

2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Frederick G. Kushner, Mary Hand, Sidney C. Smith, Jr, Spencer B. King, III, Jeffrey L. Anderson, Elliott M. Antman, Steven R. Bailey, Eric R. Bates, James C. Blankenship, Donald E. Casey, Jr, Lee A. Green, Judith S. Hochman, Alice K. Jacobs, Harlan M. Krumholz, Douglass A. Morrison, Joseph P. Ornato, David L. Pearle, Eric D. Peterson, Michael A. Sloan, Patrick L. Whitlow, and David O. Williams

J. Am. Coll. Cardiol. published online Nov 18, 2009;
doi:10.1016/j.jacc.2009.10.015

This information is current as of November 19, 2009

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://content.onlinejacc.org/cgi/content/full/j.jacc.2009.10.015v1>

JACC

JOURNAL *of the* AMERICAN COLLEGE *of* CARDIOLOGY



Table 4. Recommendations for the Use of Parenteral Anticoagulants

STEMI Recommendations	PCI Recommendations	2009 Joint STEMI/PCI Focused Update Recommendations	Comments
2007 STEMI Update, Section 8	2007 PCI Guideline Update, Table 13		
Class I			
<p>2. For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed:</p> <p>a. For prior treatment with UFH, administer additional boluses of UFH as needed to support the procedure, taking into account whether GP IIb/IIIa receptor antagonists have been administered. (<i>Level of Evidence: C</i>) Bivalirudin may also be used in patients treated previously with UFH. (<i>Level of Evidence: C</i>)</p> <p>b. For prior treatment with enoxaparin, if the last subcutaneous dose was administered within the prior 8 hours, no additional enoxaparin should be given; if the last subcutaneous dose was administered at least 8 to 12 hours earlier, an intravenous dose of 0.3 mg per kg of enoxaparin should be given. (<i>Level of Evidence: B</i>)</p> <p>c. For prior treatment with fondaparinux, administer additional intravenous treatment with an anticoagulant possessing anti-IIa activity taking into account whether GP IIb/IIIa receptor antagonists have been administered. (<i>Level of Evidence: C</i>)</p>	<p>1. For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed:</p> <p>a. For prior treatment with UFH, administer additional boluses of UFH as needed to support the procedure, taking into account whether GP IIb/IIIa receptor antagonists have been administered. (<i>Level of Evidence: C</i>) Bivalirudin may also be used in patients treated previously with UFH. (<i>Level of Evidence: C</i>)</p> <p>b. For prior treatment with enoxaparin, if the last subcutaneous dose was administered at least 8 to 12 hours earlier, an IV (intravenous) dose of 0.3 mg/kg of enoxaparin should be given; if the last subcutaneous dose was administered within the prior 8 hours, no additional enoxaparin should be given. (<i>Level of Evidence: B</i>)</p> <p>c. For prior treatment with fondaparinux, administer additional intravenous treatment with an anticoagulant possessing anti-IIa activity, taking into account whether GP IIb/IIIa receptor antagonists have been administered. (<i>Level of Evidence: C</i>)</p>	<p>1. For patients proceeding to primary PCI who have been treated with ASA and a thienopyridine, recommended supportive anticoagulant regimens include the following:</p> <p>a. For prior treatment with UFH, additional boluses of UFH should be administered as needed to maintain therapeutic activated clotting time levels, taking into account whether GP IIb/IIIa receptor antagonists have been administered. (<i>Level of Evidence: C</i>)</p> <p>b. Bivalirudin is useful as a supportive measure for primary PCI with or without prior treatment with UFH (9). (<i>Level of Evidence: B</i>)</p>	<p>Modified recommendation. (Bivalirudin was added as an acceptable anticoagulant for primary PCI; text about UFH was modified to mention activated clotting time levels. Information on enoxaparin and fondaparinux was not imported because recommendations concerning these drugs were unchanged.)</p>
Class IIa			
		<p>1. In STEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin anticoagulation is reasonable (9). (<i>Level of Evidence: B</i>)</p>	<p>New recommendation</p>

cardiac causes (1.8% versus 2.9%; RR 0.62; 95% CI 0.40 to 0.95; $P=0.03$) and death due to all causes (2.1% versus 3.1%; RR 0.66; 95% CI 0.44 to 1.00; $P=0.047$ compared with UFH plus GP IIb/IIIa inhibitors). At 1 year, MACE rates were identical, but there was a decrease in all-cause mortality with bivalirudin (3.4% versus 4.8%, $P=0.03$) (68).

Concerns about the trial include its open-label design and the administration of UFH before randomization in 66% of patients in the bivalirudin arm and 76% of patients in the UFH plus GP IIb/IIIa receptor antagonist arm. Only 615 patients received bivalirudin monotherapy, and only 60% of patients in the trial received a 600-mg clopidogrel loading dose. Major bleeding as defined in the publication included hematomas of 5 cm, intracranial hemorrhage, and bleeding that required surgery. Additionally, the study put forth a composite primary end point that combined efficacy and safety. Although there were no statistically significant interactions at 30 days between the treatment assignment and preprocedural UFH use or clopidogrel loading dose with respect to MACE or major bleeding, the occurrence of an increase in early stent thrombosis with bivalirudin and the excess bleeding with UFH and GP IIb/IIIa inhibitors may be related to the degree of platelet inhibition and antithrombin activity associated with these treatment doses.

A preliminary report suggested that the use of bivalirudin alone ($P=0.005$) and a lower loading dose of clopidogrel (300 versus 600 mg; $P=0.01$) were independent predictors of acute and subacute stent thrombosis rates, respectively (69). Probability values for secondary end points may not have been adjusted for multiple looks.

Therefore, the writing group now considers bivalirudin useful for primary PCI in STEMI whether or not the patient received pretreatment with UFH. The risk of acute stent thrombosis associated with bivalirudin appeared to be mitigated by the prior use of UFH and the risk of subacute stent thrombosis by the use of a 600-mg loading dose of clopidogrel. These data should be confirmed by prospective studies.

5. Recommendations for Triage and Transfer for PCI

(See Table 5 and Appendix 5.)

5.1. Triage and Transfer for PCI

5.1.1. STEMI Patients Who Are Candidates for Reperfusion
The 2007 STEMI Focused Update describes several strategies for reperfusion, among them *facilitated PCI* and *rescue PCI* (4). These terms are no longer used for the recommen-

Table 5. Recommendations for Triage and Transfer for PCI

2004/2005/2007 Recommendations	2009 Joint STEMI/PCI Focused Update Recommendations	Comments
Class I		
	1. Each community should develop a STEMI system of care that follows standards at least as stringent as those developed for the AHA's national initiative, Mission: Lifeline, to include the following: <ul style="list-style-type: none"> • ongoing multidisciplinary team meetings that include emergency medical services, non-PCI-capable hospitals/STEMI referral centers, and PCI-capable hospitals/STEMI receiving centers to evaluate outcomes and quality improvement data; • a process for prehospital identification and activation; • destination protocols for STEMI receiving centers; • transfer protocols for patients who arrive at STEMI referral centers who are primary PCI candidates, are ineligible for fibrinolytic drugs, and/or are in cardiogenic shock. (<i>Level of Evidence: C</i>) 	New recommendation
Class IIa		
	1. It is reasonable for high-risk* patients who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI-capable facility to be transferred as soon as possible to a PCI-capable facility where PCI can be performed either when needed or as a pharmacoinvasive strategy. Consideration should be given to initiating a preparatory antithrombotic (anticoagulant plus antiplatelet) regimen before and during patient transfer to the catheterization laboratory (14,15). (<i>Level of Evidence: B</i>)	New recommendation (see Appendix 5)
Class IIb		
(From 2007 STEMI Update, Section 5)	1. Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present: a. Patients are at high risk, b. PCI is not immediately available within 90 minutes, and c. Bleeding risk is low (younger age, absence of poorly controlled hypertension, normal body weight). (<i>Level of Evidence: C</i>)	Modified recommendation (changed text).
(From 2007 STEMI Update, Section 6)	1. A strategy of coronary angiography with intent to perform PCI in the absence of 1 or more of the above Class I or IIa indications might be reasonable in moderate- and high-risk patients, but its benefits and risks are not well established. The benefits of rescue PCI are greater the earlier it is initiated after the onset of ischemic discomfort. (<i>Level of Evidence: C</i>)	Deleted recommendation (covered by new recommendations, above)

*High risk was defined in the CARESS-in-AMI (15) study as STEMI patients with ≥ 1 high-risk feature (extensive ST-segment elevation, new-onset left bundle-branch block, previous MI, Killip class >2 , or left ventricular ejection fraction $\leq 35\%$ for inferior MIs; anterior MI alone with ≥ 2 mm of ST elevation in ≥ 2 leads also qualified the patient as being at high risk). It was defined in TRANSFER-AMI (14) as ≥ 2 mm of ST-segment elevation in 2 anterior leads or ST elevation of at least 1 mm in inferior leads with at least 1 of the following: systolic blood pressure <100 mm Hg, heart rate >100 bpm, Killip class II to III, ≥ 2 mm of ST-segment depression in the anterior leads, or ≥ 1 mm of ST elevation in right-sided lead V_4 indicative of right ventricular involvement.

dations in this update so that the contemporary therapeutic choices that lead to reperfusion as part of the treatment of patients presenting with STEMI can be described without these potentially misleading labels.

A brief review of facilitated PCI, however, is needed. This strategy involves full- or half-dose fibrinolytic therapy with or without a GP IIb/IIIa receptor antagonist, followed by immediate PCI. Two studies addressed this issue: ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy With Percutaneous Coronary Intervention) (70), which was described in detail in the 2007 PCI and STEMI focused updates, and FINESSE (71), which was a randomized, double-blind clinical trial of 2452 patients ran-

domized within 6 hours of symptom onset to receive reduced-dose reteplase plus abciximab followed by PCI (combination-facilitated PCI), abciximab alone followed by PCI (abciximab-facilitated PCI), or placebo (primary PCI).

ASSENT-4 patients treated with fibrinolytic therapy before PCI had increased rates of adverse outcomes, including in-hospital death (6% versus 3%). The investigators theorized that suboptimal antithrombotic therapy (i.e., the lack of a heparin infusion after bolus administration, no upfront loading dose of clopidogrel, and prohibition of IIb/IIIa use except for bailout) and a short time from fibrinolytic therapy to PCI contributed in part to the adverse clinical outcomes.

FINESSE (8) showed that neither PCI preceded by abciximab and reteplase nor PCI preceded by abciximab alone was superior to abciximab used at the time of PCI among patients presenting within 4 hours of medical contact. Neither the primary end point (a composite of death due to all causes, ventricular function more than 48 hours after randomization, cardiogenic shock, and congestive heart failure during the first 90 days after randomization) nor mortality was significantly different among the groups. Although the study was terminated early because of recruitment challenges, there was less than a 2% chance that the primary treatment group difference would be significant if the trial had been allowed to continue to its planned completion.

The indications for rescue PCI have been defined by a combination of clinical and electrocardiographic clues that an infarct artery has not reperfused. These are relief of pain and resolution of ST-segment elevation. Although complete relief of pain and complete resolution of ST elevation are reasonably predictive of reperfusion after fibrinolytic therapy, this is not a common occurrence. In the 2007 STEMI Focused Update, the writing committee held that at 90 minutes after initiation of fibrinolytic therapy, if there was less than 50% ST-segment resolution in the lead that showed the greatest degree of ST elevation at presentation, then fibrinolytic therapy had likely failed to reperfuse the patient (4). If the judgment was made that fibrinolytic therapy had not resulted in reperfusion after 90 minutes, then PCI performed at that time was labeled rescue PCI.

The 2007 STEMI Focused Update (4) recommended rescue PCI in the following cases: Fibrinolytic-treated STEMI patients meeting high-risk criteria (i.e., cardiogenic shock [less than 75 years of age, Class I; 75 years of age or older, Class IIa]); hemodynamic or electrical instability; persistent ischemic symptoms; and for certain moderate- and high-risk patients who did not strictly meet the above criteria (Class IIb). These recommendations were based on results of the REACT (Rescue Angioplasty Versus Conservative Treatment of Repeat Thrombolysis) trial (74) which showed a clear benefit of rescue PCI (over repeated doses of fibrinolytics or medical management) in moderate- to high-risk patients with failed reperfusion, as well as a meta-analysis of 8 rescue PCI trials (including REACT) (73–76). The 2007 focused update acknowledged that the expected benefits of rescue PCI are greater the earlier it is initiated after the onset of ischemic symptoms.

Two new trials have helped inform this update: The CARESS-in-AMI trial and the TRANSFER-AMI trial. CARESS-in-AMI (15) studied 600 STEMI patients 75 years of age or younger with at least 1 high-risk feature (extensive ST-segment elevation, new-onset left bundle-branch block, previous MI, Killip class greater than 2, or left ventricular ejection fraction 35% or less) who were treated initially at non-PCI hospitals with half-dose reteplase, abciximab, heparin, and ASA within 12 hours of symptom onset (3). All patients were randomized to immediate transfer for PCI or to standard treatment with transfer for rescue PCI if needed. PCI was performed in 85.6% of patients in the immediate PCI group, and rescue PCI was performed in 30.3% of the standard treatment/transfer for rescue PCI group. There was a

shorter median time from fibrinolytic therapy to transfer to a PCI-capable center in the immediate versus the rescue PCI group (110 versus 180 minutes, $P<0.0001$). Antiplatelet therapy with ASA and clopidogrel was used less frequently in the standard care/rescue arm than in the early intervention group. The primary outcome (composite of all-cause mortality, reinfarction, and refractory myocardial ischemia within 30 days of randomization) occurred significantly less often (4.4% versus 10.7%, $P=0.004$) in the immediate PCI group than in the standard care/rescue PCI group (NNT=17). There were no significant differences in the rates of major bleeding at 30 days (3.4% versus 2.3%, $P=0.47$) or stroke (0.7% versus 1.3%, $P=0.50$) between groups. These results suggest that high-risk STEMI patients treated at non-PCI hospitals with a preparatory pharmacological strategy of half-dose fibrinolytic therapy, abciximab, heparin, and ASA have improved outcomes when transferred immediately to a PCI facility rather than when medical therapy is continued with transfer for rescue PCI only if there is evidence of failed reperfusion.

The TRANSFER-AMI study (14) further tested the pharmacoinvasive strategy concept in high-risk STEMI patients. Accordingly, 1059 patients who presented to a non-PCI-capable hospital within 12 hours of symptom onset of STEMI who had at least 1 high-risk feature (greater than or equal to 2 mm of ST-segment elevation in 2 anterior leads, systolic blood pressure less than 100 mm Hg, heart rate higher than 100 bpm, Killip class II to III, 2 mm or more of ST-segment depression in the anterior leads, or 1 mm or more of ST elevation in right-sided lead V₄ indicative of right ventricular involvement for inferior MIs; anterior MI alone with 2 mm or more of ST-segment elevation in 2 or more leads also qualified) and who were treated with fibrinolytic therapy were randomized to a pharmacoinvasive strategy (immediate transfer for PCI within 6 hours of fibrinolytic therapy) or to standard treatment after fibrinolytic therapy, which included rescue PCI as required for ongoing chest pain and less than 50% resolution of ST elevation at 60 to 90 minutes or hemodynamic instability. Standard-treatment patients who did not require rescue PCI remained at the initial hospital for at least 24 hours, and coronary angiography within the first 2 weeks was encouraged.

All patients received standard-dose tenecteplase, ASA, and either UFH or enoxaparin. Clopidogrel loading (300 mg for patients 75 years of age or younger and 75 mg for those older than 75 years of age) was strongly encouraged in all study patients. GP IIb/IIIa receptor antagonists were administered at the PCI-capable hospitals according to standard practice at the institution. The primary end point of the trial was the 30-day composite of the first occurrence of death, reinfarction, recurrent ischemia, new or worsening heart failure, and cardiogenic shock.

The median time to administration of tenecteplase from onset of symptoms was approximately 2 hours in both groups, whereas the median time from tenecteplase administration to catheterization was 2.8 hours in the pharmacoinvasive group and 32.5 hours in the standard-treatment group. Coronary angiography was performed in 98.5% versus 88.7% and PCI

in 84.9% versus 67.4% of the pharmacoinvasive and standard-treatment groups, respectively.

The primary end point of the trial occurred in 11.0% of the pharmacoinvasive group compared with 17.2% of the standard-treatment group (RR 0.64; 95% CI 0.47 to 0.84; $P=0.004$). Importantly, the incidence of TIMI major and minor bleeding and GUSTO (Global Use of Strategies to Open Occluded Coronary Arteries) (77) moderate and severe bleeding was not different between groups, although there was a higher incidence of GUSTO mild bleeding in the pharmacoinvasive group (13.0% compared with 9.0% in the standard-treatment group, $P=0.036$). The authors concluded that after treatment with fibrinolytic therapy in STEMI patients presenting to hospitals without PCI capability, transfer to a PCI center to undergo coronary angiography and PCI should be initiated immediately without waiting to determine whether reperfusion has occurred. These results lend further support to the routine, early transfer of high-risk, fibrinolytic-treated patients to a PCI center for early PCI supported by contemporary antiplatelet and antithrombotic therapy.

On the basis of this evidence, a pathway has been suggested for the care of STEMI patients that has been divided into those patients presenting to a PCI-capable facility and those presenting to a non-PCI-capable facility (Appendix 5). Those seen at a PCI-capable facility should be moved expeditiously to the catheterization laboratory, with appropriate antithrombotic therapy for catheterization and PCI if appropriate. There has been discussion about whether the recommended door-to-balloon time (or first medical contact-to-balloon time) should be greater than 90 minutes, with the recognition that in certain patients, the mortality advantage of primary PCI compared with fibrinolytic therapy is maintained with more prolonged door-to-balloon times (78). However, the writing groups continue to believe that the focus should be on developing systems of care to increase the number of patients with timely access to primary PCI rather than extending the acceptable window for door-to-balloon time (79). Moreover, in a study of 43 801 patients with STEMI undergoing primary PCI within the National Cardiovascular Data Registry, any delay in time to reperfusion after arrival at the hospital was associated with a higher adjusted risk of in-hospital mortality in a continuous, nonlinear fashion (30 minutes=3.0%, 60 minutes=3.5%, 90 minutes=4.3%, 120 minutes=5.6%, 150 minutes=7.0%, and 180 minutes=8.4%; $P<0.001$) (80). Rather than accepting a 90-minute door-to-balloon benchmark for primary PCI, these data suggest an as-soon-as-possible standard.

Those patients presenting to a non-PCI-capable facility should be triaged to fibrinolytic therapy or immediate transfer for PCI. This decision will depend on multiple clinical observations that allow judgment of the mortality risk of the STEMI, the risk of fibrinolytic therapy, the duration of the symptoms when first seen, and the time required for transport to a PCI-capable facility (3). If primary PCI is chosen, the patient will be transferred for PCI. If fibrinolytic therapy is chosen, the patient will receive the agent(s), and a judgment as to whether the patient is high risk or not will be made. If high risk, the patient should receive appropriate antithrombotic therapy and be moved immediately to a PCI-capable

facility for diagnostic catheterization and consideration of PCI. If not high risk, the patient may be moved to a PCI-capable facility after receiving antithrombotic therapy or may be observed in the initial facility.

Patients best suited for transfer for PCI are those STEMI patients who present with high-risk features, those with high bleeding risk from fibrinolytic therapy, and patients presenting late, that is, more than 4 hours after onset of symptoms. The decision to transfer is a judgment made after consideration of the time required for transport and the capabilities of the receiving hospital (2,5). Patients best suited for fibrinolytic therapy are those who present early after symptom onset with low bleeding risk. After fibrinolytic therapy, if the patient is not at high risk, transfer to a PCI-capable facility may be considered, especially if symptoms persist and failure to reperfuse is suspected.

The duration of symptoms should continue to serve as a modulating factor in selecting a reperfusion strategy for STEMI patients. Although patients at high risk (e.g., those with congestive heart failure, shock, and contraindications to fibrinolytic therapy) are best served with timely PCI, “inordinate delays between the time from symptom onset and effective reperfusion with PCI may prove deleterious, especially among the majority of STEMI patients at relatively low risk” (p 1299) (81). Accordingly, each community and each facility in that community should have an agreed-upon plan for how STEMI patients are to be treated. This includes which hospitals should receive STEMI patients from emergency medical services units capable of obtaining diagnostic ECGs, management at the initial receiving hospital, and written criteria and agreements for expeditious transfer of patients from non-PCI-capable to PCI-capable facilities (82).

The development of regional systems of STEMI care is a matter of utmost importance (83,84). This includes encouraging the participation of key stakeholders in collaborative efforts to evaluate care using standardized performance and quality improvement measures, such as those endorsed by the ACC and the AHA for ACS (85). Standardized quality-of-care data registries designed to track and measure outcomes, complications, and adherence to evidence-based processes of care for ACS are also critical: programs such as the National Cardiovascular Data Registry ACTION Registry, the AHA’s “Get With The Guidelines” quality improvement program, and those performance-measurement systems required by the Joint Commission and the Centers for Medicare and Medicaid Services (86–89). More recently, the AHA has promoted its “Mission: Lifeline” initiative, which was developed to encourage closer cooperation and trust among prehospital emergency services, and cardiac care professionals (90). The evaluation of STEMI care delivery across traditional care-delivery boundaries with these tools and other resources is imperative to identify systems problems and to enable the application of modern quality improvement methods, such as Six Sigma, to make necessary improvements (70,91–93).

6. Recommendations for Intensive Glucose Control in STEMI

(See Table 6.) (94–96)