β-Blockers for the Post–Myocardial Infarction Patient: Current Clinical Evidence and Practical Considerations

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β-Blockers significantly decrease the risk of mortality in patients after myocardial infarction (MI). Furthermore, β-blockers reduce the risk of reinfarction and mortality in both the immediate and long term after an MI. Guidelines recommend that post-MI patients should be started on β-blocker therapy and continued indefinitely, unless absolutely contraindicated or not tolerated. Despite compelling evidence, many patients are not prescribed β-blockers after a myocardial event. In addition, some patients are treated with agents whose long-term use has not been shown to be effective. This article discusses practical implementation of β-blockers, provides the rationale for choosing specific β-blockers, and presents protocols for initiating or switching to evidence-based therapies in the acute and chronic post-MI period.
[Rev Cardiovasc Med. *2006;7(1):1-9*]

Key words: Myocardial infarction • β-blockers • Left ventricular dysfunction

Despite significant advances in pharmacologic and interventional therapies, 25% of men and 38% of women still die within 1 year of an acute myocardial infarction (MI). In addition, up to nearly half will experience subsequent physical disability from heart failure (HF).[1] Randomized clinical trials have shown that long-term β-blocker use reduces the risk of death and disability in MI survivors. Current guidelines state that all patients should be prescribed a β-blocker after an MI, unless there is an absolute contraindication to therapy. Contraindications include symptomatic bradycardia, hypotension

(systolic blood pressure < 80 mm Hg), signs of peripheral hypoperfusion (cold clammy skin, cyanosis, oliguria, impaired mental status), cardiogenic shock, acute pulmonary edema, advanced heart block (without pacemaker), or reactive airway disease.[2,3] The 2004 American Heart Association/American College of Cardiology (AHA/ACC) ST elevation MI (STEMI) guidelines give a Class I (level of evidence A) recommendation (procedure/treatment should be performed/administered) for the in-hospital and long-term postdischarge use of β-blockers in MI patients without contraindications.[3] The AHA/ACC guidelines give a Class IIa (level of evidence B) recommendation (additional studies with focused objectives needed; however, it is reasonable to perform procedure/administer treatment) for the prompt administration of intravenous (IV) β-blockers to STEMI patients without contraindications, especially if a tachyarrhythmia or hypertension is present. The presence of moderate left ventricular failure early in the course of STEMI should preclude the use of early IV β-blockade until the HF has been compensated but is a strong indication for the use of oral β-blockade before discharge from the hospital.[3] The 2002 ACC/AHA guideline update for the management of patients with unstable angina and non-STEMI supports the use of β-blocker therapy as a Class I (level of evidence B) recommendation.[4] β-Blocker therapy (with the first dose administered IV if there is ongoing chest pain) followed by oral administration, in the absence of contraindications, is recommended. Initial studies of β-blocker benefits in acute cardiac syndrome were small and uncontrolled. An overview of double-blind, randomized trials in patients with threatening or evolving MI suggests an approximately 13% reduction in the risk of progression to acute MI.[4,5] These trials lack sufficient power to assess the effects of these drugs on mortality rates for unstable angina. However, randomized trials of other patients with coronary artery disease (acute MI, recent MI, stable angina with daily-life ischemia, and HF) have all shown reductions in mortality and/or morbidity rates. Thus, the rationale for β-blocker use in all forms of coronary artery disease, including unstable angina, is very compelling, and in the absence of contraindications it is sufficient to make β-blockers a routine part of care, especially in patients who are to undergo cardiac or noncardiac surgery.[4] Therefore, the use of "post-MI" in this article will refer to all patients with MI, including STEMI and non-STEMI patients.

Despite compelling evidence and recommendations, β-blockers remain an underused therapy in the post-MI period. Physician concerns might exist regarding the safety and benefits of β-blockers in post-MI patients with left ventricular dysfunction (LVD), with or without HF symptoms, despite clinical trial evidence to the contrary. This is especially important because many post-MI patients will have left ventricular systolic dysfunction (an ejection fraction [EF] of ≤ 40%), with or without symptoms of HF. For example, the Trandolapril Cardiac Evaluation (TRACE) registry of more than 6500 MI patients assessed HF and LVD within the first few days of an MI and found that 64% of patients had either HF or LVD or both.[6,7] In addition, misunderstandings might persist regarding the safety and benefits in elderly patients or patients with diabetes or chronic obstructive airway disease.

A number of β-blockers have demonstrated safety and efficacy in large-scale, long-term, placebo-controlled, randomized clinical trials of MI survivors in which the target doses were well defined.[8-10] Nevertheless, MI patients are often treated with agents whose long-term use has not been shown to be effective and for which optimal dosing has not been defined.[11,12]

Despite compelling evidence and recommendations, β-blockers remain an underused therapy in the post-MI period.

Post-MI Risk

Within 6 years of an initial heart attack, approximately 18% of men and 35% of women will have a recurrent MI. Post-MI patients have a sudden death rate that is four to six times that of the general population.[3] Compared with post-MI patients without LVD, patients with LVD have an even worse prognosis. Post-MI patients with LVD have a fourfold increase in the rate of in-hospital mortality and a two- to threefold increase in the rate of mortality at 30 days and 6 months.[13-15] Post-MI patients with LVD also have a twofold increase in the rate of reinfarction and are at the highest risk for sudden death.[13,14] Approximately 50% of patients with LVD do not have symptoms of HF, but despite being asymptomatic they remain at similar risk as patients with symptoms of HF.[16]

β-Blocker Use After MI

The Immediate Post-MI Period (Within Hours)

β-Blocker use in the immediate post-MI period is a Class I recommenda-

Table 1
Large (>1000 Patients) IV β-Blocker Trials in Acute/Post-Myocardial Infarction

Study	Mean Duration of Follow-Up	Active Treatment	β-Blocker	Patients (N)	Background Therapy	Mortality	Fatal/Nonfatal Reinfarction	Assessed CHF/LVD?
MIAMI[20]	15 d	Metoprolol	Selective (β_1)	5778	Diuretics	P = NS	P = NS	Excluded HF
ISIS-1[11]	1 wk	Atenolol	Selective (β_1)	16,027	Diuretics, IV nitrates, calcium antagonists, antiarrhythmics, digitalis, inotropic agents	↓15% $P < .04$	P = NS	Excluded HF
TIMI-IIB[22]	6 d*	Metoprolol	Selective (β_1)	1434	Aspirin, heparin, thrombolysis	P = NS	↓47% $P = .02$	History of HF = 1%
COMMIT[23]	15 d	Metoprolol†	Selective (β_1)	45,852	Fibrinolytics (55%), anticoagulant (75%), ACEIs (68%), nitrates (94%), diuretics (23%); PCI excluded	P = NS	↓18% $P = .001$	Included Killip class II and III

IV, intravenous; CHF, congestive heart failure; LVD, left ventricular dysfunction; MIAMI, Metoprolol in Acute Myocardial Infarction; NS, not significant; ISIS, International Study of Infarct Survival; TIMI-IIB, Thrombolysis in Myocardial Infarction Study; COMMIT, Clopidogrel and Metoprolol in Myocardial Infarction Trial; ACEIs, angiotensin-converting enzyme inhibitors; PCI, percutaneous coronary intervention.
*Study analyzed acute vs delayed metoprolol tartrate at 6 weeks and 1 year.
†Study used IV metoprolol tartrate (5 mg × 3 doses) followed by oral metoprolol tartrate (50 mg q 6 hrs) and succinate (200 mg).

tion in the AHA/ACC guidelines; however, IV use is a Class IIa recommendation.[3] β-Blockers reduce the risk of reinfarction, arrhythmias, and mortality both in the early stage and long term after an MI.[17] β-Blockers provide cardioprotection by diminishing myocardial oxygen demand by reducing heart rate, systemic arterial pressure, and myocardial contractility. This limits the damage to the injured myocardium.[18] Clinical trials have demonstrated that immediate (within 24 hours) post-MI β-blocker use can provide reductions in all-cause mortality; however, these agents remain unproven in reducing nonfatal reinfarction (Table 1).[11,19,20]

β-Blockers provide cardioprotection by diminishing myocardial oxygen demand by reducing heart rate, systemic arterial pressure, and myocardial contractility.

Most of these trials were conducted before the use of thrombolysis for MI.[21] Intravenous β-blocker trials conducted after the introduction of reperfusion therapy, however, have yielded conflicting mortality results. Details of the large-scale, short-term IV β-blocker trials, including the first International Study of Infarct Survival,[11] the Metoprolol in Acute Myocardial Infarction study,[20] and the Thrombolysis in Myocardial Infarction study,[22] are displayed in Table 1. The recent large-scale Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT) showed no mortality difference with the use of IV β-blockade, supporting the weaker recommendation previously made by the ACC/AHA guidelines.[23]

The Acute MI Period and Subsequent Care: Plan for Patients With and Without LVD

Long-term β-blocker therapy has been associated with significant mortality reductions in MI patients, as demonstrated in three large-scale, randomized, clinical trials—the β-Blocker Heart Attack Trial (BHAT),[8,24] the Norwegian Timolol Trial (NTT),[9] and the Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN)[10] trial (Table 2). Although HF or LVD is present in a large number of MI patients,[7] individuals with significant cardiac decompensation have generally been excluded from randomized

Table 2
Large (>1000 Patients) Oral β-Blocker Trials in Acute/Post-Myocardial Infarction

Study	Mean Length of Trial (mo)	Active Treatment	β-Blocker	Patients (N)	Background Therapy	Mortality	Fatal/Nonfatal Reinfarction	Assessed CHF/LVD?
Goteborg[19]	3	Metoprolol*	Selective (β_1)	1395	ACEIs, aspirin = none reported; lipid-lowering agents = not available	↓36% $P = .024$	↓35% $P < .05$	Excluded HF
BHAT[8,24]	25	Propranolol	Nonselective (β_1, β_2)	3837	No acute therapies. ACEIs = none reported or not available; lipid-lowering agents (3%), aspirin (21%)	↓26% $P < .005$	↓23% $P < .01$	Excluded severe HF
NTT[9]	17	Timolol	Nonselective (β_1, β_2)	1884	ACEIs, aspirin = none reported; lipid-lowering agents = not available	↓39% $P = .0003$	↓28% $P = .0006$	Excluded uncontrolled cardiac failure
LIT[12]	12	Metoprolol	Selective (β_1)	2395	ACEIs = none reported; lipid-lowering agents = not available; aspirin = excluded	↑4% P = NS	N/A	Excluded HF
CAPRICORN[10,33]	15	Carvedilol	Nonselective (β_1, β_2, α_1)	1959	Acute: IV nitrates (73%); heparin (64%); thrombolytics (37%). Long term: ACEIs (98%); statins (23%); aspirin (86%); reperfusion therapy (46%)	↓23 $P = .031$	↓40 $P = .01$	Included acute LVD and CHF

CHF, congestive heart failure; LVD, left ventricular dysfunction; Goteborg, Goteborg Metoprolol Trial; NS, not significant; BHAT, β-Blocker Heart Attack Trial; ACEIs, angiotensin-converting enzyme inhibitors; NTT, Norwegian Timolol Trial; LIT, Lopressor Intervention Trial; CAPRICORN, Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction; IV, intravenous.
*Patients received IV (15 mg) followed by oral metoprolol tartrate (200 mg).

β-blocker trials: only 19% of BHAT and 33% of NTT participants had a history or some degree of HF on admission.[9,24] In BHAT, patients with a history of severe HF were excluded, and in NTT, patients with uncontrolled cardiac failure were excluded.[8,9] CAPRICORN specifically enlisted only patients with documented LVD and was performed in the era of thrombolysis, angioplasty, and angiotensin-converting enzyme (ACE) inhibitor therapy.[10] Patients were randomized to carvedilol as early as the day after the infarct, and the majority were randomized within the first 2 weeks of the trial. In addition to a statistically significant 23% reduction in all-cause mortality,[10] CAPRICORN demonstrated that carvedilol reduced reinfarction by 40% (Figure 1).[25,26] Approximately half of the patients in CAPRICORN were asymptomatic (no congestive HF symptoms), and approximately 46% were given acute interventional therapy (either thrombolytic therapy or

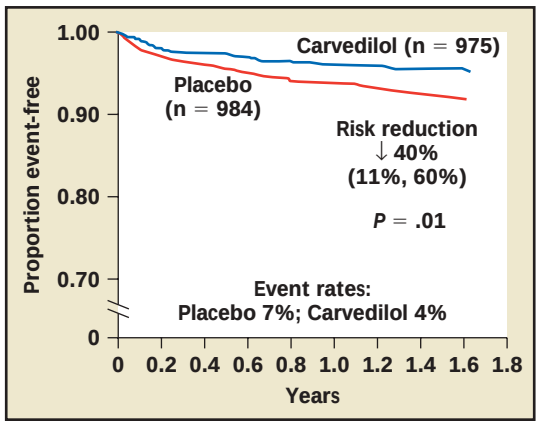

Figure 1. *CAPRICORN: reinfarction. Carvedilol treatment after a myocardial infarction significantly reduced the risk of recurrent fatal or nonfatal myocardial infarction compared with placebo. The event rates were placebo 7%, carvedilol 4%. CAPRICORN, Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction.*

angioplasty).[10] Carvedilol resulted in as great a decrease in all-cause mortality in those patients with no symptoms of HF (relative risk [RR] = 31%) as in those who had undergone revascularization (RR = 32%).[25,27] In a subset analysis, carvedilol also significantly increased left ventricular ejection fraction (LVEF), whereas placebo caused no change after 6 months of treatment.[28]

Evidence-Based Strategy for Post-MI β-Blocker Therapy

Although large-scale randomized clinical trials have demonstrated a reduced post-MI mortality risk in patients with normal ventricular function treated with long-term propranolol (BHAT)[8] and timolol (NTT)[9] and patients with LVD treated with carvedilol (CAPRICORN),[10] no similar evidence has been reported for the commonly used β_1-selective blockers metoprolol or atenolol. In general, although antiadrenergic agents are discussed as being interchangeable, the currently available clinical trial evidence does not support the view that clinical benefits of β-blockers after MI are a class effect.

Practical Implementation of β-Blocker Use: Evidence-Based Algorithm

Patients with Suspected MI Admitted to the Hospital

Initiating IV β-Blockers. In MI patients with significant ongoing chest pain, hypertension, or marked sinus tachycardia without contraindications, IV dosing can be considered; otherwise, oral dosing should be initiated. MI patients receiving IV β-blockers require strict monitoring of heart rate, blood pressure, electrocardiogram, and clinical status during initiation, and administration should be discontinued if abnormalities occur. β-Blockade can be reversed with IV isoproterenol (1–5 μg/min) if severe serious adverse effects, such as profound bradycardia or marked hypotension, occur.[3]

The AHA/ACC guidelines state that IV β-blocker use is a Class IIa recommendation.[3] The findings from COMMIT indicate that careful patient selection for IV β-blockade is important.[23] In this study, 45,852 patients were randomly allocated metoprolol (up to 15 mg IV, then 200 mg oral daily; n = 22,929) or matching placebo (n = 22,923), and study treatment was to continue until discharge or up to 4 weeks in hospital (mean = 15 days in survivors). Eligible patients included those presenting with ST-segment elevation, left bundle branch block, or ST-segment depression (7%) within 24 hours of onset of symptoms of suspected acute MI, unless their physician considered them to have clear indications for, or contraindications to, any of the study treatments. Patients scheduled for primary percutaneous coronary intervention were excluded. Other reasons for excluding patients were determined by the physician and included either a small likelihood of worthwhile benefit (eg, other life-threatening disease or unconvincing history of MI) or a high risk of adverse effects with the study treatments (which for metoprolol would have included persistently low blood pressure [eg, systolic blood pressure < 100 mm Hg] or low heart rate [eg, < 50 bpm], heart block, or cardiogenic shock). Evidence of moderate HF (Killip class II or III) was not an exclusion criterion; approximately 20% of patients were in Killip class II, and almost 5% were classified as Killip class III. There was no difference in overall mortality between the placebo and metoprolol groups (RR = 1%, $P = .7$). Importantly, patients in this study had a significantly increased risk (30%, $P < .00001$) of cardiogenic shock when administered IV metoprolol followed by oral metoprolol succinate versus placebo.[23]

Many patients are initiated intravenously on β_1-selective agents in hospital, converted to oral treatment, and discharged on these β_1-selective agents, despite their failure to demonstrate significant improvement in long-term survival after MI.[11,12] Implementation of evidence-based therapy might prompt consideration of switching patients from β_1-selective blockers to evidence-based, nonselective β-blockers. Switching was performed safely in MI patients during the CAPRICORN trial, in which prior β-blockade did not exclude participation.[10] A post hoc analysis that included the approximately 15% of CAPRICORN patients who had received at least one dose of IV or oral β-blockade was performed. The agent was discontinued before randomization. Although some of these patients were switched to carvedilol on the same day, the majority had one or more intervening days with no β-blocker therapy. Carvedilol resulted in clinical benefits, regardless of whether patients had initially been started on a different β-blocker or were started de novo at randomization. Patients initiated on an IV or oral β-blocker and subsequently receiving carvedilol had the same improved outcomes as those initiated directly on carvedilol.[27,29]

Among patients randomized in the hospital in CAPRICORN, there was no significant heterogeneity between those newly started on or those switched to carvedilol with regard to in-hospital HF or bradycardia adverse events. Importantly, patients newly started on carvedilol had similar rates of in-hospital HF and bradycardia as those receiving placebo (HF: placebo 2%, carvedilol 4%, $P = .06$; bradycardia: placebo 2%, carvedilol 1%,

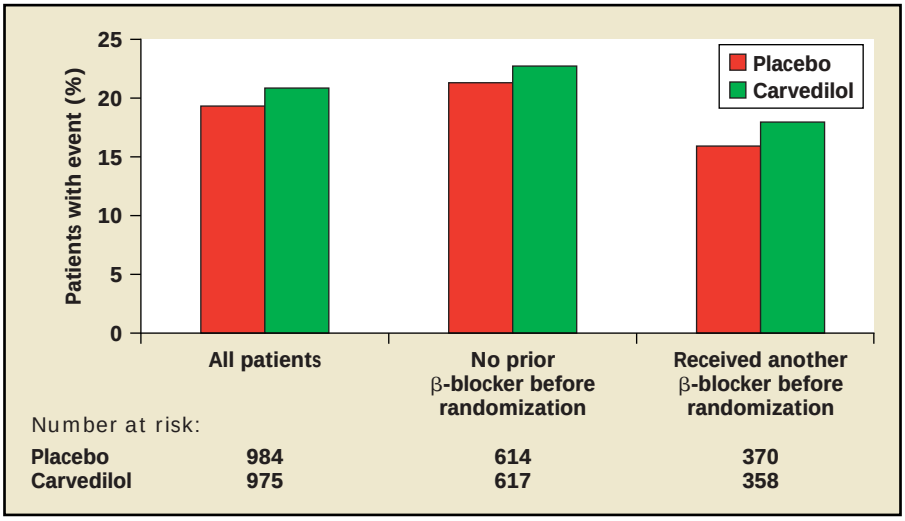

Figure 2. *CAPRICORN: HF adverse events anytime during the study. This post hoc analysis included approximately 15% of CAPRICORN patients who had received at least one dose of intravenous or oral β-blockade that was discontinued before randomization. Although some of these patients were switched to carvedilol on the same day, the majority had one or more intervening days with no β-blocker therapy. The percentage of the total patient population who had a heart failure adverse event anytime during the CAPRICORN trial was similar in patients who were started de novo on carvedilol at randomization and those who had previously received an intravenous or oral β-blocker before randomization.*

$P = .77$). This pattern was also seen for patients who had previously received IV or oral β-blockade (HF: placebo 1%, carvedilol 2%, $P = .28$; bradycardia: placebo 2%, carvedilol 3%, $P = .56$). For in-hospital hypotensive events, there was a trend toward heterogeneity between these subgroups (interaction P value = .08). Eleven percent of patients newly started on carvedilol experienced a hypotensive event, compared with 6% receiving placebo ($P = .0007$); however, there were nearly equal rates (7% placebo, 8% carvedilol) among patients previously receiving IV or oral β-blockade as part of their post-MI treatment.[25,27,29]

No difference was observed between carvedilol and placebo in the incidence of HF adverse events reported any time during the study, regardless of prior β-blocker treatment (Figure 2). For bradycardia, patients newly started on carvedilol had a rate of 7.5% any time during the study, compared with 4% for placebo ($P = .0005$); for patients who previously received a β-blocker, this rate was 8% for carvedilol and 5% for placebo ($P = .06$). For hypotension any time during the study, patients newly started on carvedilol had a rate of 24%, compared with 15% with placebo ($P < .0001$); for patients who previously received β-blockade, this rate was 21% with carvedilol and 14% with placebo ($P = .03$).[25,27,29]

Withdrawal of medication, both for in-hospital events and events reported for the entire study, showed no heterogeneity according to prior β-blocker use and no difference between carvedilol and placebo.[29] Although these data primarily reflect a population that was not directly switched from IV or oral β-blocker to carvedilol in the peri-MI period, they do suggest both the safety and efficacy of carvedilol in such patients.[27]

Initiating Oral β-Blockers. Oral β-blockers can be started before, during, or after initiation and titration of ACE inhibitor therapy in patients with or without reperfusion therapy.[3] The evidence-based β-blockers for post-MI patients without LVD include propranolol and timolol (Table 3). Both metoprolol tartrate and atenolol are US Food and Drug Administration–indicated for post-MI use, although their safety and efficacy, specifically in post-MI patients with LVD, has not been studied. Evidence from CAPRICORN shows that patients with LVD, regardless of the presence of HF symptoms, benefit greatly from treatment.[10,25] Left ventricular function should be assessed in the hospital be-

Table 3
Recommended Dosing for Evidence-Based β-Blocker in Post-Myocardial Infarction Patients

Agent	Initiation Dose	Titration Steps (3-10 d after initiation)	Target Dose
No LVD or HF			
Timolol[9]	5 mg b.i.d.		10 mg b.i.d.
Propranolol[8]	40 mg q.d.		60 to 80 mg q.d.
LVD With or Without HF			
Carvedilol[10,25]	6.25 mg b.i.d.*	12.5 mg b.i.d.	25 mg b.i.d.

*A lower starting dose can be used (3.125 mg b.i.d.) and/or the rate of up-titration can be slowed if clinically indicated (eg, due to low blood pressure, low heart rate, or fluid retention). Patients should be maintained on lower doses if higher doses are not tolerated.

fore the patient is discharged, and LVEF less than 40% warrants the use of carvedilol preferentially.[25]

In patients with LVD, carvedilol should be started at 6.25 mg b.i.d. and increased to 12.5 b.i.d. and 25 mg b.i.d. at 3- to 10-day intervals (Table 3).[10,25] The recommended dosing regimen need not be altered in patients who received treatment with an IV or oral β-blocker during the acute phase of the MI. Treatment should be initiated as soon as possible, and the target dose should be continued indefinitely. If patients are unable to achieve the full recommended dose owing to severe bradycardia or hypotension, a lower dose should be maintained, and dose escalation should be reattempted after several weeks. Dose-related clinical benefits have been demonstrated at below target doses of carvedilol in patients with chronic HF.[30]

Concomitant Drug Therapy

The ACC/AHA recommendations for pharmacologic therapy in the acute phase after MI and long-term management are listed in Table 4. Figure 3 shows evidence-based pharmacologic therapy for post-MI patients.[17] Patients with MI should be treated with ACE inhibitors and β-blockers in the absence of contraindications, irrespective of left ventricular function. In post-MI patients with LVD and HF, aldosterone antagonists are also indicated; in the absence of contraindications or intolerance, ACE inhibitors are recommended for initiation 12 to 24 hours after admission for MI. Patients might thus be started on β-blockers before, during, or after initiation of ACE inhibitors. ACE inhibitors do not need to be at target doses before the initiation of a β-blocker. Subsequent up-titration of the ACE inhibitor can be done after optimization of the β-blocker dose, and both agents can be titrated to target doses over time. Aldosterone antagonists are recommended in post-MI patients with LVD, HF, or diabetes in the absence of contraindications or significant renal dysfunction. Patients must be closely monitored for the development of hyperkalemia. Aldosterone antagonists can be initiated, continued, or dose-adjusted before or during β-blocker treatment. Although both ACE inhibitors and β-blockers are Class I recommendations in the guidelines, and the evidence is strong that both should ultimately be used in post-MI patients without contraindications or intolerance,[3] the question frequently arises as to which to initiate first. In the major clinical trials of ACE inhibitors in MI, most patients were already receiving β-blocker therapy when randomized to ACE inhibitor or placebo. In CAPRICORN, by study design, patients needed to be receiving ACE inhibitor therapy before randomization to carvedilol or placebo. The recent Cardiac Insufficiency Bisoprolol Study III indicates that the initiation of bisoprolol before enalapril in HF might result in better outcomes for the patient.[31]

In a recent clinical trial, HF patients were randomized to initiation and up-titration of ACE inhibitor

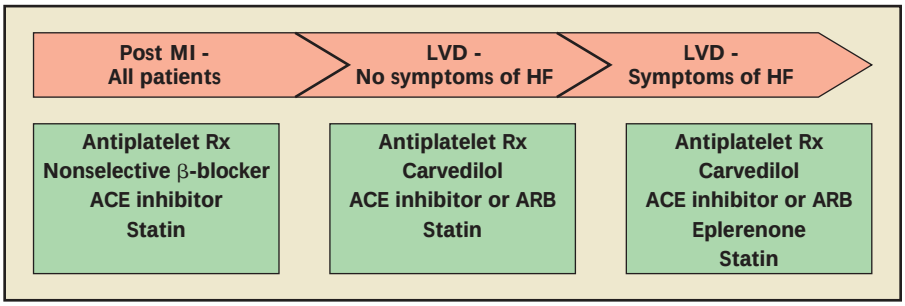

Figure 3. *Evidence-based pharmacologic treatment of patients with a recent (< 1 month prior) myocardial infarction without contraindications. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HF, heart failure; LVD, left ventricular dysfunction; MI, myocardial infarction; Rx, treatment.*

Table 4
American College of Cardiology/American Heart Association Guidelines for Management of ST-Elevation Myocardial Infarction

Acute Therapy	Discharge Therapy
Aspirin	Aspirin
Clopidogrel	Clopidogrel
β-blocker	β-blocker
Heparin (UFH or LMWH)	ACEI/ARB
GP IIb-IIIa inhibitor (if receiving PCI)	Aldosterone antagonist
Catheterization/PCI	Statin/lipid-lowering drug
	Smoking cessation
	Cardiac rehabilitation

UFH, unfractionated heparin; LMWH, low-molecular-weight heparin; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GP, glycoprotein; PCI, percutaneous coronary intervention. Data from Antman et al.[3]

therapy followed by carvedilol, compared with initiation and up-titration of carvedilol followed by ACE inhibitor.[32] Patients started first on carvedilol had better clinical status, greater LVEF, and lower B-type natriuretic peptide levels at the end of 1 year compared with those started on ACE inhibitors first. Thus, in post-MI patients with LVD and borderline blood pressures, initiation of β-blocker therapy first, followed by subsequent initiation of ACE inhibitors, should be considered.

If overt HF develops in patients with asymptomatic LVD or worsens in those who already have signs or symptoms of decompensation, diuretics should be increased and the rate of up-titration should be slowed. If hypotension limits carvedilol up-titration, the ACE inhibitor dose should be decreased temporarily.

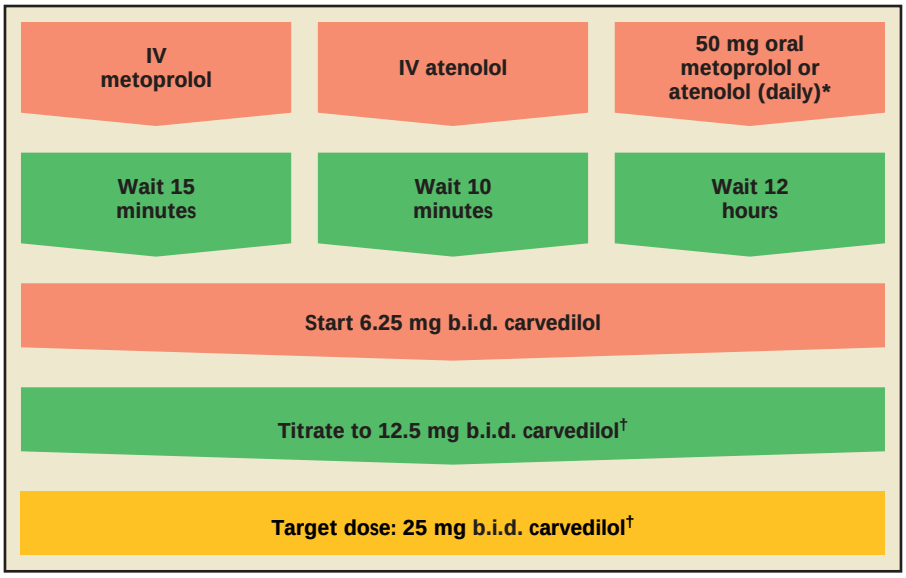

Figure 4. *Switching protocol for post–myocardial infarction patients with left ventricular dysfunction, with or without symptomatic heart failure. *After patients have been clinically stable for 72 hours. †As tolerated.*

Switching

In all MI patients without contraindication, a β-blocker should be started as soon as possible, LVD should be assessed, and then either the initiation or switching to an evidence-based β-blocker should occur.[9,10,24] Dosing of carvedilol remains the same whether the patient is newly initiated or switched from another agent. Patients should continue β-blocker therapy for life.

A simple algorithm for switching to evidence-based β-blockade with carvedilol is shown in Figure 4.[29] After patients have been clinically stable for 72 hours, oral metoprolol and atenolol can be switched to carvedilol (for LVEF ≤ 40%). Patients with LVD not at further increased risk due to persistent ischemia, arrhythmias, hypotension, HF, or large areas of jeopardized myocardium can be safely switched directly from metoprolol or atenolol to carvedilol. Other patients should be stabilized before switching. Patients taking metoprolol or atenolol should discontinue these agents and then begin carvedilol 12 hours after the last dose (carvedilol 12.5 mg b.i.d. for those taking metoprolol or atenolol 100–200 mg daily, and 6.25 mg b.i.d. for those taking 50 mg daily). Patients in either dose group should have carvedilol titrated by

Main Points

- Current guidelines state that all patients should be prescribed a β-blocker after a myocardial infarction (MI), unless there is an absolute contraindication to therapy.
- Approximately 50% of patients with LVD do not have symptoms of HF, but despite being asymptomatic they remain at similar risk as patients with symptoms of HF.
- Although large-scale randomized clinical trials have demonstrated a reduced post-MI mortality risk in patients with normal ventricular function treated with long-term propranolol (BHAT) and timolol (NTT) and patients with LVD treated with carvedilol (CAPRICORN), no similar evidence has been reported for the commonly used β_1-selective blockers metoprolol or atenolol.
- Although antiadrenergic agents are discussed as being interchangeable, the currently available clinical trial evidence does not support the view that clinical benefits of β-blockers after MI are a class effect.
- Implementation of evidence-based therapy might prompt consideration of switching patients from β_1-selective blockers to evidence-based, nonselective β-blockers.
- Thus, in post-MI patients with LVD and borderline blood pressures, initiation of β-blocker therapy first, followed by subsequent initiation of ACE inhibitors should be considered.

doubling the dose stepwise to 25 mg b.i.d. every 3 to 10 days. The measurement of LVD is the key to this management strategy and should be considered vital in all post-MI patients before an evidence-based approach to care can be chosen.

Conclusions

A convincing body of evidence supports the lifesaving benefits of β-blocker therapy in the acute and long-term period after MI. On the basis of this evidence, the latest ACC/AHA guidelines for MI indicate that all patients without contraindication should be started on β-blocker therapy promptly, irrespective of concomitant fibrinolytic therapy or performance of primary percutaneous coronary intervention.[3] There is little evidence that a class effect exists, however, and every effort should be made to use those specific agents and doses demonstrated to be effective in randomized clinical trials. Every effort should be made to initiate and maintain this evidence-based, guideline-recommended, life-prolonging therapy for the long term. ■

Dr. Fonarow discloses that he has received research support as well as speaker's honoraria and consulting fees from GlaxoSmithKline.

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