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ACC/AHA TASK FORCE HEART FAILURE GUIDELINES

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

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Preamble

It is becoming more apparent each day that despite a strong national commitment to excellence in health care, the resources and personnel are finite. It is, therefore, appropriate that the medical profession examine the impact of developing technology and new therapeutic modalities on the practice of cardiology. Such analysis, carefully conducted, could potentially have an impact on the cost of medical care without diminishing the effectiveness of that care.

To this end, the American College of Cardiology and the American Heart Association in 1980 established a Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (now the ACC/AHA Task Force on Practice Guidelines) with the following charge:

> The task force of the American College of Cardiology and the American Heart Association shall develop guidelines relative to the role of new therapeutic approaches and of specific noninvasive and invasive procedures in the diagnosis and management of cardiovascular disease.
>
> The task force shall address, when appropriate, the contribution, uniqueness, sensitivity, specificity, indications, contraindications and cost-effectiveness of such diagnostic procedures and therapeutic modalities.

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The task force shall emphasize the role and values of the developed guidelines as an educational resource.

The task force shall include a chair and eight members, four representatives from the American Heart Association and four representatives from the American College of Cardiology. The task force may select ad hoc members as needed upon the approval of the presidents of both organizations. Recommendations of the Task Force are forwarded to the President of each organization.

The members of the task force are Melvin D. Cheitlin, MD, Kim A. Eagle, MD, Timothy J. Gardner, MD, Arthur Garson, Jr., MD, MPH, Raymond J. Gibbons, MD, Richard P. Lewis, MD, Robert A. O'Rourke, MD, Thomas J. Ryan, MD and James L. Ritchie, MD, Chair.

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This document was reviewed by the officers and other responsible individuals of the American College of Cardiology and American Heart Association and received final approval in September 1995. It is being published simultaneously in *Circulation* and *Journal of the American College of Cardiology*.

James L. Ritchie
Chair, ACC/AHA Task Force on Practice Guidelines

These guidelines were approved by the American College of Cardiology Board of Trustees and the American Heart Association Science Advisory and Coordinating Committee in September 1995.

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Introduction

The American College of Cardiology and the American Heart Association (ACC/AHA) have long been involved in the joint development of practice guidelines designed to assist physicians in the management of selected cardiovascular disorders or in the selection of certain cardiovascular procedures. Selection of the disorders or procedures for which to develop guidelines is based on several factors, including their importance to physicians and whether there is sufficient scientific data from which to derive accepted guidelines.

The importance of congestive heart failure is underscored by the frequency with which the condition is encountered and its prognosis, for example, 4.7 million people (NHANES III data) in this country have congestive heart failure, and once failure develops, the 6-year mortality rate approaches 80% in men and 65% in women (1). Importantly, as our population ages, the incidence of heart failure and its mortality rate will continue to increase. Furthermore, recent advances in our understanding of the pathophysiology of heart failure and new developments in the therapy of this disorder have greatly expanded the information base on which to make decisions. However, the results of a number of ongoing clinical trials may require modification of the recommendations contained herein.

These guidelines were developed by cardiovascular specialists and were based primarily on a comprehensive review of published reports. The references listed are not all inclusive but contain those which we believe are representative of the most convincing data. In cases where the data do not appear conclusive, recommendations are based on the consensus opinion of the group.

We elected to limit our guidelines for adults to heart failure associated with left ventricular dysfunction, with the

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major focus on systolic dysfunction. This decision was based on the fact that the great majority of adults with heart failure in this country have left ventricular systolic dysfunction, and the greatest advances in our understanding and treatment of heart failure are associated with this disorder.

The guidelines for adults are based on the manner in which patients present to physicians and encompass the extremes of presentation from acute pump failure with shock to asymptomatic left ventricular dysfunction. We have included patients in the latter category because proper treatment can delay or prevent the development of heart failure. Treatment strategies frequently depend on the etiology of the heart disease, and a major focus of these guidelines is the diagnostic approach to determine correctable etiologies and precipitating factors. However, our treatment strategies do not include specific therapies for correctable causes of heart failure, such as the surgical approach to valvular disease or the treatment of thyrotoxic heart disease. Our approach is to discuss the diagnostic studies and treatment necessary to stabilize the status of adult patient with acute heart failure and the evaluation and treatment of patients presenting with chronic left ventricular dysfunction or stabilized acute heart failure.

In the pediatric population, the leading causes of heart failure are significantly different from those in the adult. Our therapeutic guidelines for the pediatric group therefore are directed more to specific causes of heart failure than for the adults.

For both groups, we have followed the format of previous ACC/AHA guidelines for classifying indications for diagnostic procedures and therapeutic interventions.

Class I

Usually indicated, always acceptable

Class II

Acceptable, but of uncertain efficacy and may be controversial

Class III

Generally not indicated

Because our goal was to develop guidelines for use by physicians, and our Task Force included only physicians, our guidelines do not include other aspects of care, such as nursing care, rehabilitation and the provision of social services. We recognize the importance of these areas in the overall management of patients with heart failure.

The task force did not deal with issues relating to the diagnosis of heart failure, nor did we attempt to analyze the cost-effectiveness of our recommendations. We were acutely aware of cost implications of our recommendations, and these implications were considered in our deliberations. However, our primary goal was to develop guidelines to assist physicians in delivering the best care possible to those with heart failure.

We emphasize that there are many factors, notably the wishes of informed patients, that ultimately determine the most appropriate therapy for an individual patient. Therefore, deviation from these guidelines may be appropriate in some circumstances. Furthermore, these guidelines are based on the assumption that the resources necessary to provide this care are readily available. Unquestionably, this is not true in all geographic areas, which further underscores our position that these are guidelines and not rigid requirements.

Acute Heart Failure in Adults

The clinical presentation of acute heart failure ranges from the sudden appearance of dyspnea to frank cardiogenic shock. The management of acute heart failure differs for the various patient groups residing within the clinical spectrum of this condition; thus, this topic is approached by separately discussing the management of each of the major clinical groups.

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We assume that the physician has excluded noncardiac disorders whose clinical presentation can be similar in many respects to that of acute heart failure (e.g., noncardiogenic pulmonary edema). Also, noncardiac support measures (e.g., ventilator therapy) are not discussed in detail despite the fact that these measures are important in the overall management of these critically ill patients.

Acute heart failure can be grouped clinically into *acute cardiogenic pulmonary edema, cardiogenic shock,* and *acute decompensation of chronic left heart failure.*

With few exceptions, patients presenting with acute heart failure require hospital admission, particularly those with an initial episode of failure (see page 1392).

Therapeutic interventions to produce hemodynamic improvement and stability must be undertaken expeditiously in these patients. In addition, it is imperative to obtain quickly those diagnostic tests necessary to detect causes of heart failure which are best treated by special therapeutic approaches. Myocardial injury/infarction, high degree atrioventricular (AV) block, ventricular tachycardia, pericardial tamponade and pulmonary embolism are examples of the latter causes of failure. Once etiologies of this type have been excluded, further diagnostic testing to determine the etiology of the heart disease generally can be deferred to a more appropriate time.

Acute Cardiogenic Pulmonary Edema

A brief medical history and directed physical examination are generally sufficient to initiate therapy. An intravenous catheter should be placed, blood obtained for essential laboratory studies and the patient placed on oxygen therapy.

The sublingual administration of nitroglycerin (0.4 to 0.6 mg, repeated every 5 to 10 min four times as needed) is of value. Nitroglycerin is effective in patients with acute cardiogenic pulmonary edema due to both ischemic and nonischemic causes. If systemic blood pressure is acceptable (generally a systolic blood pressure ≥ 95 to 100 mm Hg), nitroglycerin can be administered intravenously (starting dose 0.3 to 0.5 µg/kg body weight per min) as well (2).

Sodium nitroprusside (starting dose 0.1 µg/kg per min) may be selected for patients not immediately responsive to nitrate therapy and for those whose pulmonary edema is, in large part, attributable to severe mitral or aortic valvular regurgitation or marked, systemic hypertension (2). The dose is advanced as needed to improve the patient's overall clinical and hemodynamic status, using a systemic systolic pressure of 85 to 90 mm Hg as the usual lower limit for dose incrementation in patients previously normotensive and as long as adequate perfusion of vital organs is maintained.

Furosemide (20 to 80 mg intravenously) should be given shortly after the diagnosis of acute pulmonary edema is established.

Morphine sulfate (3 to 5 mg intravenously) is effective in ameliorating many of the symptoms of acute pulmonary edema and can be administered safely to most patients with this condition. However, morphine sulfate should be administered with caution to patients with chronic pulmonary insufficiency and those with respiratory or metabolic acidosis in whom suppression of ventilatory drive can cause a drastic lowering of systemic pH.

Intubation and mechanical ventilation are of value in patients with severe hypoxia that does not respond rapidly to therapy and in those with respiratory acidosis.

Patients with severe refractory pulmonary edema may benefit from intraaortic balloon counterpulsation (see page 1382). This procedure is of particular value if the patient is to undergo urgent cardiac catheterization and definitive intervention. Intraaortic balloon counterpulsation should not be used in patients with significant aortic valvular insufficiency or aortic dissection. A rare patient presenting with severe refractory pulmonary edema and a correctable lesion may need to proceed directly to the operating room after prompt diagnosis (usually by clinical

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examination and echocardiography) of the precipitating lesion; examples include rupture of a papillary muscle with acute, marked mitral regurgitation and acute aortic dissection complicated by proximal coronary artery occlusion or marked aortic valvular insufficiency, or both. Patients whodevelop cardiogenic shock should be approached as discussed later.

In most patients acute cardiogenic pulmonary edema can be stabilized with appropriate intervention and frequent, intermittent bedside evaluation without the routine introduction of indwelling pulmonary or systemic arterial catheters. Placement of a pulmonary artery balloon catheter should be considered in this setting if 1) the patient's clinical course is deteriorating; 2) recovery from the acute presentation is not proceeding as expected; 3) high dose nitroglycerin or nitroprusside is required for clinical stabilization; 4) dobutamine or dopamine are needed to augment systemic blood pressure and peripheral perfusion; or 5) uncertainty exists regarding the diagnosis of acute cardiogenic pulmonary edema (see page 1382).

Early in the initial evaluation of patients with acute pulmonary edema, the physician must determine whether acute myocardial injury/infarction is present. At this stage, this determination is based on clinical assessment and the electrocardiogram (ECG). Evidence of acute myocardial injury/infarction should raise consideration of urgent myocardial reperfusion therapy. Cardiac catheterization and coronary arteriography followed by the most appropriate interventional procedure (if readily available), or thrombolytic therapy should be considered. The reader is referred to other ACC/AHA guidelines (3–5) for additional, more specific information regarding the therapeutic approach to acute myocardial injury/infarction.

Transthoracic Doppler–two dimensional echocardiography is indicated in all patients who present with acute cardiogenic pulmonary edema, unless there are obvious precipitating factors and the patient's cardiac status had been adequately evaluated previously. Depending on the urgency for confirming or establishing a diagnosis, the procedure is performed as soon as possible after initial stabilization. Transesophageal echocardiography may be required to diagnose or more clearly define certain lesions (e.g., ruptured chordae tendinea, aortic dissection).

Initial Diagnostic Evaluation of Acute Pulmonary Edema

Class I

1. Focused history/physical examination

2. 12-lead ECG

3. Continuous ECG monitoring

4. Blood–serum studies: complete blood count (CBC); electrolytes, blood urea nitrogen (BUN), creatinine and cardiac enzyme levels

5. Digital pulse oximetry/arterial blood gases

6. Chest radiograph

7. Transthoracic Doppler–two dimensional echocardiography

8. Cardiac catheterization/coronary arteriography for suspected coronary artery disease 1) if acute intervention for myocardial injury/infarction is anticipated; 2) to determine the cause(s) for refractory acute pulmonary edema

Class II

1. Indwelling arterial cannula

2. Transesophageal echocardiography

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3. Tabulation of fluid volume intake and urine output

Class III

Extensive evaluation (e.g., cardiac catheterization and coronary arteriography) in a patient with a concomitant terminal illness or who would not be considered a candidate for the necessary major cardiovascular intervention.

Therapeutic Management of Acute Pulmonary Edema

Class I

1. Oxygen therapy

2. Nitroglycerin, sublingually or intravenously

3. Intravenous administration of a diuretic (e.g. furosemide)

4. Morphine sulfate

5. Administration of cardiovascular support drugs to attain and stabilize clinical–hemodynamic status (e.g. intravenous infusion of nitroprusside, dobutamine, dopamine)

6. Thrombolytic therapy or urgent revascularization (angioplasty or coronary artery bypass surgery) for acute myocardial injury/infarction

7. Intubation and mechanical ventilation for severe hypoxia that does not respond rapidly to therapy and for respiratory acidosis

8. Definitive correction of the underlying cause (e.g., mitralvalve replacement or repair of acute, severe mitral regurgitation) when indicated and clinically feasible

Additional cardiovascular laboratory testing may be necessary to exclude correctable causes of heart failure once the patient's status is stabilized, as discussed in the section on chronic and stabilized acute heart failure. Without the detection and correction of a reversible cause or lesion, the long-term prognosis of patients who present with acute cardiogenic pulmonary edema is poor(6).

Cardiogenic Shock

If cardiogenic shock is not caused by a reparable lesion, or if the lesion is not repaired in an efficient and effective manner, the mortality rate is ≥85% (7,8). Therefore, cardiogenic shock should be approached with diagnostic and therapeutic vigor in an attempt to identify a treatable lesion and to intervene in a definitive manner. Patients presenting with hypoperfusion but adequate blood pressure may be considered to be in near shock and should be approached in the same manner to prevent the progression to frank shock and death.

The general principles of management are rapid recognition of the condition; rapid exclusion or treatment, or both, of readily reversible causes; and prompt stabilization of the clinical and hemodynamic status. As in most emergency situations, many of these activities are performed simultaneously without a routine or set sequence for all patients.

An ECG should be obtained, continuous ECG monitoring instituted, an intravenous catheter inserted and an indwelling arterial cannula placed for continuous blood pressure monitoring. An indwelling pulmonary artery catheter should be inserted at an early stage of shock management, unless the patient responds rapidly to fluid infusion. The catheter should be inserted by an operator skilled in this technique in a suitable environment (e.g.,

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procedure room of the emergency department, intensive care unit or catheterization laboratory), with assistance from experienced staff.

If arrhythmias are present, their contribution to the hemodynamic state and need for rapid cardioversion or pacing must be determined.

In patients presenting with cardiogenic shock, a relative or absolute reduction in left ventricular filling pressure as the cause of hypotension must be excluded. Because of prior diuretic therapy or acute interspace volume shifts, it is estimated that 10% to 15% of patients with an acute myocardial infarction may be significantly volume depleted (7,9). Right ventricular infarction, pericardial tamponade and certain instances of pulmonary embolization are other common examples of acute heart failure that fall into this category. Unless there are signs of left heart volume overload (e.g., S_3 gallop, moist pulmonary rales, vascular or pulmonary congestion on chest radiograph), normal saline solution should be administered intravenously at a reasonably fast rate ($\leq$500-ml bolus, followed by 500 ml/h). Jugular venous pressure is not a consistently reliable indicator of left heart filling pressure (10), and, thus, elevation of jugular pressure does not obviate the need for fluid administration in a number of clinical situations (e.g., pericardial tamponade, right ventricular myocardial infarction).

In patients with an acute inferior infarction with shock, a right ventricular infarction should be suspected, resulting in right ventricular failure and inadequate filling of the left heart system. Right-sided precordial ECG leads in addition to the standard leads should be used in these patients. An injury pattern is often but not uniformly observed on the right precordial lead tracings (V_3R, V_4R) in patients with a right ventricular infarction. The diagnosis of right ventricular infarction frequently can be made on the basis of clinical findings such as an increase in jugular venous pressure during inspiration. An echocardiogram or the insertion of a pulmonary artery balloon catheter, or both, are helpful in patients in whom the diagnosis is unclear. Right-sided cardiac pressure recordings generally show mean right atrial and right ventricular filling pressures equaling or exceeding pulmonary artery occlusive (wedge) pressure with normal or low pulmonary artery pressures (11–13). Echocardiography can be used to establish or confirm the presence of right heart involvement, assess tricuspid valve competence, evaluate the extent of left heart damage and left ventricular function and exclude pericardial tamponade (which can have a similar clinical presentation). As an alternative, radionuclide angiography can be used to detect right ventricular infarction by demonstrating right ventricular enlargement and dysfunction.

Fluid volume administration is a major component of therapy for patients with right ventricular infarction to maintain the elevated right-sided filling pressure necessary to maintain cardiac output. Fluid administration initially may be guided by clinical variables (e.g., systemic blood pressure, peripheral perfusion, urine output, ventricular gallop sounds), but hemodynamic monitoring by a pulmonary artery catheter is generally required to optimize volume administration. Failure of fluid volume administration to achieve clinical and hemodynamic improvement and stabilization in these patients requires additional therapeutic approaches (e.g., dobutamine, intraaortic balloon counterpulsation or interventional procedures). The use of diuretic drugs or vasodilator agents in patients with a right ventricular infarction can result in severe hypotension.

Occasionally, vasodilator agents and diuretic drugs produce hypotension in patients with an acute myocardial infarction and pulmonary edema becasue the translocation of fluid into the lung reduces intravascular volume. These patients should be treated as described later.

Severe hypotension (systolic blood pressure $\leq$70 mm Hg) or clinical shock, or both, occurring in the presence of volume overload or persisting after bolus saline administration should be approached with moderate (4 to 5 µg/kg body weight per min), then, if necessary, increasing doses of dopamine (14,15).

If hypotension or clinical shock or near shock persists at dopamine doses $\geq$15 µg/kg per min, institution of intraaortic balloon counterpulsation should be considered for patients with a potentially reversible condition or as a bridge to transplantation. If intraaortic balloon counterpulsation is not available, norepinephrine can be added to increase systemic blood pressure to acceptable levels (systolic pressure $\geq$80 mm Hg) and the patient transferred on an emergency basis to a more comprehensive medical facility. Patients with volume overload (or after adequate volume loading) in near shock or with a lesser degree of systemic hypotension often respond favorably to

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dobutamine (2 to 3 µg/kg per min initially) or low to moderate doses of dopamine (2 to 5 µg/kg per min initially) (14,15).

During treatment, attention should remain focused on 1) the status of the patient's intravascular volume; 2) the condition of the patient's ventricular function; 3) the presence of myocardial injury/infarction, and 4) whether correctable, mechanical lesions are present.

1. Status of intravascular volume. The best means of assessing and monitoring intravascular volume in these patients is by hemodynamic measurements through the pulmonary artery catheter. However, in the presence of left ventricular dysfunction, the usual pressure criteria used to assess intravascular volume do not apply. The optimal left ventricular diastolic filling pressure, as estimated by the pulmonary artery occlusive (wedge) pressure (or pulmonary artery diastolic pressure when comparable), for most patients with shock or near shock secondary to acute myocardial infarction resides between 14 to 18 mm Hg (16).

2. Status of patient's ventricular function. Transthoracic Doppler–two dimensional echocardiography is helpful in assessing the status of ventricular function and guiding additional studies and interventions. The finding of segmental hypokinesia or akinesia suggests the presence of occlusive coronary artery disease, although similar findings may occur in some patients with acute myocarditis or idiopathic dilated cardiomyopathy. Global left ventricular enlargement and dysfunction generally indicate a more diffuse or chronic process.

The thermodilution pulmonary artery catheter can provide diagnostic information and a general functional assessment of ventricular and overall cardiovascular performance. Depressed stroke volume in the setting of elevated pulmonary artery occlusive (wedge) pressure generally indicates a significant reduction in left ventricular function. Elevated V (systolic) waves in the wedge position suggest the presence of mitral regurgitation, although the absence of elevated V waves does not exclude mitral regurgitation. Significant oxygen desaturation in mixed venous blood drawn from the pulmonary artery indicates depressed systemic oxygen delivery.

3. Existence of myocardial injury/infarction. Emergency cardiac catheterization and selective coronary arteriography should be considered in the patient with cardiogenic shock or near shock and ECG evidence of acute myocardial injury/infarction (3,17–19). Reperfusion of the injured/infarcted region of the acutely occluded coronary artery in patients with shock not responding to fluid administration has been reported (20) to reduce the mortality rate from <85% to ≤60%. Ideally, the patient is transferred to the catheterization laboratory shortly after initial stabilization. In patients in near shock/shock who do not respond to fluid administration and cannot undergo catheterization–intervention expeditiously, thrombolytic therapy should be considered. Admittedly the effect of thrombolytic therapy on mortality under these conditions is unclear.

4. Are correctable, mechanical lesions present? Clinical evaluation and transthoracic Doppler–two dimensional echocardiography are the primary methods to diagnose or exclude most of these lesions initially. The most commonly encountered potentially reversible defects in this clinical setting are pericardial tamponade; massive pulmonary embolism; rupture of chordae tendinae, papillary muscle or ventricular septum; critical valvular stenosis or acute regurgitation; aortic dissection with complicating lesions (e.g., acute coronary occlusion, acute aortic valvular regurgitation); acute obstruction or incompetency of a prosthetic heart valve; and cardiac tumors. Additional diagnostic testing, such as transesophageal echocardiography and cardiac catheterization may be necessary to more precisely define the lesion(s) and disease process before definitive surgical intervention.

Initial Diagnostic Evaluation of Cardiogenic Shock/Near Shock

Class I

1. Focused history–physical examination

2. Twelve-lead ECG (plus occasional right-sided leads)

3. Continuous ECG monitoring

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4. Blood–serum studies: complete blood count, platelet count, clotting studies, electrolytes, BUN, creatinine, glucose and cardiac and liver enzymes

5. Arterial blood gases and lactate concentration

6. Chest radiograph

7. Transthoracic Doppler–two dimensional echocardiography

8. Indwelling arterial cannula for continuous monitoring of systemic blood pressure and for arterial blood gas sampling

9. Tabulation of fluid volume intake, urine output and other fluid volume loss

10. Cardiac catheterization/coronary arteriography if acute revascularization for acute myocardial injury/infarction is anticipated

Class II

Transesophageal echocardiography

Class III

Extensive evaluation in a patient with a concomitant terminal illness or who is not a candidate for cardiovascular intervention

Therapeutic Management of Cardiogenic Shock/Near Shock

Class I

1. Oxygen therapy

2. In the absence of obvious intravascular volume overload, brisk intravenous administration of fluid volume

3. In the presence of intravascular volume overload or after adequate intravenous fluid volume therapy, intravenous administration of cardiovascular support drugs (e.g., dopamine, dobutamine, norepinephrine) to attain and maintain stable clinical–hemodynamic status

4. Urgent coronary artery revascularization for acute myocardial injury/infarction, if readily available

Class II

1. Thrombolytic therapy in the setting of acute myocardial injury/infarction if a cardiac catheterization/coronary arteriography/revascularization procedure is not readily available

2. Ventricular assist device in patients who respond inadequately to the aforementioned interventions and who are reasonable candidates for heart transplantation

Class III

Extensive evaluation and major intervention in patients with a concomitant terminal illness, those afflicted with an irreversible underlying cause or those who are not candidates for corrective intervention or heart transplantation

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Acute Decompensation of Chronic Congestive Heart Failure

The general principles of management for this group of patients are clinical and hemodynamic stabilization, diagnostic studies for reversible precipitating factor(s) and optimization of long-term therapy.

The clinical manifestations of this group of patients generally are secondary to volume overload, elevated ventricular filling pressures and depressed cardiac output.

Mild to moderate symptoms can be treated effectively with intravenously or orally administered diuretic drugs and reinstitution or optimization, or both, of the patients' long-term therapy for chronic heart failure. Unless the presentation is complicated by a precipitating factor (e.g., recent myocardial infarction) or a concurrent threatening condition (e.g., marked hypokalemia, moderate to marked azotemia, symptomatic arrhythmias), many of these patients do not require urgent hospital admission beyond several hours of observation in an emergency room or outpatient facility.

Moderate to severe symptoms usually require hospital admission, generally in a cardiac or intensive care unit. The diagnostic and therapeutic approach is similar to that for patients presenting with acute heart failure. Once symptoms at rest are largely alleviated, and reasonable clinical and hemodynamic stability is achieved for ≥ 24 h, any intravenously administered cardiovascular support drugs can be withdrawn (usually in a decremental manner) while orally administered long-term heart failure therapy is optimized.

The underlying cardiac diagnosis has been established for the majority of patients in this group, and the precipitating factors usually can be ascertained by history, physical examination, electrocardiography, serial cardiac enzyme level determinations, an echocardiogram and selected laboratory testing. Extensive diagnostic evaluation is generally not necessary if correctable causes of heart failure have been excluded previously.

Recommendations for Intraaortic Balloon Counterpulsation in Heart Failure

Class I

1. Cardiogenic shock, pulmonary edema and other acute heart failure conditions not responding to the proper administration of fluid volume or pharmacologic therapy, or both, in patients with potentially reversible heart failure or as a bridge to heart transplantation

2. Acute heart failure accompanied by refractory ischemia, in preparation for cardiac catheterization/coronary arteriography and definitive intervention

3. Acute heart failure complicated by significant mitral regurgitation or rupture of the ventricular septum; to obtain hemodynamic stabilization for definitive diagnostic studies or intervention, or both

Class II

Progressive, chronic heart failure if necessary to allow for a proper diagnostic approach, time to consider treatment options and definitive intervention (e.g., cardiac surgery, heart transplantation).

Class III

1. Significant aortic insufficiency

2. Aortic dissection

3. Patients unresponsive to therapy in whom the cause is known to be uncorrectable or irreversible and who are not candidates for transplantation

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4. Patients in the end-stage of a terminal illness

5. Bleeding diathesis or severe thrombocytopenia

Recommendations for Placement of Pulmonary Artery Balloon Catheter in Heart Failure

Class I

1. Cardiogenic shock or near shock that does not respond promptly to the proper administration of fluid volume

2. Acute pulmonary edema that does not respond to appropriate intervention or is complicated by systemic hypotension or shock/near shock

3. As a diagnostic tool to resolve any uncertainty of whether pulmonary edema is cardiogenic or noncardiogenic in origin

Class II

1. Assessment of the status of intravascular volume, ventricular filling pressures and overall cardiac function in a patient whose decompensated chronic heart failure is not responding appropriately to standard therapy

2. Evaluation of overall cardiac–hemodynamic status and exclusion of left heart failure in a patient with decompensated chronic lung disease

3. As a diagnostic tool to assess the origin and clinical and hemodynamic significance of a new systolic murmur in acute heart failure

Class III

As a routine approach to the assessment, diagnosis or treatment of heart failure

Summary

Patients presenting with acute heart failure usually should be admitted to the hospital. Initial diagnostic testing for patients with acute heart failure should be limited to those tests necessary to exclude etiologies requiring special therapeutic procedures. Further diagnostic testing generally can be deferred until hemodynamic stability and improvement have been attained.

Initial laboratory testing generally can be limited to CBC, urinalysis, serum electrolytes, creatinine, cardiac enzymes, blood urea nitrogen, arterial gases and pH, ECG, chest radiograph, and transthoracic Doppler–two dimensional echocardiography.

Patients with acute heart failure and evidence of acute myocardial injury/infarction should be considered for urgent cardiac catheterization, coronary arteriography and definitive interventional procedures. Thrombolysis should be considered if these studies cannot be done expeditiously.

Treatment of acute cardiogenic pulmonary edema consists initially of intravenous diuretic drugs, nitrates, oxygen and morphine. Intubation and mechanical ventilation are of value in selected patients.

Patients with cardiogenic shock who do not have evidence of volume overload should receive a rapid infusion of intravenous fluids initially and the response observed.

Patients with cardiogenic shock unresponsive to fluid administration or who have obvious volume overload should

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be given intravenous dopamine initially.

A pulmonary artery balloon flotation catheter should be inserted in all patients with cardiogenic shock unless there is rapid response to fluid administration. Patients with acute cardiogenic pulmonary edema generally do not require a pulmonary artery catheter. However, catheter insertion is indicated in those not responding appropriately to therapy or those in whom it is unclear whether the pulmonary edema is due to cardiac or noncardiac causes.

Intraaortic balloon counterpulsation may be indicated in patients with acute heart failure not responding adequately to therapy. The device is particularly helpful in attaining hemodynamic improvement and stability while awaiting additional diagnostic or therapeutic interventions.

Chronic and Stabilized Acute Heart Failure in Adults

Systolic Dysfunction: Evaluation

All patients presenting with chronic heart failure should undergo a diagnostic evaluation that should be limited initially to those studies necessary to 1) determine the type of cardiac dysfunction, 2) uncover correctable etiologic factors, 3) determine prognosis, and 4) guide treatment. A similar approach should be applied to patients with acute failure if not adequately evaluated during the stabilization phase. Transthoracic Doppler–two dimensional echocardiography is of particular benefit in the initial evaluation of patients with heart failure to specifically assess ventricular mass, chamber size and systolic and diastolic function and to search for causes best treated by specific therapy (e.g. aortic stenosis, segmental systolic contraction abnormalities suggestive of occlusive coronary artery disease). Magnetic resonance imaging (MRI) is a promising diagnostic tool to assess ventricular function and mass and to detect structural abnormalities. However, the cost-effectiveness of MRI in relation to other more readily available diagnostic modalities has not been adequately evaluated.

The most commonly identified causes of left ventricular systolic dysfunction in the United States are coronary artery disease, hypertension and idiopathic dilated cardiomyopathy (21). As the available treatment modalities for hypertension have improved, and large-scale detection programs have resulted in wider application of aggressive treatment to the general population, ischemic heart disease has become the most common cause of heart failure in adults (22).

The combination of ischemia and left ventricular dysfunction (with or without overt clinical heart failure) carries a poor prognosis, and it is this subset which stands to gain the greatest benefit from revascularization (5). In some patients with coronary artery disease, left ventricular systolic dysfunction may reflect the reversible effects of intermittent or prolonged ischemia ("myocardial stunning" or "hibernation"). For example, survivors of a myocardial infarction may show evidence of "hibernating" myocardium, that is, hypokinetic, hypoperfused myocardial areas that are still viable and improve after reperfusion. Even patients with very severe left ventricular dysfunction (ejection fraction <15% to 20%) may show significant improvement in ejection fraction and functional state after revascularization of hibernating myocardium (23).

Patients with angina and moderate to severe left ventricular systolic dysfunction, including those with congestive heart failure have been shown to have improved survival after coronary bypass surgery (24). Based on these data, coronary arteriography should be strongly considered in patients with coexistent angina and congestive heart failure to assess suitability for coronary revascularization.

Patients with prior myocardial infarction and congestive heart failure but without angina are commonly evaluated with noninvasive testing to detect ischemia or hibernating myocardium or with coronary arteriography to document the extent of coronary artery disease. However, coronary revascularization has not been shown (24) to improve survival in patients with coronary artery disease and heart failure without angina, although regional ventricular function may improve. Although there is a strong pathophysiologic basis to anticipate that patients with evidence of extensive myocardial ischemia or large areas of hibernating myocardium would benefit from coronary revascularization, there are no data from randomized trials directly relevant to patients with heart failure. Analysis

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of observational data suggests that the potential benefit of coronary revascularization is directly proportional to the extent of ischemic but noninfarcted myocardium that can be revascularized.

In the absence of angina or prior myocardial infarction, the probability of coronary artery disease as the cause of heart failure varies considerably among patients. After clinical assessment, the physician properly may elect to 1) not pursue further testing for coronary disease, 2) use noninvasive tests to detect myocardial ischemia, or 3) perform coronary arteriography. There are insufficient data at present to evaluate the relative efficacy of these alternative approaches. However, a more aggressive diagnostic approach can be justified as the probability of coronary artery disease increases (e.g., in patients with multiple risk factors or regional wall abnormalities on echocardiography).

Several noninvasive tests are available to detect ischemic or hibernating myocardium. Guidelines for the use of radionuclide imaging to detect these conditions have been published recently(25). The "gold standard" for the identification of myocardial viability is positron emission tomography, which is costly and not generally available. However, quantitative thallium scintigraphy using exercise with late redistribution or reinjection at rest imaging as well as rest–redistribution imaging may provide most of the clinically relevant information regarding viable myocardium in patients with left ventricular dysfunction. Technetium-99m sestamibi is of value in measuring ventricular function and detecting ischemia but appears to be of lesser value in assessing myocardial viability. Pharmacologic means for inducing "ischemia," such as the use of dipyridamole, dobutamine or adenosine, are useful in patients who cannot exercise. Stress echocardiography using exercise or dobutamine is an alternate approach for detecting ischemia (26), as is dobutamine echocardiography for assessing myocardial viability(27).

Patients whose heart failure cannot clearly be attributed to hypertension or coronary artery disease should undergo a diligent evaluation for other specific etiologies; the designation "idiopathic dilated cardiomyopathy" should only be applied as a diagnosis of exclusion after an appropriate evaluation has been completed. Table 1 presents a partial list of specific but less common etiologies of dilated cardiomyopathy; clinical features of these disorders have been reviewed extensively elsewhere(28,29). However, clinical judgment is called for when determining the extent to which other diagnoses should be pursued. There is usually little justification for aggressively pursuing conditions whose incidence is exceedingly low or for which there is no specific treatment unless there are other specific justifications for determining precise etiology (e.g., candidacy for transplantation). The diagnostic pursuit of such conditions should be based on a high index of suspicion raised by other clinical or laboratory findings.

Table 1. Less Common Causes of Left Ventricular Systolic Dysfunction

Infectious agents: viral, bacterial, fungal
Acute rheumatic fever
Infilrative disorders: amyloid, hemochromatosis, sarcoid
Toxic: heroin, cocaine, alcohol, amphetamines, adriamycin, cyclosphamide, sulfonamides, lead, arsenic, cobalt, phosphorus, ethylene glycol
Nutritional deficiencies: protein, thiamine, selenium
Electrolyte disorders: hypocalcemia, hyposphosphatemia, yponatremia, hypokalemia
Collagen vascular disorders: diabetes, thyroid disease(both hypo- and hyper-), hypoparathyroidism with hypocalcemia, pheochromocytoma, acromegaly
Tachycardia induced: incessant supraventricular tachyarrhythmias or atrial fibrillation with rapid ventricular rates
Miscellaneous: hyperreosinophilic syndrome, peripartum cardiomyopathy, sleep apnea syndrome, Whipple's disease, L-carnitine deficiency

Myocarditis frequently is considered in those with unexplained heart failure, particularly if the patients are young and the failure of acute onset. However myocarditis is an uncommon cause of heart failure. Infectious agents may cause heart failure by their direct effects on myocardial tissue or by triggering an immune response that presents as an acute inflammatory myocarditis or as a delayed response causing late, slowly progressively dysfunction. Myocarditis (often with pericarditis) usually is a mild, self-limited disease in which cardiac dysfunction is completely reversible. Fulminant myocarditis with progressive, irreversible heart failure as an immediate and direct result of viral infection is relatively rare.

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Efforts to develop noninvasive methods to screen heart failure patients for acute myocarditis have not been successful. A variety of radionuclide techniques have been proposed but either remain investigational or lack the sensitivity and specificity to be clinically useful (25). Similarly, increasing serum titers of antibody to a specific viral agent may provide circumstantial evidence for acute viral myocarditis but are of little help clinically. Biopsy evidence of significant inflammation and myocardial necrosis is required to prove the diagnosis of acute myocarditis. When strict histologic criteria for active myocarditis are applied (30), the yield is low (≤10%) among patients with systolic dysfunction and congestive heart failure of recent onset (31,32). Most important, the recently reported Myocarditis Treatment Trial (32) found no beneficial effect of prednisone with either azathioprine or cyclosporine in patients with biopsy-proven lymphocytic myocarditis. However, as the investigators note, the study does not exclude a beneficial effect of other immunosupressive regimens or therapies in other forms of myocarditis or at other stages of the disease process.

Recommended Routine Diagnostic Studies for Adult Patients With Chronic Heart Failure or Stabilized Acute Heart Failure Not Previously Performed

Class I

1. CBC and urinalysis

2. Blood–serum: electrolytes, BUN, creatinine, glucose, phosphorus, magnesium, calcium and albumin levels

3. Thyroid-stimulating hormone levels in patients with atrial fibrillation and unexplained heart failure

4. Chest radiograph and ECG

5. Transthoracic Doppler–two dimensional echocardiography

6. Noninvasive stress testing to detect ischemia in patients without angina but with a high probability of coronary artery disease who would be candidates for revascularization

7. Noninvasive testing to detect ischemia and assess myocardial viability or coronary arteriography in patients with a previous infarction but with no angina who would be candidates for revascularization

8. Cardiac catheterization/coronary arteriography in patients with angina or large areas of ischemic or hibernating myocardium; also in patients at risk for coronary artery disease who are to undergo surgical correction of noncoronary cardiac lesions

Class II

1. Serum iron and ferritin

2. Noninvasive stress testing to detect ischemia in all patients with unexplained heart failure who are potential candidates for revascularization

3. Coronary arteriography in all patients with unexplained heart failure who are potential candidates for revascularization

4. Endomyocardial biopsy in patients a) with recent onset of rapidly deteriorating cardiac function or other clinical indications of myocarditis; b) receiving chemotherapy with adriamycin or similar myocardial toxic agents; c) with a systemic disease and possible cardiac involvement (hemochromatosis, sarcoid, amyloid, Loeffler's endocarditis, endomyocardial fibroelastosis

5. Thyroid-stimulating hormone levels in patients with sinus rhythm and unexplained heart failure

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Class III

1. Repeat cardiac catheterization/coronary arteriography or stress testing in patients in whom coronary artery disease as a cause of left ventricular dysfunction has been excluded previously and no objective evidence of intercurrent ischemia or infarction has occurred

2. Endomyocardial biopsy in the routine evaluation of patients with chronic heart failure

3. Multiple echocardiographic or radionuclide studies in the routine follow-up of patients with heart failure responding to therapy

4. Routine Holter monitoring or signal-averaged electrocardiography

5. Cardiac catheterization/coronary arteriography in patients who are not candidates for revascularization, valve surgery or heart transplantation

Diastolic Dysfunction: Evaluation

The majority of patients presenting with heart failure have reduced left ventricular systolic function and variable degrees of diastolic dysfunction. However, a significant subset (30% in some series) have normal or near-normal rest systolic function and predominantly diastolic dysfunction. The management of patients with primarily systolic or diastolic dysfunction is very different, and it is critical to make the distinction. A review of diastolic dysfunction has been published recently (33).

Diastolic dysfunction impairs ventricular filling by diminishing relaxation (during early diastole) or reducing compliance (early to late diastole) of the ventricle, or both. The hemodynamic consequences include elevation of ventricular filling, left atrial, pulmonary venous and pulmonary capillary pressures, and if uncorrected, an eventual increase in pulmonary artery and right heart pressures. The elevated filling pressure is frequently sufficient to maintain a normal stroke volume and cardiac output at rest, but the latter often are compromised in situations that require an increase in cardiac output (e.g., exercise).

Myocardial ischemia, hypertrophy and fibrosis are the usual underlying pathologic processes for ventricular diastolic dysfunction, and the most common etiologies include coronary artery disease, systemic hypertension, diabetes mellitus, aortic stenosis, hypertrophic cardiomyopathy, infiltrative cardiomyopathies and endocardial fibroelastosis. Decreased ventricular compliance also occurs as part of the normal aging process.

Clinical manifestations can range from no symptoms to dyspnea, pulmonary edema, signs of right heart failure and exercise intolerance. Whereas diastolic dysfunction usually presents as a chronic condition, acute diastolic dysfunction producing acute pulmonary edema is not an uncommon manifestation of acute myocardial ischemia or uncontrolled hypertension.

Diastolic dysfunction should be suspected when a patient presents with symptoms and signs of congestive heart failure and has normal or near-normal ventricular systolic function. Doppler echocardiography or radionuclide imaging is of value in assessing systolic function and detecting diastolic dysfunction; the latter by measuring indexes of the rate of diastolic filling. Alternatively, cardiac catheterization may be used and may be of particular value when noninvasive studies are nondiagnostic. Unless another diagnosis has been established, most of these patients should be evaluated for underlying coronary artery disease and myocardial ischemia. Noninvasive testing to detect coronary artery disease may be used as in patients with systolic dysfunction. Alternatively, one could proceed directly to cardiac catheterization/coronary arteriography 1) when there is a high suspicion of occlusive coronary artery disease as the cause of the diastolic heart failure (e.g., presence of angina or previous myocardial infarction) and is potentially treatable by revascularization; 2) when the possibility of occlusive coronary artery disease cannot be reliably or safely assessed by other methods; and 3) when a patient with two or more risk factors for coronary atherosclerosis is slated to undergo cardiac surgery for what is believed to be the primary cause of the

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diastolic heart failure (e.g., aortic stenosis). Constrictive pericarditis, a surgically treatable condition, must be excluded in patients whose diastolic dysfunction appears to be secondary to a restrictive cardiomyopathy; in this setting, echocardiography, computerized tomography or MRI or the finding of significant myocardial pathology by endomyocardial biopsy (e.g., myocardial amyloidosis, hemochromatosis) can be very helpful in guiding management.

Assessment of Neurohormonal Activity in Heart Failure

A variety of endogenous neurohormonal systems are activated in patients with chronic heart failure, and such activation may play a role in the pathophysiology of the disease. Among the most important of these neurohormonal derangements is the activation of the sympathetic nervous system and the renin–angiotensin system. The sympathetic nervous system is activated early in the disease process, and its activity may be increased even in patients with asymptomatic left ventricular dysfunction. The renin–angiotensin system appears to be activated later in the disease process (once diuretic therapy has been initiated), and its activity is markedly enhanced in patients with advanced symptoms (particularly those with renal hypoperfusion). Other vasoconstrictor hormonal factors that appear to be increased in heart failure include endothelin and vasopressin. In addition to the activation of the vasoconstrictor hormonal system, the activity of several hormonal systems with vasodilator activity is also altered in patients with chronic heart failure.

Experimental and clinical observations suggest that neurohormonal activation plays an important role in the development and progression of heart failure. These hormonal systems exert hemodynamic effects that can alter cardiac function; prolonged activation may also exert direct deleterious effects on cardiac muscle cells. Such actions have led to the development of therapeutic interventions designed to block the effects of endogenous vasoconstrictor systems as well as enhance the effects of endogenous vasodilator systems. The clinical utility of many of these interventions (e.g., angiotensin converting-enzyme inhibitors and beta-adrenergic blocking agents in selected patients) is well established, whereas the efficacy of others (e.g., vasopressin antagonists and endothelin antagonists) is still under investigation.

Despite their pathophysiologic and therapeutic importance, there is little reason to measure circulating hormonal factors in patients with heart failure to guide routine clinical care. Although such measurements are useful in the setting of a research study, there is little evidence that such measurements assist in the routine assessment and management of patients. Furthermore, such measurements have not been shown to guide the rational selection of a specific therapeutic intervention in patients with heart failure.

Assessment of Functional Capacity

Assessment of functional capacity in patients with congestive heart failure is important, for functional capacity has a direct impact on patient well-being and quality of life. Improvement of functional capacity is therefore a major goal of therapy in patients with heart failure. Also, functional capacity is a predictor of mortality in patients with heart failure, even after controlling for the prognostic information contained in various laboratory tests. Risk assessment of patients is essential to the choice of therapy, particularly surgical approaches.

Functional assessment of the patient encompasses several dimensions, including physical capacity, emotional status, social function and cognitive capabilities. Assessment of physical function is most important, but the other dimensions are also relevant. Emotional, social and cognitive factors may have a strong effect on the patients' capacity to adhere or respond to a therapeutic regimen and may be adversely affected by the underlying disease or its treatment. Clinical assessment of these dimensions, especially depression, social support and cognitive capability, should be performed regularly. The established standard for assessment of physical capacity is the exercise test, particularly measurements of exercise time or distance, peak work load and maximal oxygen consumption. These measures can be assessed using a treadmill exercise test and have the advantage of objectivity. However, these tests are relatively expensive and carry a small risk.

Inquiring about the patient's tolerance for common daily activities can provide an alternative method for

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assessment of functional capacity. Because patients may gradually restrict their activities to avoid symptoms, it is preferable to inquire about tolerance for well defined activities (e.g., walking 100 ft [90 m] on level ground, climbing one or two flights of stairs).

Recommendations for Assessment of Functional Capacity in Heart Failure

Class I

1. Patient interview or questionnaire at each clinic visit

2. Exercise testing, usually with respiratory gas analysis, to determine potential candidacy for heart transplantation

Class II

1. Exercise testing to more definitively assess functional capacity and symptomatic limitations in patients in whom a disparity exists between symptoms expressed and clinical assessment

2. Exercise testing to address specific clinical questions and issues. Examples include ventricular rate changes and control during atrial fibrillation or after pacemaker placement, blood pressure control in a patient with heart failure with a history of hypertension, exercise-induced arrhythmias, quantitative evaluation of degree of disability and assessing a change in functional capacity or response to therapy

Class III

Exercise testing as a routine, serially performed procedure to follow chronic ventricular dysfunction that is clinically stable unless used to assess candidacy Table 1

Summary

Patients presenting with chronic heart failure and those patients with acute heart failure in whom the cause was not established during the stabilization period should undergo diagnostic testing to determine the etiology.

Heart failure due to diastolic dysfunction must be differentiated from that due to systolic dysfunction. This can be done by transthoracic Doppler–two dimensional echocardiography, radionuclide imaging or cardiac catheterization.

Coronary artery disease must be excluded as the causal factor in patients with heart failure., Patients with angina should undergo cardiac catheterization and coronary arteriography if they are otherwise candidates for interventional procedures., Opinion is divided as to the proper approach to patients with known coronary artery disease and heart failure but without angina. Either coronary arteriography or noninvasive testing with coronary arteriography limited to patients demonstrating ischemia or hibernating myocardium may be considered., The approach to other patients with heart failure will depend in great part on the probability of coronary artery disease as the cause of heart failure. For patients with a high probability, such as those with multiple risk factors, a more aggressive diagnostic approach may be indicated, whereas in patients with a low probability, neither coronary angiography nor stress testing may be necessary.

Myocarditis is a rare cause of rapidly progressive heart failure and requires myocardial biopsy to establish the diagnosis; there is no evidence that immunosuppressive therapy is beneficial

Measurement of circulating neurohormone levels is of little value in the routine assessment and management of patients with heart failure

Ongoing assessment of functional capacity plays an important role in the management of patients with heart failure and should include physical capacity, emotional status, social function and cognitive abilities

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Systolic Dysfunction: Therapy

The treatment of chronic heart failure has changed remarkably in the past 10 to 15 years. Heart failure is no longer considered a simple edematous state that is responsive to intermittent diuretic therapy. Many if not most patients are now nonedematous, but the condition is still disabling and lethal. Fortunately, a number of important clinical trials have led to substantial improvement in the treatment of patients with New York Heart Association functional class I to IV heart failure due to systolic dysfunction(22,34–41).

Functional class I. Patients with functional class I status have left ventricular systolic dysfunction but manifest no or minimal overt signs or symptoms of heart failure. In many cases, patients in functional class I have previously been symptomatic with heart failure but have become well compensated despite residual left ventricular systolic dysfunction. In other cases, patients may have sustained left ventricular damage as a result of myocardial infarction, onset of dilated cardiomyopathy or some other progressive disease process compromising left ventricular systolic function but remain asymptomatic or very minimally symptomatic.

Because patients in functional class I with left ventricular systolic dysfunction are asymptomatic or minimally symptomatic, pharmacologic therapy often is not prescribed. However, angiotensin-converting enzyme (ACE) inhibitor therapy is appropriate for patients in functional class I as a means of preventing heart failure(37) and may reduce mortality after acute myocardial infarction(38). In the Studies of Left Ventricular Dysfunction (SOLVD) prevention trial (37), enalapril significantly reduced the incidence of heart failure and the rate of related hospital admissions compared with that for placebo (37). In the Survival and Ventricular Enlargement (SAVE) trial(38), patients with ejection fractions ≤0.40 but without overt heart failure or myocardial ischemia 3 to 16 days (average 11 days) after myocardial infarction derived a 19% overall reduction in the risk of death from all causes ($p = 0.019$) when treated with long-term captopril for an average of 42 months. In the Gruppo Italiano per lo Studio della Sopravvienza nell'Infarto Miocardico (GISSI)-III(39) and International Study of Infarct Survival (ISIS) IV(40) trials, oral ACE inhibitor therapy begun within the first 24 h in patients with an acute myocardial infarction was also beneficial in patients with and without heart failure. However, the use of intravenous enalaprilat in the first 24 h of an acute infarction followed by oral enalapril offered no survival advantage over placebo in the Cooperative New Scandinavian Enalapril Survival Study (CONSENSUS) II trial(41), and the use of intravenous ACE inhibitors after acute myocardial infarction is not recommended. On the basis of these studies, oral ACE inhibitors should be given to all patients in functional class I with significant left ventricular systolic dysfunction (ejection fraction <35% to 40%).

Contraindications to a trial of ACE inhibitors include shock, angioneurotic edema or significant hyperkalemia. Asymptomatic hypotension (i.e., systolic blood pressure 70 to 90 mm Hg) is not a contraindication to ACE inhibitor therapy, but clinical judgment must always govern therapeutic decisions. Dosing is very important, and lower doses should be used initially and gradually increased. Enalapril should be started at 2.5 mg twice daily and titrated to 10 mg twice daily, whereas captopril should be begun at 6.25 or 12.5 mg three times a day, and gradually (over weeks) titrated to 50 mg three times a day. The larger doses are those shown to be effective in reducing mortality in large-scale studies.

Because patients in functional class I rarely retain fluid or become edematous, sodium restriction and diuretic drugs may not be uniformly indicated. Additionally, patients in functional class I may have pedal edema from a variety of causes unrelated to heart failure. When a diuretic drug is necessary because of peripheral edema or mild jugular venous distension despite sodium restriction, nonloop diuretic drugs, such as hydrochlorothiazide or chlorthalidone, may suffice. Overzealous treatment with diuretic drugs may reduce plasma volume, cardiac output and blood pressure, thus stimulating neuroendocrine activation(42–44). Therefore, for the patient in functional class I, it is prudent to withhold diuretic therapy unless there is clear evidence of salt and water retention despite a low sodium diet.

Functional classes II to IV. Reports of the SOLVD (22), Veterans Administration Cooperative Vasodilator Heart Failure Trial (V-HeFT) II(35) and Cooperative North Scandinavian Enalapril Survival Study CONSENSUS (36) trials support the use of ACE inhibitors in all patients with symptomatic heart failure, unless the inhibitors are contraindicated or not tolerated. If possible, the dose should gradually be increased to that shown to reduce

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mortality in these trials (i.e., 20 mg of enalapril or 150 mg of captopril daily). Lisinopril (5 to 20 mg/day) and quinapril (5 mg twice daily) have also been approved for the treatment of heart failure. These latter drugs have been shown to improve exercise tolerance and symptoms. In addition, in the Acute Infarction Ramipril Efficacy (AIRE) study (45), ramipril (5 mg twice daily) also reduced mortality when begun between 3 and 10 days after an acute myocardial infarction in patients with heart failure. There are insufficient data regarding the effect of lower doses and alternative ACE inhibitors on mortality in patients with heart failure. Once a patient has begun ACE inhibitor therapy, the drug should be prescribed for an indefinite period of time, probably for life if well tolerated.

Data from V-HeFT I (34) and II (35) established a role for isosorbide dinitrate and hydralazine for patients with functional class II and III heart failure. Although ACE inhibitors are the cornerstone of treatment for heart failure, isosorbide dinitrate and hydralazine should be considered when ACE inhibitors are not tolerated because of symptomatic hypotension, azotemia, hyperkalemia, cough, rash or angioneurotic edema. Isosorbide dinitrate (5 to 10 mg three times a day) and hydralazine (10 mg four times a day) should be the initial doses. If tolerated, hydralazine should be increased gradually to 75 mg four times a day and isosorbide dinitrate to 40 mg three times a day. A minimal 10-h "nitrate-free" period at night usually should be achieved to avoid nitrate tolerance. Occasionally, hydralazine and isosorbide dinitrate are added to an ACE inhibitor when symptoms of dyspnea or fatigue persist, but data to support this combination are scanty.

Patients with symptomatic heart failure are more likely to retain sodium, and a diuretic drug usually is indicated (46). Initiating diuretic therapy is highly individualized. Many physicians begin with a thiazide diuretic drug, but reduced renal perfusion may ultimately favor the use of a loop diuretic such as furosemide or bumetanide. Thiazide diuretic drugs are of less value if the glomerular filtration rate (GFR) is <30 to 40 ml/min and may actually reduce this rate further. Patients should be advised to weigh themselves daily and keep a log of their weight. An increase of 1 or 2 kg may be an indication to supplement the maintenance diuretic dose. For example, 2.5 mg of metolazone may be added for 2 or 3 days to the loop diuretic drug, followed by a return to the usual maintenance dose of loop diuretic drug when the weight stabilizes.

Eliminating the salt shaker at the table, salt in the cooking and the institution of a low sodium diet should be introduced progressively into the therapeutic program, depending on the clinical circumstances. Sodium restriction becomes a critical strategy in the treatment of heart failure as the disorder progresses, and its importance cannot be overstated. Sodium intake should be limited to ≤2 g/day before one resorts to large doses or multiple diuretic drugs.

When diuretic drug resistance develops, using a combination of diuretic drugs that act in different nephron segments (i.e., thiazide or metolazone plus a loop diuretic drug) is often effective (47,48). Severe electrolyte and volume depletion can occur when metolazone is combined with a loop diuretic drug (48), and hospital admission may be warranted in some circumstances (i.e., in the presence of hypotension, azotemia, oliguria or ascites). Careful patient and laboratory monitoring is necessary when these diuretic drugs are combined. An increase in BUN, particularly when disproportionate to serum creatinine levels, is usually corrected by reducing the diuretic dose and is not necessarily an indication to reduce or stop the ACE inhibitor. Under most circumstances, a mild increase in BUN or serum creatinine levels is well tolerated without discontinuation of the diuretic drug or ACE inhibitor. Patients with truly refractory or resistant sodium retention and heart failure may require hospital admission to receive intravenous dobutamine (2 to 5 µg/kg body weight per min), dopamine (1 to 3 µg/kg per min) or a constant infusion of furosemide (1 to 5 mg/h). Fluid restriction to 1,000 to 2,000 ml/day is of value in patients with dilutional hyponatremia.

Hypokalemia and contraction alkalosis are frequent accompaniments of vigorous diuretic drug use. Because ventricular arrhythmias occur in the majority of patients with heart failure and are aggravated by hypokalemia, potassium must be replaced or hypokalemia prevented. Potassium chloride is frequently required in doses of 20 to 60 mEq/day to maintain serum potassium in the 4.5- to 5.0-mEq/liter range. Dietary supplementation of potassium is rarely sufficient. Alternatively, potassium-sparing agents, such as amiloride, triamterene or spironolactone, can be used to maintain sufficient serum potassium levels. Dangerous hyperkalemia may occur when ACE inhibitors are used in combination with potassium-sparing agents or large doses of oral potassium, and serum potassium levels must be carefully monitored. Hyperkalemia and sodium retention are particularly common

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when nonsteroidal anti-inflammatory agents are used in patients with severe heart failure. In general, nonsteroidal anti-inflammatory agents should be avoided in patients with heart failure. Hypomagnesemia (serum magnesium level <1.6 mEq/liter) should also be corrected when observed.

Digitalis glycosides have been used for >200 years to treat heart failure, yet controversy still persists regarding their use in patients with heart failure and normal sinus rhythm (49). The role of digoxin in patients with heart failure and atrial fibrillation is accepted, and recent studies (50–52) indicate that it is an effective therapeutic agent in many patients with symptomatic left ventricular systolic dysfunction and sinus rhythm. In double-blind placebo controlled trials, digoxin has been shown to increase left ventricular ejection fraction (53) and exercise tolerance (54) in patients with chronic heart failure. It may also reduce sympathetic activity as a major mechanism of action (55). Patients receiving long-term digoxin therapy with (56) or without (57) concomitant ACE inhibitor therapy may manifest clinical deterioration when digoxin is withdrawn. Digoxin has not been shown to be efficacious in asymptomatic patients with ventricular systolic dysfunction. Uncertainty regarding the use of digoxin derives primarily from the lack of data regarding its effect on mortality. To remedy this uncertainty, the National Heart, Lung, and Blood Institute and the Department of Veterans Affairs are currently conducting a large placebo-controlled clinical trial (DIG-Digitalis Investigator Group). This study of the effect of digoxin on survival in heart failure is scheduled to report its results in 1996. Until the results of the trial are released, controversy will persist regarding the appropriate role of digoxin in patients with heart failure who are in sinus rhythm.

Calcium channel blocking agents are sometimes used as antianginal therapy or antihypertensive agents in patients with angina or hypertension who have left ventricular dysfunction, but they may worsen heart failure (58–60). The risk of worsening heart failure also appears to accompany the use of newer agents in this class (e.g., felodipine [61]). As a result, physicians should not consider calcium channel blockers as safe or effective agents in the treatment of chronic heart failure. However, in the Prospective Randomized Amlodipine Survival Evaluation (PRAISE) trial (presented at the 44th Annual Scientific Session of the ACC), the administration of amlodipine in patients with heart failure was not accompanied by an adverse effect on morbidity or mortality; rather, the study reported a favorable effect of amlodipine on the survival of patients with nonischemic dilated cardiomyopathy. This preliminary finding is being further evaluated in a follow-up trial.

There has been considerable interest in the use of beta-adrenergic blocking agents in the treatment of chronic heart failure since early reports from Sweden (62) first suggested the possible usefulness of metoprolol in patients with dilated cardiomyopathy. Metoprolol was reported (62,63) to have beneficial clinical and hemodynamic effects, whereas withdrawal of the drug was associated with symptomatic deterioration. However, these studies were uncontrolled and, thus, difficult to interpret. Small, controlled clinical studies (usually of short duration) produced conflicting results (64–66).

More recently, beta-blockers with additional pharmacologic properties have been evaluated extensively in long-term placebo-controlled clinical trials of patients with chronic heart failure. Nebivolol and bucindolol, which have both beta-blocking activity and vasodilator properties, improve left ventricular performance during long-term therapy (67–69). Carvedilol, which also has combined beta-blocker and vasodilator activity, has been shown in several placebo-controlled studies to (70–72) improve left ventricular function, symptoms and submaximal exercise tolerance in patients with symptoms of wide-ranging severity.

In addition, several trials have suggested that long-term beta-blockade may reduce morbidity and mortality in patients with chronic heart failure. Beta-blockers have been shown (73) to reduce mortality in high risk patients after an acute myocardial infarction, including many patients with heart failure. The Metoprolol in Dilated Cardiomyopathy (MDC) trial (74) demonstrated that metoprolol reduces the combined risk of mortality and the need for heart transplantation in patients with idiopathic dilated cardiomyopathy. The Cardiac Insufficiency Bisoprolol Study (CIBIS) (75) showed a significant reduction in hospital adminssions for heart failure and a nonsignificant decrease in mortality, but the trial was too small to evaluate the effect of the drug on survival. Reportedly, carvedilol has been shown (76) to reduce mortality in a large-scale clinical trial program conducted in the United States that enrolled >1,000 patients. In that trial, the beneficial effect on mortality was seen in patients with functional class II and class III or IV symptoms as well as in patients with and without coronary artery disease. This effect also was accompanied by a significant decrease in the risk of hospital admissions for cardiovascular

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causes. Additional survival trials with beta-blockers are being planned or are in progress.

At the present time, the use of beta-blockers for the treatment of chronic heart failure remains investigational, but the official status of beta-blockers may change as recent data are reviewed. Hence, physicians might consider the use of a beta-blocker in selected patients with chronic heart failure. However, this approach should be taken only with considerable caution because the initiation of beta-blockade may exacerbate heart failure in some patients (72,75).

Anticoagulation with warfarin is frequently used for patients with chronic heart failure to prevent systemic embolization. This practice is based largely on retrospective analyses of referral populations (77). In V-HeFT II (78) there were only 46 clinical embolic events in 804 patients (5.7%) followed up for an average of 2.6 years. In the SOLVD trial (79), only 5.3% of patients experienced a clinical embolism during 39.2 months of follow-up. In an analysis of the major studies (80), the incidence of arterial thromboembolism ranged from 0.9 to 5.5 events/100 patient-years, with the largest studies reporting an incidence of 2.0% and 2.4%/100 patients-years. However, clinical embolic complications were linked to a low ejection fraction (77,78), and many physicians currently administer anticoagulation to patients with an ejection fraction <20% to 25%. Similarly, many physicians will administer anticoagulation in patients with left ventricular dysfunction and an intracardiac thrombus. However, the value of this approach is unclear, except in patients with thrombus after an acute infarction. Patients with atrial fibrillation should receive anticoagulation to achieve a target range of international normalized ratio of 2.0 to 3.0 (81). A recent report (82) suggests that the optimal range of anticoagulation for patients with a documented embolism should be 2.0 to 3.9. There are no controlled trials demonstrating the efficacy of routine anticoagulation in other patients with heart failure and normal sinus rhythm, and its use here is questionable.

Patients with heart failure and atrial fibrillation should have their ventricular rate controlled. Multiple drugs may be necessary, such as digoxin, diltiazem or a beta-blocker. Uncontrolled or new-onset atrial fibrillation can worsen heart failure or lead to decompensation. It is usually prudent to convert new-onset atrial fibrillation or atrial fibrillation of uncertain duration to normal sinus rhythm. In some cases amiodarone or occasionally catheter ablation or modification of the AV node may be necessary to prevent uncontrolled, rapid ventricular rates.

Ventricular arrhythmias are nearly omnipresent in patients with heart failure (83,84). Asymptomatic ventricular arrhythmias (including mild palpitations and nonsustained ventricular tachycardia) should not be treated because there currently are no data to support this strategy (85). Antiarrhythmic therapy can worsen ventricular arrhythmias and produce negative inotropic effects in patients with heart failure (86–88). Routine Holter monitoring and signal-averaged electrocardiography are not indicated but may be useful in patients with symptoms suggestive of arrhythmias. Patients with symptoms due to ventricular arrhythmias, bradyarrhythmias or cardiac syncope (89,90) (including those who survive a cardiac arrest) should be referred to a cardiac specialist for further evaluation.

When antiarrhythmic drugs are used in patients with heart failure, they ordinarily should be initiated in the hospital. Empiric use of type I antiarrhythmic drugs should be avoided for treatment of ventricular arrhythmias in patients with heart failure. There are several large clinical trials currently underway that are designed to assess the role of amiodarone and cardioverter-defibrillator devices as therapy for this important and complex problem. The recently completed Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA) trial (91) demonstrated an improvement in survival in patients with heart failure randomized to receive amiodarone. In contrast, the Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure (92) reported no improvement in survival nor a reduction in sudden deaths in patients with heart failure and asymptomatic ventricular arrhythmias treated with amiodarone. However, there was a trend toward improved survival in patients with nonischemic cardiomyopathy (92). Therefore, the empiric use of amiodarone for patients with heart failure needs further study.

When patients with chronic heart failure become refractory to therapy, hospital admission is usually indicated. This approach is particularly useful when symptoms are progressive, and large doses of oral diuretic drugs no longer achieve adequate diuresis. Short periods of bed rest alone may produce diuresis. A change from oral to intravenous diuretic drugs may also be useful (93). The use of dobutamine or phosphodiesterase inhibitors to temporarily improve cardiac output and renal blood flow is sometimes effective in lessening symptoms and relieving refractory salt and water retention. Low dose dobutamine (2 to 5 µg/kg per min) is frequently sufficient, whereas larger doses

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of dobutamine may produce tachycardia, ventricular arrhythmias, hypokalemia and myocardial ischemia. Alternatively, intravenous milrinone (50-µg/kg loading dose, then 0.375 to 0.75 µg/kg per min) may be used. Occasionally, patients may improve symptomatically as a result of long-term low dose dobutamine infusion (2 to 5 µg/kg per min) given through an indwelling central catheter on a long-term outpatient basis (94). Continuous outpatient therapy, with gradual weaning, is most useful in patients who cannot be weaned from inotropic therapy as an inpatient. Intermittent outpatient (or inpatient) therapy for 12 to 24 h at intervals is useful in patients who require repeated hospital admissions or emergency department visits for therapy of volume overload or symptoms of low cardiac output. However, the value of long-term low dose inotropic support in an outpatient setting remains uncertain. Furthermore, concerns have been raised about its safety in light of the increase in mortality reported with high dose outpatient dobutamine infusions (95) and long-term milrinone therapy (96).

Pharmacologic Treatment of Left Ventricular Systolic Dysfunction

Class I

1. ACE inhibitors for all patients with significantly reduced left ventricular ejection fraction unless contraindicated

2. Hydralazine and isosorbide dinitrate in patients who cannot take ACE inhibitors

3. Digoxin in patients with heart failure due to systolic dysfunction not adequately responsive to ACE inhibitors and diuretic drugs

4. Digoxin in patients with atrial fibrillation and rapid ventricular rates

5. Diuretic drugs for patients with fluid overload

6. Anticoagulation in patients with atrial fibrillation, or a previous history of systemic or pulmonary embolism

7. Beta-blockers for high risk patients after an acute myocardial infarction

Class II

1. Digoxin for all patients with heart failure due to left ventricular systolic dysfunction

2. Addition of hydralazine and isosorbide dinitrate for patients who do not respond adequately to ACE inhibitors

3. Beta-blockers for patients with dilated cardiomyopathy

4. Anticoagulation in patients in sinus rhythm with a very low ejection fraction or intracardiac thrombi

5. Outpatient low dose dobutamine infusion for refractory heart failure

Class III

1. Calcium channel blockers in the absence of coexistent angina or hypertension

2. Treatment of asymptomatic ventricular arrhythmias

Heart transplantation should be considered in patients with heart failure refractory to medical or surgical therapy. The reader is referred to two recent reports (97,98) regarding the role of transplantation in the treatment of heart failure. Other surgical procedures, such as cardiomyoplasty, and the use of mechanical ventricular assist devices remain investigational.

Intense physical exertion should be discouraged, but moderate exercise to tolerance should be strongly encouraged.

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Mild to moderate dynamic exercise, such as walking or recreational bike riding, is preferred. Isometric exercise (i.e., work against gravity), such as push-ups or weight lifting, should be discouraged because it presents an acute afterload stress to the left ventricle. Restriction of activity results in skeletal muscle deconditioning, which can contribute to the fatigue associated with heart failure. With a physical conditioning program it is possible to increase blood flow to exercising muscles (99), delay anaerobic threshold (100) and improve autonomic function (101).

Diastolic Dysfunction: Therapy

The treatment of heart failure due to diastolic dysfunction has both similarities and dissimilarities to the treatment of heart failure due to systolic dysfunction. Our recommendations do not include therapy for hypertrophic cardiomyopathy because the pathophysiologic features and therapy for hypertrophic cardiomyopathy differ significantly from most other causes of diastolic dysfunction. Certainly, causal or aggravating conditions should be corrected if possible (e.g., revascularization for coronary artery disease, control of systemic hypertension). Similarly, recommendations regarding the use of anticoagulation and antiarrhythmic agents and the role of activity apply to both conditions. However, there are important differences in the pharmacologic approach to systolic and diastolic dysfunction. The goal of drug therapy in diastolic dysfunction is to reduce symptoms by lowering the elevated filling pressures without significantly reducing cardiac output. This goal can be accomplished by the judicious use of diuretic drugs and nitrates. Because an adequate cardiac output depends on the elevated filling pressure, such patients are prone to develop hypotension, and small doses of diuretic drugs or nitrates should be given initially, with careful monitoring to avoid adverse effects. Calcium channel and beta-blockers have been proposed to directly improve diastolic dysfunction by augmenting ventricular relaxation or improving compliance, but there are few data to indicate that these agents exert a clinically important effect by this mechanism of action. Beta-blockers may improve diastolic filling by reducing heart rate. ACE inhibitors are frequently used, but studies demonstrating their effectivness in patients with diastolic function are limited.

Because systolic function is generally normal or near normal, positive inotropic agents are of little use. As the disease progresses, systolic dysfunction may develop, which should then be treated accordingly. Patients with diastolic dysfunction that is refractory to optimal medical/surgical management should be evaluated for heart transplantation.

Pharmacologic Treatment of Left Ventricular Diastolic Dysfunction

Class I

1. Diuretic drugs

2. Nitrates

3. Drugs suppressing AV conduction to control ventricular rate in patients with atrial fibrillation

4. Anticoagulation in patients with atrial fibrillation or previous systemic or pulmonary embolization

Class II

1. Calcium channel blockers

2. Beta-blockers

3. ACE inhibitors

4. Anticoagulation in patients with intracardiac thrombus

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Class III

1. Drugs with positive inotropic effect in the absence of systolic dysfunction

2. Treatment of asymptomatic arrhythmias

General Measures

There are certain general measures that apply to all patients with heart failure. Factors aggravating or precipitating heart failure should be corrected (e.g., anemia, infections, hypertension, obesity). Alcohol can produce cardiomyopathy, and excessive intake can cause hypertension. Restriction of intake or abstinence should be encouraged.

The proper education of patients and their families is imperative. Failure of patients to comply with their physician's instructions is a frequent cause of recurrent heart failure. Many factors produce this failure to comply, but, unfortunately, the patient's lack of understanding is a significant cause. It is incumbent on physicians to be certain that patients and their families have an understanding of the causes of heart failure, prognosis, therapy, dietary restrictions, activity, importance of compliance and the signs and symptoms of recurrent heart failure. Home monitoring by other health care providers is of value if adequate support cannot otherwise be provided. In addition, patients should be strongly encouraged to construct written advance directives for their future care. The instruction of family members in cardiopulmonary resuscitation should be recommended.

Summary

Systolic Dysfunction: Therapy

- All patients with symptomatic heart failure and those in functional class I with significantly reduced left ventricular function should be treated with an ACE inhibitor, unless contraindicated or not tolerated.
- ACE inhibitors should be continued indefinitely.
- The recommended dose of ACE inhibitors for heart failure are the larger doses used in the clinical trials demonstrating improvement in survival.
- Patients with symptomatic heart failure should be treated with a diuretic drug, even when rendered free of edema. Diuretic drugs should be used in conjunction with an ACE inhibitor. The dose and type of diuretic drug may change according to fluid status but generally will be needed indefinitely.
- Sodium restriction is a critical strategy in the treatment of patients with heart failure.
- Calcium channel blockers are not of proven benefit for patients with systolic heart failure and may be harmful. Such risks may not accompany the use of amlodipine, which is undergoing further evaluation.
- Digoxin is an effective treatment in many patients with moderate to severe heart failure, but there is uncertainty regarding its influence on mortality.
- Asymptomatic arrhythmias should not be treated in patients with heart failure.
- The results with beta-blockers for the treatment of heart failure are encouraging, but their use remains investigational pending full review of the available data. However, beta-blockers are indicated (if tolerated) in the treatment of high risk patients after an acute myocardial infarction.
- Anticoagulation is indicated for patients with atrial fibrillation or previous embolization and is frequently administered in patients with a very low ejection fraction or intracardiac thrombus. However, there are few data to support its routine use for heart failure.
- Low dose dobutamine or milrinone infusion may benefit selected patients with refractory heart failure. The infusion of low dose dobutamine on an outpatient basis may result in symptomatic improvement, but studies are needed to determine the effect on survival.
- Dynamic exercise as tolerated should be encouraged.

Diastolic Dysfunction: Therapy

The goal of drug therapy in patients with diastolic dysfunction is to control symptoms by reducing ventricular

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filling pressure without reducing cardiac output.

Diuretic drugs and nitrates are the drugs of choice for symptomatic patients.

Calcium channel blockers, beta-blockers and ACE inhibitors may be of benefit.

Agents with positive inotropic actions are not indicated if systolic function is normal.

Recommendations for Hospital Admission of Patients With Heart Failure

Class I

1. Patients experiencing moderate to severe heart failure for the first time

2. Patients with recurrent heart failure complicated by acutely threatening events or clinical situations (e.g., recent myocardial ischemia/infarction, acute pulmonary edema, hypotension, pulmonary or systemic embolus, symptomatic arrhythmias or other severe medical illnesses)

Class II

1. Mild to moderate decompensation of chronic heart failure

2. Patients experiencing mild heart failure for the first time

Heart Failure in the Fetus, Infant and Child

Children with heart failure differ from adults in two major ways: 1) There are maturational differences in contractile function, with improvement from early fetal gestation to the adult, making perturbation of the cardiovascular system more likely to have an effect on an immature subject. 2) There are congenital, structural and genetic causes for heart failure in the fetus, infant and child that are either modified by adulthood or lead to early death such that the causes of heart failure in infancy are largely due to congenital heart disease, whereas this is not the case in the adult.

The term heart failure in pediatrics has the same definition as in adult cardiology, with many similar causes, some with reduced myocardial function. However, the most common cause of "heart failure" in infants and children is ventricular septal defect, in which myocardial function is frequently normal. Therefore, in young patients with heart failure the systemic output is most often normal, but excessive preload, afterload or pulmonary blood flow leads to pulmonary edema.

The majority of infants with heart failure have a surgically correctable cause, and surgical correction is a class I indication for treatment of such patients. The major consideration in these patients is the timing of operation, especially for those in whom the defect may become smaller (e.g., ventricular septal defect). However, for medical management of heart failure in children, there are no long-term prospective, randomized, double-blind, placebo-controlled outcomes data available. Essentially every form of treatment has either been proposed as successful or unsuccessful on the basis of uncontrolled trials. Therefore, it is not possible at present to assign treatment options clearly to class I or III. It is hoped that the present document will stimulate formal outcomes research in the fetus, infant and child to determine optimal management.

Because the management principles of heart failure in children and adults are generally similar, only the major differences from those outlined earlier in this document will be presented in this section, beginning with acute heart failure and continuing with the five common presentations of chronic heart failure.

Acute Heart Failure

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The infant or child with heart failure is generally tachypneic, with a respiratory rate (taken while asleep) greater than ~60 breaths/min at <2 years old and >40 breaths/min at ≥ 2 years old. The tachypnea generally is unlabored and requires close inspection because the infant may appear to be comfortable. The presence of retractions may indicate associated pulmonary infection or impending cardiovascular collapse. There is usually accompanying sinus tachycardia. Hepatomegaly is usually present, whereas splenomegaly is not. The patient may be diaphoretic and, depending on the state of the circulation, mottled in the presence of impending circulatory collapse. Such infants may be diagnosed incorrectly as having sepsis. The pulse volume should be examined in all four extremities and both carotid arteries. Blood pressure readings should be obtained in all four extremities. Infants with obstruction to systemic ventricular outflow, such as that found in critical aortic stenosis, may have diffusely reduced pulse volume, whereas in coarctation of the aorta or interruption of the aortic arch, there may be differential pulse volume between the arms and legs. If the coarctation involves the left subclavian artery, and there is a retroesophageal right subclavian artery originating below the coarctation site, the only normal pulses may be the carotids.

In the patient with physical findings of heart failure, a diuretic drug such as furosemide may be given before diagnostic testing is completed. In the infant with heart failure, oxygen administration generally is withheld until an anatomic diagnosis can be ascertained. In patients with anatomic outflow obstructions, such as hypoplastic left heart syndrome (in which the entire systemic outflow is through the ductus arteriosus), administration of oxygen may constrict the ductus and reduce systemic output. Initial diagnostic testing should include determination of the serum concentrations of glucose, calcium and hemoglobin because abnormalities in these variables may accompany or cause heart failure. A chest radiograph is helpful to detect pleural effusion, pneumonia or anatomic abnormalities, such as diaphragmatic hernia. It will also confirm the diagnosis of pulmonary overcirculation.

The rhythm on the ECG may be helpful in diagnosis because tachycardia or bradycardia can cause acute heart failure, and chronic tachyarrhythmias of any sort can cause "cardiomyopathy." Occasionally, additional pathognomonic abnormalities on the ECG are found, such as wide Q waves in anomalous origin of the left coronary artery from the pulmonary artery.

The essential diagnostic test is the transthoracic Doppler–two dimensional echocardiogram. The echocardiographic findings will fall into one of five major categories that determine further management. 1) *Congenital heart disease with a left-to-right shunt.* This condition generally presents after the first few weeks of age (rarely in the first week) and is initially managed with intravenous furosemide. Drug doses may be found in a number of excellent reviews (102,103). Digoxin may also be used (see later). Oxygen generally is withheld because of its properties of pulmonary vasodilation and systemic vasoconstriction. 2) *Congenital heart disease with systemic outflow obstruction* (e.g., hypoplastic left heart syndrome, interrupted aortic arch, coarctation of the aorta). Prostaglandin E_1 is given to dilate the ductus arteriosus, and oxygen is withheld because it can constrict the ductus. The infant usually undergoes intubation and hypoventilation to increase pulmonary vascular resistance and force blood into the systemic circulation. Digoxin and a diuretic drug may be given. 3) *Normally functioning heart with dilated chambers, especially the right ventricle and right atrium.* This condition may indicate a congenital extracardiac arteriovenous fistula found most commonly in the cerebral or hepatic circulation; chronic severe anemia also may present with this echocardiographic picture. 4) *Pericardial effusion with tamponade.* 5) *Dilated, poorly functioning heart.* A correctable cause of the latter condition is anomalous origin of the left coronary artery from the pulmonary artery; other causes include acute myocarditis and acute presentation of chronic cardiomyopathy.

In the infant or child with acute heart failure accompanied by decreased ventricular function, principles similar to those described for adults are followed. Diuretic drugs should be administered cautiously because an acute decrease in preload may lead to hypotension. The intravenous inotropic agents used in children (dobutamine, dopamine, epinephrine, isoproterenol) are generally similar to those used in adults. In equivalent doses, dopamine may be less effective in infants because of maturational differences in norepinephrine stores (104). Intravenous digoxin may be used. However, in the acute setting with changing renal perfusion and function, as well as potentially variable serum potassium and calcium concentrations, digoxin serum concentration and effects may be unpredictable. The use of digoxin in this setting has been questioned. Amrinone has been used as both a primary inotropic agent and as a systemic vasodilator. Other systemic vasodilators, such as sodium nitroprusside,

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hydralazine and nitroglycerin, have also been used(103). Ventricular assist devices for both the right and left ventricle are being developed for pediatric use(105).

Similar considerations apply to the immediate postoperative period after surgery for congenital heart disease in which acute heart failure and low cardiac output may occur from myocardial depression due to myocardial ischemia related to cardiopulmonary bypass, unavoidable residual defect or pericardial tamponade from bleeding.

*Diagnostic Evaluation of Acute Heart Failure in the Fetus, Infant and Child**

Class I

1. Physical examination, including blood pressure measurement in all extremities

2. CBC and urinalysis

3. Blood–serum: glucose, calcium, electrolytes, creatinine

4. Electrocardiogram, chest radiograph, transthoracic Doppler–two dimensional echocardiogram

*Follow general principles for adults.

Medical Treatment of Acute Heart Failure in the Fetus, Infant and Child

Class I

1. General: intravenous inotropes (excluding digoxin), intravenous diuretic

2. *Systemic outflow obstruction*: prostaglandin E_1, artificial ventilation without supplemental oxygen

Class II

General: digoxin

Class III

Oxygen administration until a definitive diagnosis has been established

Subacute or Chronic Heart Failure

Infants with chronic heart failure may present with difficulty in feeding (requiring >20 min to drink a bottle), diaphoresis (with damp clothes on awakening from a nap) or poor weight gain (inability to keep the same growth percentile). Occasionally, an infant or child with chronic heart failure may present with pneumonia; alternatively, heart failure may be misdiagnosed as pneumonia. In the following five areas, management of infants with heart failure may differ from that of adults.

1. Congestive cardiomyopathy. After initial stabilization, a diagnosis of idiopathic dilated cardiomyopathy must be established by exclusion. If echocardiography has not demonstrated normal proximal coronary artery anatomy, cardiac catheterization must be performed. If no anatomic cause is demonstrated, myocardial biopsy may be performed to diagnose myocarditis. In infants and children, metabolic and genetic familial causes of congestive cardiopathy, such as carnitine and selenium deficiency, are more common than in adults. Therefore, a careful family history of early death from heart disease should be sought. The management principles and drugs used to treat

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dilated cardiomyopathy in children are similar to those used in adults. Most recently, ACE inhibitors, such as enalapril and captopril, have been used in infants and children with symptoms that are refractory to treatment with digoxin and furosemide. In those patients with extremely poor function, platelet antagonists should be considered as prophylaxis against stroke. Although formal outcome studies have not been performed, it appears at present that no form of therapy in children markedly affects longevity(106). Because the prognosis is so poor in many cases, heart transplantation should be considered.

2. Congenital heart disease with a left to right shunt. In an infant with a large left to right shunt, the choice for continued medical management is weighed against the severity of the heart failure, the natural history of the defect and the expected success of operation. For example, in the infant with a large ventricular septal defect, there is approximately a 50% probability that the defect will become small enough not to require surgical intervention. Therefore, in most instances surgical intervention for ventricular septal defect is postponed as long as the infant is gaining weight and free of lower respiratory tract infection. If the infant still has a large left to right shunt after 6 months of age, increasing consideration is given to repair of the defect, especially in the presence of significantly elevated pulmonary artery pressure.

Medical management in these infants is controversial. Low sodium formulas are available, but appropriately controlled studies have not been performed to determine their efficacy. A diuretic drug such as furosemide generally is given. As long as the dose is <2 mg/kg per day orally, excess potassium loss generally does not occur. At higher doses, spironolactone generally is added, potentially obviating the need for potassium supplementation. Despite one recent study in which the use of a diuretic drug did not reduce the respiratory rate in a group of 18 infants with a large ventricular septal defect (107), many clinicians recommend the use of a diuretic drug in this situation (102,103).

The greatest controversy has surrounded the use of digoxin in infants with a left to right shunt. It has generally been accepted that in the premature infant with a patent ductus arteriosus, the risk of digoxin toxicity and the lack of demonstrated benefit do not justify the use of digoxin. The controversy currently surrounds infants with a ventricular septal defect in whom contractility, as measured by load-independent indexes, is frequently normal. The results and recommendations have been contradictory. In the study of Kimball et al.(107), digoxin did not change symptoms, although the combination of digoxin and furosemide did provide an increase in contractility over that at baseline. In all but two of the infants, right ventricular systolic pressure was <90% of left ventricular pressure, and ventricular function appeared to be normal in all. In contradistinction, in the study of Colan and Sanders(108), many patients with a large ventricular septal defect had reduced ventricular function measured by a similar load-independent index, and digoxin was found to be beneficial. It appears that in certain children with a large left to right shunt and symptomatic heart failure, digoxin may be of benefit.

Finally, controversy surrounds the use of vasodilators. In the presence of a large interventricular communication in which right and left ventricular systolic pressures are equal, the amount of left to right shunt is dependent on the balance of pulmonary and systemic vascular resistance. Because there are no specific vasodilators that affect the pulmonary and systemic circulations differentially and in the same direction, it is to be expected that some children with left to right shunt given a vasodilator might improve and others might not. In catheterization studies(109,110), it appears that captopril and enalapril are most beneficial in children with either elevated systemic vascular resistance (>20 U/m^2), or those without markedly elevated pulmonary arteriolar resistance (<3.5 U/m^2). These infants must be monitored closely for hypotension or worsening heart failure.

3. Eisenmenger's syndrome with heart failure. Patients with Eisenmenger's syndrome have elevated pulmonary vascular resistance and a communication (either atrial, ventricular or ductal) that allows right to left shunting so that systemic arterial oxygen saturation is dependent on the balance between pulmonary and systemic vascular resistance. If patients with Eisenmenger's syndrome are treated with a vasodilator, there is a risk that with relatively fixed pulmonary arteriolar resistance, there will be a greater vasodilating effect on the systemic vasculature, an increase in right to left shunting and a decrease in systemic arterial saturation. For this reason, vasodilators usually are not given to patients with Eisenmenger's syndrome unless the shunt had been corrected previously. The type of heart failure generally found in patents with Eisenmenger's syndrome is right-sided heart failure with tricuspid regurgitation, hepatomegaly, peripheral edema and low cardiac output. A diuretic drug may relieve painful hepatic

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congestion and edema. Digoxin is frequently used, although its benefit has not been studied. Phlebotomy to reduce the viscosity of the blood has been used in patients with Eisenmenger's syndrome and high hematocrits to decrease symptoms of headaches, muscle and joint aches, but its effect on myocardial function is undemonstrated. Heart/lung transplantation should be considered in those with Eisenmenger's syndrome.

4. Heart failure due to arrhythmias. Acute paroxysmal tachyarrhythmias or bradyarrhythmias may cause heart failure, and elimination of the arrhythmia is the treatment choice. Chronic, incessant tachyarrhythmias (e.g., atrial ectopic tachycardia, permanent junctional reciprocating tachycardia, atrial flutter or ventricular tachycardia) that are present >10% of the day may cause chronic heart failure. These arrhythmias may cause a dilated, poorly functioning heart or diastolic dysfunction. The identification of the tachyrhythmia generally is not difficult. However, in some patients, a right atrial ectopic focus tachycardia may masquerade as sinus tachycardia. In these patients, atrial ectopic tachycardia is more likely if the P wave is negative in lead V_2 or if the heart rate is >150% of the upper limit of normal for age(111). The causative nature of the tachyrhythmia has been demonstrated by the eventual normalization of cardiac size and function after definitive treatment of the tachyrhythmia(112).

5. Heart failure in the fetus. Heart failure in the fetus is demonstrated by the findings of pleural effusion, pericardial effusion, ascites and skin edema on the fetal echocardiogram. Fetal heart failure caused by congenital heart disease usually is an ominous finding and may be associated with spontaneous abortion. The most common cause for fetal heart failure is sustained supraventricular tachycardia. Because the infant may be in sinus rhythm at the time of the fetal echocardiogram (having just had a long episode of supraventricular tachycardia), there must be a high index of suspicion of an arrhythmia if there are signs of heart failure and the heart is anatomically normal. This arrhythmia is treated initially with digoxin given to the mother. There have been reports of success with verapamil, flecainide, procainamide and amiodarone. The majority of fetuses with supraventricular tachycardia can be treated successfully, with only a minority requiring early delivery.

*Diagnostic Evaluation of Subacute or Chronic Heart Failure in the Fetus, Infant and Child**

Class I

1. *General*: electrocardiogram, chest radiograph, transthoracic Doppler–two dimensional echocardiogram (if not previously performed)

2. *General*: cardiac catheterization/coronary arteriography to determine coronary anatomy if not established by echocardiogram

3. *General*: Holter monitor if no other cause for failure is found

4. *General*: tests for carnitine, selenium deficiency

5. *Fetus*: repeated echocardiogram for paroxysmal arrhythmia if there is evidence of hydrops fetalis

Class II

General: myocardial biopsy

*Medical Treatment of Subacute or Chronic Heart Failure in the Fetus, Infant and Child**

Class I

1. *General*: diuretic

2. *Congestive cardiomyopathy*: digoxin, ACE inhibitor

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3. *Fetus*: digoxin, specific antiarrhythmic treatment

Class II

1. *Congestive cardiomyopathy*: platelet antagonists

2. *Left to right shunt*: digoxin, ACE inhibitor

3. *Eisenmenger's syndrome*: digoxin, phlebotomy

Class III

Eisenmenger's syndrome: systemic vasodilator

Summary

The majority of infants with heart failure have a surgically correctable cause.

Initial diagnostic testing should include CBC, urinalysis, serum electrolytes, glucose, calcium, creatinine, chest radiograph and ECG. The essential diagnostic study is the transthoracic Doppler–two dimensional echocardiogram.

In infants with heart failure, oxygen administration generally is withheld until an anatomic diagnosis can be made.

Heart failure due to congenital heart disease with a left to right shunt is managed initially with intravenous furosemide. Oxygen is withheld because of its properties of pulmonary vasodilation and systemic vasoconstriction.

Infants with heart failure due to congenital heart disease with systemic outflow obstruction should receive prostaglandin E_1 to dilate the ductus arteriosus, and oxygen should be withheld.

A diagnosis of idiopathic dilated cardiomyopathy must be established by exclusion. If echocardiography has not demonstrated normal proximal coronary artery anatomy, cardiac catheterization should be performed. If no anatomic cause is demonstrated, myocardial biopsy may be indicated.

The management principles and drugs used to treat dilated cardiomyopathy in children are similar to those used in adults.

Controversy surrounds the use of digoxin in infants and children, but it may be useful in those with symptomatic heart failure.

ACE inhibitors are most beneficial in children with either elevated systemic vascular resistance or those without markedly elevated pulmonary vascular resistance.

Vasodilators generally are contraindicated in patients with Eisenmenger's syndrome, unless the shunt has been surgically corrected.

Chronic incessant tachyarrhythmias that are present >10% of the day may cause dilated cardiomyopathy and heart failure.

The most common cause of fetal heart failure is sustained supraventricular tachycardia, which is treated by administering digoxin to the mother.

Appendix

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