: C)*

3. The usefulness of digitalis to minimize symptoms of HF in patients with HF and normal LVEF is not well established. *(Level of Evidence: C)*

**Table 8. Recommendations for Treatment of Patients With Heart Failure and Normal Left Ventricular Ejection Fraction**

<b>Recommendation</b>	<b>Class</b>	<b>Level of Evidence</b>
Physicians should control systolic and diastolic hypertension, in accordance with published guidelines.	I	A
Physicians should control ventricular rate in patients with atrial fibrillation.	I	C
Physicians should use diuretics to control pulmonary congestion and peripheral edema.	I	C
Coronary revascularization is reasonable in patients with coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to be having an adverse effect on cardiac function.	IIa	C
Restoration and maintenance of sinus rhythm in patients with atrial fibrillation might be useful to improve symptoms.	IIb	C
The use of beta-adrenergic blocking agents, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, or calcium antagonists in patients with controlled hypertension might be effective to minimize symptoms of heart failure.	IIb	C
The use of digitalis to minimize symptoms of heart failure is not well established.	IIb	C

### **Table 9. Differential Diagnosis in a Patient With Heart Failure and Normal Left Ventricular Ejection Fraction**

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- Incorrect diagnosis of HF
  - Inaccurate measurement of LVEF
  - Primary valvular disease
  - Restrictive (infiltrative) cardiomyopathies  
Amyloidosis, sarcoidosis, hemochromatosis
  - Pericardial constriction
  - Episodic or reversible LV systolic dysfunction
  - Severe hypertension, myocardial ischemia
  - HF associated with high metabolic demand (high-output states)  
Anemia, thyrotoxicosis, arteriovenous fistulae
  - Chronic pulmonary disease with right HF
  - Pulmonary hypertension associated with pulmonary vascular disorders
  - Atrial myxoma
  - Diastolic dysfunction of uncertain origin
  - Obesity
- 

HF = heart failure; LV = left ventricular; and LVEF = left ventricular ejection fraction.

## D. Patients With Refractory End-Stage HF (Stage D)

Before a patient is considered to have refractory HF, physicians should confirm the accuracy of the diagnosis, identify any contributing conditions, and ensure that all conventional medical strategies have been optimally employed. Measures listed as Class I recommendations for patients in stages A, B, and C are also appropriate for patients in end-stage HF (also see Section V). When no further therapies are appropriate, careful discussion of the prognosis and options for end-of-life care should be initiated (see Section VI).

### Recommendations

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- Class I**
1. Meticulous identification and control of fluid retention is recommended in patients with refractory end-stage HF. (*Level of Evidence: B*)
  2. Referral for cardiac transplantation in potentially eligible patients is recommended for patients with refractory end-stage HF. (*Level of Evidence: B*)
  3. Referral of patients with refractory end-stage HF to an HF program with expertise in the management of refractory HF is useful. (*Level of Evidence: A*)
  4. Options for end-of-life care should be discussed with the patient and family when severe symptoms in patients with refractory end-stage HF persist despite application of all recommended therapies. (*Level of Evidence: C*)

5. Patients with refractory end-stage HF and implantable defibrillators should receive information about the option to inactivate defibrillation.

*(Level of Evidence: C)*

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**Class IIa** 1. Consideration of an LV assist device as permanent or “destination” therapy is reasonable in highly selected patients with refractory end-stage HF and an estimated 1-year mortality over 50% with medical therapy. *(Level of Evidence: B)*

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**Class IIb** 1. Pulmonary artery catheter placement may be reasonable to guide therapy in patients with refractory end-stage HF and persistently severe symptoms. *(Level of Evidence: C)*

2. The effectiveness of mitral valve repair or replacement is not established for severe secondary mitral regurgitation in refractory HF. *(Level of Evidence: C)*

3. Continuous intravenous infusion of a positive inotropic agent may be considered for palliation of symptoms in patients with refractory end-stage HF. *(Level of Evidence: C)*

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**Class III** 1. Partial left ventriculectomy is not recommended in patients with nonischemic cardiomyopathy and refractory end-stage HF. *(Level of Evidence: C)*

2. Routine intermittent infusions of positive inotropic agents are not recommended for patients with refractory end-stage HF. *(Level of Evidence: B)*

**Table 10. Indications for Cardiac Transplantation**

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**Absolute indications in appropriate patients**

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For hemodynamic compromise due to HF

- Refractory cardiogenic shock
- Documented dependence on IV inotropic support to maintain adequate organ perfusion
- Peak  $\text{VO}_2$  less than 10 ml per kg per min with achievement of anaerobic metabolism

Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention

Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities

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**Relative indications**

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Peak  $\text{VO}_2$  11 to 14 ml per kg per min (or 55% of predicted) and major limitation of the patient's daily activities

Recurrent unstable ischemia not amenable to other intervention

Recurrent instability of fluid balance/renal function not due to patient noncompliance with medical regimen

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**Insufficient indications**

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Low left ventricular ejection fraction

History of functional class III or IV symptoms of HF

Peak  $\text{VO}_2$  greater than 15 ml per kg per min (and greater than 55% of predicted) without other indications

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HF = heart failure; IV = intravenous; and  $\text{VO}_2$  = oxygen consumption per unit time.



## V. Treatment of Special Populations and Concomitant Disorders

Many patients with HF are members of subpopulations who are likely to exhibit unique responses that accelerate the development or progression of HF or complicate the management of HF.

### Recommendations

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#### Class I

1. Groups of patients including (a) high-risk ethnic minority groups (e.g., blacks), (b) groups underrepresented in clinical trials, and (c) any groups believed to be underserved should, in the absence of specific evidence to direct otherwise, have clinical screening and therapy in a manner identical to that applied to the broader population. (*Level of Evidence: B*)
  2. It is recommended that evidence-based therapy for HF be used in the elderly patient with individualized consideration of the elderly patient's altered ability to metabolize or tolerate standard medications. (*Level of Evidence: C*)
- 

#### Class IIa

1. The addition of isosorbide dinitrate and hydralazine to a standard medical regimen for HF, including angiotensin converting enzyme inhibitors and beta-blockers, is reasonable and can be effective in blacks with New York Heart

Association functional class III or IV HF. Others may benefit similarly, but this has not yet been tested.

*(Level of Evidence: A)*

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## **A. Women and Men**

Many physicians regard HF primarily as a disease of men, because coronary risk factors are common in men and primarily men are enrolled in clinical trials of treatments for HF; however, the majority of patients with HF in the general population are women (particularly elderly women), who frequently have HF associated with a normal LVEF. Even HF due to reduced LVEF may be different in women than in men. The conflicting data regarding the efficacy of digoxin in women suggests that if it is prescribed, particular attention should be paid to dosing and renal function.

## **B. Ethnic Considerations**

Race is an imprecise concept that has largely become a social and political construct, with more limited biological significance. The concept of racial “minorities” may be relevant to large populations, especially those in clinical trials, but is clearly not a concept applicable in many demographic areas and clinical practices. However, it is useful to review epidemiological and clinical trial evidence to raise awareness of potential areas of concern and guide socioeconomic and clinical remedies. This has become especially pertinent in the evaluation of HF as it affects blacks. Heart failure is a major public health problem in blacks. Heart failure is more common in the

black population, affecting approximately 3% of all black adults. This reflects a 50% higher incidence of HF in the black population than is seen in the general population.

## C. Patients With HF Who Have Concomitant Disorders

### Recommendations

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#### Class I

1. All other recommendations should apply to patients with concomitant disorders unless there are specific exceptions. *(Level of Evidence C)*
2. Physicians should control systolic and diastolic hypertension and diabetes mellitus in patients with HF in accordance with recommended guidelines. *(Level of Evidence: C)*
3. Physicians should use nitrates and beta-blockers for the treatment of angina in patients with HF. *(Level of Evidence: B)*
4. Physicians should recommend coronary revascularization according to recommended guidelines in patients who have both HF and angina. *(Level of Evidence: A)*
5. Physicians should prescribe anticoagulants in patients with HF who have paroxysmal or persistent atrial fibrillation or a previous thromboembolic event. *(Level of Evidence: A)*
6. Physicians should control the ventricular response rate in patients with HF and atrial fibrillation with a

beta-blocker (or amiodarone, if the beta-blocker is contraindicated or not tolerated).

*(Level of Evidence: A)*

7. Patients with coronary artery disease and HF should be treated in accordance with recommended guidelines for coronary artery disease.

*(Level of Evidence: C)*

8. Physicians should prescribe antiplatelet agents for prevention of MI and death in patients with HF who have underlying coronary artery disease.

*(Level of Evidence: B)*

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**Class IIa** 1. It is reasonable to prescribe digitalis to control the ventricular response in patients with HF and atrial fibrillation. *(Level of Evidence: A)*

2. It is reasonable to prescribe amiodarone to decrease recurrence of atrial arrhythmias and to decrease recurrence of implantable cardioverter-defibrillator discharge for ventricular arrhythmias.

*(Level of Evidence: C )*

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**Class IIb** 1. The usefulness of current strategies to restore and maintain sinus rhythm in patients with HF and atrial fibrillation is not well established.

*(Level of Evidence: C)*

2. The usefulness of anticoagulation is not well established in patients with HF who do not have atrial fibrillation or a previous thromboembolic event. *(Level of Evidence: B)*

3. The benefit of enhancing erythropoiesis in patients with HF and anemia is not established.

*(Level of Evidence C)*

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- Class III**
1. Class I or III antiarrhythmic drugs are not recommended in patients with HF for the prevention of ventricular arrhythmias. *(Level of Evidence: A)*
  2. The use of antiarrhythmic medication is not indicated as primary treatment for asymptomatic ventricular arrhythmias or to improve survival in patients with HF. *(Level of Evidence: A)*
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## VI. End-of-Life Considerations

### Recommendations

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- Class I**
1. Ongoing patient and family education regarding prognosis for functional capacity and survival is recommended for patients with HF at the end of life. *(Level of Evidence: C)*
  2. Patient and family education about options for formulating and implementing advance directives and the role of palliative and hospice care services with re-evaluation for changing clinical status is recommended for patients with HF at the end of life. *(Level of Evidence: C)*

3. Discussion is recommended regarding the option of inactivating an implanted cardioverter-defibrillator for patients with HF at the end of life.

*(Level of Evidence: C)*

4. It is important to ensure continuity of medical care between inpatient and outpatient settings for patients with HF at the end of life. *(Level of*

*Evidence: C)*

5. Components of hospice care that are appropriate to the relief of suffering, including opiates, are recommended and do not preclude the options

for use of inotropes and intravenous diuretics for symptom palliation for patients with HF at the end of life. *(Level of Evidence: C)*

6. All professionals working with HF patients should examine current end-of-life processes

and work toward improvement in approaches to palliation and end-of-life care. *(Level of Evidence: C)*

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**Class III**

1. Aggressive procedures performed within the final days of life (including intubation and implantation of a cardioverter-defibrillator in patients with New York Heart Association functional class IV symptoms who are not anticipated to experience clinical improvement from available treatments) are not appropriate. *(Level of Evidence: C)*

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## VII. Implementation of Practice Guidelines

### Recommendations

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- Class I**
1. Academic detailing or educational outreach visits are useful to facilitate the implementation of practice guidelines. *(Level of Evidence: A)*
  2. Multidisciplinary disease-management programs for patients at high risk for hospital admission or clinical deterioration are recommended to facilitate the implementation of practice guidelines. *(Level of Evidence: B)*
  3. Multifactorial interventions to facilitate the implementation of practice guidelines that attack different barriers to behavioral change should be used. *(Level of Evidence: A)*
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- Class IIa**
1. Chart audit and feedback of results can be effective to facilitate implementation of practice guidelines. *(Level of Evidence: A)*
  2. The use of reminder systems can be effective to facilitate implementation of practice guidelines. *(Level of Evidence: A)*
  3. The use of performance measures based on practice guidelines may be useful to improve quality of care. *(Level of Evidence: B)*

4. Statements by and support of local opinion leaders can be helpful to facilitate implementation of practice guidelines. *(Level of Evidence: A)*

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**Class IIb** 1. Multidisciplinary disease-management programs for patients at low risk for hospital admission or clinical deterioration may be considered to facilitate implementation of practice guidelines. *(Level of Evidence: B)*

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**Class III** 1. Dissemination of guidelines without more intensive behavioral change efforts is not useful to facilitate implementation of practice guidelines. *(Level of Evidence: A)*

2. Basic provider education alone is not useful to facilitate implementation of practice guidelines. *(Level of Evidence: A)*

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