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ACC/AHA PRACTICE GUIDELINES

ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure)

Developed in Collaboration with the International Society for Heart and Lung Transplantation

Endorsed by the Heart Failure Society of America

COMMITTEE MEMBERS

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RICHARD O. RUSSELL, MD, FACC*
SIDNEY C. SMITH, JR, MD, FACC

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This document, as well as the corresponding full-text guidelines, is available on the World Wide Web sites of the American College of Cardiology (www.acc.org) and the American Heart Association (www.americanheart.org). Single reprints of the executive summary are available for $5.00 each by calling 800-253-4636 (US only) or writing the American College of Cardiology, Educational Services, 9111 Old Georgetown Road, Bethesda, MD 20814-1699. To purchase additional reprints up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1466, fax 214-691-6342, or e-mail pubauth@heart.org (specify version: Executive Summary—71-0215; Full Text—71-0216).

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*Former Task Force member during this writing effort.

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I. INTRODUCTION

Heart failure (HF) is a major public health problem in the United States. Nearly 5 million patients in this country have HF, and nearly 500,000 patients are diagnosed with HF for the first time each year. The disorder is the underlying reason for 12 to 15 million office visits and 6.5 million hospital days each year (1). During the last 10 years, the annual number of hospitalizations has increased from approximately 550,000 to nearly 900,000 for HF as a primary diagnosis and from 1.7 to 2.6 million for HF as a primary or secondary diagnosis (2). Nearly 300,000 patients die of HF as a primary or contributory cause each year, and the number of deaths has increased steadily despite advances in treatment.

HF is primarily a disease of the elderly (3). Approximately 6% to 10% of people older than 65 years have HF (4), and approximately 80% of patients hospitalized with HF are more than 65 years old (2). HF is the most common Medicare diagnosis-related group, and more Medicare dollars are spent for the diagnosis and treatment of HF than for any other diagnosis (5). The total inpatient and outpatient costs for HF in 1991 were approximately $38.1 billion, which was approximately 5.4% of the healthcare budget that year (1). In the United States, approximately $500 million 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 (6). 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 generally fatal disorder. For this reason, the 2 organizations believed that the time was right to reassess and update these guidelines, fully recognizing that the optimal therapy of HF remains a work in progress and that future guidelines will supersede these.

The writing committee was composed of 7 members who represented the ACC and AHA, as well as invited participants from the American College of Chest Physicians, the Heart Failure Society of America, the International Society for Heart and Lung Transplantation, the American Academy of Family Physicians, and the American College of Physicians–American Society of Internal Medicine. Both the academic and private practice sectors were represented. This document was reviewed by 3 official reviewers nominated by the ACC, 3 official reviewers nominated by the AHA, 1 reviewer nominated by the Heart Failure Society of America, 1 reviewer nominated by the International Society for Heart and Lung Transplantation, 1 reviewer nominated by the American Academy of Family Physicians, 1 reviewer nominated by the National Heart Foundation of Australia, the ACC Hypertensive Disease Committee and 16 content reviewers.

In formulating the present document, the writing committee decided to take a new approach to the classification of HF that emphasized both the evolution and progression of the disease. In doing so, we identified 4 stages of HF. **Stage A** identifies the patient who is at high risk for developing HF but has no structural disorder of the heart; **Stage B** refers to a patient with a structural disorder of the heart but who has never developed symptoms of HF; **Stage C** denotes the patient with past or current symptoms of HF associated with underlying structural heart disease; and **Stage D** designates the patient with end-stage disease who requires specialized treatment strategies such as mechanical circulatory support, continuous inotropic infusions, cardiac transplantation, or hospice care (see Table 1 and Fig. 1). Only the latter 2 stages, of course, qualify for the traditional clinical diagnosis of HF for diagnostic or coding purposes. This classification recognizes that there are established risk factors and structural prerequisites for the development of HF and that therapeutic interventions performed even before the appearance of left ventricular dysfunction or symptoms can reduce the morbidity and mortality of HF. This classification system is intended to complement but not to replace the New York Heart Association (NYHA) functional classification, which primarily gauges the severity of symptoms in patients who are in stage C or D. It has been recognized for many years, however, that the NYHA functional classification reflects a subjective assessment by a physician and changes frequently over short periods of time and that the treatments used do not differ significantly across the classes. Therefore, the committee believed that a staging system was needed that would reliably and objectively identify patients in the course of their disease and would be linked to treatments that were uniquely appropriate at each stage of their illness. According to this new approach, patients would be expected to advance from one stage to the next unless progression of the disease was slowed or stopped by treatment. This new classification scheme adds a useful dimension to our thinking about HF similar to that achieved by staging systems for other disorders (e.g., those used in the classification of cancer).

Table 1. Stages of HF

Stage	Description	Examples
A	Patients at high risk of developing HF because of the presence of conditions that are strongly associated with the development of HF. Such patients have no identified structural or functional abnormalities of the pericardium, myocardium, or cardiac valves and have never shown signs or symptoms of HF.	Systemic hypertension; coronary artery disease; diabetes mellitus; history of cardiotoxic drug therapy or alcohol abuse; personal history of rheumatic fever; family history of cardiomyopathy.
B	Patients who have developed structural heart disease that is strongly associated with the development of HF but who have never shown signs or symptoms of HF.	Left ventricular hypertrophy or fibrosis; left ventricular dilatation or hypocontractility; asymptomatic valvular heart disease; previous myocardial infarction.
C	Patients who have current or prior symptoms of HF associated with underlying structural heart disease.	Dyspnea or fatigue due to left ventricular systolic dysfunction; asymptomatic patients who are undergoing treatment for prior symptoms of HF.
D	Patients with advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy and who require specialized interventions.	Patients who are frequently hospitalized for HF or cannot be safely discharged from the hospital; patients in the hospital awaiting heart transplantation; patients at home receiving continuous intravenous support for symptom relief or being supported with a mechanical circulatory assist device; patients in a hospice setting for the management of HF.

HF indicates heart failure.

All recommendations provided in this document follow the format of previous ACC/AHA guidelines:

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

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

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

The recommendations listed in this document are evidence based whenever possible. Pertinent medical literature in the English language was identified through a series of computerized literature searches (including Medline and EMBASE) and a manual search of selected articles. References selected and published in this document are representative but not all-inclusive.

The levels of evidence on which these recommendations are based were ranked as level A if the data were derived from multiple randomized clinical trials, level B when data were derived from a single randomized trial or nonrandomized studies, and level C when the consensus opinion of experts was the primary source of recommendation. The strength of evidence does not necessarily reflect the strength of a recommendation. A treatment may be considered controversial although it has been evaluated in controlled clinical trials; conversely, a strong recommendation may be based on years of clinical experience and be supported only by historical data or by no data at all.

The committee elected to focus this document on the prevention of HF, as well as the evaluation and management of chronic HF in the adult patient with left ventricular systolic and diastolic dysfunction. It specifically did not consider acute HF, which might merit a separate set of guidelines and which is addressed in part in the ACC/AHA guidelines for the management of patients with acute myocardial infarction (7). We have also excluded HF in children, both because the underlying causes of HF in children differ from those in adults and because none of the controlled trials of treatments for HF have included children. We have not considered the management of HF due to primary valvular disease (see ACC/AHA guidelines on management of patients with valvular heart disease) (8) or congenital malformations, and we have not included recommendations for the treatment of specific myocardial disorders (e.g., hemochromatosis, sarcoidosis, or amyloidosis).

The ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult were approved for publication by the governing bodies of the ACC and AHA. These guidelines will be reviewed annually after publication and will be considered current unless the ACC/AHA Task Force on Practice Guidelines revises or withdraws them from circulation.

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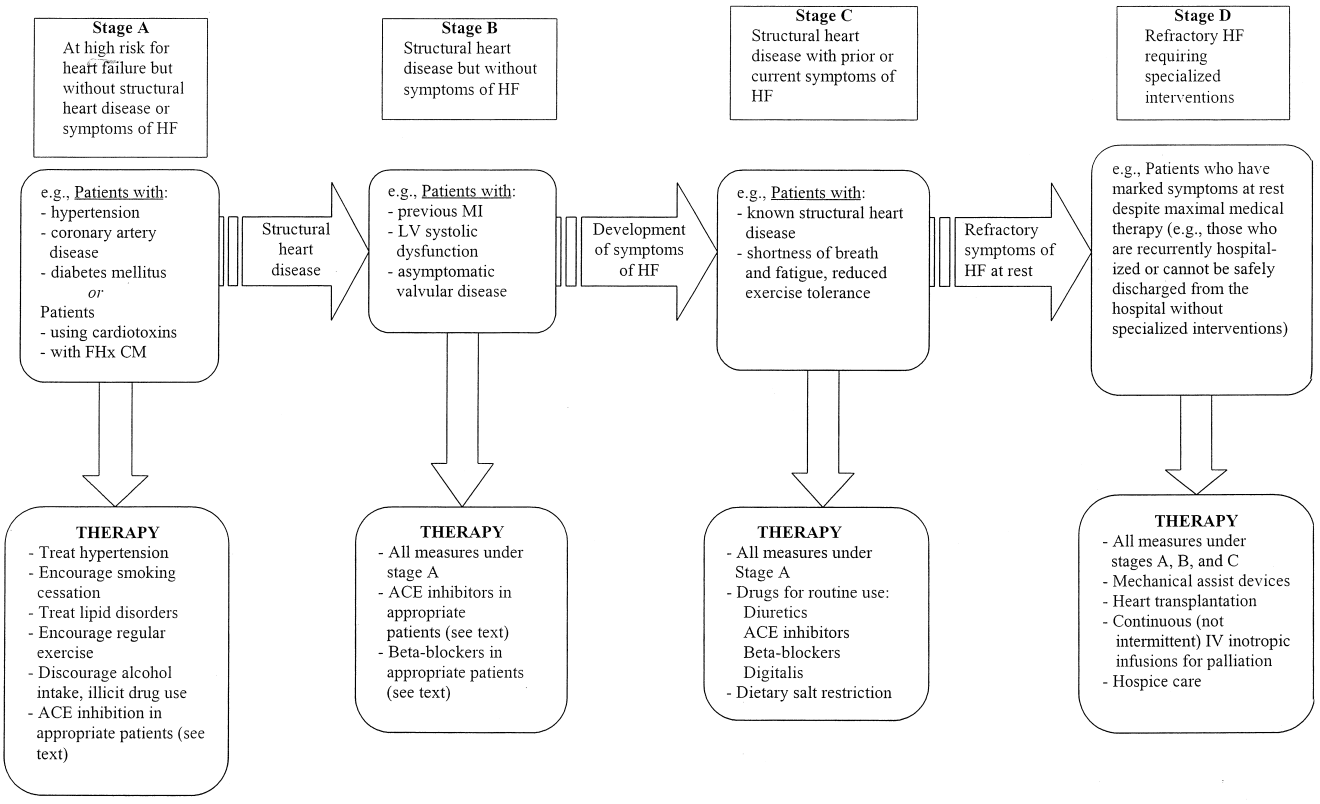

Figure 1. Stages in the evolution of HF and recommended therapy by stage. FHx CM indicates family history of cardiomyopathy; MI, myocardial infarction; LV, left ventricular; and IV, intravenous.

These practice guidelines are intended to assist physicians in clinical decision making by describing a range of generally acceptable approaches for the prevention, diagnosis, and management of HF. The guidelines attempt to define practices that meet the needs of most patients under most circumstances. However, the ultimate judgment regarding the care of a particular patient must be made by the physician in light of all of the circumstances that are relevant to that patient. The various therapeutic strategies described in this document can be viewed as a checklist to be considered for each patient in an attempt to individualize treatment for an evolving disease process. Every patient is unique, not only in terms of his or her cause and course of HF, but also in terms of his or her personal and cultural approach to the disease. Guidelines can only provide an outline for evidence-based decisions or recommendations for individual care; these guidelines are meant to provide that outline.

II. CHARACTERIZATION OF HF AS A CLINICAL SYNDROME

HF 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 and peripheral edema. Both abnormalities can impair the functional capacity and quality of life of affected individuals, but they may not necessarily dominate the clinical picture at the same time.

Coronary artery disease is the underlying cause of HF in approximately two thirds of patients with left ventricular systolic dysfunction (9). The remainder have nonischemic causes of systolic dysfunction and may have an identifiable cause (e.g., hypertension, valvular disease, myocardial toxins, or myocarditis) or may have no discernible cause (e.g., idiopathic dilated cardiomyopathy).

The classification system that is most commonly used to quantify the degree of functional limitation imposed by HF is one first developed by the NYHA (10). This system assigns patients to 1 of 4 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 that would limit normal individuals (class I). The mechanisms responsible for exercise intolerance in patients with chronic HF have not been clearly defined. Patients with a very low ejection fraction may be asymptomatic, whereas patients with preserved left ventricular systolic function may have severe disability. The apparent discordance between the severity of systolic dysfunction and the degree of functional impairment is not well understood despite intense investigation.

Left ventricular dysfunction begins with some injury to

the myocardium and is usually a progressive process, even in the absence of a new identifiable insult to the myocardium. The principal manifestation of such progression is a process known as remodeling, which occurs in association with homeostatic attempts to decrease wall stress through increases in wall thickness. This ultimately results in a change in the geometry of the left ventricle such that the chamber dilates, hypertrophies, and becomes more spherical. The process of cardiac remodeling generally precedes the development of symptoms, occasionally by months or even years. The process of remodeling continues after the appearance of symptoms and may contribute importantly to worsening of symptoms despite treatment.

The committee struggled with its perception that many clinicians do not appreciate the progressive nature of left ventricular dysfunction and HF or the importance of screening and prophylaxis for them, principles that are quite analogous to well-recognized strategies in the field of oncology. For this reason, it believed that the progression to and evolution of HF could appropriately be characterized by considering 4 stages in the evolution of the disease as described in the Introduction and Table 1. This classification scheme recognizes that HF, like coronary artery disease, has established risk factors; that the evolution of HF has asymptomatic and symptomatic phases; and that treatments prescribed at each stage can reduce the morbidity and mortality of HF.

III. ASSESSMENT OF PATIENTS

A. Initial Evaluation of Patients and Detection of Predisposing Conditions

1. Identification of Patients. In general, patients with left ventricular dysfunction present to the physician in 1 of 3 ways: with a syndrome of decreased exercise tolerance; with a syndrome of fluid retention; or with no symptoms and incidentally discovered left ventricular dysfunction.

2. Identification of Structural Abnormality. A complete history and physical examination are the first steps in evaluating the structural abnormality or cause responsible for the development of HF. Although the history and physical examination may provide important clues about the nature of the underlying cardiac abnormality, identification of the structural abnormality leading to HF generally requires either noninvasive or invasive imaging of the cardiac structures. The single most useful diagnostic test in the evaluation of patients with HF is the 2-dimensional echocardiogram, coupled with Doppler flow studies. Other tests may be used to provide information regarding the nature and severity of the cardiac abnormality. Radionuclide ventriculography can provide highly accurate measurements of global and regional function and assessment of ventricular enlargement, but it is unable to directly assess valvular abnormalities or cardiac hypertrophy. Both chest radiography and 12-lead electrocardiograms are considered to provide baseline information in most patients, but because they are both insensitive and nonspecific, neither the chest radiograph nor the electrocardiogram alone should form the primary basis for determining the specific cardiac abnormality responsible for the development of HF.

Recently, the measurement of circulating levels of brain natriuretic peptide has become available as a means of identifying patients with elevated left ventricular filling pressures who are likely to exhibit signs and symptoms of HF. The assessment of this peptide cannot reliably distinguish patients with systolic from those with diastolic dysfunction. However, it has been widely investigated as a biochemical marker of morbidity and mortality in patients with known HF (11) and as an aid in differentiating dyspnea due to HF from dyspnea due to other causes in an emergency setting (12). The role of brain natriuretic peptide measurement in the identification and management of patients with symptomatic or asymptomatic left ventricular dysfunction remains to be fully clarified.

3. Evaluation of the Cause of Ventricular Dysfunction. Identification of the disorder leading to HF may be important, because some causes of left ventricular dysfunction are reversible or treatable. However, it may not be possible to discern the cause of HF in many patients who present with this syndrome, and in others, the underlying condition may not be amenable to treatment. Hence, physicians should focus their efforts on diagnoses that have some potential for improvement with therapy directed at the underlying condition. Evaluation of potential causative factors should include taking a patient and family history, general laboratory testing, evaluation of the possibility of coronary artery disease, and evaluation of the possibility of primary myocardial disease.

B. Ongoing Evaluation of HF

Once the nature and cause of the structural abnormalities leading to the development of HF have been defined, physicians should focus on the clinical assessment of patients, both during the initial presentation and during subsequent visits. This ongoing review of the patient's clinical status is critical to the appropriate selection and monitoring of treatment. It should include assessment of functional capacity, assessment of volume status, laboratory evaluation, and assessment of prognosis.

Recommendations for the Evaluation of Patients With HF

Class I

1. **Thorough history and physical examination to identify cardiac and noncardiac disorders that might lead to the development of HF or accelerate the progression of HF. (*Level of Evidence: C*)**
2. **Initial and ongoing assessment of patient's ability to perform routine and desired activities of daily living. (*Level of Evidence: C*)**
3. **Initial and ongoing assessment of volume status. (*Level of Evidence: C*)**

4. **Initial measurement of complete blood count, urinalysis, serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum creatinine, blood glucose, liver function tests, and thyroid-stimulating hormone. (*Level of Evidence: C*)**
5. **Serial monitoring of serum electrolytes and renal function. (*Level of Evidence: C*)**
6. **Initial 12-lead electrocardiogram and chest radiograph. (*Level of Evidence: C*)**
7. **Initial 2-dimensional echocardiography with Doppler or radionuclide ventriculography to assess left ventricular systolic function. (*Level of Evidence: C*)**
8. **Cardiac catheterization with coronary arteriography in patients with angina who are candidates for revascularization. (*Level of Evidence: B*)**

Class IIa

1. **Cardiac catheterization with coronary arteriography in patients with chest pain who have not had evaluation of their coronary anatomy and who have no contraindications to coronary revascularization. (*Level of Evidence: C*)**
2. **Cardiac catheterization with coronary arteriography in patients with known or suspected coronary artery disease but without angina who are candidates for revascularization. (*Level of Evidence: C*)**
3. **Noninvasive imaging to detect ischemia and viability in patients with known coronary artery disease and no angina who are being considered for revascularization. (*Level of Evidence: C*)**
4. **Maximal exercise testing with measurement of respiratory gas exchange and/or blood oxygen saturation 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 to identify high-risk patients who are candidates for cardiac transplantation or other advanced treatments. (*Level of Evidence: B*)**
6. **Echocardiography in asymptomatic first-degree relatives of patients with idiopathic dilated cardiomyopathy. (*Level of Evidence: C*)**
7. **Repeat measurement of ejection fraction in patients 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*)**
8. **Screening for hemochromatosis. (*Level of Evidence: C*)**
9. **Measurement of serum antinuclear antibody, rheumatoid factor, urinary vanillylmandelic acid, and metanephrines in selected patients. (*Level of Evidence: C*)**

Class IIb

1. **Noninvasive imaging to define the likelihood of coronary artery disease in patients with left ventricular dysfunction. (*Level of Evidence: C*)**
2. **Maximal exercise testing with measurement of respiratory gas exchange to facilitate prescription of an appropriate exercise program. (*Level of Evidence: C*)**
3. **Endomyocardial biopsy in patients in whom an inflammatory or infiltrative disorder of the heart is suspected. (*Level of Evidence: C*)**
4. **Assessment of human immunodeficiency virus status. (*Level of Evidence: C*)**

Class III

1. **Endomyocardial biopsy in the routine evaluation of patients with HF. (*Level of Evidence: C*)**
2. **Routine Holter monitoring or signal-averaged electrocardiography. (*Level of Evidence: C*)**
3. **Repeat coronary arteriography or noninvasive testing for ischemia in patients for whom coronary artery disease has previously been excluded as the cause of left ventricular dysfunction. (*Level of Evidence: C*)**
4. **Routine measurement of circulating levels of norepinephrine or endothelin. (*Level of Evidence: C*)**

IV. THERAPY

A. Patients at High Risk of Developing Left Ventricular Dysfunction (Stage A)

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

Recommendations for Patients at High Risk of Developing HF (Stage A)

Class I

1. **Control of systolic and diastolic hypertension in accordance with recommended guidelines. (*Level of Evidence: A*)**
2. **Treatment of lipid disorders in accordance with recommended guidelines. (*Level of Evidence: B*)**
3. **Avoidance of patient behaviors that may increase the risk of HF (e.g., smoking, alcohol consumption, and illicit drug use). (*Level of Evidence: C*)**
4. **Angiotensin converting enzyme (ACE) inhibition in patients with a history of atherosclerotic vascular disease, diabetes mellitus, or hypertension and associated cardiovascular risk factors. (*Level of Evidence: B*)**
5. **Control of ventricular rate in patients with supraventricular tachyarrhythmias. (*Level of Evidence: B*)**
6. **Treatment of thyroid disorders. (*Level of Evidence: C*)**
7. **Periodic evaluation for signs and symptoms of HF. (*Level of Evidence: C*)**

Class IIa

Noninvasive evaluation of left ventricular function in patients with a strong family history of cardiomyopathy or in those receiving cardiotoxic interventions. (*Level of Evidence: C*)

Class III

1. **Exercise to prevent the development of HF. (*Level of Evidence: C*)**
2. **Reduction of dietary salt beyond that which is prudent for healthy individuals in patients without hypertension or fluid retention. (*Level of Evidence: C*)**
3. **Routine testing to detect left ventricular dysfunction in patients without signs or symptoms of HF or evidence of structural heart disease. (*Level of Evidence: C*)**
4. **Routine use of nutritional supplements to prevent the development of structural heart disease. (*Level of Evidence: C*)**

B. Patients With Left Ventricular Dysfunction Who Have Not Developed Symptoms (Stage B)

Patients without symptoms but who have had a myocardial infarction and patients without symptoms who have evidence of left ventricular dysfunction are at considerable risk of developing HF. The likelihood of developing clinical HF can be diminished by the use of therapies that reduce the risk of additional injury, the process of remodeling, and the progression of left ventricular dysfunction. However, as with patients with no structural heart disease, there is no evidence that control of dietary sodium, participation in regular exercise, or use of nutritional supplements can prevent the development of HF in patients with a recent or remote myocardial infarction with or without left ventricular systolic dysfunction.

Recommendations for Patients With Asymptomatic Left Ventricular Systolic Dysfunction (Stage B)

Class I

1. **ACE inhibition in patients with a recent or remote history of myocardial infarction regardless of ejection fraction. (*Level of Evidence: A*)**
2. **ACE inhibition in patients with a reduced ejection fraction, whether or not they have experienced a myocardial infarction. (*Level of Evidence: B*)**
3. **Beta-blockade in patients with a recent myocardial infarction regardless of ejection fraction. (*Level of Evidence: A*)**
4. **Beta-blockade in patients with a reduced ejection fraction, whether or not they have experienced a myocardial infarction. (*Level of Evidence: B*)**
5. **Valve replacement or repair for patients with hemodynamically significant valvular stenosis or regurgitation. (*Level of Evidence: B*)**
6. **Regular evaluation for signs and symptoms of HF. (*Level of Evidence: C*)**
7. **Measures listed as class I recommendations for patients in stage A. (*Levels of Evidence: A, B, and C as appropriate*).**

Class IIb

Long-term treatment with systemic vasodilators in patients with severe aortic regurgitation. (*Level of Evidence: B*)

Class III

1. **Treatment with digoxin in patients with left ventricular dysfunction who are in sinus rhythm. (*Level of Evidence: C*)**
2. **Reduction of dietary salt beyond that which is prudent for healthy individuals in patients without hypertension or fluid retention. (*Level of Evidence: C*)**
3. **Exercise to prevent the development of HF. (*Level of Evidence: C*)**
4. **Routine use of nutritional supplements to treat structural heart disease or prevent the development of symptoms of HF. (*Level of Evidence: C*)**

C. Patients With Left Ventricular Dysfunction With Current or Prior Symptoms (Stage C)

1. General Measures. Measures listed as class I recommendations for patients in stages A and B are also appropriate for patients with current or prior symptoms of HF (see Section V). In addition, moderate sodium restriction is indicated, along with daily measurement of weight, to permit effective use of lower and safer doses of diuretic drugs. 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 decompensation 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 (13–16).

Of the general measures that should be pursued in patients with HF, possibly the most effective yet least utilized is close attention and follow-up. Noncompliance with diet and medications can rapidly and profoundly affect the clinical status of patients, and increases in body weight and minor changes in symptoms commonly precede the major clinical episodes that require emergency care or hospitalization. Patient education and close supervision, which includes surveillance by the patient and his or her family between physician visits, can reduce the likelihood of noncompliance and can often lead to the detection of changes in body weight or clinical status early enough to allow the patient or a healthcare provider an opportunity to institute treatments that can prevent clinical deterioration and hospitalization. Supervision between physician visits ideally may be performed by a nurse or physician assistant

with special training in the care of patients with HF. Such an approach has been reported to have significant clinical benefits (17–20).

2. Drugs Recommended for Routine Use. Most patients with symptomatic left ventricular dysfunction should be routinely managed with a combination of 4 types of drugs: a diuretic, an ACE inhibitor, a beta-adrenergic blocker, and (usually) digitalis (21). The value of these drugs has been established in numerous large-scale clinical trials, and the evidence supporting a central role for their use is compelling and persuasive. Patients with evidence of fluid retention should be given a diuretic until a euvolemic state is achieved, and diuretic therapy should be continued to prevent the recurrence of fluid retention. Even if the patient has responded favorably to the diuretic, treatment with an ACE inhibitor and a beta-blocker should be initiated and maintained in patients who can tolerate them, because they have been shown to favorably influence the long-term prognosis of HF. Therapy with digoxin may be initiated at any time to reduce symptoms and enhance exercise tolerance.

3. Interventions to Be Considered for Use in Selected Patients. Several interventions have been shown in controlled clinical trials to be useful in a limited cohort of patients with HF. Some of these are undergoing active investigation in large-scale trials to determine whether their role in the management of HF might justifiably be expanded. They include aldosterone antagonists, angiotensin receptor blockers, hydralazine and isosorbide dinitrate, and exercise training.

4. Drugs and Interventions Under Active Investigation. Several drugs and interventions are under active evaluation in long-term large-scale trials because they showed promise in pilot studies that involved small numbers of patients. Until the results of definitive trials are available, none of these interventions can be recommended for use in patients with HF. These include vasopeptidase inhibitors, cytokine antagonists, endothelin antagonists, synchronized biventricular pacing, external counterpulsation, and techniques for respiratory support.

5. Interventions of Unproved Value and Not Recommended. Interventions of unproved value that are not recommended include nutritional supplements and hormonal therapies, intermittent intravenous positive inotropic therapy, and dynamic cardiomyoplasty.

Recommendations for Treatment of Symptomatic Left Ventricular Systolic Dysfunction (Stage C)

Class I

1. **Diuretics in patients who have evidence of fluid retention. (*Level of Evidence: A*)**
2. **ACE inhibition in all patients unless contraindicated. (*Level of Evidence: A*)**
3. **Beta-adrenergic blockade in all stable patients unless contraindicated. Patients should have no or minimal evidence of fluid retention and should not have required treatment recently with an intravenous positive inotropic agent. (*Level of Evidence: A*)**
4. **Digitalis for the treatment of symptoms of HF, unless contraindicated. (*Level of Evidence: A*)**
5. **Withdrawal of drugs known to adversely affect the clinical status of patients (e.g., nonsteroidal anti-inflammatory drugs, most antiarrhythmic drugs, and most calcium channel blocking drugs). (*Level of Evidence: B*)**
6. **Measures listed as class I recommendations for patients in stages A and B (*Levels of Evidence: A, B, and C as appropriate*).**

Class IIa

1. **Spironolactone in patients with recent or current class IV symptoms, preserved renal function, and a normal potassium concentration. (*Level of Evidence: B*)**
2. **Exercise training as an adjunctive approach to improve clinical status in ambulatory patients. (*Level of Evidence: A*)**
3. **Angiotensin receptor blockade in patients who are being treated with digitalis, diuretics, and a beta-blocker and who cannot be given an ACE inhibitor because of cough or angioedema. (*Level of Evidence: A*)**
4. **A combination of hydralazine and a nitrate in patients who are being treated with digitalis, diuretics, and a beta-blocker and who cannot be given an ACE inhibitor because of hypotension or renal insufficiency. (*Level of Evidence: B*)**

Class IIb

1. **Addition of an angiotensin receptor blocker to an ACE inhibitor. (*Level of Evidence: B*)**
2. **Addition of a nitrate, alone or in combination with hydralazine, to an ACE inhibitor in patients who are also being given digitalis, diuretics, and a beta-blocker. (*Level of Evidence: B*)**

Class III

1. **Long-term intermittent use of an infusion of a positive inotropic drug. (*Level of Evidence: C*)**
2. **Use of an angiotensin receptor blocker instead of an ACE inhibitor in patients with HF who have not been given or who can tolerate an ACE inhibitor. (*Level of Evidence: B*)**
3. **Use of an angiotensin receptor blocker before a beta-blocker in patients with HF who are taking an ACE inhibitor. (*Level of Evidence: A*)**
4. **Use of a calcium channel blocking drug as a treatment for HF. (*Level of Evidence: B*)**
5. **Routine use of nutritional supplements (coenzyme Q10, carnitine, taurine, and antioxidants) or hormonal therapies (growth hormone or thyroid hormone) for the treatment of HF. (*Level of Evidence: C*)**

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

Most patients with HF due to left ventricular systolic dysfunction respond favorably to pharmacological and non-

pharmacological treatments and enjoy a good quality of life and enhanced survival. However, despite optimal medical therapy, some patients do not improve with treatment or experience rapid recurrence of symptoms. Such patients generally have symptoms (including profound fatigue) at rest or on minimal exertion, cannot perform most activities of daily living, frequently have evidence of cardiac cachexia, and typically require repeated or prolonged hospitalizations for intensive management. These individuals represent the most advanced state of HF and should be considered for specialized treatment strategies such as mechanical circulatory support, continuous intravenous positive inotropic therapy, referral for cardiac transplantation, or hospice care. Before a patient is considered to have refractory HF, it is critical that physicians confirm the accuracy of the diagnosis; identify and reverse, if possible, any contributing conditions; and ensure that all conventional medical strategies have been optimally employed.

Many patients with advanced HF have symptoms that are related to the retention of salt and water and thus will respond favorably to interventions designed to restore sodium balance. Hence, a critical step in the successful management of end-stage HF is the recognition and meticulous control of fluid retention.

Controlled trials suggest that patients with advanced HF respond favorably to treatment with both ACE inhibitors and beta-blockers in a manner similar to those with mild to moderate disease (22,23). However, because neurohormonal mechanisms play an important role in the support of circulatory homeostasis as HF progresses, neurohormonal antagonism may be less well tolerated by patients with severe symptoms than by patients with mild symptoms. Patients who are at the end stage of their disease are at particular risk of developing hypotension and renal insufficiency after the administration of an ACE inhibitor and of experiencing worsening HF after treatment with a beta-blocker. As a result, patients with refractory HF may tolerate only small doses of these neurohormonal antagonists or may not tolerate them at all.

Many commonly performed cardiac surgical procedures (e.g., coronary artery bypass grafting and valve repair/replacement) are being performed with increasing frequency in patients with HF, including those with advanced symptoms. Revascularization is routinely recommended for patients with left ventricular dysfunction who have angina, but its role in patients without symptoms of ischemia remains controversial.

Cardiac transplantation is currently the only established surgical approach to the treatment of refractory HF, but it is available to no more than 2500 patients yearly in the United States (24). Alternative surgical and mechanical approaches for the treatment of end-stage HF are under development. Extracorporeal devices are approved for circulatory support in patients who are expected to recover from a major cardiac insult (e.g., postcardiotomy shock) or who are expected to receive a definitive treatment for HF (e.g., heart transplantation). Left ventricular assist devices provide similar degrees of hemodynamic support, but many are implantable and thus allow for patient ambulation and hospital discharge (25,26). One ongoing trial is evaluating the long-term utility of such a device in patients with refractory HF who are not candidates for a heart transplant.

Recommendations for Patients With Refractory End-Stage HF (Stage D)

Class I

1. **Meticulous identification and control of fluid retention. (*Level of Evidence: B*)**
2. **Referral for cardiac transplantation in eligible patients. (*Level of Evidence: B*)**
3. **Referral to an HF program with expertise in the management of refractory HF. (*Level of Evidence: A*)**
4. **Measures listed as class I recommendations for patients in stages A, B, and C. (*Levels of Evidence: A, B, and C as appropriate*).**

Class IIb

1. **Pulmonary artery catheter placement to guide therapy in patients with persistently severe symptoms. (*Level of Evidence: C*)**
2. **Mitral valve repair or replacement for severe secondary mitral regurgitation. (*Level of Evidence: C*)**
3. **Continuous intravenous infusion of a positive inotropic agent for palliation of symptoms. (*Level of Evidence: C*)**

Class III

1. **Partial left ventriculectomy. (*Level of Evidence: C*)**
2. **Routine intermittent infusions of positive inotropic agents. (*Level of Evidence: B*)**

V. TREATMENT OF SPECIAL POPULATIONS AND CONCOMITANT DISORDERS

Many patients with HF are members of subpopulations or have comorbid conditions that either contribute to the development of their HF or make the management of their HF symptoms more difficult. These factors need to be considered in the management of such patients.

1. Special Subpopulations. Many subgroups are underrepresented in most trials, and some present unique problems in HF management. These include women and men, racial minorities, and elderly patients.

2. Concomitant Disorders. Patients with left ventricular dysfunction frequently have associated cardiovascular and noncardiovascular disorders, the course or treatment of which may exacerbate the syndrome of HF. In many patients, appropriate management of these concomitant illnesses may produce clinical and prognostic benefits that may be as important as the treatment of HF itself. These concomitant conditions include cardiovascular disorders such as hypertension, hyperlipidemia, and diabetes mellitus; coronary artery disease; supraventricular arrhythmias; ven-

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tricular arrhythmias and prevention of sudden death; and prevention of thrombotic events. Associated noncardiovascular disorders include renal insufficiency, pulmonary disease, cancer, and thyroid disease.

Recommendations for Management of Concomitant Diseases in Patients With HF

Class I

1. **Control of systolic and diastolic hypertension in patients with HF in accordance with recommended guidelines. (*Level of Evidence: A*)**
2. **Nitrates and beta-blockers (in conjunction with diuretics) for the treatment of angina in patients with HF. (*Level of Evidence: B*)**
3. **Coronary revascularization in patients who have both HF and angina. (*Level of Evidence: A*)**
4. **Anticoagulants in patients with HF who have paroxysmal or chronic atrial fibrillation or a previous thromboembolic event. (*Level of Evidence: A*)**
5. **Control of the ventricular response 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*)**
6. **Beta-adrenergic blockade (unless contraindicated) in patients with HF to reduce the risk of sudden death. Patients should have no or minimal fluid retention and should not have recently required treatment with an intravenous positive inotropic agent. (*Level of Evidence: A*)**
7. **Implantable cardioverter-defibrillator, alone or in combination with amiodarone, in patients with HF who have a history of sudden death, ventricular fibrillation, or hemodynamically destabilizing ventricular tachycardia. (*Level of Evidence: A*)**

Class IIa

1. **Antiplatelet agents for prevention of myocardial infarction and death in patients with HF who have underlying coronary artery disease. (*Level of Evidence: B*)**
2. **Digitalis to control the ventricular response in patients with HF and atrial fibrillation. (*Level of Evidence: A*)**

Class IIb

1. **Coronary revascularization in patients who have HF and coronary artery disease but no angina. (*Level of Evidence: B*)**
2. **Restoration of sinus rhythm by electrical cardioversion in patients with HF and atrial fibrillation. (*Level of Evidence: C*)**
3. **Amiodarone to prevent sudden death in patients with HF and asymptomatic ventricular arrhythmias. (*Level of Evidence: B*)**
4. **Anticoagulation in patients with HF who do not have atrial fibrillation or a previous thromboembolic event. (*Level of Evidence: B or C*)**

Class III

1. **Routine use of an implantable cardioverter-defibrillator in patients with HF. (*Level of Evidence: C*)**
2. **Class I or III antiarrhythmic drugs (except amiodarone) in patients with HF for the prevention or treatment of asymptomatic ventricular arrhythmias. (*Level of Evidence: A*)**
3. **Ambulatory electrocardiographic monitoring for the detection of asymptomatic ventricular arrhythmias. (*Level of Evidence: A*)**

VI. DIASTOLIC DYSFUNCTION

Approximately 20% to 40% of patients with HF have preserved left ventricular systolic function and (in the absence of valvular disease) are believed to have an impairment of ventricular relaxation as the primary mechanism leading to symptoms (27–31). Several recognized myocardial disorders are associated with diastolic dysfunction, including restrictive cardiomyopathy, obstructive and nonobstructive hypertrophic cardiomyopathy, and infiltrative cardiomyopathies. However, the vast majority of patients who present with HF and normal systolic function do not have a defined myocardial disease but nevertheless have a clinically significant impairment of diastolic function.

Many of the changes that occur in the cardiovascular system as a result of aging have a greater impact on diastolic function than on systolic performance (32). HF associated with preserved systolic function is primarily a disease of elderly women, most of whom have hypertension (28). These patients suffer considerably from dyspnea and fatigue, which can limit their exercise tolerance and quality of life, and they are hospitalized frequently for clinical stabilization (33). Although the risk of death in these patients appears to be lower than in patients with HF and poor systolic function, the management of these patients still has major socioeconomic implications (34).

It is difficult to be precise about the diagnosis of diastolic dysfunction. Noninvasive methods, especially those that rely on Doppler echocardiography, have been developed to assist in such diagnosis. In practice, however, the diagnosis of diastolic HF is generally based on the finding of typical symptoms and signs of HF in a patient who is shown to have a normal left ventricular ejection fraction and no valvular abnormalities on echocardiography.

In contrast to the treatment of HF due to systolic dysfunction, few clinical trials are available to guide the management of patients with HF due to diastolic dysfunction. Although controlled studies have been performed with digitalis, ACE inhibitors, angiotensin receptor antagonists, beta-blockers, and calcium channel blockers in patients with HF who had a normal left ventricular ejection fraction, these trials have been small or have produced inconclusive results (35–39). Nevertheless, many patients with diastolic HF receive treatment with these drugs because of the presence of comorbid conditions (i.e., atrial fibrillation,

hypertension, diabetes, or coronary artery disease). In addition, recommendations regarding the use of anticoagulation and antiarrhythmic agents apply to both systolic and diastolic HF.

In the absence of controlled clinical trials, the management of patients with diastolic dysfunction is frequently determined by a set of therapeutic principles (31). These include control of blood pressure, control of tachycardia, reduction in central blood volume, and alleviation of myocardial ischemia.

Recommendations for Management of HF and Preserved Systolic Function

Class I

1. **Control of systolic and diastolic hypertension in accordance with published guidelines. (*Level of Evidence: A*)**
2. **Control of ventricular rate in patients with atrial fibrillation. (*Level of Evidence: C*)**
3. **Diuretics to control pulmonary congestion and peripheral edema. (*Level of Evidence: C*)**

Class IIa

Coronary revascularization in patients with coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to have an adverse effect on diastolic function. (*Level of Evidence: C*)

Class IIb

1. **Restoration of sinus rhythm in patients with atrial fibrillation. (*Level of Evidence: C*)**
2. **Use of beta-adrenergic blocking agents, ACE inhibitors, angiotensin receptor blockers, or calcium antagonists in patients with controlled hypertension to minimize symptoms of HF. (*Level of Evidence: C*)**
3. **Digitalis to minimize symptoms of HF. (*Level of Evidence: C*)**

VII. END-OF-LIFE CONSIDERATIONS

Although issues surrounding end-of-life care deserve attention for all chronic terminal diseases, several general principles merit particular discussion in the context of chronic HF (40,41). Education of both patient and family regarding the expected or anticipated course of illness, final treatment options, and planning should be undertaken before the patient becomes too ill to participate in decisions. Discussions regarding treatment preferences, living wills, and advance directives should encompass a variety of likely contingencies that include responses to a potentially reversible exacerbation of HF, a cardiac arrest, a sudden catastrophic event such as a severe cerebrovascular accident, and worsening of major coexisting noncardiac conditions. In reviewing these issues with families, short-term intervention in anticipation of rapid recovery should be distinguished from prolonged life support without reasonable expectation of return to good functional capacity.

Hospice services have only recently been extended to patients dying of HF. Originally developed for patients with end-stage cancer, the focus of hospice care has now been expanded to the relief of symptoms other than pain (42). This is appropriate, because the suffering of patients with HF is characteristically linked to symptoms of breathlessness, and thus, compassionate care may require the frequent administration of intravenous diuretics and (in some cases) the continuous infusion of positive inotropic agents rather than the use of potent analgesics. Physicians caring for these patients, however, are becoming more comfortable with the prescription of anxiolytics and narcotics to ease distress during the last days.

Recommendations for End-of-Life Care

Class I

1. **Ongoing patient and family education regarding prognosis for function and survival. (*Level of Evidence: C*)**
2. **Patient and family education about options for formulating and implementing advance directives. (*Level of Evidence: C*)**
3. **Continuity of medical care between inpatient and outpatient settings. (*Level of Evidence: C*)**
4. **Components of hospice care that are appropriate to the relief of suffering. (*Level of Evidence: C*)**

Class III

Implantation of a cardioverter-defibrillator in patients with class IV symptoms who are not anticipated to experience clinical improvement from available treatments. (*Level of Evidence: C*)

VIII. IMPLEMENTATION OF PRACTICE GUIDELINES

Despite the publication of evidence-based guidelines (6,21,43), the current care of patients with HF remains suboptimal. Numerous studies document underutilization of key processes of care, such as use of ACE inhibitors in patients with decreased systolic function and the measurement of left ventricular ejection fraction (44–46). The relatively sparse literature on implementing practice guidelines for patients with HF can be divided into 2 areas: isolated provider interventions and disease-management systems approaches. It is clear that dissemination of a practice guideline must be accompanied by more intensive educational and behavioral change efforts to maximize the chances of improving physician practice patterns. The disease-management approach views HF as a chronic illness spanning the home, outpatient, and inpatient settings and involves multidisciplinary team care. Observational and randomized controlled trials have generally shown that disease-management programs reduce hospitalizations and can improve quality of life and functional status (20,47).

Insufficient evidence exists to make uniform recommen-

dations about the most appropriate roles for generalist physicians and cardiologists in the care of patients with HF. Many questions remain. Do generalist physicians and cardiologists provide similar levels of care for the noncardiac comorbid conditions frequently present in patients with HF? What is the optimal time for referral to a specialist? What is the most effective system of comanagement of patients by generalists and cardiologists? What is the most cost-effective entry point into a disease-management program? Regardless of the ultimate answers to these questions, all physicians and other healthcare providers must advocate and follow care practices that have been shown to improve patient outcomes. If a physician is not comfortable following a specific recommendation (e.g., the use of beta-blockers), then the physician should refer the patient to someone with expertise in HF. A collaborative model in which generalist and specialist physicians work together to optimize the care of patients with HF is likely to be most fruitful.

Recommendations for Implementing Practice Guidelines

Class I

1. **Multifactorial interventions that attack different barriers to behavioral change. (*Level of Evidence: A*)**
2. **Multidisciplinary disease-management programs for patients at high risk for hospital admission or clinical deterioration. (*Level of Evidence: B*)**
3. **Academic detailing or educational outreach visits. (*Level of Evidence: A*)**

Class IIa

1. **Chart audit and feedback of results. (*Level of Evidence: A*)**
2. **Reminder systems. (*Level of Evidence: A*)**
3. **Local opinion leaders. (*Level of Evidence: A*)**

Class IIb

Multidisciplinary disease-management programs for patients at low risk for hospital admission or clinical deterioration. (*Level of Evidence: B*)

Class III

1. **Dissemination of guidelines without more intensive behavioral change efforts. (*Level of Evidence: A*)**
2. **Basic provider education alone. (*Level of Evidence: A*)**

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