

# β-Blockers in Heart Failure

## Clinical Applications

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ONCE THOUGHT HARMFUL FOR patients with heart failure,<sup>1,2</sup> β-blockers have been shown to reduce morbidity and mortality in heart failure patients with left ventricular (LV) systolic dysfunction and stable fluid status.<sup>3-10</sup> The appropriate use of β-blockers in heart failure is now a key aspect of high-quality cardiovascular care, requiring appropriate prescribing behavior and effective monitoring systems to maintain patient safety. The goal of this article is to distill the current scientific evidence<sup>6-10</sup> and consensus guidelines<sup>11-13</sup> into practical, immediately useful information about patient selection, discussions with patients, management and monitoring, and systems improvements to optimize quality of care and safety for all heart failure patients.

### Patient Selection

All heart failure patients with LV systolic dysfunction should be considered for β-blockers to reduce morbidity and prevent mortality.<sup>13</sup> Previous guidelines from the American College of Cardiology (ACC) and American Heart Association (AHA)<sup>14</sup> and current guidelines from the Heart Failure Society of America<sup>11</sup> have recommended β-blockers for certain patients with mild to moderate heart failure according to New York Heart Association functional classification.<sup>4,6,7</sup> Prompted by new evidence,<sup>5,10</sup> the most

β-blockers reduce morbidity and mortality in heart failure patients with left ventricular systolic dysfunction and stable fluid status. The successful adoption of β-blocker guidelines for these patients requires an understanding of the value of this therapy and effective systems to maintain safety and ensure high quality of care. This article distills scientific evidence and consensus guidelines into a series of cases and practical answers about patient selection, discussions with patients, management and monitoring, and systems improvements to optimize quality of care, safety, and benefit for all patients with heart failure.

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recent ACC–AHA guidelines<sup>13</sup> have introduced a broader disease-progression staging system (FIGURE 1) that ranges from patients without structural heart disease but at risk for heart failure (ACC–AHA stage A) to severely ill patients with a need for specialized interventions (ACC–AHA stage D). The ACC–AHA guidelines endorse the use of β-blockers for all patients with heart failure or those at risk for heart failure, except those with a history of intolerance to β-blockers and those with a contraindication. In addition, β-blockers are not recommended without a heart failure specialist first being consulted for patients with refractory heart failure, multiple hospitalizations, or a need for specialized treatments (ACC–AHA stage D) such as a mechanical circulatory-assist device or intravenous inotropic support.

The following cases are examples of the typical outpatients who have heart failure and are most appropriate for receiving β-blockers.

### Patient 1

Patient 1 is a 60-year-old man who has chronic heart failure and complains of dyspnea upon mild to moderate exer-

tion. A recent LV ejection fraction measurement was 25%. His weight is stable; he has trace pedal edema but no rales. His medications include an angiotensin-converting enzyme (ACE) inhibitor, digoxin, furosemide, and spironolactone.

This patient is ideal for a trial of β-blocker therapy. He has dyspnea with mild to moderate exertion (New York Heart Association functional class II or III; ACC–AHA stage C) and LV systolic dysfunction (LV ejection fraction <35% to 40%) and is similar to many patients enrolled in the first major clinical trials of β-blockers.<sup>4,6,7</sup>

Like most patients in clinical trials, this patient is receiving stable doses of

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a diuretic.<sup>4-7</sup> To maximize patient safety, guidelines<sup>11-13</sup> recommend that β-blockers be initiated only in heart failure patients who are clinically euvolemic or receiving stable doses of diuretics without signs of fluid overload such as pulmonary rales, jugular venous distension, or more than minimal peripheral edema (BOX 1). If fluid status worsens after a β-blocker is started, guidelines<sup>13</sup> recommend increasing the diuretic dosage (or initiating a diuretic if one is not already started), provided the patient does well, eg, has no hypotension, evidence of hypoperfusion, or requirement for intravenous positive inotropic support.

Patient 1 is also similar to many patients in clinical trials in that he is receiving stable doses of an ACE inhibitor and digoxin.<sup>4-7</sup> Evidence for β-blocker use is most applicable for patients receiving these medications, since most patients in trials of mild to moderate heart failure were receiving at least a low dose of an ACE inhibitor (90%-97% of patients) and digoxin (50%-68%). The simultaneous initiation of β-blockers and ACE inhibitors, discussed below, is feasible but was not evaluated in the clinical trials.

If patient 1 instead had dyspnea at rest (New York Heart Association class III or IV, ACC-AHA stage C) and stable fluid status, evidence for β-blocker use would be provided by the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) Trial,<sup>5</sup> a study of patients with severe heart failure (symptoms at minimal exertion or at rest).

**Patient 2**

Patient 2 is an asymptomatic 62-year-old male jogger presenting for a regular checkup. His only medication is a daily aspirin. His LV ejection fraction was 30% last year following an acute myocardial infarction (AMI) 2 years ago.

This patient has asymptomatic LV dysfunction (New York Heart Association class I, or ACC-AHA stage B) and is a good candidate for β-blockers on the basis of his history of AMI.<sup>15</sup> β-Blockers would also be recommended if he had LV systolic dysfunction from some other

**Figure 1.** American College of Cardiology–American Heart Association (ACC–AHA) Stage and New York Heart Association (NYHA) Classification of Heart Failure

| ACC-AHA Stage  | NYHA Functional Classification        |
|--|---------------------------------------|
| A At high risk for heart failure but without structural heart disease or symptoms of heart failure (eg, patients with hypertension or coronary artery disease) | None                                  |
| B Structural heart disease but without symptoms of heart failure   | I Asymptomatic                        |
| C Structural heart disease with prior or current symptoms of heart failure   | II Symptomatic with moderate exertion |
|  | III Symptomatic with minimal exertion |
| D Refractory heart failure requiring specialized interventions   | IV Symptomatic at rest                |

cause, such as idiopathic dilated cardiomyopathy.<sup>13</sup> Although there is currently insufficient clinical trial evidence to recommend β-blocker use in patients with asymptomatic LV dysfunction, studies<sup>10,16-18</sup> and recent guidelines<sup>11,13</sup> suggest that β-blockers should be initiated because they reduce progression to heart failure, as in trials of coronary artery disease or hypertension.<sup>17,19</sup>

The 2 previous patients are prototypical “ideal” examples of heart failure patients for whom β-blockers are recommended. Clinicians, however, must often decide about the use of β-blockers for a population of patients that is more diverse than the patients included in clinical trials. The following case illustrates an example of the many patients in clinical practice with chronic comorbidities and other factors that have not been well represented in clinical trials.

**Patient 3**

Patient 3 is an 81-year-old black woman who has dyspnea on minimal exertion and was hospitalized recently for intravenous diuresis. Her LV ejection fraction was measured in the hospital at 28%. She has no signs or symptoms of fluid overload when receiving appropriate doses of diuretic and ACE inhibitor. She has well-controlled diabetes mellitus, chronic obstructive pulmonary disease,

and a pacemaker that was placed for sick sinus syndrome.

This patient was only recently discharged from the hospital with fluid overload, but she appears to have good fluid balance after receiving oral diuretics and is still a good candidate for a trial of β-blockers. The results from COPERNICUS<sup>5</sup> suggest that heart failure patients who were hospitalized or given intravenous diuretics within 14 days will do well when receiving β-blockers, provided that they have stable fluid status. On the other hand, β-blockers should not be used in patients who require the intensive care unit, intravenous vasodilators, or intravenous positive inotropic agents.<sup>13</sup>

Patients with symptomatic bradycardia should not receive a β-blocker until the cause of bradycardia is ascertained and treated. The recent ACC-AHA<sup>13</sup> and Heart Failure Society of America guidelines<sup>11</sup> do not recommend a specific heart-rate threshold in asymptomatic patients, but most major trials<sup>4,5,7</sup> excluded even asymptomatic patients with an untreated heart rate of 65/min or less, and the previous ACC-AHA guideline<sup>14</sup> recommended avoiding β-blockers in patients with untreated heart rates of less than 60/min. Patient 3 had been found to have sick sinus syndrome, but β-blockers should be safe because she has a pacemaker.

**Box 1. Selection of Patients With Heart Failure for β-Blocker Therapy\***

**INDICATIONS**

**Asymptomatic Left Ventricular Dysfunction (American College of Cardiology–American Heart Association [ACC–AHA] Stage B)**

- No dyspnea on exertion (New York Heart Association [NYHA] class I)
- Left ventricular ejection fraction <35% to 40%
- No signs of fluid overload (given diuretic if necessary to maintain fluid balance)
- Medications should include an angiotensin-converting enzyme (ACE) inhibitor
- Evidence is best for patients with a risk for worsened heart failure caused by concurrent hypertension, coronary artery disease, or another cause

**Structural Heart Disease With Prior or Current Symptoms of Heart Failure (ACC–AHA Stage C)**

- Dyspnea on mild to moderate exertion or dyspnea at rest if otherwise stable (NYHA class II and III and some patients with NYHA class IV)
- Left ventricular ejection fraction <35% to 40%
- No signs of fluid overload (given diuretic if necessary to maintain fluid balance)
- Medications should include an ACE inhibitor and digoxin if indicated

**CONTRAINDICATIONS**

- Hospitalized in an intensive care unit
- Evidence of fluid overload or severe volume depletion
- Recent requirement for intravenous treatment with positive inotropic agent
- Reactive airways disease requiring inhaled β-adrenergic agonist therapy
- Symptomatic bradycardia or advanced heart block without a pacemaker

\*Abstracted from ACC–AHA guidelines.<sup>13</sup> Guidelines also recommend β-blockers for certain patients at risk for developing heart failure (ACC–AHA stage A) caused by hypertension or coronary artery disease. Patients with severe symptoms and recurrent hospitalizations (refractory heart failure or ACC–AHA stage D) should be evaluated by a physician experienced in treating heart failure.

Diabetes mellitus was once thought to be a contraindication to β-blocker use, but β-blockers have since been shown to be well tolerated in trials, with little concern of masking hypoglycemia.<sup>14,20–22</sup> Patients with bronchospasm requiring inhaled β-agonists should not receive β-blockers, but patients with nonreversible chronic obstructive pulmonary disease have been included in several studies<sup>4,7</sup> and can be expected to do well if observed for worsening respiratory status. Additionally, heart failure patients with chronic obstructive pulmonary disease<sup>20,23</sup> and diabetes<sup>21,22</sup> may have a greater absolute benefit from β-blockers than those without these comorbidities. Thus, the careful use of β-blockers in patients with diabetes or mild chronic obstructive pulmonary disease (not requiring bronchodilators) is prudent.

Some clinicians may be reluctant to initiate a β-blocker on the basis of this patient's age, since patients older than

80 years have been excluded from many trials and may be considered to have a higher risk from the medication. Nevertheless, β-blockers have been found to be safe and effective in smaller studies<sup>24,25</sup> and in a large retrospective study of patients after AMI that included more than 10 000 patients older than 75 years and receiving a β-blocker.<sup>26</sup> Thus, the potential benefits from β-blockers seem to outweigh the risks in this population.

Some experts have questioned the application of clinical trial results to subgroups such as women<sup>4,6,7</sup> and black patients,<sup>20,27</sup> but recent data<sup>28–30</sup> and the expert opinion of consensus groups<sup>13</sup> strongly endorse the extension of trial results to such groups not well represented in the trials. Thus, patient 3 has no absolute contraindications to β-blocker use despite several differences between her case and that of subjects in clinical trials. She is likely to benefit from cautious initiation of a

β-blocker and close follow-up by a physician experienced in the care of heart failure patients.

**Patient 4**

You receive a call from the emergency department physician about a 34-year-old man who has heart failure caused by progressive cardiomyopathy and returns to the hospital only 3 days after his most recent hospitalization, at which his LV ejection fraction measurement was 14%. Medications at discharge included a starting dose of a β-blocker, furosemide twice daily, an ACE inhibitor, and digoxin. He has severe dyspnea at rest, orthopnea, and pitting edema to the knees, even with high-dose diuretics and home dobutamine. The emergency physician wishes to admit patient 4 to the intensive care unit for aggressive therapy and suggests consultation with a heart failure specialist.

This patient is an example of a patient with ACC–AHA stage D heart failure. Evidence is limited regarding the general use of β-blockers in such patients, so patients must be individually evaluated to determine the balance of risk and benefit. Given this patient's complexity, β-blockers perhaps should not have been initiated until his condition was somewhat better controlled. At this point, the recent ACC–AHA guidelines<sup>13</sup> would recommend that β-blockers be discontinued when the patient enters the intensive care unit or when positive intravenous inotropic support is required, or if the patient develops signs of fluid overload.

Regarding this patient's hospitalization, it would be advisable to consult a heart failure specialist who can help with future management of this patient's β-blocker and other medications. The recent ACC–AHA guidelines<sup>13</sup> advocate a model in which primary care physicians and heart failure specialists collaborate. Heart failure specialists have more experience with severe heart failure and often have better access to systems resources such as disease-management programs.

Many heart failure patients can be treated by primary care providers, but patients who remain symptomatic or have frequent hospitalizations should be evaluated by a heart failure specialist. Referral is especially recommended for patients with complicated or stage D heart failure, a category reserved for patients with refractory symptoms, recurrent hospitalization, or the need for specialized care.<sup>13</sup> Many stage D patients may have difficulty tolerating β-blockers and may develop hypotension, bradycardia, or worsened fluid retention.

When β-blockers are indicated, how should the decision be discussed with the patient? Discussions with heart failure patients about the benefits and risks of β-blockers are important for reasons of professionalism and shared decision making. Also, patient education may help reduce nonadherence with treatment plans and prevent a delay in seeking preventive care, which may avoid readmissions and premature mortality.<sup>31,32</sup> In addition, patients should have realistic expectations of benefits and potential adverse effects.

Several key concepts should be conveyed in a standardized fashion to heart failure patients when β-blockers are initiated (BOX 2). First, patients should understand that β-blockers will immediately reduce the chances of death from heart failure or other causes.<sup>14</sup> Next, patients should know that 2 to 3 months may elapse before they notice a reduction in symptoms or need for hospitalization and that they may experience a brief worsening of symptoms in the beginning.<sup>14,33</sup> Patients should be aware of the potential for adverse effects with β-blockers, as discussed below. They should be trained to weigh themselves daily and contact their physician if their weight increases or if they develop early warning symptoms for hypotension, bradycardia, or fluid retention. Patients should also be aware of the importance of their cooperation with the plan for gradual increases in β-blocker dosage and contacting the clinician if symptoms arise. Finally, they should be counseled to not stop taking a β-blocker

**Box 2. Procedures for Using β-Blockers in Chronic Heart Failure**

**Measures to Aid Implementation in Clinical Settings**

- Maintain an adequate knowledge base about β-blocker therapy for heart failure
- Implement systems changes (such as reminder stickers on charts or an audit and feedback program) to ensure the appropriate use of β-blockers
- Periodically review the charts of patients with heart failure to ensure that they are receiving β-blockers and other appropriate medications such as angiotensin-converting enzyme inhibitors or have a documented contraindication
- Maintain a relationship with a disease-management program consultant and an experienced heart failure consultant to help heart failure patients at greater risk for developing adverse effects or complications

**Assessment Visit on Beginning β-Blockers**

- Thorough history taking, physical examination, and assessment of left ventricular ejection fraction to verify the cause and extent of heart failure
- Record baseline weight, blood pressure, pulse, respiratory rate, and document cardiopulmonary examination, including presence or absence of peripheral edema
- Determine stability of fluid status and the need for diuretics
- Educate the patient about the appropriate diet and fluid intake
- Supply the patient with written instructions for β-blocker dosage. Educate the patient about signs of hypotension, bradycardia, or worsening heart failure.
- Supply the patient with reliable contact information and instructions in case symptoms develop
- Teach patients to weigh themselves daily and, if possible, to monitor their blood pressure at home
- Maintain a specialized flow sheet to ensure that dosages are easily appraised in the chart
- Determine the date for follow-up or dosage increase according to recent stability of blood pressure, pulse rate, and fluid status (typical range, 2-4 weeks)
- After initiation and early dosage increases, schedule interim follow-up by telephone

**Follow-up Visit**

- Repeat measurements of weight, blood pressure, pulse rate, and respiratory rate, and document cardiopulmonary examination, including presence or absence of peripheral edema
- Evaluate patient to determine whether signs or symptoms of any of the following have developed: dizziness, fatigue, dyspnea, peripheral edema, hypotension, bradycardia, palpitations, atrioventricular block, bronchospasm, impotence (men), confusion, and memory loss
- Reinforce education and practice of weighing at home, blood pressure monitoring, and monitoring for adverse effects

abruptly without discussing the change with their clinician. These key concepts can be found online in a patient information page at <http://jama.ama-assn.org/issues/v287n7/jwe20004>. Other resources are available for patients to learn more about β-blockers and heart failure, including the guidelines themselves and Web sites sponsored by the AHA (<http://www.americanheart.org/chf>) and the Heart Failure Society of America (<http://www.abouthf.org>).

**Adverse Effects**

A variety of adverse effects have been reported for β-blockers.<sup>34-37</sup> Patients should be instructed about the most common adverse effects (hypotension, bradycardia, or worsened heart failure) (Box 2), which can arise in virtually any patient if the dosage of β-blocker is too high or escalated too rapidly. Patients should be provided with an educational handout that they can review at home and advised to contact the clinician immediately if symptoms develop.

**Table.** Starting and Target Dosages of β-Blockers in Heart Failure\*

| Drug                                   | Starting Dosage      | Maximum Dosage  | Approximate Cost per Month for Starting Dosage, \$† |
|--|----------------------|---|---|
| Bisoprolol                             | 1.25 mg/d            | 10 mg/d   | 34‡   |
| Carvedilol                             | 3.125 mg twice daily | 25 mg twice daily (50 mg twice daily for patients >85 kg) | 97  |
| Metoprolol succinate, extended release | 12.5-25 mg/d         | 200 mg/d  | 31-62   |

\*Based on data from Hunt et al.<sup>13</sup>

†Cost is based on the average wholesale price for the lowest target dosage given for 30 days, as provided in 2007 *Drug Topics Red Book*.<sup>42</sup> Cost per patient may be higher, depending on the fee for filling a prescription.

‡This cost is for the lowest strength available, 5 mg. Bisoprolol is also available as 2.5 mg strength with various formulations of hydrochlorothiazide.

At the follow-up visit, patients should be asked whether they have developed adverse effects other than those listed in Box 2, although the clinician should remain aware that many of these adverse effects have been reported nearly as frequently in clinical trial patients receiving a placebo. Package inserts<sup>35-37</sup> and the *Physicians' Desk Reference*<sup>34</sup> report many other rare adverse effects ranging from nausea to thrombocytopenic purpura, but these have not been commonly observed in clinical trials.

When patients develop adverse effects that do not resolve, the clinician and patient should discuss the relative risks and benefits of continuing the β-blocker. The patient should be aware that some hypotension and bradycardia is to be expected after β-blockers are initiated and that the appearance of these adverse effects does not preclude continued use of a β-blocker. Some adverse effects such as fatigue, depression, or impotence may resolve over time or may be treatable; some symptoms may be entirely unrelated to the β-blocker. Other adverse effects may be more desirable than the adverse effect of stopping the β-blocker use, eg, worsened heart failure and a shorter life expectancy.

Which β-blocker is the best choice? Opinions diverge about which β-blocker is best, since little published work has compared patient outcomes among the different β-blockers.<sup>38,39</sup> Currently, only carvedilol and long-acting metoprolol are approved by the US Food and Drug Administration for use in heart failure; bisoprolol is not yet approved for heart failure, but it has

demonstrated efficacy in clinical trials.<sup>4</sup> Pharmacologically, metoprolol and bisoprolol are highly selective for cardiac β<sub>1</sub> receptors; carvedilol is less cardioselective but also has ancillary vasodilating and antioxidant<sup>40</sup> properties. Although some have touted the advantages of one β-blocker over another, there is no evidence that differences between β-blockers are associated with differences in patient outcomes. The ongoing Carvedilol or Metoprolol European Trial (COMET)<sup>41</sup> will compare outcomes among more than 3000 heart failure patients randomized to receive either carvedilol or metoprolol. Recruitment for this trial is complete and the 2-year follow-up results are expected to be available later this year.

How should the dose be initiated and titrated to maximize benefit and lessen adverse effects? Once a patient is determined to be appropriate for receiving β-blockers, a key goal should be to initiate the medication safely and titrate the dosage to the maximum tolerable. Suggested initiation and target dosages, based on clinical trials<sup>4,6,7</sup> and guidelines,<sup>12</sup> are shown in the TABLE for bisoprolol, carvedilol, and extended-release metoprolol.<sup>7,11,14</sup> To avoid β-blockers' causing hypotension, they should be titrated upward with the "start low, go slow" approach used in most clinical trials, with a doubling of the dose every 2 to 4 weeks until the target is reached.<sup>13</sup> This approach is similar to the 2-week open-label run-in period used before randomization in 2 major trials to determine whether patients could tolerate β-blockers.<sup>6,7</sup> Cli-

nicians may wish to increase the titration interval or decrease the increment in patients with a history of systolic blood pressure less than 90 mm Hg or a pulse rate less than 60/min or in patients with a recent change in fluid status. After the 2-week run-in period, up to 90% of the ideal patients in the US Carvedilol Program were able to tolerate the study protocol of doubled dose every 2 to 4 weeks,<sup>6</sup> and nearly two thirds of those included in the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF) were receiving the target dose of 200 mg at the conclusion of the study.<sup>7</sup>

After a β-blocker dose is titrated up, the risk for symptomatic hypotension can be expected to be greatest within 24 to 48 hours<sup>14</sup> and then improve within the next few doses. Combination effects from diuretics and ACE inhibitors should be considered or drug interactions with agents such as amiodarone, nitrates, or other antihypertensives. If hypotension develops, patients should try to take the β-blocker, ACE inhibitor, and diuretic at different times of the day.<sup>14</sup> Patients should not reduce their diuretic dosages but may try temporary reductions in the dosage of an ACE inhibitor. Little evidence is available to guide these decisions, but the trials do suggest that the combination of medications is useful. Finally, other causes of hypotension should be considered, such as worsening fluid status caused by increased intake of salt or medication nonadherence.

A key remaining question is whether or how to initiate β-blockers and ACE inhibitors simultaneously, especially in patients receiving these agents for the first time. There is no evidence to help prioritize the titration of ACE inhibitors and β-blockers together, but recent guidelines observe that patients need not be receiving high doses of an ACE inhibitor to be considered for β-blockers, since most patients in clinical trials were not receiving high doses of an ACE inhibitor. In addition, there is some evidence for benefit with low doses of ACE inhibitors either by them-

selves or in combination with β-blockers<sup>43</sup> as well as for very low doses of β-blockers.<sup>13,44</sup> Finally, an early benefit for both agents together is plausible based on their separate mechanisms of action and the antiarrhythmic effects of β-blockers.<sup>43</sup> In some cases, heart failure patients with systolic blood pressure below 95 to 100 mm Hg or a pulse rate below 60/min can be treated safely with β-blockers by experienced heart failure clinicians with access to disease-management programs or other ways to arrange for close monitoring at home.

**Monitoring Doses and Adverse Effects**

What strategies can help the busy clinician ensure that effective doses of β-blockers are initiated and safely titrated? Changing clinical practice can be challenging, and a busy practice can benefit from a systematic approach to titrating β-blocker dosage and monitoring for adverse effects. A list of specific tasks for baseline and follow-up office visits is shown in Box 2.<sup>13,45,46</sup> The flow sheet in FIGURE 2 is an example of a simple charting tool that can be replicated on any word processor and placed in the records of all heart failure patients to follow titration of both β-blocker and ACE inhibitor. When hypotension or other adverse effects arise, the clinician can use the flow sheet to determine whether dose titration may have been too rapid or remind the clinician when several previous dose reductions had been necessary. In either case, a complete record of dose titration on 1 page may help the clinician decide whether it will be advisable to refer the patient to a heart failure consultant or a specialized heart failure management clinic<sup>13,46,47</sup> while the β-blocker dose is escalated.

**Systems Changes**

Many strategies can be used to help ensure that all appropriate heart failure patients receive β-blockers, even in a busy clinical practice with many patients in various stages of heart failure. Published evidence has shown that simple provider education and guideline dis-

**Figure 2.** Sample Flow Sheet for Heart-Failure Medication

|  |   |   |   |   |   |
|--|---|---|---|---|---|
| Date   |   |   |   |   |   |
| <b>Current Heart Failure Medications</b>                         |   |   |   |   |   |
| β-Blocker agent/dosage   | / | / | / | / | / |
| ACE Inhibitor agent/dosage                                       | / | / | / | / | / |
| Digoxin dosage   |   |   |   |   |   |
| Spironolactone dosage  |   |   |   |   |   |
| Loop diuretic agent/dosage                                       | / | / | / | / | / |
| Thiazide diuretic agent/dosage                                   | / | / | / | / | / |
| Other cardiovascular agents(s)/dosage(s)                         |   |   |   |   |   |
| New or increased adverse effects (Specify)                       |   |   |   |   |   |
| <b>Current Patient Data</b>                                      |   |   |   |   |   |
| NYHA class (I-IV)  |   |   |   |   |   |
| Symptoms, eg, orthopnea (Specify if increased or decreased)      |   |   |   |   |   |
| Blood pressure   |   |   |   |   |   |
| Pulse  |   |   |   |   |   |
| Weight   |   |   |   |   |   |
| Physical findings, eg, edema (Specify if increased or decreased) |   |   |   |   |   |
| <b>Plan</b>  |   |   |   |   |   |
| Medication or dosage changes                                     |   |   |   |   |   |
| Other  |   |   |   |   |   |

ACE indicates angiotensin-converting enzyme.

semination alone are unlikely to effectively improve processes of care such as β-blocker use in heart failure.<sup>48</sup> Rather, systemic change must be accomplished through the multifaceted use of several types of interventions, each of which would probably be ineffective if used alone.<sup>47-49</sup> In addition to education<sup>49,50</sup> and guideline dissemination,<sup>51</sup> effective systemic approaches include academic detailing or outreach visits,<sup>52</sup> opinion leaders/local champions,<sup>53</sup> computer and chart reminders,<sup>54,55</sup> disease management programs,<sup>46,47</sup> and chart audit and feedback to clinicians.<sup>56</sup> Since clinical change is difficult to accomplish all at

once, small manageable changes should be made according to feasibility. Care can then be monitored sequentially for effectiveness of the change.<sup>57</sup>

Although some clinics may not have the resources to provide specific heart failure case management or elaborate quality improvement projects, clinicians can still adopt this approach of small, feasible changes. An initial first step might be to place a prominent heart failure sticker and the flow sheet in Figure 2 in the charts of all heart failure patients, regardless of whether they have recently been treated in the office. A nurse or office manager can go through the list of heart failure pa-

tients, calling in each one for an assessment visit throughout a 2- or 3-month period. Heart failure patients not receiving β-blockers can be evaluated at baseline as shown in Box 1 and treated as indicated in Box 2. Follow-up can be systematized with the flow sheet in Figure 2. After a 6-month period, the clinician can ask that a sample of heart-failure-labeled charts be pulled for a simple self-directed audit. The point is that adherence to the new guideline will require a system that ensures that eligible patients are identified and appropriately treated.

### Management of β-Blocker Dosage During Heart Failure Exacerbation

Heart failure is a progressive and often fatal condition, and many heart failure patients receiving β-blockers will require admission to the hospital. Some patients may develop heart failure exacerbation or fluid overload after being given β-blockers. Other patients' heart failure may progress because of worsened hypertension or myocardial ischemia. Clinicians should be aware of how to manage β-blockers during these exacerbations as well as when they should consult a physician who specializes in the care of patients with severe heart failure.

### Patient 5

You receive a call from the inpatient residents about a 62-year-old man with heart failure admitted to the hospital. He has been compliant with medications, and his LV ejection fraction 6 months ago was 30%. He now presents with dyspnea at rest, orthopnea, and peripheral pitting edema after dietary indiscretion while on vacation. He has no chest pain, and 2 sets of laboratory and electrocardiogram test results show no evidence of ischemia. The residents wonder whether his exacerbation could be related to his longstanding use of a β-blocker. Your outpatient chart reminds you that the β-blocker had been successfully titrated to a maximal dosage 4 months ago and was well tolerated at follow-up a month ago.

This patient has experienced an exacerbation of heart failure with evidence of fluid overload. Heart failure patients being admitted to the hospital should be evaluated individually by experienced clinicians to determine whether the β-blocker should be discontinued, on the grounds that the patients may be more likely to undergo adverse consequences of bradycardia, hypotension, and worsened failure if the β-blocker use is continued.<sup>13</sup> In general, β-blockers should not be initiated in patients with unstable signs or symptoms of fluid overload,<sup>11,12</sup> but they can often be continued during treatment of heart failure exacerbation if diuretic and other therapies are intensified.<sup>13</sup> In addition, the COPERNICUS trial<sup>5</sup> established the safety and benefit of β-blockers in heart failure patients recently discharged from the hospital. Since it does not appear that this patient will require admission to the intensive care unit or intravenous inotropic support, some experienced clinicians may elect to attempt an aggressive diuresis and restart his β-blocker use as soon as fluid status begins to respond.

The ACC–AHA guidelines<sup>13</sup> suggest that primary care physicians with knowledge or experience in heart failure care will be able to direct this patient's inpatient therapy and temporary discontinuation of a β-blocker. A cardiologist will become involved at some level in the care of patients who require echocardiography or catheterization. A heart failure specialist should evaluate patients who fail to respond to diuretics or have multiple exacerbations. In addition, many heart failure patients with exacerbation, such as this patient, will benefit from renewed education or participation in a disease-management program, services that may be provided more efficiently in a heart failure specialist clinic.

The residents' question about a possible association between this patient's β-blocker use and exacerbation reflects the persistence of the longstanding myth that β-blockers are contraindicated in heart failure,<sup>3</sup> al-

though it is possible that the patient could be experiencing an adverse effect. The fact that this patient has tolerated a stable dosage of β-blocker for several months suggests that some other cause is likely, providing that no other event has occurred, such as an AMI.

### COMMENT

Now that evidence and guidelines are available to recommend β-blockers in patients with and at risk for developing heart failure, clinicians should develop a system to be able to care properly for patients with this common disorder. A key goal of these systems should be to extend in a short time the benefits of β-blockers to all patients who are likely to benefit from them. The components of the system should include (1) appropriate knowledge of β-blockers and their indications, (2) awareness of how some heart failure patients differ from the ideal prototypes for therapy, (3) strategies to assist the clinician in initiating and monitoring patients to ensure that they are treated effectively and safely, (4) effective methods for communicating to patients the risks, benefits, and effective participation in care, (5) the enlistment of support staff where possible, (6) an effective safety net for hospitalization or home therapy, with temporary discontinuation of β-blockers as indicated, and (7) appropriate safeguards for consultation with or referral to a heart failure specialist for patients with complicated heart failure or for those who have difficulty tolerating β-blockers. With better understanding and appropriate involvement of heart failure specialists and disease-management programs, more heart failure patients will be prescribed β-blockers and experience the expected improvements in morbidity and mortality.

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### What Is Heart Failure?

The main job of the heart is to pump blood, bringing fluid, oxygen, and nutrients to all parts of the body. Heart failure occurs when the heart becomes weakened and is not able to pump as well as it should. Sometimes physicians also call this condition congestive heart failure, which means that fluid is backing up in the lungs or tissues of the body. People with weakened or failing hearts can develop any of these symptoms:

- Shortness of breath with exercise (even simple exercise such as carrying groceries)
- Fatigue, loss of appetite, or generally feeling ill (physicians call this *malaise*)
- Shortness of breath during minimal activity (such as walking) or rest
- Trouble breathing when lying flat (sometimes helped with extra pillows)
- Suddenly waking up in the middle of the night, unable to breathe
- Cough or wheeze (especially at night)
- Weight gain
- Swelling of the ankles or legs
- Palpitations
- Chest pain, stomach pain, or feeling of fullness in the abdomen
- Anxiety

You should call your doctor if you develop any of these symptoms. If not treated, heart failure can get worse and eventually require hospitalization or even cause death.

### What Causes Heart Failure?

Heart failure can develop for many reasons, including the following:

- Coronary artery disease, heart attacks
- Problems with the heart muscle (cardiomyopathy) because of
  - high blood pressure
  - history of exposure to alcohol, certain drugs, or other toxins
  - viral infection
- Heart valve problems
- Rheumatic heart disease (after rheumatic fever)
- Excessive fluid volume in the body
- Heart-rhythm disturbances (heart rate too fast, too slow, or not strong enough)
- Thyroid problems
- Nutrition or specific vitamin deficiencies

Sometimes no cause can be determined for a person's heart failure

### How Can Heart Failure Be Treated?

Your physician has a number of treatments to prescribe or recommend, but many people with heart failure cannot be completely cured. Your physician may discuss special medications or any of the following with you:

- A special diet, including low amounts of salt and possibly reduced fats or cholesterol
- Restriction of the amount of fluid you drink every day
- Weight loss and exercise (your physician or a physical therapist will help you decide how much is appropriate)
- Quitting smoking
- Change in other medications that might make heart failure worse
- Avoiding certain toxins, such as alcohol
- Closely fitting stockings to help reduce swelling of ankles

Other measures such as supplemental oxygen, further testing, or even surgery may become necessary. The most common medications used to treat heart failure are diuretics, angiotensin-converting enzyme (ACE) inhibitors,  $\beta$ -blockers, and digoxin.

**Diuretics** are medications that help the body expel (via urination) excess fluid that has built up in the body. By reducing excess fluid, diuretics can reduce swelling and breathing troubles and improve blood pressure.

**ACE inhibitors** reduce blood pressure and help keep the heart from developing into the wrong shape.

**$\beta$ -Blockers** help keep the heart from beating too hard at any one time, letting it work more efficiently over a long period. They also reduce blood pressure and help prevent heart rhythm disturbances.

**Digoxin** or **digitalis** helps increase the strength of each heartbeat.

**Spirolactone** helps regulate salts in the blood and may keep the heart from developing into the wrong shape.

Each of these medications has been shown to improve quality of life and reduce the chance of death in heart failure patients.

### $\beta$ -Blockers for Heart Failure

Your physician has prescribed a  $\beta$ -blocker for your heart failure. This handout will help you learn about the ways in which a  $\beta$ -blocker can improve your quality of life, reduce the chance of hospitalization, and help to prevent a premature death.

### Treating Heart Failure With $\beta$ -Blockers

The main job of the heart is to pump blood around the body, bringing fluid, oxygen, and nutrients to all parts of the body. Heart failure is said to occur when the heart becomes weakened and is not able to pump as well as it should. Common symptoms experienced by people with heart failure include shortness of breath, fatigue, and swelling of the ankles and legs. If left untreated, heart failure will cause “fluid overload” and worsened symptoms and cause people to require hospitalization or be at risk of sudden death.

$\beta$ -Blockers are a group of heart failure medications that reduce symptoms, improve quality of life, and reduce the chances of death. They help keep the heart from beating too hard at any one time, letting it work more efficiently over a long period. They also reduce blood pressure, help prevent heart rhythm disturbances, and protect the heart of people who have had or are at risk for heart attacks.

### Benefits of $\beta$ -Blockers for Heart Failure

$\beta$ -Blockers have been used for many years for controlling blood pressure and heart attacks, but only in the last decade have they been found to be beneficial for heart failure as well. After being extensively tested and studied,  $\beta$ -blockers are now recommended for heart failure patients by several consensus groups of physicians. Other things to know about the benefits of  $\beta$ -blockers include the following:

- $\beta$ -Blockers begin to work immediately to help prevent premature death.
- Within 2 to 3 months,  $\beta$ -blockers reduce symptoms and improve a person's overall quality of life.
- Within 2 to 3 months,  $\beta$ -blockers help prevent unnecessary hospitalization.

### Cautions About $\beta$ -Blockers in Heart Failure

Although  $\beta$ -blockers are beneficial for almost everybody, patients should be aware of a few cautions. When used in heart failure,  $\beta$ -blockers are started at a very low dosage that is increased gradually to avoid adverse effects or worsened heart failure. Although many people feel fine immediately after beginning  $\beta$ -blockers, others may experience adverse effects or an initial increase in symptoms.

- The most common adverse effects of  $\beta$ -blockers are low blood pressure and slowed heart rate. These can cause the following symptoms:
  - Light-headedness
  - Fatigue or decreased tolerance for exercise
  - Palpitations or fluttering discomfort in the chest
- In some people,  $\beta$ -blockers can be associated with a temporary worsening of heart failure, with symptoms including worsened shortness of breath, swelling, fatigue, loss of appetite, or feeling generally ill.
- These adverse effects can often be prevented by taking your medication exactly as directed. You should call your physician if you develop any of these symptoms. If not treated, heart failure can get worse and eventually require hospitalization or even cause death.
- Other adverse effects are more rare but are still possible. Call the office immediately if you develop any of the following:
  - Chest pain
  - Confusion or memory loss
  - Wheezing or other trouble breathing
  - Skin rash
  - Cold hands or feet
  - Impotence in men (difficulty with erections)
- Your physician should know if you have a chronic respiratory condition or diabetes, since  $\beta$ -blockers may require special observation.
  - Patients with asthma or who require inhaled bronchodilators (such as albuterol) are more likely to develop trouble breathing when given  $\beta$ -blockers. Patients with other chronic lung diseases (such as emphysema) often do well with  $\beta$ -blockers. Make sure your physician knows if you have asthma or emphysema or require any inhaled medication.
  - Patients who have diabetes and well-controlled blood glucose levels often do well with  $\beta$ -blockers. Patients with blood glucose levels that are often less than 80  $\mu\text{g}/\text{dL}$  should call their physician to make sure that  $\beta$ -blockers will be safe for them, since  $\beta$ -blockers can mask the symptoms normally experienced by patients with low blood glucose levels.

### How to Take Your $\beta$ -Blocker

- You should take your  $\beta$ -blocker at the same time every day, in exactly the way your physician tells you to take it. Never stop taking the medication without talking to your physician first.
- If you forget to take your  $\beta$ -blocker and remember within a few hours, take it as soon as you remember. If the next dose is due in less than 12 hours, hold off and take the next day's dose at the correct time. If it has been longer than 4 hours but less than 12, call the office for instructions.
- In order to monitor your fluid balance, weigh yourself at the same time every day and write your weight for the day in a notebook. Bring the notebook to clinic visits. Once your weight has stabilized, it will be called your baseline weight. Your physician will give instructions to call the office if your weight is too high or too low.

Baseline weight: \_\_\_\_\_  
Weight too high: \_\_\_\_\_ } Call the office if your weight  
Weight too low: \_\_\_\_\_ } reaches either number.