Treatment Gaps in the Pharmacologic Management of Heart Failure

Mihai Gheorghiade, MD,* Wendy A. Gattis, PharmD,† Christopher M. O'Connor, MD†

*Division of Cardiology, Northwestern University, Chicago, IL; †Division of Pharmacology, Duke University Medical Center, Durham, NC

Chronic heart failure continues to increase in incidence and prevalence despite many pharmacologic advances over the previous decade. Morbidity and mortality remain high, with the number of hospitalizations for worsening heart failure in 1999 approaching 1 million. In addition to investigation of new therapies for the treatment of heart failure, attention must be placed on identifying effective methods for increasing the adoption of proven therapies. First, the potential barriers to implementation of evidence-based medicine must be recognized. Subsequently, strategies to overcome such barriers can be developed. Published guidelines may be helpful in educating practitioners on current standards of care. Other tools may also be considered, and testing the influence of such tools on the implementation of optimal therapy may help the scientific community better understand the factors that influence decision-making among clinicians.
[Rev Cardiovasc Med. *2002;3(suppl 3):S11–S19*]

Key words: Heart failure • Angiotensin-converting enzyme inhibitors • β-blockers • Left ventricular dysfunction

The incidence and prevalence of heart failure in the United States continue to increase, and the associated morbidity and mortality remain unacceptably high despite more than a decade of research that has produced several lifesaving therapies for the treatment of heart failure. To appreciate the significance of the heart failure problem, the epidemiology and mortality of heart failure can be compared to that of cancer. As shown in Figure 1, the incidence of heart failure is more than double that of breast cancer. Similarly, the annual mortality rate for heart failure is 85% higher than that of combined stages of lung cancer. The 5-year survival for most cancers is significantly higher than for heart failure; patients with heart failure have a 5-year survival, which is similar to that of lung cancer (Figure 2).[1,2]

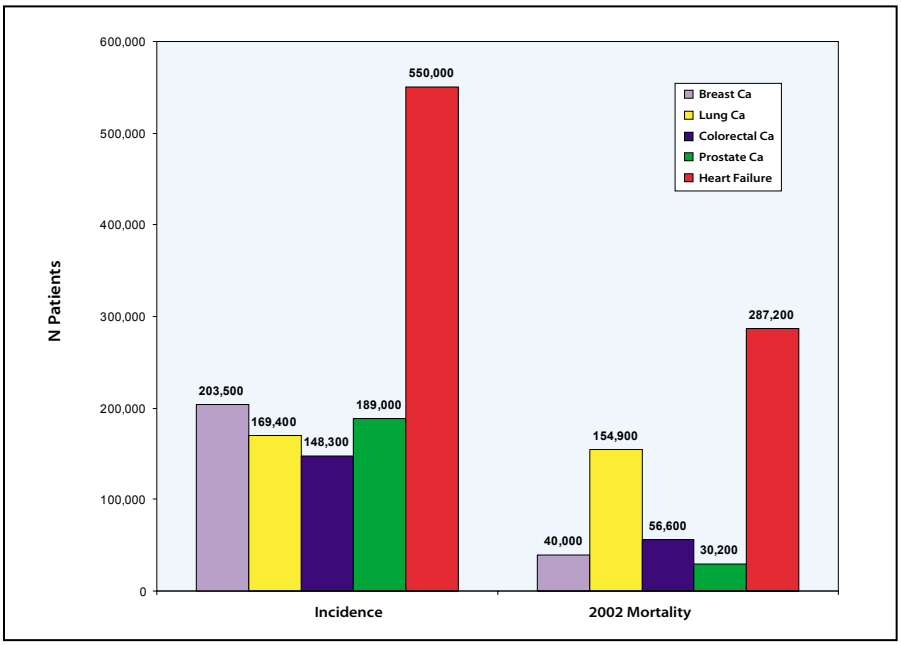

Figure 1. *Epidemiology: cancer (Ca) versus heart failure.*

These statistics are sobering and reinforce the need to implement therapies that accomplish the goals of caring for the heart failure patient. A primary goal is to prevent heart failure mortality. Heart failure morbidity is also exceedingly high and represents a significant burden on patients, caregivers, and the overall health system. Therefore, in addition to improving survival, the goals of reducing heart failure hospitalizations and improving quality of life are also extremely important. This article briefly describes the standard of care for patients with heart failure, provides hypotheses for the delayed adoption of evidence-based medicine among physicians, and outlines potential strategies that may be useful in bridging the gap between evidence-based medicine and clinical practice in the heart failure population.

Current Standard of Care

The optimal pharmacologic regimen for patients with chronic heart failure includes angiotensin-converting enzyme (ACE) inhibitors, β-blockers (limited to those β-blockers with a U.S Food and Drug Administration [FDA]-approved heart failure indication), diuretics as needed for symptomatic treatment of volume overload, and digoxin and spironolactone in patients who are persistently symptomatic despite ACE inhibitors and β-blockers.[3–12] The importance of angiotensin-receptor blockers is still being defined, but these agents may help reduce the need for hospitalization in persistently symptomatic patients already on ACE inhibitors or in patients intolerant to ACE inhibitors who are not treated with β-blockers.[13]

Data from the period immediately following publication of ACE-inhibitor trials revealed that ACE inhibitors were underused in the heart failure population, often without the patient exhibiting a clear contraindication to the therapy.[14–21] Prescription of ACE inhibitors in the majority of patients with heart failure was not observed until almost a decade after the first trials demonstrating their benefits were published, and the frequency with which ACE inhibitors are prescribed is now estimated at over 75% of all patients who are candidates for therapy.

The adoption of β-blocker therapy among clinicians has traveled a path similar to the acceptance of ACE inhibitors. It has been shown that the delay between the availability of clinical data and changing clinical

Figure 2. *Five-year survival: cancer (Ca) versus heart failure.*

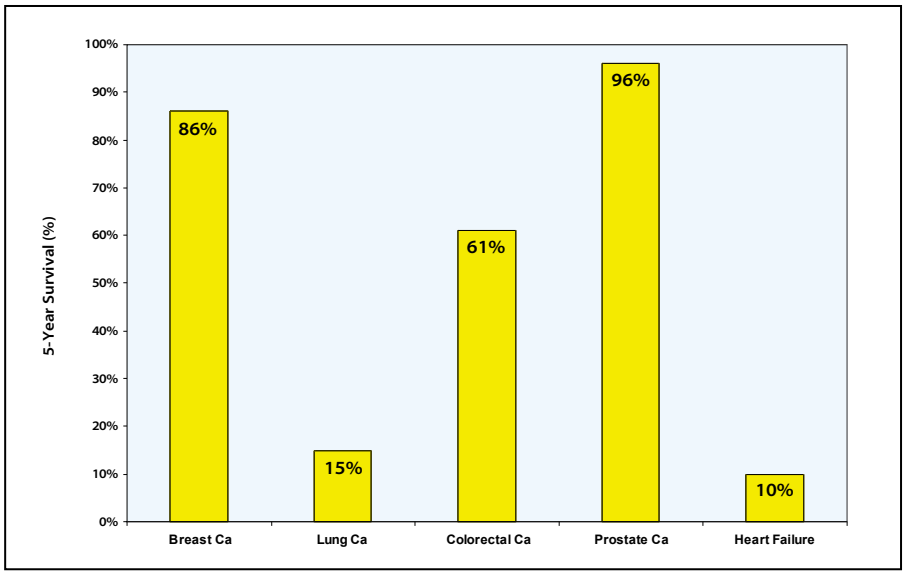

Table 1
Major Placebo-Controlled Trials of Beta Blockade in Heart Failure

Study	Drug	Heart Failure Severity	Patients (n)	Follow-up (yr)	Target Dosage (mg)	Mean Achieved Dosage	Effects on Outcomes
CIBIS[23]	Bisoprolol*	Moderate/severe	641	1.9	5 q.d.	3.8	All-cause mortality NS
CIBIS-II[10]	Bisoprolol*	Moderate/severe	2647	1.3	10 q.d.	7.5	All-cause mortality ↓34% ($P < .0001$)
MDC[24]	Metoprolol tartrate*	Mild/moderate	383	1.0	100–150 q.d.	108	Death or need for transplant (primary endpoint) NS
MERIT-HF[9]	Metoprolol succinate	Mild/moderate	3991	1.0	200 q.d.	159	All-cause mortality ↓34% ($P < .0062$)
BEST[25]	Bucindolol*	Moderate/severe	2708	2.0	50–100 b.i.d.	152	All-cause mortality NS
US Carvedilol[8]	Carvedilol	Mild/moderate	1094	6.5 months	6.25–50 b.i.d.	65	All-cause mortality ↓65% ($P < .0001$)
COPERNICUS[11]	Carvedilol	Severe	2289	10.4 months	25 b.i.d.	35	All-cause mortality ↓35% ($P < .0014$)

* Not an approved indication

practice is often substantial, even for therapies that are seemingly easy to prescribe, such as aspirin in patients with coronary disease. The adoption of β-blockers as a standard treatment for heart failure also faces additional barriers that were not a factor with ACE inhibitors and other evidence-based therapies. Traditionally, physicians have been educated to avoid β-blockers in the heart failure population due to concern that a "negative inotrope/chronotrope" would have harmful effects in these patients. This concern has been dispelled, and in fact β-blockers are the only agents that have been shown to improve ejection fraction and promote reverse remodeling over time. Despite the scientific data supporting the benefits of β-blockers in heart failure (Table 1), overcoming traditional thinking is a difficult process that takes years of education. Thus it is not surprising that 5 years after the publication of the first β-blocker trial, only 20%–50% of patients with heart failure are treated with β-blockers.

The underuse of β-blockers is of great concern when viewed in the context of the morbidity and mortality associated with heart failure. A consistent 35% reduction in mortality on top of ACE inhibitors has been observed in the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) trial, Metaprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF), and Cardiac Insufficiency Bisoprolol Study 2 (CIBIS-2) trials (Table 2). Thus, a crude analysis of the epidemiology and the mortality suggests that of the 287,000 patients who died from heart failure in 1999,[1] approximately 100,000 could have been saved with β-blocker therapy. Likewise, hospitalizations for heart failure are common, with 962,000 discharges reported in 1999. In the COPERNICUS trial, the reduction in the composite endpoint of death or rehospitalization was 31%.[11] If this figure is applied to the hospitalizations reported in 1999, then almost 300,000 hospitalizations could have been prevented. At a Medicare reimbursement rate for hospitalization of $6000 per discharge, $1.8 billion could potentially have been saved by implementing β-blocker therapy.

Of the 287,000 patients who died from heart failure in 1999, approximately 100,000 could have been saved.

One of the first steps in understanding how to optimize the use of evidence-based therapies is to recognize implementation barriers. In addition to traditional teaching to

avoid β-blockers in heart failure, other challenges exist. An important issue, but one that is likely underappreciated, is the diagnosis of heart failure. Failure to pursue diagnostic testing of left ventricular function may be particularly common for patients with a history of coronary disease or hypertension who are asymptomatic or minimally symptomatic but have left ventricular dysfunction. Thus another gap that exists in the current state of heart failure management resides in the underdiagnosis of asymptomatic or mildly symptomatic patients who are at high risk of developing heart failure because of concomitant diseases such as hypertension or coronary artery disease.

Likewise, patients who are minimally symptomatic may be less likely to receive chronic therapies such as ACE inhibitors or β-blockers because they appear to be "doing well." These patients are at the highest risk of sudden cardiac death, which is the mechanism of over 50% of deaths in patients with mild to moderate heart failure symptoms. Even though asymptomatic patients have a lower risk of sudden death as compared to patients with mild to moderate heart failure, even a low incidence is significant because of the large numbers of patients with asymptomatic left ventricular dysfunction. The heart failure population has a risk of sudden death 6–9 times that of the general population, increasing the need to implement therapies such as β blockade that reduce sudden death.

The heart failure population has a risk of sudden death 6–9 times that of the general population.

The revised American College of Cardiology/American Heart Association (ACC/AHA) guidelines address the issues of patient identification, classification, and therapeutic strategies in this population. The new approach may help clinicians refine their thinking in terms of strategies to slow or prevent the progression of heart failure and occurrence of sudden death.[22] Table 3 summarizes potential reasons for the pharmacologic gaps in the management of heart failure with specific focus on β blockade.

Table 2
Beta-Blocker Trials in Heart Failure

Trial	% Mortality Reduction	% Reduction in Death or Cardiovascular Hospitalization
U.S. Carvedilol[8]	65%; $P < .001$	38%; $P < .001$
MERIT-HF[9]	34%; $P = .006$	19%; $P = .00012$
CIBIS-II[10]	34%; $P < .0001$	20%; $P = .0006$ (all-cause hospital admission)
COPERNICUS[11]	35%; $P = .00013$	24%; $P = .0004$
CAPRICORN[22]	23%; $P = .031$	8%; $P = .296$ (all-cause mortality + cardiovascular hospitalization)

Guideline Approach to Heart Failure Management

The recent ACC/AHA guidelines are an important step in bridging the current treatment gap for patients with heart failure. First, the guidelines redefine the way patients are classified. The revised classification scheme includes patients at risk for developing heart failure and defines conditions that contribute to heart failure progression. It highlights strategies that can be used to address these risks. Table 4 describes the new classification scheme for heart failure.

Before patients can be classified, they must first be identified as at risk of or having heart failure. The revised guidelines describe for physicians common presentations for which heart failure should be included in the differential diagnosis. The specific recommendations are presented in Table 5. The guidelines appropriately discuss the fact that vague symptoms may often be attributed to other causes such as deconditioning or pulmonary disease, and as a result, heart failure is not diagnosed until symptoms progress further. It is extremely important that an accurate diagnosis of heart failure is made because of the high risk of morbidity and mortality from sudden cardiac death, even in patients who are mildly symptomatic. The underdiagnosis of heart failure is a barrier to the optimal care of this patient population, which needs to be addressed in addition to addressing the gap that exists in treating heart failure patients with evidence-based therapies such as β-blockers.

To confirm or refute heart failure as a differential diagnosis, a variety of diagnostic tests are available to

the practicing physician. As shown in Table 5, echocardiography is often the most accessible, useful, and comprehensive initial evaluation for patients suspected of having left ventricular dysfunction. Once the presence of left ventricular dysfunction is documented, treatments categorized for Stage B should be prescribed. Further testing is often indicated specifically to define the cause and degree of left ventricular dysfunction. Radionuclide ventriculography, magnetic resonance imaging, chest radiography, electrocardiography, noninvasive ischemia assessments, and coronary arteriography may be employed in the workup of the heart-failure patient. Most recently, laboratory assessment of circulating brain natriuretic peptide (BNP) has emerged as a potential diagnostic test for heart failure. The utility of BNP for diagnosing heart failure is still under investigation, but it holds promise in terms of differentiating noncardiac dyspnea from heart failure. However, its specificity is limited in terms of differentiating between patients with systolic dysfunction and preserved systolic function.

Strategies to Bridge the Gap and Optimize Heart Failure Management

The best and most effective approach to improve management of heart failure and bridge the gaps in both diagnosis and treatment is not known. However, several strategies may be considered, and it is likely that a combination of these strategies will prove to be the most efficacious.

First, the presence of guidelines supported by the leading cardiology professional organizations is important. Although the guidelines may not be widely read by practicing physicians, they provide a foundation from which a standard of care

Table 3
Potential Reasons for the Pharmacological Gap in the Treatment of Heart Failure: Focus on Beta Blockade

Issues Related to Heart Failure

- *Definition of Heart Failure:* Although the term "chronic heart failure" (CHF) is commonly used, there is no clear definition for this condition. Many patients with decreased left ventricular systolic function who are at risk for sudden death have minimal or no symptoms of heart failure. One reason patients are not treated for CHF may be related to the fact that diagnosis is not being made.
- *Pathophysiology of Heart Failure:* Although 40 years ago the goal was to improve cardiac performance (contractility and/or decrease preload and afterload), most agents that increase inotropy and/or cause vasodilatation also decrease survival. In contrast, agents that have a neutral or even a negative inotropic effect, such as ACE inhibitors and β-blockers, prolong survival—most likely by improving the neurohormonal profile. Although acute symptoms are related to abnormal hemodynamics, progression of heart failure, including death, may be related to neurohormonal activation.
- *Prognostic Considerations:* Although prognosis is poor with patients with symptoms at rest, the majority of patients with systolic dysfunction are asymptomatic or minimally symptomatic. Although mortality in this group is far less than in patients with severe CHF (10% at 2 years compared to 50% in 1 year in patients with symptoms at rest), most patients who are going to die are patients with minimal symptoms, because there are approximately 5 million of them compared to 200,000 patients who have symptoms at rest.
- *Prevention of Sudden Death:* Most patients who are going to die will do so suddenly and unexpectedly, in spite of clinical compensation. Sudden death may account for 60%–70% of patients with CHF who die. Accordingly, the goal is no longer to control symptoms but to decrease the rate of sudden death. Beta-blockers are probably the best agents to prevent sudden death.
- *Patient Evaluation:* There is dissociation between physical findings and severity of left ventricular dysfunction. Most patients with low systolic function have minimal or no symptoms. Often those patients are not identified as having heart failure; therefore they are not being treated.
- *Available Therapies:* Although there are many therapies utilized for heart failure, such as nitrates, hydralazine, calcium-channel-blockers, diuretics, and digoxin, only two are truly lifesaving—β-blockers and ACE inhibitors. Most therapies tested to date, including milrinone, xamoterol, enoximone, diltiazem, mibefradil, tumor necrosis factor, and endothelin blocking agents, have given negative results. This consideration should be taken into account when approaching a patient with mild to moderate heart failure, in order to concentrate on truly lifesaving therapies.

Issues Related to Beta-Blockers

- *Paradigm Shift:* For many years β-blockers were contraindicated in heart failure patients because of their negative inotropic effects. However, the overwhelming data suggest that in spite of a short-term negative inotropic effect, β-blockers would actually increase cardiac contractility related to their positive biological effect, and this would result in a major decrease in mortality in patients already taking an ACE inhibitor.
- *Patient Selection and Initiation of Therapy:* The available data suggest that β-blockers, particularly carvedilol, are safe for all heart-failure patients, providing that the starting dose is low and the patient is not dependent on intravenous inotropics or intravenous diuretics. Physicians should prescribe β-blockers because approximately 60 million patients are at risk for heart failure, 10 million patients have asymptomatic systolic dysfunction, and 5 million patients with symptomatic heart failure are responding to therapy. It is unrealistic to think that the cardiologist should be the only one to prescribe this therapy. A standard should be created, and the primary care physician is the main player in prescribing and optimizing this therapy.

Data from Gheorghiade and Bonow.[26]

Table 4
Heart Failure Stages

Stage	Description	Examples	Therapies
A	Estimated population: 60 million; Patients at high risk of developing heart failure because of the presence of conditions strongly associated with development of heart failure. Such patients have no identified structural or functional abnormalities of the pericardium, myocardium, or cardiac valves and have never shown signs or symptoms of heart failure	Systemic hypertension; coronary artery disease; diabetes mellitus; history of cardiotoxic drug therapy or alcohol abuse; personal history of rheumatic fever; family history of cardiomyopathy	• Treat hypertension • Encourage smoking cessation • Encourage regular exercise • Discourage alcohol intake, illicit drug use • ACE inhibition ○ History of atherosclerotic vascular disease ○ Diabetes mellitus ○ Hypertension ○ Other cardiovascular risk factors
B	Estimated population: 10 million; Patients who have structural heart disease that is strongly associated with the development of heart failure but who show no signs or symptoms of heart failure	Left ventricular hypertrophy or fibrosis; left ventricular dilatation or hypocontractility; asymptomatic valvular heart disease; previous myocardial infarction	• All measures under Stage A • ACE inhibitors ○ Post–myocardial infarction regardless of ejection fraction ○ Reduced ejection fraction • Beta-blockers ○ Recent myocardial infarction regardless of ejection fraction ○ Reduced ejection fraction
C	Estimated population: 5 million; Patients who have current or prior symptoms of heart failure associated with underlying structural heart disease	Dyspnea or fatigue due to left ventricular systolic dysfunction; asymptomatic patients who are undergoing treatment for prior symptoms of heart failure	• All measures under Stage A • Routine drugs ○ ACE inhibitors ○ Beta-blockers ○ Diuretics ○ Digoxin ○ Spironolactone or angiotensin-receptor blockers in patients with persistent symptoms treated with the above • Dietary salt restriction
D	Estimated population: 200,000 Patients with advanced structural heart disease and marked symptoms of heart failure at rest despite maximal medical therapy and who require specialized interventions	Patients frequently hospitalized hospitalized for heart failure or who cannot cannot be safely discharged; hospitalized awaiting heart transplant; at home receiving continuous IV support for symptom relief or mechanical circulatory assist device support; hospice	• All measures under A, B, and C • Mechanical assist devices • Heart transplantation • Continuous IV inotropic infusions for palliative care • Hospice care • Refer to heart failure disease management program

Reproduced with permission. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol*. 2001;38:2101–2113.

can be established. Educational programs promoting the guidelines can be conducted. Care maps, pathways, and standard orders for hospitals can be developed based on these guidelines. Protocols guiding physicians as to how and when diagnostic testing and medications should be employed may also be useful. The protocol-guided strategy is currently being tested in the Initiation Management Predischarge Process for Assessment of Carvedilol Therapy for Heart Failure (IMPACT-HF) study, which is described in an article by

Table 5
Diagnosing Heart Failure

Patient Presentation	Differential Diagnosis	
• Decreased exercise tolerance	• Heart failure • Coronary artery disease • Aging	• Deconditioning • Pulmonary disease
• Syndrome of fluid retention	• Heart failure • Liver failure	• Renal failure • Myxedema (hypothyroidism)
• No symptoms or symptoms of another cardiac or noncardiac disorder	• Heart failure • Myocardial infarction	• Arrhythmia • Pulmonary or systemic thromboembolic event

Diagnostic Tool	Specific Focus	
History and physical exam	• Identify concomitant diseases ❍ Hypertension ❍ Diabetes ❍ Hyperlipidemia ❍ Degree/extent of ischemia ❍ Valvular disease ❍ Peripheral vascular disease ❍ Rheumatic fever	❍ Radiation therapy to the chest ❍ Cardiotoxin exposure (chemotherapy) ❍ Illicit alcohol or drug use ❍ Sexually transmitted diseases ❍ Collagen vascular disease ❍ Thyroid abnormality ❍ Pheochromocytoma
	• Family history • Signs ❍ Displaced point of maximum intensity ❍ Jugular venous distension • Abnormal blood pressure response to Valsalva maneuver	❍ 3rd heart sound ❍ Leg edema
Echocardiography with Doppler	• Left and right ventricular ejection fraction • Segmental wall motion abnormalities • Diastolic function • Quantitative assessments • Valvular disease (insufficiency or stenosis) • Other structural abnormalities ❍ Pericardial disease • Pulmonary artery pressure	
Radionuclide ventriculography	• Accurate measurements of global and regional function	
Magnetic resonance imaging	• Left ventricular mass, shape, hyperenhancement (myocardial infarction) • Myocardium viability • Right ventricular dysplasia • Pericardial disease	
Chest radiography	• CT ratio • Alveolar edema, interstitial edema • Estimated degree of cardiac enlargement • Pulmonary congestion	• Pulmonary disease • Upper lobe redistribution • Pleural effusions
12-lead electrocardiography	• Evidence of previous myocardial infarction • Left ventricular hypertrophy	• Arrhythmia • Left bundle branch block
Coronary angiography, ventriculography, right heart catheterization	• Presence and extent of coronary disease • Left ventricular ejection fraction	• Valvular abnormalities • Hemodynamic measurements (includes pulmonary artery pressure)
Noninvasive ischemia assessments	• Presence/degree of coronary disease • Ischemia and/or hibernation	• Left ventricular function • Myocardial perfusion scintigraphy with technetium and thallium
Myocardial biopsy	• Myocardial inflammation or infiltration	• Selective cases only (eg, posttransplant)
Circulatory brain natriuretic peptide	• Potential for diagnosis, assess prognosis and response to therapy • Cardiac vs noncardiac dyspnea	• Correlates to elevated filling pressures

Wendy Gattis and colleagues in this supplement.

In order to be completely successful, it is very likely that the mandate to incorporate evidence-based practices will need to come from a source linked to reimbursement for services. Heart failure is the most common diagnosis among Medicare beneficiaries, and as the population continues to age, the incidence of heart failure will continue to climb. Reducing hospitalizations will be important for the financial viability of the Medicare budget. Ensuring the use of agents that reduce the rate of hospitalization by more than 30% should become a focus of health care agencies such as Medicare. Currently, the Health Care Financing Administration evaluates institutions based on their adherence to standards of care for heart failure. Currently, these standards include prescription of ACE inhibitors, assessment of left ventricular function, and patient education. Use of β-blocker therapy may become incorporated into these standards, and Medicare reimbursements may ultimately be tied to an institution's adherence to such guideline standards. If institution reimbursements are contingent on adherence to practice standards, a rapid adoption of evidence-based therapies among clinicians may be observed. This strategy may prove to be the most effective to begin to close the gap that exists between clinical practice and available evidence from clinical trials.

Conclusion

Although the prevalence of heart failure continues to increase, related to the aging population and more patients surviving their initial insult from a myocardial infarction, mortality and morbidity can be substantially reduced by instituting lifesaving therapies such as ACE inhibitors and β-blockers.[27] The problem remains that the majority of patients who would benefit from those therapies, particularly β-blockers, do not receive this therapy. When used appropriately, β-blockers will reduce the devastating toll of heart failure. ■

References

1. 2002 Heart and Stroke Statistical Update. American Heart Association. Available from http://www.americanheart.org.
2. Cancer Facts and Figures 2002. American Cancer Society. Available from http://www.cancer.org.
3. CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure: results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med*. 1987;316:1429–1435.
4. Cohn JN, Johnson G, Ziesche S, et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. *N Engl J Med*. 1991;325:303–310.
5. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med*. 1991;325:293–302.
6. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med*. 1992;327:685–691.
7. The Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med*. 1997;336:525–533.
8. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. *N Engl J Med*. 1996;334:1349–55.
9. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF). *Lancet*. 1999;353:2001–2007.
10. CIBIS-II Investigators and Committee. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. *Lancet*. 1999;353:9–13.
11. Packer M, Coats AJS, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med*. 2001;344:1651–1658.
12. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med*. 1999;341:709–717.
13. Cohn JN, Tognoni G for the Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med*. 2001;345:1667–1675.
14. Bourassa MG, Gurne O, Bangdiwala SI, et al. Natural history and patterns of current practice in heart failure. *J Am Coll Cardiol*. 1993;22(suppl A):14A–19A.

Main Points

- The 5-year survival for most cancers is significantly higher than for heart failure; patients have a 5-year survival similar to that of lung cancer.
- Despite conclusive data supporting their benefits, only 20%–40% of patients with heart failure are treated with β-blockers.
- Physicians have avoided β-blockers in the heart failure population due to concern that a "negative inotrope/chronotrope" would have harmful effects; this is now known not to be the case.
- Beta-blockers are the only agents that have been shown consistently to improve ejection fraction.
- Vague symptoms may be attributed to other causes, such as deconditioning or pulmonary disease, and so heart failure may not be diagnosed until symptoms progress.
- Echocardiography is often the most accessible, useful, and comprehensive initial evaluation for patients suspected of having left ventricular dysfunction; further testing can define the cause and degree of dysfunction.

15. Packer M. Do angiotensin-converting enzyme inhibitors prolong life in patients with heart failure treated in clinical practice? *J Am Coll Cardiol*. 1996;28:1323–1327.
16. Philbin EF, Andreou C, Rocco TA, et al. Patterns of angiotensin-converting enzyme inhibitor use in congestive heart failure in two community hospitals. *Am J Cardiol*. 1996;77:832–838.
17. Rich MW, Beckham V, Wittenberg C, et al. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. *N Engl J Med*. 1995;333:1190–1195.
18. Luther P, Baldus D, Beckham V, et al. Adherence to prescribed medications in elderly patients with congestive heart failure. *Geriatr Cardiol*. 1995;32–40.
19. Clinical Quality Improvement Network Investigators. Mortality risk and patterns of practice in 4606 acute care patients with congestive heart failure. The relative importance of age, sex, and medical therapy. *Arch Intern Med*. 1996;156:1669–1673.
20. The Large State Peer Review Organization Consortium. Heart failure treatment with angiotensin-converting enzyme inhibitors in hospitalized Medicare patients in 10 large states. *Arch Intern Med*. 1997;157:1103–1108.
21. Bart BA, Gattis WA, Diem SJ, O'Connor CM. Reasons for underuse of angiotensin-converting enzyme inhibitors in patients with heart failure and left ventricular dysfunction. *Am J Cardiol*. 1997;79:1118–1120.
22. CAPRICORN Investigators. Effect of carvedilol outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. *Lancet*. 2001;357:1385–1390.
23. CIBIS Investigators and Committees. A randomized trial of beta-blockade in heart failure. The Cardiac Insufficiency Bisoprolol Study (CIBIS). *Circulation*. 1994;90:1765–1773.
24. Waagstein F, Bristow MR, Swedberg K, et al, for the Metoprolol in Dilated Cardiomyopathy (MDC) Trial Study Group. Beneficial effects of metoprolol in idiopathic dilated cardiomyopathy. *Lancet*. 1993;342:1441–1446.
25. The Beta-Blocker Evaluation of Survival Trial Investigators. A trial of the beta-blocker bucindolol in patients with advanced chronic heart failure. *N Engl J Med*. 2001;344:1659–1667.
26. Gheorghiade M, Bonow RO. Introduction and overview: use of beta-blocker therapy for mild to moderate chronic heart failure. *Am J Med*. 2001;110:1S–5S.
27. Gheorghiade M, Eichhorn EJ. Practical aspects of using beta-adrenergic blockade in systolic heart failure. *Am J Med*. 2001;110:685–735.