

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

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A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

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*The opinions expressed in this article should not be construed as necessarily representing an official position of the US Department of Health and Human Services, the Agency for Healthcare Research and Quality, or the US Government, by whom M. Hand is employed.

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§Recused from Section 6, Intensive Glucose Control.

||Recused from Section 2, Glycoprotein IIb/IIIa Receptor Antagonists; Section 3, Thienopyridines.

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2009 STEMI and PCI Focused Updates

Preamble

A primary challenge in the development of clinical practice guidelines is keeping pace with the stream of new data on which recommendations are based. In an effort to respond promptly to new evidence, the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Task Force on Practice Guidelines has created a “focused update” process to revise the existing guideline recommendations that are affected by evolving data or opinion. Before the initiation of this focused approach, periodic updates and revisions of existing guidelines required up to 3 years to complete. Now, however, new evidence will be reviewed in an ongoing fashion to more efficiently respond to important science and treatment trends that could have a major impact on patient outcomes and quality of care. Evidence will be reviewed at least twice a year, and updates will be initiated on an as-needed basis as quickly as possible, while maintaining the rigorous methodology that the ACCF and AHA have developed during their 25 years of partnership.

These updated guideline recommendations reflect a consensus of expert opinion after a thorough review primarily of late-breaking clinical trials identified through a broad-based vetting process as being important to the relevant patient population, as well as a review of other new data deemed to have an impact on patient care (see Section 1.1, *Methodology and Evidence Review*, for details). This focused update is not intended to represent an update based on a full literature review from the date of the previous guideline publication. Specific criteria/considerations for inclusion of new data include the following:

- publication in a peer-reviewed journal;
- large randomized, placebo-controlled trial(s);
- nonrandomized data deemed important on the basis of results that affect current safety and efficacy assumptions;
- strength/weakness of research methodology and findings;
- likelihood of additional studies influencing current findings;
- impact on current performance measure(s) and/or likelihood of need to develop new performance measure(s);
- requests and requirements for review and update from the practice community, key stakeholders, and other sources free of relationships with industry or other potential bias;
- number of previous trials showing consistent results; and
- need for consistency with a new guideline or guideline revision.

In analyzing the data and developing updated recommendations and supporting text, the focused update writing group used evidence-based methodologies developed by the ACCF/AHA Task Force on Practice Guidelines, which are described elsewhere.¹

The schema for classification of recommendations and level of evidence is summarized in Table 1, which also illustrates how the grading system provides an estimate of the

size of the treatment effect and an estimate of the certainty of the treatment effect. Note that a recommendation with level of evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although randomized trials may not be available, there may be a very clear clinical consensus that a particular test or therapy is useful and effective. Both the classification of recommendations and level of evidence listed in the focused updates are based on consideration of the evidence reviewed in previous iterations of the guideline and the focused update. Of note, the implications of older studies that have informed recommendations but have not been repeated in contemporary settings are considered carefully.

The ACCF/AHA practice guidelines address patient populations (and healthcare providers) residing in North America. As such, drugs that are not currently available in North America are discussed in the text without a specific class of recommendation. For studies performed in large numbers of subjects outside of North America, each writing group reviews the potential impact of different practice patterns and patient populations on the treatment effect and on the relevance to the ACCF/AHA target population to determine whether the findings should inform a specific recommendation.

The ACCF/AHA practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient. Thus, there are circumstances in which deviations from these guidelines may be appropriate. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. These guidelines may be used as the basis for regulatory or payer decisions, but the ultimate goals are quality of care and serving the patient's best interests.

Prescribed courses of treatment in accordance with these recommendations are effective only if they are followed by the patient. Because a lack of patient adherence may adversely affect treatment outcomes, healthcare providers should engage the patient in active participation with the prescribed treatment.

The ACCF/AHA Task Force on Practice Guidelines makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the writing committee. Specifically, all members of the writing committee, as well as reviewers of the document, are asked to disclose all such relevant relationships pertaining to the trials and other evidence under consideration (see Appendixes 1, 2, and 3). All guideline recommendations require a confidential vote by the writing group and must be approved by a consensus of the members voting. Members who recused themselves from voting are noted on the title page of this document. Members must recuse themselves from voting on any recommendations to which their relationships with industry and other entities

Table 1. Applying Classification of Recommendations and Level of Evidence

		SIZE OF TREATMENT EFFECT →			
		CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/administered	CLASS IIa <i>Benefit >> Risk</i> Additional studies with <i>focused objectives</i> needed IT IS REASONABLE to perform procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> Additional studies with <i>broad objectives</i> needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>Risk ≥ Benefit</i> Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses
	LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies
	LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†		should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACCF/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

apply. Writing group members who did not participate are not listed as authors of this focused update. The work of the writing group was supported exclusively by the ACCF and AHA without commercial support. Writing group members volunteered their time for this effort.

With the exception of the recommendations presented here, the full-text guidelines remain current.^{2,3} Only the recommendations from the affected section(s) of the full-text guidelines are included in this focused update. Recommendations from any section of a guideline affected by a change are presented with notation as to whether they are new or have been modified; however, recommendations that remain unchanged in each section are not included in this focused update. When evidence affects recommendations in more than 1 set of guidelines, those guidelines are updated concurrently whenever possible.

The recommendations in this focused update will be considered current until they are superseded by another

focused update or the full-text guidelines are revised. This focused update is published in the December 1, 2009, issues of the *Journal of the American College of Cardiology* and *Circulation* as an update to the full-text guideline, and it is also posted on the American College of Cardiology (ACC; www.acc.org), AHA (my.americanheart.org), and Society for Cardiovascular Angiography and Interventions (SCAI; scai.org) World Wide Web sites.

Alice K. Jacobs, MD, FACC, FAHA
Chair, ACCF/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

Late-breaking clinical trials presented at the 2007 and 2008 annual scientific meetings of the ACC, AHA, Transcatheter Cardiovascular Therapeutics, the European Society of Cardi-

ology, and the 2009 annual scientific sessions of the ACC were reviewed by the standing guideline writing committee along with the parent Task Force and other experts to identify those trials and other key data that may impact guideline recommendations. On the basis of the criteria/considerations noted above, recent trial data and other clinical information were considered important enough to prompt a focused update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction and the ACC/AHA 2005 Guidelines for Percutaneous Coronary Intervention, inclusive of their respective 2007 focused updates.²⁻⁵

The ST-elevation myocardial infarction (STEMI) and percutaneous coronary intervention (PCI) writing groups together considered the following studies: Two meta-analyses, “A Comparison of Abciximab and Small Molecule Glycoprotein IIb/IIIa Inhibitors in Patients Undergoing Primary Percutaneous Coronary Intervention,”⁶ and “Benefits From Small Molecule Administration as Compared With Abciximab Among Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Angioplasty,”⁷ FINESSE (Facilitated PCI in Patients With ST-Elevation Myocardial Infarction),⁸ the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction),⁹ BRAVE-3 (Bavarian Reperfusion Alternatives Evaluation-3),¹⁰ MULTISTRATEGY (Multicentre Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare Metal Stent in Acute Myocardial Infarction Study),¹¹ ON-TIME 2 (Ongoing Tirofiban in Myocardial Infarction Evaluation),¹² TRITON-TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel—Thrombolysis in Myocardial Infarction),¹³ TRANSFER-AMI (Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction),¹⁴ CARESS-in-AMI (Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction),¹⁵ NICE-SUGAR (Normoglycemia in Intensive Care Evaluation—Survival Using Glucose Algorithm Regulation),¹⁶ TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study),¹⁷ and EXPIRA (Thrombectomy With Export Catheter in Infarct-Related Artery During Primary Percutaneous Coronary Intervention).¹⁸ Additionally, the PCI writing group considered the CARE (Cardiac Angiography in Renally Impaired Patients),¹⁹ FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) study,²⁰ SYNTAX (Synergy Between Percutaneous Intervention With Taxus and Cardiac Surgery),²¹ Early ACS (Early versus Delayed, Provisional Eptifibatide in Acute Coronary Syndromes),²² and TIMACS (Timing of Intervention in Patients With Acute Coronary Syndromes) studies.²³ When considering the new data for this focused update, the writing group faced the task of weighing evidence from studies that had enrolled large numbers of subjects outside North America. Although noting that practice patterns and the rigor applied to data collection, as well as the genetic makeup of subjects, may influence the observed magnitude of a treatment’s effect, the writing group believed the data were relevant to the formulation of recommendations for management of STEMI and PCI in North

America. The writing group also notes that the AHA/ACCF and the Heart Rhythm Society have published updated recommendations for the standardization and interpretation of the electrocardiogram with a separate section on acute ischemia/infarction.²⁴

To provide clinicians with a comprehensive set of data, whenever possible, the exact event rates in various treatment arms of clinical trials are presented to permit calculation of the absolute risk difference and number needed to treat (NNT) or harm; the relative treatment effects are described either as odds ratio, relative risk (RR), or hazard ratio (HR) depending on the format used in the original publication. Along with all other statistical point estimates, the confidence interval (CI) for those statistics are added when available.

Consult the full-text or executive summary versions of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction or the ACC/AHA/SCAI 2005 Guidelines for Percutaneous Coronary Intervention, as well as their respective 2007 focused updates, for policy on clinical areas not covered by the present focused update.²⁻⁵ Unchanged recommendations from previous iterations of the guidelines are not listed in this document and remain current policy. Individual recommendations updated in this focused update will be incorporated into future revisions of the full-text guidelines.

1.2. Organization of Committee and Relationships With Industry and Other Entities

For this focused update, all members of the 2004 STEMI guideline, 2007 STEMI focused update, 2005 PCI guideline, and 2007 PCI focused update writing committees were invited to participate; those who agreed (referred to as the 2009 Focused Update Writing Group) were required to disclose all relationships with industry and other entities relevant to the data under consideration. The policies used for relationships with industry were those in effect at the initial meeting of this committee, which included disclosure of relationships 12 months prior to initiation and a chair with no relevant relationships except in a situation where more than one chair is named. In this circumstance, one chair will have no relevant relationships and the other may have relationships. Each recommendation required a confidential vote by the writing group members before and after external review of the document. Any writing group member with a relationship with industry relevant to the recommendation was recused from voting on that recommendation. The PCI writing group included 2 representatives from SCAI.

1.3. Document Review and Approval

This document was reviewed by 3 official reviewers nominated by the ACCF and 4 official reviewers nominated by the AHA, 1 official reviewer nominated by the SCAI, 6 reviewers from the ACCF Interventional Council, 2 reviewers from the ACCF Imaging Council, and 22 content reviewers. All reviewer information on relationships with industry and other entities was collected and distributed to the writing committee and is published in Appendix 3. This document was approved for publication by the governing bodies of the ACCF, the AHA, and the SCAI (specifically, the PCI portion of the guideline).

Table 2. Recommendations for the Use of Glycoprotein IIb/IIIa Receptor Antagonists

2004/2005/2007 Recommendations: 2004 STEMI Guideline Section 6.3.1.6.8.2.3; Also 2005 PCI Guideline Section 6.2.2		2009 Joint STEMI/PCI Focused Update Recommendations	Comments
Class IIa			
1. It is reasonable to start treatment with abciximab as early as possible before primary PCI (with or without stenting) in patients with STEMI. (<i>Level of Evidence: B</i>)	1. It is reasonable to start treatment with glycoprotein IIb/IIIa receptor antagonists (abciximab ^{9,11} [<i>Level of Evidence: A</i>], tirofiban ^{11,12} [<i>Level of Evidence: B</i>] or eptifibatide ^{6,7,9} [<i>Level of Evidence: B</i>]) at the time of primary PCI (with or without stenting) in selected patients with STEMI.		Modified recommendation (class of recommendation changed from IIb to IIa for tirofiban and eptifibatide).
Class IIb			
1. Treatment with tirofiban or eptifibatide may be considered before primary PCI (with or without stenting) in patients with STEMI. (<i>Level of Evidence: C</i>)	1. The usefulness of glycoprotein IIb/IIIa receptor antagonists (as part of a preparatory pharmacological strategy for patients with STEMI before their arrival in the cardiac catheterization laboratory for angiography and PCI) is uncertain. ^{8,10} (<i>Level of Evidence: B</i>)		Modified recommendation (text modified; level of evidence changed from C to B).

STEMI and PCI Focused Update Section

2. Recommendations for the Use of Glycoprotein IIb/IIIa Receptor Antagonists

(See Table 2 and Appendix 4.)

2.1. Glycoprotein IIb/IIIa Receptor Antagonists

In considering the use of intravenous glycoprotein (GP) IIb/IIIa receptor antagonists for STEMI, the writing group noted that much of the evidence favoring the use of these agents was established in the era before dual oral antiplatelet therapy and largely by placebo-controlled comparisons. Contemporary management of STEMI patients involves a complex array of antithrombotics, including dual oral antiplatelet therapy (aspirin [acetylsalicylic acid; ASA] plus a thienopyridine) and an anticoagulant. There is a paucity of trials adequately powered for assessment of clinical end points that have reevaluated the current relative role of intravenous GP IIb/IIIa receptor antagonists with respect to other pharmacological therapy in STEMI patients. Accordingly, a reevaluation of the value of GP IIb/IIIa antagonists in STEMI is appropriate, but the ability to draw definitive conclusions is limited.

At least 3 trials evaluated GP IIb/IIIa antagonists as adjuncts to oral antiplatelet therapy in the setting of primary PCI. The findings of these trials question whether GP IIb/IIIa antagonists provide significant additional benefit to STEMI patients who have received dual-antiplatelet therapy before catheterization. In the BRAVE-3 study, 800 patients presenting within 24 hours of a STEMI were pretreated with 600 mg of clopidogrel and then randomly assigned in a double-blind manner to receive either abciximab or placebo in the intensive care unit before being sent for PCI.¹⁰ The primary end point was infarct size measured by single photon emission computed tomography before hospital discharge. At 30 days, the composite of death, recurrent myocardial infarction (MI), stroke, or urgent revascularization of the infarct-related artery was not significantly different in the 2 groups (abciximab 5%, placebo 3.8%; 95% CI 0.7 to 2.6; $P=0.4$). There was no significant difference in infarct size or major bleeding.

ON-TIME 2 was a randomized, placebo-controlled, multicenter European trial that included 491 patients receiving high-dose tirofiban and 493 receiving placebo within a median of 76 minutes from onset of symptoms.¹² Patients

receiving high-dose tirofiban (25 mcg/kg bolus followed by 0.15 mcg/kg per min for 18 hours) at first medical contact before transport for primary PCI were also treated with unfractionated heparin (UFH; 5000 U), clopidogrel (600 mg), and ASA. Patients in the high-dose tirofiban group had improved ST-segment resolution (primary end point) before and 1 hour after PCI ($P=0.003$) compared with those receiving placebo (NNT=100). However, there was no significant difference in Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow or blush grade and no significant difference in major bleeding or minor bleeding. There was no significant difference in death, recurrent MI, or urgent target-vessel revascularization (TVR) between the tirofiban and placebo groups at 30 days.²⁵

In the HORIZONS-AMI trial,⁹ patients undergoing primary PCI for STEMI were randomized to treatment with UFH plus a GP IIb/IIIa receptor antagonist (abciximab or double-bolus eptifibatide) or to bivalirudin alone with provisional IIb/IIIa. Aspirin and a thienopyridine were administered before catheterization. (See the full discussion of the trial under Section 4, Recommendations for the Use of Parenteral Anticoagulants.) Seven hundred fifty-seven of the 1661 patients who received UFH received a double bolus of eptifibatide and infusion, whereas 53 of 1661 in the bivalirudin arm received eptifibatide. At 30 days, rates of major bleeding and total adverse events were higher among patients treated with GP IIb/IIIa antagonists and heparin than among those given bivalirudin alone.

Two meta-analyses of randomized trials were published that compared small-molecule GP IIb/IIIa antagonists with abciximab in STEMI patients undergoing primary PCI.^{6,7} In each case, there was no statistically significant difference in 30-day mortality, reinfarction, or major TIMI bleeding, and there was no significant difference in death or reinfarction at 8 months between groups. There was also no statistically significant difference in postprocedural TIMI flow grade 3 or ST-segment resolution. On the basis of these studies, the present writing group judged that the totality of evidence indicates that the various GP IIb/IIIa antagonists demonstrate similar effectiveness in the setting of primary PCI.

MULTISTRATEGY was an open-label, multicenter, randomized European trial with a 2-by-2 factorial design that

randomized 745 STEMI patients undergoing primary PCI to high-dose bolus tirofiban versus abciximab infusion and sirolimus-eluting stent versus bare-metal stent (BMS).¹¹ The prespecified primary end points were the achievement of 50% resolution of ST-segment elevation at 90 minutes after PCI, powered for noninferiority, and the rate of major adverse cardiac events (MACE) at 8 months, powered for superiority. All patients received ASA at the usual doses, clopidogrel 300 mg orally then 75 mg per day, and UFH. There was a similar rate of at least 50% ST-segment resolution at 90 minutes after primary PCI with abciximab and tirofiban (RR 1.020; 97.5% CI 0.958 to 1.086; $P=0.001$ for noninferiority). Rates of MACE, including all-cause death, clinical reinfarction, or TVR, and hemorrhagic (major and minor bleeding) complications were similar. The incidence of severe or moderate thrombocytopenia was more common with abciximab than with tirofiban (4.0% versus 0.8%, $P=0.004$).

In an analysis of the predictors of stent thrombosis after primary PCI in acute MI presented at the 2009 ACC Scientific Sessions, titled "Predictors of Stent Thrombosis After Primary Angioplasty in Acute Myocardial Infarction: The HORIZONS-AMI Trial,"⁶⁹ there was no significant difference in the 1-year rate of stent thrombosis with the heparin plus GP IIb/IIIa receptor antagonists compared with eptifibatide and abciximab (3.6% versus 2.8%, $P=0.93$), which suggests that eptifibatide has the same impact as abciximab on stent thrombosis incidence.

One investigation, FINESSE, addressed the issue of timing of GP IIb/IIIa antagonist administration. This double-blind, randomized, placebo-controlled study of 2453 patients with STEMI explored the use of pre-PCI treatment with a half-dose fibrinolytic agent plus abciximab, pre-PCI abciximab alone, and abciximab at the time of PCI.⁸ The primary end point was the composite of death due to all causes, ventricular fibrillation that occurred more than 48 hours after randomization, cardiogenic shock, and congestive heart failure during the first 90 days after randomization. The results of the trial are discussed in Section 5.1, Triage and Transfer for PCI. This trial showed no benefit (and a tendency toward excess bleeding) with prehospital abciximab compared with abciximab at the time of PCI. The writing group concluded there was no benefit of administration of abciximab before primary PCI, alone or in combination with reteplase. On the basis of this trial and ON-TIME 2, the writing group concluded that the use of GP IIb/IIIa antagonists before primary PCI is of uncertain benefit.

Given the results of the studies cited above, the writing group concluded that in the setting of dual-antiplatelet therapy with UFH or bivalirudin as the anticoagulant, current evidence indicates that adjunctive use of a GP IIb/IIIa antagonist can be useful at the time of primary PCI but cannot be recommended as routine therapy. These agents might provide more benefit in selective use, for example, for the patient with a large thrombus burden or for patients who have not received adequate thienopyridine loading.

3. Recommendations for the Use of Thienopyridines

(See Table 3 and Appendix 4.)

3.1. Thienopyridines

Since the publication of the last guidelines,^{4,5} evidence has emerged about prasugrel, a thienopyridine that achieves greater inhibition of platelet aggregation than clopidogrel.²⁷ The pivotal trial for prasugrel, TRITON-TIMI 38, focused on patients with ACS who were referred for PCI.

TRITON-TIMI 38 randomly assigned 13 608 patients with moderate- to high-risk ACS, 3534 of whom had STEMI, to receive prasugrel (6813 patients received a 60-mg loading dose and a 10-mg daily maintenance dose) or clopidogrel (6795 patients received a 300-mg loading dose and a 75-mg daily maintenance dose) for an average follow-up of 14.5 months. Aspirin was prescribed within 24 hours of PCI. Clinical end points were assessed at 30 and 90 days and then every 3 to 15 months.²⁷

Prasugrel was associated with a significant 2.2% absolute reduction and a 19% relative reduction in the primary efficacy end point, a composite of the rate of death due to cardiovascular causes (including arrhythmia, congestive heart failure, shock, and sudden or unwitnessed death), nonfatal MI, or nonfatal stroke during the follow-up period. The primary efficacy end point occurred in 9.9% of patients receiving prasugrel and 12.1% of patients receiving clopidogrel (HR for prasugrel versus clopidogrel 0.81; 95% CI 0.73 to 0.90; $P<0.001$). A significant reduction in the primary end point was seen in the prasugrel group by the first prespecified time point, which was 3 days (4.7% in the prasugrel group versus 5.6% in the clopidogrel group; HR 0.82; 95% CI 0.71 to 0.96; $P=0.01$), and persisted throughout the follow-up period. From Day 3 to the end of the study, the primary end point had occurred in 5.6% of patients receiving prasugrel and in 6.9% of patients receiving clopidogrel (HR 0.80; 95% CI 0.70 to 0.93; $P=0.003$). Prasugrel decreased cardiovascular death, MI, and stroke by 138 events (NNT=46).²⁷ The rate of MI with subsequent death due to cardiovascular causes was also reduced in the prasugrel group ($P=0.02$). The difference in the primary end point was largely related to the difference in rates of nonfatal MI (7.3% for prasugrel versus 9.5% for clopidogrel; HR 0.76; 95% CI 0.67 to 0.85; $P<0.001$). There were no significant differences in the 2 treatment groups in the rates of stroke or of death due to cardiovascular causes not preceded by recurrent MI (at 15 months, the nonfatal stroke rate was 1.0% for both prasugrel and clopidogrel; HR for prasugrel=1.02; CI 0.71 to 1.45; $P=0.93$; the rate of deaths due to cardiovascular causes not preceded by recurrent MI was 2.1% for prasugrel versus 2.4% for clopidogrel; HR 0.89; CI 0.70 to 1.12; $P=0.31$). There were significant reductions in the rates of ischemic events in the prasugrel group compared with the clopidogrel group: Rates of MI were 7.4% for prasugrel versus 9.7% for clopidogrel ($P<0.001$); urgent TVR rates were 2.5% for prasugrel versus 3.7% for clopidogrel ($P<0.001$); and rates of stent thrombosis were 1.1% for prasugrel versus 2.4% for clopidogrel (HR 0.48; 95% CI 0.36 to 0.64; $P<0.001$).

Prasugrel was associated with a significant increase in the rate of bleeding, notably, TIMI major hemorrhage, which was observed in 2.4% of patients taking prasugrel and in 1.8% of patients taking clopidogrel (HR for prasugrel versus clopidogrel

Table 3. Recommendations for the Use of Thienopyridines

STEMI Recommendations	PCI Recommendations	2009 Joint STEMI/PCI Focused Update Recommendations	Comments (All Modified Recommendations Are for Patients With ACS)
Class I			
2004 STEMI Guidelines, Section 7.4.4	2007 PCI Update, Table 14		
4. For patients who have undergone diagnostic cardiac catheterization and for whom PCI is planned, clopidogrel should be started and continued for at least 1 month after bare metal stent implantation and for several months after drug-eluting stent implantation (3 months for sirolimus, 6 months for paclitaxel) and for up to 12 months in patients who are not at high risk for bleeding. (<i>Level of Evidence: B</i>)	4. A loading dose of clopidogrel,* generally 600 mg, should be administered before or when PCI is performed. (<i>Level of Evidence: C</i>) In patients undergoing PCI within 12 to 24 hours of receiving fibrinolytic therapy, a clopidogrel oral loading dose of 300 mg may be considered. (<i>Level of Evidence: C</i>)	1. A loading dose of thienopyridine is recommended for STEMI patients for whom PCI is planned. Regimens should be 1 of the following: a. At least 300 to 600 mg of clopidogrel† should be given as early as possible before or at the time of primary or nonprimary PCI. (<i>Level of Evidence: C</i>) b. Prasugrel 60 mg should be given as soon as possible for primary PCI. ^{26,27} (<i>Level of Evidence: B</i>) c. For STEMI patients undergoing nonprimary PCI, the following regimens are recommended: (i) If the patient has received fibrinolytic therapy and has been given clopidogrel, clopidogrel should be continued as the thienopyridine of choice (<i>Level of Evidence: C</i>); (ii) If the patient has received fibrinolytic therapy without a thienopyridine, a loading dose of 300 to 600 mg‡ of clopidogrel should be given as the thienopyridine of choice (<i>Level of Evidence: C</i>); (iii) If the patient did not receive fibrinolytic therapy, either a loading dose of 300 to 600 mg of clopidogrel should be given or, once the coronary anatomy is known and PCI is planned, a loading dose of 60 mg of prasugrel should be given promptly and no later than 1 hour after the PCI. ^{26,27} (<i>Level of Evidence: B</i>)	Modified recommendation (changed text).
	5. For all post-PCI stented patients receiving a DES, clopidogrel 75 mg daily should be given for at least 12 months if patients are not at high risk of bleeding. For post-PCI patients receiving a BMS, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks). (<i>Level of Evidence: B</i>)	2. The duration of thienopyridine therapy should be as follows: a. In patients receiving a stent (BMS or drug-eluting stent [DES]) during PCI for ACS, clopidogrel 75 mg daily† ^{27–29} (<i>Level of Evidence: B</i>) or prasugrel 10 mg daily§ ²⁷ (<i>Level of Evidence: B</i>) should be given for at least 12 months; b. If the risk of morbidity because of bleeding outweighs the anticipated benefit afforded by thienopyridine therapy, earlier discontinuation should be considered. (<i>Level of Evidence: C</i>)	Modified recommendation (pertains to STEMI and unstable angina [UA]/non-STEMI [NSTEMI] based on TRITON-TIMI 38).
2007 STEMI Update, Section 9			
2. In patients taking clopidogrel in whom CABG is planned, the drug should be withheld for at least 5 days and preferably for 7 days unless the urgency for revascularization outweighs the risks of excess bleeding. (<i>Level of Evidence: B</i>)		3. In patients taking a thienopyridine in whom CABG is planned and can be delayed, it is recommended that the drug be discontinued to allow for dissipation of the antiplatelet effect. (<i>Level of Evidence: C</i>) The period of withdrawal should be at least 5 days in patients receiving clopidogrel ^{2,30} (<i>Level of Evidence: B</i>) and at least 7 days in patients receiving prasugrel† ²⁷ (<i>Level of Evidence: C</i>), unless the need for revascularization and/or the net benefit of the thienopyridine outweighs the potential risks of excess bleeding. ³¹ (<i>Level of Evidence: C</i>)	Modified recommendation (added prasugrel).
Class IIa			
2004 STEMI Guidelines, Section 7.4.4	2007 PCI Update, Table 14		
	1. If clopidogrel is given at the time of procedure, supplementation with GP IIb/IIIa receptor antagonists can be beneficial. (<i>Level of Evidence: B</i>)		Deleted recommendation
	2. For patients with an absolute contraindication to aspirin, it is reasonable to give a 300-mg to 600-mg loading dose of clopidogrel, administered at least 6 hours before PCI, and/or GP IIb/IIIa antagonists, administered at the time of PCI. (<i>Level of Evidence: C</i>)		Deleted recommendation
Class IIb			
2004 STEMI Guidelines, Section 7.4.4	2007 PCI Update, Table 14		
	1. Continuation of clopidogrel therapy beyond 1 year may be considered in patients undergoing DES placement. (<i>Level of Evidence: C</i>)	1. Continuation of clopidogrel or prasugrel§ beyond 15 months may be considered in patients undergoing DES placement. ²⁷ (<i>Level of Evidence: C</i>)	Modified recommendation (changed text).

(Continued)

Table 3. Continued

STEMI Recommendations	PCI Recommendations	2009 Joint STEMI/PCI Focused Update Recommendations	Comments (All Modified Recommendations Are for Patients With ACS)
Class III			
		1. In STEMI patients with a prior history of stroke and transient ischemic attack for whom primary PCI is planned, prasugrel is not recommended as part of a dual-antiplatelet therapy regimen. (Level of Evidence: C)	New recommendation

*Available data for prasugrel use are for PCI for acute coronary syndrome (ACS) and not elective PCI. Recommendations for elective PCI with clopidogrel use are not being updated in this guideline focused update.

†The optimum loading dose of clopidogrel has not been established. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral dose of 75 mg.^{26,27} Higher oral loading doses such as 600 mg or more than 900 mg³⁶ of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and safety of higher oral loading doses have not been rigorously established. The necessity for giving a loading dose of clopidogrel before PCI is driven by the pharmacokinetics of clopidogrel, for which several hours are required to achieve desired levels of platelet inhibition. For post-PCI patients receiving a stent (BMS or DES), a daily maintenance dose should be given for at least 12 months and for up to 15 months unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine.

‡Clopidogrel loading dose after fibrinolytic therapy: For patients given fibrin- and non-fibrin-specific fibrinolytic drugs who are undergoing PCI within 24 hours, 300 mg; for patients given a fibrin-specific fibrinolytic undergoing PCI after more than 24 hours, 300 to 600 mg; for patients given a non-fibrin-specific fibrinolytic undergoing PCI between 24 and 48 hours, 300 mg; for patients given a non-fibrin-specific fibrinolytic undergoing PCI after 48 hours, 300 to 600 mg.

§Patients weighing <60 kg have an increased exposure to the active metabolite of prasugrel and an increased risk of bleeding on a 10-mg once-daily maintenance dose. Consideration should be given to lowering the maintenance dose to 5 mg in patients who weigh <60 kg. The effectiveness and safety of the 5-mg dose have not been studied prospectively. For post-PCI patients receiving a stent (BMS or DES), a daily maintenance dose should be given for at least 12 months and for up to 15 months unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine. Do not use prasugrel in patients with active pathological bleeding or a history of transient ischemic attack or stroke. In patients ≥75 years of age, prasugrel is generally not recommended because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI) in which its effect appears to be greater and its use may be considered. Do not start prasugrel in patients likely to undergo urgent CABG. When possible, discontinue prasugrel at least 7 days before any surgery. Additional risk factors for bleeding include body weight <60 kg, propensity to bleed, and concomitant use of medications that increase the risk of bleeding (eg, warfarin, heparin, fibrinolytic therapy, or chronic use of nonsteroidal anti-inflammatory drugs).

1.32; 95% CI 1.03 to 1.68, $P=0.03$), which represented an increase in the relative rate of major bleeding of 32%. From the standpoint of safety, prasugrel was associated with an increase of 35 TIMI major and non-coronary artery bypass graft bleeds (number needed to harm=167).²⁷ Also, greater rates of life-threatening bleeding were evident in the prasugrel group than in the clopidogrel group: 1.4% versus 0.9%, respectively (HR for prasugrel 1.52; 95% CI 1.08 to 2.13; $P=0.01$), which included nonfatal bleeding (1.1% versus 0.9%; HR for prasugrel 1.25; 95% CI 0.87 to 1.81; $P=0.23$) and fatal bleeding (0.4% versus 0.1%; HR for prasugrel 4.19; 95% CI 1.58 to 11.11; $P=0.002$). In the few patients who underwent coronary artery bypass graft (CABG), TIMI major bleeding through 15 months was also greater with prasugrel than with clopidogrel (13.4% versus 3.2%, respectively; HR for prasugrel 4.73; 95% CI 1.90 to 11.82; $P<0.001$).²⁷ Despite the increase in bleeding, the net clinical-benefit end point, which included all-cause mortality, ischemic events, and major bleeding events, favored prasugrel.²⁷

Prasugrel showed superior efficacy in major prespecified subgroups in the overall ACS population. The benefit tended to be greater among the 3146 patients with diabetes (12.2% of whom had the primary end point in the prasugrel group versus 17.0% in the clopidogrel group; HR 0.70; 95% CI 0.58 to 0.85; $P<0.001$) than among the 10 462 patients without diabetes (9.2% of whom had the primary end point in the prasugrel group versus 10.6% in the clopidogrel group; HR 0.86; 95% CI 0.76 to 0.98; $P=0.02$). The rate of definite or probable stent thrombosis was significantly reduced in the prasugrel group compared with the clopidogrel group, as noted.²⁷

A post hoc analysis suggested there were 3 subgroups of ACS patients who did not have a favorable net clinical benefit (defined as the rate of death due to any cause, nonfatal MI, nonfatal stroke, or non-CABG-related nonfatal TIMI major bleeding) from the use of prasugrel or who had net harm: Patients with a history of stroke or transient ischemic attack (TIA) before enrollment had net harm from prasugrel (HR 1.54; 95% CI 1.02 to 2.32; $P=0.04$), patients 75 years of age and older had no net benefit from prasugrel (HR 0.99; 95% CI 0.81 to 1.21; $P=0.92$); and patients with a body weight of less than 60 kg had no net benefit from prasugrel (HR 1.03; 95% CI 0.69 to 1.53; $P=0.89$). In both treatment groups, patients with at least 1 of these risk factors had higher rates of bleeding than those without them.²⁷ A pharmacokinetic analysis showed greater exposure to the active metabolite of prasugrel for patients who weighed less than 60 kg and who were 75 years old or older.³⁸

The US Food and Drug Administration (FDA) approved prasugrel in July 2009 and incorporated the aforementioned subgroup findings into its labeling by citing a contraindication against prasugrel use in patients with a history of TIA or stroke and active pathological bleeding. The FDA further recommends that consideration be given to lowering the maintenance dose of prasugrel to 5 mg in patients who weigh less than 60 kg, with a note that the effectiveness and safety of the 5-mg dose have not been studied prospectively to date. The FDA labeling information includes a general warning against the use of prasugrel in patients older than 75 years of age because of concerns of an increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior

MI), in which case its effect appears to be greater and its use may be considered.³⁷

In focusing specifically on patients with STEMI, the primary composite end point of cardiovascular death, nonfatal MI, or nonfatal stroke was significantly reduced in patients assigned to prasugrel at 30 days compared with patients who received clopidogrel (6.5% versus 9.5%; HR 0.68; 95% CI 0.54 to 0.87; $P=0.0017$), and this trend persisted to 15 months (HR 0.79; 95% CI 0.65 to 0.97; $P=0.0221$).¹³ Furthermore, in the STEMI group, the key secondary end point of cardiovascular death, MI, or urgent TVR was significantly reduced with prasugrel at 30 days ($P=0.0205$) and 15 months ($P=0.0250$).¹³ At 30 days and 15 months, the individual end points of cardiovascular death and MI, as well as stent thrombosis, were reduced with prasugrel.¹³

The interaction testing for efficacy and safety showed no significant difference in bleeding risk regardless of the type of ACS (eg, UA/NSTEMI versus STEMI). Thus, the STEMI results for efficacy and safety are consistent with the main results of the trial. In a post hoc analysis of patients with anterior MI, event rates at 15 months for the primary end point were lower with prasugrel (9.8% for prasugrel versus 16.3% for clopidogrel; HR 0.57; 95% CI 0.42 to 0.78; $P=0.0003$). In patients with nonanterior MI, treatment effects did not differ for the primary end point (10.1% for prasugrel versus 9.9% for clopidogrel; HR 1.02; 95% CI 0.78 to 1.34; $P=0.8749$). The test for heterogeneity of the effect of prasugrel was significant ($P=0.0053$), which suggests that the benefit might vary by the location of the MI. Data were consistent in both the primary and secondary PCI subgroups.¹³

The writing group weighed the current data regarding the use of thienopyridine therapy in patients who remain hospitalized after STEMI and are candidates for CABG and retained the 2007 focused update recommendation of empiric discontinuation of clopidogrel therapy for at least 5 days and at least 7 days in patients receiving prasugrel before planned CABG.^{2,27,30}

Platelet function testing to determine the degree of platelet inhibition³⁹ may be used, and if platelet function has normalized, CABG may be performed at an earlier time. Additionally, other strategies of platelet inhibition (GP IIb/IIIa receptor antagonists) may be used if recurrent ischemia is a concern during the waiting period for CABG. Ultimately, the patient's clinical status will determine the risk-to-benefit ratio of CABG compared with awaiting restoration of platelet function.

The results of TRITON-TIMI 38 influenced dosing recommendations for loading and chronic thienopyridine therapy with prasugrel. Sixty milligrams of prasugrel is now recommended as a loading dose for primary PCI in STEMI. For secondary PCI in those patients who have recurrent ischemia or other reasons for planned intervention during their course of treatment, 60 mg of prasugrel may be given after the coronary anatomy has been identified (to avoid dosing those patients who require CABG) either before, during, or within 1 hour of PCI.²⁷ Furthermore, 10 mg of prasugrel may be used in addition to ASA for chronic dual-antiplatelet therapy.²⁷

Determination of patient groups that should be considered for continuation of dual-antiplatelet treatment beyond 12 months is based on patient-level factors (eg, age, history of bleeding) and lesion characteristics (eg, bifurcation, small-diameter vessel).²⁸

In previous studies of patients with prior stroke or TIA, use of dual-antiplatelet therapy has been associated with an increased risk of adverse outcomes, notably intracranial bleeding, compared with single-antiplatelet therapy. In the MATCH (Management of Atherothrombosis With Clopidogrel in High-Risk Patients With TIA or Stroke) trial⁴⁰ in which patients with prior stroke or TIA and additional risk factors ($n=7599$) were allocated to clopidogrel 75 mg or combination therapy with clopidogrel 75 mg plus ASA 75 mg per day, there was no significant benefit of combination therapy compared with clopidogrel alone in reducing the primary outcome of the composite of ischemic stroke, MI, vascular death, or rehospitalization due to ischemic events, or any of the secondary outcomes. The risk of major hemorrhage was significantly increased in the combination-therapy group compared with those given clopidogrel alone, with a 1.3% absolute increase in life-threatening bleeding. Although clopidogrel plus ASA is recommended over ASA alone for patients with ACS,^{41–43} the results of MATCH do not suggest a similar risk-benefit ratio for stroke and TIA survivors. The AHA/American Stroke Association's Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Stroke contain a Class III recommendation for the use of ASA in combination with clopidogrel in patients with prior stroke or TIA.⁴⁴ On the other hand, a post hoc analysis from the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) trial, which included 9478 patients, suggested that patients with documented prior MI, ischemic stroke, or symptomatic peripheral artery disease derive benefit from dual-antiplatelet therapy with clopidogrel plus ASA.⁴⁵ Although MATCH and CHARISMA did not involve STEMI patients, the writing group recommended weighing the benefits and risks of prescribing clopidogrel and ASA in patients with a recent history of TIA or stroke. Given prasugrel's greater tendency to cause intensive inhibition of platelet aggregation in general and the findings of increased levels of bleeding compared with clopidogrel in this population, the use of prasugrel as part of a dual-antiplatelet therapy regimen in patients with prior stroke or TIA is contraindicated.³⁷

3.1.1. Additional Thienopyridine Information

Although clopidogrel in combination with ASA has been shown to reduce recurrent coronary events in the posthospitalized ACS population,^{32,43,46} the response to clopidogrel varies among patients, and clopidogrel resistance has been observed.⁴³ Information is accumulating about the variations in the antiplatelet effect of clopidogrel in patients with loss-of-function alleles in the gene encoding CYP450 2C19.^{32,46–50} These patients form a subgroup in which failure of clopidogrel effectiveness has been linked to adverse clinical outcomes.^{30,47–51} In TRITON-TIMI 38 and 3 of the cohort studies,^{47,49,52} patients who were carriers of a reduced-function CYP450 2C19 allele had significantly lower levels

of the active metabolite of clopidogrel, diminished platelet inhibition, and increased rates of cardiovascular events (eg, death, MI, stroke), including stent thrombosis,⁵³ compared with the extensive metabolizers.⁵⁴ In another cohort study with 2208 patients,⁵⁰ the increased event rate was observed only in poor metabolizers. (Prasugrel has a higher level of inhibition of platelet aggregation than clopidogrel and a more rapid onset of action.⁵⁵ Its metabolism is not affected by the 2C19 allele variant.⁵⁶)

Accordingly, the effective clopidogrel dose for an individual undergoing PCI for STEMI may not be known. A large randomized trial⁵⁷ is attempting to determine whether adjustment of clopidogrel therapy on the basis of platelet function testing with a point-of-care assay safely improves outcomes after PCI with DES. As noted in the drug dosing table (Appendix 4), the current recommended loading dose for clopidogrel is uncertain. In addition, a period of several hours is required to metabolize clopidogrel to its active metabolite, which leaves a window of time during which there is a reduced level of effectiveness even in responders.

With regard to clopidogrel loading for PCI after a patient has received fibrinolytic therapy, there are no studies that have formally tested a 600-mg (or higher) clopidogrel loading dose administered with fibrinolytic treatment. The only study that tested any clopidogrel dose with a fibrinolytic was the CLARITY-TIMI 28 (Clopidogrel as Adjunctive Reperfusion Therapy–Thrombolysis in Myocardial Infarction 28) study, which randomized 3491 patients 75 years of age and younger who were receiving fibrinolytic therapy within 12 hours of STEMI to clopidogrel (300-mg oral loading dose; 75-mg oral daily maintenance dose) or placebo.⁵⁸ As described in the 2007 STEMI focused update,⁴ patients who received clopidogrel had a reduced rate of an occluded infarct artery, accomplished by preventing infarct-related reocclusion rather than by facilitating early reperfusion.

When considering a loading dose of clopidogrel for PCI after a patient has received a fibrinolytic agent, the available level of evidence is limited (Level of Evidence: C), and consensus opinion suggests it is dependent on how many hours have elapsed since fibrinolytic therapy was administered before PCI. For patients who have received any fibrinolytic agent and subsequently proceed to PCI within 24 hours, a dose of 300 mg of clopidogrel as a loading dose is suggested. If the patient received a fibrin-specific fibrinolytic agent and then proceeds to PCI after 24 hours has elapsed, a loading dose of 300 to 600 mg may be considered. If at least 48 hours has elapsed after treatment with a non-fibrin-specific fibrinolytic agent, a dose of 300 to 600 mg may be considered.

Prasugrel has not been studied in patients who have received fibrinolytic therapy. Thus, for STEMI patients undergoing nonprimary PCI who received prior fibrinolytic therapy without a thienopyridine, only a loading dose with clopidogrel should be given as the thienopyridine of choice.

3.1.2. Choice of Thienopyridine for PCI in STEMI

The guidelines do not endorse explicitly one of the thienopyridines over the other. There were several reasons for this decision. Although the composite efficacy end point favored prasugrel, driven predominantly by a difference in nonfatal

MIs, with deaths and nonfatal strokes being similar, bleeding was increased in the prasugrel group.²⁷ In addition, the comparison of the 2 drugs is based on a single large trial. Also, the loading dose of clopidogrel in TRITON-TIMI 38 was lower than is currently recommended in these guidelines. Furthermore, there are some emerging studies that suggest there may be some patients who are resistant to clopidogrel, but there is little information about the use of strategies to select patients who might do better with prasugrel. There is not yet experience with the use of prasugrel in routine community practice. As a result, the writing group believes that there is some uncertainty regarding the net benefit and risks of 1 drug over another for a given patient. Considerations of efficacy in the prevention of thrombosis and risk of an adverse effect related to bleeding, as well as experience with a given medication, may best guide decisions about the choice of thienopyridine for individual patients.

3.2. Proton Pump Inhibitors and Dual-Antiplatelet Therapy for ACS

Proton pump inhibitors (PPIs) are often prescribed prophylactically when clopidogrel is started, to prevent gastrointestinal complications such as ulceration and related bleeding⁵⁹ due to dual-antiplatelet therapy, in particular ASA and clopidogrel.³² Coupled with concern about the gastrointestinal precautions, there has been increased emphasis on the prevention of premature discontinuation of dual-antiplatelet therapy, particularly in patients who have received a stent (BMS or DES), for whom 12 months of antiplatelet therapy is recommended.²⁸ PPI medications* have been found to interfere with the metabolism of clopidogrel.³⁴

Although there are studies that show a pharmacodynamic interaction on ex vivo platelet function testing, to date there are no convincing randomized clinical trial data for an important clinical drug–drug interaction. Retrospective claims-based reports suggesting clinical harm, some detailed below, may be confounded by different baseline characteristics and lack of compliance data. There have been retrospective reports of adverse cardiovascular outcomes (eg, readmission for ACS) when the antiplatelet regimen of clopidogrel and ASA is accompanied by PPIs, assessed as a group, compared with the use of this regimen without a PPI.^{32–34,60} In a retrospective cohort study from the Veterans Affairs' medical records and pharmacy database, concomitant clopidogrel and PPI therapy (with omeprazole, rabeprazole, lansoprazole, or pantoprazole) at any time point during follow-up of 8205 patients discharged for ACS was associated with an increased risk of death or rehospitalization for ACS.³² Other post hoc study analyses^{50,61} and a retrospective data analysis from the NHLBI Dynamic Registry⁶² in which PPIs were assessed as a class in combination with a clopidogrel and an ASA regimen have not found an effect of PPI therapy on the clinical effect of clopidogrel in ACS patients, after ACS, or in a general post-PCI population, respectively.^{50,61,62}

Some studies have suggested that adverse cardiovascular outcomes with the combination of clopidogrel and a PPI are

*PPIs include omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole (which are all available by prescription). Omeprazole is also sold over the counter for frequent heartburn.⁶⁶

explained by the individual PPI, in particular the use of a PPI that inhibits CYP450 2C19, which includes omeprazole, lansoprazole, and rabeprazole. The PPI omeprazole notably has been reported to significantly decrease the inhibitory effect of clopidogrel on platelet aggregation.^{63,64} One study reported that the PPI pantoprazole was not associated with recurrent MI among patients receiving clopidogrel, possibly because of its lack of inhibition of CYP450 2C19.³³

Other studies have examined the thienopyridine agent prescribed with the PPI. One open-label drug study evaluated the effects of the PPI lansoprazole on the pharmacokinetics and pharmacodynamics of prasugrel and clopidogrel in healthy subjects given single doses of prasugrel (60 mg) and clopidogrel (300 mg) with and without concurrent lansoprazole 30 mg per day. The data suggest that inhibition of platelet aggregation was reduced in patients who took the combination of clopidogrel and lansoprazole, whereas it was unaffected after a prasugrel dose.⁵⁶

Another study³⁵ assessed the association of PPIs with the pharmacodynamics and clinical efficacy of clopidogrel and prasugrel, based on populations from 2 randomized trials, the PRINCIPLE (Prasugrel In Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation) TIMI-44 trial⁶⁵ and the TRITON-TIMI 38 trial.²⁷ The findings indicated that first, PPI treatment attenuated the pharmacodynamic effects of clopidogrel and, to a lesser extent, those of prasugrel. Secondly, PPI treatment did not affect the clinical outcome of patients given clopidogrel or prasugrel. This finding was true for all PPIs that were studied, including omeprazole and pantoprazole.

The FDA communication concerning an ongoing safety review of clopidogrel bisulfate⁶⁶ advises that healthcare providers avoid the use of clopidogrel in patients with impaired CYP2C19 function due to known genetic variation or due to drugs that inhibit CYP2C19 activity. The FDA notes that there is no evidence that other drugs that reduce stomach acid, such as H₂ blockers or antacids, interfere with the antiplatelet activity of clopidogrel.

Further research with thienopyridines and PPI combinations, particularly drugs that are not dependent on CYP450 2C19, is needed. Consideration may be given to the use of H₂ antagonists as an alternative to PPIs in the setting of dual-antiplatelet therapy, although they cannot be relied on to protect as well as PPIs, and there are few data about their use with ASA.⁵⁹ The FAMOUS (Famotidine for the Prevention of Peptic Ulcers in Users of Low-Dose Aspirin) trial, a phase II, double-blind, randomized, placebo-controlled trial, found that among patients with a history of coronary heart disease, diabetes mellitus, or cerebrovascular disease who were taking low-dose ASA, 12 weeks of famotidine 20 mg twice daily (n=204) compared with placebo twice daily (n=200) was beneficial in reducing the incidence of peptic ulcer or esophagitis during follow-up endoscopy at 12 weeks. The rate of occurrence of a gastric ulcer at endoscopy at 12 weeks was 3.4% in the famotidine group versus 15% in the placebo group ($P=0.0002$), duodenal ulcer occurred in 0.5% versus 8.5% ($P=0.0045$), and erosive esophagitis was seen in 4.4% versus 19% ($P<0.0001$), respectively. Of note, in the famotidine group, clopidogrel use was 19% and dipyridamole use

was 6%.⁶⁷ The writing committee concluded that additional data, notably randomized controlled clinical trial data that have been peer reviewed and published, are needed before an official recommendation can be made about the use of dual antiplatelet therapy with PPIs in the setting of ACS.

4. Recommendations for the Use of Parenteral Anticoagulants

(See Table 4 and Appendix 4.)

4.1. Parenteral Anticoagulants

Parenteral anticoagulants include intravenous UFH, bivalirudin, enoxaparin, and fondaparinux. Bivalirudin was briefly cited in the 2007 STEMI focused update. The HORIZONS-AMI trial, which was reported subsequently, was a prospective, open-label, randomized, multicenter, international trial that included 3602 patients with STEMI undergoing primary PCI. Patients were randomized to treatment with UFH plus a GP IIb/IIIa receptor antagonist or to bivalirudin alone (with provisional abciximab or double-bolus eptifibatide). The primary efficacy end point was a composite of net adverse clinical events, including major bleeding plus MACE, a composite of cardiovascular death, reinfarction, TVR for ischemia, and stroke within 30 days. Bivalirudin alone resulted in a lower incidence of net adverse clinical events at 30 days (9.2% versus 12.1%; RR 0.76; 95% CI 0.63 to 0.92; $P=0.005$; NNT=34) and at 1 year (15.7% versus 18.3%, HR 0.84; 95% CI 0.71 to 0.98; $P=0.3$).⁹ The difference was driven by a significant decrease in major bleeding complications with bivalirudin at 30 days (4.9% versus 8.3%, $P=0.001$; number needed to harm=33) and 1 year (5.8% versus 9.2%, $P=0.001$). There was a statistically significant 1% increase in stent thrombosis (n=17) within the first 24 hours with bivalirudin but no subsequent difference (1.3% versus 0.3%, $P<0.001$). More deaths at 30 days occurred after major bleeding (n=26) than after reinfarction (n=10) or definite stent thrombosis (n=5).⁹ Treatment with bivalirudin resulted in significantly lower 30-day rates of death due to 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

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			
2. For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed: <ol style="list-style-type: none"> 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>) 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>) 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>) 	1. For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed: <ol style="list-style-type: none"> 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>) 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>) 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>) 	1. For patients proceeding to primary PCI who have been treated with ASA and a thienopyridine, recommended supportive anticoagulant regimens include the following: <ol style="list-style-type: none"> 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>) Bivalirudin is useful as a supportive measure for primary PCI with or without prior treatment with UFH.⁹ (<i>Level of Evidence: B</i>) 	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.)
Class IIa			
		1. In STEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin anticoagulation is reasonable. ⁹ (<i>Level of Evidence: B</i>)	New recommendation

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 recommendations 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 randomized 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 (ie, 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

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>)	1. Patients who are not at high risk who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI-capable facility may be considered for transfer 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. (<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-AMI¹⁵ 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-AMI¹⁴ 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 V₄ indicative of right ventricular involvement.

from fibrinolytic therapy to PCI contributed in part to the adverse clinical outcomes.

FINESS⁸ 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 Update⁴ recommended rescue PCI in the following cases: Fibrinolytic-treated STEMI patients meeting high-risk criteria (ie, 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) trial⁷⁴ 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-AMI¹⁵ 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 study¹⁴ 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 (eg, 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.)

6.1. Intensive Glucose Control

As detailed in the 2004 STEMI guideline and the 2007 UA/NSTEMI guideline revision, randomized trial evidence supported the use of insulin infusion to control hyperglycemia.^{3,97} A recently published randomized clinical trial of intensive versus conventional glucose control in critically ill patients raised uncertainty regarding the optimal level to target when achieving glucose control. NICE-SUGAR, a large, international randomized trial (n=6104) of adults admitted to the intensive care unit with either medical or surgical conditions, compared intensive glucose control (target glucose range 81 to 108 mg/dL) with conventional glucose control (to achieve a glucose level less than 180 mg/dL, with reduction and discontinuation of insulin if the blood glucose level dropped below 144 mg/dL).¹⁶ Time-weighted glucose levels achieved were 115 ± 18 mg/dL in the intensive glucose control group versus 144 ± 23 mg/dL in the conventional glucose control group. The risk of death was increased at 90 days in the intensive glucose control group by 2.6% (27.5% versus 24.9%; odds ratio 1.14; 95% CI 1.02 to 1.08; $P=0.02$; number needed to harm=38). The result remained the same after adjustment for potential confounders. There were significantly more episodes of treatment-related hypoglycemia in the intensely managed group (6.8% versus 0.5%, $P=0.001$), although the contribution of hypoglycemia

Table 6. Recommendations for Intensive Glucose Control in STEMI

2004/2005/2007 Recommendations: 2004 STEMI Guidelines	2009 Joint STEMI/PCI Focused Update Recommendations	Comments
Class I		
1. An insulin infusion to normalize blood glucose is recommended for patients with STEMI and complicated courses. (<i>Level of Evidence: B</i>)		Recommendation is no longer current. See 2009 Class IIa recommendation #1.
Class IIa		
	1. It is reasonable to use an insulin-based regimen to achieve and maintain glucose levels less than 180 mg/dL while avoiding hypoglycemia* for patients with STEMI with either a complicated or uncomplicated course. ^{16,94–96} (<i>Level of Evidence: B</i>)	New recommendation
1. During the acute phase (first 24 to 48 hours) of the management of STEMI in patients with hyperglycemia, it is reasonable to administer an insulin infusion to normalize blood glucose even in patients with an uncomplicated course. (<i>Level of Evidence: B</i>)		Recommendation is no longer current. See 2009 Class IIa recommendation #1.

*There is uncertainty about the ideal target range for glucose necessary to achieve an optimal risk-benefit ratio.

to excess mortality is uncertain.^{94,98} Overall, the hospital course and proximate causes of death were similar in the 2 groups. Excess deaths in the intensive-control group were predominantly due to cardiovascular causes (absolute difference 5.8%; $P=0.02$). More patients in the intensive-control group than in the conventional-control group were treated with corticosteroids.

Because NICE-SUGAR enrolled critically ill medical and surgical patients, the degree to which its results can be extrapolated to the management of patients with STEMI is unclear. Although recent data from a small, mechanistic clinical trial^{28,29,98} suggest that glucose control may reduce inflammation and improve left ventricular ejection fraction in patients with acute myocardial infarction (AMI), whether it will improve patient outcomes remains uncertain.

A consensus statement by the American Association of Clinical Endocrinologists and the American Diabetes Association⁹⁹ summarized that “although hyperglycemia is associated with adverse outcomes after AMI, reduction of glycemia per se, and not necessarily the use of insulin, is associated with improved outcomes. It remains unclear, however, whether hyperglycemia is a marker of underlying health status or is a mediator of complications after AMI. Noniatrogenic hypoglycemia has also been associated with adverse outcomes and is a predictor of higher mortality” (p 1120).⁹⁹

There is a clear need for a well-designed, definitive randomized trial of target-driven glucose control in STEMI that has meaningful clinical end points to determine glucose treatment thresholds and glucose targets. Until such a trial is completed, and based on the balance of current evidence,^{99–101} the writing group concluded that it was prudent to change the recommendation for the use of insulin to control blood glucose in STEMI from a Class I to a Class IIa recommendation (*Level of Evidence: B*) and to recommend treatment for hyperglycemia greater than 180 mg/dL while avoiding hypoglycemia.

7. Recommendation for Thrombus Aspiration During PCI for STEMI

(See Table 7.)

7.1. Thrombus Aspiration

Since the publication of the last STEMI and PCI focused updates, 2 new trials of manual thrombus aspiration have been published. TAPAS was a single-center, unblinded, randomized clinical trial that compared 2 catheter-based reperfusion strategies in 1071 patients with STEMI.^{17,102} Before coronary angiography, patients were randomized to manual thrombus aspiration before PCI (55.1% by direct stenting, 28.6% by balloon angioplasty followed by stenting, 10.1% by PCI without thrombus aspiration) or conventional PCI with balloon angioplasty followed by stenting. BMS were implanted in 92% of PCI procedures. All patients were treated with ASA, 600 mg of clopidogrel, UFH, and abciximab unless contraindicated. TIMI myocardial blush grade 0 or 1 occurred in 17.1% of patients with thrombus aspiration and 26.3% of those with conventional PCI ($P<0.001$). Complete resolution of ST-segment elevation occurred in 56.6% and 44.2%, respectively ($P<0.001$). Death, reinfarction, and TVR rates at 30 days were not significantly different (6.8% versus 9.4%).¹⁷ However, at 1 year, rates of cardiac death (3.6% versus 6.7%, $P=0.02$) and cardiac death or nonfatal reinfarction (5.6% versus 9.9%, $P=0.009$) were lower with thrombus aspiration. Low myocardial blush grade and incomplete ST-segment resolution were associated with clinical events.¹⁰²

EXPIRA was a smaller ($n=175$) randomized clinical trial that also compared thrombus aspiration with conventional PCI, but only in patients with TIMI flow 0/1.¹⁸ TIMI myocardial blush grade of 2 or more (88% versus 60%,

Table 7. Recommendation for Thrombus Aspiration During PCI for STEMI

2009 Joint STEMI/PCI Focused Update Recommendation	Comments
Class IIa	
1. Aspiration thrombectomy is reasonable for patients undergoing primary PCI. ^{17,18,102} (<i>Level of Evidence: B</i>)	New recommendation

Table 8. Recommendations for the Use of Stents in STEMI

2004/2005/2007 Recommendations	2009 Joint STEMI/PCI Focused Update Recommendations	Comments
Class IIa		
	1. It is reasonable to use a DES as an alternative to a BMS for primary PCI in STEMI. ^{11,105} (<i>Level of Evidence: B</i>)*	New recommendation
Class IIb		
2007 PCI Guideline Update, Table 16		
1. A DES may be considered for clinical and anatomic settings in which the effectiveness/safety profile appears favorable but has not been fully confirmed by clinical trials. (<i>Level of Evidence: C</i>)	1. A DES may be considered for clinical and anatomic settings† in which the efficacy/safety profile appears favorable. ^{106–109} (<i>Level of Evidence: B</i>)	Modified recommendation (level of evidence changed from C to B).

*Consideration for the use of stents (DES or BMS) in STEMI should include the ability of the patient to comply with prolonged dual-antiplatelet therapy, the bleeding risk in patients undergoing chronic oral anticoagulation, and the possibility that the patient may need surgery during the ensuing year.²⁸

†For example, small vessels, long lesions, or diabetes mellitus. This recommendation applies to primary and nonprimary PCI patients with STEMI.

$P<0.001$) and 90-minute ST-segment resolution greater than 70% (64% versus 39%, $P<0.001$) occurred more frequently in the thrombus aspiration group. Infarct size measured by contrast-enhanced magnetic resonance imaging in 75 patients at 3 months was significantly reduced only in the thrombus aspiration group.

Both of these trials, as well as a meta-analysis by Bavry et al¹⁰³ and a large pooled analysis of randomized trials,¹⁰⁴ support the use of aspiration thrombectomy for STEMI. In developing a recommendation for the role of routine aspiration thrombectomy, however, it is noteworthy that TAPAS was a study of routine thrombus aspiration versus no thrombus aspiration rather than a study of routine thrombus aspiration versus selective thrombus aspiration. It is not known whether a strategy of selective thrombus aspiration in patients with a large thrombus burden might be superior to no thrombus aspiration or equivalent to routine thrombus aspiration. Clinically, it is reasonable to assume that this strategy can be useful in STEMI patients with short ischemic times and large thrombus burden. It may not be helpful in STEMI patients with long ischemic times, side branches with small infarct territories, or lesions with low thrombus burden.

8. Recommendations for the Use of Stents in STEMI

(See Table 8.)

8.1. Stent Selection for STEMI

Primary PCI is generally the preferred reperfusion strategy for patients with STEMI.¹¹⁰ Compared with balloon angioplasty, routine BMS implantation during primary PCI decreases risk for TVR and possibly reduces MI rates but does not reduce mortality rates.^{111,112}

Two-year data from the Massachusetts registry¹¹³ from 1221 propensity score–matched pairs of DES and BMS patients demonstrated a reduction in mortality and TVR rates with DES in primary PCI, and an analysis from the New York State registry¹¹⁴ found a reduction in mortality rates but not TVR rates with DES. These reports were limited to patients treated before 2005, so they represent the earliest experience with DES, in which selection bias may have influenced stent choice and off-label use may have been pursued more

cautiously. Additionally, duration of clopidogrel therapy was longer in the DES group.

More recently, several relatively small randomized clinical trials have shown an inconsistent efficacy for DES over BMS in primary PCI. Three meta-analyses of these trials have concluded that there were no differences in death, MI, or stent thrombosis rates, but TVR rates were decreased with DES.^{115–117} Variably included were 12 studies that differed in trial design, inclusion criteria, end-point definitions, stent types, duration of clopidogrel treatment, and type of follow-up (angiographic versus clinical). They were limited by sample size and duration of follow-up and by usually requiring angiographic documentation of stent thrombosis, which may have underestimated its true incidence.

The HORIZONS-AMI trial randomized, in a 3-to-1 ratio, 3006 patients to DES or BMS.^{9,68,105} There was no difference in the 12-month composite safety end point of death, reinfarction, stroke, or stent thrombosis. The rates of ischemia-driven TVR and target-lesion revascularization were significantly lower in the DES group (5.8% versus 8.7% and 4.5% versus 7.5%, respectively; NNT=33 at 1 year), as was the 13-month binary restenosis rate (10.0% versus 22.9%).

In summary, there appears to be no difference between BMS and DES in mortality or MI rates and no difference in stent thrombosis risk. The major advantage of DES over BMS is a small reduction in TVR rates. Given cost considerations, it could be argued that selective use of DES to prevent restenosis and TVR in high-risk patients (ie, patients with diabetes) and in high-risk lesions (longer and smaller-diameter stents) could be recommended,¹¹⁸ as it has been for elective PCI. The greatest challenge in selecting patients for DES implantation, however, is determining in an emergency situation whether the patient is a candidate for prolonged thienopyridine therapy. As with elective procedures, DES should be avoided in the presence of financial barriers to continuing prolonged dual-antiplatelet therapy, social barriers that may limit patient compliance, or medical issues that involve bleeding risks or the need for invasive or surgical procedures in the following year that would interrupt antiplatelet therapy.

Table 9. Recommendation for Angiography in Patients With Chronic Kidney Disease

2004/2005/2007 Recommendation: 2007 PCI Guidelines Update, Table 9		2009 PCI Focused Update Recommendation	Comments
Class I			
2. In chronic kidney disease patients undergoing angiography, isosmolar contrast agents are indicated and are preferred. (<i>Level of Evidence: A</i>)	1. In patients with chronic kidney disease undergoing angiography who are not undergoing chronic dialysis, either an isosmolar contrast medium ^{19,119} (<i>Level of Evidence: A</i>) or a low-molecular-weight contrast medium other than ioxaglate or iohexol is indicated. ¹⁹ (<i>Level of Evidence: B</i>)		Modified recommendation (changed text).

PCI Focused Update Section

9. Recommendation for Angiography in Patients With Chronic Kidney Disease

(See Table 9.)

9.1. Angiography in Patients With Chronic Kidney Disease

Patients with chronic kidney disease (CKD) with or without diabetes who undergo angiography are at high risk for a contrast-induced nephropathy (CIN). At issue is the selection of a contrast agent to minimize this risk. The 2007 UA/NSTEMI guideline recommended that in patients with chronic kidney disease undergoing angiography, “isosmolar contrast agents are indicated and are preferred (*Level of Evidence: A*)” (p e112).⁹⁷ In patients with CKD or CKD and diabetes mellitus who are undergoing angiography, isosmolar contrast material was shown to lessen the rise in creatinine. This was based on evidence up to mid-2007 that suggested that isosmolar agents also reduced the risk of CIN in both a moderate-sized randomized clinical trial (RECOVER [Renal Toxicity Evaluation and Comparison Between Visipaque (Iodixanol) and Hexabrix (Ioxaglate) in Patients With Renal Insufficiency Undergoing Coronary Angiography]) that compared iodixanol with ioxaglate¹¹⁹ and a meta-analysis of 16 smaller, earlier clinical trials.¹²⁰

However, in mid-2007, a major US randomized trial of contrast agents in patients with CAD and an estimated glomerular filtration rate of 20 to 59 mL/min who were undergoing angiography, the CARE study, was published. CARE compared the low-osmolar agent iopamidol and the isosmolar agent iodixanol and found no difference in the primary end point (serum creatinine increase of 0.5 mg/dL or higher over baseline) between iopamidol (4.4%) and iodixanol (6.7%, $P=0.39$).¹⁹

Since then, several larger randomized trials have been published that reported no difference in CIN when iodixanol was compared with various other low-osmolar contrast media (LOCM).^{19,121–123} These and other randomized trials comparing isosmolar iodixanol with LOCM have been summarized in 2 mutually supportive and complementary meta-analyses involving 16 trials in 2763 patients¹²⁴ and 25 trials in 3260 patients,¹²⁵ respectively. When more recent trials were combined with the older studies, trends in CIN favoring iodixanol were no longer significant (summary RR 0.79; 95% CI 0.56 to 1.12; $P=0.29$; summary RR 0.80; CI 0.61 to 1.04; $P=0.10$, respectively).^{124,125} However, subanalyses showed variations in relative renal safety by specific LOCM: A reduction in CIN was observed when iodixanol was compared with ioxaglate,

the only ionic LOCM (RR 0.58, CI 0.37 to 0.92, $P=0.02$)¹²⁴, and with iohexol, a nonionic LOCM (RR 0.19 to 0.38, $P<0.01$)^{124,125}, but no difference was noted in comparisons of iodixanol with iopamidol, iopromide, or ioversal,¹²⁴ and a single trial favored iomeprol.¹²³ A pooled comparison of iodixanol with all nonionic LOCM other than iohexol indicated equivalent safety (RR 0.97; CI 0.72 to 1.32, $P=0.86$)¹²⁵. Results were consistent regardless of ancillary preventive therapies (hydration, acetylcysteine), route of administration (intravenous or intra-arterial), age, sex, dose, or preexisting CKD or diabetes. Of further interest, findings were similar in the 8 studies ($n=1793$ patients) performed in the setting of coronary angiography.¹²⁴

These more recent observations indicate that the CIN risk of contrast media cannot be attributed to osmolality alone, but that ionicity and other and unknown characteristics of specific agents may play a role. Thus, the updated evidence base suggests that the recommended choices of contrast media during coronary angiography be expanded to either isosmolar media or LOCM other than ioxaglate or iohexol.

10. Recommendations for Use of Fractional Flow Reserve

(See Table 10.)

10.1. Fractional Flow Reserve

Coronary angiography is often performed in clinical situations in which preprocedural functional testing has not been obtained. Additionally, in the setting of multivessel disease, the need to treat individual stenosis is often difficult to determine. Although revascularization of ischemia-producing lesions improves patient outcomes, the clinical benefits of revascularization of stenotic but non-ischemia-producing lesions are less clear. Intraprocedural assessment of the functional significance of individual stenosis may help define the optimal revascularization strategy.

The objective of the FAME trial²⁰ was to compare clinical outcomes after PCI on the basis of conventional angiographic determination of lesion severity versus fractional flow reserve (FFR) combined with angiography in patients with multivessel disease. This prospective, randomized, multicenter trial included 1005 patients selected from 1905 screened patients at 20 medical centers who were randomized to either angiography-guided or FFR-guided (for lesions with FFR less than or equal to 0.80) PCI. Before randomization, lesions that required PCI were prespecified on the basis of the angiographic appearance. Patients assigned to angiography-guided PCI had all identified lesions treated with DES, whereas those assigned to FFR-guided PCI had only identified lesions with an FFR of 0.80 or less

Table 10. Recommendations for Use of Fractional Flow Reserve

2004/2005/2007 Recommendation: 2005 PCI Guideline, Section 5.6.2.		2009 PCI Focused Update Recommendations	Comments
Class IIa			
1. It is reasonable to use intracoronary physiologic measurements (Doppler ultrasound, fractional flow reserve) in the assessment of the effects of intermediate coronary stenoses (30% to 70% luminal narrowing) in patients with anginal symptoms. Coronary pressure or Doppler velocimetry may also be useful as an alternative to performing noninvasive functional testing (eg, when the functional study is absent or ambiguous) to determine whether an intervention is warranted. (<i>Level of Evidence: B</i>)		1. Coronary pressure (fractional flow reserve [FFR]) or Doppler velocimetry can be useful to determine whether PCI of a specific coronary lesion is warranted. FFR or Doppler velocimetry can also be useful as an alternative to performing noninvasive functional testing (eg, when the functional study is absent or ambiguous) to determine whether an intervention is warranted. It is reasonable to use intracoronary physiological measurements (coronary pressure [FFR] ^{20,126–137} [<i>Level of Evidence: A</i>] or Doppler velocimetry [<i>Level of Evidence: C</i>]) in the assessment of the effects of intermediate coronary stenoses (30% to 70% luminal narrowing) in patients with anginal symptoms.	Modified recommendation (level of evidence changed from B to A for FFR; C for Doppler).
Class III			
1. Routine assessment with intracoronary physiologic measurements such as Doppler ultrasound or fractional flow reserve to assess the severity of angiographic disease in patients with a positive, unequivocal noninvasive functional study is not recommended. (<i>Level of Evidence: C</i>)		1. Routine assessment with intracoronary physiological measurements such as coronary pressure (FFR) or Doppler ultrasound to assess the severity of angiographic disease in concordant vascular distribution in patients with angina <u>and</u> a positive, unequivocal noninvasive functional study is not recommended. (<i>Level of Evidence: C</i>)	Modified recommendation

treated with DES. The primary end point of the trial was the rate of death, nonfatal MI, and repeat revascularization at 1 year.

No difference was evident in the number of intended lesions to be treated per patient (2.7 ± 0.9 versus 2.8 ± 1.0 , $P=0.34$) in the angiography- and FFR-guided groups, respectively. In the FFR group, 37% of lesions had an FFR greater than 0.80. Evaluation of ischemia, as defined by an FFR less than 0.80, resulted in fewer lesions receiving stents (2.7 ± 1.2 versus 1.9 ± 1.3 , $P<0.001$). At 1 year, the composite event rate was 18.3% in the angiography-guided group compared with 13.2% in the FFR-guided group ($P=0.02$).

The results of the FAME trial suggest that identification of ischemia-producing lesions by use of systematic assessment of FFR in patients undergoing multivessel PCI is associated with improved clinical outcomes compared with angiographic assessment alone. Further evidence is needed regarding the added value of assessing FFR in lesions with greater than 90% stenosis.

11. Recommendations for PCI for Unprotected Left Main Coronary Artery Disease

(See Table 11.)

11.1. Unprotected Left Main Coronary Artery Disease

Although listed as a Class III indication in the 2003 guideline on the management of chronic stable angina,¹⁴⁵ PCI of an unprotected left main coronary artery has increased in frequency.¹⁴⁶ Early studies (listed in Appendix 6) involved short follow-up periods, which gave CABG a disadvantage, because the apparent benefits of surgery over PCI in other settings have not typically been fully evident until 1 to 5 years after the procedure. In the ACC/AHA/SCAI 2005 guideline update for PCI, the performance of PCI for left main CAD is given a Class III, Level of Evidence C recommendation if the patient is eligible for CABG and a Class IIa, Level of

Evidence B recommendation for patients who are not eligible for CABG. Thus, it has been recommended that CABG still be considered the standard of care for left main CAD.^{147–149}

Several studies comparing CABG to PCI, however, indicated that the advantage of CABG consists primarily of fewer repeat revascularizations.^{139,149–155} The study by Brener et al¹⁵⁶ indicates no significant mortality difference between PCI and CABG after 3 years of follow-up. Longer-term follow-up is needed.

The present focused update specifically addresses the findings of SYNTAX, an unblinded, randomized clinical trial that assigned patients with 3-vessel and/or left main CAD to an initial treatment strategy of CABG or PCI.²¹ The primary prespecified end point for the 1800 enrolled patients was the composite of death, stroke, and myocardial revascularization determined at 12 months. Prespecified stratification occurred for diabetes mellitus and left main CAD. Ninety-seven percent of CABG patients received at least 1 arterial graft.

In SYNTAX, for the subgroup with left main CAD, there were no significant differences in the incidence of the composite end point (death, MI, stroke, or repeat revascularization) between the 2 groups (PCI 15.8% versus CABG 13.7%, $P=0.44$), although rates of repeat revascularization were higher (11.8% versus 6.5%, $P=0.02$) and rates of stroke were lower (0.3% versus 2.7%, $P=0.01$) in the PCI group.²¹ Left main stented patients with limited CAD (lower SYNTAX score) displayed a trend toward fewer adverse events at 12 months than did similar patients assigned to CABG. Specifically, MACE in patients with isolated left main CAD occurred in 8.5% with CABG versus 7.1% with PCI, and in 13.2% with CABG versus 7.5% with PCI in patients with left main CAD and disease of 1 other vessel. In contrast, MACE with CABG versus PCI were numerically less frequent in patients with disease of the left main coronary artery and disease of 2 other vessels (14.4% versus 19.8%) and in

Table 11. Recommendations for PCI for Unprotected Left Main Coronary Artery Disease

2004/2005/2007 Recommendation	2009 PCI Focused Update Recommendations	Comments
Class IIa		
2005 PCI Guideline, Section 6.3.4.		
1. It is reasonable that patients undergoing PCI to unprotected left main coronary obstructions be followed up with coronary angiography between 2 and 6 months after PCI. (<i>Level of Evidence: C</i>)		Deleted recommendation (no longer recommended).
Class IIb		
	1. PCI of the left main coronary artery with stents as an alternative to CABG may be considered in patients with anatomic conditions that are associated with a low risk of PCI procedural complications and clinical conditions that predict an increased risk of adverse surgical outcomes.*21,138,139 (<i>Level of Evidence: B</i>)	New recommendation
Class III		
2005 PCI Guideline, Section 5.1		
PCI is not recommended in patients with [. . .] f. Left main disease and eligibility for CABG. (<i>Level of Evidence: C</i>)		Modified recommendation (bullet “f” from Section 5.1 and bullet “e” from Sections 5.2. and 5.3. are no longer current; see 2009 Class IIb recommendation #1).
2005 PCI Guideline, Sections 5.2, 5.3		
PCI is not recommended in patients with [. . .] e. Left main disease and eligibility for CABG. (<i>Level of Evidence: C</i>)		

*Stenting for unprotected left main CAD is relatively more favorable for patients with isolated left main coronary artery lesions or left main coronary artery plus single-vessel disease,²¹ for patients with ostial or mid left main coronary artery lesions,^{138,140–144} and for patients with factors (such as severe lung disease, prior thoracic surgery, or poor bypass graft targets) that would make CABG a high-risk procedure or unlikely to be successful. Conversely, CABG surgery for unprotected left main CAD may be relatively more favorable for patients with left main CAD plus multivessel disease,²¹ distal/bifurcation left main coronary artery lesions,^{138,140–144} or low surgical risk with a good chance of technical success.

patients with both left main CAD and 3 other vessels involved (15.4% versus 19.3%).²¹

These data from a post hoc subgroup analysis in SYNTAX must be interpreted with caution for several reasons. The number of patients with isolated left main (or left main plus single vessel) CAD was relatively small, and the differences in outcomes were not statistically significant. Furthermore, SYNTAX reported outcomes at 1 year, and longer follow-up is needed before left main PCI (in patients who are otherwise surgical candidates) should become standard clinical practice. Moreover, because the overall study did not reach its primary end point, subset analyses are less robust; because noninferiority was not proven in this cohort, specific information for each subgroup is of an observational nature and is hypothesis-generating.

On the basis of the evidence in aggregate, prior to and within the present focused update, the writing group has modified the class of recommendation for PCI to unprotected left main coronary from Class III to Class IIb, now citing the Level of Evidence as B. The writing group noted 3 important caveats in classifying unprotected left main CAD as a Class IIb indication. First, patients undergoing PCI in cohort or randomized studies represent merely a subset of all patients with left main CAD. Because only certain left main coronary lesions are amenable to PCI, the Class IIb indication is intended to apply only to those left main lesions that are suitable for PCI. The primary conclusion of SYNTAX is that PCI failed to be shown to be noninferior to CABG in left main and triple-vessel disease. Because patients in SYNTAX

with left main and 2- or 3-vessel disease compared with patients with left main and no other vessel or 1-vessel disease had higher rates of MACE, it is recommended that PCI to left main lesions be limited to patients without significant multivessel disease. Second, because of the narrow margin for error, operators undertaking PCI of left main coronary lesions should be experienced and backed by highly competent support staff and surgeons.¹⁵⁷ Although routine use of intravascular ultrasound has been advocated by some authors for the evaluation of left main lesions, there is no definitive evidence at present that this technique improves outcomes.^{138,157} Finally, not all left main lesions respond equally well to PCI. Bifurcation lesions are technically more challenging¹³⁸ and have higher rates of restenosis.^{140,141,143,144} In contrast, results of PCI of ostial or mid-body left main coronary lesions more closely approximate the results of CABG, even with respect to the need for subsequent procedures.¹⁴² The best case for PCI as an alternative to CABG for left main CAD is in ostial and mid-body lesions without additional multivessel disease.

The writing group discussed the previous Class IIa recommendation for follow-up between 2 and 6 months with coronary angiography. They focused on the inability of angiography to predict a situation that might be prone to acute, sudden stent thrombosis, as well as the risk associated with angiography in a patient who has undergone placement of a left main stent. In view of these factors, the writing group decided that the Class IIa recommendation for angiographic follow-up should be omitted from the guidelines.

Table 12. Recommendations for the Timing of Angiography and Antiplatelet Therapy in UA/NSTEMI

2004/2005/2007 Recommendation	2009 PCI Focused Update Recommendations	Comments
Class I		
	1. Patients with definite or likely UA/NSTEMI selected for an invasive approach should receive dual-antiplatelet therapy. ^{158,159} (<i>Level of Evidence: A</i>) Aspirin should be initiated on presentation. ^{158,159} (<i>Level of Evidence: A</i>) Clopidogrel (before or at the time of PCI) ^{158,159} (<i>Level of Evidence: A</i>) or prasugrel (at the time of PCI) ²⁷ (<i>Level of Evidence: B</i>) is recommended as a second antiplatelet agent.	New recommendation
Class IIa		
	1. It is reasonable for initially stabilized <i>high-risk</i> patients with UA/NSTEMI* (GRACE [Global Registry of Acute Coronary Events] risk score greater than 140) to undergo an early invasive strategy within 12 to 24 hours of admission. For patients <i>not at high risk</i> , an early invasive approach is also reasonable. ^{22,23} (<i>Level of Evidence: B</i>)	New recommendation

*Immediate catheterization/angiography is recommended for unstable patients.

12. Recommendations for the Timing of Angiography and Antiplatelet Therapy in UA/NSTEMI

(See Table 12.)

12.1. Timing of Angiography

A routine invasive strategy in UA/NSTEMI patients with high-risk features has been associated with improved outcomes, but the optimal timing of intervention has not been well established. Early intervention might prevent ischemic events that could occur while the patient awaits a delayed procedure. Alternatively, with intensive antithrombotic therapy with a delay for up to a few days, procedure-related complications might be avoided by intervening on a more stable, “passivated” plaque. Although one study has suggested greater benefit with relatively early intervention,¹⁰⁶ the evidence base for a definitive recommendation on timing is weak. Thus, the question of when to intervene in UA/NSTEMI has not been answered conclusively. Given this uncertainty, the TIMACS investigators²³ undertook a large, multicenter randomized trial to determine whether a strategy of early coronary angiography and intervention was superior to a delayed strategy in patients with UA/NSTEMI assigned to an invasive approach.

TIMACS randomly assigned 3031 non-ST-elevation ACS patients to routine early intervention (coronary angiography within 24 hours) or to delayed intervention (coronary angiography at 36 hours or more). The primary outcome was the composite of death, MI, or stroke at 6 months, and a prespecified secondary outcome was death, MI, or refractory ischemia.²³

Coronary angiography was performed at a median of 14 hours in the early-intervention group and 50 hours in the delayed-intervention group. At 6 months, 9.7% of patients in the early-intervention group experienced a primary outcome versus 11.4% in the delayed-intervention group (HR 0.85; 95% CI 0.68 to 1.06; $P=0.15$). Death, MI, or refractory ischemia was reduced by 28% in favor of early intervention (9.6% versus 13.1%; HR 0.72; 95% CI 0.58 to 0.89; $P=0.002$). Prespecified analyses showed that early intervention improved the primary outcome in the one third of patients at highest risk (HR 0.65; 95% CI 0.48 to 0.88), as determined by a GRACE (Global Registry of Acute Coronary Events) risk score greater than 140, but not in the two thirds at low to intermediate risk (HR 1.14; 95% CI 0.82 to 1.58; P for heterogeneity=0.01). There were no safety issues related

to early intervention; major bleeding occurred in 3.1% of patients in the early invasive group and 3.5% in the delayed invasive group.

Overall in TIMACS, early intervention trended to be superior to delayed intervention in preventing the composite of death, MI, or stroke (primary end point), but the difference was not statistically significant.²³ However, early intervention reduced the composite of death, MI, or refractory ischemia (the secondary end point) and, in high-risk patients, was superior to a delayed invasive strategy. The trial was underpowered to discern a clinically meaningful 15% advantage to early invasive therapy for the primary end point, with recruitment stopped at 3000 because of recruitment and funding challenges. This provided a power of 80% to detect a risk reduction of 28% in the primary end point. Subgroup analysis (high-risk subset) of this overall negative trial was not robust and must be viewed cautiously.

Taken together with the earlier ISAR-COOL (Intracoronary Stenting With Antithrombotic Regimen Cooling Off) study,¹⁰⁶ the favorable secondary end-point results, the subgroup analysis in patients at higher risk, and the lack of a safety issue with early therapy, TIMACS suggests the following conclusions: an early invasive strategy within 12 to 24 hours (median 14 hours) is preferred in high-risk patients and may be chosen in patients at low to intermediate risk at the physician's or institution's preference (eg, efficiency and cost savings), whereas a more delayed approach may be beneficial in low- to intermediate-risk patients.²³ In contrast, results from the recent ABOARD (Angioplasty to Blunt the rise Of troponin in Acute coronary syndromes Randomized for an immediate or Delayed intervention) trial¹⁶⁰ indicate that an immediate invasive strategy (median time 1.1 hour) in UA/NSTEMI is not associated with further incremental benefit.

Typically, early versus delayed angiography is defined with reference to a 12- to 48-hour time window. The ISAR-COOL study¹⁰⁶ supports an earlier compared with a more delayed time to angiography, but the data supporting this general timing suggestion are limited.

12.2. Timing of GP IIb/IIIa Receptor Antagonist Therapy in UA/NSTEMI Patients Undergoing Angiography

The optimal timing of initiation of GP IIb/IIIa receptor antagonist therapy in patients with UA/NSTEMI (ie, whether

to administer therapy upstream on presentation or later at the time of angiography/PCI) and the optimal application of this therapy (ie, whether routine, selective, or provisional) have not been resolved. The 2007 ACC/AHA Guidelines for the Management of Patients With UA/NSTEMI recommend that patients with definite or likely UA/NSTEMI selected for an invasive approach should receive ASA and either clopidogrel or a GP IIb/IIIa receptor antagonist before angiography (Class I, Level of Evidence: A).⁹⁷ They further state that it is reasonable to initiate both clopidogrel and a GP IIb/IIIa receptor antagonist, especially in the setting of delays to angiography, high-risk features, or recurrent ischemic discomfort (Class IIa, Level of Evidence: B). The 2007 European Society of Cardiology guidelines recommend early dual-antiplatelet therapy with ASA and clopidogrel (Class I), with the addition of a GP IIb/IIIa receptor antagonist for those patients with the specific high-risk features of an elevated troponin level, ST-segment depression, or diabetes (Class IIa).¹⁶³

The EARLY ACS (Early Glycoprotein IIb/IIIa Inhibition in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome) trial²² tested the hypothesis that a strategy of early, routine administration of the GP IIb/IIIa receptor antagonist eptifibatide would be superior to delayed, provisional administration in reducing ischemic complications among high-risk patients. EARLY ACS enrolled 9492 non-ST-segment elevation ACS (UA/NSTEMI) patients who presented within 24 hours of an episode of ischemic rest discomfort and who were assigned to an invasive treatment strategy no sooner than the next calendar day (amended later to at least 12 hours but less than 96 hours after randomization). Eligibility required at least 2 of the following features: ST-segment depression or transient ST-segment elevation, an elevated biomarker (creatinine kinase-MB or troponin), and age of 60 years or older (amended to include patients 50 to 59 years with known vascular disease). The key primary end point was all-cause death, MI, recurrent ischemia that required urgent revascularization, or thrombotic bailout at 96 hours. The key secondary efficacy end point was all-cause death or MI within 30 days. Safety end points included major hemorrhage and transfusions through 120 hours after randomization. The study was powered to detect 22.5% and 15% relative reductions in the primary and key secondary end points, respectively.

The primary end point occurred in 9.3% of patients in the early therapy arm versus 10.0% of patients in the provisional GP IIb/IIIa therapy arm (odds ratio 0.92; 95% CI 0.80 to 1.06; $P=0.23$). Secondary end-point event rates were 11.2% versus 12.3% (odds ratio 0.89; CI 0.79 to 1.01; $P=0.08$). Early, routine eptifibatide administration occurred at the cost of a greater risk of TIMI major hemorrhage (2.6% versus 1.8%, $P=0.02$). Moderate and less severe bleeding also occurred more commonly. Rates of red cell transfusion were 8.6% and 6.7%, respectively ($P=0.001$).

EARLY ACS represents a large, carefully executed trial with potentially important implications; however, these results are best taken in the context of previous major trials. As a single trial, EARLY ACS does not establish the superiority of early versus delayed, provisional eptifibatide in non-ST-elevation ACS. A trend toward fewer recurrent ischemic complications was noted at 30 days, but this was counterbalanced by more frequent episodes of bleeding and need for transfusions. Given

the use of eptifibatide at PCI (39% of patients in the delayed, provisional group), EARLY ACS does not contradict the benefit of GP IIb/IIIa therapy over placebo in UA/NSTEMI in previous studies. Rather, its findings relate specifically to the timing of such therapy and selective versus routine use.

In another similar study, ACUTY (Acute Catheterization and Urgent Intervention Triage strategy), superiority of early GP IIb/IIIa therapy also was not found, but investigators could not exclude as much as a 29% benefit with GP IIb/IIIa therapy nor show noninferiority of delayed administration. In addition, drug exposure before angiography was much shorter (4 hours), which might substantially diminish the opportunity for differential efficacy.¹⁶¹

The results of the EARLY ACS study are similar to a meta-analysis of 6 prior large, randomized trials of GP IIb/IIIa therapy versus placebo in non-ST-elevation ACS in which an invasive strategy was not mandated, which showed a relative reduction in death/MI of 9% (CI 2% to 16%).¹⁶² In those patients who underwent PCI, the RR reduction was a more robust 23% (CI 8% to 36%). This finding also was consistent with EARLY ACS. Both studies found no benefit in troponin-negative patients. The investigators ascribed the less than expected benefit of early GP IIb/IIIa therapy in EARLY ACS to convergence of eptifibatide use in the 2 arms at the time of PCI and more aggressive contemporary cotherapies compared with earlier studies, including frequent use of clopidogrel, low-molecular-weight heparin, and statins. A further caution is the lack of follow-up for several years.

Despite a lack of clarity from the overall and subgroup results, an argument can be made against the routine upstream use of GP IIb/IIIa therapy in all non-ST-elevation ACS patients intended for an invasive strategy. In particular, those with a normal baseline troponin level and those over the age of 75 years, in whom there was no evidence for benefit but who showed an increased risk of bleeding, might be excluded. On the other hand, findings in those with a positive troponin at baseline and those with diabetes, although not definitive in EARLY ACS alone, trend positively and are in line with previous results. The EARLY ACS trial showed no significant benefit in the composite outcome comparing early versus delayed eptifibatide as defined by the study. Thus, at this time, a high-risk group that would clearly benefit from the early administration of eptifibatide upstream before cardiac catheterization has not been identified. Early GP IIb/IIIa therapy in patient groups continues to appear reasonable if they are judged clinically to be at high risk of thrombotic events relative to bleeding risk.

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Appendix 1. Author Relationships With Industry and Other Entities—ST-Elevation Myocardial Infarction

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*Significant (greater than \$10 000) relationship.

Appendix 2. Author Relationships With Industry and Other Entities—Percutaneous Coronary Intervention

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DSMB indicates data and safety monitoring board; SCAI, Society for Cardiovascular Angiography and Interventions.

This table represents the relationships of committee members with industry that were reported at the Task Force on Practice Guidelines meeting and updated in conjunction with all meetings. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity or ownership of \$10 000 or more of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships noted in this table are modest unless otherwise noted.

*Significant (greater than \$10 000) relationship.

Appendix 3. Reviewer Relationships With Industry and Other Entities—2009 STEMI and PCI Focused Updates

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Sanjay Kaul	Official Reviewer—AHA	None	None	None	None	None	None
Mikhail Kosiborod	Official Reviewer—AHA	Sanofi-aventis	None	None	None	None	None
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ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; and SCAI, Society for Cardiovascular Angiography and Interventions.

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*Significant (greater than \$10 000) relationship.

Appendix 4. Dosing Table for Antiplatelet and Anticoagulant Therapy Discussed in This Focused Update to Support PCI in STEMI

	During PCI		
Drug*	Patient Received Initial Medical Treatment (With an Anticoagulant and/or Fibrinolytic Therapy)	Patient Did Not Receive Initial Medical Treatment (With an Anticoagulant and/or Fibrinolytic Therapy)	Comments: All Patients to Receive ASA (162–325 mg)
Glycoprotein IIb/IIIa Receptor Antagonists (Section 2)			
Abciximab	Of uncertain benefit	LD of 0.25 mg/kg IV bolus MD of 0.125 mcg/kg per minute (maximum 10 mcg/min) (<i>Class IIa</i> , <i>LOE: A</i>)	Continue for up to 12 hours at the discretion of the physician. ^{9,11}
Eptifibatide	Of uncertain benefit	LD of 180 mcg/kg IV bolus followed 10 minutes later by second IV bolus of 180 mcg/kg MD of 2.0 mcg/kg per minute, started after first bolus; reduce infusion by 50% in patients with estimated creatinine clearance <50 mL/min (<i>Class IIa</i> , <i>LOE: B</i>)	Double bolus recommended to support PCI in STEMI as the recommended adult dosage of eptifibatide in patients with normal renal function. ^{6,7} Infusion should be continued for 12 to 18 hours at the discretion of the physician. ⁹
Tirofiban	Of uncertain benefit	LD of 25 mcg/kg IV bolus MD of IV infusion of 0.15 mcg/kg per min; reduce rate of infusion by 50% in patients with estimated creatinine clearance <30 mL/min (<i>Class IIa</i> , <i>LOE: B</i>)	Increased dosing over previous recommendation. ^{11,12} Continue for up to 18 hours at the discretion of the physician. ¹²
Thienopyridines (Section 3)			
Clopidogrel†	If 600 mg given orally, then no additional treatment A second LD of 300 mg may be given orally to supplement a prior LD of 300 mg (<i>Class I</i> , <i>LOE: C</i>)	LD 300–600 mg orally MD of 75 mg orally per day (<i>Class I</i> , <i>LOE: C</i>)	Optimum LD has not been established. Dose for patients >75 years of age has not been established. There is a recommended duration of therapy for all post-PCI patients receiving a BMS or DES. Period of withdrawal before surgery should be at least 5 days. (For full explanations, see footnote.)
Prasugrel‡	No data are available to guide decision making	LD of 60 mg orally MD of 10 mg orally per day (<i>Class I</i> , <i>LOE: B</i>)	There is no clear need for treatment with prasugrel before PCI. MD of 5 mg orally per day in special circumstances. Special dosing for patients <60 kg or >75 years of age. There is a recommended duration of therapy for all post-PCI patients receiving a DES. Contraindicated for use in patients with prior history of TIA or stroke. (For full explanations, see footnote.)
Parenteral Anticoagulants (Section 4)			
Bivalirudin	For patients who have received UFH, wait 30 minutes, then give 0.75 mg/kg bolus, then 1.75 mg/kg per hour infusion (<i>Class I</i> , <i>LOE: B</i>)	0.75 mg/kg bolus, 1.75 mg/kg per hour infusion	Bivalirudin may be used to support PCI and STEMI with or without previously administered UFH with the addition of 600 mg of clopidogrel. ⁹ In STEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin anticoagulation is reasonable. ⁹

(Continued)

Appendix 4. Continued

Drug*	During PCI		Comments: All Patients to Receive ASA (162–325 mg)
	Patient Received Initial Medical Treatment (With an Anticoagulant and/or Fibrinolytic Therapy)	Patient Did Not Receive Initial Medical Treatment (With an Anticoagulant and/or Fibrinolytic Therapy)	
UFH	IV GP IIb/IIIa planned: target ACT 200–250 seconds No IV GP IIb/IIIa planned: target ACT 250–300 seconds for HemoTec, 300–350 seconds for Hemochron (<i>Class I, LOE: C</i>)	IV GP IIb/IIIa planned: 50–70 U/kg bolus to achieve an ACT of 200–250 seconds No IV GP IIb/IIIa planned: 70–100 U/kg bolus to achieve target ACT of 250–300 seconds for HemoTec, 300–350 seconds for Hemochron (<i>Class I, LOE: C</i>)	

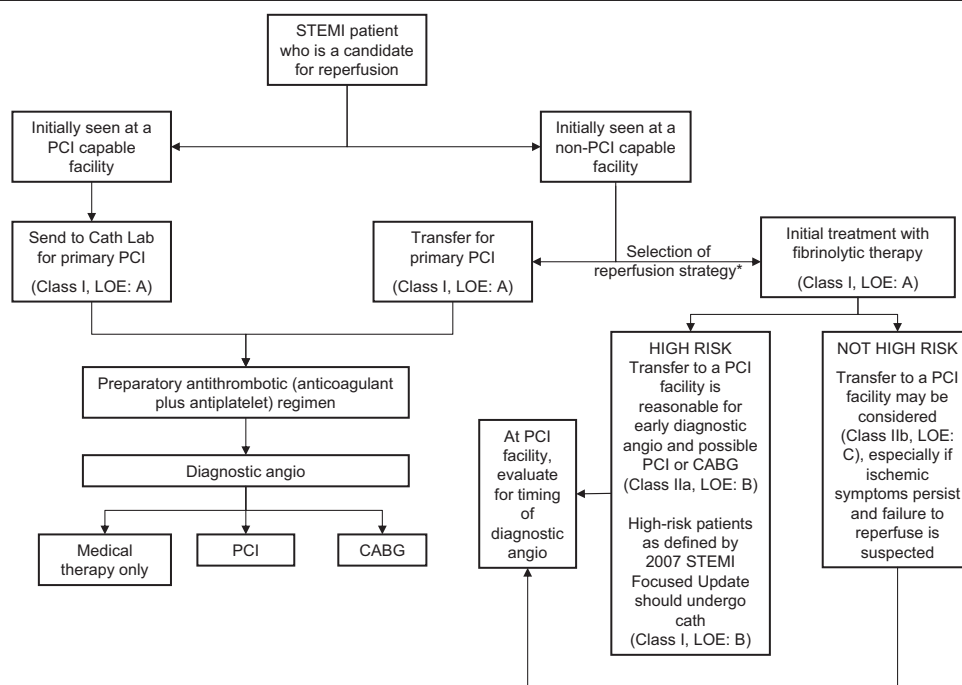
ACT indicates activated clotting time; BMS, bare-metal stent; CABG, coronary artery bypass graft; DES, drug-eluting stent; GP, glycoprotein; IV, intravenous; LD, loading dose; LOE, level of evidence; MACE, major adverse cardiac events; MD, maintenance dose; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; and UFH, unfractionated heparin.

*This list is in alphabetical order and is not meant to indicate a particular therapy preference. This drug table does not make recommendations for combinations of listed drugs. It is only meant to indicate approved dosages if a drug is chosen for a given situation.

†The optimum LD of clopidogrel has not been established. Randomized trials establishing its efficacy and providing data on bleeding risks used an LD of 300 mg orally followed by a daily oral dose of 75 mg.^{26,27} Higher oral LDs such as 600 mg or more than 900 mg³⁶ of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and safety of higher oral LD have not been rigorously established. For post-PCI patients receiving a DES, a daily MD should be given for at least 12 months unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine. For post-PCI patients receiving a BMS, an MD should be given for a minimum of 1 month²⁸ and ideally up to 12 months (unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine; then it should be given for a minimum of 2 weeks). The necessity of giving an LD of clopidogrel before PCI is driven by the pharmacokinetics of clopidogrel, for which a period of several hours is required to achieve desired levels of platelet inhibition. Patients who have a reduced-function CYP2C19 allele have significantly lower levels of the active metabolite of clopidogrel, diminished platelet inhibition, and a higher rate of MACE, including stent thrombosis.⁵³ In STEMI patients taking clopidogrel for whom CABG is planned and can be delayed, it is reasonable to discontinue the clopidogrel to allow for dissipation of the antiplatelet effect, unless the urgency for revascularization and/or the net benefit of clopidogrel outweighs the potential risks of excess bleeding. The period of withdrawal should be at least 5 days in patients receiving clopidogrel.³⁰ Clopidogrel LD after fibrinolytic therapy: For patients given fibrin- and non-fibrin-specific fibrinolytic drugs who are undergoing PCI within 24 hours, 300 mg; for patients given a fibrin-specific fibrinolytic undergoing PCI after more than 24 hours, 300 to 600 mg; for patients given a non-fibrin-specific fibrinolytic undergoing PCI between 24 and 48 hours, 300 mg; for patients given a non-fibrin-specific fibrinolytic undergoing PCI after 48 hours, 300 to 600 mg.

‡Patients weighing <60 kg have an increased exposure to the active metabolite of prasugrel and an increased risk of bleeding on a 10-mg once-daily MD. Consider lowering the MD to 5 mg in patients who weigh <60 kg. The effectiveness and safety of the 5-mg dose have not been studied prospectively. For post-PCI patients receiving a DES, a daily MD should be given for at least 12 and up to 15 months unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine. Do not use prasugrel in patients with active pathological bleeding or a history of TIA or stroke. In patients ≥75 years of age, prasugrel is generally not recommended because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI) for which its effect appears to be greater and its use may be considered. Do not start prasugrel in patients likely to undergo urgent CABG. When possible, discontinue prasugrel at least 7 days before any surgery. Additional risk factors for bleeding include body weight <60 kg, propensity to bleed, concomitant use of medications that increase the risk of bleeding (eg, warfarin, heparin, fibrinolytic therapy, or chronic use of nonsteroidal antiinflammatory drugs).

Appendix 5. Triage and Transfer for PCI



Angio indicates angiography; CABG, coronary artery bypass graft surgery; Cath Lab, catheterization laboratory; LOE, level of evidence; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

Each community and each facility in that community should have an agreed-on plan for how STEMI patients are to be treated that includes which hospitals should receive STEMI patients from emergency medical services units capable of obtaining diagnostic electrocardiograms, management at the initial receiving hospital, and written criteria and agreements for expeditious transfer of patients from non-PCI-capable to PCI-capable facilities. Consideration should be given to initiating a preparatory pharmacological regimen as soon as possible in preparation for and during patient transfer to the catheterization laboratory. The optimal regimen is not yet established, although published studies (see text for details) have used various combinations of the following: anticoagulant, oral antiplatelet agents, intravenous antiplatelet.

*Time since onset of symptoms; risk of STEMI; risks associated with fibrinolytic therapy; time required for transport to a skilled PCI laboratory.

Appendix 6. Outcomes of PCI Versus CABG for Unprotected Left Main Coronary Artery Disease

Reference, Year	Type of Study, Years of Recruitment	PCI/CABG	Short-Term Results	Long-Term Results
Chieffo et al, ¹⁴¹ 2006	Cohort, 2002–2004	107/142	In-hospital outcomes for PCI versus CABG: Death: 0% versus 2.1%; $P=NS$ MI: 9.3% versus 26.1%; $P=0.0009$ Stroke: 0% versus 2%; $P=NS$	1-Year adjusted ORs for PCI versus CABG: Death or MI: 0.26; 95% CI 0.078–0.597; $P=0.0005$ Death, MI, or stroke: 0.385; 95% CI 0.180–0.819; $P=0.01$ Revascularization: 4.2; 95% CI 1.486–14.549; $P=0.005$
Lee et al, ¹⁵¹ 2006	Cohort, 2003–2005	50/123	30-Day outcomes for PCI versus CABG: Death: 2% versus 5%; $P=NS$ MI: 0% versus 2%; $P=NS$ Stroke: 0% versus 8%; $P=0.03$ Death/MI/stroke/revascularization: 17% versus 2%; $P<0.01$	1-Year follow-up for PCI versus CABG: Death: 4% versus 15%; $P=0.2$ Death, MI, stroke: 4% versus 21%; HR=4.4; 95% CI 1.0–18.6; $P=0.03$ Revascularization: 13.3% versus 5.5%; $P=0.2$
Palmerini et al, ¹⁵² 2006	Cohort, 2002–2005	157/154	30-Day outcomes for PCI versus CABG: Death: 3.2% versus 4.5%; $P=NS$ MI: 4.5% versus 1.9%; $P=NS$ Revascularization: 0.6% versus 0.6%; $P=NS$	1- to 2-Year follow-up for PCI and CABG: Death: 13.4% versus 12.3%; 95% CI 0.51–1.77; $P=0.8$ MI: 8.3% versus 4.5%; 95% CI 0.21–1.32; $P=0.17$ Revascularization: 2.6% versus 25.5%; 95% CI 0.03–0.23; $P=0.0001$
Buszman et al, ¹⁵⁰ 2008	Randomized, 2001–2004	52/53	30-Day outcomes for PCI versus CABG: Death: 0% versus 0% MI: 2% versus 4%; $P=NS$ MACE: 2% versus 14%; 95% CI 0.79–0.99; $P=0.03$	1-Year follow-up for PCI versus CABG: Death: 2% versus 8%; $P=NS$ MI: 2% versus 6%; $P=NS$ Revascularization: 30% versus 10%; 95% CI 1.05–1.54; $P=0.01$ MACE: 32% versus 26%; 95% CI 0.85–1.38; $P=NS$

(Continued)

Appendix 6. Continued

Reference, Year	Type of Study, Years of Recruitment	PCI/CABG	Short-Term Results	Long-Term Results
Sanmartin et al, ¹⁵⁴ 2007	Cohort, 2000–2005	96/245	At 30 days for PCI versus CABG: Death: 2.1% versus 6.1%; $P=0.17$ Death/MI/stroke/revascularization: 2.1% versus 9.0%; $P=0.03$	At 1 year, for PCI versus CABG: Death: 5.2% versus 8.4%; $P=0.37$ MI: 0% versus 1.3%; $P=0.44$ Repeat revascularization: 5.2% versus 0.8%; $P=0.02$ Death/MI/stroke/revascularization: 10.4% versus 11.4%; $P=0.5$
Brener et al, ¹⁵⁶ 2008	Cohort with matched CABG controls, 1997–2006	97/190		At 3 years, outcomes for PCI versus CABG: Death: 20% versus 15%; $P=0.14$
Seung et al, ¹³⁹ 2008	Matched cohort, 2000–2006	542/542		At 3 years, HRs for PCI versus CABG: Death: 1.18; HR=1.18; 95% CI 0.77–1.80; $P=0.45$ Death/MI/stroke: 1.10; HR=1.10; 95% CI 0.75–1.62; $P=0.61$ Revascularization: 4.76; HR=4.76; 95% CI 2.80–8.11; $P<0.001$
White et al, ¹⁵⁵ 2008	Cohort, 2003–2007	120/223		At 30 months, HRs for PCI versus CABG: Death: 1.93; 95% CI 0.89–4.19; $P=0.10$
Serruys et al, ²¹ 2009	Randomized, 2005–2007	348/357		At 1 year, HRs for PCI versus CABG: Death/MI/CVA/revascularization: 15.8 versus 13.7; $P=0.44$

CABG indicates coronary artery bypass graft surgery; CI, confidence interval; CVA, cerebrovascular accident; HR, hazard ratio; MACE, major adverse cardiac events; MI, myocardial infarction; NS, not significant; OR, odds ratio; RR, relative risk; and PCI, percutaneous coronary intervention.

When possible, 95% CIs reported were provided for RR, OR, or HR calculations along with probability values.

References

1. ACCF/AHA Task Force on Practice Guidelines. Methodologies and Policies from the ACCF/AHA Task Force on Practice Guidelines. Available at: <http://www.acc.org/qualityandscience/clinical/manual/pdfs/methodology.pdf>. Accessed August 1, 2009.
2. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *J Am Coll Cardiol*. 2006;47:e1–121.
3. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *J Am Coll Cardiol*. 2004;44:e1–e211.
4. Antman EM, Hand M, Armstrong PW, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. *J Am Coll Cardiol*. 2008;51:210–47.
5. King SB III, Smith SC Jr, Hirshfeld JW Jr, et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention). *J Am Coll Cardiol*. 2008;51:172–209.
6. Gurm H, Tamhane U, Meier P, et al. A comparison of abciximab and small molecule glycoprotein IIb/IIIa inhibitors in patients undergoing primary percutaneous coronary intervention: a meta-analysis of contemporary randomized controlled trials. *Circ Cardiovasc Intervent*. 2009;2:230–6.
7. De Luca G, Ucci G, Cassetti E, et al. Benefits from small molecule administration as compared with abciximab among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: a meta-analysis. *J Am Coll Cardiol*. 2009;53:1668–73.
8. Ellis SG, Tendera M, de Belder MA, et al. Facilitated PCI in patients with ST-elevation myocardial infarction. *N Engl J Med*. 2008;358:2205–17.
9. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med*. 2008;358:2218–30.
10. Mehilli J, Kastrati A, Schulz S, et al. Abciximab in patients with acute ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention after clopidogrel loading: a randomized double-blind trial. *Circulation*. 2009;119:1933–40.
11. Valgimigli M, Campo G, Percoco G, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. *JAMA*. 2008;299:1788–99.
12. Van't Hof AW, Ten Berg J, Heestermaas T, et al. Prehospital initiation of tirofiban in patients with ST-elevation myocardial infarction undergoing primary angioplasty (On-TIME 2): a multicentre, double-blind, randomised controlled trial. *Lancet*. 2008;372:537–46.
13. Montalescot G, Wiviott SD, Braunwald E, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial. *Lancet*. 2009;373:723–31.
14. Cantor WJ, Fitchett D, Borgundvaag B, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med*. 2009;360:2705–18.
15. Di Mario C, Dudek D, Piscione F, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. *Lancet*. 2008;371:559–68.
16. Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283–97.
17. Svilaas T, Vlaar PJ, van der Horst I, et al. Thrombus aspiration during primary percutaneous coronary intervention. *N Engl J Med*. 2008;358:557–67.
18. Sardella G, Mancone M, Bucciarelli-Ducci C, et al. Thrombus aspiration during primary percutaneous coronary intervention improves myocardial reperfusion and reduces infarct size: the EXPIRA (thrombectomy with export catheter in infarct-related artery during primary percutaneous coronary intervention) prospective, randomized trial. *J Am Coll Cardiol*. 2009;53:309–15.
19. Solomon RJ, Natarajan MK, Doucet S, et al. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. *Circulation*. 2007;115:3189–96.
20. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213–24.

21. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–72.
22. Giugliano RP, White JA, Bode C, et al. Early versus delayed, provisional eptifibatide in acute coronary syndromes. *N Engl J Med*. 2009;360:2176–90.
23. Mehta SR, Granger CB, Boden WE, et al. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med*. 2009;360:2165–75.
24. Wagner GS, Macfarlane P, Wellens H, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. *J Am Coll Cardiol*. 2009;53:1003–11.
25. Hamm C. ON-TIME-2. Ongoing-Tirofiban In Myocardial Infarction evaluation 1 year follow-up. Available at: www.clinicaltrialresults.org/slides/OnTime2-Orlando.ppt. Accessed March 30, 2009.
26. Wiviott SD, Antman EM, Gibson CM, et al. Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet Inhibition with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38). *Am Heart J*. 2006;152:627–35.
27. Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007;357:2001–15.
28. Grines CL, Bonow RO, Casey DE Jr, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *J Am Dent Assoc*. 2007;138:652–5.
29. Hochholzer W, Trenk D, Frundi D, et al. Time dependence of platelet inhibition after a 600-mg loading dose of clopidogrel in a large, unselected cohort of candidates for percutaneous coronary intervention. *Circulation*. 2005;111:2560–4.
30. Plavix (clopidogrel bisulfate) [package insert]. Bridgewater, NJ: Bristol-Myers Squibb Sanofi-aventis. Sanofi-aventis, 2009.
31. Kim JH, Newby LK, Clare RM, et al. Clopidogrel use and bleeding after coronary artery bypass graft surgery. *Am Heart J*. 2008;156:886–92.
32. Ho PM, Maddox TM, Wang L, et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. *JAMA*. 2009;301:937–44.
33. Juurlink DN, Gomes T, Ko DT, et al. A population-based study of the drug interaction between proton pump inhibitors and clopidogrel. *CMAJ*. 2009;180:713–8.
34. Stanek E. Medco study: PPIs reduce clopidogrel efficacy post-stenting. Available at: <http://cardiobrief.org/2009/05/06/scai-clopidogrelppi-wed-1130am/>. Accessed July 29, 2009.
35. O'Donoghue ML, Braunwald E, Antman EM, et al. Pharmacodynamic effect and clinical efficacy of clopidogrel and prasugrel with or without a proton-pump inhibitor: an analysis of two randomised trials. *Lancet*. 2009;374:989–97.
36. Bonello L, Camoin-Jau L, Arques S, et al. Adjusted clopidogrel loading doses according to vasodilator-stimulated phosphoprotein phosphorylation index decrease rate of major adverse cardiovascular events in patients with clopidogrel resistance: a multicenter randomized prospective study. *J Am Coll Cardiol*. 2008;51:1404–11.
37. Prasugrel [drug label]. Indianapolis, Ind: Eli Lilly and Co., 2009.
38. Wrishko RE, Ernest CS, Small DS, et al. Population pharmacokinetic analyses to evaluate the influence of intrinsic and extrinsic factors on exposure of prasugrel active metabolite in TRITON-TIMI 38. *J Clin Pharmacol*. 2009;49:984–98.
39. Michelson AD. Platelet function testing in cardiovascular diseases. *Circulation*. 2004;110:e489–93.
40. Diener HC, Bogousslavsky J, Brass LM, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet*. 2004;364:331–7.
41. Jneid H, Bhatt DL, Corti R, et al. Aspirin and clopidogrel in acute coronary syndromes: therapeutic insights from the CURE study. *Arch Intern Med*. 2003;163:1145–53.
42. Mehta SR, Yusuf S. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. *Eur Heart J*. 2000;21:2033–41.
43. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet*. 2001;358:527–33.
44. Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke. *Stroke*. 2006;37:577–617.
45. Bhatt DL, Flather MD, Hacke W, et al. Patients with prior myocardial infarction, stroke, or symptomatic peripheral arterial disease in the CHARISMA trial. *J Am Coll Cardiol*. 2007;49:1982–8.
46. Lau WC, Gurbel PA. The drug-drug interaction between proton pump inhibitors and clopidogrel. *CMAJ*. 2009;180:699–700.
47. Collet JP, Hulot JS, Pena A, et al. Cytochrome P450 2C19 polymorphism in young patients treated with clopidogrel after myocardial infarction: a cohort study. *Lancet*. 2009;373:309–17.
48. Roden DM, Stein CM. Clopidogrel and the concept of high-risk pharmacokinetics. *Circulation*. 2009;119:2127–30.
49. Sibbing D, Stegheer J, Latz W, et al. Cytochrome P450 2C19 loss-of-function polymorphism and stent thrombosis following percutaneous coronary intervention. *Eur Heart J*. 2009;30:916–22.
50. Simon T, Verstuyft C, Mary-Krause M, et al. Genetic determinants of response to clopidogrel and cardiovascular events. *N Engl J Med*. 2009;360:363–75.
51. Mega J, Thakuria JV, Cannon CP, Sabatine MS. Sequence variations in CYP metabolism genes and cardiovascular outcomes following treatment with clopidogrel: insights from the CLARITY-TIMI 28 genomic study. Available at: http://content.onlinejacc.org/cgi/reprint/51/10_Suppl_A/A178.pdf. Accessed May 25, 2009.
52. Giusti B, Gori AM, Marcucci R, et al. Relation of cytochrome P450 2C19 loss-of-function polymorphism to occurrence of drug-eluting coronary stent thrombosis. *Am J Cardiol*. 2009;103:806–11.
53. Mega J, Close S, Wiviott S, et al. Cytochrome p-450 polymorphisms and response to clopidogrel. *N Engl J Med*. 2009;360:354–62.
54. Aspirin for the prevention of cardiovascular disease. Available at: [http://www.pharmacistsletter.com/\(S\(ea4ssifcnyu01j45v2124zqc\)\)/pl/detaildocuments/250601.pdf?cs=&s=PL](http://www.pharmacistsletter.com/(S(ea4ssifcnyu01j45v2124zqc))/pl/detaildocuments/250601.pdf?cs=&s=PL). Accessed May 26, 2009.
55. Michelson AD, Frelinger AL III, Braunwald E, et al. Pharmacodynamic assessment of platelet inhibition by prasugrel vs. clopidogrel in the TRITON-TIMI 38 trial. *Eur Heart J*. 2009;30:1753–63.
56. Small DS, Farid NA, Payne CD, et al. Effects of the proton pump inhibitor lansoprazole on the pharmacokinetics and pharmacodynamics of prasugrel and clopidogrel. *J Clin Pharmacol*. 2008;48:475–84.
57. Price MJ, Berger PB, Angiolillo DJ, et al. Evaluation of individualized clopidogrel therapy after drug-eluting stent implantation in patients with high residual platelet reactivity: design and rationale of the GRAVITAS trial. *Am Heart J*. 2009;157:818–24.
58. Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med*. 2005;352:1179–89.
59. Bhatt DL, Scheiman J, Abraham NS, et al. ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2008;52:1502–17.
60. Aubert RE, Epstein RS, Teagarden JR, et al. Proton pump inhibitors effect on clopidogrel effectiveness: the Clopidogrel Medco Outcomes Study. *Circulation*. 2008;118:S-815. Abstract.
61. Dunn SP, Macaulay TE, Brennan DM, et al. Baseline proton pump inhibitor use is associated with increased cardiovascular events with and without the use of clopidogrel in the CREDO trial. *Circulation*. 2008;118:S-815. Abstract.
62. Ramirez JF, Selzer F, Chakrapani R. Proton pump inhibitor and clopidogrel combination is not associated with adverse clinical outcomes after PCI: the NHLBI Dynamic Registry. *J Am Coll Cardiol* 2009;53: A27–A28. Abstract.
63. Gilard M, Arnaud B, Cornily JC, et al. Influence of omeprazole on the antiplatelet action of clopidogrel associated with aspirin: the randomized, double-blind OCLA (Omeprazole CLopidogrel Aspirin) study. *J Am Coll Cardiol*. 2008;51:256–60.

64. Sibbing D, Morath T, Stegheer J, et al. Impact of proton pump inhibitors on the antiplatelet effects of clopidogrel. *Thromb Haemost*. 2009;101:714–9.
65. Wiviott SD, Trenk D, Frelinger AL, et al. Prasugrel compared with high loading- and maintenance-dose clopidogrel in patients with planned percutaneous coronary intervention: the Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44 trial. *Circulation*. 2007;116:2923–32.
66. US Food and Drug Administration. Clopidogrel (Marketed as Plavix) and Omeprazole (Marketed as Prilosec): Drug Interaction. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm190848.htm>. Accessed November 17, 2009.
67. Taha AS, McCloskey C, Prasad R, et al. Famotidine for the prevention of peptic ulcers and oesophagitis in patients taking low-dose aspirin (FAMOUS): a phase III, randomised, double-blind, placebo-controlled trial. *Lancet*. 2009;374:119–25.
68. Mehran R, Brodie B, Cox DA, et al. The Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial: study design and rationale. *Am Heart J*. 2008;156:44–56.
69. Dangas GD, Lansky AJ, Brodie BR. Predictors of Stent Thrombosis After Primary Angioplasty in Acute Myocardial Infarction: The HORIZONS-AMI Trial. Available at: <http://www.cardiosource.com/rapidnewsummaries/summary.asp?SumID=406>. Accessed August 3, 2009.
70. ASSENT-4 PCI Investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet*. 2006;367:569–78.
71. Ellis SG, Armstrong P, Betriu A, et al. Facilitated percutaneous coronary intervention versus primary percutaneous coronary intervention: design and rationale of the Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial. *Am Heart J*. 2004;147:E16.
72. Deleted in proof.
73. Alp NJ, Gershlick AH, Carver A, et al. Rescue angioplasty for failed thrombolysis in older patients: insights from the REACT trial. *Int J Cardiol*. 2008;125:254–7.
74. Gershlick AH, Stephens-Lloyd A, Hughes S, et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. *N Engl J Med*. 2005;353:2758–68.
75. Collet JP, Montalescot G, Le May M, et al. Percutaneous coronary intervention after fibrinolysis: a multiple meta-analyses approach according to the type of strategy. *J Am Coll Cardiol*. 2006;48:1326–35.
76. Wijeyesundera HC, Vijayaraghavan R, Nallamothu BK, et al. Rescue angioplasty or repeat fibrinolysis after failed fibrinolytic therapy for ST-segment myocardial infarction: a meta-analysis of randomized trials. *J Am Coll Cardiol*. 2007;49:422–30.
77. Lincoff AM, Califf RM, Van de Werf F, et al. Mortality at 1 year with combination platelet glycoprotein IIb/IIIa inhibition and reduced-dose fibrinolytic therapy vs conventional fibrinolytic therapy for acute myocardial infarction: GUSTO V randomized trial. *JAMA*. 2002;288:2130–5.
78. Pinto DS, Kirtane AJ, Nallamothu BK, et al. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. *Circulation*. 2006;114:2019–25.
79. Antman EM. Time is muscle: translation into practice. *J Am Coll Cardiol*. 2008;52:1216–21.
80. Rathore SS, Curtis JP, Chen J, et al. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. *BMJ*. 2009;338:b1807.
81. Armstrong PW, Westerhout CM, Welsh RC. Duration of symptoms is the key modulator of the choice of reperfusion for ST-elevation myocardial infarction. *Circulation*. 2009;119:1293–303.
82. Jacobs AK, Antman EM, Faxon DP, et al. Development of systems of care for ST-elevation myocardial infarction patients: executive summary. *Circulation*. 2007;116:217–30.
83. Jacobs AK. Regional systems of care for patients with ST-elevation myocardial infarction: being at the right place at the right time. *Circulation*. 2007;116:689–92.
84. Bonow RO, Masoudi FA, Rumsfeld JS, et al. ACC/AHA classification of care metrics: performance measures and quality metrics: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol*. 2008;52:2113–7.
85. Krumholz HM, Anderson JL, Bachelder BL, et al. ACC/AHA 2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Performance Measures for ST-Elevation and Non-ST-Elevation Myocardial Infarction). *Circulation*. 2008;118:2596–648.
86. American Heart Association. Get With The Guidelines. Available at: <http://www.americanheart.org/presenter.jhtml?identifier=1165>. Accessed June 10, 2009.
87. Measure Comparison (Inpatient Hospital Quality Measures). Available at: <http://www.qualitynet.org/dcs/ContentServer?c=Page&pagename=QnetPublic%2FPages%2FQnetTier3&cid=1138900297065>. Accessed June 10, 2009.
88. National Cardiovascular Data Registry. Action Registry – GWTG. Available at: <http://www.ncdr.com/webncdr/ACTION/Default.aspx>. Accessed June 10, 2009.
89. The Joint Commission. Acute Myocardial Infarction Core Measure Set. Available at: <http://www.jointcommission.org/PerformanceMeasurement/PerformanceMeasurement/Acute+Myocardial+Infarction+Core+Measure+Set.htm>. Accessed June 10, 2009.
90. American Heart Association. Mission: lifeline. Available at: <http://www.americanheart.org/presenter.jhtml?identifier=3050213>. Accessed June 10, 2009.
91. Henry TD, Sharkey SW, Burke MN, et al. A regional system to provide timely access to percutaneous coronary intervention for ST-elevation myocardial infarction. *Circulation*. 2007;116:721–8.
92. Le May MR, So DY, Dionne R, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2008;358:231–40.
93. Ting HH, Rihal CS, Gersh BJ, et al. Regional systems of care to optimize timeliness of reperfusion therapy for ST-elevation myocardial infarction: the Mayo Clinic STEMI Protocol. *Circulation*. 2007;116:729–36.
94. Kosiborod M, Inzucchi SE, Goyal A, et al. Relationship between spontaneous and iatrogenic hypoglycemia and mortality in patients hospitalized with acute myocardial infarction. *JAMA*. 2009;301:1556–64.
95. Malmberg K, Norhammar A, Wedel H, et al. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. *Circulation*. 1999;99:2626–32.
96. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. *N Engl J Med*. 2006;354:449–61.
97. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction). *J Am Coll Cardiol*. 2007;50:e1–157.
98. Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. *JAMA*. 2008;300:933–44.
99. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care*. 2009;32:1119–31.
100. Deedwania P, Kosiborod M, Barrett E, et al. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Anesthesiology*. 2008;109:14–24.
101. Marfella R, Di Filippo C, Portoghesi M, et al. Tight glycemic control reduces heart inflammation and remodeling during acute myocardial infarction in hyperglycemic patients. *J Am Coll Cardiol*. 2009;53:1425–36.
102. Vlaar PJ, Svilaas T, van der Horst I, et al. Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study. *Lancet*. 2008;371:1915–20.
103. Bavry AA, Kumbhani DJ, Bhatt DL. Role of adjunctive thrombectomy and embolic protection devices in acute myocardial infarction: a comprehensive meta-analysis of randomized trials. *Eur Heart J*. 2008;29:2989–3001.

104. Burzotta F, De Vita M, Gu YL, et al. Clinical impact of thrombectomy in acute ST-elevation myocardial infarction: an individual patient-data pooled analysis of 11 trials. *Eur Heart J*. 2009;30:2193–203.
105. Stone GW, Lansky AJ, Pocock SJ, et al. Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. *N Engl J Med*. 2009;360:1946–59.
106. Neumann FJ, Kastrati A, Pogatsa-Murray G, et al. Evaluation of prolonged antithrombotic pretreatment ('cooling-off' strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. *JAMA*. 2003;290:1593–9.
107. Marroquin OC, Selzer F, Mulukutla SR, et al. A comparison of bare-metal and drug-eluting stents for off-label indications. *N Engl J Med*. 2008;358:342–52.
108. Garg P, Normand SL, Silbaugh TS, et al. Drug-eluting or bare-metal stenting in patients with diabetes mellitus: results from the Massachusetts Data Analysis Center Registry. *Circulation*. 2008;118:2277–85.
109. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med*. 2004;350:221–31.
110. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13–20.
111. Zhu MM, Feit A, Chadow H, et al. Primary stent implantation compared with primary balloon angioplasty for acute myocardial infarction: a meta-analysis of randomized clinical trials. *Am J Cardiol*. 2001;88:297–301.
112. Nordmann AJ, Hengstler P, Harr T, et al. Clinical outcomes of primary stenting versus balloon angioplasty in patients with myocardial infarction: a meta-analysis of randomized controlled trials. *Am J Med*. 2004;116:253–62.
113. Mauri L, Silbaugh TS, Garg P, et al. Drug-eluting or bare-metal stents for acute myocardial infarction. *N Engl J Med*. 2008;359:1330–42.
114. Hannan EL, Racz M, Walford G, et al. Drug-eluting versus bare-metal stents in the treatment of patients with ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv*. 2008;1:129–35.
115. Pasceri V, Patti G, Speciale G, et al. Meta-analysis of clinical trials on use of drug-eluting stents for treatment of acute myocardial infarction. *Am Heart J*. 2007;153:749–54.
116. Kastrati A, Dibra A, Spaulding C, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. *Eur Heart J*. 2007;28:2706–13.
117. De Luca G, Stone GW, Suryapranata H, et al. Efficacy and safety of drug-eluting stents in ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. *Int J Cardiol*. 2009;133:213–22.
118. Van de Werf F. Drug-eluting stents in acute myocardial infarction. *N Engl J Med*. 2006;355:1169–70.
119. Jo SH, Youn TJ, Koo BK, et al. Renal toxicity evaluation and comparison between visipaque (iodixanol) and hexabrix (ioxaglate) in patients with renal insufficiency undergoing coronary angiography: the RECOVER study: a randomized controlled trial. *J Am Coll Cardiol*. 2006;48:924–30.
120. McCullough PA, Bertrand ME, Brinker JA, et al. A meta-analysis of the renal safety of isosmolar iodixanol compared with low-osmolar contrast media. *J Am Coll Cardiol*. 2006;48:692–9.
121. Kuhn MJ, Chen N, Sahani DV, et al. The PREDICT study: a randomized double-blind comparison of contrast-induced nephropathy after low- or isoosmolar contrast agent exposure. *AJR Am J Roentgenol*. 2008;191:151–7.
122. Rudnick MR, Davidson C, Laskey W, et al. Nephrotoxicity of iodixanol versus ioversol in patients with chronic kidney disease: the Visipaque Angiography/Interventions with Laboratory Outcomes in Renal Insufficiency (VALOR) Trial. *Am Heart J*. 2008;156:776–82.
123. Thomsen HS, Morcos SK, Erley CM, et al. The ACTIVE Trial: comparison of the effects on renal function of iomeprol-400 and iodixanol-320 in patients with chronic kidney disease undergoing abdominal computed tomography. *Invest Radiol*. 2008;43:170–8.
124. Reed M, Meier P, Tamhane UU, et al. The relative renal safety of iodixanol compared with low-osmolar contrast media: a meta-analysis of randomized controlled trials. *JACC Cardiovasc Interv*. 2009;2:645–54.
125. Heinrich MC, Haberle L, Muller V, et al. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. *Radiology*. 2009;250:68–86.
126. Bech GJ, De Bruyne B, Bonnier HJ, et al. Long-term follow-up after deferral of percutaneous transluminal coronary angioplasty of intermediate stenosis on the basis of coronary pressure measurement. *J Am Coll Cardiol*. 1998;31:841–7.
127. Berger A, Botman KJ, MacCarthy PA, et al. Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary intervention in patients with multivessel disease. *J Am Coll Cardiol*. 2005;46:438–42.
128. Botman KJ, Pijls NH, Bech JW, et al. Percutaneous coronary intervention or bypass surgery in multivessel disease? A tailored approach based on coronary pressure measurement. *Catheter Cardiovasc Interv*. 2004;63:184–91.
129. Caymaz O, Fak AS, Tezcan H, et al. Correlation of myocardial fractional flow reserve with thallium-201 SPECT imaging in intermediate-severity coronary artery lesions. *J Invasive Cardiol*. 2000;12:345–50.
130. Chamuleau SA, Meuwissen M, Koch KT, et al. Usefulness of fractional flow reserve for risk stratification of patients with multivessel coronary artery disease and an intermediate stenosis. *Am J Cardiol*. 2002;89:377–80.
131. Christou MA, Siontis GC, Katritsis DG, et al. Meta-analysis of fractional flow reserve versus quantitative coronary angiography and non-invasive imaging for evaluation of myocardial ischemia. *Am J Cardiol*. 2007;99:450–6.
132. Costa MA, Sabate M, Staico R, et al. Anatomical and physiologic assessments in patients with small coronary artery disease: final results of the Physiologic and Anatomical Evaluation Prior to and After Stent Implantation in Small Coronary Vessels (PHANTOM) trial. *Am Heart J*. 2007;153:296–7.
133. Curtis J, Rodes-Cabau J, Larose E, et al. Comparison of medical treatment and coronary revascularization in patients with moderate coronary lesions and borderline fractional flow reserve measurements. *Catheter Cardiovasc Interv*. 2008;71:541–8.
134. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. *N Engl J Med*. 1996;334:1703–8.
135. Verna E, Lattanzio M, Ghiringhelli S, et al. Performing versus deferring coronary angioplasty based on functional evaluation of vessel stenosis by pressure measurements: a clinical outcome study. *J Cardiovasc Med (Hagerstown)*. 2006;7:169–75.
136. Yanagisawa H, Chikamori T, Tanaka N, et al. Correlation between thallium-201 myocardial perfusion defects and the functional severity of coronary artery stenosis as assessed by pressure-derived myocardial fractional flow reserve. *Circ J*. 2002;66:1105–9.
137. Yanagisawa H, Chikamori T, Tanaka N, et al. Application of pressure-derived myocardial fractional flow reserve in assessing the functional severity of coronary artery stenosis in patients with diabetes mellitus. *Circ J*. 2004;68:993–8.
138. Park SJ, Hong MK, Lee CW, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. *J Am Coll Cardiol*. 2001;38:1054–60.
139. Seung KB, Park DW, Kim YH, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med*. 2008;358:1781–92.
140. Chieffo A, Stankovic G, Bonizzoni E, et al. Early and mid-term results of drug-eluting stent implantation in unprotected left main. *Circulation*. 2005;111:791–5.
141. Chieffo A, Morici N, Maisano F, et al. Percutaneous treatment with drug-eluting stent implantation versus bypass surgery for unprotected left main stenosis: a single-center experience. *Circulation*. 2006;113:2542–7.
142. Chieffo A, Park SJ, Valgimigli M, et al. Favorable long-term outcome after drug-eluting stent implantation in nonbifurcation lesions that involve unprotected left main coronary artery: a multicenter registry. *Circulation*. 2007;116:158–62.
143. Kim YH, Dangas GD, Solinas E, et al. Effectiveness of drug-eluting stent implantation for patients with unprotected left main coronary artery stenosis. *Am J Cardiol*. 2008;101:801–6.
144. Takagi T, Stankovic G, Finci L, et al. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. *Circulation*. 2002;106:698–702.
145. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol*. 2003;41:159–68.

146. Huang HW, Brent BN, Shaw RE. Trends in percutaneous versus surgical revascularization of unprotected left main coronary stenosis in the drug-eluting stent era: a report from the American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR). *Catheter Cardiovasc Interv.* 2006;68:867–72.
147. Baim DS, Mauri L, Cutlip DC. Drug-eluting stenting for unprotected left main coronary artery disease: are we ready to replace bypass surgery? *J Am Coll Cardiol.* 2006;47:878–81.
148. Brinker J. The left main facts: faced, spun, but alas too few. *J Am Coll Cardiol.* 2008;51:893–8.
149. Taggart DP, Kaul S, Boden WE, et al. Revascularization for unprotected left main stem coronary artery stenosis stenting or surgery. *J Am Coll Cardiol.* 2008;51:885–92.
150. Buszman PE, Kiesz SR, Bochenek A, et al. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. *J Am Coll Cardiol.* 2008;51:538–45.
151. Lee MS, Kapoor N, Jamal F, et al. Comparison of coronary artery bypass surgery with percutaneous coronary intervention with drug-eluting stents for unprotected left main coronary artery disease. *J Am Coll Cardiol.* 2006;47:864–70.
152. Palmerini T, Marzocchi A, Marrozzini C, et al. Comparison between coronary angioplasty and coronary artery bypass surgery for the treatment of unprotected left main coronary artery stenosis (the Bologna Registry). *Am J Cardiol.* 2006;98:54–9.
153. Rodes-Cabau J, Deblois J, Bertrand OF, et al. Nonrandomized comparison of coronary artery bypass surgery and percutaneous coronary intervention for the treatment of unprotected left main coronary artery disease in octogenarians. *Circulation.* 2008;118:2374–81.
154. Sanmartin M, Baz JA, Claro R, et al. Comparison of drug-eluting stents versus surgery for unprotected left main coronary artery disease. *Am J Cardiol.* 2007;100:970–3.
155. White A, Kedia G, Mirocha J, et al. Comparison of coronary artery bypass surgery and percutaneous drug-eluting stent implantation for treatment of left main coronary artery stenosis. *JACC Cardiovasc Interv.* 2008;1:236–45.
156. Brener SJ, Galla JM, Bryant R III, et al. Comparison of percutaneous versus surgical revascularization of severe unprotected left main coronary stenosis in matched patients. *Am J Cardiol.* 2008;101:169–72.
157. Kereiakes DJ, Faxon DP. Left main coronary revascularization at the crossroads. *Circulation.* 2006;113:2480–4.
158. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494–502.
159. Steinhubl SR, Berger PB, Mann JT III, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. *JAMA.* 2002;288:2411–20.
160. Montalescot G. Angioplasty to Blunt the rise Of troponin in Acute coronary syndromes Randomized for an immediate or Delayed intervention. Available at: <http://www.theheart.org/article/954535.do>. Accessed August 3, 2009.
161. Stone GW, Bertrand ME, Moses JW, et al. Routine upstream initiation vs deferred selective use of glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: the ACUTY Timing trial. *JAMA.* 2007;297:591–602.
162. Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *Lancet.* 2002;359:189–98.
163. Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J.* 2007;28:1598–660.

KEY WORDS: ACCF/AHA practice guidelines ■ focused update ■ ST-elevation myocardial infarction ■ percutaneous coronary intervention ■ thienopyridines ■ parenteral anticoagulants ■ antiplatelet therapy ■ glycoprotein IIb/IIIa receptor antagonists

Correction

In the article by Kushner et al, “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,” which published ahead of print on November 18, 2009, and appeared in the December 1, 2009, issue of the journal (*Circulation*. 2009;120:2271–2306), a correction is needed.

On page 2299, in Appendix 4, in the tirofiban row, in the third column, the phrase “MD of IV infusion of 0.1 mcg/kg per min;” should be changed to “MD of IV infusion of 0.15 mcg/kg per min;” for the dosing to read correctly.

This correction has been made to the current online version of the article, which is available at <http://circ.ahajournals.org/cgi/content/full/120/22/2271>.

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In the article by Kushner et al, “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,” which published ahead of print on November 18, 2009, and appeared in the December 1, 2009, issue of the journal (*Circulation*. 2009;120:2271–2306), a correction is needed.

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