Heart failure is a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood. It may result from disorders of the pericardium, myocardium, endocardium, heart valves, or great vessels, or from metabolic abnormalities, but most patients have symptoms resulting from impaired left ventricular myocardial function. Manifestations include dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema.

The American College of Cardiology Foundation (ACCF) and American Heart Association (AHA) recently developed guidelines on the diagnosis and treatment of heart failure. The guidelines are based on four progressive stages of heart failure; progression from one stage to the next is associated with reduced five-year survival and increased plasma natriuretic peptide concentrations. Stage A includes patients at risk of heart failure who are asymptomatic and do not have structural heart disease. Stage B describes those with structural heart disease who do not have signs or symptoms of heart failure; it includes New York Heart Association (NYHA) class I, in which there are no limitations on physical activity. Stage C describes patients with structural heart disease who are currently symptomatic or have a history of heart failure symptoms, and includes NYHA classes I, II (slight limitation of physical activity), III (marked limitation), and IV (unable to engage in physical activity without symptoms, or symptoms that occur at rest). Stage D describes patients with refractory heart failure who require specialized interventions; it includes NYHA class IV. Interventions at each stage are aimed at modifying risk factors (stage A), treating structural heart disease (stage B), and reducing morbidity and mortality (stages C and D).

Diagnostic Testing
Because heart failure is largely a clinical diagnosis based on findings from the history and physical examination, there is no single diagnostic test. The initial laboratory evaluation should include a complete blood count, urinalysis, fasting lipid profile, liver function testing, and measurement of serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum creatinine, glucose, and thyroid-stimulating hormone. When indicated, serial monitoring should include renal function testing and measurement of serum electrolytes. For all patients with heart failure, 12-lead electrocardiography should be obtained. In select patients, screening for hemochromatosis or human immunodeficiency virus infection may be considered. Diagnostic testing for rheumatologic diseases, amyloidosis, or pheochromocytoma is reasonable in patients with heart failure in whom there is clinical suspicion for these diseases.

BIOMARKER TESTING
Cardiac biomarkers have been reported to predict response and progression of disease and survival. In outpatients with dyspnea, measurement of B-type natriuretic peptide...
(BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP) is useful to support clinical decision making in the diagnosis of heart failure, especially when there is clinical uncertainty. Measurement of BNP or NT-proBNP is also useful in establishing the prognosis or disease severity in outpatients with chronic heart failure. BNP- or NT-proBNP–guided therapy can be useful to achieve optimal dosing of medical therapy in select clinically euvolemic outpatients in structured disease-management programs. However, the usefulness of serial measurement of BNP or NT-proBNP to reduce hospitalizations or mortality in patients with heart failure has not been established. Measurement of other biomarkers of myocardial injury or fibrosis may be considered for additional risk stratification in outpatients with chronic heart failure.

In hospitalized patients, measurement of BNP or NT-proBNP may be useful to support clinical judgment for the diagnosis of acutely decompensated heart failure, especially when the diagnosis is uncertain. Measurement of BNP or NT-proBNP and/or cardiac troponin levels may be useful for determining prognosis or disease severity in hospitalized patients with acutely decompensated heart failure. However, the usefulness of BNP- or NT-proBNP–guided therapy in these patients is not well established. Measurement of other biomarkers of myocardial injury or fibrosis may be considered for additional risk stratification in patients with acutely decompensated heart failure.

NONINVASIVE IMAGING
Chest radiography should be performed in patients with suspected or new-onset heart failure and in those with acutely decompensated heart failure to evaluate heart size and pulmonary congestion, and to detect any cardiac, pulmonary, or other disease that may cause or contribute to the patient’s symptoms. Two-dimensional echocardiography with Doppler should be performed during the initial evaluation to assess ventricular function, size, wall thickness, wall motion, and valve function. Repeat measurement of ejection fraction and measurement of the severity of structural remodeling are useful in patients who have had a significant change in clinical status, experienced or recovered from a clinical event, undergone treatment that may have had a significant effect on cardiac function, or who may be candidates for device therapy.

Treatment
STAGE A
Hypertension and lipid disorders should be controlled in patients with stage A heart failure. Long-term man-
agement of systolic and diastolic hypertension reduces the risk of incident heart failure by approximately 50%. Diuretic-based therapy has consistently been shown to prevent heart failure in a range of patients; angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and beta blockers are also effective. Patients with atherosclerotic disease are at increased risk of heart failure. Aggressive treatment of hyperlipidemia with statins reduces the risk of heart failure in at-risk patients; long-term treatment with ACE inhibitors may also reduce risk.

Other conditions that may lead to or contribute to heart failure (e.g., obesity, diabetes mellitus, tobacco use) should be controlled or avoided. Obesity and overweight have been repeatedly linked to an increased risk of heart failure. Similarly, diabetes is an important risk factor for women, and may triple their risk of developing heart failure. Dysglycemia appears to be directly related to risk, with A1C levels predicting incident heart failure. Tobacco use is strongly associated with the risk of incident heart failure, and patients who smoke should be strongly advised to quit.

STAGE B

As with patients with stage A heart failure, patients with stage B heart failure should maintain control of hyperlipidemia and hypertension. ACE inhibitors should be used to prevent symptomatic heart failure and reduce mortality in patients with stage B heart failure and a recent or remote history of myocardial infarction (MI) or acute coronary syndrome and reduced ejection fraction. Angiotensin receptor blockers are an alternative for patients who cannot tolerate ACE inhibitors. Beta blockers should also be used to reduce mortality in these patients, and statins should be used to prevent symptomatic heart failure and cardiovascular events. Blood pressure should be controlled in accordance with clinical practice guidelines in patients with stage B heart failure and structural cardiac abnormalities—including left ventricular hypertrophy—who do not have a history of MI or acute coronary syndrome. ACE inhibitors and beta blockers should be used in all patients with a reduced ejection fraction to prevent symptomatic heart failure, even if they do not have a history of MI.

To prevent sudden death, placement of an implantable cardioverter-defibrillator is reasonable in patients with stage B heart failure and asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have a left ventricular ejection fraction of 30% or less, are on appropriate medical therapy, and have a reasonable expectation of survival with good functional status for more than one year.

Nondihydropyridine calcium channel blockers that have negative inotropic effects may be harmful in asymptomatic patients with low left ventricular ejection fraction and no symptoms of heart failure after MI.

STAGE C

In addition to interventions discussed for patients with stage A and B heart failure, patients with stage C heart failure require interventions for symptom management. Diuretics should be used in these patients if there is evidence or history of fluid retention, and they should be monitored for adverse effects such as electrolyte abnormalities and dehydration. Aldosterone receptor antagonists should be used in patients with NYHA class II through IV heart failure who have an ejection fraction of 35% or less, and these patients should be monitored for hyperkalemia and renal insufficiency.

The guidelines also discuss nonpharmacologic interventions such as sodium restriction, treatment of sleep disorders, and exercise training. Other medications discussed include combination therapy with isosorbide dinitrate and hydralazine, digoxin, anticoagulants, and omega-3 polyunsaturated fatty acids. The role of device therapy, including implantable cardioverter-defibrillators and cardiac resynchronization therapy, is also discussed.

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