

What Do Guidelines Say We Should Do in Patients with ST Elevation Myocardial Infarction?

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Abstract

Clinical statements and guidelines dynamically regenerate with rapidly growing new evidence and regulate our daily clinical practice. On the other hand, our obedience on traditional experiences might lead us to manage patients inappropriately. Recently published guidelines on ST elevation myocardial infarction (STEMI) by the European Society of Cardiology (ESC) and American College of Cardiology (ACC) have altered and changed many previously accurate managements. The aim of this review is to evaluate the recommendations of the new STEMI guidelines and the inappropriate management practices we perform in our daily practice. (*JAEM 2014; 13: 199-203*)

Key words: Myocardial infarction, guideline, ST elevation

1. Emergency Management

Recent guidelines recommend assuming acute myocardial infarction (AMI) in any patient who applies to emergency services with the complaints of chest pain. American College of Cardiology (ACC) guidelines recommend obtaining a 12-derivation electrocardiogram (ECG) immediately after the first medical contact (FMC) where European Society of Cardiology (ESC) guidelines recommends not more than in 10 minutes. Furthermore, ESC details the management by utilizing laboratory evaluation and echocardiography but also points out that they should not permit any delay in revascularization therapy. Moreover, ESC also suggests opioid analgesics for chest pain relief and oxygen supplementation in case of dyspnea or hypoxemia (pulse oximetry <95%). Finally, both guidelines recommend primary percutaneous coronary intervention (PCI) as a class I recommendation in all cases if cardiac arrest occurs at FMC (1, 2).

Clinicians should be aware of any ECG abnormality, especially ST-segment elevation AMI and should start therapy without waiting for blood test results. ESC states this as a class I recommendation. Starting long-term high-dose oxygen supplementation in the emergency room or coronary intensive care immediately is not indicated, because it may lead to vasoconstriction. Instead, oxygenation is recommended in patients with oxygen saturation <95%. Additionally, intramuscular injections may lead to hematomas later if patients receive antiaggregant, anticoagulant, or fibrinolytic therapy.

2. Reperfusion Therapy

Reperfusion therapy should be performed in all patients with STEMI if primary PCI (it should absolutely be performed within the first 12 hours of initial symptoms and in 12-24 hours if ischemia persists with obvious clinical and ECG findings) is not capable. Any patients who are candidates for percutaneous intervention should be admitted to a coronary angiography (CAG) laboratory (both ACC and ESC recommend a door-to-needle interval <90 minutes in the FMC) (1, 2).

If the hospital does not contain a CAG laboratory, then the patient should be transferred to another center that is capable of primary intervention in a door-to-balloon interval of less than 120 minutes. In the absence of such a center and if fibrinolytic therapy is available in the first hospital, the patient should receive a fibrinolytic in the first 30 minutes (ESC recommends fibrin-specific agents). Also, the ESC recommends fibrinolytic therapy in any patient who is admitted to the hospital early (<2 hours) with a wide infarction area and low risk of hemorrhage if the FMC-balloon interval is <90 minutes (2).

Both guidelines recommend an immediate transfer in the first 24 hours to a center capable of coronary angiography if 1) reperfusion is unsuccessful after fibrinolysis, 2) the patient experiences re-infarction, heart failure, or cardiogenic shock or 3) symptoms of ischemia do not resolve, and 3 hours within the fibrinolytic therapy if the patient is stable (1, 2).

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Diagnosis and transfer of these patients in our country have become extremely rapid after utilization of the Emergency Medical Service (112) of the Turkish Ministry of Health. Centers that are capable of PCI are identified, and such patients are referred to these clinics, especially in megapoles. Despite this, in smaller city hospitals without available CAG laboratories, fibrinolytic therapy is preferred, since there is no nearby center that provides PCI <120 minutes as the FMC-to-balloon interval.

The major mistake in reperfusion therapy is not performing it for patients who are admitted between the 6th and 12th hours of the onset of chest pain. Clinicians still think that reperfusion is indicated in the first 6 hours and manage their patients, as well. Even patients who are admitted later than the 12th hour of initial symptoms are accepted as having subacute myocardial infarction, and despite ECG and clinical findings of ischemia, they do not receive any reperfusion therapy. However, new guidelines are clear in this manner in **absolutely starting reperfusion therapy in the first 12 hours and between the 12th and 24th hours depending on ongoing clinical and ECG findings.**

Although the timing is the most important fact in reperfusion treatment, because of challenges, such as insufficient knowledge of ECG and experience of the first clinician who takes care of the patient, waiting for serum marker results, delays in the cardiology consultation, ambulance arrival or CAG staff to come together, fibrinolysis initiation (which should be <30 minutes) and FMC-balloon interval (which should be <30 minutes) are also delayed, unfortunately.

1.1 Primary Percutaneous Intervention Therapy

Both guidelines recommend performing primary PCI in STEMI patients applying in the first 12 hours and at any time for patients having concomitant cardiogenic shock or heart failure (HF) as a class I recommendation. ESC guidelines recommend primary PCI as a class I recommendation in patients with obvious clinical and ECG findings of ischemia who apply between the 12th and 24th hours, where ACC determines the same intervention in the same patient population as a class IIa recommendation. Both of the guidelines recommend primary PCI as a class IIb recommendation in asymptomatic patients applying in the same time interval (1, 2). ACC does not recommend intervention for uninvolved arteries in ischemia (class III), whereas ESC does not recommend intervention to totally occluded artery in stable patients without any ischemic symptoms within the first 24 hours of symptom onset (class III) (1).

Additionally, both guidelines recommend stenting instead of a balloon. ACC recommends bare-metal stents (BMS) as a class I recommendation for patients who have a high risk for bleeding and are inappropriate for dual antiplatelet therapy (DAPT) for 2 years, whereas ESC recommends drug-eluting stents (DES) in patients who are not contra-indicated to receive DAPT as a class IIb recommendation. Again, both guidelines recommend usage of thrombectomy catheters as a class IIa recommendation. Finally, ESC recommends radial artery intervention for experienced clinicians as a class IIa recommendation (1, 2).

Besides, ACC recommends emergency coronary artery by-pass graft surgery (CABG) for STEMI patients. Patients having ischemia, cardiogenic shock, severe HF, and mechanical defects who have coronary anatomy that is amenable to PCI are candidates for CABG as a class I recommendation. But, for patients without cardiogenic shock, this indication in the first 6 hours is a class IIb recommendation (1).

Experienced clinics are known to perform successful interventions in STEMI patients. Despite this, guidelines are not followed especially strictly in daily practice. Stable patients applying later than 24 hours with totally occluded arteries without any obvious symptoms of ischemia undergo inaccurate interventions. Additionally, besides infarction-related arteries, it is a common fault to perform interventions in other arteries unrelated to infarction.

Another mistake is to forward the patient to urgent surgery instead of performing reperfusion intervention for the culprit vessel if the patient has 3-vessel disease in CAG performed during STEMI.

We are familiar with extremely expensive thrombectomy catheters that our social security system does not cover, which means that additional bills are paid by the patient. Thus, only limited numbers of clinics buy and use such devices, as well as DES, since it is unethical to ask any patients or accompanying relatives if more expensive but effective stents can be used or not, although ESC recommends them.

2.1.1 Antiplatelet therapy in centers performing primary PCI

Aspirin should be given orally or intravenously in a loading and maintenance dose if the patient is unable to swallow before intervention in patients with STEMI (class I). Again, both guidelines recommend loading and maintenance doses of one of the ADP receptor blockers (clopidogrel, prasugrel, or ticagrelor) (class I). At this point, ESC points out that clopidogrel should only be used when ticagrelor or prasugrel is unavailable or contra-indicated, whereas prasugrel should be used in patients under 75 years old who did not receive clopidogrel previously and have no transient ischemic attack (TIA) or stroke history. There are no limitations for ticagrelor in ESC guidelines (2).

None of the guidelines recommends glycoprotein IIb/IIIa receptor blockers (GP2b/3a RB) as a class I recommendation. ACC recommends glycoprotein IIb/IIIa inhibitors as a class IIa recommendation in selected patients who receive unfractionated heparin (UFH), whereas ESC defines these patients in detail as having thrombus, diagnosed thrombotic complications, slow flow, or no reflow. Use double boluses of eptifibatid and a high-dose bolus of tirofiban should not be forgotten. Finally administration of these drugs during transfer and administration to all patients are class IIb recommendations (1, 2).

Intravenous (IV) aspirin is available in only a few centers and thus can not always be applied to patients who can not swallow aspirin tablets. For this reason, unfortunately, the right management is impossible in such centers.

The most frequent mistake committed in our country is not giving a loading dose of ADP receptor blockers in the pre-intervention period. Loading doses of these drugs are not being applied in many clinics because of the possibility of referral of these patients to urgent surgery after CAG and the resistance of cardiovascular surgeons in operating these patients who receive such medications. As a general practice, loading doses are given after primary intervention in many clinics.

Because of problems in payment by the social security system of our country, the experience with ADP receptor blockers other than clopidogrel is extremely low. Thus, misuse of these drugs are also little. But, it should not be forgotten that ESC guidelines recommend other antiaggregants instead of clopidogrel.

Finally, although GP2b/3a RBs are recommended for selected patients, they are never used in some clinics, even is indicated, because of high costs.

2.1.2 Anticoagulant Therapy in Primary PCI Centers

Both guidelines recommend anticoagulant therapy with UFH (using activated clotting time=ACT level for follow-up) or bivalirudin and discourage fondaparinux in patients in whom primary intervention was performed. Moreover, ACC does not mention any enoxaparin usage, while ESC recommends enoxaparin instead of UFH (class IIb) (1, 2).

Since bivalirudin is not available in our country and there is not too much experience with fondaparinux in cardiology clinics, we do not notice any misuse. But, a common error is not to regulate dosages of UFH according to ACT and to start enoxaparin instead of UFH, since it is easier to administer.

2.2 Fibrinolytic Therapy

Fibrinolytic therapy is a class I recommendation within the first 12 hours of chest pain if the clinic has no CAG laboratory, FMC-balloon interval is >120 minutes, and there is no contra-indication of fibrinolysis. If the patient is admitted in the first 12-24 hours of pain with obvious clinical ischemia and ongoing ECG abnormality, fibrinolysis is recommended as a class IIb recommendation. ESC also recommends fibrinolytic therapy for patients who are admitted within the first 2 hours of chest pain with wide infarction, low bleeding possibility, and FMC-balloon interval >90 minutes (class IIa). Pre-hospital administration of fibrinolytic (class IIa), especially with fibrin-specific agents (class I), is encouraged by ESC. Fibrinolysis is discouraged in patients with ST depression, except those with true posterior MI and ST elevation in aVR.

Finally, immediate transfer to a CAG unit is recommended in cases of unsuccessful reperfusion with fibrinolysis, reinfarction, HF, cardiogenic shock, and ongoing symptoms of ischemia. If the patient is stable and fibrinolysis is successful, transfer is recommended in 3-24 hours.

Fibrinolytic therapy is frequently administered because of former experiences and difficulties in reaching centers capable of CAG, although primary interventions are performed frequently. Absolute and relative contraindications of fibrinolytics should be realized very well. An accompanying clinician should be ready to follow up and treat any complication that will occur during fibrinolysis, like hypotension, hypertension, and arrhythmia. Another error in the management of these patients is to transfer patients to clinics capable of CAG too late, 3-4 days after fibrinolytic therapy.

2.2.1 Antiplatelet Therapy in Clinics Administering Fibrinolysis

These patients have to receive aspirin and clopidogrel. According to ACC, aspirin should be given continuously at a dose of 162-325 mg, whereas clopidogrel should be given at least 14 days but for 1 year preferably at a dose of 300 mg to patients <75 years old and at 75 mg for those >75 years old (1). None of the guidelines recommends GP2b/3a RBs to patients who receive fibrinolytics (1, 2).

Although clopidogrel should be given, as well as aspirin, directly to any patient with STEMI, either lack of knowledge or former habits cause low dose or any treatment with clopidogrel.

2.2.2 Anticoagulant Therapy in Clinics Administering Fibrinolysis

Again, both guidelines recommend anticoagulation, and UFH infusion has to be monitored with aPTT (targeting 1.5-2 times normal value) follow-ups. If enoxaparin is preferred, then the dosage should be adjusted according to patient age at loading boluses and main-

tenance doses. Similarly, fondaparinux is also convenient in patients who receive fibrinolytics (1, 2).

The most frequent mistake in daily practice is to administer IV heparin at a constant dose of 1000 U/hour instead of adjusting a given dose according to aPTT monitoring. Administration of clinically effective anticoagulants (enoxaparin and fondaparinux) in such patients may help to minimize this mistake. Additionally, another fact not to miss is to adjust the dose of enoxaparin in patients >75 years old.

3. Other Treatment Strategies

3.1 Glycose

ESC recommends regulating blood glycose level between 90-200 mg/dL as a class IIa recommendation in hyperglycemic patients with diabetes but discourages using glycose-potassium-insulin infusion routinely (class III) (2).

Serum glycose levels increase in AMI due to stress. Closely monitoring serum glycose levels and regulating glycemia strictly may cause hypoglycemia episodes. Hypoglycemia may lead to clinical deterioration by a sympathomimetic stimulus. Moreover, some clinics still use glycose-potassium-insulin infusion routinely.

3.2 Beta-blockers and Verapamil

Oral beta-blockers should be initiated in the first 24 hours of STEMI unless contraindicated and should be continued during hospitalization and after discharge. Intravenous beta-blocker is a class IIa recommendation for patients whose hypertension and tachycardia are not secondary to HF (1, 2). Beta-blockers are contraindicated in cases of hypotension or HF.

ESC recommends verapamil (class IIb) for patients without HF but absolute contraindications for beta-blockers (2).

Habits on administering IV beta-blockers routinely to any patient with STEMI give rise to an increase in mortality in patients with HF. Despite this, uncontrolled use of IV beta-blockers is ongoing. Furthermore, it is a common mistake to start IV beta-blockers despite contraindications due to lack of a detailed physical examination and ECG evaluation.

Diltiazem is another drug frequently used in our country to replace when beta-blockers are contraindicated, even if it does not take part in any of the guidelines. Such drugs are absolutely contraindicated in patients with HF.

3.3 Renin-angiotensin-aldosterone System Inhibitors

Angiotensin-converting enzyme inhibitors (ACEIs) should be initiated in the first 24 hours in patients with HF, left ventricular dysfunction, diabetes, or anterior wall infarction who do not have any contraindications (class I). It is a class IIa recommendation to initiate routine ACEI in all patients (1). Angiotensin receptor blockers (ARBs) may replace ACEIs in patients who can not tolerate.

Aldosterone antagonists that are not contraindicated should be initiated simultaneously with ACEIs or beta-blockers in patients with HF, left ventricular ejection fraction <40%, or diabetes, along with close monitoring for renal failure and hyperpotassemia as a class 1 recommendation (1).

Patients with ventricular systolic dysfunction and anterior wall ischemia are usually normotensive. But, these patients are those who have a class I recommendation for ACEI initiation. Avoiding starting

ACEIs in these normotensive STEMI patients is a frequent mistake because of the fear of consequent hypotension as a complication. Besides, ARB is the first choice in some clinics instead of ACEI for the same reasons.

Although it is a class I recommendation, aldosterone antagonists are also rarely initiated in STEMI patients.

3.4 Lipid Therapy

Both guidelines recommend obtaining a fasting lipid profile as soon as possible. Irrespective of initial cholesterol levels, according to both guidelines, it is a class I recommendation to initiate and continue high-dose statin in STEMI patients if there are no contraindications (1, 2). Besides, ESC recommends re-obtaining LDL levels 4-6 weeks after STEMI and adjusting the therapy, targeting and LDL level <70 mg/dL as a class IIa recommendation (2).

Despite these, lipid therapy is still managed according to ATP III guidelines, and usually, lipid-lowering therapy is never initiated if LDL level is <130 mg/dL. Because of social security payment rules in our country, we can not initiate high-dose statin without obtaining a lipid profile. Furthermore, the targeted LDL level according to guidelines (<70 mg/dL) is lower than our security system accepts (lipid-lowering therapy can only be accepted if serum LDL is >130 mg/dL).

3.5 Anticoagulant Therapy

Anticoagulation with vitamin K antagonists is obligatory for obviously indicated patients [CHADS₂ ≥ 2 atrial fibrillation (AF), mechanical heart valve, venous thromboembolism, hypercoagulability]. If the patient has mural thrombi, continuing anticoagulation for a minimum of 3 months is recommended (class IIa) (1). Additionally, ACC recommends achieving an INR of 2.0-2.5 in patients under DAPT and adding anticoagulation if anterior apical wall dyskinesia or akinesia exists (1).

Some clinicians hesitate adding anticoagulants to DAPT, especially to patients who live in rural areas that are far away from hospitals. For this reason, anticoagulation is not initiated, despite being indicated, especially in patients with AF.

4. Suggestions for Post-STEMI Complications

4.1 Cardiogenic Shock

Primary PCI is indicated in STEMI patients with cardiogenic shock, if incapable, fibrinolysis should be performed regardless of admission time (class I). An intra-aortic balloon pump should be inserted if possible (class IIa) (2). ESC recommends the use of dopamine, dobutamine (class IIa), levosimendan (class IIb), and ultrafiltration (class IIa) in patients with HF Killip III. Epinephrine use in patients with HF Killip IV is a class IIb recommendation (2).

Owing to the high mortality of these patients, many unexperienced clinicians avoid performing intervention and prefer medical therapy. Although it is a class I recommendation, fibrinolytic therapy is avoided or delayed in patients do not receive intervention as a common mistake.

4.2 Arrhythmias

Beta-blockers or non-dihydropyridine calcium channel blockers (verapamil, diltiazem) may be initiated in patients with AF who do not have HF. But, if hypotension and HF occur due to rapid ventricular response, digitalis or amiodarone is the drug of choice. If medical

therapy is not effective and can not heal the HF, ischemia, or hemodynamics of the patient, then cardioversion is indicated. Besides, medical cardioversion with amiodarone can be performed in stable patients with new onset of AF. Digoxin, verapamil, sotalol, metoprolol, and others are discouraged for use for medical cardioversion of AF, as well as rhythm control.

ESC recommends cardioversion in sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). If sustained monomorphic VT episodes repeat, then amiodarone (class IIa) and lidocaine or sotalol (class IIb), added to cardioversion, is recommended. Furthermore, it is a class IIa recommendation to terminate VT by transcatheter pacing in these patients. Finally, IV beta-blockers in addition to other therapies are a class IIa recommendation in patients with non-sustained VT episodes (2).

If the patient has polymorphic VT, IV beta-blocker or amiodarone (by paying attention to QT interval), correcting electrolyte imbalances, magnesium supplementation, and performing CAG to exclude ischemia are class I recommendations. Whereas transvenous pacing and isoproterenol therapy are class IIa recommendations, lidocaine is a class IIb recommendation (1, 2).

In clinical practice, patients having newly onset AF during STEMI receive amiodarone. However, digoxin, verapamil, sotalol, and metoprolol are preferred as antiarrhythmic, and hypotension and HF are ignored and cardioversion is delayed.

Although lidocaine is a class IIb recommendation in these patients, it is frequently used due to habits. Besides, terminating VT by transcutaneous pacing or beta-blocker therapy is rarely administered.

4.3 ICD Implantation

An ICD is recommended in patients experiencing ventricular tachycardia or fibrillation within the first 48 hours of STEMI that is unrelated to ischemia, re-infarction, or metabolic causes (class I) (1, 2). Social security regulations and old-fashioned knowledge on the subject cause rare ICD implantation in our country.

1.4 Pericarditis

In the case of pericarditis, the pain responds to high-dose aspirin (class I), and if needed, acetaminophen, colchicine, and opioid analgesics as additives (class IIa) are recommended. Glucocorticoids and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided (class III) (1, 2).

STEMI patients are misdiagnosed as re-infarction after elevation of ST segments in ECG due to pericarditis. Common errors in these patients are performing recurrent CAG although not indicated, misdiagnosing pericarditis as myalgia, and starting NSAIDs.

5. Discharging

ESC recommends 24-hour observation at least in coronary intensive care units as a class 1 recommendation; selected cases with low risk may be hospitalized in earlier (nearly, 72 hours later) patients (class IIb) (2).

Sometimes, patients with STEMI are discharged the next day after CAG, as in elective patients in whom percutaneous intervention is performed. Nevertheless, it does not mean myocardial healing when arterial lesions are opened up. Despite this, some clinicians quickly discharge their patients after stenting as if he/she is healed. This is also the result of social security payments that equalize STEMI patients with elective CAG-indicated ones.

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References

1. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al, American College of Emergency Physicians; Society for Cardio-
2. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST segment elevation. Task Force on the management of ST segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *Eur Heart J* 2012; 33: 2569-619. [\[CrossRef\]](#)

vascular Angiography and Interventions,. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive-summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013; 61: 485-510. [\[CrossRef\]](#)

PRACTICE GUIDELINE

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: Executive Summary

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

*Developed in Collaboration With the American College of Emergency Physicians and
Society for Cardiovascular Angiography and Interventions*

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Preamble

The medical profession should play a central role in evaluating the evidence related to drugs, devices, and procedures for the detection, management, and prevention of disease. When properly applied, expert analysis of available data on the benefits and risks of these therapies and procedures can improve the quality of care, optimize patient outcomes, and favorably affect costs by focusing resources on the most effective strategies. An organized and directed approach to a thorough review of evidence has resulted in the production of clinical practice guidelines that assist physicians in selecting the best management strategy for an individual patient. Moreover, clinical practice guidelines can provide a foundation for other applications, such as performance measures, appropriate use criteria, and both quality improvement and clinical decision support tools.

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) have jointly produced guidelines in the area of cardiovascular disease since 1980. The ACCF/AHA Task Force on Practice Guidelines (Task Force), charged with developing, updating, and revising practice guidelines for cardiovascular diseases and procedures, directs and oversees this effort. Writing committees are charged with regularly reviewing and evaluating all available evidence to develop balanced, patient-centric recommendations for clinical practice.

Experts in the subject under consideration are selected by the ACCF and AHA to examine subject-specific data and write guidelines in partnership with representatives from other medical organizations and specialty groups. Writing committees are asked to perform a literature review; weigh the strength of evidence for or against particular tests, treatments, or procedures; and include estimates of expected outcomes where such data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of tests or therapies are considered. When available, information from studies on cost is considered, but data on efficacy and outcomes constitute the primary basis for the recommendations contained herein.

In analyzing the data and developing recommendations and supporting text, the writing committee uses evidence-based methodologies developed by the Task Force (1). The Class of Recommendation (COR) is an estimate of the size of the treatment effect considering risks versus benefits in addition to evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing committee reviews and ranks evidence supporting each recommendation with the weight of evidence ranked as LOE A, B, or C according to specific definitions that are included in Table 1. Studies are identified as observational, retrospective, prospective, or randomized where appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues for which sparse data are available, a survey of current practice among the clinician members of the writing committee is the basis for LOE C recommendations and no references are cited. The schema for COR and LOE is summarized in Table 1, which also provides suggested phrases for writing recommendations within each COR.

A new addition to this methodology is separation of the Class III recommendations to delineate whether the recommendation is determined to be of “no benefit” or is associated with “harm” to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another are included for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term *guideline-directed medical therapy (GDMT)* to represent optimal medical therapy as defined by ACCF/AHA guideline-

recommended therapies (primarily Class I). This new term, *GDMT*, will be used throughout subsequent guidelines.

Because the ACCF/AHA practice guidelines address patient populations (and healthcare providers) residing in North America, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing committee reviews the potential influence of different practice patterns and patient populations on the treatment effect and 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 to 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. As a result, situations may arise for which deviations from these guidelines may be appropriate. Clinical decision making should involve consideration of the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas are identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if followed. Because lack of patient understanding and adherence may adversely affect outcomes, physicians and other healthcare providers should make every effort to engage the patient’s active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and should be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of relationships with industry and other entities (RWI) among the members of the writing committee. All writing committee members and peer reviewers of the guideline are required to disclose all current healthcare related relationships, including those existing 12 months before initiation of the writing effort. In December 2009, the ACCF and AHA implemented a new RWI policy that requires the writing committee chair plus a minimum of 50% of the writing committee to have no *relevant* RWI. (Appendix 1 includes the ACCF/AHA definition of *relevance*.) These statements are reviewed by the Task Force and all members during each conference call and/or meeting of the writing committee, and members provide updates as changes occur. All guideline recommendations require a confidential vote by the writing committee and must be approved by a consensus of the voting members. Members may not draft or vote on any text or recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing committee

Table 1. Applying Classification of Recommendation 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> <i>Additional studies with focused objectives needed</i> IT IS REASONABLE to per- form procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>No Benefit</i> or CLASS III <i>Harm</i>	
				Procedure/ Test	Treatment	
				COR III: No benefit	No Proven Benefit	
				COR III: Harm	Excess Cost w/o Benefit or Harmful	
					Harmful to Patients	
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	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†		treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B			

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. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

members, and specific section recusals are noted in Appendix 1. Authors’ and peer reviewers’ RWI pertinent to this guideline are disclosed in Appendixes 1 and 2, respectively. In addition, to ensure complete transparency, writing committee members’ comprehensive disclosure information—including RWI not pertinent to this document—is available as an online supplement. Comprehensive disclosure information for the Task Force is also available online at <http://www.cardiosource.org/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx>. The work of writing committees is supported exclusively by the ACCF and AHA without commercial support. Writing committee members volunteered their time for this activity.

In an effort to maintain relevance at the point of care for practicing physicians, the Task Force continues to oversee an

ongoing process improvement initiative. As a result, in response to pilot projects, several changes to these guidelines will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: *Finding What Works in Health Care: Standards for Systematic Reviews* and *Clinical Practice Guidelines We Can Trust* (2,3). It is noteworthy that the IOM cited ACCF/AHA practice guidelines as being compliant with many of the proposed standards. A thorough review of these reports and of our current methodology is under way, with further enhancements anticipated.

The recommendations in this guideline are considered current until they are superseded by a focused update or the full-text guideline is revised. The reader is encouraged to consult the full-text guideline (4) for additional guidance and details about the care of the patient with ST-elevation myocardial infarction (STEMI), because the Executive Summary contains only the recommendations. Guidelines are official policy of both the ACCF and AHA.

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Chair, ACCF/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. The current document constitutes a full revision and includes an extensive evidence review which was conducted through November 2010, with additional selected references added through August 2012. Searches were limited to studies conducted in human subjects and reviews and other evidence pertaining to human subjects; all were published in English. Key search words included but were not limited to: *acute coronary syndromes, percutaneous coronary intervention, coronary artery bypass graft, myocardial infarction, ST-elevation myocardial infarction, coronary stent, revascularization, anticoagulant therapy, antiplatelet therapy, antithrombotic therapy, glycoprotein IIb/IIIa inhibitor therapy, pharmacotherapy, proton-pump inhibitor, implantable cardioverter-defibrillator therapy, cardiogenic shock, fibrinolytic therapy, thrombolytic therapy, nitrates, mechanical complications, arrhythmia, angina, chronic stable angina, diabetes, chronic kidney disease, mortality, morbidity, elderly, ethics, and contrast nephropathy*. Additional searches cross-referenced these topics with the following subtopics: *percutaneous coronary intervention, coronary artery bypass graft, cardiac rehabilitation, and secondary prevention*. Additionally, the committee reviewed documents related to the subject matter previously published by the ACCF and AHA. References selected and published in this document are representative and not all inclusive.

The focus of this guideline is the management of patients with STEMI. Updates to the 2004 STEMI guideline were published in 2007 and 2009 (5–7). Particular emphasis is placed on advances in reperfusion therapy, organization of regional systems of care, transfer algorithms, evidence-based antithrombotic and medical therapies, and secondary prevention strategies to optimize patient-centered care. By design, the document is narrower in scope than the 2004 STEMI Guideline, in an attempt to provide a more focused tool for practitioners. References related to management guidelines are provided whenever appropriate, including those pertaining to percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), heart failure (HF), cardiac devices, and secondary prevention.

1.2. Organization of the Writing Committee

The writing committee was composed of experts representing cardiovascular medicine, interventional cardiology, electrophysiology, HF, cardiac surgery, emergency medicine, inter-

nal medicine, cardiac rehabilitation, nursing, and pharmacy. The American College of Physicians, American College of Emergency Physicians, and Society for Cardiovascular Angiography and Interventions assigned official representatives.

1.3. Document Review and Approval

This document was reviewed by 2 outside reviewers each nominated by the ACCF and the AHA, as well as 2 reviewers each from the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions and 22 individual content reviewers (including members from the ACCF Interventional Scientific Council and ACCF Surgeons’ Scientific Council). All reviewer RWI information was distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACCF and the AHA and was endorsed by the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions.

2. Onset of Myocardial Infarction: Recommendations

2.1. Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals

See Figure 1.

CLASS I

1. All communities should create and maintain a regional system of STEMI care that includes assessment and continuous quality improvement of emergency medical services and hospital-based activities. Performance can be facilitated by participating in programs such as Mission: Lifeline and the Door-to-Balloon Alliance (8–11). (Level of Evidence: B)
2. Performance of a 12-lead electrocardiogram (ECG) by emergency medical services personnel at the site of first medical contact (FMC) is recommended in patients with symptoms consistent with STEMI (11–15). (Level of Evidence: B)
3. Reperfusion therapy should be administered to all eligible patients with STEMI with symptom onset within the prior 12 hours (16,17). (Level of Evidence: A)
4. Primary PCI is the recommended method of reperfusion when it can be performed in a timely fashion by experienced operators (17–19). (Level of Evidence: A)
5. Emergency medical services transport directly to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI, with an ideal FMC-to-device time system goal of 90 minutes or less* (11,14,15). (Level of Evidence: B)
6. Immediate transfer to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI who initially arrive at or are transported to a non-PCI-capable hospital, with an FMC-to-device time system goal of 120 minutes or less* (18–21). (Level of Evidence: B)
7. In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI at non-PCI-capable

* The proposed time windows are system goals. For any individual patient, every effort should be made to provide reperfusion therapy as rapidly as possible.

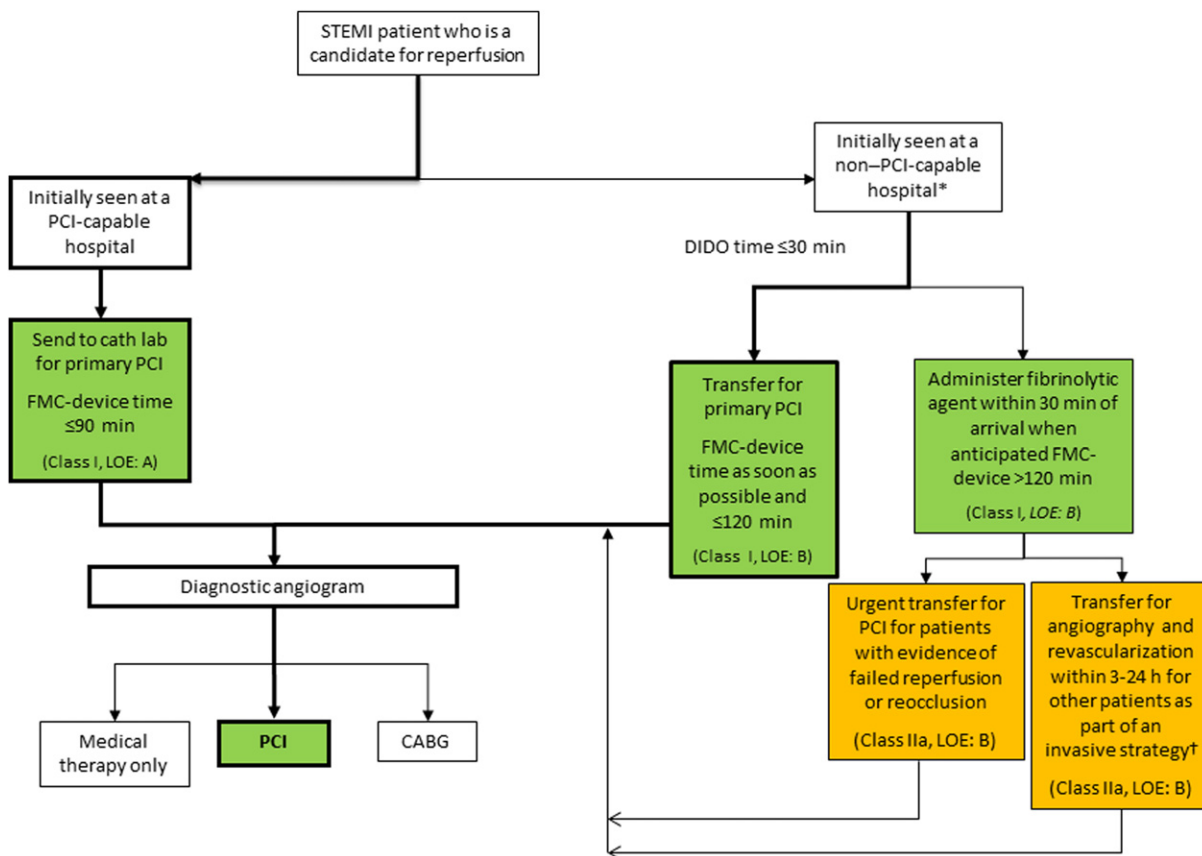


Figure 1. Reperfusion therapy for patients with STEMI. The bold arrows and boxes are the preferred strategies. Performance of PCI is dictated by an anatomically appropriate culprit stenosis. *Patients with cardiogenic shock or severe heart failure initially seen at a non-PCI-capable hospital should be transferred for cardiac catheterization and revascularization as soon as possible, irrespective of time delay from MI onset (Class I, LOE: B). †Angiography and revascularization should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy. CABG indicates coronary artery bypass graft; DIDO, door-in–door-out; FMC, first medical contact; LOE, Level of Evidence; MI, myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

hospitals when the anticipated FMC-to-device time at a PCI-capable hospital exceeds 120 minutes because of unavoidable delays (16,22,23). (Level of Evidence: B)

8. When fibrinolytic therapy is indicated or chosen as the primary reperfusion strategy, it should be administered within 30 minutes of hospital arrival* (24–28). (Level of Evidence: B)

CLASS IIa

1. Reperfusion therapy is reasonable for patients with STEMI and symptom onset within the prior 12 to 24 hours who have clinical and/or ECG evidence of ongoing ischemia. Primary PCI is the preferred strategy in this population (16,29,30). (Level of Evidence: B)

2.2. Evaluation and Management of Patients With STEMI and Out-of-Hospital Cardiac Arrest

CLASS I

1. Therapeutic hypothermia should be started as soon as possible in comatose patients with STEMI and out-of-hospital cardiac arrest caused by ventricular fibrillation or pulseless ventricular tachycardia, including patients who undergo primary PCI (31–33). (Level of Evidence: B)

2. Immediate angiography and PCI when indicated should be performed in resuscitated out-of-hospital cardiac arrest patients whose initial ECG shows STEMI (34–49). (Level of Evidence: B)

3. Reperfusion at a PCI-Capable Hospital: Recommendations

3.1. Primary PCI in STEMI

See Table 2 for a summary of recommendations from this section.

Table 2. Primary PCI in STEMI

	COR	LOE	References
Ischemic symptoms <12 h	I	A	(17,50,51)
Ischemic symptoms <12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC	I	B	(52,53)
Cardiogenic shock or acute severe HF irrespective of time delay from MI onset	I	B	(54–57)
Evidence of ongoing ischemia 12 to 24 h after symptom onset	IIa	B	(29,30)
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B	(58–60)

COR indicates Class of Recommendation; FMC, first medical contact; HF, heart failure; LOE, Level of Evidence; MI, myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

CLASS I

1. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours’ duration (17,50,51). (*Level of Evidence: A*)
2. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours’ duration who have contraindications to fibrinolytic therapy, irrespective of the time delay from FMC (52,53). (*Level of Evidence: B*)
3. Primary PCI should be performed in patients with STEMI and cardiogenic shock or acute severe HF, irrespective of time delay from myocardial infarction (MI) onset (Section 8.1) (54–57). (*Level of Evidence: B*)

CLASS IIa

1. Primary PCI is reasonable in patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia between 12 and 24 hours after symptom onset (29,30). (*Level of Evidence: B*)

CLASS III: HARM

1. PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable (58–60). (*Level of Evidence: B*)

3.2. Aspiration Thrombectomy

CLASS IIa

1. Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI (61–64). (*Level of Evidence: B*)

3.3. Use of Stents in Patients With STEMI

CLASS I

1. Placement of a stent (bare-metal stent or drug-eluting stent) is useful in primary PCI for patients with STEMI (65,66). (*Level of Evidence: A*)
2. Bare-metal stents[†] should be used in patients with high bleeding risk, inability to comply with 1 year of dual antiplatelet therapy (DAPT), or anticipated invasive or surgical procedures in the next year. (*Level of Evidence: C*)

CLASS III: HARM

1. Drug-eluting stents should not be used in primary PCI for patients with STEMI who are unable to tolerate or comply with a prolonged course of DAPT because of the increased risk of stent thrombosis with premature discontinuation of one or both agents (67–73). (*Level of Evidence: B*)

3.4. Antiplatelet Therapy to Support Primary PCI for STEMI

See Table 3 for a summary of recommendations from this section.

CLASS I

1. Aspirin 162 to 325 mg should be given before primary PCI (74–76). (*Level of Evidence: B*)
2. After PCI, aspirin should be continued indefinitely (77,78,80). (*Level of Evidence: A*)
3. A loading dose of a P2Y₁₂ receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include

- a. Clopidogrel 600 mg (76,81,82) (*Level of Evidence: B*); or
 - b. Prasugrel 60 mg (83) (*Level of Evidence: B*); or
 - c. Ticagrelor 180 mg (84). (*Level of Evidence: B*)
4. P2Y₁₂ inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (bare-metal or drug-eluting) during primary PCI using the following maintenance doses:
 - a. Clopidogrel 75 mg daily (83,85) (*Level of Evidence: B*); or
 - b. Prasugrel 10 mg daily (85) (*Level of Evidence: B*); or
 - c. Ticagrelor 90 mg twice a day (84).[‡] (*Level of Evidence: B*)

CLASS IIa

1. It is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses after primary PCI (76,77,86,87). (*Level of Evidence: B*)
2. It is reasonable to start treatment with an intravenous glycoprotein (GP) IIb/IIIa receptor antagonist such as abciximab (88–90) (*Level of Evidence: A*), high-bolus-dose tirofiban (91,92) (*Level of Evidence: B*), or double-bolus eptifibatid (93) (*Level of Evidence: B*) at the time of primary PCI (with or without stenting or clopidogrel pretreatment) in selected patients with STEMI who are receiving unfractionated heparin (UFH).

CLASS IIb

1. It may be reasonable to administer intravenous GP IIb/IIIa receptor antagonist in the precatheterization laboratory setting (e.g., ambulance, emergency department) to patients with STEMI for whom primary PCI is intended (91,94–101). (*Level of Evidence: B*)
2. It may be reasonable to administer intracoronary abciximab to patients with STEMI undergoing primary PCI (64,102–108). (*Level of Evidence: B*)
3. Continuation of a P2Y₁₂ inhibitor beyond 1 year may be considered in patients undergoing drug-eluting stent placement. (*Level of Evidence: C*)

CLASS III: HARM

1. Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack (83). (*Level of Evidence: B*)

3.5. Anticoagulant Therapy to Support Primary PCI

CLASS I

1. For patients with STEMI undergoing primary PCI, the following supportive anticoagulant regimens are recommended:
 - a. UFH, with additional boluses administered as needed to maintain therapeutic activated clotting time levels, taking into account whether a GP IIb/IIIa receptor antagonist has been administered (*Level of Evidence: C*); or
 - b. Bivalirudin with or without prior treatment with UFH (109). (*Level of Evidence: B*)

CLASS IIa

1. In patients with STEMI undergoing PCI who are at high risk of bleeding, it is reasonable to use bivalirudin monotherapy in

[†]Balloon angioplasty without stent placement may be used in selected patients.

[‡]The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

Table 3. Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI

	COR	LOE	References
Antiplatelet therapy			
Aspirin			
• 162- to 325-mg load before procedure	I	B	(74–76)
• 81- to 325-mg daily maintenance dose (indefinite)*	I	A	(77,78,80)
• 81 mg daily is the preferred maintenance dose*	IIa	B	(76,77,86,87)
P2Y₁₂ inhibitors			
Loading doses			
• Clopidogrel: 600 mg as early as possible or at time of PCI	I	B	(76,81,82)
• Prasugrel: 60 mg as early as possible or at time of PCI	I	B	(83)
• Ticagrelor: 180 mg as early as possible or at time of PCI	I	B	(84)
Maintenance doses and duration of therapy			
<i>DES placed: Continue therapy for 1 y with:</i>			
• Clopidogrel: 75 mg daily	I	B	(83,85)
• Prasugrel: 10 mg daily	I	B	(85)
• Ticagrelor: 90 mg twice a day*	I	B	(84)
<i>BMS† placed: Continue therapy for 1 y with:</i>			
• Clopidogrel: 75 mg daily	I	B	(83,85)
• Prasugrel: 10 mg daily	I	B	(85)
• Ticagrelor: 90 mg twice a day*	I	B	(84)
<i>DES placed:</i>			
• Clopidogrel, prasugrel, or ticagrelor* continued beyond 1 y	IIb	C	N/A
• Patients with STEMI with prior stroke or TIA: prasugrel	III: Harm	B	(83)
IV GP IIb/IIIa receptor antagonists in conjunction with UFH or bivalirudin in selected patients			
• Abciximab: 0.25-mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min)	IIa	A	(88–90)
• Tirofiban: (high-bolus dose): 25-mcg/kg IV bolus, then 0.15 mcg/kg/min • In patients with CrCl <30 mL/min, reduce infusion by 50%	IIa	B	(91,92)
• Eptifibatide: (double bolus): 180-mcg/kg IV bolus, then 2 mcg/kg/min; a second 180-mcg/kg bolus is administered 10 min after the first bolus • In patients with CrCl <50 mL/min, reduce infusion by 50% • Avoid in patients on hemodialysis	IIa	B	(93)
• Pre-catheterization laboratory administration of intravenous GP IIb/IIIa receptor antagonist	IIb	B	(91,94–101)
• Intracoronary abciximab 0.25-mg/kg bolus	IIb	B	(64,102–108)
Anticoagulant therapy			
• UFH:	I	C	N/A
• With GP IIb/IIIa receptor antagonist planned: 50- to 70-U/kg IV bolus to achieve therapeutic ACT‡	I	C	N/A
• With no GP IIb/IIIa receptor antagonist planned: 70- to 100-U/kg bolus to achieve therapeutic ACT§	I	C	N/A
• Bivalirudin: 0.75-mg/kg IV bolus, then 1.75-mg/kg/h infusion with or without prior treatment with UFH. An additional bolus of 0.3 mg/kg can be given if needed. • Reduce infusion to 1 mg/kg/h with estimated CrCl <30 mL/min	I	B	(109)
• Preferred over UFH with GP IIb/IIIa receptor antagonist in patients at high risk of bleeding	IIa	B	(109)
• Fondaparinux: Not recommended as sole anticoagulant for primary PCI	III: Harm	B	(110)

ACT indicates activated clotting time; BMS, bare-metal stent; CrCl, creatinine clearance; COR, Class of Recommendation; DES, drug-eluting stent; GP, glycoprotein; IV, intravenous; LOE, Level of Evidence; N/A, not available; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; and UFH, unfractionated heparin.

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

†Balloon angioplasty without stent placement may be used in selected patients. It might be reasonable to provide P2Y₁₂ inhibitor therapy to patients with STEMI undergoing balloon angioplasty alone according to the recommendations listed for BMS. (LOE: C)

‡The recommended ACT with planned GP IIb/IIIa receptor antagonist treatment is 200 to 250 s.

§The recommended ACT with no planned GP IIb/IIIa receptor antagonist treatment is 250 to 300 s (HemoTec device) or 300 to 350 s (Hemochron device).

preference to the combination of UFH and a GP IIb/IIIa receptor antagonist (109). (Level of Evidence: B)

CLASS III: HARM

1. Fondaparinux should not be used as the sole anticoagulant to support primary PCI because of the risk of catheter thrombosis (110). (Level of Evidence: B)

4. Reperfusion at a Non-PCI-Capable Hospital: Recommendations

4.1. Fibrinolytic Therapy When There Is an Anticipated Delay to Performing Primary PCI Within 120 Minutes of FMC

See Table 4 for a summary of recommendations from this section.

CLASS I

1. In the absence of contraindications, fibrinolytic therapy should be given to patients with STEMI and onset of ischemic symptoms within the previous 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of FMC (16,111–116). (Level of Evidence: A)

CLASS IIa

1. In the absence of contraindications and when PCI is not available, fibrinolytic therapy is reasonable for patients with STEMI if there is clinical and/or electrocardiographic evidence of ongoing ischemia within 12 to 24 hours of symptom onset and a large area of myocardium at risk or hemodynamic instability. (Level of Evidence: C)

CLASS III: HARM

1. Fibrinolytic therapy should not be administered to patients with ST depression except when a true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR (16,117–120). (Level of Evidence: B)

4.2. Adjunctive Antithrombotic Therapy With Fibrinolysis

See Table 5 for a summary of recommendations from this section.

Table 4. Indications for Fibrinolytic Therapy When There Is a >120-Minute Delay From FMC to Primary PCI (Figure 1)

	COR	LOE	References
Ischemic symptoms <12 h	I	A	(16,111–116)
Evidence of ongoing ischemia 12 to 24 h after symptom onset, and a large area of myocardium at risk or hemodynamic instability	IIa	C	N/A
ST depression except if true posterior (inferobasal) MI suspected or when associated with ST-elevation in lead aVR	III: Harm	B	(16,117–120)

COR indicates Class of Recommendation; FMC, first medical contact; LOE, Level of Evidence; MI, myocardial infarction; N/A, not available; and PCI, percutaneous coronary intervention.

4.2.1. Adjunctive Antiplatelet Therapy With Fibrinolysis

CLASS I

1. Aspirin (162- to 325-mg loading dose) and clopidogrel (300-mg loading dose for patients ≤75 years of age, 75-mg dose for patients >75 years of age) should be administered to patients with STEMI who receive fibrinolytic therapy (113,121,122). (Level of Evidence: A)
2. Aspirin should be continued indefinitely (113,121,122) (Level of Evidence: A) and clopidogrel (75 mg daily) should be continued for at least 14 days (121,122) (Level of Evidence: A) and up to 1 year (Level of Evidence: C) in patients with STEMI who receive fibrinolytic therapy.

CLASS IIa

1. It is reasonable to use aspirin 81 mg per day in preference to higher maintenance doses after fibrinolytic therapy (77,80,86,87). (Level of Evidence: B)

4.2.2. Adjunctive Anticoagulant Therapy With Fibrinolysis

CLASS I

1. Patients with STEMI undergoing reperfusion with fibrinolytic therapy should receive anticoagulant therapy for a minimum of 48 hours, and preferably for the duration of the index hospitalization, up to 8 days or until revascularization if performed (123,124). (Level of Evidence: A) Recommended regimens include
 - a. UFH administered as a weight-adjusted intravenous bolus and infusion to obtain an activated partial thromboplastin time of 1.5 to 2.0 times control, for 48 hours or until revascularization (Level of Evidence: C);
 - b. Enoxaparin administered according to age, weight, and creatinine clearance, given as an intravenous bolus, followed in 15 minutes by subcutaneous injection for the duration of the index hospitalization, up to 8 days or until revascularization (124–127) (Level of Evidence: A); or
 - c. Fondaparinux administered with initial intravenous dose, followed in 24 hours by daily subcutaneous injections if the estimated creatinine clearance is greater than 30 mL/min, for the duration of the index hospitalization, up to 8 days or until revascularization (110). (Level of Evidence: B)

4.3. Transfer to a PCI-Capable Hospital After Fibrinolytic Therapy

4.3.1. Transfer of Patients With STEMI to a PCI-Capable Hospital for Coronary Angiography After Fibrinolytic Therapy

See Table 6 for a summary of recommendations from this section; *Online Data Supplement 4* for additional data on early catheterization and rescue PCI for fibrinolytic failure in the stent era; and *Online Data Supplement 5* for additional data on early catheterization and PCI after fibrinolysis in the stent era.

CLASS I

1. Immediate transfer to a PCI-capable hospital for coronary angiography is recommended for suitable patients with STEMI who develop cardiogenic shock or acute severe HF, irrespective of the time delay from MI onset (128). (Level of Evidence: B)

Table 5. Adjunctive Antithrombotic Therapy to Support Reperfusion With Fibrinolytic Therapy

	COR	LOE	References
Antiplatelet Therapy			
Aspirin			
• 162- to 325-mg loading dose	I	A	(113,121,122)
• 81- to 325-mg daily maintenance dose (indefinite)	I	A	(113,121,122)
• 81 mg daily is the preferred maintenance dose	Ia	B	(77,80,86,87)
P2Y₁₂ receptor inhibitors			
• Clopidogrel:	I	A	(121,122)
• Age ≤75 y: 300-mg loading dose			
• Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding	I	A (14 d) C (up to 1 y)	(121,122) N/A
• Age >75 y: no loading dose, give 75 mg	I	A	(121,122)
• Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding	I	A (14 d) C (up to 1 y)	(121,122) N/A
Anticoagulant Therapy			
• UFH:	I	C	N/A
• Weight-based IV bolus and infusion adjusted to obtain aPTT of 1.5 to 2.0 times control for 48 h or until revascularization. IV bolus of 60 U/kg (maximum 4000 U) followed by an infusion of 12 U/kg/h (maximum 1000 U) initially, adjusted to maintain aPTT at 1.5 to 2.0 times control (approximately 50 to 70 s) for 48 h or until revascularization.			
• Enoxaparin:	I	A	(124–127)
• If age <75 y: 30-mg IV bolus, followed in 15 min by 1 mg/kg subcutaneously every 12 h (maximum 100 mg for the first 2 doses)			
• If age ≥75 y: no bolus, 0.75 mg/kg subcutaneously every 12 h (maximum 75 mg for the first 2 doses)			
• Regardless of age, if CrCl <30 mL/min: 1 mg/kg subcutaneously every 24 h			
• Duration: For the index hospitalization, up to 8 d or until revascularization			
• Fondaparinux:	I	B	(110)
• Initial dose 2.5 mg IV, then 2.5 mg subcutaneously daily starting the following day, for the index hospitalization up to 8 d or until revascularization			
• Contraindicated if CrCl <30 mL/min			

aPTT indicates activated partial thromboplastin time; COR, Class of Recommendation; CrCl, creatinine clearance; IV, intravenous; LOE, Level of Evidence; N/A, not available; and UFH, unfractionated heparin.

CLASS IIa

1. Urgent transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who demonstrate evidence of failed reperfusion or reocclusion after fibrinolytic therapy (129–132). (Level of Evidence: B)

Table 6. Indications for Transfer for Angiography After Fibrinolytic Therapy

	COR	LOE	References
Immediate transfer for cardiogenic shock or severe acute HF irrespective of time delay from MI onset	I	B	(128)
Urgent transfer for failed reperfusion or reocclusion	Ia	B	(129–132)
As part of an invasive strategy in stable* patients with PCI between 3 and 24 h after successful fibrinolysis	Ia	B	(133–138)

COR indicates Class of Recommendation; HF, heart failure; LOE, Level of Evidence; MI, myocardial infarction; N/A, not available; and PCI, percutaneous coronary intervention.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

2. Transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who have received fibrinolytic therapy even when hemodynamically stable[§] and with clinical evidence of successful reperfusion. Angiography can be performed as soon as logistically feasible at the receiving hospital, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy (133–138). (Level of Evidence: B)

5. Delayed Invasive Management: Recommendations

5.1. Coronary Angiography in Patients Who Initially Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion

See Table 7 for a summary of recommendations from this section.

§Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

CLASS I

1. Cardiac catheterization and coronary angiography with intent to perform revascularization should be performed after STEMI in patients with any of the following:
 - a. Cardiogenic shock or acute severe HF that develops after initial presentation (57,128,139,140) (Level of Evidence: B);
 - b. Intermediate- or high-risk findings on predischARGE noninvasive ischemia testing (141,142) (Level of Evidence: B); or
 - c. Myocardial ischemia that is spontaneous or provoked by minimal exertion during hospitalization. (Level of Evidence: C)

CLASS IIa

1. Coronary angiography with intent to perform revascularization is reasonable for patients with evidence of failed reperfusion or reocclusion after fibrinolytic therapy. Angiography can be performed as soon as logistically feasible (129–132). (Level of Evidence: B)
2. Coronary angiography is reasonable before hospital discharge in stable^S patients with STEMI after successful fibrinolytic therapy. Angiography can be performed as soon as logistically feasible, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy (133–138,143). (Level of Evidence: B)

5.2. PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy

See Table 8 for a summary of recommendations from this section.

CLASS I

1. PCI of an anatomically significant stenosis in the infarct artery should be performed in patients with suitable anatomy and any of the following:
 - a. Cardiogenic shock or acute severe HF (128) (Level of Evidence: B);

Table 7. Indications for Coronary Angiography in Patients Who Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion Therapy

	COR	LOE	References
Cardiogenic shock or acute severe HF that develops after initial presentation	I	B	(57,128, 139,140)
Intermediate- or high-risk findings on predischARGE noninvasive ischemia testing	I	B	(141,142)
Spontaneous or easily provoked myocardial ischemia	I	C	N/A
Failed reperfusion or reocclusion after fibrinolytic therapy	IIa	B	(129–132)
Stable* patients after successful fibrinolysis, before discharge and ideally between 3 and 24 h	IIa	B	(133–138,143)

COR indicates Class of Recommendation; HF, heart failure; LOE, Level of Evidence; N/A, not available.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

Table 8. Indications for PCI of an Infarct Artery in Patients Who Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion Therapy

	COR	LOE	References
Cardiogenic shock or acute severe HF	I	B	(128)
Intermediate- or high-risk findings on predischARGE noninvasive ischemia testing	I	C	(141,142)
Spontaneous or easily provoked myocardial ischemia	I	C	N/A
Patients with evidence of failed reperfusion or reocclusion after fibrinolytic therapy (as soon as possible)	IIa	B	(130,130a–130c)
Stable* patients after successful fibrinolysis, ideally between 3 and 24 h	IIa	B	(133–138)
Stable* patients >24 h after successful fibrinolysis	IIb	B	(55,141–148)
Delayed PCI of a totally occluded infarct artery >24 h after STEMI in stable patients	III: No Benefit	B	(55,146)

COR indicates Class of Recommendation; HF, heart failure; LOE, Level of Evidence; N/A, not available; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

- b. Intermediate- or high-risk findings on predischARGE noninvasive ischemia testing (141,142) (Level of Evidence: C); or
- c. Myocardial ischemia that is spontaneous or provoked by minimal exertion during hospitalization. (Level of Evidence: C)

CLASS IIa

1. Delayed PCI is reasonable in patients with STEMI and evidence of failed reperfusion or reocclusion after fibrinolytic therapy. PCI can be performed as soon as logistically feasible at the receiving hospital (130,130a–130c) (Level of Evidence: B)
2. Delayed PCI of a significant stenosis in a patent infarct artery is reasonable in stable^S patients with STEMI after fibrinolytic therapy. PCI can be performed as soon as logistically feasible at the receiving hospital, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy (133–138). (Level of Evidence: B)

CLASS IIb

1. Delayed PCI of a significant stenosis in a patent infarct artery greater than 24 hours after STEMI may be considered as part of an invasive strategy in stable^S patients (55,141–148). (Level of Evidence: B)

CLASS III: NO BENEFIT

1. Delayed PCI of a totally occluded infarct artery greater than 24 hours after STEMI should not be performed in asymptomatic patients with 1- or 2-vessel disease if they are hemodynamically and electrically stable and do not have evidence of severe ischemia (55,146). (Level of Evidence: B)

§Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.

Table 9. Adjunctive Antithrombotic Therapy to Support PCI After Fibrinolytic Therapy

	COR	LOE	References
Antiplatelet Therapy			
Aspirin			
• 162- to 325-mg loading dose given with fibrinolytic agent (before PCI). See Section 4.2.1 and Table 5.	I	A	(113,121,122)
• 81- to 325-mg daily maintenance dose after PCI (indefinite)	I	A	(76,77,80,82,121,122)
• 81 mg daily is the preferred daily maintenance dose	IIa	B	(76,82,86,87)
P2Y₁₂ receptor inhibitors			
Loading doses			
<i>For patients who received a loading dose of clopidogrel with fibrinolytic therapy:</i>			
• Continue clopidogrel 75 mg daily without an additional loading dose	I	C	(83,85,121,122)
<i>For patients who have not received a loading dose of clopidogrel:</i>			
• If PCI is performed ≤24 h after fibrinolytic therapy: clopidogrel 300-mg loading dose before or at the time of PCI	I	C	N/A
• If PCI is performed >24 h after fibrinolytic therapy: clopidogrel 600-mg loading dose before or at the time of PCI	I	C	N/A
• If PCI is performed >24 h after treatment with a fibrin-specific agent or >48 h after a non-fibrin-specific agent: prasugrel 60 mg at the time of PCI	IIa	B	(83,85)
<i>For patients with prior stroke/TIA: prasugrel</i>	III: Harm	B	(83)
Maintenance doses and duration of therapy			
<i>DES placed: Continue therapy for at least 1 y with:</i>			
• Clopidogrel: 75 mg daily	I	C	(83,85,121,122)
• Prasugrel: 10 mg daily	IIa	B	(83,85)
<i>BMS* placed: Continue therapy for at least 30 d and up to 1 y with:</i>			
• Clopidogrel: 75 mg daily	I	C	(121,122)
• Prasugrel: 10 mg daily	IIa	B	(83,85)
Anticoagulant Therapy			
• Continue UFH through PCI, administering additional IV boluses as needed to maintain therapeutic ACT depending on use of GP IIb/IIIa receptor antagonist†	I	C	N/A
• Continue enoxaparin through PCI: <ul style="list-style-type: none"> • No additional drug if last dose was within previous 8 h • 0.3-mg/kg IV bolus if last dose was 8 to 12 h earlier 	I	B	(127,149)
• Fondaparinux: <ul style="list-style-type: none"> • As sole anticoagulant for PCI 	III: Harm	C	(110)

ACT indicates activated clotting time; BMS, bare-metal stent; COR, Class of Recommendation; DES, drug-eluting stent; GP, glycoprotein; IV, intravenous; LOE, Level of Evidence; N/A, not available; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; and UFH, unfractionated heparin.

*Balloon angioplasty without stent placement may be used in selected patients. It might be reasonable to provide P2Y₁₂ inhibitor therapy to patients with STEMI undergoing balloon angioplasty after fibrinolysis alone according to the recommendations listed for BMS. (Level of Evidence: C)

†The recommended ACT with no planned GP IIb/IIIa receptor antagonist treatment is 250–300 s (HemoTec device) or 300–350 s (Hemochron device).

5.3. PCI of a Noninfarct Artery Before Hospital Discharge

CLASS I

1. PCI is indicated in a noninfarct artery at a time separate from primary PCI in patients who have spontaneous symptoms of myocardial ischemia. (Level of Evidence: C)

CLASS IIa

1. PCI is reasonable in a noninfarct artery at a time separate from primary PCI in patients with intermediate- or high-risk findings on noninvasive testing (58,141,142). (Level of Evidence: B)

5.4. Adjunctive Antithrombotic Therapy to Support Delayed PCI After Fibrinolytic Therapy

See Table 9 for a summary of recommendations from this section.

5.4.1. Antiplatelet Therapy to Support PCI After Fibrinolytic Therapy

CLASS I

1. After PCI, aspirin should be continued indefinitely (76,77, 80,82,121,122). (Level of Evidence: A)
2. Clopidogrel should be provided as follows:
 - a. A 300-mg loading dose should be given before or at the time of PCI to patients who did not receive a previous loading dose and who are undergoing PCI within 24 hours of receiving fibrinolytic therapy (Level of Evidence: C);
 - b. A 600-mg loading dose should be given before or at the time of PCI to patients who did not receive a previous loading dose and who are undergoing PCI more than 24 hours after receiving fibrinolytic therapy (Level of Evidence: C); and
 - c. A dose of 75 mg daily should be given after PCI (83,85, 121,122). (Level of Evidence: C)

CLASS IIa

1. After PCI, it is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses (76,82,86,87). (*Level of Evidence: B*)
2. Prasugrel, in a 60-mg loading dose, is reasonable once the coronary anatomy is known in patients who did not receive a previous loading dose of clopidogrel at the time of administration of a fibrinolytic agent, but prasugrel should not be given sooner than 24 hours after administration of a fibrin-specific agent or 48 hours after administration of a non-fibrin-specific agent (83,85). (*Level of Evidence: B*)
3. Prasugrel, in a 10-mg daily maintenance dose, is reasonable after PCI (83,85). (*Level of Evidence: B*)

CLASS III: HARM

1. Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack (83). (*Level of Evidence: B*)

5.4.2. Anticoagulant Therapy to Support PCI After Fibrinolytic Therapy

CLASS I

1. For patients with STEMI undergoing PCI after receiving fibrinolytic therapy with intravenous UFH, additional boluses of intravenous UFH should be administered as needed to support the procedure, taking into account whether GP IIb/IIIa receptor antagonists have been administered. (*Level of Evidence: C*)
2. For patients with STEMI undergoing PCI after receiving fibrinolytic therapy 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 between 8 and 12 hours earlier, enoxaparin 0.3 mg/kg IV should be given (127,149). (*Level of Evidence: B*)

CLASS III: HARM

1. Fondaparinux should not be used as the sole anticoagulant to support PCI. An additional anticoagulant with anti-IIa activity should be administered because of the risk of catheter thrombosis (110). (*Level of Evidence: C*)

6. Coronary Artery Bypass Graft Surgery: Recommendations

6.1. CABG in Patients With STEMI

CLASS I

1. Urgent CABG is indicated in patients with STEMI and coronary anatomy not amenable to PCI who have ongoing or recurrent ischemia, cardiogenic shock, severe HF, or other high-risk features (150–152). (*Level of Evidence: B*)
2. CABG is recommended in patients with STEMI at time of operative repair of mechanical defects (153–157). (*Level of Evidence: B*)

CLASS IIa

1. The use of mechanical circulatory support is reasonable in patients with STEMI who are hemodynamically unstable and require urgent CABG. (*Level of Evidence: C*)

CLASS IIb

1. Emergency CABG within 6 hours of symptom onset may be considered in patients with STEMI who do not have cardiogenic shock and are not candidates for PCI or fibrinolytic therapy. (*Level of Evidence: C*)

6.2. Timing of Urgent CABG in Patients With STEMI in Relation to Use of Antiplatelet Agents

CLASS I

1. Aspirin should not be withheld before urgent CABG (158). (*Level of Evidence: C*)
2. Clopidogrel or ticagrelor should be discontinued at least 24 hours before urgent on-pump CABG, if possible (159–163). (*Level of Evidence: B*)
3. Short-acting intravenous GP IIb/IIIa receptor antagonists (epitifibatide, tirofiban) should be discontinued at least 2 to 4 hours before urgent CABG (164,165). (*Level of Evidence: B*)
4. Abciximab should be discontinued at least 12 hours before urgent CABG (137). (*Level of Evidence: B*)

CLASS IIb

1. Urgent off-pump CABG within 24 hours of clopidogrel or ticagrelor administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding (160,166–168). (*Level of Evidence: B*)
2. Urgent CABG within 5 days of clopidogrel or ticagrelor administration or within 7 days of prasugrel administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding. (*Level of Evidence: C*)

7. Routine Medical Therapies: Recommendations

7.1. Beta Blockers

CLASS I

1. Oral beta blockers should be initiated in the first 24 hours in patients with STEMI who do not have any of the following: signs of HF, evidence of a low-output state, increased risk for cardiogenic shock,^{||} or other contraindications to use of oral beta blockers (PR interval more than 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airways disease) (169–171). (*Level of Evidence: B*)
2. Beta blockers should be continued during and after hospitalization for all patients with STEMI and with no contraindications to their use (172,173). (*Level of Evidence: B*)
3. Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility. (*Level of Evidence: C*)

CLASS IIa

1. It is reasonable to administer intravenous beta blockers at the time of presentation to patients with STEMI and no contraindications.

^{||}Risk factors for cardiogenic shock (the greater the number of risk factors present, the higher the risk of developing cardiogenic shock) are age >70 years, systolic blood pressure <120 mm Hg, sinus tachycardia >110 bpm or heart rate <60 bpm, and increased time since onset of symptoms of STEMI.

dications to their use who are hypertensive or have ongoing ischemia (169–171). (Level of Evidence: B)

7.2. Renin-Angiotensin-Aldosterone System

Inhibitors

CLASS I

1. An angiotensin-converting enzyme inhibitor should be administered within the first 24 hours to all patients with STEMI with anterior location, HF, or ejection fraction less than or equal to 0.40, unless contraindicated (174–177). (Level of Evidence: A)
2. An angiotensin receptor blocker should be given to patients with STEMI who have indications for but are intolerant of angiotensin-converting enzyme inhibitors (178,179). (Level of Evidence: B)
3. An aldosterone antagonist should be given to patients with STEMI and no contraindications who are already receiving an angiotensin-converting enzyme inhibitor and beta blocker and who have an ejection fraction less than or equal to 0.40 and either symptomatic HF or diabetes mellitus (180). (Level of Evidence: B)

CLASS IIa

1. Angiotensin-converting enzyme inhibitors are reasonable for all patients with STEMI and no contraindications to their use (181–183). (Level of Evidence: A)

7.3. Lipid Management

CLASS I

1. High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use (184,188,189). (Level of Evidence: B)

CLASS IIa

1. It is reasonable to obtain a fasting lipid profile in patients with STEMI, preferably within 24 hours of presentation. (Level of Evidence: C)

8. Complications After STEMI: Recommendations

8.1. Treatment of Cardiogenic Shock

CLASS I

1. Emergency revascularization with either PCI or CABG is recommended in suitable patients with cardiogenic shock due to pump failure after STEMI irrespective of the time delay from MI onset (54,190,191). (Level of Evidence: B)
2. In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI and cardiogenic shock who are unsuitable candidates for either PCI or CABG (16,192,193). (Level of Evidence: B)

CLASS IIa

1. The use of intra-aortic balloon pump counterpulsation can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy (194–197,197a). (Level of Evidence: B)

CLASS IIa

1. Alternative left ventricular (LV) assist devices for circulatory support may be considered in patients with refractory cardiogenic shock. (Level of Evidence: C)

8.2. Implantable Cardioverter-Defibrillator Therapy Before Discharge

CLASS I

1. Implantable cardioverter-defibrillator therapy is indicated before discharge in patients who develop sustained ventricular tachycardia/ventricular fibrillation more than 48 hours after STEMI, provided the arrhythmia is not due to transient or reversible ischemia, reinfarction, or metabolic abnormalities (198–200). (Level of Evidence: B)

8.3. Pacing in STEMI

CLASS I

1. Temporary pacing is indicated for symptomatic bradyarrhythmias unresponsive to medical treatment. (Level of Evidence: C)

8.4. Management of Pericarditis After STEMI

CLASS I

1. Aspirin is recommended for treatment of pericarditis after STEMI (201). (Level of Evidence: B)

CLASS IIa

1. Administration of acetaminophen, colchicine, or narcotic analgesics may be reasonable if aspirin, even in higher doses, is not effective. (Level of Evidence: C)

CLASS III: HARM

1. Glucocorticoids and nonsteroidal antiinflammatory drugs are potentially harmful for treatment of pericarditis after STEMI (202,203). (Level of Evidence: B)

8.5. Anticoagulation[¶]

CLASS I

1. Anticoagulant therapy with a vitamin K antagonist should be provided to patients with STEMI and atrial fibrillation with CHADS₂[#] score greater than or equal to 2, mechanical heart valves, venous thromboembolism, or hypercoagulable disorder. (Level of Evidence: C)
2. The duration of triple-antithrombotic therapy with a vitamin K antagonist, aspirin, and a P2Y₁₂ receptor inhibitor should be

[¶]These recommendations apply to patients who receive intracoronary stents during PCI for STEMI. Among individuals with STEMI who do not receive an intracoronary stent, the duration of DAPT beyond 14 days has not been studied adequately for patients who undergo balloon angioplasty alone, are treated with fibrinolysis alone, or do not receive reperfusion therapy. In this subset of patients with STEMI who do not receive an intracoronary stent, the threshold for initiation of oral anticoagulation for secondary prevention, either alone or in combination with aspirin, may be lower, especially if a shorter duration (i.e., 14 days) of DAPT is planned (204).

[#]CHADS₂ (Congestive heart failure, Hypertension, Age \geq 75 years, Diabetes mellitus, previous Stroke/transient ischemic attack [doubled risk weight]) score.

minimized to the extent possible to limit the risk of bleeding.**
(Level of Evidence: C)

CLASS IIa

1. Anticoagulant therapy with a vitamin K antagonist is reasonable for patients with STEMI and asymptomatic LV mural thrombi. (Level of Evidence: C)

CLASS IIa

1. Anticoagulant therapy may be considered for patients with STEMI and anterior apical akinesis or dyskinesis. (Level of Evidence: C)
2. Targeting vitamin K antagonist therapy to a lower international normalized ratio (e.g., 2.0 to 2.5) might be considered in patients with STEMI who are receiving DAPT. (Level of Evidence: C)

9. Risk Assessment After STEMI: Recommendations

9.1. Use of Noninvasive Testing for Ischemia Before Discharge

CLASS I

1. Noninvasive testing for ischemia should be performed before discharge to assess the presence and extent of inducible ischemia in patients with STEMI who have not had coronary angiography and do not have high-risk clinical features for which coronary angiography would be warranted (209–211). (Level of Evidence: B)

CLASS IIa

1. Noninvasive testing for ischemia might be considered before discharge to evaluate the functional significance of a noninfarct artery stenosis previously identified at angiography. (Level of Evidence: C)
2. Noninvasive testing for ischemia might be considered before discharge to guide the postdischarge exercise prescription. (Level of Evidence: C)

9.2. Assessment of LV Function

CLASS I

1. LV ejection fraction should be measured in all patients with STEMI. (Level of Evidence: C)

9.3. Assessment of Risk for Sudden Cardiac Death

CLASS I

1. Patients with an initially reduced LV ejection fraction who are possible candidates for implantable cardioverter-defibrillator therapy should undergo reevaluation of LV ejection fraction 40 or more days after discharge (212–215). (Level of Evidence: B)

**Individual circumstances will vary and depend on the indications for triple therapy and the type of stent placed during PCI. After this initial treatment period, consider therapy with a vitamin K antagonist plus a single antiplatelet agent. For patients treated with fibrinolysis, consider triple therapy for 14 days, followed by a vitamin K antagonist plus a single antiplatelet agent (205–208).

10. Posthospitalization Plan of Care: Recommendations

CLASS I

1. Posthospital systems of care designed to prevent hospital readmissions should be used to facilitate the transition to effective, coordinated outpatient care for all patients with STEMI (216–220). (Level of Evidence: B)
2. Exercise-based cardiac rehabilitation/secondary prevention programs are recommended for patients with STEMI (221–224). (Level of Evidence: B)
3. A clear, detailed, and evidence-based plan of care that promotes medication adherence, timely follow-up with the health-care team, appropriate dietary and physical activities, and compliance with interventions for secondary prevention should be provided to patients with STEMI. (Level of Evidence: C)
4. Encouragement and advice to stop smoking and to avoid secondhand smoke should be provided to patients with STEMI (225–228). (Level of Evidence: A) 79,185–187

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References

1. ACCF/AHA Task Force on Practice Guidelines. Manual for ACCF/AHA Guideline Writing Committees: Methodologies and Policies from the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association. 2006. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/professional/StatementsGuidelines/PoliciesDevelopment/Development/Methodologies-and-Policies-from-the-CCAHA-Task-Force-on-Practice-Guidelines_UCM_320470_Article.jsp. Accessed July 26, 2012.

- Eden J, Levit L, Berg A, et al, eds; Committee on Standards for Systematic Reviews of Comparative Effectiveness Research; Institute of Medicine. *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: The National Academies Press; 2011.
- Graham R, Mancher M, Miller Wolman D, et al, eds; Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Institute of Medicine. *Clinical Practice Guidelines We Can Trust*. Washington, DC: The National Academies Press; 2011.
- O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2012 Dec 17 [E-pub ahead of print], doi:10.1016/j.jacc.2012.11.019.
- 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:e1-212.
- 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. *J Am Coll Cardiol*. 2008;51:210-47.
- Kushner FG, Hand M, Smith SC Jr, 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. *J Am Coll Cardiol*. 2009;54:2205-41. Erratum in: *J Am Coll Cardiol*. 2010;54:2464.
- Aguirre FV, Varghese JJ, Kelley MP, et al. Rural interhospital transfer of ST-elevation myocardial infarction patients for percutaneous coronary revascularization: the Stat Heart Program. *Circulation*. 2008;117:1145-52.
- 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.
- Jollis JG, Roettig ML, Aluko AO, et al. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. *JAMA*. 2007;298:2371-80.
- 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.
- Dieker H-J, Liem SSB, El Aidi H, et al. Pre-hospital triage for primary angioplasty: direct referral to the intervention center versus interhospital transport. *J Am Coll Cardiol Interv*. 2010;3:705-11.
- Diercks DB, Kontos MC, Chen AY, et al. Utilization and impact of pre-hospital electrocardiograms for patients with acute ST-segment elevation myocardial infarction: data from the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry. *J Am Coll Cardiol*. 2009;53:161-6.
- Rokos IC, French WJ, Koenig WJ, et al. Integration of pre-hospital electrocardiograms and ST-elevation myocardial infarction receiving center (SRC) networks: impact on door-to-balloon times across 10 independent regions. *J Am Coll Cardiol Interv*. 2009;2:339-46.
- Sørensen JT, Terkelsen CJ, Nørgaard BL, et al. Urban and rural implementation of pre-hospital diagnosis and direct referral for primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction. *Eur Heart J*. 2011;32:430-6.
- Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. *Lancet*. 1994;343:311-22. Erratum in: *Lancet*. 1994;343:742.
- 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.
- Andersen HR, Nielsen TT, Vesterlund T, et al. Danish multicenter randomized study on fibrinolytic therapy versus acute coronary angioplasty in acute myocardial infarction: rationale and design of the DANish trial in Acute Myocardial Infarction-2 (DANAMI-2). *Am Heart J*. 2003;146:234-41.
- Dalby M, Bouzamondo A, Lechat P, et al. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. *Circulation*. 2003;108:1809-14.
- Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med*. 2003;349:733-42.
- Nielsen PH, Terkelsen CJ, Nielsen TT, et al. System delay and timing of intervention in acute myocardial infarction (from the Danish Acute Myocardial Infarction-2 [DANAMI-2] trial). *Am J Cardiol*. 2011;108:776-81.
- Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything? *Am J Cardiol*. 2003;92:824-6.
- 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.
- Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet*. 1996;348:771-5.
- Chareonthaitawee P, Gibbons RJ, Roberts RS, et al., for the CORE Investigators (Collaborative Organisation for RheothRx Evaluation). The impact of time to thrombolytic treatment on outcome in patients with acute myocardial infarction. *Heart*. 2000;84:142-8.
- McNamara RL, Herrin J, Wang Y, et al. Impact of delay in door-to-needle time on mortality in patients with ST-segment elevation myocardial infarction. *Am J Cardiol*. 2007;100:1227-32.
- Milavetz JJ, Giebel DW, Christian TF, et al. Time to therapy and salvage in myocardial infarction. *J Am Coll Cardiol*. 1998;31:1246-51.
- Newby LK, Rutsch WR, Calif RM, et al., GUSTO-1 Investigators. Time from symptom onset to treatment and outcomes after thrombolytic therapy. *J Am Coll Cardiol*. 1996;27:1646-55.
- Schömig A, Mehilli J, Antoniucci D, et al. Mechanical reperfusion in patients with acute myocardial infarction presenting more than 12 hours from symptom onset: a randomized controlled trial. *JAMA*. 2005;293:2865-72.
- Gierlotka M, Gasior M, Wilczek K, et al. Reperfusion by primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction within 12 to 24 hours of the onset of symptoms (from a prospective national observational study [PL-ACS]). *Am J Cardiol*. 2011;107:501-8.
- Peberdy MA, Callaway CW, Neumar RW, et al. Part 9: post-cardiac arrest care: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122:S768-86. Errata in: *Circulation*. 2011;124:e403 and *Circulation*. 2011;123:e237.
- Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002;346:557-63.
- Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med*. 2002;346:549-56. Erratum in: *N Engl J Med*. 2002;346:1756.
- Nichol G, Aufderheide TP, Eigel B, et al. Regional systems of care for out-of-hospital cardiac arrest: a policy statement from the American Heart Association. *Circulation*. 2010;121:709-29. Erratum in: *Circulation*. 2010;122:e439.
- Bendz B, Eritsland J, Nakstad AR, et al. Long-term prognosis after out-of-hospital cardiac arrest and primary percutaneous coronary intervention. *Resuscitation*. 2004;63:49-53.
- Borger van der Burg AE, Bax JJ, Boersma E, et al. Impact of percutaneous coronary intervention or coronary artery bypass grafting on outcome after nonfatal cardiac arrest outside the hospital. *Am J Cardiol*. 2003;91:785-9.
- Bulut S, Aengevaeren WR, Luijten HJ, et al. Successful out-of-hospital cardiopulmonary resuscitation: what is the optimal in-hospital treatment strategy? *Resuscitation*. 2000;47:155-61.
- Garot P, Lefevre T, Eltchaninoff H, et al. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. *Circulation*. 2007;115:1354-62.
- Gorjup V, Radsel P, Kocjancic ST, et al. Acute ST-elevation myocardial infarction after successful cardiopulmonary resuscitation. *Resuscitation*. 2007;72:379-85.
- Hosmane VR, Mustafa NG, Reddy VK, et al. Survival and neurologic recovery in patients with ST-segment elevation myocardial infarction resuscitated from cardiac arrest. *J Am Coll Cardiol*. 2009;53:409-15.

41. Kahn JK, Glazier S, Swor R, et al. Primary coronary angioplasty for acute myocardial infarction complicated by out-of-hospital cardiac arrest. *Am J Cardiol.* 1995;75:1069–70.
42. Keelan PC, Bunch TJ, White RD, et al. Early direct coronary angioplasty in survivors of out-of-hospital cardiac arrest. *Am J Cardiol.* 2003;91:1461–3, A6.
43. Kern KB, Rahman O. Emergent percutaneous coronary intervention for resuscitated victims of out-of-hospital cardiac arrest. *Catheter Cardiovasc Interv.* 2010;75:616–24.
44. Marcusohn E, Markusohn E, Roguin A, et al. Primary percutaneous coronary intervention after out-of-hospital cardiac arrest: patients and outcomes. *Isr Med Assoc J.* 2007;9:257–9.
45. Pleskot M, Babu A, Hazukova R, et al. Out-of-hospital cardiac arrests in patients with acute ST elevation myocardial infarctions in the East Bohemian region over the period 2002–2004. *Cardiology.* 2008;109:41–51.
46. Quintero-Moran B, Moreno R, Villarreal S, et al. Percutaneous coronary intervention for cardiac arrest secondary to ST-elevation acute myocardial infarction: influence of immediate paramedical/medical assistance on clinical outcome. *J Invasive Cardiol.* 2006;18:269–72.
47. Richling N, Herkner H, Holzer M, et al. Thrombolytic therapy vs primary percutaneous intervention after ventricular fibrillation cardiac arrest due to acute ST-segment elevation myocardial infarction and its effect on outcome. *Am J Emerg Med.* 2007;25:545–50.
48. Spaulding CM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med.* 1997;336:1629–33.
49. Werling M, Thorén A-B, Axelsson C, et al. Treatment and outcome in post-resuscitation care after out-of-hospital cardiac arrest when a modern therapeutic approach was introduced. *Resuscitation.* 2007;73:40–5.
50. Zijlstra F, Hoorntje JC, de Boer MJ, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. *N Engl J Med.* 1999;341:1413–9.
51. The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. *N Engl J Med.* 1997;336:1621–8. Erratum in: *N Engl J Med.* 1997;337:287.
52. Grzybowski M, Clements EA, Parsons L, et al. Mortality benefit of immediate revascularization of acute ST-segment elevation myocardial infarction in patients with contraindications to thrombolytic therapy: a propensity analysis. *JAMA.* 2003;290:1891–8.
53. Zahn R, Schuster S, Schiele R, et al; Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Study Group. Comparison of primary angioplasty with conservative therapy in patients with acute myocardial infarction and contraindications for thrombolytic therapy. *Catheter Cardiovasc Interv.* 1999;46:127–33.
54. Hochman JS, Sleeper LA, Webb JG, et al., for the SHOCK Investigators. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med.* 1999;341:625–34.
55. Hochman JS, Lamas GA, Buller CE, et al. Coronary intervention for persistent occlusion after myocardial infarction. *N Engl J Med.* 2006;355:2395–407.
56. Thune JJ, Hoefsten DE, Lindholm MG, et al. Simple risk stratification at admission to identify patients with reduced mortality from primary angioplasty. *Circulation.* 2005;112:2017–21.
57. Wu AH, Parsons L, Every NR, et al. Hospital outcomes in patients presenting with congestive heart failure complicating acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMII-2). *J Am Coll Cardiol.* 2002;40:1389–94.
58. Hannan EL, Samadashvili Z, Walford G, et al. Culprit vessel percutaneous coronary intervention versus multivessel and staged percutaneous coronary intervention for ST-segment elevation myocardial infarction patients with multivessel disease. *J Am Coll Cardiol Intv.* 2010;3:22–31.
59. Toma M, Buller CE, Westerhout CM, et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. *Eur Heart J.* 2010;31:1701–7.
60. Vlaar PJ, Mahmoud KD, Holmes DR Jr, et al. Culprit vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction: a pairwise and network meta-analysis. *J Am Coll Cardiol.* 2011;58:692–703.
61. 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.
62. Vlaar PJ, Svilaas T, van der Horst IC, 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.
63. 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.
64. Stone GW, Maehara A, Witzenbichler B, et al. Intracoronary abciximab and aspiration thrombectomy in patients with large anterior myocardial infarction: the INFUSE-AMI randomized trial. *JAMA.* 2012;307:1817–26.
65. 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.
66. 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.
67. Spertus JA, Kettelkamp R, Vance C, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. *Circulation.* 2006;113:2803–9.
68. Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol.* 2000;35:1288–94.
69. 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. *Circulation.* 2007;115:813–8.
70. Park D-W, Park S-W, Park K-H, et al. Frequency of and risk factors for stent thrombosis after drug-eluting stent implantation during long-term follow-up. *Am J Cardiol.* 2006;98:352–6.
71. Jeremias A, Sylvia B, Bridges J, et al. Stent thrombosis after successful sirolimus-eluting stent implantation. *Circulation.* 2004;109:1930–2.
72. Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. *J Am Coll Cardiol.* 2006;48:2584–91.
73. Nasser M, Kapeliovich M, Markiewicz W. Late thrombosis of sirolimus-eluting stents following noncardiac surgery. *Catheter Cardiovasc Interv.* 2005;65:516–9.
74. Jolly SS, Pogue J, Haladyn K, et al. Effects of aspirin dose on ischaemic events and bleeding after percutaneous coronary intervention: insights from the PCI-CURE study. *Eur Heart J.* 2009;30:900–7.
75. Barnathan ES, Schwartz JS, Taylor L, et al. Aspirin and dipyridamole in the prevention of acute coronary thrombosis complicating coronary angioplasty. *Circulation.* 1987;76:125–34.
76. Mehta SR, Bassand J-P, Chrolavicius S, et al. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. *N Engl J Med.* 2010;363:930–42. Erratum in: *N Engl J Med.* 2010;363:1585.
77. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ.* 2002;324:71–86. Erratum in: *BMJ.* 2002;324:141.
78. Schömig A, Neumann FJ, Kastrati A, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. *N Engl J Med.* 1996;334:1084–9.
79. Deleted in press.
80. Smith SC Jr, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *J Am Coll Cardiol.* 2011;58:2432–46.
81. Patti G, Bárczi G, Orlic D, et al. Outcome comparison of 600- and 300-mg loading doses of clopidogrel in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: results from the ARMYDA-6 MI (Antiplatelet therapy

- for Reduction of MYocardial Damage during Angioplasty-Myocardial Infarction) randomized study. *J Am Coll Cardiol.* 2011;58:1592-9.
82. Mehta SR, Tanguay J-F, Eikelboom JW, et al. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. *Lancet.* 2010;376:1233-43.
83. 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.
84. Steg PG, James S, Harrington RA, et al. Ticagrelor versus clopidogrel in patients with ST-elevation acute coronary syndromes intended for reperfusion with primary percutaneous coronary intervention: a Platelet Inhibition and Patient Outcomes (PLATO) trial subgroup analysis. *Circulation.* 2010;122:2131-41.
85. 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.
86. Serebruany VL, Steinhubl SR, Berger PB, et al. Analysis of risk of bleeding complications after different doses of aspirin in 192,036 patients enrolled in 31 randomized controlled trials. *Am J Cardiol.* 2005;95:1218-22.
87. Steinhubl SR, Bhatt DL, Brennan DM, et al. Aspirin to prevent cardiovascular disease: the association of aspirin dose and clopidogrel with thrombosis and bleeding. *Ann Intern Med.* 2009;150:379-86.
88. Brener SJ, Barr LA, Burchenal JE, et al; for the ReoPro and Primary PTCA Organization and Randomized Trial (RAPPORT) Investigators. Randomized, placebo-controlled trial of platelet glycoprotein IIb/IIIa blockade with primary angioplasty for acute myocardial infarction. *Circulation.* 1998;98:734-41.
89. Stone GW, Grines CL, Cox DA, et al. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. *N Engl J Med.* 2002;346:957-66.
90. Montalescot G, Barragan P, Wittenberg O, et al. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. *N Engl J Med.* 2001;344:1895-903.
91. ten Berg JM, van 't Hof AWJ, Dill T, et al. Effect of early, pre-hospital initiation of high bolus dose tirofiban in patients with ST-segment elevation myocardial infarction on short- and long-term clinical outcome. *J Am Coll Cardiol.* 2010;55:2446-55.
92. 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.
93. Akerblom A, James SK, Koutouzis M, et al. Eptifibatid is noninferior to abciximab in primary percutaneous coronary intervention: results from the SCAAR (Swedish Coronary Angiography and Angioplasty Registry). *J Am Coll Cardiol.* 2010;56:470-5.
94. 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.
95. Ellis SG, Tendera M, de Belder MA, et al. 1-Year survival in a randomized trial of facilitated reperfusion: results from the FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) trial. *J Am Coll Cardiol Intv.* 2009;2:909-16.
96. Montalescot G, Borentain M, Payot L, et al. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. *JAMA.* 2004;292:362-6.
97. Maioli M, Bellandi F, Leoncini M, et al. Randomized early versus late abciximab in acute myocardial infarction treated with primary coronary intervention (RELAX-AMI Trial). *J Am Coll Cardiol.* 2007;49:1517-24.
98. Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. *Lancet.* 2006;367:579-88. Erratum in: *Lancet.* 2006;367:1656.
99. van't Hof AWJ, 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.
100. El Khoury C, Dubien P-Y, Mercier C, et al. Prehospital high-dose tirofiban in patients undergoing primary percutaneous intervention: the AGIR-2 study. *Arch Cardiovasc Dis.* 2010;103:285-92.
101. De Luca G, Bellandi F, Huber K, et al. Early glycoprotein IIb-IIIa inhibitors in primary angioplasty-abciximab long-term results (EGYPT-ALT) cooperation: individual patient's data meta-analysis. *J Thromb Haemost.* 2011;9:2361-70.
102. 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.
103. Bellandi F, Maioli M, Gallopin M, et al. Increase of myocardial salvage and left ventricular function recovery with intracoronary abciximab downstream of the coronary occlusion in patients with acute myocardial infarction treated with primary coronary intervention. *Catheter Cardiovasc Interv.* 2004;62:186-92.
104. Romagnoli E, Burzotta F, Trani C, et al. Angiographic evaluation of the effect of intracoronary abciximab administration in patients undergoing urgent PCI. *Int J Cardiol.* 2005;105:250-5.
105. Iversen A, Galatius S, Jensen JS. The optimal route of administration of the glycoprotein IIb/IIIa receptor antagonist abciximab during percutaneous coronary intervention: intravenous versus intracoronary. *Curr Cardiol Rev.* 2008;4:293-9.
106. Kakkak AK, Moustapha A, Hanley HG, et al. Comparison of intracoronary vs. intravenous administration of abciximab in coronary stenting. *Catheter Cardiovasc Interv.* 2004;61:31-4.
107. Wöhrle J, Grebe OC, Nusser T, et al. Reduction of major adverse cardiac events with intracoronary compared with intravenous bolus application of abciximab in patients with acute myocardial infarction or unstable angina undergoing coronary angioplasty. *Circulation.* 2003;107:1840-3.
108. Bertrand OF, Rodés-Cabau J, Larose E, et al. Intracoronary compared to intravenous abciximab and high-dose bolus compared to standard dose in patients with ST-segment elevation myocardial infarction undergoing transradial primary percutaneous coronary intervention: a two-by-two factorial placebo-controlled randomized study. *Am J Cardiol.* 2010;105:1520-7.
109. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med.* 2008;358:2218-30.
110. Yusuf S, Mehta SR, Chrolavicius S, et al. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. *JAMA.* 2006;295:1519-30.
111. AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. *Lancet.* 1988;1:545-9.
112. EMERAS (Estudio Multicéntrico Estreptoquinasa Repúblicas de América del Sur) Collaborative Group. Randomised trial of late thrombolysis in patients with suspected acute myocardial infarction. *Lancet.* 1993;342:767-72.
113. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet.* 1988;2:349-60.
114. Late Assessment of Thrombolytic Efficacy (LATE) study with alteplase 6-24 hours after onset of acute myocardial infarction. *Lancet.* 1993;342:759-66.
115. Rossi P, Bolognese L. Comparison of intravenous urokinase plus heparin versus heparin alone in acute myocardial infarction: Urokinasi per via Sistemica nell'Infarto Miocardico (USIM) Collaborative Group. *Am J Cardiol.* 1991;68:585-92.
116. The I.S.A.M. Study Group. A prospective trial of Intravenous Streptokinase in Acute Myocardial infarction (I.S.A.M.): mortality, morbidity, and infarct size at 21 days. *N Engl J Med.* 1986;314:1465-71.
117. de Winter RJ, Verouden NJW, Wellens HJJ, et al. A new ECG sign of proximal LAD occlusion. *N Engl J Med.* 2008;359:2071-3.
118. The TIMI IIIA Investigators. Early effects of tissue-type plasminogen activator added to conventional therapy on the culprit coronary lesion in patients presenting with ischemic cardiac pain at rest: results of the Thrombolysis in Myocardial Ischemia (TIMI IIIA) Trial. *Circulation.* 1993;87:38-52.
119. Barrabés JA, Figueras J, Moure C, et al. Prognostic value of lead aVR in patients with a first non-ST-segment elevation acute myocardial infarction. *Circulation.* 2003;108:814-9.
120. Jong G-P, Ma T, Chou P, et al. Reciprocal changes in 12-lead electrocardiography can predict left main coronary artery lesion in patients with acute myocardial infarction. *Int Heart J.* 2006;47:13-20.

121. Chen ZM, Jiang LX, Chen YP, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet*. 2005;366:1607–21.
122. 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.
123. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med*. 1993;329:673–82.
124. Antman EM, Morrow DA, McCabe CH, et al. Enoxaparin versus unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction. *N Engl J Med*. 2006;354:1477–88.
125. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *Lancet*. 2001;358:605–13.
126. Ross AM, Molhoek P, Lundergan C, et al. Randomized comparison of enoxaparin, a low-molecular-weight heparin, with unfractionated heparin adjunctive to recombinant tissue plasminogen activator thrombolysis and aspirin: second trial of Heparin and Aspirin Reperfusion Therapy (HART II). *Circulation*. 2001;104:648–52.
127. Antman EM, Louwrenburg HW, Baars HF, et al. Enoxaparin as adjunctive antithrombin therapy for ST-elevation myocardial infarction: results of the ENTIRE-Thrombolysis in Myocardial Infarction (TIMI) 23 Trial. *Circulation*. 2002;105:1642–9. Erratum in: *Circulation*. 2002;105:2799.
128. Hochman JS, Sleeper LA, White HD, et al. One-year survival following early revascularization for cardiogenic shock. *JAMA*. 2001;285:190–2.
129. 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.
130. Sutton AGC, Campbell PG, Graham R, et al. A randomized trial of rescue angioplasty versus a conservative approach for failed fibrinolysis in ST-segment elevation myocardial infarction: the Middlesbrough Early Revascularization to Limit Infarction (MERLIN) trial. *J Am Coll Cardiol*. 2004;44:287–96.
- 130a. Gibson CM, Murphy SA, Rizzo MJ, et al; Thrombolysis In Myocardial Infarction (TIMI) Study Group. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. *Circulation*. 1999;99:1945–50.
- 130b. Gibson CM, Cannon CP, Murphy SA, et al. Relationship of the TIMI myocardial perfusion grades, flow grades, frame count, and percutaneous coronary intervention to long-term outcomes after thrombolytic administration in acute myocardial infarction. *Circulation*. 2002;105:1909–13.
- 130c. Sutton AG, Campbell PG, Price DJ, et al. Failure of thrombolysis by streptokinase: detection with a simple electrocardiographic method. *Heart*. 2000;84:149–56.
131. 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.
132. Collet J-P, 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.
133. Bøhmer E, Hoffmann P, Abdelnoor M, et al. Efficacy and safety of immediate angioplasty versus ischemia-guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances results of the NORDISTEMI (NORwegian study on DIstrict treatment of ST-elevation myocardial infarction). *J Am Coll Cardiol*. 2010;55:102–10.
134. Borgia F, Goodman SG, Halvorsen S, et al. Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis. *Eur Heart J*. 2010;31:2156–69.
135. 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.
136. 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.
137. Fernandez-Avilés F, Alonso JJ, Castro-Beiras A, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet*. 2004;364:1045–53.
138. White HD. Systems of care: need for hub-and-spoke systems for both primary and systematic percutaneous coronary intervention after fibrinolysis. *Circulation*. 2008;118:219–22.
139. Steg PG, Kerner A, Van de Werf F, et al. Impact of in-hospital revascularization on survival in patients with non-ST-elevation acute coronary syndrome and congestive heart failure. *Circulation*. 2008;118:1163–71.
140. Steg PG, Dabbous OH, Feldman LJ, et al. Determinants and prognostic impact of heart failure complicating acute coronary syndromes: observations from the Global Registry of Acute Coronary Events (GRACE). *Circulation*. 2004;109:494–9.
141. Erne P, Schoenenberger AW, Burckhardt D, et al. Effects of percutaneous coronary interventions in silent ischemia after myocardial infarction: the SWISSI II randomized controlled trial. *JAMA*. 2007;297:1985–91.
142. Madsen JK, Grande P, Saunamäki K, et al. Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI): DANish trial in Acute Myocardial Infarction. *Circulation*. 1997;96:748–55.
143. D’Souza SP, Mamas MA, Fraser DG, et al. Routine early coronary angioplasty versus ischaemia-guided angioplasty after thrombolysis in acute ST-elevation myocardial infarction: a meta-analysis. *Eur Heart J*. 2011;32:972–82.
144. Gupta M, Chang W-C, Van de Werf F, et al. International differences in in-hospital revascularization and outcomes following acute myocardial infarction: a multilevel analysis of patients in ASSENT-2. *Eur Heart J*. 2003;24:1640–50.
145. Gibson CM, Karha J, Murphy SA, et al. Early and long-term clinical outcomes associated with reinfarction following fibrinolytic administration in the Thrombolysis In Myocardial Infarction trials. *J Am Coll Cardiol*. 2003;42:7–16.
146. Ioannidis JPA, Katritsis DG. Percutaneous coronary intervention for late reperfusion after myocardial infarction in stable patients. *Am Heart J*. 2007;154:1065–71.
147. Steg PG, Thuare C, Himbert D, et al. DECOPI (DEsobstruction COronaire en Post-Infarctus): a randomized multi-centre trial of occluded artery angioplasty after acute myocardial infarction. *Eur Heart J*. 2004;25:2187–94.
148. Wilson SH, Bell MR, Rihal CS, et al. Infarct artery reocclusion after primary angioplasty, stent placement, and thrombolytic therapy for acute myocardial infarction. *Am Heart J*. 2001;141:704–10.
149. Gibson CM, Murphy SA, Montalescot G, et al. Percutaneous coronary intervention in patients receiving enoxaparin or unfractionated heparin after fibrinolytic therapy for ST-segment elevation myocardial infarction in the ExTRACT-TIMI 25 trial. *J Am Coll Cardiol*. 2007;49:2238–46.
150. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease: long-term CASS experience. *Circulation*. 1995;91:2325–34.
151. Hochman JS, Buller CE, Sleeper LA, et al. Cardiogenic shock complicating acute myocardial infarction: etiologies, management and outcome: a report from the SHOCK Trial Registry: SHOULD we emergently revascularize Occluded Coronaries for cardiogenic shock? *J Am Coll Cardiol*. 2000;36:1063–70.
152. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2011;58:e123–210.
153. Dalrymple-Hay MJ, Langley SM, Sami SA, et al. Should coronary artery bypass grafting be performed at the same time as repair of a post-infarct ventricular septal defect? *Eur J Cardiothorac Surg*. 1998;13:286–92.
154. Menon V, Webb JG, Hillis LD, et al. Outcome and profile of ventricular septal rupture with cardiogenic shock after myocardial infarction: a report from the SHOCK Trial Registry: SHOULD we emergently revascularize Occluded Coronaries in cardiogenic shock? *J Am Coll Cardiol*. 2000;36:1110–6.
155. Slater J, Brown RJ, Antonelli TA, et al. Cardiogenic shock due to cardiac free-wall rupture or tamponade after acute myocardial infarction: a report from the SHOCK Trial Registry: Should we emergently revascularize occluded coronaries for cardiogenic shock? *J Am Coll Cardiol*. 2000;36:1117–22.

156. Tavakoli R, Weber A, Vogt P, et al. Surgical management of acute mitral valve regurgitation due to post-infarction papillary muscle rupture. *J Heart Valve Dis.* 2002;11:20-5; discussion 26.
157. Thompson CR, Buller CE, Sleeper LA, et al. Cardiogenic shock due to acute severe mitral regurgitation complicating acute myocardial infarction: a report from the SHOCK Trial Registry: SHould we use emergently revascularize Occluded Coronaries in cardiogenic shock? *J Am Coll Cardiol.* 2000;36:1104-9.
158. Jacob M, Smedira N, Blackstone E, et al. Effect of timing of chronic preoperative aspirin discontinuation on morbidity and mortality in coronary artery bypass surgery. *Circulation.* 2011;123:577-83.
159. Kim JH-J, Newby LK, Clare RM, et al. Clopidogrel use and bleeding after coronary artery bypass graft surgery. *Am Heart J.* 2008;156:886-92.
160. Held C, Asenblad N, Bassand JP, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes undergoing coronary artery bypass surgery: results from the PLATO (Platelet Inhibition and Patient Outcomes) trial. *J Am Coll Cardiol.* 2011;57:672-84.
161. Nijjer SS, Watson G, Athanasiou T, et al. Safety of clopidogrel being continued until the time of coronary artery bypass grafting in patients with acute coronary syndrome: a meta-analysis of 34 studies. *Eur Heart J.* 2011;32:2970-88.
162. Barker CM, Anderson HV. Acute coronary syndromes: don't bypass the clopidogrel. *J Am Coll Cardiol.* 2009;53:1973-4.
163. Ebrahimi R, Dyke C, Mehran R, et al. Outcomes following pre-operative clopidogrel administration in patients with acute coronary syndromes undergoing coronary artery bypass surgery: the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial. *J Am Coll Cardiol.* 2009;53:1965-72.
164. Bizzarri F, Scolletta S, Tucci E, et al. Perioperative use of tirofiban hydrochloride (Aggrastat) does not increase surgical bleeding after emergency or urgent coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 2001;122:1181-5.
165. Dyke CM, Bhatia D, Lorenz TJ, et al. Immediate coronary artery bypass surgery after platelet inhibition with eptifibatid: results from PURSUIT: Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrelin Therapy. *Ann Thorac Surg.* 2000;70:866-71; discussion 871-2.
166. Shim JK, Choi YS, Oh YJ, et al. Effects of preoperative aspirin and clopidogrel therapy on perioperative blood loss and blood transfusion requirements in patients undergoing off-pump coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg.* 2007;134:59-64.
167. Woo YJ, Grand T, Valettas N. Off-pump coronary artery bypass grafting attenuates postoperative bleeding associated with preoperative clopidogrel administration. *Heart Surg Forum.* 2003;6:282-5.
168. Maltais S, Perrault LP, Do Q-B. Effect of clopidogrel on bleeding and transfusions after off-pump coronary artery bypass graft surgery: impact of discontinuation prior to surgery. *Eur J Cardiothorac Surg.* 2008;34:127-31.
169. Chen ZM, Pan HC, Chen YP, et al. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet.* 2005;366:1622-32.
170. Roberts R, Rogers WJ, Mueller HS, et al. Immediate versus deferred beta-blockade following thrombolytic therapy in patients with acute myocardial infarction: results of the Thrombolysis In Myocardial Infarction (TIMI) II-B Study. *Circulation.* 1991;83:422-37.
171. First International Study of Infarct Survival Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. *Lancet.* 1986;2:57-66.
172. A randomized trial of propranolol in patients with acute myocardial infarction, I: mortality results. *JAMA.* 1982;247:1707-14.
173. Freemantle N, Cleland J, Young P, et al. beta Blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ.* 1999;318:1730-7.
174. Pfeffer MA, Braunwald E, Moyé LA, et al; for the SAVE Investigators. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: results of the Survival and Ventricular Enlargement Trial. *N Engl J Med.* 1992;327:669-77.
175. Ball SG, Hall AS, Murray GD. ACE inhibition, atherosclerosis and myocardial infarction: the AIRE Study in practice: Acute Infarction Ramipril Efficacy Study. *Eur Heart J.* 1994;15 Suppl B:20-5; discussion 26-30.
176. Køber L, Torp-Pedersen C, Carlsen JE, et al; for the Trandolapril Cardiac Evaluation (TRACE) Study Group. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med.* 1995;333:1670-6.
177. Pfeffer MA, Greaves SC, Arnold JM, et al. Early versus delayed angiotensin-converting enzyme inhibition therapy in acute myocardial infarction: the Healing and Early Afterload Reducing Therapy trial. *Circulation.* 1997;95:2643-51.
178. Pfeffer MA, McMurray JJV, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med.* 2003;349:1893-906. Erratum in: *N Engl J Med.* 2004;350:203.
179. Maggioni AP, Fabbri G. VALIANT (VALsartan In Acute myocardial iNfarctiOn) trial. *Expert Opin Pharmacother.* 2005;6:507-12.
180. Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med.* 2003;348:1309-21. Erratum in: *N Engl J Med.* 2003;348:2271.
181. ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. *Circulation.* 1998;97:2202-12.
182. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. *Lancet.* 1994;343:1115-22.
183. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet.* 1995;345:669-85.
184. Cannon CP, Steinberg BA, Murphy SA, et al. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. *J Am Coll Cardiol.* 2006;48:438-45.
185. Deleted in press.
186. Deleted in press.
187. Deleted in press.
188. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet.* 2010;376:1670-81.
189. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004;350:1495-504. Erratum in: *N Engl J Med.* 2006;354:778.
190. Babaev A, Frederick PD, Pasta DJ, et al. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA.* 2005;294:448-54.
191. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA.* 2006;295:2511-5.
192. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation.* 2000;102:2031-7.
193. French JK, Feldman HA, Assmann SF, et al. Influence of thrombolytic therapy, with or without intra-aortic balloon counterpulsation, on 12-month survival in the SHOCK trial. *Am Heart J.* 2003;146:804-10.
194. Barron HV, Every NR, Parsons LS, et al. The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock complicating acute myocardial infarction: data from the National Registry of Myocardial Infarction 2. *Am Heart J.* 2001;141:933-9.
195. Chen EW, Canto JG, Parsons LS, et al. Relation between hospital intra-aortic balloon counterpulsation volume and mortality in acute myocardial infarction complicated by cardiogenic shock. *Circulation.* 2003;108:951-7.
196. Sanborn TA, Sleeper LA, Bates ER, et al. Impact of thrombolysis, intra-aortic balloon pump counterpulsation, and their combination in cardiogenic shock complicating acute myocardial infarction: a report from the SHOCK Trial Registry: SHould we emergently revascularize Occluded Coronaries for cardiogenic shock? *J Am Coll Cardiol.* 2000;36:1123-9.
197. Sjaauw KD, Engström AE, Vis MM, et al. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? *Eur Heart J.* 2009;30:459-68.
- 197a. Ohman EM, Nanas J, Stomel RJ, et al. Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by

- hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS Trial. *J Thromb Thrombolysis*. 2005;19:33–9.
198. Wever EF, Hauer RN, van Capelle FL, et al. Randomized study of implantable defibrillator as first-choice therapy versus conventional strategy in postinfarct sudden death survivors. *Circulation*. 1995;91:2195–203.
199. Siebels J, Kuck KH. Implantable cardioverter defibrillator compared with antiarrhythmic drug treatment in cardiac arrest survivors (the Cardiac Arrest Study Hamburg). *Am Heart J*. 1994;127:1139–44.
200. Connolly SJ, Hallstrom AP, Cappato R, et al; for the AVID, CASH and CIDS studies: Antiarrhythmics vs Implantable Defibrillator study: Cardiac Arrest Study Hamburg: Canadian Implantable Defibrillator Study. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. *Eur Heart J*. 2000;21:2071–8.
201. Berman J, Haffajee CI, Alpert JS. Therapy of symptomatic pericarditis after myocardial infarction: retrospective and prospective studies of aspirin, indomethacin, prednisone, and spontaneous resolution. *Am Heart J*. 1981;101:750–3.
202. Bulkley BH, Roberts WC. Steroid therapy during acute myocardial infarction: a cause of delayed healing and of ventricular aneurysm. *Am J Med*. 1974;56:244–50.
203. Silverman HS, Pfeifer MP. Relation between use of anti-inflammatory agents and left ventricular free wall rupture during acute myocardial infarction. *Am J Cardiol*. 1987;59:363–4.
204. Andreotti F, Testa L, Biondi-Zoccai GGL, et al. Aspirin plus warfarin compared to aspirin alone after acute coronary syndromes: an updated and comprehensive meta-analysis of 25,307 patients. *Eur Heart J*. 2006;27:519–26.
205. You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e531S–e575S.
206. Vandvik PO, Lincoff AM, Gore JM, et al. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e637S–e668S. Erratum in: *Chest*. 2012;141:1129.
207. Lip GYH, Huber K, Andreotti F, et al. Antithrombotic management of atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing coronary stenting: executive summary: a Consensus Document of the European Society of Cardiology Working Group on Thrombosis. *Eur Heart J*. 2010;31:1311–8.
208. Faxon DP, Eikelboom JW, Berger PB, et al. Consensus document: antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North-American perspective. *Thromb Haemost*. 2011;106:572–84.
209. Théroux P, Waters DD, Halphen C, et al. Prognostic value of exercise testing soon after myocardial infarction. *N Engl J Med*. 1979;301:341–5.
210. Villella A, Maggioni AP, Villella M, et al. Prognostic significance of maximal exercise testing after myocardial infarction treated with thrombolytic agents: the GISSI-2 data-base: Gruppo Italiano per lo Studio della Sopravvivenza Nell'Infarto. *Lancet*. 1995;346:523–9.
211. Leppo JA, O'Brien J, Rothendler JA, et al. Dipyridamole-thallium-201 scintigraphy in the prediction of future cardiac events after acute myocardial infarction. *N Engl J Med*. 1984;310:1014–8.
212. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346:877–83.
213. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. *N Engl J Med*. 2004;351:2481–8.
214. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). *J Am Coll Cardiol*. 2008;51:e1–62. Erratum in: *J Am Coll Cardiol*. 2009;53:147.
215. Steinbeck G, Andresen D, Seidl K, et al. Defibrillator implantation early after myocardial infarction. *N Engl J Med*. 2009;361:1427–36.
216. Naylor M, Brooten D, Jones R, et al. Comprehensive discharge planning for the hospitalized elderly: a randomized clinical trial. *Ann Intern Med*. 1994;120:999–1006.
217. Coleman EA, Parry C, Chalmers S, et al. The care transitions intervention: results of a randomized controlled trial. *Arch Intern Med*. 2006;166:1822–8.
218. Young W, Rewa G, Goodman SG, et al. Evaluation of a community-based inner-city disease management program for postmyocardial infarction patients: a randomized controlled trial. *CMAJ*. 2003;169:905–10.
219. Jack BW, Chetty VK, Anthony D, et al. A reengineered hospital discharge program to decrease rehospitalization: a randomized trial. *Ann Intern Med*. 2009;150:178–87.
220. Lappé JM, Muhlestein JB, Lappé DL, et al. Improvements in 1-year cardiovascular clinical outcomes associated with a hospital-based discharge medication program. *Ann Intern Med*. 2004;141:446–53.
221. Leon AS, Franklin BA, Costa F, et al. Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation*. 2005;111:369–76. Erratum in: *Circulation*. 2005;111:1717.
222. Suaya JA, Stason WB, Ades PA, et al. Cardiac rehabilitation and survival in older coronary patients. *J Am Coll Cardiol*. 2009;54:25–33.
223. Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med*. 2004;116:682–92.
224. Goel K, Lennon RJ, Tilbury RT, et al. Impact of cardiac rehabilitation on mortality and cardiovascular events after percutaneous coronary intervention in the community. *Circulation*. 2011;123:2344–52.
225. Wilson K, Gibson N, Willan A, et al. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. *Arch Intern Med*. 2000;160:939–44.
226. Thomson CC, Rigotti NA. Hospital- and clinic-based smoking cessation interventions for smokers with cardiovascular disease. *Prog Cardiovasc Dis*. 2003;45:459–79.
227. Dawood N, Vaccarino V, Reid KJ, et al. Predictors of smoking cessation after a myocardial infarction: the role of institutional smoking cessation programs in improving success. *Arch Intern Med*. 2008;168:1961–7.
228. Shah AM, Pfeffer MA, Hartley LH, et al. Risk of all-cause mortality, recurrent myocardial infarction, and heart failure hospitalization associated with smoking status following myocardial infarction with left ventricular dysfunction. *Am J Cardiol*. 2010;106:911–6.

KEY WORDS: ACCF/AHA Practice Guidelines ■ anticoagulants ■ antiplatelets ■ door-to-balloon ■ fibrinolysis ■ percutaneous coronary intervention ■ reperfusion ■ ST-elevation myocardial infarction.

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

Committee Member	Employment	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Patrick T. O’Gara, Chair	Harvard Medical School—Professor of Medicine	None	None	None	None	None	None	None
Frederick G. Kushner, Vice Chair	Tulane University School of Medicine—Clinical Professor of Medicine; Heart Clinic of Louisiana—Medical Director	None	None	None	None	• Novartis†	None	8.1 8.2
Deborah D. Ascheim	Mount Sinai School of Medicine—Associate Professor; InCHOIR—Clinical Director of Research	None	None	None	None	None	None	None
Donald E. Casey, Jr	Atlantic Health—Chief Medical Officer and Vice President of Quality	None	None	None	None	None	None	None
Mina K. Chung	Cleveland Clinic Foundation—Associate Professor of Medicine	<ul style="list-style-type: none"> • Biotronik† • Boston Scientific† • Nexcura † • PGx† • Sanofi-aventis† • St. Jude Medical† 	None	None	<ul style="list-style-type: none"> • Biotronik† • Boston Scientific† • GlaxoSmithKline† • Medtronic† • Siemens Medical Solutions† • St. Jude Medical† • ZOLL† 	<ul style="list-style-type: none"> • Medtronic† • Boston Scientific† • St. Jude Medical† 	None	4.4.1 5.1.4 7.2 9.5.2
James A. de Lemos	UT Southwestern Medical School—Professor of Medicine	<ul style="list-style-type: none"> • Johnson & Johnson • Tethys • AstraZeneca • Daiichi-Sankyo 	• BMS/Sanofi-aventis	None	<ul style="list-style-type: none"> • Bristol-Myers Squibb (DSMB) • Roche • Merck/Schering-Plough • Daiichi-Sankyo 	None	None	4.4.1 4.4.2 5.1.4.1 5.1.4.2 6.4.1 6.4.2 7.2 9.6 4.3.1
Steven M. Ettinger	Penn State Heart & Vascular Institute—Professor of Medicine and Radiology	None	None	None	• Medtronic§	None	None	4.3.1
James C. Fang	University Hospitals Case Medical Center—Director, Heart Transplantation	<ul style="list-style-type: none"> • Accorda • Novartis • Thoratec 	None	None	None	• Medtronic	None	9.5.4.1
Francis M. Fesmire	Heart Stroke Center—Director	• Abbott	None	None	None	None	• Plaintiff, Missed ACS, 2010	8.3
Barry A. Franklin	William Beaumont Hospital—Director, Cardiac Rehabilitation and Exercise Laboratories	None	None	None	None	None	None	None
Christopher B. Granger	Duke Clinical Research Institute—Director, Cardiac Care Unit; Assistant Professor of Medicine	<ul style="list-style-type: none"> • AstraZeneca • Boehringer Ingelheim‡ • Bristol-Myers Squibb • GlaxoSmithKline • Hoffman La Roche • Novartis • Sanofi-aventis‡ • The Medicines Company 	None	None	<ul style="list-style-type: none"> • Astellas • AstraZeneca • Boehringer Ingelheim‡ • Bristol-Myers Squibb • Eli Lilly • GlaxoSmithKline • Medtronic • Merck • Sanofi-aventis‡ • The Medicines Company 	None	None	4.4.1 6.4.2 9.7.1
Harlan M. Krumholz	Yale University School of Medicine—Professor of Medicine	• United HealthCare (Science Advisory Group)	None	None	None	None	None	None

(Continued)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Jane A. Linderbaum	Mayo Clinic—Assistant Professor of Medicine	None	None	None	None	None	None	None
David A. Morrow	Harvard Medical School—Associate Professor of Medicine	<ul style="list-style-type: none"> ● Beckman-Coulter ● Boehringer Ingelheim ● Daiichi-Sankyo ● Eli Lilly ● Genentech ● Merck ● Novartis ● OrthoClinical Diagnostics/Johnson & Johnson ● Roche Diagnostics ● Sanofi-aventis ● Schering-Plough Research Institute ● Siemens Medical Solutions 	None	None	<ul style="list-style-type: none"> ● AstraZeneca‡ ● Beckman-Coulter‡ ● Daiichi-Sankyo‡ ● Eli Lilly‡ ● GlaxoSmithKline‡ ● Merck‡ ● Nanosphere‡ ● Novartis‡ ● Roche Diagnostics‡ ● Sanofi-aventis‡ ● Schering-Plough Research Institute‡ ● Siemens Medical Solutions‡ ● Singulex‡ 	<ul style="list-style-type: none"> ● AstraZeneca‡ 	None	<ul style="list-style-type: none"> 3.2 4.4.1 4.4.2 5.1 5.1.4.1 6.4.1 6.4.2 7.2 8.2 8.3 9.6
L. Kristin Newby	Duke University Medical Center, Division of Cardiology—Professor of Medicine	<ul style="list-style-type: none"> ● Amgen‡ ● AstraZeneca ● BioVascular ● Johnson & Johnson ● Novartis 	None	None	<ul style="list-style-type: none"> ● BG Medicine ● Bristol-Myers Squibb ● diaDexus‡ ● Eli Lilly ● GlaxoSmithKline‡ ● Johnson & Johnson ● Merck‡ ● Regado ● Schering-Plough‡ ● NIH/NINDS Neurological Emergency Treatment Trials Consortium—PI‡ 	None	None	<ul style="list-style-type: none"> 4.4.1 7.2
Joseph P. Ornato	Department of Emergency Medicine Virginia Commonwealth University— Professor and Chairman Mayo	<ul style="list-style-type: none"> ● European Resuscitation Council‡ ● ZOLL Circulation 	None	None	<ul style="list-style-type: none"> ● NIH/NINDS Neurological Emergency Treatment Trials Consortium—PI‡ 	None	None	None
Narith Ou	Clinic—Pharmacotherapy Coordinator, Cardiology	None	None	None	None	None	None	None
Martha J. Radford	NYU Langone Medical Center—Chief Quality Officer; NYU School of Medicine—Professor of Medicine (Cardiology)	None	None	None	None	None	None	None
Jacqueline E. Tamis-Holland	St Luke’s-Roosevelt Hospital Center— Director, Interventional Cardiology Fellowship Program; Columbia University, College of Physicians and Surgeons— Assistant Professor of Clinical Medicine	None	None	None	None	None	None	None
Carl L. Tommaso	Skokie Hospital—Director of Catheterization Laboratory; North Shore University Health Systems	None	None	None	None	None	None	None
Cynthia M. Tracy	George Washington University Medical Center—Associate Director, Division of Cardiology	None	None	None	None	None	None	None

(Continued)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Y. Joseph Woo	Hospital of the University of Pennsylvania—Associate Professor of Surgery	None	None	None	None	None	None	None
David X. Zhao	Vanderbilt University Medical Center—Director, Cardiac Catheterization and Interventional Cardiology	None	None	None	<ul style="list-style-type: none"> ● Abbot Vascular ● Accumetrics ● AGA Medical ● Osiris ● Volcano 	None	None	4.3.1

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥\$10,000 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. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACCF/AHA, a person has a *relevant* relationship IF: a) The *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) The *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) The *person or a member of the person’s household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities could apply. Section numbers apply to the full-text guideline.

- †No financial benefit.
- ‡Significant relationship.

§Dr. Ettinger’s relationship with Medtronic was added just before balloting of the recommendations, so it was not relevant during the writing stage; however, the addition of this relationship makes the writing committee out of compliance with the minimum 50% no relevant RWI requirement.

ACS indicates acute coronary syndromes; DSMB, data safety monitoring board; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; and PI, principal investigator.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

Reviewer	Representation	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Elliott M. Antman	Official Reviewer—ACCF Board of Trustees	None	None	None	<ul style="list-style-type: none"> ● Accumetrics ● AstraZeneca ● Beckman Coulter ● Bristol-Myers Squibb Pharmaceutical Research Institute ● Daiichi-Sankyo* ● Eli Lilly* ● GlaxoSmithKline ● Merck ● Millennium Pharmaceuticals ● Novartis Pharmaceuticals ● Ortho-Clinical Diagnostics ● Sanofi-Synthelabo Recherche ● Schering-Plough Research Institute 	None	None
Gary J. Balady Christopher P. Cannon	Official Reviewer—AHA Official Reviewer—AHA	None ● Novartis†	None None	None None	<ul style="list-style-type: none"> None ● Accumetrics* ● AstraZeneca* ● Bristol-Myers Squibb† ● GlaxoSmithKline ● Merck* 	None ● GlaxoSmithKline ● Merck (DSMB)	None None

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Appendix 2. Continued

Reviewer	Representation	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Judith S. Hochman	Official Reviewer—ACCF/ AHA Task Force on Practice Guidelines	<ul style="list-style-type: none"> ● BMS/Sanofi ● Eli Lilly ● GlaxoSmithKline 	None	None	None	<ul style="list-style-type: none"> ● Johnson & Johnson Pharmaceutical Research & Development (DSMB) ● Merck/Schering Plough (DSMB) 	None
Austin H. Kutscher	Official Reviewer—ACCF Board of Governors	None	None	None	None	None	None
Charles J. Davidson	Organizational Reviewer—SCAI	<ul style="list-style-type: none"> ● Abbott* ● Abbott Vascular 	None	None	<ul style="list-style-type: none"> ● Edwards Lifesciences* 	None	None
Deborah B. Diercks	Organizational Reviewer—ACEP	<ul style="list-style-type: none"> ● Abbott ● Cardiovascular Daiichi-Sankyo 	None	None	<ul style="list-style-type: none"> ● Beckman Coulter† ● Nanosphere† 	None	None
Jonathan M. Tobis	Organizational Reviewer—SCAI	None	<ul style="list-style-type: none"> ● AGA Medical ● Boston Scientific 	None	<ul style="list-style-type: none"> ● AGA Medical* 	None	None
Jeffrey L. Anderson	Content Reviewer— ACCF/AHA Task Force on Practice Guidelines	None	None	None	<ul style="list-style-type: none"> ● Toshiba† 	<ul style="list-style-type: none"> ● AstraZeneca (DSMB) 	<ul style="list-style-type: none"> ● Defendant, Postoperative Ablation Case, 2010
James C. Blankenship	Content Reviewer	None	None	None	<ul style="list-style-type: none"> ● AstraZeneca† ● Boston Scientific† ● Novartis† ● Schering-Plough† 	None	None
Jeffrey J. Cavendish	Content Reviewer—ACCF Prevention of Cardiovascular Disease Committee	None	None	None	None	None	None
Harold L. Dauerman John S. Douglas, Jr.	Content Reviewer Content Reviewer	None None	None None	None None	<ul style="list-style-type: none"> ● None ● Abbott† ● Medtronic† ● The Medicines Company† 	None None	None None
Stephen G. Ellis	Content Reviewer	<ul style="list-style-type: none"> ● Abbott Vascular ● Boston Scientific† 	None	None	None	None	None
Joseph Fredi	Content Reviewer—ACCF Surgeons’ Scientific Council	<ul style="list-style-type: none"> ● AGA Medical† 	None	None	None	None	None
Anthony Gershlick	Content Reviewer	<ul style="list-style-type: none"> ● Abbott ● AstraZeneca ● Boehringer Ingelheim ● Boston Scientific ● Cordis ● Eli Lilly ● Medtronic 	None	None	<ul style="list-style-type: none"> ● Boehringer Ingelheim 	None	None
Howard C. Herrmann	Content Reviewer	<ul style="list-style-type: none"> ● AstraZeneca ● Merck Sharpe and Dohme 	None	None	<ul style="list-style-type: none"> ● Accumetrics ● Boston Scientific* ● Edwards Lifesciences* ● eValve ● Medtronic* ● St. Jude Medical ● The Medicines Company* 	None	None
James Bernard Hermiller	Content Reviewer—ACCF Interventional Scientific Council	<ul style="list-style-type: none"> ● Abbott ● Boston Scientific ● St. Jude Medical 	<ul style="list-style-type: none"> ● Eli Lilly 	None	None	None	None
Fred M. Kosumoto	Content Reviewer	None	None	None	None	None	None
Glenn Levine	Content Reviewer	None	None	None	None	None	None
Roxana Mehran	Content Reviewer	<ul style="list-style-type: none"> ● Abbott Vascular ● AstraZeneca ● Ortho-McNeill 	None	None	<ul style="list-style-type: none"> ● BMS/Sanofi-aventis* ● The Medicines Company* 	None	None
M. Eugene Sherman	Content Reviewer—ACCF Board of Governors	None	<ul style="list-style-type: none"> ● Eli Lilly* 	None	None	None	None

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Appendix 2. Continued

Reviewer	Representation	Consultant	Speaker’s Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Daniel I. Simon	Content Reviewer	<ul style="list-style-type: none"> ● Cordis/Johnson & Johnson ● Daiichi-Sankyo ● Eli Lilly ● Medtronic ● Sanofi-aventis ● The Medicines Company 	None	None	None	None	<ul style="list-style-type: none"> ● Defendant, DES Intellectual Property Case, 2010
Richard W. Smalling	Content Reviewer—ACCF Interventional Scientific Council	<ul style="list-style-type: none"> ● AGA Medical 	None	None	<ul style="list-style-type: none"> ● AGA Medical* ● Cordis* ● eValve* 	<ul style="list-style-type: none"> ● AGA Medical ● Cordis ● eValve 	None
William G. Stevenson	Content Reviewer—ACCF/AHA Task Force on Practice Guidelines	None	None	None	None	None	None
William A. Tansey III	Content Reviewer	None	None	None	None	None	None
David D. Waters	Content Reviewer	<ul style="list-style-type: none"> ● Bristol-Myers Squibb ● Pfizer 	None	None	None	<ul style="list-style-type: none"> ● Merck/Schering-Plough ● Sanofi-aventis (DSMB) 	None
Christopher J. White	Content Reviewer	None	None	None	<ul style="list-style-type: none"> ● Boston Scientific† ● St. Jude Medical 	None	None
Clyde W. Yancy	Content Reviewer—ACCF/AHA Task Force on Practice Guidelines	None	None	None	None	None	None
Yerem Yeghiazarians	Content Reviewer	None	None	None	None	None	None

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq 5\%$ of the voting stock or share of the business entity, or ownership of $\geq \$10,000$ 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 that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

*Significant relationship.

†No financial benefit.

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ACCF indicates American College of Cardiology Foundation; ACEP, American College of Emergency Physicians; AHA, American Heart Association; DES, drug-eluting stent; DSMB, data safety monitoring board; and SCAI, Society for Cardiovascular Angiography and Interventions.