

# Part 9: Acute Coronary Syndromes

## 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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### Introduction

Clinicians often struggle with uncertainty and complexity in deciding which course of treatment will likely lead to an optimal outcome for an individual patient. Scientific research provides information on how patient populations have responded to treatment regimens, and this information, combined with a knowledge of the individual patient, can help guide the clinician's decisions.

The recommendations in this *2015 American Heart Association (AHA) Guidelines Update for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care (ECC)* are based on an extensive evidence review process that was begun by the International Liaison Committee on Resuscitation (ILCOR) after the publication of the *ILCOR 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations*<sup>1,2</sup> and was completed in February 2015.<sup>3,4</sup>

In this in-depth evidence review process, ILCOR examined topics and then generated a prioritized list of questions for systematic review. Questions were first formulated in PICO (population, intervention, comparator, outcome) format,<sup>5</sup> and then a search for relevant articles was performed. The evidence was evaluated by the ILCOR task forces by using the standardized methodologic approach proposed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.<sup>6</sup>

The quality of the evidence was categorized based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias). Then, where possible, consensus-based treatment recommendations were created.

To create this *2015 AHA Guidelines Update for CPR and ECC*, the AHA formed 15 writing groups, with careful attention to avoid conflicts of interest, to assess the ILCOR treatment recommendations, and to write AHA treatment recommendations by using the AHA Class of Recommendation and Level of Evidence (LOE) system. The recommendations made in the *2015 Guidelines Update for CPR and ECC* are informed by the

ILCOR recommendations and GRADE classification, in the context of the delivery of medical care in North America. In the online version of this publication, live links are provided so the reader can connect directly to the systematic reviews on the Scientific Evidence Evaluation and Review System (SEERS) website. These links are indicated by a superscript combination of letters and numbers (eg, ACS 873).

This 2015 Guidelines Update offers recommendations for the care of patients with acute coronary syndromes (ACS). The recommendations made here update those made in the 2010 Guidelines and address only those issues that were reviewed in 2015. The ILCOR ACS Task Force did not review areas in which it found a paucity of new evidence between 2010 and 2015; therefore, the 2010 Guidelines for these unreviewed areas remain current. For example, acetylsalicylic acid administration has been shown to be of benefit in ACS and was recommended by the 2010 Guidelines.<sup>7</sup> Acetylsalicylic acid was not reviewed by the ACS Task Force in 2015, so the recommendations from 2010 should be used. (Note: The First Aid section of this 2015 Guidelines Update makes recommendations on acetylsalicylic acid administration by nonmedical personnel—see “Part 15: First Aid”). The recommendations that were not reviewed in 2015 will either be reviewed and included in future *AHA Guidelines for CPR and ECC* or will be in the most recent ACC/AHA Guidelines.<sup>8–10</sup>

A table of recommendations made in this update, as well as the recommendations made in “Part 10: Acute Coronary Syndromes” of the 2010 Guidelines,<sup>7</sup> can be found in the Appendix.

The 2015 Guidelines for ACS are directed toward practitioners who provide care for patients with suspected ACS from the time of first medical contact until disposition from the emergency department (ED). Care providers during this time may include emergency medical service (EMS) dispatchers, first responders, EMT-Bs, paramedics, nurses, physicians, and other independent practitioners.

### Methodology

ILCOR performed 18 systematic reviews (14 based on meta-analyses) on more than 110 relevant studies that span

The American Heart Association requests that this document be cited as follows: O'Connor RE, Al Ali AS, Brady WJ, Ghaemmaghami CA, Menon V, Welsford M, Shuster M. Part 9: acute coronary syndromes: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015;132(suppl 2):S483–S500.

(*Circulation*. 2015;132[suppl 2]:S483–S500. DOI: 10.1161/CIR.0000000000000263.)

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*Circulation* is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIR.0000000000000263

40 years. Based on these reviews, the ACS Writing Group assessed the evidence and assigned an LOE by using AHA definitions. The LOE for a given intervention supports the class or “strength” of recommendation that the writing group assigned. This update uses the newest AHA Class of Recommendation and LOE classification system, which contains modifications to the Class III recommendation and introduces LOE B-R (randomized studies) and B-NR (non-randomized studies), as well as LOE C-LD (limited data) and LOE C-EO (consensus of expert opinion). For further information, see “Part 2: Evidence Evaluation and Management of Conflicts of Interest.”

## Diagnostic Interventions in ACS

### Prehospital ECG and Prehospital STEMI Activation of the Catheterization Laboratory

ACS 873, ACS 336

Prehospital acquisition of 12-lead electrocardiograms (ECGs) has been recommended by the *AHA Guidelines for CPR and Emergency Cardiovascular Care* since 2000. The 2015 ILCOR systematic review examined whether acquisition of a prehospital ECG with transmission of the ECG to the hospital, notification of the hospital of the need for fibrinolysis, or activation of the catheterization laboratory changes any major outcome.

#### 2015 Evidence Summary

Obtaining an ECG early in the assessment of patients with possible ACS ensures that dynamic ECG changes suggestive of cardiac ischemia and ACS will be identified, even if they normalize before initial treatment.<sup>11</sup>

An early ECG may also enable ST elevation myocardial infarction (STEMI) to be recognized earlier. Acquiring a prehospital ECG and determining the presence of STEMI effectively makes the prehospital provider the first medical contact. The prehospital ECG can reliably enable identification of STEMI before arrival at the hospital,<sup>12</sup> but if notification of the receiving facility does not occur, any benefit to prehospital STEMI recognition is lost.

Prehospital ECG acquisition coupled with hospital notification if STEMI is identified consistently reduces the time to reperfusion in-hospital (first medical contact-to-balloon time, first medical contact-to-needle time, door-to-balloon time, door-to-needle time).<sup>13</sup> To reduce time to STEMI reperfusion in-hospital, rapid transport and early treatment must occur in parallel with hospital preparation for the arriving patient.

Prehospital ECGs reduce the time to reperfusion with fibrinolytic therapy and also reduce the time to primary percutaneous coronary intervention (PPCI) and facilitate triage of STEMI patients to specific hospitals.<sup>4</sup> Prehospital activation of the catheterization laboratory (as opposed to delaying cardiac catheterization laboratory activation until the patient arrives at the hospital) is independently associated with improved times to PPCI and reduced mortality.<sup>4</sup>

Prehospital ECG acquisition and hospital notification reduce mortality by 32% when PPCI is the reperfusion strategy (benefit is accentuated when prehospital activation occurs) and by 24% when ED fibrinolysis is the reperfusion strategy.<sup>4</sup>

#### 2015 Recommendations—Updated

Prehospital 12-lead ECG should be acquired early for patients with possible ACS (Class I, LOE B-NR).

Prehospital notification of the receiving hospital (if fibrinolysis is the likely reperfusion strategy) and/or prehospital activation of the catheterization laboratory should occur for all patients with a recognized STEMI on prehospital ECG (Class I, LOE B-NR).

#### Computer-Assisted ECG STEMI Interpretation<sup>ACS 559</sup>

The identification of STEMI in patients with suspected STEMI is often made on clinical grounds in combination with ECG findings as interpreted by a physician. The 2015 ILCOR systematic review addressed whether computer-assisted ECG interpretation improves identification of STEMI while minimizing unnecessary intervention.

#### 2015 Evidence Summary

Studies examined both underdiagnosis (false-negative results) and overdiagnosis (false-positive results)<sup>14,15</sup> or overdiagnosis alone<sup>16–20</sup> by computer ECG interpretation. There was wide variation in the proportion of false-positive results (0% to 42%) and of false-negative results (22% to 42%).

These variations in accuracy seemed to occur because different ECG machines use different algorithms and because the computer interpretations are compared variously with interpretation by cardiologists, emergency physicians, and discharge diagnosis of STEMI. Moreover, the sensitivity and specificity of the test will differ depending on the prevalence of STEMI.

Both studies that examined false-negative results suggest that computer interpretation of ECG tracing produces unacceptably high rates of false-negative results in the identification of STEMI. A few studies show that computer interpretation can produce an unacceptably high rate of false-positive diagnoses. Interpretation by trained personnel in conjunction with computer interpretation may lower the rate of false results obtained when using computer interpretation alone.

#### 2015 Recommendations—New

Because of high false-negative rates, we recommend that computer-assisted ECG interpretation not be used as a sole means to diagnose STEMI (Class III: Harm, LOE B-NR).

We recommend that computer-assisted ECG interpretation may be used in conjunction with physician or trained provider interpretation to recognize STEMI (Class IIb, LOE C-LD).

#### Nonphysician STEMI ECG Interpretation<sup>ACS 884</sup>

When physicians are not present or not available to interpret an ECG, other methods for interpretation must be used so that timely patient care is not adversely affected. The 2015 ILCOR systematic review examined whether nonphysicians such as paramedics and nurses could identify STEMI on an ECG so that earlier identification of STEMI could be made with acceptable rates of either underdiagnosis (false-negative results) or overdiagnosis (false-positive results).

#### 2015 Evidence Summary

Three observational studies compared the diagnostic accuracy of the interpretation of ECGs as either STEMI or No STEMI

by physicians and paramedics.<sup>21–23</sup> While the studies used different methods to adjudicate the diagnosis, including World Health Organization criteria,<sup>21</sup> discharge diagnosis,<sup>22</sup> and catheterization laboratory activation,<sup>23</sup> all 3 studies showed a fairly high rate of agreement between physician and paramedic rates of distinguishing STEMI from No STEMI.

Overidentification of STEMI may have a significant adverse effect on resource utilization. An additional 6 studies examined the accuracy of paramedic identification of STEMI and reported false-positive rates (patients incorrectly diagnosed with STEMI by paramedics when no STEMI was present) ranging from 8% to 40%.<sup>17,24–28</sup> One study reported that transmission of the ECG to the ED for emergency physician interpretation, compared with paramedic interpretation alone, improves the positive predictive value of the prehospital 12-lead ECG for triage and therapeutic decision making.<sup>24</sup> The time from hospital arrival to percutaneous coronary intervention (PCI) with balloon inflation was significantly shorter if EMS activated the catheterization laboratory than if the laboratory was activated by hospital staff<sup>25,26,28</sup> or if the patient was directly admitted to the catheterization laboratory.<sup>27</sup>

### 2015 Recommendation—New

While transmission of the prehospital ECG to the ED physician may improve positive predictive value (PPV) and therapeutic decision-making regarding adult patients with suspected STEMI, if transmission is not performed, it may be reasonable for trained nonphysician ECG interpretation to be used as the basis for decision-making, including activation of the catheterization laboratory, administration of fibrinolysis, and selection of destination hospital (Class IIa, LOE B-NR).

### Biomarkers in ACS<sup>ACS 737</sup>

Cardiac troponin measurement, along with the ECG, is an integral part of the evaluation of patients with signs and symptoms suspicious for ACS. The detection of an elevated troponin (Tn) above the 99th percentile upper reference limit is highly sensitive and specific for myocardial necrosis, and is required in the universal definition of myocardial infarction (MI).<sup>29</sup>

Contemporary troponin assays are termed “high-sensitivity” (hs) if they are able to detect measurable troponin levels even in healthy individuals, with a threshold of detection of 0.006 ng/ml for hs-cTnI and 0.005 for hs-cTnT. Positive results are an order of magnitude higher than the threshold for detection and are usually defined as exceeding the 99th percentile of values with a coefficient of variation of less than 10%.<sup>30</sup>

More than 8 million patients are evaluated for potential ischemic chest pain in US EDs each year, with troponin measurement serving as one of the crucial diagnostic tests.<sup>31</sup> Because of this vast number of patients with potential ischemic chest pain, it is highly desirable to find some combination of diagnostic testing that can reliably identify patients who are not experiencing ischemia and can be safely discharged from the ED.

The 2015 ILCOR systematic review examined whether a negative troponin test could be used to identify patients at low risk for ACS when they did not have signs of STEMI,

ischemia, or changes on the ECG that could mask signs of acute ischemia or MI.

The clinician should bear in mind that unstable angina can present without any objective data of myocardial ischemic injury (ie, with normal ECG and normal troponin), in which case the initial diagnosis depends solely on the patient’s clinical history and the clinician’s interpretation and judgment.

### 2015 Evidence Summary

Two observational studies used troponin (cTnI, cTnT, or hs-cTnT) measured at 0 and 2 hours to assess whether patients could be safely discharged from the ED.<sup>32,33</sup> In these studies, 2.5% to 7.8% of patients with ACS had (false-) negative tests. That is, ACS would have been missed in 2.5% to 7.8% of the patients studied. With an unstructured risk assessment used in addition to the troponin testing, 2.3% of patients identified as being at low risk have a major adverse cardiac event (MACE) on 30-day follow-up. A formal risk assessment instrument was not used in either of these 2 studies.

Six additional observational studies combined troponin testing (using cTnI, cTnT, hs-cTnI, or hs-cTnT) with use of clinical decision rules such as TIMI, Vancouver, North American, or HEART. The proportion of false-negative results among patients with 30-day MACE ranged from 0% to 1.2%.<sup>34–39</sup> When the age cutoff for low-risk patients was increased from 50 years to 60 years for the North American Chest Pain Rule, the proportion of false-negative results rose from 0% to 1.1%.<sup>37</sup> Because the rules were used in combination with different troponin measurements, and each test identified 99% of patients with ACS as defined by 30-day MACE, it was difficult to directly compare rule or assay performance. One study<sup>36</sup> identified 1 additional ACS patient by using the Vancouver rule when the hs-cTnI was used instead of the cTnI.

### 2015 Recommendations—New

We recommend against using hs-cTnT and cTnI alone measured at 0 and 2 hours (without performing clinical risk stratification) to identify patients at low risk for ACS (Class III: Harm, LOE B-NR).

We recommend that hs-cTnI measurements that are less than the 99th percentile, measured at 0 and 2 hours, may be used together with low-risk stratification (TIMI score of 0 or 1 or low risk per Vancouver rule) to predict a less than 1% chance of 30-day MACE (Class IIa, LOE B-NR).

We recommend that negative cTnI or cTnT measurements at 0 and between 3 and 6 hours may be used together with very low-risk stratification (TIMI score of 0, low-risk score per Vancouver rule, North American Chest Pain score of 0 and age less than 50 years, or low-risk HEART score) to predict a less than 1% chance of 30-day MACE (Class IIa, LOE B-NR).

## Therapeutic Interventions in ACS

### ADP Inhibition: Adjunctive Therapy in Patients With Suspected STEMI—ADP Inhibitors<sup>ACS 335</sup>

The 2015 ILCOR systematic review addressed the clinical impact of the timing of administration of adenosine diphosphate (ADP) inhibition in the treatment of patients with suspected STEMI. The relative merit of early prehospital as compared with hospital administration of ADP inhibition as a

general treatment strategy was assessed. Differences between individual ADP inhibitors were not examined.

The preferred reperfusion strategy for patients with STEMI is identification and restoration of normal flow in the infarct-related artery using primary percutaneous intervention. The use of potent dual antiplatelet therapy in STEMI patients undergoing PPCI is associated with improved clinical outcomes as well as lower rates of acute stent thrombosis.<sup>40,41</sup> Given the short time from first medical contact to balloon inflation, treatment with oral ADP inhibitors in a prehospital setting has the potential to enhance platelet inhibition and improve procedural and clinical outcomes after PCI.

### 2015 Evidence Summary

Three randomized controlled trials (RCTs)<sup>42–44</sup> showed no additional benefit to the outcome of 30-day mortality and no additional benefit or harm with respect to major bleeding with prehospital administration compared with in-hospital administration of an ADP-receptor antagonist.

### 2015 Recommendation—New

In patients with suspected STEMI intending to undergo PPCI, initiation of ADP inhibition may be reasonable in either the prehospital or in-hospital setting (Class IIb, LOE C-LD).

## Prehospital Anticoagulants Versus None in STEMI<sup>ACS 562</sup>

In patients with suspected STEMI, anticoagulation is standard treatment recommended by the American College of Cardiology Foundation/AHA Guidelines.<sup>9,10</sup> The 2015 ILCOR systematic review sought to determine if any important outcome measure was affected if an anticoagulant was administered prehospital compared with whether that same anticoagulant was administered in-hospital.

### 2015 Evidence Summary

A single nonrandomized, case-control study found that while flow rates were higher in an infarct-related artery when heparin and aspirin were administered in the prehospital setting versus the ED, there was no significant difference in death, PCI success rate, major bleeding, or stroke.<sup>45</sup>

### 2015 Recommendations—New

While there seems to be neither benefit nor harm to administering heparin to patients with suspected STEMI before their arrival at the hospital, prehospital administration of medication adds complexity to patient care. We recommend that EMS systems that do not currently administer heparin to suspected STEMI patients do not add this treatment, whereas those that do administer it may continue their current practice (Class IIb, LOE B-NR).

In suspected STEMI patients for whom there is a planned PPCI reperfusion strategy, administration of unfractionated heparin (UFH) can occur either in the prehospital or in-hospital setting (Class IIb, LOE B-NR).

## Prehospital Anticoagulation for STEMI<sup>ACS 568</sup>

The 2015 ILCOR systematic review examined whether the prehospital administration of an anticoagulant such as bivalirudin, dalteparin, enoxaparin, or fondaparinux instead of UFH,

in suspected STEMI patients who are transferred for PPCI, changes any major outcome.

### 2015 Evidence Summary

One RCT provided evidence in patients transferred for PCI for STEMI that there was no significant difference between prehospital bivalirudin compared with prehospital UFH with respect to 30-day mortality, stroke, or reinfarction. However, this same study did demonstrate a decreased incidence of major bleeding with bivalirudin.<sup>46</sup> Another study (this one a non-RCT) also demonstrated no difference between prehospital bivalirudin compared with prehospital UFH with respect to 30-day mortality, stroke, and reinfarction. In contrast to the RCT, this study did not find a difference in major bleeding.<sup>47</sup>

Although stent thrombosis was not considered as an *a priori* outcome, bivalirudin was strongly associated with the risk of acute stent thrombosis (relative risk, 6.11; 95% confidence interval, 1.37–27.24).<sup>46</sup> Such association is also consistently reported in other published in-hospital studies and meta-analyses of this agent in patients undergoing PCI.<sup>48–50</sup> While the benefit of bivalirudin over UFH alone in reducing bleeding complications has been shown, this benefit may be offset by the risk of stent thrombosis.

We have identified 1 RCT<sup>51</sup> enrolling 910 patients transferred for PPCI for STEMI that showed no significant difference between prehospital enoxaparin compared with prehospital UFH with respect to 30-day mortality, stroke, reinfarction, or major bleeding.

It is important to consider the results of the comparison between anticoagulants given in prehospital versus in-hospital settings in STEMI patients. Only UFH has been evaluated directly in this setting, and because there is no clear evidence of benefit, we are not recommending that EMS systems implement anticoagulant administration in the prehospital setting.

### 2015 Recommendations—New

It may be reasonable to consider the prehospital administration of UFH in STEMI patients or the prehospital administration of bivalirudin in STEMI patients who are at increased risk of bleeding (Class IIb, LOE B-R).

In systems in which UFH is currently administered in the prehospital setting for patients with suspected STEMI who are being transferred for PPCI, it is reasonable to consider prehospital administration of enoxaparin as an alternative to UFH (Class IIa, LOE B-R).

## Routine Supplementary Oxygen Therapy in Patients Suspected of ACS<sup>ACS 887</sup>

The 2010 AHA Guidelines for CPR and ECC noted that there was insufficient evidence to recommend the routine use of oxygen therapy in patients who had an uncomplicated ACS without signs of hypoxemia or heart failure and that older literature suggested harm with supplementary oxygen administration in uncomplicated ACS without demonstrated need for supplementary oxygen.<sup>52,53</sup> The 2010 Guidelines, however, did recommend that oxygen be administered to patients with breathlessness, signs of heart failure, shock, or an oxygen saturation less than 94%.<sup>7</sup>

In 2015, the ILCOR systematic review specifically addressed the use of oxygen as an adjunctive medication in the

treatment of patients who had normal oxygen saturation but had suspected ACS. The 2 treatment approaches (either providing or withholding oxygen) were compared with respect to outcomes: rate of death, infarction size, resolution of chest pain, and ECG abnormality resolution. The new recommendation in this 2015 Guidelines Update applies only to the use of oxygen for patients suspected of ACS who have normal oxygen saturations.

### Adjunctive Therapy in Patients Suspected of ACS: Oxygen

Respiratory compromise, manifested by oxygen desaturation, can occur during ACS, most often as a result of either acute pulmonary edema or chronic pulmonary disease. Supplementary oxygen has previously been considered standard therapy for the patient suspected of ACS, even in patients with normal oxygen saturation. The rationale for oxygen therapy was a belief that maximization of oxygen saturation may improve delivery of oxygen to the tissues and thus reduce the ischemic process and related negative outcomes. In other patient groups, such as resuscitated cardiac arrest patients, hyperoxia has been associated with worse outcomes as compared with normoxia.<sup>54–56</sup>

#### 2015 Evidence Summary

There is limited evidence regarding the use of supplementary oxygen therapy in suspected ACS patients with normal oxygen saturation. The practice of administering oxygen to all patients regardless of their oxygen saturation is based on both rational conjecture and research performed before the current reperfusion era in acute cardiac care.<sup>52</sup> More recent study of this issue is also limited,<sup>57,58</sup> although 2 trials addressing this question are in progress or are recently completed. The AVOID trial,<sup>59</sup> a multicentered prospective RCT published since the 2015 ILCOR systematic review, compared oxygen administration with no oxygen administration in suspected STEMI patients without respiratory compromise. When oxygen was administered, the patients experienced increased myocardial injury at presentation and larger infarction size at 6 months. Reinfarction and the incidence of cardiac arrhythmias were also increased in the oxygen therapy group.<sup>59</sup> Because this study was published after the ILCOR systematic review, it was not considered in our treatment recommendation.

There is no evidence that withholding supplementary oxygen therapy in normoxic patients suspected of ACS affects the rate of death and/or resolution of chest pain; there is only a very low level of evidence that withholding supplementary oxygen reduces infarction size, and there is no evidence that withholding supplementary oxygen therapy affects the resolution of ECG abnormality.<sup>52,53,57,58</sup>

#### 2015 Recommendation—Updated

The provision of supplementary oxygen to patients with suspected ACS who are normoxic has not been shown to reduce mortality or hasten the resolution of chest pain. Withholding supplementary oxygen in these patients has been shown to minimally reduce infarct size.

The usefulness of supplementary oxygen therapy has not been established in normoxic patients. In the prehospital, ED, and hospital settings, the withholding of supplementary

oxygen therapy in normoxic patients with suspected or confirmed acute coronary syndrome may be considered (Class IIb, LOE C-LD).

### Reperfusion Decisions in STEMI Patients

The 2010 ILCOR systematic review addressed the use of reperfusion therapy, including fibrinolysis and PPCI, in patients with STEMI who present initially to non-PCI-capable hospitals. The 2015 *AHA Guidelines Update for CPR and ECC* examines the most appropriate reperfusion therapy in STEMI patients presenting to non-PCI-capable hospitals as well as the need for hospital transfer for PCI, or ischemia-guided (ie, rescue) coronary angiography and/or PCI.

#### Prehospital Fibrinolysis, Hospital Fibrinolysis, and Prehospital Triage to PCI Center<sup>ACS 338, ACS 341</sup>

Prehospital fibrinolysis requires a sophisticated system of provider expertise, well-established protocols, comprehensive training programs, medical oversight, and quality assurance.<sup>4</sup> In many European systems, a physician provides prehospital fibrinolysis, but nonphysicians can also safely administer fibrinolytics.<sup>60</sup> The 2015 ILCOR systematic review evaluated whether prehospital fibrinolysis is preferred to reperfusion in-hospital where the prehospital fibrinolysis expertise, education, and system support exists.

#### 2015 Evidence Summary

Prehospital fibrinolysis will achieve earlier treatment as compared with ED fibrinolysis. Where transport times are more than 30 to 60 minutes, the time advantage conferred by prehospital fibrinolysis provides a mortality benefit.<sup>4</sup> This benefit from prehospital fibrinolysis was found consistently by 3 RCTs performed more than 20 years ago.<sup>61–63</sup> However, these studies were performed at a time when hospital fibrinolytic administration typically took well in excess of 60 minutes. It is not clear the extent to which that mortality benefit would be maintained today when the hospital time to fibrinolytic treatment is typically considerably shorter than it was 20 years ago. The only recent evidence for this therapy comes from a non-RCT that confirms a small mortality benefit to prehospital fibrinolysis.<sup>64</sup> When transport times are shorter than 30 to 60 minutes, the mortality benefit from administering fibrinolytics before hospital arrival may be lost and may no longer outweigh the relative complexity of providing this therapy outside of a hospital.

However, PPCI is generally preferred to in-hospital fibrinolysis for STEMI reperfusion.<sup>65</sup> Prehospital providers can transport STEMI patients directly to PCI centers, and activation of the team before arrival allows the team to assemble and prepare in parallel with transport. Several studies in the past 15 years have compared transport directly for PPCI with prehospital fibrinolysis and found no mortality benefit of either therapy, although the relatively rare harm from intracranial hemorrhage is greater with fibrinolysis.<sup>66–69</sup>

#### 2015 Recommendations—Updated

Where prehospital fibrinolysis is available as part of a STEMI system of care, and in-hospital fibrinolysis is the alternative treatment strategy, it is reasonable to administer prehospital

fibrinolysis when transport times are more than 30 minutes (Class IIa, LOE B-R).

Where prehospital fibrinolysis is available as part of the STEMI system of care and direct transport to a PCI center is available, prehospital triage and transport directly to a PCI center may be preferred because of the small relative decrease in the incidence of intracranial hemorrhage without evidence of mortality benefit to either therapy (Class IIb, LOE B-R).

### ED Fibrinolysis and Immediate PCI Versus Immediate PCI Alone<sup>ACS 882</sup>

Delays in the performance of PPCI are commonly observed in clinical practice. In many regions, the delay arises because of the relative paucity of dedicated PPCI centers, resulting in the need for prolonged transfer times. In this context, combining the availability and ease of administration of fibrinolytic with the downstream certainty of mechanical reperfusion with facilitated PCI was an attractive concept, with its promise of both restoring early flow to the infarct-related artery while addressing the concerns of pharmacologic failure and need for rescue. This was counterbalanced by the concern for a heightened risk of bleeding complications and detrimental procedural outcomes in this prothrombotic milieu.

The 2015 ILCOR systematic review addressed the merits for reperfusion in STEMI patients with a strategy of initial fibrinolysis followed by immediate PCI versus immediate PCI alone.

#### 2015 Evidence Summary

A number of randomized clinical trials have addressed clinical outcomes after initial treatment with a half- or full-dose fibrinolytic agent followed by dedicated immediate PCI compared with immediate PCI alone.

The studies showed no benefit to mortality,<sup>70–74</sup> nonfatal MI,<sup>70–74</sup> or target vessel revascularization<sup>70–73</sup> when fibrinolytic administration is combined with immediate PCI as compared with immediate PCI alone.

The studies did, however, identify harm from intracranial hemorrhage<sup>70–72</sup> or major bleeding<sup>70–74</sup> when fibrinolytic administration is combined with immediate PCI versus immediate PCI alone.

#### 2015 Recommendation—New

In the treatment of patients with suspected STEMI, the combined application of fibrinolytic therapy followed by immediate PCI (as contrasted with immediate PCI alone) is not recommended (Class III: Harm, LOE B-R).

### Delayed PCI Versus Fibrinolysis Stratified by Time From Symptom Onset<sup>ACS 337</sup>

Although the overall survivability benefits of reperfusion therapy are time dependent, the loss of efficacy caused by delay is more pronounced with fibrinolysis than with PCI.<sup>75</sup> The success of PCI in achieving TIMI-3 flow in the early hours after STEMI does not change with time, whereas the ability of fibrinolytic therapy to achieve TIMI-3 flow decreases significantly with increasing ischemic time.<sup>76</sup> In this context, the choice of reperfusion therapy for a STEMI patient when access to PCI is delayed is a challenging one. The clinician has to weigh the

advantages of immediate fibrinolysis, which includes ease of administration and potential to open the infarct-related artery in a timely manner versus the limitations of fibrinolysis, which include the risk of intracranial hemorrhage and bleeding and the time sensitivity of the intervention's efficacy to open the infarct-related artery. Thus, total ischemic time is an important variable in weighing the merits of delayed PCI versus immediate fibrinolysis.

In the 2010 AHA Guidelines for CPR and ECC,<sup>7</sup> the recommendations were directed at patients in whom PCI could not be accomplished within 90 minutes of first medical contact.

The 2015 ILCOR systematic review compared the relative benefits of immediate fibrinolysis versus primary but delayed PCI in treating STEMI patients, stratifying patients by time from initial medical contact.

#### 2015 Evidence Summary

In STEMI patients presenting less than 2 hours after symptom onset in whom immediate PPCI will delay treatment 60 to 160 minutes compared with fibrinolysis, 2 RCTs (combined into a single analysis) using an outcome of 30-day mortality<sup>77</sup> and 1 RCT using an outcome of 5-year mortality showed greater harm with delayed PPCI compared with fibrinolysis.<sup>78</sup> No differences were found to incidence of reinfarction<sup>77</sup> or severe bleeding.<sup>79</sup>

For STEMI patients presenting 2 to 6 hours after symptom onset in whom PPCI will delay treatment 60 to 160 minutes compared with fibrinolysis, 2 RCTs using an outcome of 1-year mortality<sup>77</sup> and 1 RCT using an outcome of 5-year mortality showed no benefit of delayed PPCI over fibrinolysis.<sup>78</sup> There was also no difference in the incidence of reinfarction,<sup>77</sup> but 1 RCT<sup>79</sup> showed more severe bleeding with fibrinolysis as compared with delayed PPCI.

In STEMI patients presenting 3 to 12 hours after symptom onset in whom PPCI will delay treatment 60 to 120 minutes as compared with fibrinolysis, 1 RCT<sup>80</sup> using a 30-day mortality outcome showed that delayed PPCI conferred a benefit as compared with immediate fibrinolysis.

A reanalysis of the raw data from 16 RCTs<sup>81</sup> has suggested that the acceptable fibrinolysis to PPCI delay varies depending on the patient's baseline risk and delay to presentation. A pragmatic simplification of the formula derived in the analysis has been suggested in an editorial<sup>82</sup> associated with the publication of the analysis: Patients older than 65 years and all patients in Killip class greater than 1 should be treated with PPCI. Patients older than 65 years in Killip class 1 should have PPCI unless delay is greater than 35 minutes.

#### 2015 Recommendations—Updated

The following recommendations are not in conflict with, and do not replace, the 2013 ACC/AHA STEMI Guidelines, which are endorsed by this ACS Writing Group. These 2015 Guidelines Update recommendations are derived from a different set of studies that examined the interval between *symptom onset* and reperfusion, rather than the interval between *first medical contact* and reperfusion. The symptom onset interval is appropriate to consider when time of symptom onset is known. However, time from symptom onset may be difficult to ascertain or may be unreliable. When time from symptom onset is uncertain, it is appropriate to follow the ACC/AHA

STEMI Guidelines recommendation that PPCI is the preferred reperfusion strategy when time from symptom onset is less than 12 hours and time to PPCI from first medical contact in these patients is anticipated to be less than 120 minutes. Regardless of whether time of symptom onset is known, the interval between first medical contact and reperfusion should not exceed 120 minutes (Class I, LOE C-EO).

In STEMI patients presenting within 2 hours of symptom onset, immediate fibrinolysis rather than PPCI may be considered when the expected delay to PPCI is more than 60 minutes (Class IIb, LOE C-LD).

In STEMI patients presenting within 2 to 3 hours after symptom onset, either immediate fibrinolysis or PPCI involving a possible delay of 60 to 120 minutes might be reasonable (Class IIb, LOE C-LD).

In STEMI patients presenting within 3 to 12 hours after symptom onset, performance of PPCI involving a possible delay of up to 120 minutes may be considered rather than initial fibrinolysis (Class IIb, LOE C-LD).

It is acknowledged that fibrinolysis becomes significantly less effective more than 6 hours after symptom onset, and thus a longer delay to PPCI may be the better option for patients more than 6 hours after symptom onset.

In STEMI patients, when delay from first medical contact to PPCI is anticipated to exceed 120 minutes, a strategy of immediate fibrinolysis followed by routine early (within 3 to 24 hours) angiography and PCI if indicated may be reasonable for patients with STEMI (Class IIb, LOE B-R).

### Reperfusion Therapy for STEMI in Non-PCI-Capable Hospitals<sup>ACS 332, ACS 334, ACS 779</sup>

The rapid restoration of perfusion in the infarct-related coronary artery, using either fibrinolytic therapy or PPCI, provides the opportunity for an optimal outcome.

Fibrinolytic therapy unequivocally improves survival in patients presenting with STEMI and has widespread availability.<sup>83</sup> STEMI patients with contraindications to fibrinolytic therapy and who are in cardiogenic shock are not appropriate candidates for this form of reperfusion therapy.<sup>84</sup> PPCI is superior to fibrinolytic therapy in the management of STEMI,<sup>85</sup> because PPCI also improves survival rates and enhances other important outcomes in the STEMI patient. However, this form of reperfusion therapy is not widely available.

The superiority of PPCI over fibrinolytic therapy is not absolute. For STEMI patients presenting to a non-PCI-capable hospital, the decision to administer fibrinolytic therapy at the initial facility as compared with immediate-transfer PPCI requires consideration of several factors, including the location of the MI, patient age, the duration of STEMI at time of initial ED presentation, time required to complete transfer for and performance of PPCI, and the abilities of the PPCI cardiologist and hospital.<sup>85</sup> Furthermore, the hemodynamic status of the patient is important; specifically, patients in cardiogenic shock are most appropriately managed with PPCI.<sup>84</sup>

#### 2015 Evidence Summary

##### *Fibrinolysis Versus Transfer for PPCI*

In a non-PCI-capable hospital, the choice of reperfusion therapy in the STEMI patient is either immediate fibrinolytic

therapy or transfer for PPCI; the time required for transfer of the patient to a PCI-capable hospital must be considered in making the choice. Comparison studies showed benefit of immediate transfer to a PCI center with respect to 30-day mortality, stroke, and/or reinfarction.<sup>80,86-92</sup> There was no difference in major hemorrhage.<sup>88,91</sup>

##### *Fibrinolysis and Routine Transfer for Angiography Versus Immediate Transfer for PPCI*

When immediate fibrinolysis in a non-PCI-capable hospital followed by routine transfer for angiography was compared with immediate transfer to a PCI center for PPCI, 3 studies showed no benefit to 30-day mortality, stroke, and/or reinfarction and no difference in the rates of intracranial hemorrhage or major bleeding.<sup>67,93,94</sup>

##### *Fibrinolysis and Routine Transfer for Angiography Versus No Routine Transfer: 30-Day Mortality*

In patients who received a fibrinolytic agent for STEMI in a non-PCI-capable hospital, studies comparing either routine transfer for angiography at 3 to 6 hours and up to 24 hours or no transfer except for ischemia-driven PCI (rescue PCI) in the first 24 hours showed no benefit with respect to 30-day mortality<sup>67,92,95-99</sup> or 1-year mortality.<sup>67,95,96,99-101</sup>

##### *Fibrinolysis and Routine Transfer for Angiography Versus No Routine Transfer: Intracranial Hemorrhage or Major Bleeding*

In patients who received a fibrinolytic agent for STEMI in a non-PCI-capable hospital, studies comparing either routine transfer for angiography at 3 to 6 hours and up to 24 hours or no transfer except for ischemia-driven PCI (rescue PCI) in the first 24 hours demonstrated no difference in incidence of intracranial hemorrhage,<sup>67,95-99</sup> major bleeding,<sup>67,95-99</sup> or stroke.<sup>92,95,97,99</sup>

##### *Fibrinolysis and Routine Transfer for Angiography Versus No Routine Transfer: Reinfarction*

When immediate fibrinolysis for STEMI was followed by routine transfer for angiography at 3 to 6 hours and up to 24 hours as compared with no transfer except for ischemia-driven PCI (rescue PCI) in the first 24 hours, a decrease in the rate of reinfarction was demonstrated.<sup>67,92,95-99</sup>

#### 2015 Recommendations—New

In adult patients presenting with STEMI in the ED of a non-PCI-capable hospital, we recommend immediate transfer without fibrinolysis from the initial facility to a PCI center instead of immediate fibrinolysis at the initial hospital with transfer only for ischemia-driven PCI (Class I, LOE B-R). When STEMI patients cannot be transferred to a PCI-capable hospital in a timely manner, fibrinolytic therapy with routine transfer for angiography may be an acceptable alternative to immediate transfer to PPCI (Class IIb, LOE C-LD).

When fibrinolytic therapy is administered to a STEMI patient in a non-PCI-capable hospital, it may be reasonable to transport all postfibrinolysis patients for early routine angiography in the first 3 to 6 hours and up to 24 hours rather than transport postfibrinolysis patients only when they require ischemia-guided angiography (Class IIb, LOE B-R). It is recognized that there may be practical and logistical circumstances, including geographic limitations, where transfer

for angiography within 24 hours is difficult or impossible. In these cases, the small but measurable decrease in reinfarction rates may not justify a prolonged or difficult transfer.

## Hospital Reperfusion Decisions After ROSC

### PCI After ROSC With and Without ST Elevation<sup>ACS 340, ACS 885</sup>

In 2010, the ILCOR systematic review combined ST-elevation and non-ST-elevation patients after ROSC. However, the 2010 AHA Guidelines for CPR and ECC did make separate recommendations for each of these distinct groups of patients, recommending emergency coronary angiography for ST-elevation patients after ROSC, while supporting the consideration of coronary angiography for non-ST-elevation patients after ROSC.

The 2015 ILCOR systematic review examined whether immediate coronary angiography (angiography performed within 24 hours after ROSC) for patients with and without ST elevation after cardiac arrest improved outcomes.

#### 2015 Evidence Summary

Evidence regarding the timing of coronary angiography immediately after cardiac arrest (defined variously, but within 24 hours) is limited to observational studies.

Aggregated data from 15 studies of 3800 patients having ST elevation on ECG after ROSC after cardiac arrest demonstrated a benefit of immediate coronary angiography, favoring

survival to hospital discharge,<sup>102–116</sup> while 9 of these studies enrolling a total of 2819 patients also demonstrated a benefit favoring neurologically favorable outcomes.<sup>102–104,107,109–111,114,117</sup>

In patients without ST elevation on initial postarrest ECG, 2 studies demonstrated a benefit favoring improved survival to hospital discharge and improved neurologically favorable outcome when patients received immediate coronary angiography.<sup>102,107</sup>

In these studies, the decision to undertake the intervention was influenced by a variety of factors such as patient age, duration of CPR, hemodynamic instability, presenting cardiac rhythm, neurologic status upon hospital arrival, and perceived likelihood of cardiac etiology.

#### 2015 Recommendations—Updated

Coronary angiography should be performed emergently (rather than later in the hospital stay or not at all) for OHCA patients with suspected cardiac etiology of arrest and ST elevation on ECG (Class I, LOE B-NR).

Emergency coronary angiography is reasonable for select (eg, electrically or hemodynamically unstable) adult patients who are comatose after OHCA of suspected cardiac origin but without ST elevation on ECG (Class IIa, LOE B-NR).

Coronary angiography is reasonable in post-cardiac arrest patients where coronary angiography is indicated regardless of whether the patient is comatose or awake (Class IIa, LOE C-LD).

## Disclosures

### Part 9: Acute Coronary Syndromes: 2015 Guidelines Update Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

\*Modest.

†Significant.



## Appendix

## 2015 Guidelines Update: Part 9 Recommendations

Year Last Reviewed	Topic	Recommendation	Comments
2015	Diagnostic Interventions in ACS	Prehospital 12-lead ECG should be acquired early for patients with possible ACS (Class I, LOE B-NR).	new for 2015
2015	Diagnostic Interventions in ACS	Prehospital notification of the receiving hospital (if fibrinolysis is the likely reperfusion strategy) and/or prehospital activation of the catheterization laboratory should occur for all patients with a recognized STEMI on prehospital ECG (Class I, LOE B-NR).	updated for 2015
2015	Diagnostic Interventions in ACS	Because of high false-negative rates, we recommend that computer-assisted ECG interpretation not be used as a sole means to diagnose STEMI (Class III: Harm, LOE B-NR).	new for 2015
2015	Diagnostic Interventions in ACS	We recommend that computer-assisted ECG interpretation may be used in conjunction with physician or trained provider interpretation to recognize STEMI (Class IIb, LOE C-LD).	updated for 2015
2015	Diagnostic Interventions in ACS	While transmission of the prehospital ECG to the ED physician may improve PPV and therapeutic decision-making regarding adult patients with suspected STEMI, if transmission is not performed, it may be reasonable for trained non-physician ECG interpretation to be used as the basis for decision-making, including activation of the catheterization laboratory, administration of fibrinolysis, and selection of destination hospital (Class IIa, LOE B-NR).	new for 2015
2015	Diagnostic Interventions in ACS	We recommend against using hs-cTnT and cTnI alone measured at 0 and 2 hours (without performing clinical risk stratification) to exclude the diagnosis of ACS (Class III: Harm, LOE B-NR).	new for 2015
2015	Diagnostic Interventions in ACS	We recommend that hs-cTnI measurements that are less than the 99th percentile, measured at 0 and 2 hours, may be used together with low-risk stratification (TIMI score of 0 or 1) to predict a less than 1% chance of 30-day MACE (Class IIa, LOE B-NR).	new for 2015
2015	Diagnostic Interventions in ACS	We recommend that negative cTnI or cTnT measurements at 0 and between 3 and 6 hours may be used together with very low-risk stratification (Vancouver score of 0 or North American Chest Pain score of 0 and age less than 50 years) to predict a less than 1% chance of 30-day MACE (Class IIa, LOE B-NR).	new for 2015
2015	Therapeutic Interventions in ACS	In patients with suspected STEMI intending to undergo PPCI, initiation of ADP inhibition may be reasonable in either the prehospital or in-hospital setting (Class IIb, LOE C-LD).	new for 2015
2015	Therapeutic Interventions in ACS	We recommend that EMS systems that do not currently administer heparin to suspected STEMI patients do not add this treatment, whereas those that do administer it may continue their current practice (Class IIb, LOE B-NR).	new for 2015
2015	Therapeutic Interventions in ACS	In suspected STEMI patients for whom there is a planned PPCI reperfusion strategy, administration of unfractionated heparin (UFH) can occur either in the prehospital or in-hospital setting (Class IIb, LOE B-NR).	new for 2015
2015	Therapeutic Interventions in ACS	It may be reasonable to consider the prehospital administration of UFH in STEMI patients or the prehospital administration of bivalirudin in STEMI patients who are at increased risk of bleeding (Class IIb, LOE B-R).	new for 2015
2015	Therapeutic Interventions in ACS	In systems in which UFH is currently administered in the prehospital setting for patients with suspected STEMI who are being transferred for PPCI, it is reasonable to consider prehospital administration of enoxaparin as an alternative to UFH (Class IIa, LOE B-R).	updated for 2015
2015	Therapeutic Interventions in ACS	The usefulness of supplementary oxygen therapy has not been established in normoxic patients. In the prehospital, ED, and hospital settings, the withholding of supplementary oxygen therapy in normoxic patients with suspected or confirmed acute coronary syndrome may be considered (Class IIb, LOE C-LD).	updated for 2015
2015	Therapeutic Interventions in ACS	Where prehospital fibrinolysis is available as part of a STEMI system of care, and in-hospital fibrinolysis is the alternative treatment strategy, it is reasonable to administer prehospital fibrinolysis when transport times are more than 30 minutes (Class IIa, LOE B-R).	updated for 2015
2015	Therapeutic Interventions in ACS	Where prehospital fibrinolysis is available as part of the STEMI system of care and direct transport to a PCI center is available, prehospital triage and transport directly to a PCI center may be preferred because of the small relative decrease in the incidence of intracranial hemorrhage without evidence of mortality benefit to either therapy (Class IIb, LOE B-R).	new for 2015
2015	Therapeutic Interventions in ACS	In the treatment of patients with suspected STEMI, the combined application of fibrinolytic therapy followed by immediate PCI (as contrasted with immediate PCI alone) is not recommended. (Class III: Harm, LOE B-R).	new for 2015
2015	Therapeutic Interventions in ACS	If fibrinolytic therapy is provided, immediate transfer to a PCI center for cardiac angiography within 3 to 24 hours may be considered (Class IIb, LOE C-LD).	new for 2015

(Continued)

**2015 Guidelines Update: Part 9 Recommendations, *Continued***

Year Last Reviewed	Topic	Recommendation	Comments
2015	Therapeutic Interventions in ACS	Regardless of whether time of symptom onset is known, the interval between first medical contact and reperfusion should not exceed 120 minutes (Class I, LOE C-EO).	new for 2015
2015	Therapeutic Interventions in ACS	In STEMI patients presenting within 2 hours of symptom onset, immediate fibrinolysis rather than PPCI may be considered when the expected delay to PPCI is more than 60 minutes (Class IIb, LOE C-LD).	updated for 2015
2015	Therapeutic Interventions in ACS	In STEMI patients presenting within 2 to 3 hours after symptom onset, either immediate fibrinolysis or PPCI involving a possible delay of 60 to 120 minutes might be reasonable (Class IIb, LOE C-LD).	updated for 2015
2015	Therapeutic Interventions in ACS	In STEMI patients presenting within 3 to 12 hours after symptom onset, performance of PPCI involving a possible delay of up to 120 minutes may be considered rather than initial fibrinolysis (Class IIb, LOE C-LD).	updated for 2015
2015	Therapeutic Interventions in ACS	In STEMI patients when long delays to PPCI are anticipated (more than 120 minutes), a strategy of immediate fibrinolysis followed by routine early (within 3 to 24 hours) angiography and PCI if indicated, is reasonable (Class IIb, LOE B-R).	updated for 2015
2015	Therapeutic Interventions in ACS	In adult patients presenting with STEMI in the ED of a non-PCI-capable hospital, we recommend immediate transfer without fibrinolysis from the initial facility to a PCI center instead of immediate fibrinolysis at the initial hospital with transfer only for ischemia-driven PCI (Class I, LOE B-R).	new for 2015
2015	Therapeutic Interventions in ACS	When STEMI patients cannot be transferred to a PCI-capable hospital in a timely manner, fibrinolytic therapy with routine transfer for angiography may be an acceptable alternative to immediate transfer to PPCI (Class IIb, LOE C-LD).	new for 2015
2015	Therapeutic Interventions in ACS	When fibrinolytic therapy is administered to a STEMI patient in a non-PCI-capable hospital, it may be reasonable to transport all postfibrinolysis patients for early routine angiography in the first 3 to 6 hours and up to 24 hours rather than transport postfibrinolysis patients only when they require ischemia-guided angiography (Class IIb, LOE B-R).	new for 2015
2015	Hospital Reperfusion Decisions After ROSC	Coronary angiography should be performed emergently (rather than later in the hospital stay or not at all) for OHCA patients with suspected cardiac etiology of arrest and ST elevation on ECG (Class I, LOE B-NR).	updated for 2015
2015	Hospital Reperfusion Decisions After ROSC	Emergency coronary angiography is reasonable for select (eg, electrically or hemodynamically unstable) adult patients who are comatose after OHCA of suspected cardiac origin but without ST elevation on ECG (Class IIa, LOE B-NR).	updated for 2015
2015	Hospital Reperfusion Decisions After ROSC	Coronary angiography is reasonable in post-cardiac arrest patients where coronary angiography is indicated regardless of whether the patient is comatose or awake (Class IIa, LOE C-LD).	updated for 2015
The following recommendations were not reviewed in 2015. For more information, see the <i>2010 AHA Guidelines for CPR and ECC</i> , "Part 10: Acute Coronary Syndromes."			
2010	Prehospital ECGs	If providers are not trained to interpret the 12-lead ECG, field transmission of the ECG or a computer report to the receiving hospital is recommended (Class I, LOE B).	not reviewed in 2015
2010	Prehospital Fibrinolysis	It is strongly recommended that systems which administer fibrinolytics in the prehospital setting include the following features: protocols using fibrinolytic checklists, 12-lead ECG acquisition and interpretation, experience in advanced life support, communication with the receiving institution, medical director with training and experience in STEMI management, and continuous quality improvement (Class I, LOE C).	not reviewed in 2015
2010	Prehospital Triage and EMS Hospital Destination	If PCI is the chosen method of reperfusion for the prehospital STEMI patient, it is reasonable to transport patients directly to the nearest PCI facility, bypassing closer EDs as necessary, in systems where time intervals between first medical contact and balloon times are <90 minutes and transport times are relatively short (ie, <30 minutes) (Class IIa, LOE B).	not reviewed in 2015
2010	Focused Assessment and ECG Risk Stratification	This initial evaluation must be efficient because if the patient has STEMI, the goals of reperfusion are to administer fibrinolytics within 30 minutes of arrival (30-minute interval "door-to-drug") or to provide PCI within 90 minutes of arrival (90-minute interval "door-to-balloon") (Class I, LOE A).	not reviewed in 2015
2010	Cardiac Biomarkers	If biomarkers are initially negative within 6 hours of symptom onset, it is recommended that biomarkers should be remeasured between 6 to 12 hours after symptom onset (Class I, LOE A).	not reviewed in 2015
2010	STEMI	If the patient meets the criteria for fibrinolytic therapy, a door-to-needle time (initiation of fibrinolytic agent) <30 minutes is recommended—the earlier the better (Class I, LOE A).	not reviewed in 2015

*(Continued)*

2015 Guidelines Update: Part 9 Recommendations, *Continued*

Year Last Reviewed	Topic	Recommendation	Comments
2010	STEMI	Consultation delays therapy and is associated with increased hospital mortality rates (Class III, LOE B).	not reviewed in 2015
2010	Indicators for Early Invasive Strategies	An early invasive PCI strategy is indicated for patients with non-ST-elevation ACS who have no serious comorbidity and who have coronary lesions amenable to PCI and an elevated risk for clinical events (Class I, LOE A).	not reviewed in 2015
2010	Indicators for Early Invasive Strategies	An early invasive strategy (ie, diagnostic angiography with intent to perform revascularization) is indicated in non-ST-elevation ACS patients who have refractory angina or hemodynamic or electric instability (without serious comorbidities or contraindications to such procedures) (Class I, LOE B).	not reviewed in 2015
2010	Indicators for Early Invasive Strategies	In initially stabilized patients, an initially conservative (ie, a selectively invasive) strategy may be considered as a treatment strategy for non-ST-elevation ACS patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events including those with abnormal troponin elevations (Class IIb, LOE B).	not reviewed in 2015
2010	The Chest Pain Unit Model	In patients with suspicion for ACS, normal initial biomarkers, and nonischemic ECG, chest pain observation protocols may be recommended as a safe and effective strategy for evaluating patients in the ED (Class I, LOE A).	not reviewed in 2015
2010	Fibrinolytics	If fibrinolysis is chosen for reperfusion, the ED physician should administer fibrinolytics to eligible patients as early as possible according to a predetermined process of care developed by the ED and cardiology staff (Class I, LOE A).	not reviewed in 2015
2010	Fibrinolytics	In fact, fibrinolytic therapy is generally not recommended for patients presenting between 12 and 24 hours after onset of symptoms based on the results of the LATE and EMERAS trials, unless continuing ischemic pain is present with continuing ST-segment elevation (Class IIb, LOE B).	not reviewed in 2015
2010	Fibrinolytics	Fibrinolytic therapy should not be administered (Class III, LOE B) to patients who present greater than 24 hours after the onset of symptoms.	not reviewed in 2015
2010	Percutaneous Coronary Intervention (PCI)	Coronary angioplasty with or without stent placement is the treatment of choice for the management of STEMI when it can be performed effectively with a door-to-balloon time <90 minutes by a skilled provider (performing >75 PCIs per year) at a skilled PCI facility (performing >200 PCIs annually, of which at least 36 are primary PCI for STEMI) (Class I, LOE A).	not reviewed in 2015
2010	PCI Following ROSC After Cardiac Arrest	It is reasonable to include cardiac catheterization and coronary angiography in standardized post-cardiac arrest protocols as part of an overall strategy to improve neurologically intact survival in this patient group (Class IIa, LOE B).	not reviewed in 2015
2010	PCI Following ROSC After Cardiac Arrest	Angiography and/or PCI need not preclude or delay other therapeutic strategies including therapeutic hypothermia (Class IIa, LOE B).	not reviewed in 2015
2010	PCI Following ROSC After Cardiac Arrest	A 12-lead ECG should be performed as soon as possible after ROSC (Class I, LOE A).	not reviewed in 2015
2010	PCI Versus Fibrinolytic Therapy	In summary, for patients presenting within 12 hours of symptom onset and electrocardiographic findings consistent with STEMI, reperfusion should be initiated as soon as possible – independent of the method chosen (Class I, LOE A).	not reviewed in 2015
2010	PCI Versus Fibrinolytic Therapy	Primary PCI performed at a high-volume center within 90 minutes of first medical contact by an experienced operator that maintains an appropriate expert status is reasonable, as it improves morbidity and mortality as compared with immediate fibrinolysis (<30 minutes door-to-needle) (Class I, LOE A).	not reviewed in 2015
2010	PCI Versus Fibrinolytic Therapy	For those patients with a contraindication to fibrinolysis, PCI is recommended despite the delay, rather than foregoing reperfusion therapy (Class I, LOE A).	not reviewed in 2015
2010	Clopidogrel	On the basis of these findings, providers should administer a loading dose of clopidogrel in addition to standard care (aspirin, anticoagulants, and reperfusion) for patients determined to have moderate- to high-risk non-ST-segment elevation ACS and STEMI (Class I, LOE A).	not reviewed in 2015
2010	Clopidogrel	It is reasonable to administer a 300-mg oral dose of clopidogrel to ED patients with suspected ACS (without ECG or cardiac marker changes) who are unable to take aspirin because of hypersensitivity or major gastrointestinal intolerance (Class IIa, LOE B).	not reviewed in 2015
2010	Clopidogrel	Providers should administer a 300-mg oral dose of clopidogrel to ED patients up to 75 years of age with STEMI who receive aspirin, heparin, and fibrinolysis (Class I, LOE B).	not reviewed in 2015
2010	Prasugrel	Prasugrel (60 mg oral loading dose) may be substituted for clopidogrel after angiography in patients determined to have non-ST-segment elevation ACS or STEMI who are more than 12 hours after symptom onset prior to planned PCI (Class IIa, LOE B).	not reviewed in 2015

*(Continued)*

2015 Guidelines Update: Part 9 Recommendations, *Continued*

Year Last Reviewed	Topic	Recommendation	Comments
2010	Prasugrel	There is no direct evidence for the use of prasugrel in the ED or prehospital settings. In patients who are not at high risk for bleeding, administration of prasugrel (60-mg oral loading dose) prior to angiography in patients determined to have STEMI $\leq$ 12 hours after the initial symptoms may be substituted for administration of clopidogrel (Class IIa, LOE B).	not reviewed in 2015
2010	Initial EMS Care	Because aspirin should be administered as soon as possible after symptom onset to patients with suspected ACS, it is reasonable for EMS dispatchers to instruct patients with no history of aspirin allergy and without signs of active or recent gastrointestinal bleeding to chew an aspirin (160 to 325 mg) while awaiting the arrival of EMS providers (Class IIa, LOE C).	not reviewed in 2015
2010	Initial EMS Care	If the patient is dyspneic, hypoxemic, or has obvious signs of heart failure, providers should titrate therapy, based on monitoring of oxyhemoglobin saturation, to 94% (Class I, LOE C).	not reviewed in 2015
2010	Initial EMS Care	EMS providers should administer nonenteric aspirin (160 [Class I, LOE B] to 325 mg [Class I, LOE C]).	not reviewed in 2015
2010	Initial EMS Care	Morphine is indicated in STEMI when chest discomfort is unresponsive to nitrates (Class I, LOE C).	not reviewed in 2015
2010	Initial EMS Care	Morphine should be used with caution in unstable angina (UA)/NSTEMI due to an association with increased mortality in a large registry (Class IIa, LOE C).	not reviewed in 2015
2010	Interfacility Transfer	These include patients who are ineligible for fibrinolytic therapy or who are in cardiogenic shock (Class I, LOE C).	not reviewed in 2015
2010	Interfacility Transfer	Transfer of high-risk patients who have received primary reperfusion with fibrinolytic therapy is reasonable (Class IIa, LOE B).	not reviewed in 2015
2010	TIMI Risk Score	These findings confirm the value of the TIMI risk score as a guide to therapeutic decisions (Class IIa, LOE B).	not reviewed in 2015
2010	Indicators for Early Invasive Strategies	The decision to implement an initial conservative (versus initial invasive) strategy in these patients may be made by considering physician and patient preference (Class IIb, LOE C).	not reviewed in 2015
2010	Advanced Testing to Detect Coronary Ischemia and CAD	For ED/CPU patients who are suspected of having ACS, have nonischemic ECG's and negative biomarkers, a noninvasive test for inducible myocardial ischemia or anatomic evaluation of the coronary arteries (eg, computed tomography [CT] angiography, cardiac magnetic resonance, myocardial perfusion imaging, stress echocardiography) can be useful in identifying patients suitable for discharge from the ED (Class IIa, LOE B).	not reviewed in 2015
2010	Advanced Testing to Detect Coronary Ischemia and CAD	MPS can also be used for risk stratification, especially in low- to intermediate likelihood of cardiac events according to traditional cardiac markers (Class IIa, LOE B).	not reviewed in 2015
2010	Advanced Testing to Detect Coronary Ischemia and CAD	The use of MDCT angiography for selected low-risk patients can be useful to allow for safe early discharge from the ED (Class IIa, LOE B).	not reviewed in 2015
2010	Safety of Discharge and Risk of Major Adverse Cardiac Events After Discharge From the ED/CPU	The use of inpatient-derived risk scoring systems are useful for prognosis (Class I, LOE A) but are not recommended to identify patients who may be safely discharged from the ED (Class III, LOE C).	not reviewed in 2015
2010	Aspirin and Nonsteroidal Anti-inflammatory Drugs	Therefore, unless the patient has a known aspirin allergy or active gastrointestinal hemorrhage, nonenteric aspirin should be given as soon as possible to all patients with suspected ACS (Class I, LOE A).	not reviewed in 2015
2010	Aspirin and Nonsteroidal Anti-inflammatory Drugs	NSAIDs (except for aspirin), both nonselective as well as COX-2 selective agents, should not be administered during hospitalization for STEMI because of the increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use (Class III, LOE C).	not reviewed in 2015
2010	Nitroglycerin (or Glyceryl Trinitrate)	Patients with ischemic discomfort should receive up to 3 doses of sublingual or aerosol nitroglycerin at 3- to 5-minute intervals until pain is relieved or low blood pressure limits its use (Class I, LOE B).	not reviewed in 2015
2010	Nitroglycerin (or Glyceryl Trinitrate)	The use of nitrates in patients with hypotension (SBP $<$ 90 mm Hg or $\geq$ 30 mm Hg below baseline), extreme bradycardia ( $<$ 50 bpm), or tachycardia in the absence of heart failure ( $>$ 100 bpm) and in patients with right ventricular infarction is contraindicated (Class III, LOE C).	not reviewed in 2015
2010	Analgesia	Providers should administer analgesics, such as intravenous morphine, for chest discomfort unresponsive to nitrates. Morphine is the preferred analgesic for patients with STEMI (Class I, LOE C).	not reviewed in 2015
2010	$\beta$ -Adrenergic Receptor Blockers	IV $\beta$ -blocker therapy may be considered as reasonable in specific situations such as severe hypertension or tachyarrhythmias in patients without contraindications (Class IIa, LOE B).	not reviewed in 2015

*(Continued)*

2015 Guidelines Update: Part 9 Recommendations, *Continued*

Year Last Reviewed	Topic	Recommendation	Comments
2010	$\beta$ -Adrenergic Receptor Blockers	In the absence of contraindications, PO $\beta$ -blockers should be administered within the first 24 hours to patients with suspected ACS (Class I, LOE A).	not reviewed in 2015
2010	$\beta$ -Adrenergic Receptor Blockers	It is reasonable to start oral $\beta$ -blockers with low doses after the patient is stabilized prior to discharge (Class IIa, LOE B).	not reviewed in 2015
2010	Treatment Recommendations for UA/NSTEMI	For in-hospital patients with NSTEMI managed with a planned initial conservative approach, either fondaparinux (Class IIa, LOE B) or enoxaparin (Class IIa, LOE A) are reasonable alternatives to UFH or placebo.	not reviewed in 2015
2010	Treatment Recommendations for UA/NSTEMI	For in-hospital patients with NSTEMI managed with a planned invasive approach, either enoxaparin or UFH are reasonable choices (Class IIa, LOE A).	not reviewed in 2015
2010	Treatment Recommendations for UA/NSTEMI	Fondaparinux may be used in the setting of PCI, but requires co-administration of UFH and does not appear to offer an advantage over UFH alone (Class IIb, LOE A).	not reviewed in 2015
2010	Treatment Recommendations for UA/NSTEMI	For in-hospital patients with NSTEMI and renal insufficiency, bivalirudin or UFH may be considered (Class IIb, LOE A).	not reviewed in 2015
2010	Treatment Recommendations for UA/NSTEMI	For in-hospital patients with NSTEMI and increased bleeding risk, where anticoagulant therapy is not contraindicated, fondaparinux (Class IIa, LOE B) or bivalirudin (Class IIa, LOE A) are reasonable and UFH may be considered (Class IIb, LOE C).	not reviewed in 2015
2010	Enoxaparin	For patients with STEMI managed with fibrinolysis in the hospital, it is reasonable to administer enoxaparin instead of UFH (Class IIa, LOE A).	not reviewed in 2015
2010	Enoxaparin	In addition, for prehospital patients with STEMI managed with fibrinolysis, adjunctive enoxaparin instead of UFH may be considered (Class IIb, LOE A).	not reviewed in 2015
2010	Enoxaparin	Patients initially treated with enoxaparin should not be switched to UFH and vice versa because of increased risk of bleeding (Class III, LOE C).	not reviewed in 2015
2010	Enoxaparin	In younger patients <75 years the initial dose of enoxaparin is 30 mg IV bolus followed by 1 mg/kg SC every 12 hours (first SC dose shortly after the IV bolus) (Class IIb, LOE A).	not reviewed in 2015
2010	Enoxaparin	Patients $\geq$ 75 years may be treated with 0.75 mg/kg SC enoxaparin every 12 hours without an initial IV bolus (Class IIb, LOE B).	not reviewed in 2015
2010	Enoxaparin	Patients with impaired renal function (creatinine clearance <30 mL/min) may be given 1 mg/kg enoxaparin SC once daily (Class IIb, LOE B).	not reviewed in 2015
2010	Enoxaparin	Patients with known impaired renal function may alternatively be managed with UFH (Class IIb, LOE B).	not reviewed in 2015
2010	Fondaparinux	Fondaparinux (initially 2.5 mg IV followed by 2.5 mg SC once daily) may be considered in the hospital for patients treated specifically with non-fibrin-specific thrombolytics (ie, streptokinase), provided the creatinine is 3 mg/dL (Class IIb, LOE B).	not reviewed in 2015
2010	Unfractionated Heparin Versus Low-Molecular-Weight Heparin With PPCI in STEMI	For patients with STEMI undergoing contemporary PCI (ie, additional broad use of glycoprotein IIb/IIIa inhibitors and a thienopyridine) enoxaparin may be considered a safe and effective alternative to UFH (Class IIb, LOE B).	not reviewed in 2015
2010	Unfractionated Heparin Versus Low-Molecular-Weight Heparin With PPCI in STEMI	Patients initially treated with enoxaparin should not be switched to UFH and vice versa to avoid increased risk of bleeding. Fondaparinux may be considered as an alternative to UFH, however, there is an increased risk of catheter thrombi with fondaparinux alone. Additional UFH (50 to 100 U/kg bolus) may help to avoid this complication (Class IIb, LOE B), but using these two agents is not recommended over UFH alone.	not reviewed in 2015
2010	Unfractionated Heparin Versus Low-Molecular-Weight Heparin With PPCI in STEMI	For fondaparinux and enoxaparin it is necessary to adjust the dose in patients with renal impairment. Bivalirudin may be considered as an alternative to UFH and GP IIb/IIIa inhibitors (Class IIb, LOE A).	not reviewed in 2015
2010	ACE Inhibitors and ARBs in the Hospital	Administration of an oral ACE inhibitor is recommended within the first 24 hours after onset of symptoms in STEMI patients with pulmonary congestion or LV ejection fraction <40%, in the absence of hypotension (SBP <100 mm Hg or $\geq$ 30 mm Hg below baseline) (Class I, LOE A).	not reviewed in 2015
2010	ACE Inhibitors and ARBs in the Hospital	Oral ACE inhibitor therapy can also be useful for all other patients with AMI with or without early reperfusion therapy (Class IIa, LOE B).	not reviewed in 2015
2010	ACE Inhibitors and ARBs in the Hospital	IV administration of ACE inhibitors is contraindicated in the first 24 hours because of risk of hypotension (Class III, LOE C).	not reviewed in 2015
2010	ACE Inhibitors in the Prehospital Setting	In conclusion, although ACE inhibitors and ARBs have been shown to reduce long-term risk of mortality in patients suffering an AMI, there is insufficient evidence to support the routine initiation of ACE inhibitors and ARBs in the prehospital or ED setting (Class IIb, LOE C).	not reviewed in 2015

*(Continued)*

2015 Guidelines Update: Part 9 Recommendations, *Continued*

Year Last Reviewed	Topic	Recommendation	Comments
2010	HMG Coenzyme A Reductase Inhibitors (Statins)	There is little data to suggest that this therapy should be initiated within the ED; however, early initiation (within 24 hours of presentation) of statin therapy is recommended in patients with an ACS or AMI (Class I, LOE C).	not reviewed in 2015
2010	HMG Coenzyme A Reductase Inhibitors (Statins)	If patients are already on statin therapy, continue the therapy (Class IIb, LOE C).	not reviewed in 2015
2010	HMG Coenzyme A Reductase Inhibitors (Statins)	Statins should not be discontinued during the index hospitalization unless contraindicated (Class III, LOE C).	not reviewed in 2015
2010	HMG Coenzyme A Reductase Inhibitors (Statins)	In conclusion, intensive (target LDL values optimally 70 mg/dL) statin treatment should be initiated within the first 24 hours after onset of an ACS event (eg, immediately after hospital admission) in all patients presenting with any form of ACS unless strictly contraindicated (eg, by proven intolerance) (Class I, LOE A).	not reviewed in 2015
2010	Glucose-Insulin-Potassium	At this time there is little evidence to suggest that this intervention is helpful (Class IIb, LOE C).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	the practice of prophylactic administration of lidocaine is not recommended (Class III, LOE A).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	Sotalol has not been adequately studied (Class IIb, LOE C).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	Amiodarone in a single RCT did not appear to improve survival in low doses and may increase mortality in high doses when used early in patients with suspected myocardial infarction (Class IIb, LOE C).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	prophylactic antiarrhythmics are not recommended for patients with suspected ACS or myocardial infarction in the prehospital or ED (Class III, LOE A).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	Routine IV administration of $\beta$ -blockers to patients without hemodynamic or electric contraindications is associated with a reduced incidence of primary VF (Class IIb, LOE C).	not reviewed in 2015
2010	Ventricular Rhythm Disturbances	It is prudent clinical practice to maintain serum potassium $>4$ mEq/L and magnesium $>2$ mEq/L (Class IIb, LOE A).	not reviewed in 2015

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KEY WORDS: electrocardiogram ■ fibrinolytics ■ myocardial infarction ■ ST-segment elevation ■ unstable angina

## Part 9: Acute Coronary Syndromes: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

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*Circulation*. 2015;132:S483-S500

doi: 10.1161/CIR.0000000000000263

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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