

2007 Focused Update of the ACC/AHA Guidelines

Managing patients with ST-elevation myocardial infarction.

BY ERIC R. BATES, MD

The 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction (STEMI) is a new effort by the Writing Committee to revise existing guidelines that are affected by evolving data or opinion.¹ It is complementary to the full-text guideline,² which remains current until the next full revision. The class of recommendation and level of evidence schema used in previous documents is again employed to estimate the size and certainty of the treatment effect. Nine major areas were selected for updated recommendations.

ANALGESIA

Use of morphine remains a class I recommendation for patients with STEMI, despite retrospective data questioning the safety of morphine in patients with unstable angina/non-ST-elevation myocardial infarction. However, cyclo-oxygenase-2 inhibitors and other nonsteroidal anti-inflammatory drugs should be discontinued immediately at the time of STEMI because of the known increased risk of mortality, reinfarction, hypertension, heart failure, and

myocardial rupture associated with their use.³⁻⁵ A stepped-care approach for chronic pain management should be used for treatment selection, beginning with acetaminophen or aspirin, small doses of narcotics, or nonacetylated salicylates. If pain relief is inadequate, nonselective nonsteroidal anti-inflammatory drugs, such as naproxen, are reasonable.

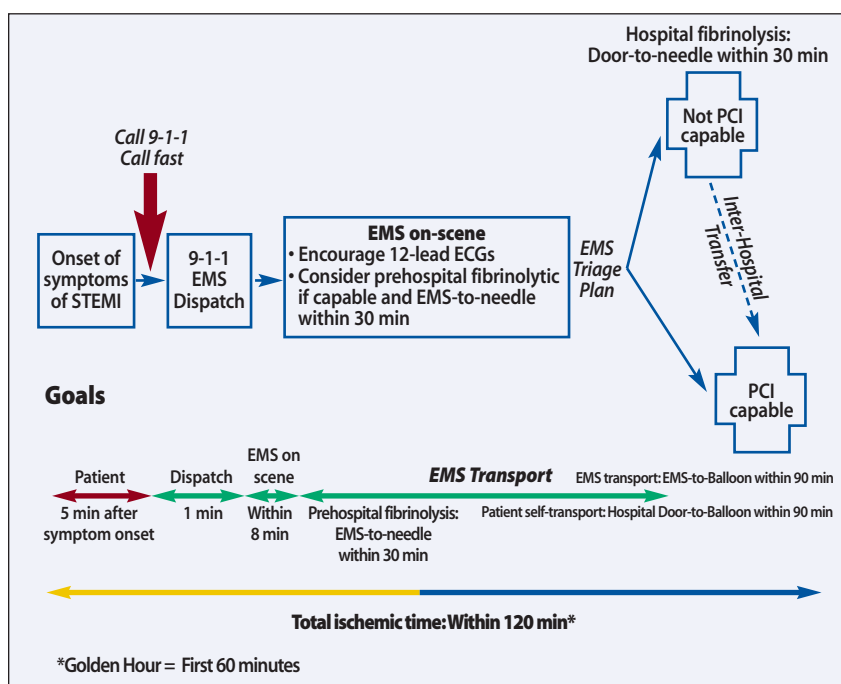


Figure 1. Options for transportation of STEMI patients and initial reperfusion treatment goals. (Adapted from Antman et al. J Am Coll Cardiol. 2008;51:210-247.¹)

BETA-BLOCKERS

Previous recommendations have supported the use of beta-blockers to reduce the incidence of reinfarction and recurrent ischemia in patients receiving fibrinolytic therapy. However, uncertainty about the use of intravenous (IV) beta-blockers has increased after subsequent reports that did not find significant reductions in mortality.⁶ These concerns were confirmed by the Clopidogrel and Metoprolol in Myocardial Infarction Trial/Second Chinese Cardiac Study (COMMIT/CCS-2) trial⁷ that randomized 45,852 patients within 24 hours of onset of suspected myocardial infarction to receive IV followed by oral metoprolol or placebo for a mean of 15 days. There was no difference in mortality, and there was an excess of cardiogenic shock, hypotension, and bradycardia, seen chiefly in the first day after hospitalization.

Therefore, the 2007 Focused Update concludes that it is only reasonable to use IV beta-blocker therapy at the time of presentation when hypertension is present and the patient is not at an increased risk of cardiogenic shock. Patients with sinus tachycardia or atrial fibrillation should have left ventricular function rapidly evaluated before administration of IV beta-blockers (or other negative inotropes, such as nondihydropyridine calcium channel blockers). In the other patients, oral beta-blocker therapy should be initiated within the first 24 hours, after hemodynamic stability is confirmed, if they do not have any of the following: (1) signs of heart failure, (2) evidence of a low output state, (3) increased risk for cardiogenic shock, or (4) other relative contraindications to beta blockade (PR interval >0.24 s, second- or third-degree heart block, active asthma, or reactive airway disease). Long-term use of oral beta-blockers is strongly recommended for secondary prevention in patients at highest risk (low ejection fraction, heart failure, or after-shock), once they have stabilized, with gradual dose titration.

LOGISTICS OF CARE

The overarching goal in STEMI is to initiate reperfusion therapy within 2 hours (ideally within 60 minutes) of symptom onset (Figure 1). The Writing Committee continues to endorse the concept that faster times to reperfusion and better systems of care are associated with important reductions in morbidity and mortality

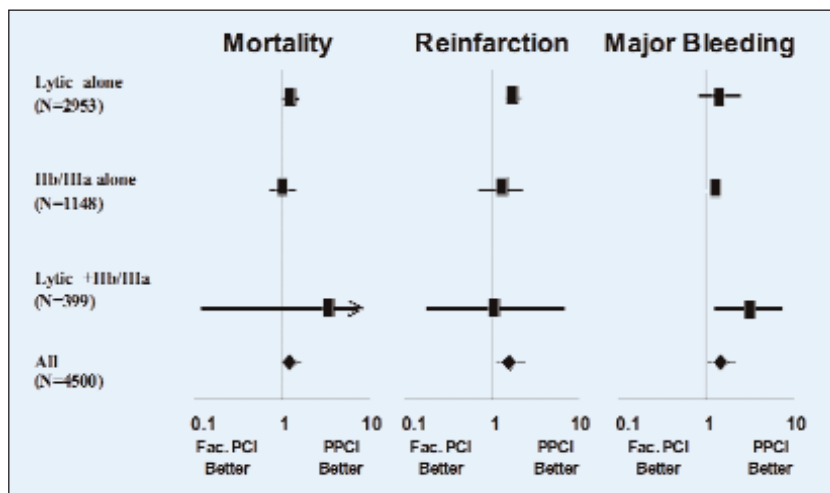


Figure 2. Outcomes in patients treated with facilitated or primary PCI. (Adapted from Keeley et al. *Lancet*. 2006;367:579-588.¹²)

rates. An underutilized strategy for improving systems of care for STEMI patients is to expand the use of prehospital 12-lead electrocardiography programs by emergency medical systems.

It is increasingly clear that two types of hospital systems provide reperfusion therapy: those with percutaneous coronary intervention (PCI) capability and those without PCI capability. STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 minutes of first medical contact as a systems goal. The best outcomes are achieved by offering this strategy 24 hours per day, 7 days per week.⁸ The goal of the “Door-to-Balloon (D2B): An Alliance for Quality” campaign (www.d2balliance.org) is to have at least 75% of patients treated within 90 minutes of hospital presentation, with a recommendation for the use of evidence-based strategies to reduce needless delays.⁹

The 75% goal was set in recognition that some patients have clinically relevant nonsystem-based delays that do not represent quality-of-care issues. These delays include patient variables (uncertainty about diagnosis, evaluation and treatment of other life-threatening conditions, obtaining informed consent, etc.) that delay the patient’s arrival in the interventional cardiology laboratory or anatomical challenges (issues of arterial, coronary, or lesion access) that prolong the PCI procedure. In the absence of such circumstances, however, reperfusion should be achieved as soon as possible within this time frame, and many hospitals with refined systems are approaching median door-to-balloon times of 60 to 70 minutes. The new focus for primary PCI is from first medical contact because in regionalization strategies, extra time may be taken to transport patients to a PCI

TABLE 1. OUTCOMES IN PATIENTS TREATED WITH RESCUE PCI

Outcome	Rescue PCI	Conservative Treatment	Relative Risk (95% CI)	P Value
Mortality, % (n)	7.3 (454)	10.4 (457)	0.69 (0.46–1.05)	.09
Heart failure, % (n)	12.7 (424)	17.8 (427)	0.73 (0.54–1.00)	.05
Reinfarction, % (n)	6.1 (346)	10.7 (354)	0.58 (0.35–0.97)	.04
Stroke, % (n)	3.4 (297)	0.7 (295)	4.98 (1.10–22.48)	.04
Minor bleeding, % (n)	16.6 (313)	3.6 (307)	4.58 (2.46–8.55)	<.001

In three trials enrolling 700 patients that reported the composite endpoint of all-cause mortality, reinfarction, and heart failure, rescue PCI was associated with a significant relative risk reduction of 28% (relative risk, 0.72; 95% CI, 0.59–0.88; $P=.001$)

Adapted from Wijeyesundera et al. J Am Coll Cardiol. 2007;49:422–430.¹⁶

center. Immediate transfer for primary PCI is a treatment option when the expected door-to-balloon time is within 90 minutes of first medical contact.¹⁰

Because of the critical importance of time to treatment, however, fibrinolytic therapy is generally preferred in hospital systems that do not have the capability of meeting the time goal for primary PCI. Transfer protocols need to be in place for arranging rescue PCI when clinically indicated. For fibrinolytic therapy, the systems goal is to deliver drug within 30 minutes of hospital presentation.

FACILITATED PCI

Facilitated PCI refers to a strategy of planned immediate PCI after administration of an initial pharmacologic regimen intended to improve coronary patency before the procedure. Potential advantages include earlier time to reperfusion, smaller infarct size, improved patient stability, lower infarct artery thrombus burden, greater procedural success rates, higher TIMI (Thrombolysis in Myocardial Infarction trial) flow rates, and improved survival rates. Potential risks include increased bleeding complications, especially in older patients. Potential limitations include additional cost.

Despite the possible advantages, clinical trials of facilitated PCI have not demonstrated any benefit in reducing infarct size or improving outcomes (Figure 2).^{11,12} Nevertheless, selective use of the facilitated strategy with regimens other than full-dose fibrinolytic therapy in subgroups of patients at high risk (large myocardial infarction or hemodynamic or electrical instability) with low risk of bleeding (younger age, absence of poorly controlled hypertension, normal body weight) who present to hospitals without PCI capability might be performed when transfer delays for primary PCI are anticipated.

EMERGENCY INVASIVE STRATEGY

In unstable patients, such as those with cardiogenic shock (especially those younger than 75 years), severe congestive heart failure/pulmonary edema, or hemodynamically compromising ventricular arrhythmias (regardless of age), a strategy of coronary angiography with intent to perform PCI is a useful approach regardless of the time since initiation of fibrinolytic therapy, provided further invasive management is not considered futile or unsuitable given the clinical circumstances.

In stable patients, rescue PCI may be reasonable if there is clinical suspicion of failure of fibrinolytic therapy (Table 1).^{13–16} The clinical diagnosis of failed fibrinolysis is difficult but is best made when there is <50% ST-segment resolution 90 minutes after initiation of therapy in the lead showing the greatest degree of ST-segment elevation at presentation.

Given the association between bleeding events and subsequent ischemic events,¹⁷ it might be reasonable to select moderate- and high-risk patients for rescue PCI and to treat low-risk patients with medical therapy. An ECG estimate of potential infarct size in patients with persistent ST-segment elevation and ongoing ischemic pain can be useful. Anterior MI or inferior MI with right ventricular involvement or precordial ST-segment depression usually predicts increased risk.¹⁸ Conversely, patients with symptom resolution, improving ST-segment elevation, or inferior myocardial infarction localized to three ECG leads probably gain little benefit. Likewise, it is doubtful that PCI of a branch artery (diagonal or obtuse marginal branch) will change prognosis in the absence of high-risk criteria noted previously. The benefits of rescue PCI are greater the earlier it is initiated after the onset of ischemic discomfort.

ELECTIVE INVASIVE STRATEGY

PCI of a hemodynamically significant stenosis in a patent infarct artery >24 hours after STEMI may be considered as part of an invasive strategy to maintain long-term patency. The open artery hypothesis suggested that late patency of an infarct artery is associated with improved left ventricular function, increased electrical stability, and provision of collateral vessels to other coronary beds for protection against future events. However, small studies have demonstrated inconsistent benefit for late PCI in stable patients with an occluded infarct artery. The Occluded Artery Trial (OAT)¹⁹ and its substudy, the second Total Occlusion Study of Canada (TOSCA-2),²⁰ enrolled 2,166 stable patients with an occluded infarct artery and left ventricular ejection fraction <50% or proximal occlusion of a major epicardial artery with a large risk region. Importantly, exclusion criteria included NYHA class III or IV heart failure, rest angina, serum creatinine >2.5 mg/dL, left main or three-vessel disease, clinical instability, or severe inducible ischemia on stress testing if the infarct zone was not akinetic or dyskinetic. Elective PCI of the occluded infarct artery 1 to 28 days after myocardial infarction had no incremental benefit beyond optimal medical therapy with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and statins in preserving left ventricular function and preventing subsequent cardiovascular events. The potential benefit of PCI in attenuating remodeling may have been decreased by periprocedural myocardial infarction and the high rate of beta-blocker and angiotensin-converting enzyme inhibitor use. Therefore, PCI for an occluded infarct artery in asymptomatic patients with one- or two-vessel disease is not recommended.

ANTICOAGULANTS

Patients treated with fibrinolytics, including streptokinase, and patients who do not receive reperfusion therapy should receive anticoagulant therapy for a minimum of 48 hours and preferably for the duration of the index hospitalization, up to 8 days.²¹⁻²³ Regimens other than unfractionated heparin (UFH) are recommended if anticoagulant therapy is given for more than 48 hours because of the risk of heparin-induced thrombocytopenia with prolonged UFH treatment. Anticoagulant regimens with established efficacy include UFH, enoxaparin,²² and fondaparinux.²³ Potential exists for accumulation of anti-Xa activity with increasing degrees of renal failure when enoxaparin and fondaparinux are used. Therefore, estimation of creatinine clearance should be calculated and doses adjusted accordingly.

For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommen-

dations should be followed. For previous treatment with UFH, administer additional boluses of UFH as needed to support the procedure taking into account whether glycoprotein IIb/IIIa receptor antagonists have been administered. Bivalirudin may also be used in patients treated previously with UFH. For previous treatment with enoxaparin, if the last dose was administered within the previous 8 hours, no additional enoxaparin should be given. If the last dose was administered at least 8 to 12 hours earlier, an IV dose of 0.3 mg/kg of enoxaparin should be given. For previous treatment with fondaparinux, administer additional intravenous treatment with an anticoagulant possessing anti-IIa activity, taking into account whether glycoprotein IIb/IIIa receptor antagonists have been administered. Because of the risk of catheter thrombosis, fondaparinux should not be used as the sole anticoagulant to support PCI.

THIENOPYRIDINES

Clopidogrel (75 mg/d orally) should be added to aspirin in patients with STEMI, regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy.^{24,25} Treatment with clopidogrel should continue for at least 14 days. In patients younger than 75 years who receive fibrinolytic therapy or who do not receive reperfusion therapy, it is reasonable to administer an oral clopidogrel loading dose of 300 mg. No data are available to guide decision making regarding an oral loading dose in older patients. Long-term maintenance therapy (eg, 1 year) with clopidogrel (75 mg/d orally) can be useful in STEMI patients regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy. Recommendations for continuing clopidogrel after PCI or stopping it before surgery remain unchanged.

SECONDARY PREVENTION

Revised recommendations adapted from the 2006 AHA/ACC Guidelines for Secondary Prevention for Patients with Coronary and Other Atherosclerotic Vascular Disease²⁶ are incorporated in the Focused Update. New recommendations for antiplatelet therapy have been added. Other changes include the addition of recommended daily physical activity, a recommendation for lowered low-density lipoprotein cholesterol, and a new recommendation for an annual influenza vaccination. ■

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