

Higher Expectations for Management of Heart Failure: Current Recommendations

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Background: Some 4.6 million Americans are estimated to suffer from heart failure, and approximately 400,000 new cases are diagnosed each year. Each year 260,000 patients die as a direct or indirect result of the disorder, with annual costs estimated between \$21 billion to \$40 billion.

Methods: The medical literature was searched using the key words “heart failure,” “beta-adrenergic blockade,” “angiotensin-converting enzyme inhibition,” and “carvedilol.” A case study illustrates the value of an emerging pharmacologic approach for some heart failure patients and places it in clinical perspective.

Results: During the past decade, placebo-controlled clinical trials have shown decreased morbidity and mortality resulting from timely intervention using a targeted multidrug approach: first, diuresis; then angiotensin-converting enzyme inhibition and β -adrenergic-receptor blockade, possibly with digoxin for symptomatic relief.

Conclusions: An emerging approach to therapy aims to reverse the course of left ventricular dysfunction and arrest the underlying disease process, as well as improve hemodynamic function. Management of heart failure has thus entered a new era of more effective pharmacotherapy, often delivered within the primary care setting. (J Am Board Fam Pract 2002;15:39–49.)

Until recently, the prognosis for patients who have symptomatic heart failure was discouraging, with most patients dying within 5 years of diagnosis.¹ Management of this disabling and progressive disorder has entered a new era, however. The Advisory Council to Improve Outcomes Nationwide in Heart Failure (ACTION HF) published consensus recommendations in 1999, based on the results of randomized, controlled clinical trials,² that map out an evolving approach to treatment of heart failure caused by left ventricular systolic dysfunction. The revised goal of therapy is not merely to control such symptoms as edema and dyspnea, but to arrest disease progression by altering the neurohormonal mechanisms that govern heart failure.

Heart failure is increasingly more common for reasons that include aging populations and im-

provement in survival rates from its major causative factors (coronary artery disease, hypertension, valvular heart disease).³ At the same time, however, the outlook for patients has never been better. In fact, selective polytherapy for patients with mild-to-moderate heart failure has been shown to reduce its progression and mortality risk,⁴ making the management both feasible and rewarding for the primary care physician. Despite these recent advances in the treatment of heart failure, the clinical complexity and poor dissemination of knowledge among physicians has resulted in primary care physicians not being kept up to date with current recommendations derived from various trials.⁵ It is disappointing that, although the benefits of polytherapy on survival are now clear, up to 50% of patients admitted with chronic heart failure are discharged without a prescription for angiotensin-converting enzyme (ACE) inhibitors.⁶ This statistic highlights the need of motivating primary care physicians toward learning more about current developments in heart failure management. In this article, we describe a typical case history of moderate heart failure to illustrate the contemporary approach to the evaluation and management of this disease syndrome.

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Table 1. Major Risk Factors for Heart Failure.

- Coronary artery disease or history of myocardial infarction
- Diabetes
- Hypertension
- Congenital heart defects
- Valvular heart disease
- Asymptomatic left ventricular dysfunction
- Obesity
- Alcoholism

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Methods

The medical literature was searched using the key words “heart failure,” “beta-adrenergic blockade,” “angiotensin-converting enzyme inhibition,” and “carvedilol.” In addition to reports of landmark clinical trials, published clinical practice guidelines and authoritative reviews on the evaluation and management of chronic systolic heart failure served as the basis for the present clinical review. A case study illustrates the value of an emerging pharmacologic approach for some heart failure patients and places it in clinical perspective.

Prevalence and Impact

Heart failure has been termed the single most expensive health care problem in the United States.⁷ The fastest growing cardiovascular disorder in developed countries, its impact is accelerating among aging populations. It is estimated that some 4.6 million Americans suffer from heart failure, with approximately 400,000 new cases diagnosed each year.⁸ Advancing age is the most striking risk factor; data from the Framingham Study indicate that heart failure occurs in 1% of adults in their 50s and in as many as 10% of those in their 80s.⁹ Major risk factors for heart failure include coronary artery disease, hypertension, diabetes mellitus, previous myocardial infarction, and obesity (Table 1).¹⁰ Obesity acts directly or indirectly in inducing dyslipidemia, hypertension, diabetes, and left ventricular hypertrophy, hence promoting cardiac failure.¹¹

Heart failure caused about 870,000 hospitalizations in 1995,⁸ and for several years it has been the single, most frequent cause of hospitalization among persons aged 65 years and older. Among cardiovascular disorders, it alone is increasing in

incidence and prevalence. Deaths from heart failure increased by 91.9% from 1979 to 1996, and each year about 260,000 patients die as a direct or indirect result of the disorder.⁸ Unless treatment is given in the early stages of heart failure, when it can decrease mortality and reverse the disease process, the aging population factor and the availability of treatment to halt heart failure only postpone mortality. The annual combined direct and indirect costs of heart failure have been estimated between \$21 billion to \$40 billion.^{7,8}

Treatment: A More Ambitious Approach

An improved understanding of the mechanisms that mediate the symptoms and progression of heart failure has guided an emerging approach to therapy, one that aims not only to relieve symptoms but also to reverse the course of left ventricular dysfunction and arrest the underlying disease process.

Standard therapy for heart failure had focused on improving hemodynamic function to relieve symptoms and improve functional status, primarily through the use of diuretics and digoxin. It has now become clear, however, that the progressive cardiac remodeling damage wrought by heart failure is conducted by means of neurohormonal pathways, specifically, the renin-angiotensin system and the sympathetic nervous system. Intervention in both pathways is necessary to slow heart failure progression.

During the past decade, placebo-controlled clinical trials have shown decreases in morbidity and mortality from timely intervention using a targeted multidrug approach: first, diuresis; then angiotensin-converting enzyme (ACE) inhibition and β -adrenergic receptor blockade, with the possible addition of digoxin for symptomatic relief. The addition of β -blockers to heart failure therapy represents a turnaround in understanding how these agents affect the pathophysiology of heart failure progression. Based on these data, the newly developed ACTION HF consensus recommendations offer detailed guidance on the optimal management of heart failure,² as follows.

Illustrative Case Study

The patient was a 52-year-old man with newly diagnosed moderate heart failure caused by idiopathic dilated cardiomyopathy. He described being

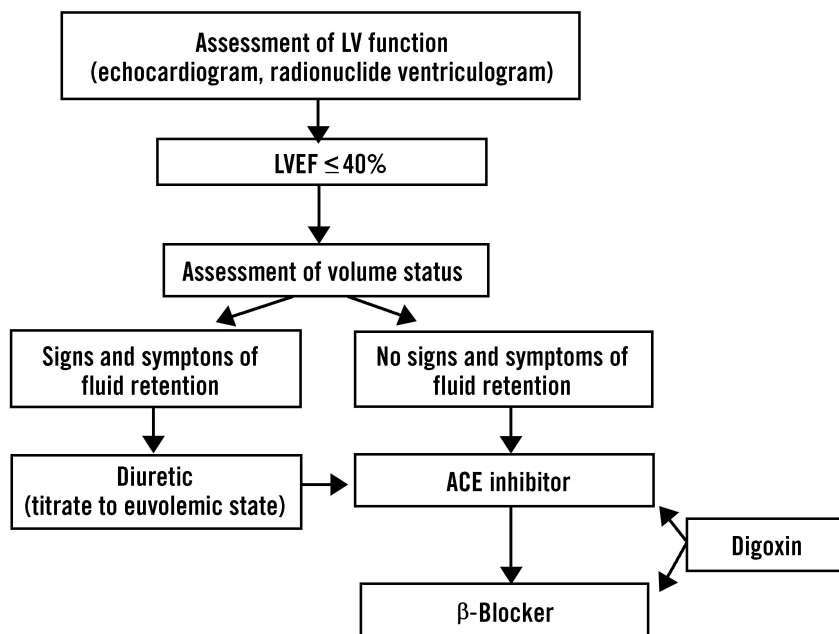


Figure 1. Algorithm for the management of heart failure. From Packer M, Cohn JN. Consensus recommendations for the management of chronic heart failure. *Am J Cardiol* 1999;83:1A-38A. Reprinted with permission. ACE, angiotensin-converting enzyme; LV, left ventricular; LVEF, left ventricular ejection fraction.

limited by dyspnea and fatigue with mild exertional activity (New York Heart Association class III heart failure). When examined, he had jugular venous distention of 10 cm of water, a few bibasilar pulmonary rales, a third heart sound, and mild peripheral edema. The patient's baseline left ventricular ejection fraction (LVEF) was 23%, as determined by two-dimensional echocardiography. Blood pressure was approximately 115/70 mm Hg. Ischemic heart disease was ruled out; the patient had normal coronary arteries and no other obvious cause of heart failure.

Therapeutic goals for heart failure patients include not only alleviating symptoms and improving functional status and left ventricular function, but also slowing disease progression and reducing the patient's risk of worsening disability and death. These complementary goals are best met by using a contemporary pharmacologic management algorithm (Figure 1).² Therapeutic intervention for this patient involved a two-pronged strategy: hemodynamic intervention, including diuretics and digoxin, to provide symptomatic relief; and neurohormonal intervention (ACE inhibitors and β -adrenergic-receptor blockers) to impede disease progression.

Diuretic and Angiotensin-Converting Enzyme Inhibitor Therapy

Initial pharmacologic treatment consisted of a loop diuretic and an ACE inhibitor. Published guidelines from the Agency for Health Care Policy and Research,¹² the American College of Cardiology and American Heart Association Task Force,¹³ and the European Society of Cardiology Task Force¹⁴ all recommend an ACE inhibitor as first-line therapy for asymptomatic left ventricular systolic dysfunction.

The initial priority in managing symptomatic heart failure, however, is resolving fluid overload, and ACE inhibitors are generally ineffective in reducing excess extracellular fluid volume. To relieve edema, this patient with moderately impaired functional capacity also required treatment with a diuretic. (Loop diuretics are the agents of choice in most cases of heart failure; Table 2).¹⁵ ACE inhibition may be begun before diuretic therapy is well established, however. Concomitant treatment with an ACE inhibitor and a diuretic may be initiated by carefully avoiding excessive diuresis and slowly titrating the ACE inhibitor upward to a target dose. Several ACE inhibitors are approved for use in heart failure; target doses are those that have been

Table 2. Loop Diuretics Used in Heart Failure

Drug	Dose Range (mg)	Frequency
Furosemide	20–240	Daily or twice daily
Bumetanide	0.5–8.0	Daily or twice daily
Torsemide	5–100	Daily or twice daily

Reprinted with permission from Cohn JN. The management of chronic heart failure. *N Engl J Med* 1996;335:490–8.

found to be effective in controlled, randomized clinical trials (Table 3).^{2,15}

After approximately 2 months, diuresis had resolved the patient's edema, and the ACE inhibitor dosage had been successfully increased to a target level. At this point, the patient had improved but remained mildly symptomatic (New York Heart Association class II). Office visits continued to be scheduled about every 2 or 3 weeks. When examined at a follow-up visit, there was compensated heart failure with a blood pressure of 95/60 mm Hg and no signs of fluid retention or low cardiac output.

Adding a β -Blocker

The next agent to be considered was a β -blocker. β -Adrenergic blockade has been shown to improve LVEF to an extent greater than any other form of pharmacologic therapy for systolic heart failure. Recent data show that when a β -blocker is added to an ACE inhibitor and diuretic, with or without digoxin, disease progression is slowed and morbidity and mortality are significantly reduced.^{16–18}

Use of β -blockers is contraindicated in patients with bronchospasm, symptomatic bradycardia, or

Table 3. Angiotensin-Converting Enzyme Inhibitors Approved for Heart Failure Treatment.

Drug	Dose Range (mg)	Frequency	Target Dosage
Captopril	6.25–150	Thrice daily	50 mg tid*
Enalapril	2.5–20	Twice daily	10 mg bid
Lisinopril	2.5–40	Daily	20 mg qd
Ramipril	2.5–10	Once or twice daily	5 mg qd or bid
Quinapril	5–20	Twice daily	10 mg bid
Fosinopril	10–40	Twice daily	20 mg bid
Trandolapril	1–4	Daily	4 mg qd

*tid—three times a day, bid—twice a day, qd—each day.

Adapted from Packer and Cohn² and Cohn.¹⁵

advanced heart block (unless treated with a pacemaker). β -Blockers should also be avoided in patients who have severe or acutely decompensated heart failure, ie, those requiring intensive diuresis, intravenous therapy, or hospitalization for heart failure.² Their use should be avoided in patients with severe hepatic impairment.

Carvedilol, a nonselective β -blocker, was started and successfully titrated up to a target dosage. “Start low and go slow” is the watchword for starting β -adrenergic blockade in patients with heart failure, as explained more fully in the discussion to follow.

Six months after the addition of β -adrenergic blockade to the therapeutic regimen, the patient had returned to a fully active lifestyle, with an LVEF of 38% and an heart failure status of New York Heart Association class I (asymptomatic).

Digoxin

Although the patient did not require digoxin therapy, it remains an important tool in treating symptoms of heart failure. For patients with systolic heart failure who remain substantially symptomatic despite diuretic therapy, digoxin is considered an appropriate addition to therapy in some patients and may be added, based on clinical judgment, before or after treatment with neurohormonal antagonists. Because this patient's symptoms improved after the addition of a β -adrenergic blockade, digoxin was not added to the regimen. Clinical trials have shown that, although digoxin reduces the risk of hospitalization for heart failure, it neither improves nor worsens survival.¹⁹ In practice, most patients with heart failure receive digoxin, and those already taking the drug might experience worsening of heart failure if digoxin is withdrawn.²⁰

The patient was reassured that any generalized fatigue was a common and often short-lived side effect associated with the use of β -blockers. As was observed in this patient, after LVEF improves and heart failure is compensated (usually after 1 or 2 weeks), this adverse effect normally disappears, after which there is eventually a marked improvement in clinical status.

From Theory to Practice

This case illustrates key points in effective, up-to-date management of heart failure in primary care. Evaluation begins with a functional assessment for

Table 4. Diagnosing Mild Heart Failure.

Diagnosis Characteristics	Signs, Symptoms, and Findings
Nonspecific signs and symptoms	Exertional dyspnea Edema Fatigue
Physical findings	Elevated jugular venous pressure Third heart sound Laterally displaced apical impulse
Establish diagnosis	Echocardiography or radionuclide ventriculography to measure ejection fraction

Adapted from Konstam et al,¹² Armstrong and Moe,²¹ and McCall D.²²

coronary ischemia, an echocardiogram to detect valvular abnormalities, and appropriate imaging studies to determine whether coronary blockages might benefit from revascularization procedures. The degree of systolic dysfunction can be determined by measuring the LVEF using echocardiography, radionuclide imaging, or ventriculography. In the absence of a murmur in patients with heart failure, echocardiography can be delayed to immediately before discharge to avoid the difficulty that might arise in differentiating diastolic from systolic dysfunction. Left ventricular dysfunction is indicated by an LVEF of less than 45%, with or without symptoms.¹⁵ Key points in determining which patients have heart failure and establishing a functional classification are recapped in Table 4^{12,21,22} and Table 5. One should keep in mind that symptoms of heart failure are poorly correlated with the actual degree of underlying cardiac dysfunction.²

For patients with a confirmed diagnosis of mild to moderate heart failure, ample data now attest to the benefits of combination drug therapy, not only to control symptoms, but to break the vicious cycle of neurohormonal activation and worsening left ventricular function (Figure 2).^{15,23} In heart failure patients with edema, the first step is to control volume retention with diuresis. The next step is to attenuate disease progression with the ultimate aim of reducing morbidity and mortality.

ACE inhibitors were the first class of agent shown to contribute to this goal. Meta-analysis of long-term, placebo-controlled trials with ACE inhibitors in heart failure, involving some 7,000 patients, has shown a significant overall 20% to 25% decrease in all-cause mortality among patients receiving treatment compared with control patients,

Table 5. New York Heart Association Functional Classification.

- I. No limitations of physical activity, no symptoms with ordinary activities
- II. Mild to slight limitation, symptoms* with ordinary activities
- III. Moderate to marked limitation, symptoms* with less-than-ordinary activities
- IV. Severe limitation, symptoms* at rest

and

Key questions to assess mild heart failure status (FACES Screening Tool)

Do you ever feel **F**atigue?

Have you experienced an altered **A**ctivity or exercise pattern?

Are you **C**omfortable walking up 1 flight?

Do you ever get **E**dema (swelling)?

Are you ever **S**hort of breath?

*Dyspnea or fatigue.

Developed at a roundtable congestive heart failure meeting chaired by Len Scarpinato, DO, and attended by Jan Basile, MD, Gary L. Chan, MD, Robert C. Lavender, MD, and Kenneth J. Smith, MD. Sponsored by GlaxoSmithKline.

with the combined risk of death and hospitalization reduced by 30%. ACE inhibition has also been associated with consistent improvement of cardiac function, symptomatic relief, and enhancement of clinical status.²⁴ When compared with ACE inhibitors, angiotensin receptor blockers have shown similar efficacy.^{25,26} Angiotensin receptor blockers are not associated with the same high incidence of cough (15% of patients), which is the most common cause for withdrawal of ACE inhibitors. More recently, the addition of β -blockers was found to produce further attenuation of progressive heart failure. For years, physicians believed that the sympathetic nervous system provided needed support for the failing heart and avoided the use of β -blockers in fear that it would worsen heart failure.²³ A deepening understanding of the dynamics of disease progression in heart failure has reversed this belief.

It became apparent that activation of the sympathetic nervous system and the renin-angiotensin system wrought damage directly on the heart, independent of the hemodynamic effects of heart failure that caused such symptoms as edema and dyspnea.²³ In patients with left ventricular dysfunction, prolonged sympathetic nervous system activation damaged the heart through several mechanisms mediated by the interaction of catecholamines with α_1 -, β_1 -, and β_2 -adrenergic re-

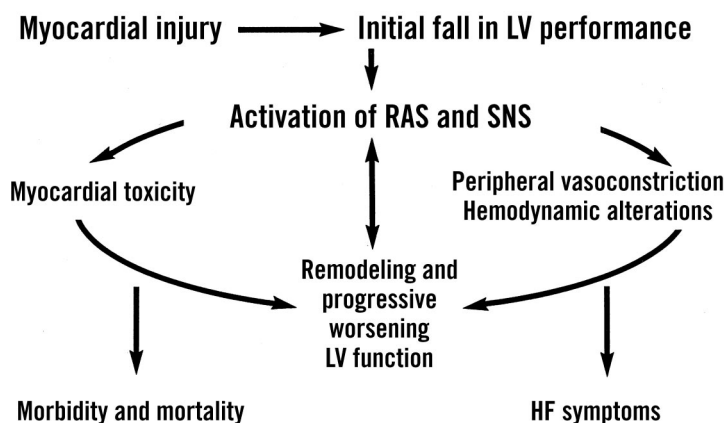


Figure 2. Neurohormonal activation in heart failure. Adapted from Cohn JN. The management of chronic heart failure. *N Engl J Med* 1996;335:490 to 498; and Packer M. The neurohormonal hypothesis: a theory to explain the mechanism of disease progression in heart failure. *J Am Coll Cardiol* 1992;20:248 to 254. LV, left ventricular; RAS, renin-angiotensin system; SNS, sympathetic nervous system; HF, heart failure.

ceptors. This direct cardiac damage includes dysfunction and death of cardiac myocytes, increased ventricular size and pressure, arrhythmia, and increased heart rate.¹⁰

Subsequently, a succession of landmark clinical trials in patients with heart failure showed alleviation of both cardiac dysfunction and symptoms with the addition of β -adrenergic blockade to standard therapy (diuresis plus ACE inhibition). To date, β -blockers have been evaluated in nearly 10,000 patients with heart failure through more than 20 placebo-controlled clinical trials involving metoprolol and bisoprolol (which selectively block the β_1 -receptor) and carvedilol (which blocks β_1 -, β_2 -, and α_1 -receptors). Although with short-term use β -blockers can depress left ventricular function, they are associated with an increase in LVEF with long-term therapy.²⁷ Like ACE inhibitors, β -blockers were shown to decrease the risk of death and the combined risk of death or hospitalization.¹⁶⁻¹⁸

Indeed, ACE inhibition and β -adrenergic blockade might provide synergistic benefits. The two major neurohormonal systems shown to affect disease progression in heart failure, the renin-angiotensin system and the sympathetic nervous system, are coactivated in heart failure. Sympathetic activation appears to stimulate the renin-angiotensin system, and vice versa. Activation of the sympathetic nervous system stimulates renin release from the kidneys, and angiotensin II facilitates the neuronal release of norepinephrine. Therapy that down-regulates one system tends to reduce activation of the other: ACE inhibitors modestly de-

crease plasma norepinephrine levels and β -blockers inhibit renal renin release.

Carvedilol (an α_1 -, β_1 -, and β_2 -receptor blocker) and controlled-release, extended-release metoprolol (a β_1 -receptor blocker) are the only β -blockers currently approved by the US Food and Drug Administration for use in heart failure. The short-acting form of metoprolol has not been shown to produce a significant decrease in mortality; propranolol is not used because of the range and extent of its adverse effects, and atenolol and timolol have not proved to be efficacious in heart failure. Carvedilol blocks all three adrenergic receptors that can mediate catecholamine toxicity in the heart, vasculature, and kidneys. This third-generation β -blocker has been associated with an apparently greater effect on survival than the selective second-generation agents.²⁸ Because of its effects on the α_1 -receptor, carvedilol produces renal and systemic vasodilatory effects that other β -blockers do not. Whether this characteristic confers a lower risk of initial hemodynamic adverse effects and whether multiple adrenergic-receptor blockade has advantages compared with single-receptor blockade are still under investigation. A recent large study showed similar, although smaller, mortality and morbidity effects for metoprolol.

β -Adrenergic Blockade: Current Recommendations

Based on this ongoing research, the recent ACTION HF consensus guidelines recommend the addition of β -adrenergic blockade to therapy with

Table 6. β -Blockers Commonly Used in Treatment of Heart Failure.

Drug	Starting Dosage	Target Dosage
Carvedilol	3.125 mg bid*	6.25–25 mg bid [†]
Bisoprolol	1.25 mg qd	10 mg qd
Metoprolol CR/XL	12.5 mg qd	200 mg qd

*bid—twice a day, qd—each day, CR/XL—controlled release, extended release.

[†]50 mg bid if patient weighs >85 kg.

diuretics and ACE inhibitors for most patients with mild to moderate heart failure and left ventricular systolic dysfunction.² (Even patients with mild symptoms have a high risk of undergoing clinical progression within a year.²³) The benefits of β -adrenergic blockade in patients with asymptomatic heart failure have yet to be shown.

The recently published results of the COPENICUS Trial show that the benefits of carvedilol, previously reported for patients with mild to moderate heart failure, are also observed in patients with severe heart failure.²⁹ As it has been elegantly pointed out by Braunwald,³⁰ it is now clear that β -blockers represent “another important arrow in the physician quiver for the management of heart failure,” but that, at the same time, contraindications (ie, reactive airway disease, sinus-node dysfunction, and abnormalities in the cardiac conduction system), as well as adverse effects of β -blockers, should not be forgotten.

A low starting dose and careful titration upward are keys to successful use of both ACE inhibition and β -adrenergic blockade in heart failure. The starting dose for carvedilol in heart failure, for example, is 3.125 mg twice a day; the dose should be slowly increased to the highest tolerable level, not to exceed the maximum recommended dosage (25 mg twice a day in patients weighing <187 lb [85 kg], 50 mg twice a day in those weighing >187 lb [85 kg]) (Table 6).³¹ There is evidence to suggest that patients derive benefits from carvedilol even at doses as low as 6.25 mg twice a day.²⁸ Accordingly, although the optimal goal is to titrate the drug to a target dose of 25 mg twice a day, patients who are unable to tolerate this dose or who experience problems with titration should still derive considerable benefits at lower doses. Comparable low-dose effectiveness has not been shown for metoprolol.

Patients should be maintained at each dose for at least 2 weeks while blood pressure, heart rate, respirations, temperature, weight, and clinical status are monitored. If dizziness, light-headedness, or fluid retention occur, temporary adjustment of the dose of β -blocker or concomitant medications might be necessary. Early transient hypotension can be managed by adjusting the timing of the ACE inhibitor, and fluid retention can be alleviated by adjusting the dosage of the diuretic. In patients who have a contraindication for or are intolerant of ACE inhibitors, angiotensin receptor blockers or a combination of nitrates and hydralazine may be used. Data from the Veterans Cooperative Study showed that 19% of patients discontinued one or both of these drugs because of side effects.³²

β -Adrenergic Blockade: Cost-Effectiveness

Some studies have also addressed the issue of the effects of β -adrenergic blockade on hospitalizations and costs. In particular, it has been shown that carvedilol used for heart failure reduces hospitalization risk, number of hospitalizations per patient, severity of illness, mean length of stay, and intensive care unit or coronary care unit days, therefore diminishing resource utilization during admission of patients with chronic heart failure.³³ Furthermore, the recent results of a claims analysis have shown that carvedilol has proven economical advantages when compared with metoprolol, as exemplified by fewer hospitalizations, fewer emergency department visits, and lower medical and hospitalization costs.³⁴

Primary Care for Heart Failure: Rewards and Challenges

Early intervention in heart failure is the key to lowering the daunting morbidity and mortality rates resulting from this disorder. Now that available effective therapy can slow disease progression and cut the risk of hospitalization and death, management of heart failure can begin to shift from the domain of specialty care to a partnership between cardiology and primary care.

This partnership, which must also include the patient, begins with a focus on prevention and detection and continues with treatment and follow-up.

Prevention

The best management of heart failure, of course, is to keep it from occurring in the first place. Two primary strategies will help prevent heart failure: decreasing the risk of initial cardiac injury (primarily through effective prevention and treatment of coronary artery disease and hypertension), and lowering the risk of additional injury in patients who have left ventricular systolic dysfunction from a previous cardiac event.²

Detection

Patients should be questioned to detect mild heart failure (Table 5, FACES Screening Tool.) It is important to be alert to heart failure in patients with cardiovascular risk factors, particularly hypertension, left ventricular dysfunction, and previous myocardial infarction. For example, in about 20% of heart failure cases, there has been antecedent left ventricular hypertrophy,³⁵ and myocardial infarction increases the risk of heart failure four- to fivefold compared with the general population.³⁵ Approximately 22% of male and 46% of female patients with myocardial infarction will be disabled by heart failure within 6 years.³⁶

Treatment

Research on actual practice patterns suggests that more rigorous adherence to current recommendations could greatly improve outcomes. Recently the use of ACE inhibitors at discharge in patients hospitalized for congestive heart failure was found to be 46% to 74%.^{6,37,38} Even in congestive heart failure patients who were ideal candidates for ACE inhibition (those for whom there is no reason to withhold ACE inhibitors), use at discharge was 72% to 96%.^{6,38,39} In addition, multiple studies show that only 26% to 44% of patients taking ACE inhibitors are receiving the target dosage.³⁹⁻⁴¹

Making Polypharmacy Work

Concerns about cost, compliance, and drug interactions have given polypharmacy a pejorative connotation, but heart failure is a classic exception to the notion that "less is more." Few patients relish a regimen of multiple pill taking, but this disorder, similar to some cases of diabetes and asthma, is unquestionably one in which multiple drugs offer clearcut advantages compared with monotherapy. The challenge, then, is making it work in real life.

Educating patients about their condition and motivating their adherence to a course of therapy are steps toward success. The physician or a well-prepared office staff member must take the time to explain the basic purpose and action of each drug in clear, comprehensible language. ("The diuretic helps your body get rid of excess fluid. The ACE inhibitor and the β -blocker work together to stop ongoing damage to your heart. The digoxin helps relieve symptoms like shortness of breath.") It should be emphasized that current therapy is keeping other patients alive and healthy who otherwise would have been disabled or even dead under older, simpler regimens. In practice, after they gain this understanding, few patients object to a multidrug regimen, even a challenging one.

Another critical aspect in patient compliance is the physician's support and reassurance in managing side effects. Patients should be alerted that, initially, they might experience some mild, intermittent postural light-headedness. Obviously, moderate to severe dizziness calls for the regimen to be adjusted. In these cases, the real problem might be overdiuresis; reducing the dosage of diuretic could permit upward titration of the ACE inhibitor or β -blocker to target doses. Therapy must also be individualized to the patient's lifestyle; for example, a patient who operates heavy machinery on the job will be less able to tolerate light-headedness than a retired patient living quietly at home.

Although patients should be made aware of possible adverse effects, the case need not be overstated. Patients should be reminded that most patients tolerate this drug regimen very well, and any discomforts associated with the beginning of therapy are likely to be mild and temporary.

Conscientious case management of heart failure does take time, but some routine functions can be delegated. An office staff member can be chosen to serve as a heart failure point person, responsible for education, compliance, and monitoring. A nurse coordinator, clinical nurse specialist, nurse practitioner, physician assistant, or other staff member can serve in this capacity. Having patients keep a daily chart of their weight and some basic standards of well-being (exercise tolerance, for example) is an excellent way to involve them in their own care. At clinic or office follow-up visits, the designated staff member can review these data, update medications,

and refresh patients' understanding of their drug regimen.

Cardiovascular Risk Management

In general, patients with heart failure are a population at high risk for cardiovascular disease. They should be considered as candidates for daily cardioprotective aspirin therapy and, if dyslipidemia is present, for lipid-lowering drug therapy. Hypertension must be adequately treated. In addition to drug therapy, patients should be encouraged to adopt the basic lifestyle measures associated with cardiovascular risk reduction.

Moderate, Regular Physical Activity

Any form of safe aerobic activity that is enjoyable and practical enough to be pursued several times a week—walking, gardening, and housework—should be encouraged. Strenuous isometric exercise such as competitive weight training is inadvisable.¹⁵

Moderate Sodium Intake

Extreme sodium restriction is seldom necessary, but moderate restriction permits the use of lower doses of diuretics.² Sodium should be limited to a maximum of 2 to 3 g/d for mild to moderate heart failure, and less than 2 g/d for severe heart failure. During diuretic therapy, patients might require an increase in dietary or supplemented potassium. Those receiving spironolactone (a potassium-sparing diuretic), however, should be monitored for hyperkalemia.

Smoking Cessation

For patients who are not ready to attempt quitting (or to try again), readiness should be assessed at every follow-up visit.

Moderate Alcohol Intake

In general, this means no more than 2 ounces, or 2 drinks per day.¹⁵ Those with an alcoholic cardiomyopathy should eliminate alcohol consumption altogether.

Maintaining Appropriate Body Weight

Patients with heart failure should be advised to weigh themselves daily to check for fluid retention and to report any gain of 2 pounds or more.

When to Refer

Most patients with heart failure can be cared for appropriately and effectively within the primary care setting. Success might be even more likely if β -adrenergic blockade therapy is begun and stabilized by a cardiologist during the early weeks of treatment, when close supervision of medications is essential.

Not all cases of heart failure are appropriate for primary care. Cardiology referral is indicated for patients who do not have a clearcut diagnosis, for those who have refractory moderate to severe heart failure, for patients who have been hospitalized more than once in the previous year for decompensated heart failure, and for those who have cardiac complications, such as ischemic or valvular heart disease. Consultation is also advisable before initiating β -adrenergic blockade in a patient with markedly low blood pressure (90/60 mm Hg or lower). Other candidates for referral are patients who remain substantially symptomatic on standard medical therapy as already outlined and those who, despite a fair trial, cannot tolerate the recommended regimen.

Why β -Blockers for Heart Failure?

β -Blockers were formerly considered to be contraindicated in heart failure therapy because they depressed left ventricular function. Despite this short-term effect, it is now evident that long-term β -adrenergic blockade reduces damage to heart and blood vessels caused by prolonged activation of the sympathetic nervous system in heart failure. The mechanisms of cardiotoxicity mediated by norepinephrine and epinephrine include:²⁷

1. Dysfunction and death of cardiac myocytes
2. Increased ventricular size and pressures, caused by peripheral vasoconstriction and increased intravascular volume (resulting from sympathetic impairment of renal salt and water excretion)
3. Provocation of arrhythmias
4. Increased heart rate (through stimulation of β_1 - and β_2 -receptors)

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