Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting With Suspected Acute Myocardial Infarction or Unstable Angina

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Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting With Suspected Acute Myocardial Infarction or Unstable Angina

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Approved by the ACEP Board of Directors, January 17, 2000.

This clinical policy focuses on critical issues in the evaluation and management of patients with acute myocardial infarction or unstable angina. A MEDLINE search for articles published between January 1993 and December 1998 was performed using combinations of the key words chest pain, acute myocardial infarction, unstable angina, thrombolytics, primary angioplasty, 12-lead ECG, ST-segment monitoring, cardiac serum markers, and chest pain centers. Subcommittee members and expert peer reviewers also supplied articles with direct bearing on the policy. This policy focuses on 5 areas of current interest and/or controversy: (1) ECG eligibility criteria for fibrinolytic therapy, (2) role of primary angioplasty in patients with acute myocardial infarction, (3) use of serum markers to diagnose acute myocardial infarction, (4) serial 12-lead ECGs during the initial evaluation, and (5) chest pain evaluation units. Recommendations for patient management are provided for each of these 5 topics based on strength of evidence (Standards, Guidelines, Options). *Standards* represent patient management principles that reflect a high degree of clinical certainty; *Guidelines* represent patient management principles that reflect moderate clinical certainty; and *Options* represent other patient management strategies based on preliminary, inconclusive, or conflicting evidence, or based on panel consensus. This guideline is intended for physicians working in hospital-based emergency departments or chest pain evaluation units.

[American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting with suspected acute myocardial infarction or unstable angina. *Ann Emerg Med.* May 2000;35:521-544.]

INTRODUCTION

Chest pain is one of the most common and complex symptoms for which patients seek emergency department care. The diagnoses for patients with chest pain range from minor disease processes such as chest wall strain or indigestion to life-threatening conditions such as acute myocardial infarction (AMI) or aortic dissection. Not only does missing a life-threatening condition result in potential serious morbidity and mortality to the patient, but this represents a frequent cause of malpractice suits against emergency physicians and the most dollars awarded.[1,2] For these reasons, the American College of Emergency Physicians (ACEP) chose chest pain as the topic of its first clinical policy, which was published in 1990[3] and revised in 1995.[4] The format of the initial and revised chest pain clinical policies focused on the evaluation of a patient presenting with a chief complaint of chest pain as opposed to specific disease processes. It was a broad-based attempt to focus on key history, physical, and diagnostic findings to drive the diagnosis of potentially serious medical conditions with emphasis on AMI, aortic dissection, pericarditis, myocarditis, pneumonia, pulmonary embolus, pneumothorax, and pulmonary edema. Because of the all-inclusive nature of the previous policies, the format did not allow specific emphasis on critical issues in the evaluation of selected subsets of chest pain patients.

Over the past decade there has been an explosion of published research and development of new diagnostic modalities and therapies relating to disorders causing chest pain. These newer diagnostic and therapeutic modalities are being developed at a pace that far exceeds the ability of one physician to keep track. This current policy is a scheduled revision of the previous chest pain clinical policy. However, the Clinical Policies Committee believed that the format of the previous complaint-based clinical policy had gone as far as possible in directing the appropriate evaluation and treatment of patients presenting with chest pain. The committee was satisfied that the original policy had met the original goals of ACEP. This has been exemplified by the use of clinical policies to direct physician education and research, its utilization by quality improvement personnel in individual hospitals, its use in medical malpractice cases for establishing a reasonable standard of care, and its utilization by private companies in creating templates for physician history and physicals. A decision was made to develop a revised policy that focuses on critical issues in the evaluation and management of patients with AMI or unstable angina. It is hoped that departure from the previous format will not only improve patient care, but also direct critical areas of future research.

Methodology

This clinical policy was created after careful review and critical analysis of the peer-reviewed literature. A MEDLINE search for articles published between January 1993 and December 1998 was performed using combinations of the key words chest pain, AMI, unstable angina, and thrombolytics. Abstracts were reviewed by subcommittee members, who then selected the following topics on which to focus this policy: (1) ECG eligibility criteria for fibrinolytic therapy, (2) role of primary angioplasty in patients with AMI, (3) use of serum markers to diagnose AMI, (4) serial 12-lead ECGs during the initial evaluation, and (5) chest pain evaluation units. Additional MEDLINE searches were performed using the key words 12-lead ECG, ST-segment monitoring, cardiac serum markers, and chest pain centers. Pertinent articles were selected from the reviewed abstracts and from bibliographies of initially selected papers. Committee members and expert reviewers also supplied papers from their own knowledge base. All publications were stratified by at least 2 of the subcommittee members into 1 of 3 categories of strength of evidence, and some were downgraded 1 or more levels as necessary based on a standardized formula that graded papers on size, methodology, validity of conclusions, and potential sources of bias.

This policy is not intended to be a complete manual on the initial evaluation and management of patients with AMI and unstable angina. Some areas suggested by expert peer reviewers for addition of further discussion included utilization of serum markers to risk stratify unstable angina patients,[4-15] use of combinations of serum markers to exclude AMI,[16,17] risk stratification tools such as the acute time-insensitive predictive instrument (ACI-TIPI)[18] and Goldman criteria for predicting need of intensive care admission,[19] and discussion of multiple technologies for identifying acute coronary syndromes (ACS).[20-37] These areas have been discussed to some degree in other clinical policies[37-40] and represent areas that ACEP may address in future updates of this current policy.

The reasons for developing clinical policies in emergency medicine and the approaches used in their development have been enumerated.[41] This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the existing literature; where literature was not available, consensus of emergency physicians was used. Expert review comments were

received from emergency physicians, physicians from other specialties, such as cardiologists, and specialty societies including members of the American Academy of Family Physicians, American Association for Clinical Chemistry, and the American Society of Nuclear Cardiologists. Their responses were used to further refine and enhance this policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly.

During the review process, all papers were given a baseline "strength of evidence" by the subcommittee members according to the following criteria:

Strength of evidence A—Interventional studies including clinical trials, observational studies including prospective cohort studies, aggregate studies including meta-analyses of randomized clinical trials only.

Strength of evidence B—Observational studies including retrospective cohort studies, case-controlled studies, aggregate studies including other meta-analyses.

Strength of evidence C—Descriptive cross-sectional studies, observational reports including case series, case reports; consensual studies including published panel consensus by acknowledged groups of experts.

Strength of Evidence A and B papers were then rated on elements the committee believed were most important in creating a quality work. A and B papers with significant flaws or design bias were downgraded from 1 to 3 levels based on a set formula. Strength of Evidence C articles were downgraded 1 level if they demonstrated significant flaws or bias. Articles downgraded below a "C" strength of evidence were given an "X" rating and were not used in formulating this policy.

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

Evidence-based standards. Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on "strength of evidence A" or overwhelming evidence from "strength of evidence B" studies that directly address all the issues).

Guidelines. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on "strength of evidence B" that directly addresses the issue, decision analysis that directly addresses the issue, or strong consensus of "strength of evidence C").

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

Scope of Application

This guideline is intended for physicians working in hospital-based emergency departments or chest pain center evaluation units.

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ECG ELIGIBILITY CRITERIA FOR EMERGENT FIBRINOLYTIC THERAPY

Introduction

Large randomized trials involving fibrinolytic therapy have demonstrated that fibrinolytic therapy reduces mortality in some patients with AMI. The Fibrinolytic Therapy Trialists Collaborative Group analyzed all randomized fibrinolytic therapy trials of more than 1,000 patients and found that benefit of fibrinolytic therapy was observed only in patients with ST-segment elevation (ie, injury) or bundle branch block (BBB).[1] Benefit was demonstrated regardless of age, gender, systolic blood pressure, heart rate, history of prior MI, or diabetes. Benefit also was seen at all time intervals within the first 12 hours of symptom onset with greater benefit the earlier treatment is begun. Benefit was greatest in patients with BBB and anterior AMI and least in inferior AMI. Inferior AMI patients with precordial ST-segment depression or elevation in right ventricular leads have a worse prognosis and benefit more from fibrinolytic agents than patients with isolated inferior ST-segment elevation.[2-11] Benefit from fibrinolytic therapy in patients with injury or BBB who present more than 12 hours after symptom onset has yet to be established.[1,12-14]

Bundle branch block and AMI

Much confusion exists in the medical community regarding BBB criteria for fibrinolytic administration with many physicians believing that these criteria apply only to patients with *left* (L) BBB or *new* LBBB. Because the repolarization abnormalities of BBB are thought to obscure injury on the ECG, the Grupo Italiano per lo Studio della Streptochinasi nell'Infarto miocardico (GISSI) and Second International Study of Infarct Survival (ISIS-2) studies only looked at BBB with no distinction being made between right, left, atypical, old, or new BBB.[15,16] Likewise, the Fibrinolytic Therapy Trialists Collaborative Group made no attempt to make a distinction between type of BBB when analyzing their meta-analysis data.[1] Thus, the 1999 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for AMI recommend "BBB (obscuring ST-segment analysis) and history suggesting AMI" as one of the class I eligibility criteria for fibrinolytic therapy.[17,18] Since AMI frequently presents with atypical symptoms,[19-21] reliance on history to guide fibrinolytic treatment means that many patients with AMI in the presence of BBB are not treated. One study in consecutive chest pain patients presenting to the ED for evaluation demonstrated that only 11% of admitted chest pain patients with BBB are actually having an AMI.[22] So the dilemma is either to treat all patients with BBB and any type of chest pain with the result that many non-AMI patients are subjected to the risks of fibrinolytic therapy (ie, low specificity, high sensitivity) or to treat only the patients with classic presentation of AMI with the result that many AMI patients with BBB are not treated (ie, high specificity, low sensitivity). It is common knowledge that the ECG diagnosis of completed MI in the presence of LBBB is extremely difficult and often impossible. More than 50 rules have been proposed as criteria for interpreting Q-wave equivalents superimposed on the QRS complex in the presence of LBBB.[23-25] However, a multitude of studies and case reports have demonstrated that acute injury can be read in the presence of LBBB or paced rhythm, and may be seen as often as in the presence of normal conduction.[23-28] Understanding the interpretation of injury in the presence of BBB or paced rhythm requires a basic understanding of the expected ECG pattern. Typically, one finds ST-segment discordant with the direction of the major QRS deflection. Injury should be suspected when one observes ST-segment concordant with the direction of QRS deflection or an abnormal amount of discordance of the ST-segment with the direction of the QRS deflection. Wackers[23] reported on findings of 96 patients with LBBB and suspected AMI. Fifty-five patients were diagnosed as AMI. ST-segment changes were considered significant if they demonstrated a concordance of 2 mm or more or a discordance of 7 mm or more with the direction of QRS deflection. The sensitivity, specificity, and positive predictive value of these findings for AMI were 54%, 97%, and 96%, respectively. Hands et al[24] described 35 patients with suspected AMI in the presence of LBBB; AMI was diagnosed in 20. ST-segment concordance had a sensitivity for AMI of 16.7% with a specificity and positive predictive value (PPV) of 90.9% and 80%, respectively. Hands et al did not study discordance of ST segments. Sgarbossa et al[26] reported on the ECG findings in 131 patients with LBBB enrolled in the Global Use of Strategies To open Occluded coronary arteries (GUSTO-1) trial. Three ECG findings were found to be independently predictive of AMI: ST-segment elevation of 1 mm or more and concordant with the QRS complex (sensitivity 73%, specificity 92%), ST-segment depression of 1 mm or more and concordant with the QRS in 1 or more precordial leads V_1 through V_3 (sensitivity 25%, specificity 96%), and ST-segment elevation of 5 mm or more and discordant with the QRS complex (sensitivity 31%, specificity 92%). Shiplak et al[29] retrospectively reported on Sgarbossa et al's criteria for predicting AMI in the presence of LBBB and concluded that these criteria are a poor indicator of AMI and that all patients with LBBB should be considered for fibrinolytic treatment. However, the study by Shiplak et al[29] comprised 103 patient visits with one of the following presentations: (1) acute chest pain of 20 minutes or more within 12 hours of presentation, (2) acute pulmonary edema without chest pain occurring within 12 hours of presentation, and (3) cardiac arrest prior to arrival. AMI was defined as having occurred if one of the following serum marker criteria occurred either on presentation or in the hospital: troponin I of 1.5 ng/mL or more or CK-MB activity of 7 U/L or more with index greater than 3%. Although this study has serious design flaws in that acute pulmonary edema and cardiac arrest are known to induce cardiac serum marker elevations in the absence of AMI, this study still found high specificities for the Sgarbossa et al criteria. ST-segment elevation concordant with QRS complex had a sensitivity of 7% and specificity of 100%. ST-segment depression concordant with the QRS complex in leads V_1, V_2, or V_3 had a sensitivity of 3% and specificity of 100%, and ST-elevation of 5 mm or more in discordant leads had a sensitivity of 19% with specificity of 82%. Although the Shiplak et al data shed no light on whether the criteria of Sgarbossa et al are sensitive in identifying acute injury in

patients with LBBB presenting with acute chest pain, the data still support utilization of fibrinolytic therapy in patients with atypical presentation and ECG concordance of 1 mm or more or discordance of 5 mm or more.

In a related study, Sgarbossa et al[27] reported on the findings in 32 patients with AMI and paced rhythm who were enrolled in the GUSTO-1 study. Just as in patients with LBBB, 3 ECG findings were found to be independently predictive of AMI in paced rhythm: ST-segment elevation of 5 mm or more and discordant with the QRS complex (sensitivity 53%, specificity 88%), ST-segment elevation of 1 mm or more and concordant with the QRS complex (sensitivity 18%, specificity 94%), and ST-segment depression of 1 mm or more in 1 or more precordial leads V_1 through V_3 (sensitivity 29%, specificity 82%). Theoretically, these rules of concordance and discordance can be applied to patients with RBBB (Figure 1) and atypical BBB, but studies currently are lacking.[30-32]

ST-segment depression and AMI

Analysis of patients with ST-segment depression on the initial ECG in the Fibrinolytic Therapy Trialists Collaborative Group revealed a mortality of 13.8% in control versus 15.2% in patients who received fibrinolytic treatment.[1] This finding of greater mortality in patients treated for ST-segment depression has led to recommendations that patients with ST-segment depression should not be treated with fibrinolytic therapy. The 1999 ACC/AHA Guidelines for AMI[17] categorized ST-segment depression as a class III indication for fibrinolytic drugs (ie, no benefit, possibly harmful). However, this subgroup of patients with ST-segment depression is a very heterogeneous subgroup and includes patients with ischemia, reciprocal injury, and ST-segment depressions due to repolarization abnormalities from left ventricular hypertrophy (LVH), electrolyte disturbances, drug effects, and so on. To date, no study has prospectively investigated the role of fibrinolytic therapy in patients presenting in the initial hours of symptom onset with ongoing chest pain and predefined ECG criteria for reciprocal injury. Theoretically, patients with large posterior acute infarcts should benefit from fibrinolytic agents if their infarct is due to acute occlusion of the circumflex artery or posterior descending artery. In the discussion that follows the 1999 AHA/ACC Guideline recommendation of ST-segment depression as a class III indication for fibrinolytic therapy, the following statement is made: "When marked ST-segment depression is confined to leads V_1 through V_4, there is a likelihood that this reflects a posterior current of injury and suggests a circumflex artery occlusion for which thrombolytic therapy would be considered appropriate. Very recent retrospective analysis of the Late Assessment of Thrombolytic Efficacy (LATE) Trial also casts some uncertainties about withholding thrombolytic therapy from this heterogeneous group of patients."[18] Patients with large posterior infarcts have been shown to have a significant amount of myocardium in jeopardy.[33] To date, only one study has attempted to elucidate the ECG criteria for diagnosing acute posterior injury. Boden et al[34] retrospectively analyzed 50 of 576 patients from the Diltiazem Reinfarction Study who presented with isolated precordial ST-segment depression of 1 mm or more in 2 or more leads V_1 through V_4. All 23 patients with posterior AMI had horizontal ST-segment depression and upright precordial T waves (Figure 2), whereas all 27 patients with anterior non–Q-

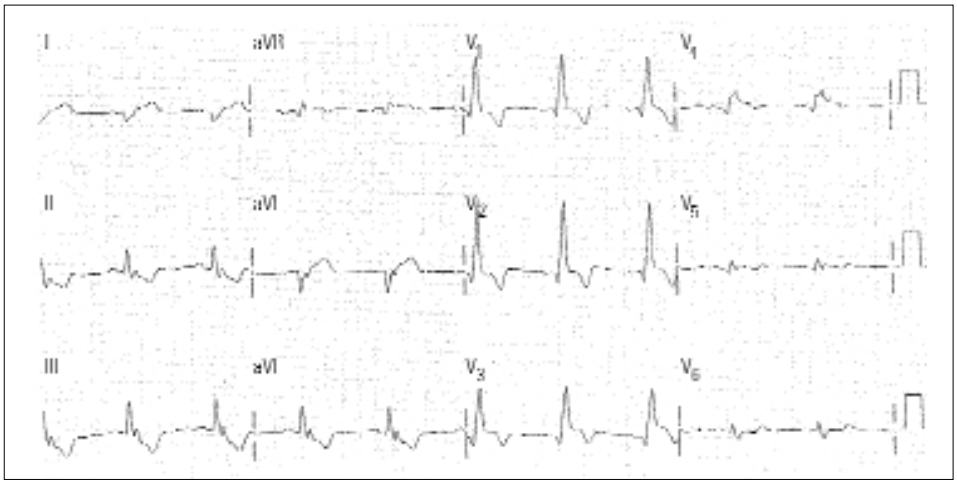

Figure 1.
AMI in presence of RBBB. Note the pseudonormalization of ST segments in leads V_1 and V_2 with concordant ST-segment elevation ≥1 mm in leads V_3 through V_5. Also note the early Q-wave formation in leads V_1 through V_5. Unlike LBBB, anterior Q waves are not obscured by the presence of RBBB.

wave AMI had downsloping ST-segment depression with precordial T-wave inversion. The major limitation of the study is that it diagnosed posterior MI strictly on the criteria of evolving Q-wave equivalents in leads V_1 and V_2 (R wave ≥0.04 sec in V_1 and R:S≥1 in lead V_2) with no coronary arteriography or scintigraphic confirmation of infarct location. The authors conclude that because posterior injury is projected as reciprocal precordial ST-segment depression, patients with anterior precordial ST-segment depression with upright T waves in 2 or more contiguous leads should be considered eligible for fibrinolytic therapy.

Interestingly, the LATE study, which investigated outcomes in patients with a discharge diagnosis of non–Q-wave AMI who were treated with fibrinolytic drugs 6 to 24 hours after symptom onset,[14] found only that patients with ST-segment depression of 2 mm or more had a significant reduction in mortality (31.9% versus 20.1% control). Patients with ST-segment elevation demonstrated no benefit from fibrinolytic therapy (21.2% versus 22.4% control). Because this study only analyzed patients with a discharge diagnosis of non–Q-wave AMI, the ST-segment elevation cohort was composed of patients with relatively small infarcts as opposed to the findings if all patients

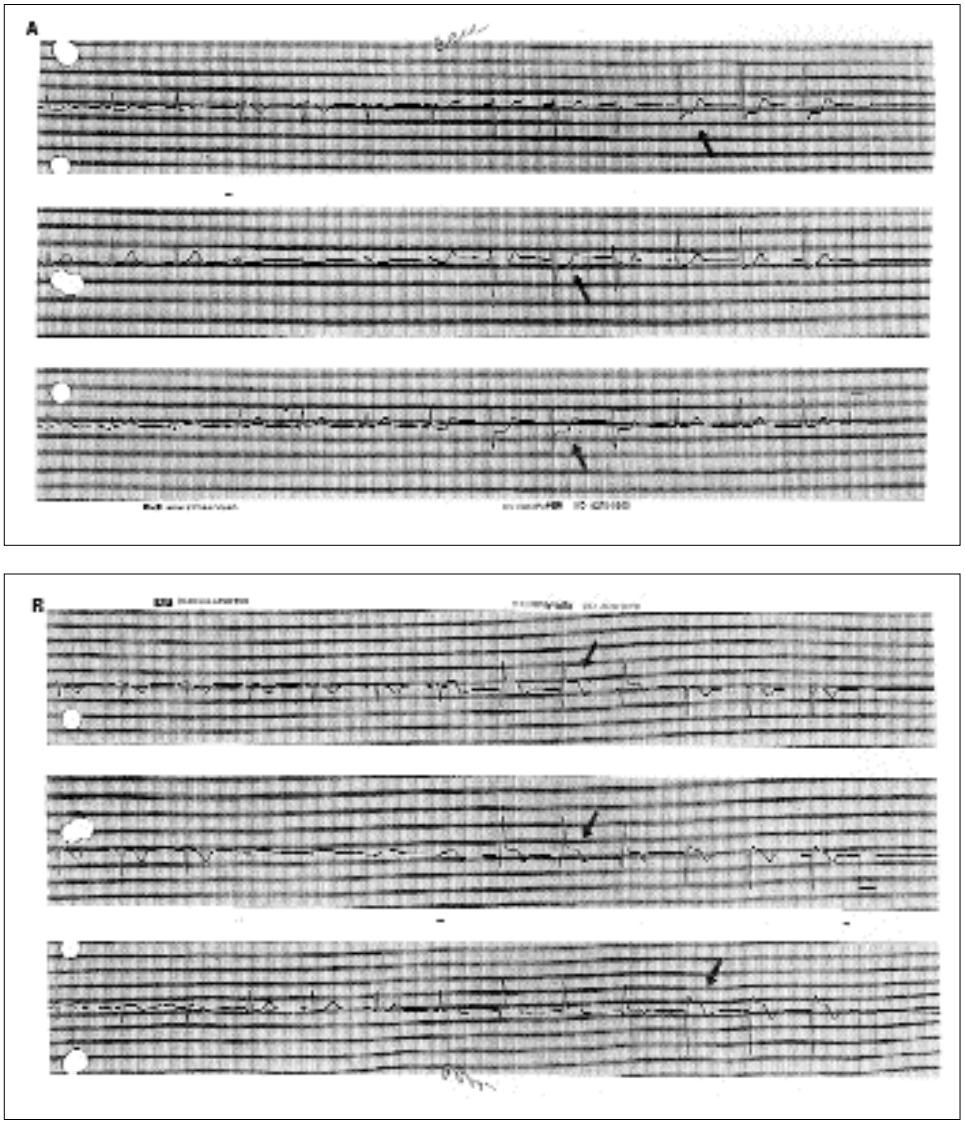

Figure 2.
A, True posterior AMI. Note the horizontal ST-segment depressions in V_1 through V_5 with terminal upright T waves. B, Upside-down mirror image of A representing classical ST-segment elevation in leads V_1 through V_5.

with ST-segment elevation were included. It has been hypothesized that the subgroup of patients with ST-segment depression actually represented patients with large posterior transmural infarcts that would thus account for the results.[35]

Isolated right ventricular AMI (Figure 3) and true posterior AMI may present only with ST-segment depression on the initial ECG as the standard 12-lead ECG does not look directly at the posterior or right ventricular wall. Theoretically, obtaining posterior leads when one sees anterior ST-segment depression, and right ventricular leads when one sees lateral ST-segment depression may increase the yield of ST elevation in AMI patients. Zalenski et al[36] reported on the findings in 149 admitted chest pain patients with suspected AMI who underwent a 15-lead ECG (12-lead ECG + V_8 through V_9 + V_4R). Addition of the extra leads led to an increase in detection of injury from 35% to 44%, although the small study size limited the conclusions. In a larger follow-up study, Zalenski et al[37] described 533 patients who underwent an 18-lead ECG (12-lead ECG + V_7 through V_9 + V_4R through V_6R). Detection of injury by obtaining the 6

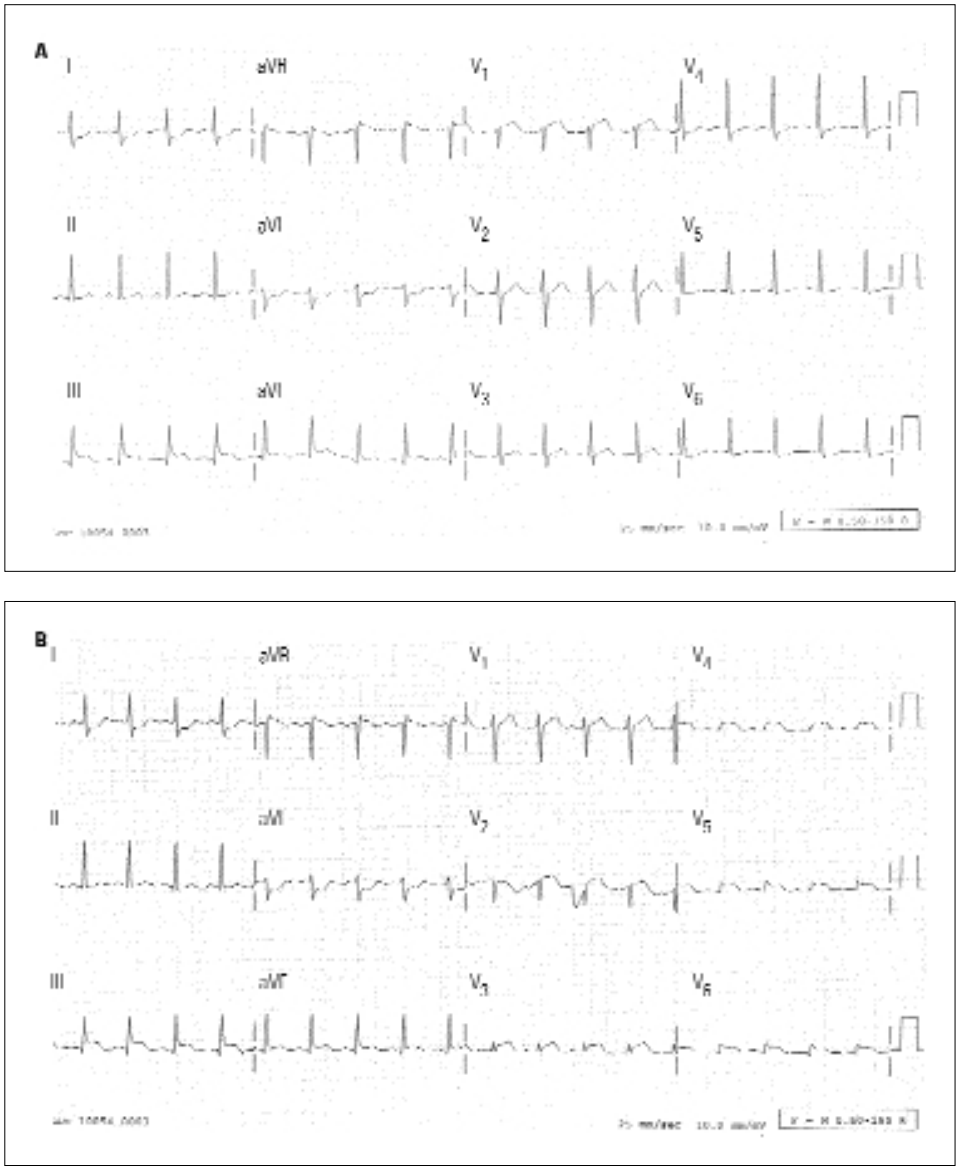

Figure 3.
A, Isolated right ventricular AMI. Note the diagnostic ST-segment elevations in leads III and V_1 and ST depressions with terminal upright T waves in leads I and aVL (reciprocal changes from right lateral injury). Because injury in lead V_1 corresponds to injury in V_2R (V_1=V_2R), and right lateral injury corresponds to V_6R injury, theoretically this patient should demonstrate injury in leads V_2R through V_6R.
B, Right ventricular leads in same patient confirming injury in leads V_2R through V_6R.

nonstandard leads resulted in an incremental increase in sensitivity for AMI of 8.4% with a decrease in specificity of 7.0%. It is unknown how many of these patients in these 2 studies with ST-segment elevation on nonstandard leads had diagnostic ECG changes of reciprocal injury on the traditional 12-lead ECG (ie, ST-segment depression with upright T waves on the standard 12-lead ECG) that potentially would render the additional information from these nonstandard leads of confirmational value before proceeding with fibrinolytic therapy.

Patient management recommendations: ECG eligibility criteria for emergent reperfusion therapy

Evidence-based standards. Assess for fibrinolytic therapy in patients presenting within 12 hours of symptom onset if ECG reveals:

1. ST-segment elevations greater than 0.1 mV in 2 or more contiguous leads that are not characteristic of early repolarization or pericarditis, nor of a repolarization abnormality from LVH or BBB in patients with clinical presentation suggestive of AMI.

2. Any type of BBB (right, left, paced, and atypical—new or old) in patients with clinical presentation suggestive of AMI.

Guidelines. Assess for fibrinolytic therapy if ECG reveals LBBB and ST-segment deviations of 1 mm or more toward the major QRS deflection or 5 mm or more away from the major QRS deflection in 2 or more contiguous leads in patients with atypical presentation of AMI.

Options. Assess for fibrinolytic therapy if ECG reveals:
1. ST-segment depressions of 1 mm or more with upright T waves in 2 or more contiguous anterior precordial leads in patients with clinical presentation suggestive of posterior AMI.

2. ST elevations of 1 mm or more in 2 or more contiguous nonstandard leads (V_4R through V_6R, V_7 through V_9) in patients with clinical presentation suggestive of isolated right ventricular or posterior AMI.

3. RBBB, atypical BBB, or paced BBB and ST-segment deviations of 1 mm or more toward the major QRS deflection or of 5 mm or more away from the major QRS deflection in 2 or more contiguous leads in patients with atypical presentation of AMI.

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THE ROLE OF PRIMARY ANGIOPLASTY IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

The role of primary coronary angioplasty in AMI patients presenting to the ED in cardiogenic shock or who have an absolute contraindication to fibrinolytic administration is well established.[1,2] In contrast, the role of primary angioplasty in patients with AMI eligible for fibrinolytic therapy is controversial.[3] A number of prospective trials have been conducted to address the issue of primary angioplasty versus fibrinolytic therapy with varying results.[4-12] Several of these studies have found modest but statistically significant benefits in short-term mortality, reinfarction rates, infarct size, and/or complication rates.[4-8] Other studies failed to confirm these benefits and found the 2 therapies to be of equal value.[9-12] Emergency physicians who practice in centers that offer primary angioplasty are frequently faced with the conundrum of whether to activate the emergency cardiac catheterization team or give fibrinolytic therapy in the ED. Likewise, emergency physicians who practice in a hospital that does not offer angioplasty face a similar dilemma if they have a patient with an AMI who they believe might benefit from immediate transfer to a facility with cardiac catheterization capabilities.

A recent meta-analysis analyzed 10 prospective studies comparing primary angioplasty with intravenous fibrinolytic therapy and found that the mortality rate for 30 days or less was 4.4% for 1,290 patients treated with primary angioplasty compared with 6.5% for 1,316 patients treated with fibrinolytic agents (95% confidence intervals 0.46 to 0.49, P=.02).[13] When death was combined with nonfatal reinfarction, the rates were 7.2% for angioplasty and 11.9% for fibrinolytic therapy. In addition, angioplasty was associated with a statistically significant reduction in total strokes (0.7% versus 2.0%) and hemorrhagic stroke (0.1% versus 1.1%). Although the apparent benefit of primary angioplasty found in this analysis is enticing, 3 caveats must be considered before reaching a definitive conclusion. First, there is acknowledged potential for bias in both the quantitative review techniques and the enrollment practices of the individual studies reviewed.[14] Second, the time from presentation to the ED to inflation of the balloon in the angiography suite is relatively rapid in most of the studies used for the analysis, and in order for a center to duplicate these results, it is reasonable to presume they must be able to consistently equal or improve on the door-to-balloon times in the published studies. Although no clinical study definitively establishes the ideal door-to-balloon time, it may be reasonable to extrapolate that the balloon time ideally would be less than 90 minutes from time of ED diagnosis of AMI. Likewise, the experience of the interventionist is of critical importance and the procedure must be done at a high-volume center similar to those used in the reported trials. Third, there continue to be advances in interventional techniques, such as the use of platelet inhibitors and coronary stents, that may modify future results. Currently it can be concluded that primary angioplasty, when conducted in a timely manner in experienced hands, is a viable alternative to fibrinolytic therapy. When the element of time or experience is uncertain or cannot meet stringent criteria, fibrinolytic therapy remains the treatment of choice.

Patient management recommendations: Role of primary angioplasty in patients with AMI

Evidence-based standards. Primary coronary angioplasty when performed by experienced personnel within 90 minutes of diagnosis of AMI is as effective as fibrinolytic therapy in AMI patients meeting standard criteria for emergency reperfusion therapy.

Guidelines. If resources are available, consider primary coronary angioplasty as an alternative to fibrinolytic therapy in AMI patients meeting standard criteria for emergent reperfusion therapy providing it can be performed within 90 minutes of diagnosis of AMI.

Options. None specified.

References—Role of primary angioplasty in patients with AMI

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SERUM MARKER ANALYSIS IN ACUTE MYOCARDIAL INFARCTION

Introduction

There has been much controversy in recent years regarding which serum marker is the best measure of myocardial necrosis in patients with AMI.[1] In the 1980s, creatine kinase (CK)-MB activity measurements supplanted lactate dehydrogenase (LDH) and its isoenzymes as the best marker of myocardial necrosis. In the early 1990s, CK-MB mass became the *gold* standard. Currently CK-MB subforms and myoglobin have been proposed to be the best serum markers early in symptom onset, whereas cardiac troponin T (cTnT) and cardiac troponin I (cTnI) have been purported to be equally sensitive to CK-MB but more specific for unstable ischemic syndromes. cTnT and cTnI also have the advantage of remaining elevated for days following an AMI. In addition to the multitude of studies on serum marker use in AMI, there have been a multitude of studies using serum marker analysis for risk stratification of all chest pain patients (and not just AMI patients).[2-12] Although these studies indicate that CK-MB mass, cTnT, and cTnI demonstrate an ability to risk-stratify patients, the sensitivity for adverse outcome is low. For this reason, this discussion focuses on the ability of serum marker analysis to identify and exclude AMI and does not further address which marker is more sensitive for non-AMI unstable ischemic syndromes. This discussion also excludes all bedside qualitative measurements of serum markers because their ultimate utility will be determined by information gathered from quantitative measurements. Finally, because this committee found no new experimental evidence regarding the use of CK-MB index, and because the total CK level is not routinely used in this country to identify AMI, this discussion focuses only on the following markers of AMI: CK-MB activity, CK-MB mass, CK-MB subforms, myoglobin, cTnT, and cTnI.

The determination of when an assay result becomes positive must take into consideration the time of symptom onset, the amount of myocardium that is infarcting, and the cutoff value chosen. To date, studies comparing the various assays used to detect myocardial necrosis suffer from a multitude of experimental biases. A frequent source of experimental bias is that a positive value of the assay under investigation is used as the criterion for making the diagnosis of AMI. Another type of bias frequently encountered is the use of a receiver operator characteristic (ROC) curve to determine the "optimum" cutoff value for a new test with subsequent comparison of this optimum value with either the hospital's "gold standard" or the manufacturer's recommendation of abnormal values. Other problems in the comparison of differing studies in a particular serum marker's ability to detect AMI are the discrepancies that arise from the vast differences in patient populations (eg, critical care unit admission versus general ED population), as well as vast discrepancies in terms of symptom onset in relationship to ED presentation. Also, the different cutoff values for a serum marker used in the various studies and the lack of an international standardization of serum marker calibrations render direct comparison between studies meaningless. In the studies reviewed by this committee,[2-41] 7 different cutoff values were used for CK-MB activity (range 5 to 23 IU/L), 14 different cutoff values for CK-MB mass (range 4 to 20 ng/mL), 2 cutoff values for subform (range of MB_2/MB_1 ratio of 1.5 to 2.3), 9 cutoff values for myoglobin (range 35 to 110 ng/mL), 5 different cutoff values for cTnT (range 0.06 to 0.2 ng/mL), and 5 different cutoff values for cTnI (range 0.1 to 2.5 ng/mL). Finally, there is a gray zone between unstable angina and non–Q-wave AMI, and researchers have had difficulty in how to best deal with a test result that is false positive for AMI but true positive for unstable angina. This also poses problems for newer tests that are actually superior for identification of trace myocardial necrosis in unstable angina but are judged against the standard of the old tests. The result is that despite all researchers declaring that they use World Health Organization Criteria for AMI, almost all studies have their own unique definitions for AMI and unique definitions for inclusion and exclusion criteria of patient population under study.

In analyzing the serum marker data for this policy, the committee determined that the following conditions should be met for a study to be a valid comparison between 2 or more marker's ability to detect AMI: (1) the diagnosis of AMI should not be defined by the positive value of any marker under investigation, (2) figures of ROC curves should be supplied, and statistical comparison of areas should be performed, (3) sensitivity and specificity comparisons should be performed at a point on the individual ROC curves with equivalent and clinically meaningful likelihood ratios for AMI,[42] and (4) sensitivity analysis should be supplied relative to time from symptom onset for patients in whom a definite time of symptom onset can be determined. No study reviewed by this committee met all of the criteria discussed above as being a valid comparison between 2 or more markers.

Due to the bias inherent in all the studies reviewed by this policy, and the belief that no serum marker can have a 100% sensitivity for AMI if a truly unbiased definition of

AMI is used, this policy defines the term *reliably identifies* as sensitivity of the serum marker assay for AMI of 90% or more with positive likelihood ratio of 10 or more and defines the term *reliably excludes* as specificity of the serum marker assay for AMI of 90% or more with negative likelihood ratio of 0.1 or less. The ideal serum marker of AMI should both reliably identify and reliably exclude AMI within a specified time interval from symptom onset.

Which serum marker is best?

Both theoretically and clinically, cTnI and cTnT are the best markers 24 hours after clinical onset as CK-MB activity, CK-MB mass, CK-MB subforms, and myoglobin are declining back toward baseline.[1,13,14] Studies are consistent in their conclusion that no serum marker level reliably identifies AMI in all patients on presentation to the ED nor in patients presenting within 6 hours of symptom onset.[12-40,41] Only 2 of the studies[15,21] reviewed reported any marker with a sensitivity of 100% within 6 hours of symptom onset. Mair et el[15] reported a sensitivity of 100% for CK-MB mass of 5 ng/mL or more 5 hours after symptom onset. However, the study population consisted of 37 patients with AMI, of whom 35 patients were treated with fibrinolytic therapy. Tucker et al[21] likewise reported a sensitivity of 100% for CK-MB mass 6 hours after symptom onset; however, the study population consisted of 177 patients, of whom only 27 were diagnosed as AMI. Also, a positive value of CK-MB mass was one of the criteria used for diagnosis of AMI. Studies also are consistent in that CK-MB activity, CK-MB mass, CK-MB subforms, cTnT, and cTnI all reliably identify AMI 12 to 24 hours after symptom onset if appropriate cutoff values are chosen.[12-22,41] CK-MB activity, cTnT, and cTnI do not reliably identify AMI within 8 hours of symptom onset,[13,15-18,41] but can identify AMI in the 8- to 12-hour range.[12-14,17,18,41,43]

CK-MB mass and CK-MB subforms can reliably identify AMI during the 6- to 10-hour time frame from symptom onset if appropriate cutoff values are chosen.[12-18,33,37,41] The role of myoglobin in diagnosing AMI is unclear. It reportedly has a rapid increase and early decrease and is widely believed to be the earliest marker of myocardial necrosis.[1,14-18,20,23,41] However, studies to date indicate similar myoglobin sensitivities for AMI during the first 6 hours of symptom onset[14-18,20,23,41] compared with other serum markers. Four studies report a declining myoglobin sensitivity for AMI within 5 to 12 hours of symptom onset.[14,16,17,41] For this reason, myoglobin should never be used as the sole marker of myocardial necrosis.

The Table summarizes recent studies in sensitivity for AMI in relationship to time from symptom onset in 2-hour increments over the initial 12 hours. Several studies reported findings in 3- to 6-hour increments[12-14,20-23,37] and were not used for the initial 12-hour data in this table except for cTnI, in which only 1 study reported 2-hour incremental data. Also, only data derived from baseline serum marker analysis were used from Mair et al's[15] study as 95% of the patients received thrombolytic drugs. Six studies reported the following ranges of sensitivity and specificity for AMI at 6 hours from symptom onset: CK-MB activity: sensitivity 48% to 76%, specificity 90% to 99%[16,27,33]; CK-MB mass: sensitivity 87% to 100%, specificity 95%

Table.
Relationship of reported sensitivities of various serum markers in relationship to time of symptom onset.

Time (h)	CK-MB Activity (%)	CK-MB Mass (%)	CK-MB Subform (%)	Myoglobin (%)	cTnT (%)	cTnI (%)
0–2	0–21[15,17,33,41]	7–49[15,17,18,41]	8–47[15,18,33,41]	22–53[15,17,18,41]	11–55[15,17,41]	16–47[15,41]
2–4	14–41[15-17,33,41]	12–64[15-18,41]	32–59[15,18,33,41]	27–84[15-18,41]	34–55[15-17,41]	36–59[15,41]
4–6	19–59[16,17,33,41]	58–87[16-18,38,41]	85–96[18,33,41]	55–90[16-18,41]	58–73[16,17,41]	41–58[13,*41]
6–8	50–81[16,17]	72–94[16-18,38]	95[18]	61–95[16-18]	78–84[16,17]	71[13†]
8–10	90–96[17,41]	90–98[17,18,41]	96–100[18,41]	76–98[17,18,41]	87–95[17,41]	92–93[14,‡41]
10–12	88–100[16,17]	97–100[16-18]	100[18]	71–98[16-18]	94–100[16,17]	88[13§]
12–24	84–98[16,41]	89–100[12,13,16,41]	53–91[41]	41–66[14,16,41]	79–99[12-16,41]	83–100[13,14,41]
24–48	—	57–91[13,14]	—	39[14]	—	100[13,14]

*3–6 h.
†6–9 h.
‡6–12 h.
§9–12 h.

to 100%[16,21,27,39]; CK-MB subform: sensitivity 95% to 96%, specificity 94% to 96%[27,33]; myoglobin: sensitivity 78% to 91%, specificity 59% to 100%[16,21,24,27,39]; cTnT: sensitivity 67% to 89%, specificity 84% to 95%[16,21,24]; cTnI: sensitivity 63% to 82%, specificity 98% to 99%.[21]

Caution must be exercised in using the time of symptom onset to interpret the relevance of the baseline serum marker. AMI is frequently preceded by preinfarction angina associated with plaque rupture and intermittent coronary closure and opening as the cycle of platelet aggregation and fibrin deposition is initiated. *If the 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.*

Delta measurements

A different approach to identifying AMI with serum markers is to rely on time changes in the serum marker level (slope or delta values) as opposed to an absolute threshold value for normalcy. Because newer assays are becoming ever more sensitive and precise, this approach has the potential to both reliably identify and reliably exclude AMI if an appropriate time interval and cutoff value is chosen while the marker value is still in the normal range. Lott et al[36] performed ROC analysis of time changes of CK-MB values (ie, slope) versus discrimination values of CK-MB and index values of CK-MB in 266 chest pain patients (44 AMI). The ROC curve area for AMI of the slope of CK-MB over the initial 12 hours from symptom onset was statistically higher compared with ROC curve areas for the absolute CK-MB values and CK-MB index values. Young et al[37] performed baseline and 3-hour CK-MB testing in 1,042 chest pain patients (67 AMI). A positive serial test result was defined as a baseline or 3-hour CK-MB of 8 ng/mL or more or an increase in CK-MB of +3 ng/mL or more (ΔCK-MB) in the 3-hour time interval. The addition of the ΔCK-MB in comparison with an abnormal baseline or 3-hour CK-MB resulted in a small incremental increase in sensitivity from 88% to 93% with no significant change in specificity. Fesmire et al[38] performed baseline and 2-hour CK-MB mass measurements in 710 chest pain patients (113 AMI) whose baseline CK-MB did not meet the study criteria for AMI on presentation. A ΔCK-MB of +1.6 ng/mL or more was 92% sensitive for AMI and 95% specific compared with 75% sensitivity and 96% specificity for a 2-hour CK-MB of 6 ng/mL or more in patients presenting a mean of 108 minutes after symptom onset and both *reliably identified* (sensitivity=92% and positive likelihood ratio=19.6) and *reliably excluded* (specificity=95% and negative likelihood ratio=0.08) AMI. A finding of a ΔCK-MB of +1.6 ng/mL or more in AMI patients was independent from time of symptom onset with no differences found in sensitivity in patients presenting within 1, 2, 4, and 6 hours from symptom onset.

The time changes in serum marker value have also been applied to myoglobin testing. Tucker et al[39] investigated baseline and 2-hour myoglobin in 133 patients with suspected AMI (39 AMI). Sensitivity of a myoglobin value of 90 ng/mL or more at 2 hours after onset of symptoms was 37% and increased to 87% 6 hours after onset. Combining a doubling of the baseline myoglobin value in 2 hours to an abnormal myoglobin 6 hours after symptom onset increased the sensitivity to 95% at 6 hours. Brogan et al[20] investigated 189 patients with suspected AMI (22 AMI) and performed myoglobin measurements at baseline and 1 hour after symptom onset. A baseline or 1-hour myoglobin value of 110 ng/mL or more had a sensitivity for AMI of 73%. Combining an increase of myoglobin of +40 ng/mL or more in 1 hour to an abnormal baseline or 1-hour myoglobin value raised the sensitivity of myoglobin to 91% for identification of AMI. Davis et al[40] performed myoglobin testing at baseline, 1, and 2 hours in 42 admitted chest pain patients (14 AMI). A positive myoglobin test result was defined as any myoglobin level greater than 100 ng/mL or a change (increase or decrease) of 50% or more from baseline at either the 1- or 2-hour measurement intervals. Sensitivity for AMI was 57% for an abnormal myoglobin value and increased to 93% if the myoglobin value underwent a 50% or greater change from baseline.

Patient management recommendations: serum marker analysis in AMI

Evidence-based standards. No single determination of one serum biochemical marker of myocardial necrosis *reliably identifies*[*] or *reliably excludes*[†] AMI less than 6 hours of symptom onset. No serum biochemical marker identifies or excludes unstable angina at any time after symptom onset.

Guidelines. In patients presenting with acute chest pain and a negative baseline serum marker level, consider repeat serum marker testing at the following time intervals from symptom onset[‡] before making an exclusionary diagnosis of non-AMI chest pain:

CK-MB activity	8–12 hours
CK-MB mass	6–10 hours
CK-MB subforms	6–10 hours

[*] *Reliably identifies* = sensitivity ≥90% with positive likelihood ratio ≥10.
[†] *Reliably excludes* = specificity ≥90% with negative likelihood ratio ≤0.1.
[‡] If 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.

cTnT	8–12 hours
cTnI	8–12 hours

The exact timing of the repeat determination of the serum marker value should take into account the sensitivity, precision, and institutional norms of the assay being used, as well as the release kinetics of the marker being measured. CK-MB activity, CK-MB mass, cTnT, and cTnI all reliably identify and exclude AMI 12 to 24 hours after symptom onset. Because of its rapid release kinetics, myoglobin alone does not reliably identify or exclude AMI at any time interval after symptom onset and is best used in conjunction with the other common serum markers. cTnT and cTnI are the preferred serum markers in patients presenting greater than 24 hours after symptom onset.

Options. Consider repeat determination of CK-MB mass 2 to 3 hours after baseline or repeat myoglobin at 1 to 2 hours after baseline for utilization of the ΔCK-MB or Δmyoglobin when the repeat serum marker level is drawn at a time interval before the time intervals discussed in the Guidelines recommendation above.

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SERIAL 12-LEAD ECGS IN THE EMERGENCY DEPARTMENT

Introduction

Early identification of patients with ACS, defined as AMI and unstable angina in the ED, is of paramount importance. However, establishing this diagnosis is often challenging, as patients' symptoms may be atypical in nature and the initial ECG in patients with AMI can be normal or nondiagnostic up to 55% of the time.[1] Complicating matters further is a mounting body of evidence indicating that ST-segment depression or elevation is frequently an unstable phenomenon in the early stages of AMI and unstable angina.[2,3] Thus, a single ECG represents a "snapshot" of what is actually a dynamic process, and may happen to be obtained at a moment when the ST-segment changes are nondiagnostic. Instability of ST segments in patients with ongoing cardiac ischemia, as well as the potential for evolving changes, is the theoretical basis for the implementation of automated serial 12-lead ECG monitoring (SECG). There are currently several automated SECG monitors on the market and most share the following features: (1) the ability to continuously monitor ST-segment trends in the standard 12-leads, (2) storage of ECGs at a predetermined interval (generally every 20 minutes or less), (3) frequent computer analysis of the ECGs (generally at intervals of <2 minutes), (4) the ability of the computer analysis to detect changes in ST-segment elevation or depression from an initial baseline reading, and (5) alarms to notify the clinician of ST-segment variability meeting preset criteria. Current SECG monitors do not include T-wave morphology analysis and some have limited analysis of QRS area trends. Although the use of automated SECG systems has the principal advantage of being nearly continuous, some of the same potential benefits may be reaped by routinely obtaining conventional serial 12-lead ECGs in chest pain patients with possible ACS at select time intervals after presentation to the ED.

In AMI patients receiving fibrinolytic therapy, SECG or a repeat ECG at 60 to 180 minutes has been shown to be predictive of successful reperfusion and is used to alert clinicians to patients in whom reperfusion therapy is failing.[4-8] SECG monitoring also has been shown to have prognostic value in detecting complications after coronary artery bypass graft surgery, as well as detecting episodes of silent ischemia in CCU patients.[9,10] Silent myocardial ischemia has been found to occur frequently in patients with unstable angina and has been shown to be a marker for unfavorable outcomes including death.[11-13] In a British study of 212 CCU patients that used SECG monitoring for the first 48 hours of hospitalization, Patel et al[14] found that transient ST-segment changes predicted an increased risk of myocardial infarction or death. No patients with a normal ECG and without changes on SECG monitoring died or had an MI.

Clinical trials

Two trials evaluating the benefit of obtaining a second routine ECG on ED patients with possible ACS have been conducted.[15,16] Hedges et al[15] conducted a multicenter prospective observational study comparing 2 ECGs with serial CK-MB in 261 patients with possible ACS. They found a repeat ECG at 3 to 4 hours had a 39% sensitivity and 88% specificity for AMI, and 25% sensitivity and 92% specificity for ACS. The study found that combining serial CK-MB with a repeat ECG was more sensitive and specific than either used alone. A second multicenter trial of similar design enrolled 1,055 patients for serial cardiac markers and a

second ECG. They reported that the second ECG diagnosed an additional 3% of MI patients not diagnosed by the initial ECG and serial cardiac markers.[16]

Research in automated SECG monitoring in the ED setting is limited. Fesmire et al[17] reported on 1,000 admitted chest pain patients (204 AMI patients, 295 unstable angina) who underwent SECG monitoring during the initial ED evaluation. The study objective was to determine whether the use of SECG monitoring was more sensitive and specific than a single 12-lead ECG in the detection of injury and ischemia in patients with ACS. The initial ECG was obtained on average 17 minutes after arrival in the ED, and the SECG monitoring was initiated 46 minutes after arrival to the ED. The mean duration of SECG monitoring was 128 minutes±41 minutes. This study found SECG monitoring was more sensitive and specific than the initial ECG for detection of AMI and ACS. Perhaps most importantly, SECG detected injury in an additional 16.2% of AMI patients, which represented a relative increase of 34% in patients eligible for emergency reperfusion therapy. Also, when compared with patients who had no changes on their SECG, those patients with diagnostic changes on SECG had a 2.5 times greater risk of ACS, a 4.9 times greater risk of percutaneous transluminal coronary angioplasty/coronary artery bypass graft (PTCA/CABG), a 9.6 times greater risk of life-threatening complications, and a 12.3 times greater risk of death.

In a retrospective study, Gibler et al[18] described 1,010 low-risk chest pain patients in whom SECG monitoring was used as part of their chest pain unit evaluation protocol. In this study, only 11 patients were found to have evidence of ischemia or evolving MI on SECG. However, this was a population with a low prevalence of disease as evidenced by 43 of 1,010 patients ultimately being discharged with an ACS diagnosis (12 AMI, 31 angina). Gibler et al[19] also reported on SECG monitoring in 86 admitted patients who underwent SECG monitoring during the ED evaluation. Of the 86 patients admitted, 18 (20.9%) were discharged with a cardiac-related diagnosis. Seven of those 18 patients had suggested abnormalities on SECG monitoring. However, an additional 10 of the 86 patients had findings suggestive of ACS or MI but were ultimately discharged with a noncardiac diagnosis. Finally, a number of case reports[1,2,20] demonstrate various aspects of the potential value of SECG monitoring in the ED including diagnosis of AMI in the presence of LBBB.

Patient management recommendations: Serial 12-lead ECGs in the ED

Evidence-based standards. Performing SECG or repeat ECGs at select time intervals after presentation results in an incremental increase in identification of injury or ischemia in patients with AMI and unstable angina compared with the baseline ECG. Its greatest value appears to be when it is used in patients with intermediate or high clinical likelihood of AMI or unstable angina who are spending at least 1 hour in the ED or in identification of successful reperfusion from fibrinolytic treatment.

Guidelines. Perform repeat ECG at a set time interval after presentation or automated SECG monitoring during the ED evaluation of patients in whom the initial ECG is nondiagnostic for injury and who have symptoms consistent with ongoing or recurrent ischemic chest pain.

Options. Perform repeat ECG at a set time interval after presentation or automated SECG monitoring during the ED evaluation of patients with a low suspicion of AMI or unstable angina.

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CHEST PAIN EVALUATION UNITS

Introduction

The evaluation of patients presenting to the ED with chest pain remains a complex and difficult issue for emergency physicians. Perhaps the most challenging aspect of this evaluation is the determination of the presence or absence of an ACS in such patients. Not only does ACS assume a variety of atypical and subtle forms in its clinical presentation, but its misdiagnosis also can result in potentially catastrophic and subsequently litigious outcomes. The competing forces of the emergency clinician's desire to establish a diagnosis in patients with chest pain and avoid dismissing patients with ACS, versus the increasing emphasis of cost containment has led to the implementation of chest pain evaluation units (CPEU) for patients presenting to the ED with chest pain. A CPEU may involve an inpatient or ED-based protocol. Either way, an algorithm is established that uses a predetermined observation period and battery of tests to reliably identify and/or exclude AMI and ACS. The use of CPEUs is increasing, and currently approximately 15% to 22% of metropolitan EDs have established CPEUs.[1,2]

Although the exact protocol and tests used varies, the underlying goals and principles of the CPEUs are fairly consistent.

The premise of the CPEU is to rapidly risk-stratify patients into those who are at a very low likelihood of having an adverse outcome related to ACS (death or nonfatal AMI) and can be safely dismissed for outpatient follow-up, and those patients who have ACS and require further treatment or inpatient evaluation. The primary goal is not to establish a definitive diagnosis, but rather establish the patient's short-term risk of death or life-threatening complication. After an initial evaluation by the emergency physician, which generally includes a 12-lead ECG and an initial serum cardiac marker determination, those patients who do not have an obvious AMI or ACS are entered into the CPEU. Over a predetermined observation period (most commonly 6 to 12 hours), serial cardiac marker determinations and ECGs are obtained, and any change in the patient's clinical status, including the recurrence of chest pain, is noted and addressed. At the end of the predetermined observation period, the patient is reevaluated and depending on the CPEU protocol, generally undergoes functional cardiac testing and/or stress testing if he or she still is considered to be at risk for ACS.[3] To date, treadmill exercise testing,[4-9] resting nuclear scans,[10-15] resting echos,[5,16] stress nuclear scans,[17] stress echos,[18,19] and electron-beam CT scanning[20] have all been used in evaluation of chest pain patients. No information is available regarding which is the optimal modality; however, theoretically these tests should be used selectively and not as a mandatory part of a CPEU protocol.[21] Those patients who have a recurrence of chest pain strongly suggestive of ACS, a positive serum marker value, a significant ECG change, or a positive functional test result, are generally admitted for inpatient evaluation. Those patients who "pass" all of these tests are usually discharged to home with outpatient follow-up recommended. There will always be an occasional patient with a diagnosis of noncardiac chest pain who is dismissed and ultimately has a later diagnosis of an ACS or other life-threatening non-ACS condition (eg, aortic dissection). There are currently no controlled studies available that address whether the utilization of CPEUs will decrease the prevalence of missed MIs and ACS during the initial ED evaluation.

Clinical trials

The majority of research published regarding CPEUs is observational in nature. However, 3 prospective randomized studies have been published. Farkouh et al[22] performed a community-based, randomized trial of 424 patients who met Agency for Health Care Policy and Research criteria for unstable angina at intermediate risk for short-term death or nonfatal MI. Among the 212 patients cared for in a 6-hour CPEU protocol, 97 were able to be discharged home, and none of those 97 had cardiac-related events (MI, death, congestive heart failure) during a 30-day follow-up period. Resource use was found to be significantly reduced in CPEU patients including those who were subsequently admitted.

Roberts et al[23] randomly assigned 163 chest pain patients with low probability for an acute MI but intermediate probability for ACS, no acute ECG changes, and no history of coronary artery disease to a CPEU or routine admission to a telemetry bed in the hospital. The CPEU protocol uses 12 hours of observation on a cardiac monitor with CK-MB level determinations at 0, 4, 8, and 12 hours, ECGs at 0, 6, and 12 hours, and a clinical examination by the physician at 0, 6, and 12 hours. Patients with recurrent ischemic chest pain or any positive test results in the first 12 hours were hospitalized. Those whose tests results were negative and remained pain-free went on to an ECG exercise test using a modified Bruce protocol. Compared with routine admission, the patients in the CPEU protocol had lower costs and shorter hospital stays with no adverse outcome.

In the Rapid Rule-Out of Myocardial Ischemia Observation (ROMIO) trial,[24] a similar CPEU protocol was used, utilizing a 9-hour observation period with serial cardiac marker determinations at 0, 3, 6, and 9 hours, serial ECGs, and a predischarge treadmill stress test. In this study, 50 patients were randomly assigned to the CPEU and 50 to routine hospital care. MI or ACS were diagnosed in 6% of patients in the study group within 30 days and no diagnoses were missed. Again, hospital stay was shorter overall, and costs less in those patients assigned to the CPEU.

Gibler et al[5] have described an observational series on 1,010 patients considered at low risk for ACS enrolled in an ED-based CPEU. Patients underwent initial evaluation and then were observed for a 9-hour period, which included serial cardiac marker determinations and automated SECG. At the end of the 9 hours, patients who remained pain-free and had no elevated markers or ECG changes had 2-dimensional echocardiography and graded exercise testing. Among the 1,010 patients, 82.1% were released to home from the ED, whereas 15.1% required admission for further evaluation. Overall, 43 of the patients had ACS (12

AMIs, 31 angina or unstable angina). A number of other observational and retrospective studies have reported decreased length of stay and decreased cost or charges.[6-8,15,25-28]

Rydman et al[29] conducted a satisfaction survey in conjunction with a larger study assessing the utilization of CPEUs. They found that patients were more satisfied with the care they received in the CPEU than those who participated in an inpatient evaluation. A prospective observational study designed to assess the cost-effectiveness of mandatory stress testing found that the utilization of stress testing in a CPEU setting was safe and cost-effective.[7]

Patient management recommendations: Chest pain evaluation units

Evidence-based standards. Chest pain evaluation units are a safe and effective alternative to routine admission for evaluation of low- to intermediate-risk chest pain patients. Further investigation needs to be performed to determine the most cost-effective and efficient utilization of available diagnostic modalities.

Guidelines. As an alternative to admission, consider use of a CPEU protocol consisting of serial serum marker determinations, serial ECGs, and selective stress testing for evaluation and risk stratification of patients at low- to intermediate-risk for AMI and ACS.

Options. None stated.

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