



Complete Summary

GUIDELINE TITLE

Clinical policy: critical issues in the evaluation and management of adult patients with non-ST-segment elevation acute coronary syndromes.

BIBLIOGRAPHIC SOURCE(S)

Fesmire FM, Decker WW, Diercks DB, Ghaemmaghami CA, Nazarian D, Brady WJ, Hahn S, Jagoda AS, American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients with non-ST-segment elevation acute coronary syndromes. *Ann Emerg Med* 2006 Sep;48(3):270-301. [115 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- [June 8, 2007, Troponin-I Immunoassay](#): Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Non-ST-segment elevation acute coronary syndromes

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To provide evidence-based recommendations for the medical evaluation and management of adult patients who present to the emergency department (ED) with non-ST-segment elevation acute coronary syndromes
- To address the following critical questions:
 - Are serial electrocardiograms useful during the ED evaluation of patients with suspected acute coronary syndromes?
 - Is there a preferred regimen of serum marker testing in the ED for the exclusion of non-ST-segment elevation acute myocardial infarction (AMI)?
 - What are the indications for ED administration of glycoprotein IIb/IIIa inhibitors in patients with non-ST-segment elevation acute coronary syndromes?
 - What are the indications for ED administration of clopidogrel in patients with non-ST-segment elevation acute coronary syndromes?

TARGET POPULATION

Adult patients presenting to the emergency department with suspected non-ST-segment elevation acute coronary syndromes

This guideline is not intended for pediatric patients, patients in cardiogenic shock, or patients with injury on the initial 12-lead electrocardiogram.

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Repeat electrocardiogram (ECG) or automated serial 12-lead ECG monitoring in the emergency department (ED)
2. Cardiac serum marker tests to exclude non–ST-segment elevation acute myocardial infarction in the ED

Treatment

1. ED administration of glycoprotein IIb/IIIa inhibitors (abciximab, tirofiban, or eptifibatide)
2. ED administration of clopidogrel

MAJOR OUTCOMES CONSIDERED

- Utility and prognostic value of serial electrocardiograms (ECGs) and serum markers in the emergency department
- Efficacy of treatment:
 - In-hospital and 30-day mortality rate
 - Death from cardiovascular causes
 - Non-fatal acute myocardial infarction
 - Urgent revascularization
- Bleeding complications

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The American College of Emergency Physicians (ACEP) Clinical Policies Subcommittee performed multiple MEDLINE searches. The medical literature was reviewed for articles that pertained to each critical question posed, and pertinent articles were selected. Those articles were evaluated, and those addressing the questions considered in this document were chosen for grading. Subcommittee members also supplied articles from bibliographies of initially selected articles or from their own files.

See the original guideline document for specific search strategies for each critical question.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Literature Classification Schema[^]

Design/Class	Therapy*	Diagnosis **	Prognosis***
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

[^] Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

*Objective is to measure therapeutic efficacy comparing ≥ 2 interventions.

**Objective is to determine the sensitivity and specificity of diagnostic tests.

*** Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence*

	Design/Class		
Downgrading	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See "Description of Methods Used to Analyze the Evidence" field for more information.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

This clinical policy was created after careful review and critical analysis of the medical literature.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic clinical reports respectively (see Appendix A in the original guideline document and the "Rating Scheme for the Strength of the Evidence" field). Articles were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (e.g., selection, detection, transfer), external validity (i.e., generalizability), and sufficient sample size. Articles received a final grade (I, II, III) on the basis of a predetermined formula taking into account design and quality of study (see Appendix B in the original guideline document and the "Rating Scheme for the Strength of the Evidence" field). Articles with fatal flaws were given an "X" grade and not used in the creation of this policy. Evidence grading was done with respect to the specific data being extracted, and the specific critical question being reviewed. Thus, the level of evidence for any one study may vary according to the question, and it is possible for a single article to receive different levels of grading as different critical questions are answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of the original guideline document.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This policy is a product of the American College of Emergency Physicians (ACEP) clinical policy development process and is based on the existing literature; where literature was not available, consensus of emergency physicians was used.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Clinical findings and strength of recommendations regarding patient management were made according to the following criteria:

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all the issues)

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies)

Level C recommendations. Other strategies for patient management based on preliminary, inconclusive, or conflicting evidence, or, in the absence of any published literature, based on panel consensus

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Expert review comments were received from individual emergency physicians and individual members of the American College of Cardiology, the Emergency Medicine Cardiac Research and Education Group, and the Society of Chest Pain Centers. Their responses were used to further refine and enhance this policy.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the strength of evidence (Class I-III) and strength of recommendations (Level A-C) are repeated at the end of the "Major Recommendations" field.

1. **Are serial electrocardiograms (ECGs) useful during the emergency department (ED) evaluation of patients with suspected acute coronary syndromes?**

Level A recommendations. None specified.

Level B recommendations. Perform repeat ECG or automated serial ECGs during the ED evaluation of patients in whom the initial ECG is nondiagnostic for injury and who have symptoms consistent with ongoing or recurrent ischemia.

No recommendations can be made in regards to the exact timing of repeat ECGs. Studies suggest that 30 to 60 minutes after baseline may be a reasonable time interval for repeat ECG.

Level C recommendations. None specified.

2. **Is there a preferred regimen of serum marker testing in the ED for the exclusion of non-ST-segment elevation acute myocardial infarction (AMI)?**

Inclusion Criteria. Patients with symptoms suggestive of acute coronary syndromes presenting less than or equal to 12 hours of symptom onset.

Level A recommendations. Do not utilize cardiac serum marker tests to exclude non-AMI acute coronary syndromes (i.e., unstable angina).

Level B recommendations. Utilize any of the following cardiac serum marker tests to exclude non-ST-segment elevation AMI as defined by the World Health Organization (WHO) or modified WHO criteria (see below):*

1. A single negative creatine kinase MB band (CK-MB) mass, Troponin I, or Troponin T measured 8 to 12^a hours after symptom onset^b
2. A negative myoglobin in conjunction with a negative CK-MB mass, or negative Troponin^c when measured at baseline and 90 minutes in patients presenting less than 8 hours after symptom onset^b
3. A negative 2-hour delta^d CK-MB mass in conjunction with a negative 2-hour delta^d Troponin^c in patients presenting less than 8 hours after symptom onset^b

Level C recommendations. None specified.

*There is insufficient evidence at this time to make any recommendations in regards to utilization of cardiac serum markers to exclude non-ST-segment elevation AMI using current Joint European Society of Cardiology (ESC)/ACC criteria for AMI (see Figure 2 in the original guideline document).

^aThe exact timing of serum marker measurement as it relates to time of symptom onset should take into account the sensitivity, precision, and institutional norms of the assay being utilized, as well as the release kinetics of the marker being measured.

^bIf time of symptom onset is unknown, unreliable, or more consistent with preinfarctional angina, then time of symptom onset should be referenced to the time of ED presentation.

^cOnly Troponin I has been investigated in the serial 90 minute multimarker protocol and the 2-hour delta protocol.

^dThe appropriate delta values for exclusion of AMI should take into account the sensitivity and precision of the assay utilized and confirmed by in-house studies. It is also important that delta serum marker levels are measured on the same instrument due to subtle variations in calibration among individual instruments of the same model.

WHO Diagnostic Criteria for Acute Myocardial Infarction (One of following):

1. Definite ECG*, or
2. Symptoms** typical or atypical or inadequately described, together with probable ECG*** and abnormal enzymes[^], or
3. Symptoms typical** and abnormal enzymes[^] with ischemic or noncodable

- ECG or ECG not available, or
4. Fatal case, whether sudden or not, with naked-eye appearance of fresh myocardial infarction and/or recent coronary occlusion found at necropsy.

*Definite ECG:

- a. The development in serial records of a diagnostic Q wave and/or
- b. The evolution of an injury current that lasts more than 1 day.

**Duration of more than 20 minutes

***Probable ECG: Evolution of major ST-elevation, major ST-depression, and/or major T-wave inversion

^Abnormal enzymes: if at least one reading is more than twice the upper limit of normal

Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*. 1994;90:583-612. Reprinted with permission.

3. **What are the indications for ED administration of glycoprotein IIB/IIIa inhibitors in patients with non-ST-segment elevation acute coronary syndromes?**

Exclusion Criteria: Contraindications for a glycoprotein inhibitor (bleeding disorder, renal insufficiency, etc).

Level A recommendations. None specified.

Level B recommendations. Consider administration of glycoprotein IIB/IIIa inhibitors (abciximab, tirofiban, or eptifibatide) prior to percutaneous coronary intervention to patients with positive troponin or ischemic ST-segment depression in whom an early interventional strategy is anticipated.* Studies suggest that benefit is greatest in patients in whom treatment was initiated within 6 hours of symptom onset and in patients in whom there will be a delay in percutaneous coronary intervention.

Level C recommendations. Consider administration of glycoprotein IIB/IIIa inhibitors (tirofiban or eptifibatide) to patients with positive troponin or ischemic ST-segment depression in whom a *non-interventional* strategy is planned.*

*There is insufficient information at this time to make any recommendations in regards to the exact location or timing for initiation of glycoprotein IIB/IIIa inhibitor therapy (i.e., ED versus in-hospital).

4. **What are the indications for ED administration of clopidogrel in patients with non-ST-segment elevation acute coronary syndromes?**

Exclusion Criteria: Aspirin allergy; contraindications for clopidogrel therapy (e.g., bleeding disorder, other).

Level A recommendations. None specified.

Level B recommendations. Administer a loading dose of clopidogrel in patients with elevated troponin or ischemic ST-segment depression*:

1. In whom a non-interventional approach is planned
2. Prior to percutaneous coronary intervention in patients in whom an interventional approach is planned and who are not at significant risk for urgent coronary artery bypass graft.

Level C recommendations. None specified.

*There is insufficient information at this time to make any recommendations in regard to the exact location or timing for administration of the initial clopidogrel loading dose (i.e., ED versus in-hospital administration). Studies in elective percutaneous coronary intervention suggest benefit is greatest if clopidogrel is administered at least 6 hours prior to percutaneous coronary intervention.

Definitions:

Literature Classification Schema[^]

Design/Class	Therapy*	Diagnosis **	Prognosis***
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
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**Objective is to determine the sensitivity and specificity of diagnostic tests.

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Approach to Downgrading Strength of Evidence*

	Design/Class		
Downgrading	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See "Description of Methods Used to Analyze the Evidence" field for more information.

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all the issues)

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies)

Level C recommendations. Other strategies for patient management based on preliminary, inconclusive, or conflicting evidence, or, in the absence of any published literature, based on panel consensus

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CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and management of adult patients with non-ST-segment elevation acute coronary syndromes

POTENTIAL HARMS

Adverse Effects of Medications

Glycoprotein IIb/IIIa inhibitors and *clopidogrel* are associated with bleeding complications.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contraindications to *glycoprotein IIb/IIIa inhibitors*: bleeding disorder, renal insufficiency etc.
- Contraindications to *clopidogrel* therapy: bleeding disorder, other

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. The American College of Emergency Physicians (ACEP) clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the crucial questions addressed in this policy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Fesmire FM, Decker WW, Diercks DB, Ghaemmaghami CA, Nazarian D, Brady WJ, Hahn S, Jagoda AS, American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients with non-ST-segment elevation acute coronary syndromes. *Ann Emerg Med* 2006 Sep;48(3):270-301. [115 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Sep

GUIDELINE DEVELOPER(S)

American College of Emergency Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Emergency Physicians

GUIDELINE COMMITTEE

Clinical Policies Subcommittee on Non-ST-Segment Elevation Acute Coronary Syndromes

ACEP Clinical Policies Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [American College of Emergency Physicians Web site](#).

Print copies: Available from the American College of Emergency Physicians, P.O. Box 619911, Dallas, TX 75261-9911, or call toll free: (800) 798-1822.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 28, 2006. The information was verified by the guideline developer on January 5, 2007. This summary was updated by ECRI Institute on July 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Troponin-1 Immunoassay.

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