Polypharmacy, the use of multiple medications resulting in complex drug regimens, is increasing among patients with heart failure. Ideally, at discharge from the hospital, each patient should be prescribed evidence-based medications (ie, medications that published evidence indicates are effective for the patient’s condition). The list of such medications is becoming long. According to the National Heart Care Project for 2000-2001, the mean numbers of heart failure medications and doses per day were 7.5 and 11.1, respectively. National guidelines rarely address the problem of polypharmacy for high-risk patients, and they do not consider patients’ adherence, the risk of adverse effects, or pharmacoeconomic considerations. Patients who have had a myocardial infarction, especially those who have concomitant heart failure, are prescribed an equal, if not higher, number of medications than are patients with just heart failure.

Perhaps the easiest way to improve clinical and health outcomes is to improve adherence to the drug treatment plan by simplifying the medication regimen (Figure 1). Among patients with heart failure and other cardiovascular conditions, such as hypertension, changing regimens from doses taken 2 or 3 times a day to a dose taken once a day increased adherence. In a large meta-analysis, increased treatment adherence improved health outcomes, including survival, readmission rates, blood pressure, cholesterol level, and hemoglobin A1c level. Fewer pills per day may be particularly beneficial for patients after myocardial infarction or for patients with heart failure.

Medication adherence was previously thought to be in the domain of the patient, but a recent shift in philosophy advocates forming a partnership between healthcare provider and patient, who enter into a contractual agreement to support self-care by the patient once the patient is discharged from the hospital.
This approach has been evaluated in several studies,11-16 which showed successful health outcomes in patients who were better educated about drug regimens in nurse-directed intervention programs. By using education and communication facilitated by a heart failure or cardiac nurse and reducing the numbers of pills required by choosing once-daily regimens over twice-daily or more frequent treatments, adherence to therapy can be improved. Cardiac nurses, especially advanced practice nurses, are well positioned to discuss drug adherence issues with patients and determine whether a once-daily agent would increase patients’ ability to take heart failure medications as prescribed.

In this article, I discuss the practical considerations of the use of evidence-based β-blockers. Specifically, I propose changing from twice-daily to once-daily β-blockers and changing from commonly used non-evidence-based agents to evidence-based, once-daily β-blockers in patients with heart failure and patients with left ventricular systolic dysfunction (LVSD) after myocardial infarction. In patients with chronic systolic heart failure and LVSD and heart failure after myocardial infarction, β-blockade is considered a key pharmaceutical therapy.17-18 Simplifying the β-blocker regimen with once-daily dosing offers an opportunity to improve patients’ outcomes by boosting the probability of adherence to treatment. Availability of once-daily formulations of evidence-based β-blockers should prompt nurses to consider a new treatment model to help overcome the barrier to adherence created by high dosing frequency.

**Literature Review**

Simplifying a patient’s medical regimen by reducing dosing frequency to once a day is likely to be associated with improved adherence to therapy, greater satisfaction among patients, and possibly more favorable outcomes. In a recent study,19 researchers compared patients’ compliance (measured electronically) and treatment effectiveness in patients with stable angina pectoris treated with oral nitrates administered once daily versus twice daily. Patients receiving once-daily therapy had significantly greater overall medication adherence than did patients receiving twice-daily therapy (88.9% vs 73.8%; P<.001), a higher percentage of days with the correct number of doses taken (85.5% vs 59.5%; P<.001), and a greater reduction in mean number of episodes of weekly chest pain (94% less vs 30% less; P<.001).20

Many researchers20-27 have studied the effects of daily doses on drug adherence in both observational studies and randomized clinical trials. Simply put, once-daily agents were taken more regularly than were twice-daily agents,20-27 supporting better adherence to drug regimens; however, whether the use of once-daily β-blockers improves adherence has not yet been assessed in a clinical trial.

Specific to β-blocker therapy, improved adherence has been associated with improved outcomes in 2 studies.20,28 In patients with heart failure, lower adherence to metoprolol tartrate was associated with a higher rate of emergency room visits (P<.001) and hospital admissions (P<.001).29 After surviving a myocardial infarction, patients in the Beta Blocker Heart Attack Trial who took 75% or less of prescribed β-blockers were 2.6 times more likely to die in the first year of follow-up than were patients who were adherent to therapy.29

**β-Blockers in Heart Failure**

The American College of Cardiology/American Heart Association management guidelines include recommendations that long-term therapy with β-blockers be started and continued indefinitely in all survivors of acute myocardial infarction who do not have absolute...
contraindications\(^7\) and in patients with mild to severe heart failure.\(^8\) \(\beta\)-Blockers significantly reduced mortality in patients with heart failure and acute myocardial infarction in several large-scale randomized clinical trials\(^{17-20,25}\) and in a national registry of patients hospitalized for acute decompensated heart failure.\(^{26}\)

Only carvedilol and metoprolol succinate are approved in the United States for the treatment of heart failure (Table 1).\(^8\) Carvedilol (both formulations, see following) is the only \(\beta\)-blocker approved by the US Food and Drug Administration for patients with LVSD after myocardial infarction; approval was based on mortality benefits of the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) trial.\(^{35}\) Carvedilol is also the only \(\beta\)-blocker approved for use in patients with severe advanced, chronic heart failure.\(^{27}\)

### Switching From Carvedilol to Carvedilol CR (Carvedilol Phosphate Extended-Release)

A once-daily controlled-release formulation of carvedilol (carvedilol phosphate extended-release, or carvedilol CR) was approved by the Food and Drug Administration with the same indications as the original twice-daily formulation of carvedilol: mild to severe heart failure, LVSD after myocardial infarction with or without signs and symptoms of heart failure, and hypertension.\(^{28}\) An ongoing trial of adherence to once-daily carvedilol CR versus twice-daily carvedilol will provide more information about adherence to \(\beta\)-blocker use in patients with heart failure.\(^{29}\)

### Bioequivalence

The 2 formulations of carvedilol (twice-daily dosing with the original formulation and once-daily dosing with carvedilol CR) have equivalent steady-state pharmacokinetic characteristics and pharmacodynamic properties.\(^{40,41}\) The pharmacokinetic profile of the 2 formulations was compared in patients with mild to severe heart failure and in patients with asymptomatic LVSD after myocardial infarction.\(^{42}\) The mean steady-state concentration-time profile of the \(\beta\)-blocking enantiomer, \(S(-)\)-carvedilol, was equivalent between the 2 formulations in a crossover pharmacokinetic study of 188 patients with mild to severe heart failure or asymptomatic LVSD after myocardial infarction, reflecting no discernible difference between carvedilol and carvedilol CR.\(^{42}\) Additionally, medication adherence was better in the carvedilol CR group (93% vs 85%); however, this open-label clinical trial did not have sufficient power to allow statistical evaluation of differences in adherence between the groups.\(^{42}\)

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**Table 1** \(\beta\)-Blockers indicated for treatment in various stages of heart failure\(^8\)

<table>
<thead>
<tr>
<th>Drug(^a)</th>
<th>Drug type(^b)</th>
<th>Stage B(^c)</th>
<th>Stage C(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>2, 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>2</td>
<td>After myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Betaxolol</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carteolol</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carvedilol (f)</td>
<td>3, 4</td>
<td>Left ventricular systolic dysfunction after myocardial infarction</td>
<td>Heart failure; left ventricular systolic dysfunction after myocardial infarction</td>
</tr>
<tr>
<td>Labetalol</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>2</td>
<td></td>
<td>Heart failure</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>2</td>
<td>After myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td>1, 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>1</td>
<td>After myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Timolol</td>
<td>1</td>
<td></td>
<td>After myocardial infarction</td>
</tr>
</tbody>
</table>

\(^a\) All drugs listed here are indicated for treatment of hypertension in patients with stage A heart failure.

\(^f\) \(f\), noncardioselective: blocks \(\beta_1\)- and \(\beta_2\)-adrenergic receptors located mainly in the heart (\(\beta_1\)) and the bronchial and vascular smooth muscle and uterus (\(\beta_2\)); 2, cardioselective: blocks \(\beta_1\)-adrenergic receptors located mainly in the heart; 3, noncardioselective +: blocks \(\beta_1\)- and \(\beta_2\)-adrenergic receptors and has other properties such as \(\alpha_1\)-adrenergic blocking, antioxidant, direct vasodilating and/or calcium antagonist properties; 4, intrinsic sympathomimetic action that may result in less bradycardia than occurs with other agents.

\(^c\) Stage B: pre-heart failure; patients with left ventricular systolic dysfunction but without symptoms.

\(^d\) Stage C: clinical heart failure; patients currently have or in the past had symptoms of heart failure.

\(^e\) Bisoprolol is not approved by the Food and Drug Administration for use in patients with heart failure.

\(^g\) Both formulations of carvedilol (carvedilol and carvedilol phosphate extended-release) are indicated in patients with hypertension, left ventricular systolic dysfunction after myocardial infarction, and heart failure.
Tolerability

Less-frequent dosing regimens combined with a favorable tolerability profile result in better medication-taking behavior. Surveys have repeatedly indicated that the occurrence of adverse effects is an important predictor of nonadherence by patients. The original twice-daily carvedilol formulation had a favorable tolerability profile; common adverse effects reported by patients with heart failure that were deemed likely to be related to the drug were dizziness, fatigue, hypotension, and bradycardia.

Data from the US Carvedilol Heart Failure trial and the Carvedilol Prospective Randomized Cumulative Survival study revealed that fewer patients receiving carvedilol than patients receiving placebo discontinued therapy because of adverse events. In elderly patients with heart failure who were receiving carvedilol, overall tolerability at 6 months was between 77% and 84%. In a study of carvedilol CR in patients with LVSD, the once-daily formulation had similar tolerability to the twice-daily carvedilol formulation, indicating equivalence in safety when patients are switched from twice-daily carvedilol to once-daily carvedilol CR.

Switching patients from twice-daily carvedilol to once-daily carvedilol CR is straightforward; the once-daily doses of 10, 20, 40, and 80 mg of carvedilol CR are equivalent to the 4 twice-daily dose levels of carvedilol, respectively. Patients currently taking twice-daily carvedilol should start the equivalent dose of carvedilol CR the following morning after their last evening dose of carvedilol.

Clinical Rationale for Choosing a Specific Evidence-Based β-Blocker

Carvedilol may be preferable to metoprolol succinate in some clinical situations. Carvedilol has neutral metabolic effects in patients with hypertension for example, it causes no increases in insulin resistance or level of hemoglobin A1c, a property not shared by β1-specific blocking agents, including metoprolol succinate. In single-center studies, carvedilol had no negative metabolic effects in patients after a myocardial infarction, whereas insulin resistance was increased in similar patients receiving metoprolol tartrate. Carvedilol may also be warranted in heart failure patients with diabetes because of its neutral metabolic profile, which was shown in hypertensive patients.

In a substudy of adverse events from the Carvedilol or Metoprolol European Trial, more events related to new onset of diabetes (diabetic coma, peripheral gangrene [diabetic foot], decreased glucose tolerance, hyperglycemia) occurred in patients with heart failure who were taking metoprolol tartrate than in patients taking carvedilol (13.0% vs 10.6%; hazard ratio = 0.78; 95% confidence interval [CI], 0.61-0.99; P=.04). Additionally, patients with LVSD after myocardial infarction should be preferentially switched to carvedilol CR, because other β-blockers are not indicated in such patients.

Some clinical situations may warrant choosing metoprolol succinate over carvedilol. Patients with reactive airway disease could have an exacerbation of their underlying disease by the β2-receptor–blocking property of carvedilol. Because of its relative β1-selectivity, metoprolol succinate can be used with caution in patients with bronchospastic disease. However, because β1-selectivity is not absolute, a β2-stimulating agent should be administered concomitantly and the lowest possible dose of metoprolol succinate should be used.

Dosing requirement is an important factor in medication nonadherence and may adversely affect elderly patients. Reductions in mortality have been observed for patients with heart failure who were consistently treated with low doses of carvedilol (6.25 twice daily), yet a similar mortality benefit was observed only in patients who had their doses of metoprolol succinate adjusted to a higher equivalent. Thus, when the

Table 2: Dose conversion chart for switching from carvedilol to carvedilol phosphate extended-release (carvedilol CR) in patients with heart failure or after myocardial infarction

<table>
<thead>
<tr>
<th>Current twice-daily dose of carvedilol, mg</th>
<th>Starting once-daily dose of carvedilol CR, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.125</td>
<td>10</td>
</tr>
<tr>
<td>6.25</td>
<td>20</td>
</tr>
<tr>
<td>12.5</td>
<td>40</td>
</tr>
<tr>
<td>25</td>
<td>80</td>
</tr>
</tbody>
</table>

a When patients switch from the twice-daily to the once-daily formulation, it is recommended that patients wait 12 hours, that is, take their nighttime dose of carvedilol and then start carvedilol CR the next morning with food.
b Doses listed for carvedilol CR are greater than the doses listed for carvedilol because carvedilol CR uses carvedilol phosphate, which has a higher molecular weight than carvedilol. Additionally, the amount of carvedilol free base (formulation used in twice-daily carvedilol) in each capsule of carvedilol CR is greater to create equivalency between twice-daily carvedilol and once-daily carvedilol CR.
Clinically, switching from a non–evidence-based β-blocker to an evidence-based agent was safe in the Carvedilol or Metoprolol European Trial. The recommended starting dose was half the equivalent of the last study medication dose; for example, if the current metoprolol dose was 100 mg/day, then the starting dose of carvedilol would be the equivalent of 50 mg/day metoprolol (6.25 mg twice daily). Among patients taking carvedilol who were switched to metoprolol tartrate, 9.4% experienced a serious adverse event (discontinuation of therapy due to dizziness, bradycardia, headache, or presyncope), and 4.7% experienced worsening heart failure (worsening New York Heart Association functional class).

In patients switched from metoprolol tartrate to carvedilol, 3.1% experienced a serious adverse event, and 1.5% experienced worsening heart failure. In a single-center study of 30 patients with baseline mean left ventricular ejection fractions of 29%, compared with patients maintained on metoprolol therapy, patients who switched treatment from metoprolol to carvedilol had an improvement in left ventricular ejection fraction (+7%, standard error of the mean [SEM] ±3% vs -1%, SEM ±2%; \(P = .04\)). In a comparison of the effects of metoprolol tartrate and carvedilol in 150 patients, patients receiving carvedilol had a significantly greater improvement in ejection fraction after 12 months of treatment (carvedilol: from 20.4% [SEM ±7.6%] to 31.2% [SEM ±11.9%] vs metoprolol: 21.6% [SEM ±7.2%] to 28.8.2% [SEM ±11.3%], \(P = .03\)).

Ultimately, nurses with prescriptive privileges should consider switching patients with heart failure from a non–evidence-based β-blocker (eg, atenolol or metoprolol tartrate) to an evidence-based agent (carvedilol, carvedilol CR, metoprolol succinate, or bisoprolol). Cardiac nurses without prescriptive privileges are key team members in ensuring implementation of processes that optimize ordering and administration of drug therapy and should ensure that patients are on an evidence-based β-blocker therapy before discharge from the hospital.

### Practical Aspects of Switching Strategies for Switching

Table 3 shows a strategy for switching patients with heart failure from 2 common non–evidence-based β-blockers to carvedilol CR, metoprolol succinate, or bisoprolol, once-daily agents. The strategy is based on suggestions from previous publications as well as the dose equivalency observed in the carvedilol and carvedilol CR profiles. Figure 2 shows a strategy for switching from non–evidence-based β-blockers to carvedilol CR in patients with LVSD after myocardial infarction.

The suggested equivalent dose conversions from a non–evidence-based β-blocker to the original

### Table 3 Recommended algorithm for switching from commonly used non–evidence-based β-blockers to once-daily evidence-based β-blockers in patients with heart failure

<table>
<thead>
<tr>
<th>Non–evidence-based β-blockers</th>
<th>Timing</th>
<th>Evidence-based β-blockers, daily dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>When switching from</td>
<td>To carvedilol CR</td>
<td>To metoprolol succinate XL</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Wait 24 hours</td>
<td></td>
</tr>
<tr>
<td>50 mg daily from last dose of once-daily atenolol</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>≥100 mg daily</td>
<td>40d</td>
<td>100</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>Wait 12 hours</td>
<td></td>
</tr>
<tr>
<td>25 mg twice daily from last dose of metoprolol tartrate</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>≥50 mg twice daily</td>
<td>40d</td>
<td>100</td>
</tr>
</tbody>
</table>

* Suggestion: Patients taking atenolol should start taking the evidence-based once-daily agent the next morning. Recommend that patients take their nighttime dose of metoprolol tartrate and start the new once-daily agent the next morning with food.

b The dose equivalencies provided in this table have not been studied in clinical trials; they are based on references that discuss dose equivalency and clinical judgment.

c Patients can start with 1.25 mg bisoprolol daily if they do not tolerate 2.5 mg.

d After the switch, adjust dosage to target or maximal tolerated dose over successive intervals of at least 2 weeks. Patients can be started with 10 mg carvedilol CR daily if they do not tolerate 20 mg. Patients more than 65 years old, patients with diabetic neuropathy, and patients predisposed to orthostatic hypotension should generally switch to 20 mg carvedilol CR if receiving a low dose of another β-blocker and to 40 mg carvedilol CR if receiving a high dose of another β-blocker. These patients may then have their dosages increased as tolerated; switching directly to 80 mg (the target dose) is not recommended in these patients.

### Key Points

- Switching from a non–evidence-based β-blocker to an evidence-based agent was safe in the Carvedilol or Metoprolol European Trial.
- The recommended starting dose was half the equivalent of the last study medication dose.
- Among patients taking carvedilol who were switched to metoprolol tartrate, 9.4% experienced a serious adverse event.
- In patients switched from metoprolol tartrate to carvedilol, 3.1% experienced a serious adverse event.
- Cardiac nurses without prescriptive privileges are key team members in ensuring implementation of processes that optimize ordering and administration of drug therapy.

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</tr>
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</tr>
<tr>
<td>≥100 mg daily</td>
<td>40d</td>
<td>100</td>
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<td></td>
</tr>
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<td>20</td>
<td>50</td>
</tr>
<tr>
<td>≥50 mg twice daily</td>
<td>40d</td>
<td>100</td>
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</table>

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twice-daily carvedilol formulation in patients with heart failure and LVSD after myocardial infarction were used as the starting point in Figure 2 and Table 3.\textsuperscript{59,62} The dose equivalencies used were derived from clinical experience\textsuperscript{59,62} and the degree of β\textsubscript{1}-blockade (heart rate lowering) and blood pressure lowering that can be expected with each dose.

Considerations in Patients With Heart Failure

Patients with heart failure who are currently being treated with a non–evidence-based agent such as metoprolol tartrate or atenolol should be switched to metoprolol succinate, carvedilol CR, or bisoprolol. When patients with hypertension are treated with β-blockers such as atenolol or metoprolol tartrate and then LVSD or heart failure develops, the patients’ treatment should be switched to a β-blocker that has proved effective in reducing poor outcomes in heart failure (Table 3). When β-blockers are being switched, especially to a nonselective agent with α-blocking effects, patients should be started at a low dose to ensure tolerance. Once the β-blocker has been tolerated for 2 weeks, the
dose can be titrated up to the maximal dose as tolerated over time by doubling the dose stepwise every 2 weeks. Although a change from one β-blocker to another is generally safe and well tolerated, monitoring for adverse effects should be routine whenever medications are switched.

The switch to a once-daily evidence-based β-blocker can be done 12 hours after the last dose of a twice-daily agent by beginning the first dose of the new agent the next morning after the last dose of the old agent was taken the previous evening. Likewise, treatment with a once-daily evidence-based β-blocker can be started 24 hours after a once-daily non–evidence-based agent is discontinued. In patients at high risk for precipitating or worsening ischemia, an option rather than direct switching is maintaining full β₁-blockade and gradually increasing β₁-mediated vasodilatation in a stepwise fashion by overlapping decreasing doses of metoprolol tartrate or atenolol with increasing doses of carvedilol every 2 weeks.

It is crucial not to add agents with vasodilatory properties, such as calcium antagonists, nitrates, or other antihypertensives, directly before carvedilol. The details on how to switch β-blockers with this overlapping protocol were developed by W. T. Abraham.

If switching to another β-blocker is being considered because of a lack of clinical response, the patient’s condition should first be stabilized by modulating his or her diuretic or angiotensin-converting enzyme inhibitor. Switching β-blockers as a form of rescue therapy while a patient’s clinical condition is deteriorating is not recommended. For patients experiencing severe decompensation of heart failure, destabilization of clinical condition, marked hypotension, or continuing requirements for intravenous inotropes or diuretics, switching β-blockers is not recommended. On the other hand, a switch in β-blocker therapy, all other medication dosing should be stable (steady state), and patients should be free of volume overload.

**Considerations in Patients With LVSD After Myocardial Infarction**

Treatment of patients with LVSD after myocardial infarction should start with carvedilol CR, because it is the only once-daily β-blocker indicated in this setting. Before the CAPRICORN trial, which specifically enrolled patients with LVSD after myocardial infarction, large-scale trials provided evidence that atenolol, metoprolol tartrate, and timolol were beneficial in patients without overt heart failure or uncontrolled cardiac failure after myocardial infarction; therefore, nurses may encounter patients receiving these agents who should be switched to an evidence-based agent. In patients with acute myocardial infarction without evidence of cardiogenic shock, intravenous administration of metoprolol tartrate or atenolol should be started immediately, then patients should be switched to

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Switching between once-daily dose of evidence-based β-blockers in patients with heart failurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose, mg</td>
<td>Starting daily dose, mg</td>
</tr>
<tr>
<td>From metoprolol succinate</td>
<td>To carvedilol</td>
</tr>
<tr>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>100-200</td>
<td>40</td>
</tr>
<tr>
<td>&gt;200</td>
<td>40</td>
</tr>
<tr>
<td>From bisoprololc</td>
<td>To carvedilol CR</td>
</tr>
<tr>
<td>1.25</td>
<td>10</td>
</tr>
<tr>
<td>2.5</td>
<td>20</td>
</tr>
<tr>
<td>5.0</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>From bisoprololc</td>
<td>To metoprolol succinate</td>
</tr>
<tr>
<td>2.5</td>
<td>50</td>
</tr>
<tr>
<td>5.0</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>150-200</td>
</tr>
</tbody>
</table>

a The dose equivalencies provided in this table have not been studied in clinical trials. The following references were used in the generation of these recommendations: the equivalent dose levels suggested in the open-label phase of the Carvedilol or Metoprolol European Trial (carvedilol CR was substituted for carvedilol); dose equivalencies from previously published article that represented best clinical judgment; and the prescrib-ing information for doses of each drug in heart failure. Once a patient's condition should first be stabilized by modulating his or her diuretic or angiotensin-converting enzyme inhibitor. Switching β-blockers as a form of rescue therapy while a patient’s clinical condition is deteriorating is not recommended. For patients experiencing severe decompensation of heart failure, destabilization of clinical condition, marked hypotension, or continuing requirements for intravenous inotropes or diuretics, switching β-blockers is not recommended. On the other hand, a switch in β-blocker therapy, all other medication dosing should be stable (steady state), and patients should be free of volume overload.

<table>
<thead>
<tr>
<th>Starting daily dose, mg</th>
<th>Daily dose, b mg</th>
<th>To carvedilol CR</th>
<th>From carvedilol CR</th>
<th>To metoprolol succinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>50</td>
<td>20</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>150-200</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>2.5</td>
<td>1.25</td>
<td>1.25</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>5</td>
<td>2.5</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

b In all cases, wait 24 hours from the last dose before starting the new daily dose.

c Bisoprolol is not approved for heart failure by the US Food and Drug Administration.
oral carvedilol CR because the oral equivalents of metoprolol tartrate or atenolol have not been studied in patients with LVSD after myocardial infarction. After treatment with carvedilol CR is started, upward titration of the dose should be attempted every 3 to 10 days until the target dose is achieved. If severe bradycardia or hypotension prevents titration up to the recommended dose, a lower final dose can be used.35

Switching from non–evidence-based oral agents to carvedilol CR is shown in Figure 2. In patients with LVSD after myocardial infarction and recent symptomatic heart failure, carvedilol CR may be started at 10 mg rather than 20 mg and titrated to the highest dose tolerated. In hospitalized patients with LVSD after myocardial infarction, twice-daily carvedilol may be selected because of its shorter half-life and caregiver familiarity. Nurses can be the gatekeepers in ensuring that patients are switched to a once-daily dose formulation before discharge to increase the probability of better adherence to the medication regimen.

Monitoring During the Switch

During any switch of β-blocking agents, nurses should closely monitor each patient’s tolerance and medication adherence. Careful objective and subjective assessment may be warranted. Additionally, before a patient is discharged from the hospital, nurses should provide clear instructions about signs and symptoms of worsening heart failure and should assess the patient’s understanding of what he or she has been taught. These precautions may increase recognition of an adverse event before the event becomes serious or severe.

Importance of Nurse-Based Management

Critical care, cardiac, and advanced practice nurses are charged with the day-to-day care of hospitalized patients with heart failure and LVSD after myocardial infarction. Through the use of therapy recommended in guidelines and thoughtful prescribing patterns, nurses can improve patients’ clinical outcomes (fewer hospitalizations and improved quality of life); however, results of research on patients’ overall well-being in relation to once-daily vs twice-daily dosing of drug therapies are not available. In the Carvedilol or Metoprolol European Trial, assessment of well-being was associated with New
York Heart Association functional class but not with the patient’s age or sex or with the β-blocker used. If once-daily β-blocker therapy creates a large enough change in total dose regularly received, functional class possibly could improve to a greater degree, improving subjective well-being.

A nurse’s responsibilities include educating patients and caregivers, initiating treatment with and titrating doses of therapeutic drugs, identifying and following a nursing plan of care (in addition to physicians’ orders), supervising adherence to drug and nonpharmacological care strategies, and advocating for patients. If agents known to decrease mortality and improve functional status are used, patients are more likely to have fewer emergency room visits and unplanned hospitalizations, greater satisfaction with well-being, and improved quality of life.

The success of patients’ treatment is affected by expert multidisciplinary care and also by the level of involvement of nurse caregivers, who are often the mediators of evidence-based practice and are responsible for ongoing collaboration and communication with other members of the healthcare team. For example, physicians may be reluctant to initiate a switch in β-blocker treatment because switching requires closer monitoring and upward titration of the dose. Or a physician may tell a patient why the patient is being treated with a β-blocker but not explain the expectations related to starting treatment with that drug. Thus, if patients become more fatigued or dizziness develops, they may think the drug is not for them and stop taking it. A gap clearly exists between the evidence that supports treatments used in heart failure and patients who have had a myocardial infarction and actual practice in day-to-day patient care. Because multiple registries have shown that the prescription of lifesaving therapies is not yet optimal, and studies have shown that patients’ adherence to therapies is poor, innovative practice improvement programs, clinical leaders, and system tools are needed to close the gap. As part of a multidisciplinary team of healthcare providers, nurses can use clinical pathways/protocols, interdisciplinary rounds, and case study discussions to facilitate processes that advance planning of patients’ care and promote effective care delivery.

In a randomized controlled clinical trial of 169 patients with heart failure, ejection fraction of 45% or less, and no contraindications to use of β-blockers, primary providers were randomly stratified to 1 of 3 interventions: (1) physician education (including substantial education on the use of β-blockers in heart failure, including grand rounds presentations, conferences, and distribution of letters and e-mails with guidelines for β-blocker initiation and upward titration of the dose); (2) provider and patient notification (physicians were alerted via computer messages when they accessed a patient’s electronic record for the first 2 visits after randomization, and patients were alerted via letters informing them that they might be candidates for β-blocker therapy and that they should discuss this treatment with their primary provider); and (3) use of a nurse facilitator (a nurse practitioner supervised by 2 cardiologists assumed responsibility for initiating treatment with β-blockers, titrating the dose, and stabilizing a patient’s clinical condition in appropriate patients with heart failure).

The primary outcome, the proportion of patients who started treatment with β-blockers or had the dose titrated upward and were maintained on β-blockers, was achieved in 67% (36 of 54) of patients in the nurse facilitator group compared with 16% (10 of 64) of patients in the provider-patient notification group and 27% (14 of 51) of patients in the physician education group ($P < .001$ for the comparisons between the nurse facilitator group and both other groups). The proportion of patients receiving target doses of β-blockers at the end of the study (median follow-up 12 months) was also higher ($P < .001$) in the nurse facilitator group (43%) than in the physician education group (10%) and the provider/patient notification group (2%). The frequency of adverse events did not differ among groups.

Cardiac nurses are well placed to facilitate improvements in care and advocate for changes in therapy when warranted. As evidenced in the study just described, advanced practice nurses with prescription privileges can successfully implement treatment with an evidence-based β-blocker in indicated patients. The switching algorithms provided here can be instrumental in helping nurses improve care.

Conclusion
Adherence to pharmacological therapies in cardiovascular disease is poor, leading to worsening disease...
severity and rehospitalization. Barriers to medication adherence are numerous, including complex medication regimens, adverse effects, and poor education of patients. Nurses can increase the use of lifesaving therapies by implementing treatment at discharge and using once-daily agents that will result in easier regimens that, in turn, may improve patients’ adherence and lead to better outcomes. After assessing a patient’s current medical and device therapies and his or her ability to adhere to medication, nurses may find that switching β-blockers is warranted. Nurse-led management programs have shown that nurses can markedly influence patients’ outcomes by educating patients about medication regimens. The availability of once-daily formulations of β-blocker therapies with favorable tolerability may enhance adherence to therapy with evidence-based agents. Three once-daily β-blocker therapies are acceptable for treatment of patients with heart failure: carvedilol CR, metoprolol succinate, and bisoprolol. Carvedilol CR is also indicated for the treatment of patients with LVSD after myocardial infarction. Once-daily formulations can promote use of evidence-based β-blocker therapy that assist nurses in providing quality care and ensuring patients’ safety.

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References


Switching to Once-Daily Evidence-Based β-Blockers in Patients With Systolic Heart Failure or Left Ventricular Dysfunction After Myocardial Infarction
Nancy M. Albert

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