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Practical Implementation of the Guidelines for Unstable Angina/Non-ST-Segment Elevation Myocardial Infarction in the Emergency Department: A Scientific Statement From the American Heart Association Council on Clinical Cardiology (Subcommittee on Acute Cardiac Care), Council on Cardiovascular Nursing, and Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration With the Society of Chest Pain Centers

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Practical Implementation of the Guidelines for Unstable Angina/Non–ST-Segment Elevation Myocardial Infarction in the Emergency Department

A Scientific Statement From the American Heart Association Council on Clinical Cardiology (Subcommittee on Acute Cardiac Care), Council on Cardiovascular Nursing, and Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration With the Society of Chest Pain Centers

W. Brian Gibler, MD, Chair; Christopher P. Cannon, MD, Co-Chair; Andra L. Blomkalns, MD; Douglas M. Char, MD; Barbara J. Drew, RN, PhD; Judd E. Hollander, MD; Allan S. Jaffe, MD; Robert L. Jesse, MD, PhD; L. Kristin Newby, MD; E. Magnus Ohman, MD; Eric D. Peterson, MD; Charles V. Pollack, MA, MD

Abstract—In the United States each year, >5.3 million patients present to emergency departments with chest discomfort and related symptoms. Ultimately, >1.4 million individuals are hospitalized for unstable angina and non–ST-segment elevation myocardial infarction. For emergency physicians and cardiologists alike, these patients represent an enormous challenge to accurately diagnose and appropriately treat. This update of the 2002 American College of Cardiology/American Heart Association Guidelines for the Management of Patients with Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction (UA/NSTEMI) provides an evidence-based approach to the diagnosis and treatment of these patients in the emergency department, in-hospital, and after hospital discharge. Despite publication of the guidelines several years ago, many patients with UA/NSTEMI still do not receive guideline-indicated therapy. (*Circulation*. 2005;111:2699-2710.)

Key Words: AHA Scientific Statements ■ unstable angina ■ emergency management
■ non–ST-myocardial infarction ■ acute coronary syndrome

Through this statement, the authors hope to provide a practical approach to implementing the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Management of Patients with Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction (UA/NSTEMI) by succinctly summarizing the diagnostic elements such as electrocardiography and cardiac biomarker testing, as well as treatment regimens including nitrates, morphine, β -blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, antiplatelet agents, and anti-thrombin drugs for acute coronary syndrome (ACS). Risk stratification of patients with ACS is emphasized so that the patients at highest risk are identified for guideline-directed

pharmacological therapy and early invasive therapy for revascularization. Two quality improvement tools, a template for an emergency department (ED) ACS risk assessment record and an initial therapeutic order template, are provided to help emergency physicians and cardiologists at every hospital integrate care in an evidence-based approach for their patients.

Finally, 4 quality improvement initiatives—Guidelines Applied in Practice (GAP), UCLA Cardiovascular Atherosclerosis Management Program (CHAMP), American Heart Association “Get With the Guidelines,” and the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of

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These Guidelines will also appear in the August 2005 issue of *Annals of Emergency Medicine*.

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the ACC/AHA guidelines)—are presented. Each of these programs attempts to improve care for patients with ACS by emphasizing guidelines awareness and implementation. Through the implementation of and adherence to the guidelines, improvement in care and outcomes for patients with ACS can be realized.

The 2002 ACC/AHA UA/NSTEMI guidelines represent an evidence-based approach to the care of patients with ACS.^{1,2} For patients presenting to the ED, these guidelines represent an opportunity to standardize the diagnosis and treatment of patients with ACS across the United States. Several summaries of the guidelines emphasizing emergency care have been published.^{3,4} Now, 3 years after the publication of the 2002 guidelines, adoption into routine practice in the emergency setting remains variable.⁵ The purpose of the present effort is to provide the emergency physician and cardiologist at any hospital with a practical approach, along with quality improvement tools, to implement the guidelines.

The 2002 ACC/AHA UA/NSTEMI guidelines provide extensive evidence for diagnostic and treatment regimens that provide substantial benefit in the early period after the patient with ACS presents to the ED. The evaluation of ACS in the emergency setting remains a challenge across the United States. More than 5.3 million patients present to EDs each year, resulting in 1.4 million patients being hospitalized for UA and NSTEMI.^{6,7} This undifferentiated population must be evaluated and risk stratified, not only for ACS but also for a number of other potentially fatal disease processes such as pulmonary embolism and aortic dissection. It is the hope of the present authors that this statement will prove useful to improve care for patients with UA/NSTEMI presenting to EDs across the United States.

Recommendations/Evidence Weighting

The 2002 ACC/AHA UA/NSTEMI guidelines use recommendation classes that rapidly provide the reader with sufficient information to make choices regarding diagnostic and treatment strategies. A Class I recommendation is generally considered to be useful and effective. Aspirin serves as an excellent example of a Class I treatment. Designation of a regimen as Class IIa identifies a treatment as generally considered effective, but some controversy may be present about the usefulness of a treatment. A Class IIb recommendation suggests that a treatment is controversial but leans toward efficacy. A therapy or diagnostic strategy that is Class III is not useful and may actually be harmful in some cases. Weighting of evidence for these Class I, II, and III recommendations is straightforward. If data from multiple large, randomized trials support a recommendation, then the weight of evidence is A. An evidence grade of B for a therapy is provided if fewer, smaller randomized trials, analyses of nonrandomized studies, or observational registries support a recommendation. Expert consensus provides an evidence grade of C¹ (Figure 1).

Risk Stratification

Emergency physicians must be expert in identifying patients with ACS presenting to the ED. It is critical to quickly perform risk stratification early in the course of a patient's

ACC/AHA Classification of Recommendations and Levels of Evidence

| | |
|---------------------|--|
| Class I: | Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. |
| Class II: | Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. IIa. Weight of evidence/opinion is in favor of usefulness/efficacy IIb. Usefulness/efficacy is less well established by evidence/opinion. |
| Class III: | Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful. |
| Level of Evidence A | Data derived from multiple randomized clinical trials |
| Level of Evidence B | Data derived from a single randomized trial, or non-randomized studies |
| Level of Evidence C | Consensus opinion of experts |

Adapted from: Braunwald E, Antman EM, Beasley JW et al. ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—2002: Summary Article: A Report of the American College of Cardiology/American Heart Associate Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). *Circulation* 2002; 106:1893-1900.

Figure 1. ACC/AHA classification of recommendations and levels of evidence. Adapted from *Circulation*. 2002;106:1893-1900.

evaluation to promptly provide guidelines-directed therapy. The history, including risk factors for coronary artery disease (CAD) development, as well as the physical examination help the clinician to screen patients for ACS (Table 1). The 12-lead ECG and cardiac biomarkers such as troponin and creatine kinase-MB (CK-MB) serve as the major ancillary testing tools for risk stratification in the emergency setting, a process that involves assessing (1) the likelihood that the patient's symptoms are the result of ACS and (2) among patients with probable/definite ACS, to identify patients who are at higher or lower risk of death and myocardial infarction (MI) as a complication of their ACS event.

The history taken from a patient with ACS typically but not always includes chest discomfort as a central feature. Older adults, patients with diabetes, chronic renal failure, and women may present with less-typical symptoms, yet they are at significant risk for complications with ACS. The older adult patient (>75 years old) in particular requires identification in the emergency setting because typically the benefits afforded this group by therapies recommended in the 2002 ACC/AHA guidelines exceed those of younger patients with ACS. The characterization of this discomfort, location, severity, frequency, and possible radiation help to identify the patient with ACS. The patient's age, sex, family history of CAD, smoking, dyslipidemia, hypertension, diabetes, previous CAD, and cocaine use help to increase the pretest likelihood of ACS in the individual presenting to the ED. The possibility of non-ACS causes for the patient's symptoms also must be considered, including pulmonary embolism, aortic dissection, parenchymal lung disease, esophageal reflux, biliary disease, psychiatric illnesses including depression and panic disorder, musculoskeletal pain, and trauma. A history of underlying illnesses such as intracranial tumor, gastrointestinal or other major bleeding, aortic dissection, and hemorrhagic stroke, or a major surgery in the previous 2 weeks can make antithrombotic or antiplatelet therapy dangerous.

Physical examination of the patient with possible ACS should focus on identifying features that cause the patient to

TABLE 1. Likelihood That Signs and Symptoms Represent an ACS Secondary to CAD

| Feature | High Likelihood <i>Any of the following:</i> | Intermediate Likelihood <i>Absence of high-likelihood features and presence of any of the following:</i> | Low Likelihood <i>Absence of high- or intermediate-likelihood features, but may have:</i> |
|-----------------|--|---|---|
| History | Chest or left arm pain or discomfort as chief symptom reproducing previously documented angina Known history of CAD, including MI | Chest or left arm pain or discomfort as chief symptom Age >70 y Male sex Diabetes mellitus | Probable ischemic symptoms in absence of any of intermediate-likelihood characteristics Recent cocaine use |
| Examination | Transient MR, hypotension diaphoresis, pulmonary edema, or rales | Extracardiac vascular disease | Chest discomfort reproduced by palpation |
| ECG | New, or presumably new, transient ST-segment deviation (≥ 0.05 mV) or T-wave inversion (≥ 0.2 mV) with symptoms | Fixed Q waves Abnormal ST segments or T waves not documented to be new | T-wave flattening or inversion in leads with dominant R waves Normal ECG |
| Cardiac markers | Elevated cardiac troponin I, troponin T, or CK-MB | Normal | Normal |

MR indicates mitral regurgitation; all other abbreviations as in text.

Adapted with permission from: Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE III, Steward DE, Thérout P. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). 2002. Available at: <http://www.acc.org/clinical/guidelines/unstable/unstable.pdf>. Accessed May 9, 2005.

be at high risk for death and nonfatal MI. Evidence of cardiogenic failure, including jugular venous distension, rales, cardiac murmurs, S₃ or S₄ gallops, and peripheral edema, increase the likelihood that ACS is the cause of the patient’s symptoms and portends a patient at high risk for ischemic complication. A new mitral regurgitation murmur, hypotension (systolic blood pressure <100 mm Hg), tachycardia (pulse >100 bpm), and bradycardia (pulse <60 bpm) also should alert the clinician to a patient at high risk. The physical examination also should be used to identify contraindications to antithrombotic or antiplatelet therapy such as gross rectal bleeding^{1,2} (Figure 2).

Twelve-Lead ECG

The 12-lead ECG is one of the most useful ancillary tools for detecting ACS. ST-segment depression has been shown to be a significant risk indicator for mortality and MI.⁸ Bundle-branch blocks that are new or presumed to be new can indicate a high-risk presentation in the emergency setting. A new bundle-branch block serves as a criterion for STEMI in the appropriate clinical setting, such as prolonged ischemic chest pain. It then indicates a need for rapid reperfusion therapy with immediate intervention in the cardiac catheterization laboratory. Old bundle-branch blocks may suggest underlying coronary disease; however, they also may indicate primary conduction system disease. A paced rhythm can mask underlying electrocardiographic high-risk features, making other cardiac testing such as radionuclide imaging or echocardiography extremely important. Approximately half of the patients with ST-segment depression will develop MI within hours after presentation to the ED. T-wave inversion on the initial 12-lead ECG portends a less-adverse prognosis in patients with ACS; $\approx 5\%$ of these patients will have an MI or die within 30 days. Deep symmetrical T-wave inversion across the precordial leads may indicate a critical stenosis of the left anterior descending coronary artery (Wellen’s phenomenon). Patients with suggestive histories and ST changes

in the anterior precordial leads and/or I and L should have posterior leads recorded to detect possible posterior ST-elevation events. A normal 12-lead ECG on presentation to the ED represents the lowest risk for a given patient;

Template for Emergency Department Record which Includes Acute Coronary Syndrome Risk Assessment

Demographics: Patient Name, Age, Sex, Race, Date/Time Seen

History of Present Illness:

- 1) Time of chest pain onset/symptom onset; duration of longest episode of pain prompting visit
- 2) Other locations of pain: Neck, Left shoulder/arm, Right shoulder/arm, Left hand, Right hand, Abdomen, Back, Other _____
- 3) Quality of Pain: Pressing/Crushing/Tightness, Sharp/Stabbing, Burning, Ache, Indigestion/Gas, Numbness, Indescribable, Other _____
- 4) Pain is reproduced by: Deep breathing, Palpation, Change in position, Other _____
- 5) Associated Symptoms: Diaphoresis, Nausea, Vomiting, Dyspnea, Dizziness, Other _____
- 6) Diagnosis of most similar chest pain: MI, Angina, Other _____
- 7) Recent pain compared with previously diagnosed angina: Worse, Similar, Better, No previous diagnosis of angina, Different

Cardiac Risk Factors: Family history of premature coronary artery disease in first degree relatives <60 years old, Elevated Cholesterol (>200 or taking medication), hypertension (systolic blood pressure >140, diastolic blood pressure >90 or taking medication), diabetes mellitus, smoking (current, past, never)

Past Medical History: MI, Angina, Cardiac Catheterization, Percutaneous Coronary Intervention, Coronary Artery Bypass Grafting

Medications

Allergies

Physical Examination: Vital signs including O₂ saturation

General: Distress - None; Mild; Moderate; Severe; Diaphoresis

HEENT: JVD; Carotid Bruits

Pulmonary: Clear; Rales (bibasilar or less); Rales (>bibasilar), Other _____

Heart: Mitral regurgitation murmur S₃; S₄

Abdomen: Abdominal Aortic Aneurysm; Renal/Femoral Artery Bruits; Rectal Examination/Guaic results: positive/negative

Extremities: Decreased Peripheral Pulses/ Decreased Perfusion

Laboratory

Electrocardiogram: Normal; Probable new ST-segment elevation MI (≥ 1.0 mm ST-segment elevation in ≥ 2 leads) or new bundle branch block (left or right); New ischemia (> 1.0 mm ST-segment depression in ≥ 2 leads); Transient ST-segment elevation or ST-segment elevation not reaching 1.0 mm (0.5 mm < ST-segment elevation < 1.0 mm); Other new ST-segment or T-wave changes of ischemia; old infarction, old ischemia; non-specific ST-segment or T-wave abnormality

Cardiac Biomarkers: Troponin T or I Level
CK/CK-MB Level

Adapted from: Emergency Department Chest Pain/ACS Evaluation template, Brigham & Women’s Hospital, Boston, Massachusetts and the University Hospital, Cincinnati, Ohio.

Figure 2. Template for emergency department record that includes ACS risk assessment. Adapted from Brigham & Women’s Hospital, Boston, Mass, and the University Hospital, Cincinnati, Ohio.

however, up to a 6% rate of NSTEMI still exists for these patients. The initial ECG results therefore provide the clinician with substantial risk stratification information. The ACC/AHA guidelines support obtaining serial 12-lead ECGs in the ED to improve sensitivity for detecting ACS if the initial ECG is nondiagnostic.¹

Cardiac Biomarkers

The cardiac biomarkers troponin (I and T) and CK-MB represent the second principal method for identifying patients with ACS at risk for significant complications, including death and MI in the ED. Although CK-MB has been the predominant marker of myocardial necrosis used, the troponins I and T have in many centers replaced this traditional marker in accordance with the recent criteria for the redefinition of acute MI promulgated by the European Society of Cardiology and the ACC.⁹⁻¹³

Point-of-care testing can accelerate decision making in the ED by providing CK-MB and troponin levels within 15 to 20 minutes after presentation¹⁴; however, many point-of-care devices are less sensitive than are central laboratory analyzers.¹⁵ Thus, some patients with minor and/or modest elevations in troponin may be missed. This factor must be considered by clinicians relying on these results. Some assays lack adequate sensitivity and/or sufficient precision to allow for accurate low-level measurements. Insufficient precision means that too much variability is present in an assay when multiple testing is performed on a uniform set of samples. When central laboratory testing is used, the turnaround time for laboratory results should not exceed 1 hour.

During the last decade, numerous studies have demonstrated that any detectable elevation of troponin identifies patients at high risk for ischemic complications, including patients with renal failure.¹⁶ Elevated troponin in the setting of ischemic symptoms indicates that the patient has experienced an MI. Elevation of troponin is associated with increased risk of death, and the risk of this complication increases proportionately with the absolute level.¹⁷ Like the 12-lead ECG, troponin serves as an independent predictor of substantial patient risk. Studies also have confirmed that patients with ACS and elevated troponins derive greater benefit from treatment with platelet glycoprotein (GP) IIb/IIIa inhibitors, low-molecular-weight heparin, and early percutaneous coronary intervention (PCI) than those not having elevated troponin levels. It should be emphasized that a normal level of troponin (or CK-MB) on ED presentation, particularly within 6 hours of chest pain onset, does not exclude MI. Serial testing in the ED, at 3 and 6 hours, and at an interval of 6 to 10 hours in-hospital, is necessary to exclude myocardial injury.

The best predictive accuracy for elevated troponin occurs with the use of the 99th percentile of the normal value for troponin. To improve specificity, however, some have suggested using the value when the assay precision is <10%.¹⁸ This approach to improving troponin sensitivity and specificity has been proposed recently and should improve diagnostic accuracy in patients with ACS. When troponin is used at these cutoff values, CK-MB may be useful for timing of the infarction. Neither CK-MB nor other markers, however, have

been shown to add substantially to predictive accuracy when serial samples are analyzed with sensitive assays for troponin.

An elevated troponin is indicative of cardiac injury but not necessarily ischemic cardiac injury.¹⁹ If the clinical presentation is not one of acute ischemic heart disease, then a careful search for alternative causes of cardiac injury is essential, such as congestive heart failure or pulmonary embolus. It is important in patients with borderline elevated troponin levels to obtain a careful clinical history so that potent antithrombin and antiplatelet agents, which can cause bleeding, are given to appropriate patients with myocardial necrosis resulting from ACS.

Other Diagnostic Testing

In the emergency setting, other modalities such as radionuclide imaging can provide additional evidence for ACS in patients who present with symptoms that are consistent with ischemia but nondiagnostic 12-lead ECGs and normal levels of cardiac biomarkers.¹ Multiple other tests such as echocardiography for wall motion abnormality, contrast echo perfusion, and radionuclide perfusion such as sestamibi can be performed at rest, providing compelling risk stratification information for patients presenting to the ED. When performed while the patient is complaining of chest pain, these studies can provide excellent negative predictive value for acute myocardial ischemia. Patients with chronic electrocardiographic changes such as bundle-branch block or ST-segment/T-wave abnormalities also can be evaluated more extensively with these modalities. The availability of these techniques at a hospital depends on the particular expertise of the cardiologists or nuclear radiologists at the institution. Standard graded exercise testing and stress echocardiography can be performed in patients with nondiagnostic ECGs, negative cardiac biomarkers, and no recent (<6 hours) pain at rest; however, exercise testing is contraindicated in patients with acute ischemia. New blood tests such as myeloperoxidase and ischemia-modified albumin are being evaluated to better diagnose ACS.^{20,21} For patients without high-risk features presenting to the ED, negative serial cardiac biomarkers, no evidence of ST-segment or T-wave changes, and negative perfusion imaging at rest, discharge from the ED after a chest pain center evaluation may be appropriate. An Algorithm for the Evaluation and Management of Patients Suspected of Having an Acute Coronary Syndrome is available in the 2002 ACC/AHA UA/NSTEMI guidelines for the clinician in such circumstances.

2002 ACC/AHA Treatment Guidelines—Management Strategies

Basic Therapy for ACS

For all patients with probable ACS, the following therapies are recommended by the 2002 ACC/AHA guidelines. These therapies should be provided in addition to routine therapy such as bed rest, oxygen if needed, and continuous cardiac rhythm monitoring:

1. Nitrates (IC). Nitrates should be given via sublingual administration followed by intravenous administration for the relief of ischemia and associated symptoms. There are no randomized, placebo-controlled clinical trials of nitrate use in

unstable angina; however, small studies from the prethrombolytic era suggested a reduction in mortality rate of $\approx 35\%$. More contemporary studies (fourth International Study of Infarct Survival [ISIS-4], Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico II [lisinopril and transdermal glyceryl trinitrate] [GISSI-3]) are confounded by their being STEMI trials and to a lesser extent by the prehospital use of nitrates. As a result, the recommendations are largely extrapolated from pathophysiological principles and uncontrolled observations.²²

2. Morphine (IC). Morphine is indicated in the initial treatment of acute coronary syndromes. Although no randomized, controlled trials have been performed with morphine, it remains recommended because of its venodilation properties and modest reductions in heart rate. Morphine sulfate is recommended when symptoms are not immediately relieved with nitroglycerin and a β -blocker or when acute pulmonary congestion or agitation is present.

3. β -Blockers (IB). Intravenous administration is recommended in the emergency setting when there is ongoing chest pain without contraindications to β -blockade and the patient is not already taking β -blockers before presentation. An overview of double-blind, randomized, controlled trials in patients with threatening or evolving MI suggests an $\approx 13\%$ reduction in risk of progression to MI for patients. There are no trials with enough power to evaluate β -blockade in patients with unstable angina; however, the proven efficacy of β -blockers in patients with acute MI, recent acute MI, congestive heart failure, and angina led to their use being recommended in unstable angina.²³

4. Nondihydropyridine calcium-channel blockers (verapamil or diltiazem) (IB). Nondihydropyridine calcium-channel blockers are recommended in patients with continuing or frequently recurring ischemia when β -blockers are contraindicated and there is no left ventricular (LV) dysfunction or other contraindication to their use. When administered to patients with LV dysfunction, there is strong evidence that they are detrimental (Class III).^{24–26}

5. Angiotensin-converting enzyme inhibitors (ACEIs) (IB). ACEIs are recommended when hypertension persists despite treatment with nitroglycerin and β -blockers in patients with LV systolic dysfunction or congestive heart failure. They are also recommended for patients with ACS and diabetes. ACEI initiation in the ED is appropriate; however, it is not necessary to be started in this setting. Angiotensin renin blockers can be substituted if the patient is ACEI intolerant.^{27–29}

6. Antiplatelet agents. Agents that inhibit the aggregation of platelets serve as a principal approach to preventing thrombosis in the 2002 ACC/AHA UA/NSTEMI guidelines. There are 3 different classes of agents that have distinct and separate mechanisms of action: aspirin, clopidogrel, and the GP IIb/IIIa receptor inhibitors.

- Aspirin serves as the prototypical platelet inhibitor by blocking the thromboxane A_2 pathway. It is inexpensive and has been proved effective in a wide variety of thrombotic diseases. The use of aspirin is a Class IA recommendation, and it should be started as soon as possible. Many prehospital emergency medical services programs rou-

tinely provide aspirin to patients with possible ACS in the field. If not given there, then it should be given in the ED shortly after presentation. Four randomized trials of aspirin versus placebo in patients with UA have confirmed the salutary effect of this simple treatment. In these studies, there was an $\approx 50\%$ reduction in death and MI with aspirin.^{1,30,31}

- Another antiplatelet agent, a thienopyridine clopidogrel, has been shown to be effective in blocking adenosine diphosphate-stimulated platelet aggregation. Clopidogrel irreversibly blocks the P_2Y_{12} receptor on platelets, which partially blocks subsequent platelet activation by adenosine diphosphate. The Clopidogrel in Unstable Angina to prevent Recurrent Events (CURE) trial confirmed the additional benefit of clopidogrel with aspirin for UA/NSTEMI. There was a 20% reduction in the primary outcome of cardiac death, MI, or stroke in the CURE trial. This agent was incorporated into the 2002 ACC/AHA UA/NSTEMI guidelines as a Class IA recommendation.³²
- The GP IIb/IIIa receptor inhibitors are the third class of antiplatelet agents that are important therapies in the 2002 ACC/AHA UA/NSTEMI guidelines. Activated platelets express surface GP IIb/IIIa receptors, which bind fibrinogen to allow aggregation. Eptifibatid and tirofiban (small-molecule agents) and abciximab (a monoclonal antibody fragment) are approved for use in patients with ACS and are recommended for patients undergoing early invasive therapy based on the CAPTURE, PURSUIT, PRISM-PLUS, and TACTICS-TIMI 18 (c7E3 Antiplatelet Therapy in Unstable Refractory Angina, Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin™ Therapy, Platelet Receptor Inhibition for ischemic Syndrome Management in Patients Limited to very Unstable Signs and symptoms, and Treat angina with Aggrastat® and determine Costs of Therapy with Invasive or Conservative Strategies-Thrombolysis In Myocardial Infarction-18, respectively) trials (Class IA). The 2 small-molecule agents eptifibatid and tirofiban provide reversible inhibition of the GP IIb/IIIa receptor and are indicated for patients receiving conservative therapy or early invasive therapy for ACS (Class IIaA).^{1,33–37}
- Abciximab is not indicated for patients receiving only medical management without cardiac catheterization; this is a Class IIIA recommendation based on the GUSTO-IV (Global Utilization of Streptokinase and tPA for Occluded arteries) ACS trial. It is indicated for use in patients in whom early PCI is planned.³⁸

7. Antithrombin agents. The use of heparin is essential to the treatment of patients with ACS. Heparin blocks thrombin formation, when given intravenously, by accelerating the action of antithrombin. Unfractionated heparin binds to a variety of proteins, which reduces the heparin available to affect antithrombin, resulting in variable anticoagulant responses in patients. Intravenous heparin, however, is considered a fundamental therapy for treating ACS and is a Class IA therapy when given in conjunction with antiplatelet agents.^{1,39–41} In a number of trials, low-

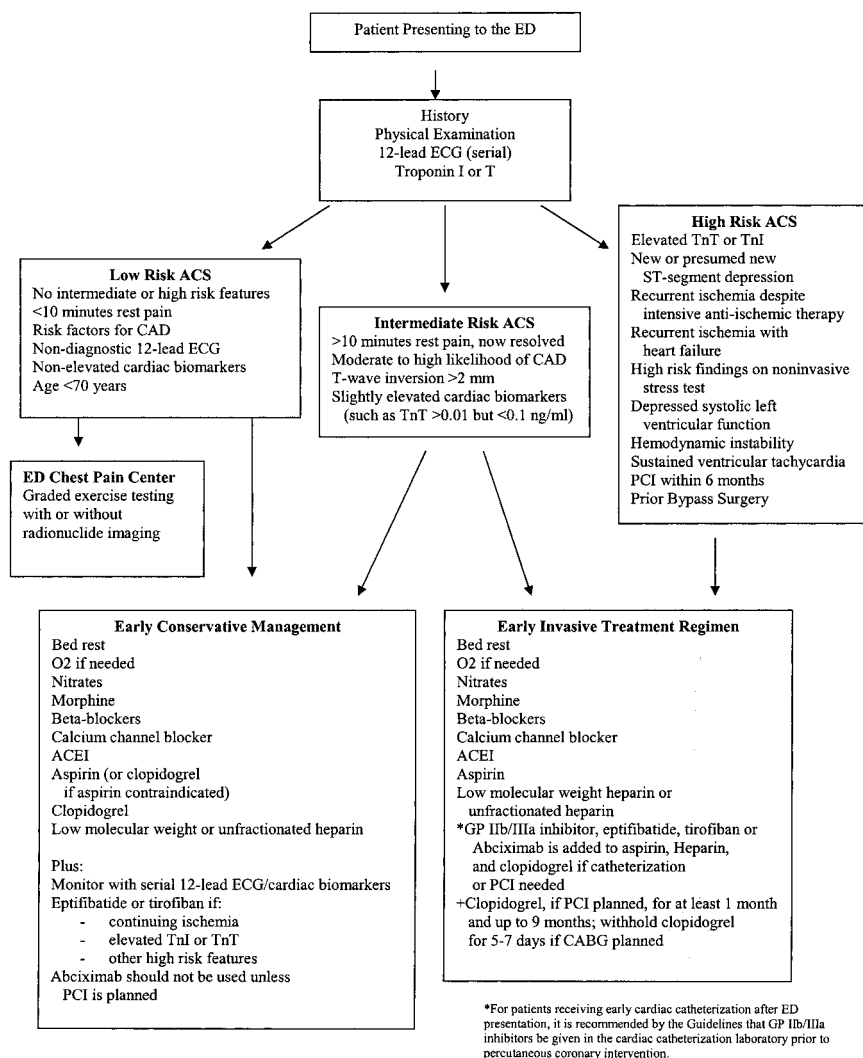


Figure 3. Integration of the 2002 ACC/AHA Guidelines for Diagnostic and Treatment Strategies in the Emergency Department for Patients with ACS.

molecular-weight heparin has been found to have improved efficacy as compared with unfractionated heparin. The low-molecular-weight heparin enoxaparin has been shown to be superior to unfractionated heparin in 2 large clinical trials, ESSENCE (Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-wave Coronary Events) and TIMI-II-B, but was equivalent in the most recent study, SYNERGY (Superior Yield of the New strategy of Enoxaparin, Revascularization, and Glycoprotein IIb/IIIa inhibitors).^{42,43} The guidelines suggest enoxaparin, but not the other low-molecular-weight heparins, is preferred over unfractionated heparin unless coronary artery bypass grafting (CABG) surgery is planned within 24 hours (Class IIaA).⁴⁴ Patients with elevated troponin values are the ones who seem to benefit. The use of low-molecular-weight heparin should be coordinated with the cardiac catheterization team before PCI. Some laboratories prefer not to perform these procedures on patients who have received low-molecular-weight heparin.

Figure 3 is an algorithm that depicts the integration of the 2002 ACC/AHA UA/NSTEMI guidelines for these diagnostic and treatment strategies in the ED.

Patients With ACS at Risk for Complications

The 2002 ACC/AHA UA/NSTEMI guidelines define high, intermediate, and low risk for death or nonfatal MI.¹ Initially, in the ED, emergency physicians must risk stratify patients for ACS. Once it is determined that a patient likely has ACS, then it is necessary to identify those patients at high risk for ischemic complications, including death and nonfatal MI. Patients with ACS at low risk for ischemic complications, including death and MI, should be admitted and treated with early conservative management, as shown in Figure 3. Early invasive therapy should be considered for all patients with ACS who are deemed to be at high risk for ischemic complications. Patients at intermediate risk for death or nonfatal MI should receive appropriate therapy for ACS and be considered for possible intervention by a cardiologist.

Some low-risk ACS patients are candidates for evaluation in an ED chest pain center. In these individuals with nondiagnostic 12-lead ECGs and nonelevated cardiac biomarkers, graded exercise testing with or without radionuclide imaging can be performed safely. If negative, then the patient can be discharged home from the ED for further follow-up by a cardiologist.

TABLE 2. Short-Term Risk of Death or Nonfatal MI in Patients With UA/NSTEMI

| Feature | High Risk <i>At least 1 of the following features must be present:</i> | Intermediate Risk <i>No high-risk features but must have 1 of the following:</i> | Low Risk <i>No high- or intermediate-risk features but may have any of the following features:</i> |
|-------------------|--|---|--|
| History | Accelerating tempo of ischemic symptoms in preceding 48 h | Previous MI, peripheral or cerebrovascular disease, or CABG, previous aspirin use | |
| Character of pain | Prolonged ongoing (>20 min) rest pain | Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD Rest angina (>20 min) or relieved with rest or sublingual NTG | New-onset or progressive CCS Class III or IV angina previous 2 wk without prolonged (>20 min) rest pain but with moderate or high likelihood of CAD* |
| Clinical findings | Pulmonary edema, most likely result of ischemia New or worsening MR murmur, S ₃ or new/worsening rales Hypotension, bradycardia, tachycardia Age >75 y | Age >70 y | |
| ECG | Angina at rest with transient ST-segment changes >0.05 mV Bundle-branch block, new or presumed new Sustained ventricular tachycardia | T-wave inversions >0.2 mV Pathological Q waves | Normal or unchanged ECG during episode of chest discomfort |
| Cardiac markers | Elevated (eg, troponin T >0.1 ng/mL) | Slightly elevated (eg, troponin T >0.01 but <0.1 ng/mL) | Normal |

Estimation of the short-term risks of death and nonfatal cardiac ischemic events in UA is a complex, multivariable problem that cannot be fully specified in a table such as this; therefore, this table is meant to offer general guidance and illustration rather than rigid algorithms.

CCS indicates Canadian Cardiovascular Society; NTG, nitroglycerin; MR, mitral regurgitation; all other abbreviations as in text.

*See Table 1.

Adapted with permission from: Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE III, Steward DE, Thérout P. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). 2002. Available at: <http://www.acc.org/clinical/guidelines/unstable/unstable.pdf>. Accessed May 9, 2005.

Early Conservative Strategy

Patients presenting to the ED with ACS who are at low risk for ischemic complications should be treated with an early conservative management strategy that includes the following^{1,35}:

1. Aspirin (Class IA); clopidogrel if aspirin is contraindicated (Class IA)
2. Clopidogrel for at least 1 month (Class IA) and for up to 9 months (Class IB); clopidogrel should be given to these patients in the ED if cardiac catheterization is not planned.
3. Enoxaparin or unfractionated heparin (Class IA)
4. Eptifibatid or tirofiban in patients with:
 - continuing ischemia (Class IIaA)
 - elevated TnI or TnT (Class IIaA)
 - other high-risk features (Class IIaA)
5. Abciximab should not be used unless PCI is planned (Class IIIA).³⁹

Patients can evolve in the emergency setting from low through intermediate to high risk. Serial ECGs and cardiac biomarkers should be performed on any patient suspected of having ACS but with initially negative cardiac biomarkers or a nondiagnostic 12-lead ECG. Should a patient be low risk initially, warranting a conservative strategy, surveillance through serial ECGs and cardiac biomarkers may detect intermittent ischemic events that require a switch to an invasive treatment strategy.

Early Invasive Treatment Strategy

An early invasive treatment strategy defined as coronary angiography and revascularization within 12 to 48 hours after presentation to the ED is a Class IA level of evidence for all patients considered to be at high risk for UA/NSTEMI.^{35,36,45} The following criteria are indicative of the high-risk patient as noted in Table 2¹:

1. New or presumed new ST-segment depression
2. Elevated troponin I or T
3. Recurrent angina/ischemia at rest or with low levels of activity despite intensive anti-ischemic treatment
4. Recurrent ischemia with associated heart failure (S₃ gallop, pulmonary edema, worsening rales, or new or worsening mitral regurgitation)
5. High-risk findings on noninvasive stress testing
6. Depressed systolic LV function (EF <0.40 on noninvasive study)
7. Hemodynamic instability
8. Sustained ventricular tachycardia
9. PCI within the last 6 months
10. Previous coronary artery bypass surgery

In these high-risk patients, in addition to O₂ (if needed), nitrates, morphine, β -blockers, calcium-channel blockers, and ACEI therapies in the early invasive strategy should include the following:

1. Aspirin (Class IA); clopidogrel if aspirin is contraindicated (Class IA).

UA/Non-ST-segment Elevation (NSTEMI) Initial Management Standing Orders.

MEDICATION ALLERGIES
 Specify: _____

DIAGNOSTIC STUDIES
 12-lead ECG; Now _____; In AM _____; Date: _____
 12-lead ECG for recurrent chest pain
 Cardiac markers → Specify:
 Troponin I OR } 0, 3, 6, 12, 24 hours
 Troponin T }
 CK AND } 0, 3, 6, 12, 24 hours
 CK-MB }

LABS
 Fasting lipid profile in AM CBC q AM
 Chemistry Panels in ED and q AM Other labs: _____

INITIAL TREATMENT
Oral Antiplatelet Therapies:
 Aspirin → Specify:
 160-325 mg Enteric-coated ASA } _____ mg per day
 OR Non-enteric coated ASA }
 If aspirin intolerant, clopidogrel: 300 mg loading dose followed by 75 mg po QD

Nitrates and Morphine:
 SL NTG 0.4 mg as needed for recurrent chest pain
 NTG paste: _____ inches q 6 hours, off from midnight-6 AM
 IV NTG: Start at 10 mcg/min if pain not relieved by SL or transmucosal NTG and titrate (up to 200 mg/min) for relief of chest pain (keep SBP > 90 mmHg)
 Morphine Sulfate 1-2 mg every _____ hours as needed for recurrent chest pain

Beta Blockers:
 Metoprolol → Specify:
 IV: _____ mg q 5 min X _____ doses OR
 po: _____ mg q _____ hours OR
 Atenolol → Specify:
 IV: _____ mg q 5 min X _____ doses OR
 po: _____ mg qd
 Other → Specify: _____

Non-Dihydropyridine Calcium Antagonist (if Beta-blocker contraindicated):
 Diltiazem → Specify:
 po: _____ mg q 8 hours OR
 Diltiazem CD/XR: _____ mg po qd
 Verapamil → Specify:
 po: _____ mg q 8 hours OR
 Verapamil SR: _____ mg po qd

ACE Inhibitor (Angiotensin receptor blocker can be substituted if ACE intolerant):
 Enalapril po: _____ mg q 12 hours
 Lisinopril po: _____ mg qd

MANAGEMENT STRATEGY

■ **NSTEMI ACS patients with high-risk features should be managed according to the Early Invasive Protocol.**
 ■ **Patients with moderate-risk features can be managed with either Protocol.**
 ■ **Patients with low-risk features should be managed according to the Early Conservative Protocol.**

High-risk: Elevated Cardiac Marker, ST depression, Transient ST elevation > 20 min, rest pain, Hemodynamic instability, signs of CHF
Moderate-risk: No high-risk features, Prior MI, Prior CABG, T-wave inversions, Rest angina (< 20 min) relieved promptly with NTG, Age > 70 years
Low-risk: No high- or moderate-risk features, progressive angina without prolonged rest pain, Normal cardiac markers, Normal ECG with pain

| EARLY INVASIVE PROTOCOL | EARLY CONSERVATIVE PROTOCOL |
|--|--|
| Intravenous Anti-thrombotic Therapies: <input type="checkbox"/> IV unfractionated heparin → Initial bolus of 60-70 U/kg bolus (not to exceed 5000 U) + 12-15 U/kg/hr infusion (not to exceed 1000 U/hr) to target aPTT range of 50-70 sec, or 1.5-2.5 times control <input type="checkbox"/> Low-molecular-weight heparin → Specify: <input type="checkbox"/> Enoxaparin: 1 mg/kg SC q 12 hrs | Intravenous Anti-thrombotic Therapies: <input type="checkbox"/> IV unfractionated heparin → Initial bolus of 60-70 U/kg bolus (not to exceed 5000 U) + 12-15 U/kg/hr infusion (not to exceed 1000 U/hr) to target aPTT range of 50-70 sec, or 1.5-2.5 times control <input type="checkbox"/> Low-molecular-weight heparin → Specify: <input type="checkbox"/> Enoxaparin: 1 mg/kg SC q 12 hrs |
| Intravenous Antiplatelet Therapies: GP IIb/IIIa Inhibitor → Specify: <input type="checkbox"/> Abciximab: 0.25 mg/kg IV bolus + 0.125 mcg/kg/min infusion (only for patients planned to undergo PCI within 12-24 hrs) OR <input type="checkbox"/> Eptifibatid: 180 mcg/kg IV bolus + 2.0 mcg/kg/min infusion* OR <input type="checkbox"/> Tirofiban: 0.4 mcg/kg/min IV bolus for 30 min + 0.1 mcg/kg/min infusion* <small>* For patients with renal impairment, administer 1/2 the rate of infusion for eptifibatid and tirofiban</small> <input type="checkbox"/> Schedule for Early Cardiac Catheterization Date: _____ Day: _____ Month: _____ Year: _____ | Intravenous Antiplatelet Therapies: <input type="checkbox"/> Clopidogrel: 300 mg loading dose → 75 mg po QD Oral Antiplatelet Therapies: <input type="checkbox"/> Clopidogrel: 300 mg loading dose → 75 mg po QD NOTE: Add clopidogrel after diagnostic catheterization unless CABG is planned. <input type="checkbox"/> Clopidogrel: 300 mg loading dose → 75 mg po QD |
| Oral Antiplatelet Therapies: NOTE: Add clopidogrel after diagnostic catheterization unless CABG is planned. <input type="checkbox"/> Clopidogrel: 300 mg loading dose → 75 mg po QD | Oral Antiplatelet Therapies: <input type="checkbox"/> Clopidogrel: 300 mg loading dose → 75 mg po QD Intravenous Antiplatelet Therapies: NOTE: Eptifibatid or tirofiban are indicated for patients with high-risk features who are managed conservatively. GP IIb/IIIa Inhibitor → Specify: <input type="checkbox"/> Eptifibatid: 180 mcg/kg IV bolus + 2.0 mcg/kg/min infusion* OR <input type="checkbox"/> Tirofiban: 0.4 mcg/kg/min IV bolus for 30 min + 0.1 mcg/kg/min infusion* <small>* For patients with renal impairment, administer 1/2 the rate of infusion for eptifibatid and tirofiban</small> <input type="checkbox"/> Schedule for assessment of left ventricular function → Type(s): <input type="checkbox"/> Echocardiogram <input type="checkbox"/> Nuclear ventriculogram <input type="checkbox"/> Schedule for stress test → Type(s): <input type="checkbox"/> Exercise treadmill test <input type="checkbox"/> Exercise nuclear perfusion study <input type="checkbox"/> Dobutamine nuclear perfusion study <input type="checkbox"/> Persantine nuclear perfusion study <input type="checkbox"/> Exercise stress echocardiography <input type="checkbox"/> Dobutamine echocardiography |

Lipid-lowering agent: Name and dose of drug prescribed: _____

Name of Physician: _____ Date: _____ Time: _____
 Signature: _____

Adapted from: CRUSADE Quality Improvement Initiative tool (<http://www.crusadeqi.com>)

Figure 4. UA/NSTEMI initial treatment standing orders. Adapted from <http://www.crusadeqi.com>.

2. Low-molecular-weight heparin or unfractionated heparin (Class IA); low-molecular-weight heparin is considered preferable to unfractionated heparin unless bypass surgery is planned within 24 hours (Class IIaA).

3. GP IIb/IIIa inhibitor if catheterization or PCI is planned (Class IA); the 2002 ACC/AHA UA/NSTEMI guidelines recommend that this therapy be given immediately before PCI in patients receiving early invasive therapy for non-ST-segment elevation ACS.

4. GP IIb/IIIa inhibitor is added to aspirin, heparin, and clopidogrel if cardiac catheterization or PCI is planned (Class IIaB).

5. Clopidogrel, if PCI is planned, should be given for at least 1 month (Class IA) and for up to 9 months (Class IB). In most situations in which the patient with ACS is receiving early cardiac catheterization, clopidogrel therapy can be postponed until coronary anatomy can be defined. It should be noted that some cardiologists prefer the initial use of clopidogrel even if cardiac catheterization/PCI is planned because the likelihood of the patient's needing CABG is low and many cardiac surgeons feel that if CABG is urgently required, then a 5- to 7-day wait is not necessary. If CABG is necessary, then clopidogrel therapy should be withheld until after surgery. It is suggested that CABG be delayed for 5 to 7 days if clopidogrel has already been administered.

Improving Guideline Adherence

The development of expert-prepared strategies such as the 2002 ACC/AHA UA/NSTEMI guidelines presents enormous

challenges to the general implementation of this best-practice approach. Several quality improvement initiatives have been developed to demonstrate methods for changing physician behavior and improving patient outcomes for patients with ACS.⁴⁶⁻⁵⁸

The GAP project, undertaken in Michigan, used educational tools distributed to healthcare providers and patients describing the newest therapies for acute MI. Indicators such as smoking cessation, biomarker use, and cholesterol levels improved after GAP use. These tools improved the appropriate use of aspirin, beta-blockers, and cholesterol-lowering agents.⁵⁹

In a similar fashion, CHAMP stressed the initiation of aspirin, cholesterol-lowering treatment, ACEIs, and beta-blockers in the hospital. The researchers used adherence guidelines, standardized treatment orders, and precise tracking of medication use rates. Treatment rates and clinical outcomes were improved in patients with acute MI after CHAMP was implemented.^{60,61}

Another proactive approach to improving adherence, the AHA's "Get With the Guidelines" program, demonstrated that didactic best-practice presentations, interactive multidisciplinary team workshops, a customized guideline tool kit, and an interactive Web-based management tool significantly improved the performance of practitioners. Measurements of aspirin, beta-blocker, and ACEI use; cholesterol level management; smoking cessation counseling; blood pressure control; and cardiac rehabilitation referral demonstrated an improved

use of these therapies for patients with ACS for early, in-hospital, and discharge therapies.⁶²

Finally, the CRUSADE Quality Improvement Initiative is an ongoing effort to track adherence to the 2002 ACC/AHA UA/NSTEMI guidelines and to provide mechanisms to improve performance. This initiative is a partnership of academicians, industry, and emergency physicians and cardiologists at hospitals throughout the United States. The objectives of CRUSADE include the following:

1. Determine the current awareness and adherence to the 2002 ACC/AHA UA/NSTEMI guidelines for ACS.
2. Implement quality improvement initiatives at site hospitals to promote ACC/AHA diagnostic and treatment recommendations for high-risk ACS patients.
3. Improve clinical outcomes through early guideline implementation, for example, in the ED.

Early evidence with >100 000 patients enrolled suggests that this effort has been successful in increasing awareness and adherence to the 2002 ACC/AHA UA/NSTEMI guidelines. Since October 2003, data have been collected on ED guideline adherence for UA/NSTEMI that provide information that emergency physicians and cardiologists can use to improve the care of these patients.^{63,64} A structured order set provides specific guideline-based therapy for patients with ACS enrolled in the CRUSADE Quality Improvement Initiative (Figure 4).

Barriers to Guideline Implementation

A variety of barriers to guideline implementation are experienced in the emergency setting. Delays in receiving cardiac biomarker data because of slow laboratory turnaround, high patient volume in the ED decreasing throughput, and a lack of standardized diagnostic and treatment approaches are only some of the barriers that can inhibit providing appropriate care to patients. Specialties other than cardiology provide inpatient care to individuals with ACS. Making all physicians who care for these patients aware of the 2002 ACC/AHA UA/NSTEMI guidelines is a significant challenge in any hospital setting. Finally, multiple cardiology groups at an institution can make an agreement on specific diagnostic and treatment regimens for patients with ACS difficult to achieve.

Predictors for Successful Guideline Implementation

A variety of circumstances can predict a high likelihood for improvement in guideline implementation. Strong clinical champions in emergency medicine and cardiology who have effective communication with other emergency physicians, cardiologists, internists, and family physicians at their institutions can develop consensus on clear diagnostic and treat-

ment pathways that incorporate guidelines directives. Physicians must demonstrate a clear willingness to partner with other hospital healthcare specialists.

Support from the laboratory and hospital administration also is essential. Improving laboratory turnaround time for cardiac biomarkers can ensure that high-risk patients are identified early while in the ED. Hospital administration can provide needed resources and clear support, which encourages involvement in quality improvement efforts by all hospital departments, including pharmacy and nursing. Having the significant involvement of nursing, administration, laboratory, and pharmacy is essential to reaching agreement on a pathway. Aligning the incentives of all parties to provide guideline-directed care is extremely important.

Careful data analyses, which can be used to provide high-quality feedback to ED and coronary care unit personnel (physicians and nurses), can serve as a ready stimulus for quality improvement. These data, compared with national benchmarks, can be shared with multiple physician groups across the hospital (emergency medicine, cardiology, internal medicine, family medicine, and cardiac surgery) and nonphysician members of the healthcare team to identify areas of success and potential improvement. Quality management teams having constituents from all of these physician disciplines as well as the laboratory, nursing, pharmacy, and hospital administration can use these high-quality data to improve adherence to guidelines.

In addition, the use of quality improvement tools such as standard diagnostic evaluations for the ED that readily identify high-risk criteria in ED patients as well as standardized medication order sets also can increase adherence to guidelines. Early identification of high-risk patients with ACS in the emergency setting can decrease time to cardiac catheterization and revascularization. The combination of improved communication between all members of the care team involved with ACS patients, the collection of high-quality data on these patients, and the use of quality improvement tools can provide improved, more consistent care for these patients.

Conclusions

The 2002 ACC/AHA UA/NSTEMI guidelines represent an evidence-based approach to the care of patients with ACS. Adherence to the guidelines can be improved by enhanced communication between emergency physicians and cardiologists, as well as by the implementation of quality improvement initiatives. Through this approach, better, more consistent care can be provided for patients with ACS and can lead to improved outcomes.

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