

# New Guidelines for Evaluating Acute Coronary Syndrome

The American College of Cardiology and the American Heart Association

[Clinician Reviews 11(1):73-86, 2001. © 2001 Clinicians Publishing Group]

## Introduction

Myocardial infarction continues to be missed in too many patients who present with chest pain. New guidelines issued by the American College of Cardiology and the American Heart Association can help primary care providers—including NPs and PAs—to identify acute coronary syndrome (ACS); categorize a patient's immediate risk; and use clinical findings, new cardiac markers, and electrocardiographic readings to take decisive action, providing the optimal level of care for patients with confirmed ACS. Early management guidelines include changes in the recommended use of oxygen and address use of fractionated (low-molecular weight) heparin and glycoprotein IIb/IIIa inhibitors.

## Defining Acute Coronary Syndrome

*Acute coronary syndrome* (ACS) refers to a constellation of clinical symptoms that may indicate acute myocardial infarction (MI). In spite of newly identified cardiac markers that enhance diagnosis of ACS and newer medical and surgical therapeutic options, coronary artery disease (CAD) continues to be the leading cause of death in the United States. Missed MI is a leading cause of malpractice suits in emergency medicine.<sup>[1]</sup>

A new report by the American College of Cardiology (ACC) and the American Heart Association (AHA) provides guidelines for primary care providers evaluating a patient who presents with chest pain.\* The guidelines focus on two components of ACS: unstable angina (UA) and non-ST-segment elevation MI (NSTEMI). The apparent result of disrupted atherosclerotic plaque and subsequent decrease of coronary blood flow, UA/NSTEMI may lead to development of acute MI or sudden death.

## Unstable Angina

The diagnosis of UA may be based on any of three presentations.<sup>[2]</sup> *Rest angina* occurs without any exertional provocation and generally lasts for 20 minutes or longer. *Increasing angina* occurs in a patient with a prior diagnosis of angina; episodes become "distinctly more frequent, longer in duration, or lower in threshold" (ie, severity increased by one or more Canadian Cardiovascular Society [CCS] classes to at least CCS class III; see Table 1). *New-onset, severe angina*, the third form of UA, is of CCS class III or greater.

## Non-ST-segment Elevation Myocardial Infarction

NSTEMI differs from UA primarily in severity and the two may be indistinguishable at presentation. NSTEMI involves ischemia severe enough to result in myocardial damage, although cardiac markers or enzymes may not be elevated until several hours after onset of chest pain. Of patients with NSTEMI, only one fourth will develop Q-wave MI; the remaining patients will go on to experience non-Q-wave MI.

## Initial Evaluation

The clinician evaluating a patient with chest pain must first address two critical questions:

- Are the symptoms caused by ACS?
- If the patient has ACS, what is the prognosis?

The answers to these questions will help guide important management issues, including where the patient is best managed- in the coronary care unit, a step-down unit, or a monitored bed; or through outpatient management. It will also determine what medications and/or invasive procedures may be indicated.

## Identifying ACS

Patients who call ahead for advice should be told that possible heart disease cannot be assessed by phone. Although a careful history can help the practitioner determine the likelihood that a patient has ACS due to CAD, this information must be supplemented by electrocardiography (ECG) and biochemical cardiac markers. All patients who present with pressure-type or heavy chest pain or tightness (which may radiate to the jaw, the neck, or either or both arms) must be assumed to have possible ACS. In addition, the patient who complains of "indigestion" or "heartburn"-as well as belching, cramping, epigastric pain or persistent shortness of breath, weakness, dizziness, lightheadedness, or loss of consciousness-should also be evaluated for ACS.

Associated dyspnea, diaphoresis, nausea, and/or vomiting should be taken as added evidence of possible ACS. Additional history should focus on prior or current CAD, exertional angina, MI, coronary artery bypass graft surgery, and any measures the patient has taken to relieve chest discomfort, including use of nitroglycerin. Risk factors such as family history, cocaine use, smoking, diabetes, hypertension, and hyperlipidemia should also be considered.

Elderly patients with ACS may present with isolated syncope, a change in mental status, weakness, or even a stroke without experiencing chest pain. Women are more likely than men to present with atypical symptoms. Similarly, the presentation may be atypical in diabetic patients because of impaired autonomic function.

The five most important features, listed in descending order of likelihood of ACS are the nature of the patient's chest pain, prior history of CAD, gender, age, and the number of risk factors (see Table 2).

The following symptoms are *not* characteristic of ischemic chest pain: pleuritic pain (sharp or knife-like pain induced by cough or taking a deep breath); mid or lower abdominal pain without associated chest or epigastric pain; pain that the patient can localize with one finger; pain that can be reproduced by palpation or movement of the chest wall or arms; continuous chest pain that lasts for many hours; fleeting chest pain lasting only for a few seconds; and pain that radiates into the legs.

Although historical information can "substantially raise the probability of CAD, features not characteristic of [ACS], such as sharp stabbing pain or reproduction of pain on palpation, *do not exclude* the possibility of ACS," according to the ACC/AHA report. In fact, authors of the Multicenter Chest Pain Study<sup>3</sup> found that among patients presenting to the emergency department with sharp or stabbing pain, 22% were found to have acute ischemia. Among patients with "pleuritic" chest pain, 13% had acute ischemia-as did 7% of patients whose pain was reproduced on palpation.

Acute ischemia is not always present in patients with symptoms of "possible" ACS. According to a study of 10,689 patients evaluated for suspected ACS, three fourths were found not to have acute ischemia.<sup>[4]</sup>

## Physical Examination

Vital signs should be documented, including blood pressure in both arms, heart rate, and temperature. The heart and lungs should be auscultated for an S3 gallop, the murmur of mitral regurgitation, and rales. Peripheral vessels should also be examined for bruits or pulse deficits. Pain in the back, unequal pulses, or a murmur of aortic regurgitation may suggest aortic dissection. Pericarditis may produce a friction rub, while pulsus paradoxus may indicate cardiac tamponade. Acute dyspnea, pleuritic chest pain, and differential breath sounds may indicate pneumothorax.

## Electrocardiogram

For all patients with suspected ACS, an ECG should be performed within 10 minutes of arrival. In fact, Eugene Braunwald, MD, lead author of the ACC/AHA report, told Clinician Reviews that patients should preferably have the ECG within five minutes of presentation-without delays for detailed history, sign-in, or even finding them a bed. The ECG should be repeated as necessary. It is especially important to obtain a recording during any recurrences of remitting chest pain. ECGs should be compared with prior recordings, if any are available. ST-segment changes, especially if they resolve with resolution of chest pain, strongly suggest acute ischemia.

In a departure from prior recommendations, the report advises that clinicians use ST-segment deviations of 0.05 mV to identify ischemic changes. Although clinical decisions may be based on ECG findings, an entirely normal ECG does not rule out ACS: 1% to 6% of patients with acute ischemia will not have ECG changes.

A patient with ST-segment elevation should be scrutinized closely for alternative diagnoses (eg, early repolarization, pericarditis, left ventricular aneurysm, Prinzmetal's angina, and Wolff-Parkinson-White syndrome). Patients with T-wave inversion, new bundle branch block, left ventricular hypertrophy, or paced rhythms are all at increased risk of acute ischemia and death.

## Cardiac Markers

Creatine kinase MB band (CK-MB) may not be elevated until six hours after infarction onset. Subforms CK-MB<sub>1</sub> and CK-MB<sub>2</sub> improve early sensitivity and may rise as quickly as three hours after infarction onset. A CK-MB<sub>2</sub>:CK-MB<sub>1</sub> ratio exceeding 1.5 or an absolute level of CK-MB<sub>2</sub> higher than 1 U/L indicates myocardial necrosis.

Troponin I and troponin T have equal sensitivity and specificity. Although elevated troponin values were previously thought simply to indicate a higher-risk category of UA, current histologic evidence shows that high levels indicate focal myocardial necrosis. Thus, patients with angina and no CK-MB but elevated troponin levels constitute a subgroup of NSTEMI patients with "microinfarction."<sup>[5]</sup> These patients may benefit from platelet glycoprotein (GP) IIb/IIIa inhibitors and low-molecular weight heparin. Troponin levels may not rise until six hours after symptom onset; if these levels are undetectable, they should be measured again at eight to 12 hours.

Myoglobin is a very early marker of myonecrosis and may be elevated as early as two hours after MI onset. Because it is released during muscle damage of any origin, however, it is very nonspecific. Nevertheless, a *negative* test result for myoglobin may be informative.

## Early Risk Assessment

Clinicians should assess the risk of death or recurrent MI by noting the following determinants: age over 65 years, elevation of cardiac markers on admission, lower body weight, CCS class III or IV chronic angina prior to admission, pulmonary rales, and depressed ST-segments on the admitting ECG.<sup>[6,7]</sup> High-risk patients, the new guidelines add, are also identified by pulmonary edema, angina with S3 gallop, new or worsening mitral regurgitation, and hypotension. In one study, patients who were prospectively stratified as low risk according to these factors had virtually no risk of death or MI within 30 days after presentation. The risk rose to 1.2% in intermediate-risk patients and to 1.7% in the high-risk group.<sup>[8]</sup>

Patients who meet criteria for high risk should be treated with aspirin, a  $\beta$ -blocker, antithrombin therapy, and a GP IIb/IIIa inhibitor, and evaluated for angiography and revascularization.

## Treatment Measures

Because the risk of death rises with treatment delays, providers must make certain clinical decisions immediately after obtaining the ECG: identifying the appropriate level of care and the safest mode of transport for the patient who presents to an outpatient office or emergency department and requires transfer.

If symptoms have been continuous for more than 20 minutes, UA/NSTEMI must be considered. The patient must be evaluated at a site where MI can be ruled out or treated. Patients who are hemodynamically unstable require ambulance transfer. If an ambulance may be delayed more than 20 to 30 minutes, transport by a driver in a personal vehicle may be an acceptable alternative.

### **Immediate Actions**

Dr. Braunwald emphasized the importance of starting an intravenous (IV) line and administering aspirin in all patients with no history of aspirin sensitivity. Recommendations for oxygen administration have also changed with this new report; only patients with documented hypoxemia or questionable respiratory status should receive it. "A lot of oxygen is wasted," explained Dr. Braunwald, who also chairs the ACC/AHA Committee on Management of Patients with Unstable Angina. "Check their pulse oxygenation. If it's under 90%, give oxygen."

Several agents may be recommended to treat ischemia. *Nitroglycerin*, through its peripheral and coronary artery dilating effects, reduces preload and myocardial oxygen consumption. However, this benefit may be offset in part by reflex heart rate increases unless a  $\beta$ -blocker is prescribed. Patients who fail to improve with three 0.4-mg nitroglycerin tablets (taken sublingually at five-minute intervals) and IV  $\beta$ -blocker medication, should be started on continuous-infusion IV nitroglycerin at 10  $\mu$ g/min, with 10- $\mu$ g increases every three to five minutes until the patient responds. Upon partial response, dosage increments should be reduced or the interval between increments lengthened. Caution is required when the systolic value drops below 110 mm Hg in a previously normotensive patient.

*Morphine* is recommended only for patients who fail to respond to nitroglycerin; morphine's anxiolytic and potent analgesic effects can be useful, but patients may experience hypotension or respiratory depression. Symptomatic hypotension can often be resolved by placing the patient in Trendelenburg's position or (in the event of bradycardia) by giving saline boluses with atropine; respiratory depression can be reversed with naloxone.

$\beta$ -Blockers reduce myocardial oxygen consumption through their negative chronotropic and negative inotropic effects. All  $\beta$ -blockers, except those with intrinsic sympathomimetic effects, are considered equally effective. Patients with ongoing chest pain and no contraindications should receive the initial dose by IV, followed by oral therapy. Contraindications to  $\beta$ -blockade include atrioventricular block (unless the patient has a functioning pacemaker), asthma, and severe left ventricular dysfunction with congestive heart failure.  $\beta$ -Blocker therapy may reduce progression from ACS to MI by approximately 13%.<sup>[9]</sup>

Oral, long-acting *calcium antagonists* may be appropriate for recurrent ischemia. These agents vary in structure and mechanism of action; but generally, they inhibit myocardial and vascular smooth muscle contraction, and they share coronary dilatory properties. In theory, they could benefit left ventricular relaxation and arterial compliance. Major adverse effects include hypotension, worsening congestive heart failure, bradycardia, and atrioventricular block.

For platelet inhibition, *aspirin* is the first choice and should be given as soon as possible (first dose, 162 to 325 mg). Patients who are not already taking aspirin may chew the tablet to achieve high blood levels quickly. Those who cannot take aspirin may be given clopidogrel or ticlopidine.

Antiplatelet therapy should be followed by anticoagulation therapy with *unfractionated IV heparin* or subcutaneous *low-molecular weight heparin*.

*Platelet GP IIb/IIIa inhibitors* are then administered to patients with high-risk features or continuing ischemia, and to patients awaiting invasive treatment such as angioplasty.

### Subsequent Management

After further risk stratification, patients with UA/NSTEMI are generally managed according to one of two different strategies.

In the *early conservative strategy*, only patients with recurrent ischemia or a strongly positive stress test (despite "vigorous medical therapy") undergo coronary angiography. Otherwise, the guidelines authors point out, treatment with low-molecular weight heparin and GP IIb/IIIa inhibitors can help prevent adverse outcomes in patients managed with this strategy-as opposed to costly invasive procedures.

Candidates for the *early invasive strategy* (patients without obvious clinical contraindications to coronary revascularization) routinely undergo early angiography, an invasive means of risk stratification. Coronary revascularization can improve prognosis, relieve symptoms, prevent ischemic complications, and improve function. Patient anatomy, life expectancy, ventricular function, and comorbidities are all considered in the decision to perform revascularization.

Thanks to high rates of immediate success and low complication rates, percutaneous coronary intervention-increasingly enhanced by stenting and treatment with GP IIb/IIIa inhibitors-has become more commonly used to treat UA/NSTEMI. Coronary artery bypass grafting may be appropriate for high-risk patients with left ventricular systolic dysfunction, diabetes, or certain forms of two- or three-vessel disease. In lower-risk patients, the choice between continued medical management and a revascularization procedure depends on patients' preferences and quality of life rather than "strict clinical outcomes."

**Acknowledgement:** This article is based on Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guidelines 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). J Am Coll Cardiol. 2000;36: 970-1062. Most of the remaining references were cited in the guidelines.

### Table 1. Grading of Angina Pectoris by CCS Classification

Class	Description
I	Ordinary physical activity (eg, walking or climbing stairs under normal conditions) does not cause angina
II	Slight limitations following ordinary physical activity
III	Marked limitations following ordinary physical activity
IV	Inability to carry on any physical activity without discomfort, or presence of angina symptoms at rest

CCS, Canadian Cardiovascular Society.

Adapted from Table 4, Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guidelines 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). J Am Coll Cardiol. 2000;36:976.

**Table 2. Likelihood of Presence of CAD-Related ACS**

<b>Feature</b>	<b>High likelihood</b> Any of the following:	<b>Intermediate likelihood</b> Absence of high-likelihood features and presence of any of the following:	<b>Low likelihood</b> Absence of high- or intermediate-likelihood features, but may have:
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina; known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom; age >70 years; male sex; diabetes mellitus	Probable ischemic symptoms in absence of any 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 or T-wave inversion with symptoms	Fixed Q waves; abnormal ST segments or T waves not documented as new	T-wave flattening or inversion in leads with dominant R waves, or normal ECG
Cardiac markers	Elevated troponin I, troponin T, or CK-MB	Normal	Normal

CAD, coronary artery disease; ACS, acute coronary syndrome; MI, myocardial infarction; MR, mitral regurgitation; ECG, electrocardiography; CK-MB, MB isoenzyme of creatine phosphokinase.

Reprinted from Table 5, Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guidelines 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). *J Am Coll Cardiol.* 2000;36:978.

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