

CME CREDIT **EDUCATIONAL OBJECTIVES:** Readers will understand the new definition of acute myocardial infarction (MI) and how to make the diagnosis of acute MI

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A new, precise definition of acute myocardial infarction

ABSTRACT

Several international cardiovascular societies have revised their diagnostic criteria for acute myocardial infarction (MI) (*J Am Coll Cardiol* 2007; 50:2173–2188). The cornerstone of diagnosis remains a high level of clinical suspicion, serial electrocardiograms, and troponin levels. This article reviews the new definition and the appropriate clinical tools necessary to diagnose acute MI accurately.

KEY POINTS

The clinical presentation of acute MI varies considerably from patient to patient. Therefore, one must consider the symptoms, serial electrocardiographic findings, and serial biomarker results in concert.

Troponin I or T is now the preferred biomarker of myocardial necrosis. Still, troponin can be elevated in many conditions other than ischemic heart disease.

Electrocardiographic signs of acute ischemia have been precisely defined, but electrocardiography can give false-positive or false-negative results in a number of conditions.

MI is now categorized into five types depending on cause.

ACUTE MYOCARDIAL INFARCTION (MI) portends important and substantial consequences. Angioplasty or fibrinolytic therapy to open the blocked coronary artery is proven to improve the patient's chances of surviving without consequent morbidity or death. But the diagnosis is not always straightforward. The presentation of acute MI can vary widely, and a number of other conditions—many of them equally serious emergencies—can mimic its symptoms, electrocardiographic signs, and biomarker patterns.

In an attempt to improve the accuracy of the diagnosis of MI, a multinational task force met in 1999 under the auspices of the European Society of Cardiology and the American College of Cardiology. The goal was to develop a simple, clinically oriented definition of MI that could be widely adopted. A document was created and published simultaneously in 2000 in the *European Heart Journal* and the *Journal of the American College of Cardiology*.¹ These organizations updated their paper in 2007 with a new definition of acute MI to account for advances in diagnosis and management.²

In this article we will review the new definition and how to make the diagnosis of acute MI today. Specifically, the updated definition includes:

- Subtypes of acute MI
- Imaging tests supporting the diagnosis
- Biomarker thresholds after percutaneous coronary intervention or bypass grafting.

TROPONIN: BETTER THAN CK, BUT NOT PERFECT

The original 2000 paper¹ and the 2007 update² featured the use of the cardiac bio-

TABLE 1

Conditions other than MI that can elevate troponin

- Acute neurologic disease, including stroke or subarachnoid hemorrhage
- Aortic dissection
- Aortic valve disease
- Apical ballooning syndrome
- Burns, especially if affecting > 30% of body surface area
- Cardiac contusion or other trauma including surgery, ablation, cardioversion, defibrillation
- Congestive heart failure—acute and chronic
- Critical illness, especially with respiratory failure or sepsis
- Drug toxicity or toxins
- Extreme exertion
- Hypertrophic cardiomyopathy
- Infiltrative diseases, eg, amyloidosis, hemochromatosis, sarcoidosis, and scleroderma
- Inflammatory diseases, eg, myocarditis or myocardial extension of endocarditis or pericarditis
- Pulmonary embolism, severe pulmonary hypertension
- Renal failure
- Rhabdomyolysis with cardiac injury
- Tachyarrhythmias, bradyarrhythmias, or heart block

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marker troponin, which is considerably more sensitive and specific for heart damage than total creatine kinase (CK) or its isoform, CK-MB.

The new, more-sensitive biomarker-based definition of MI resulted in more cases of MI being diagnosed, and this has attracted the attention and scrutiny of many, especially population scientists and interventional cardiologists.³ This change has caused some controversy, especially when dealing with small rises in troponin following percutaneous coronary intervention.

In addition, some confusion over terminology remains. For example, the phrase

“troponin leak” is often used to describe cases in which serum troponin levels rise but there is no MI. However, most experts believe that a rise and fall in troponin is due to true myocardial cell death. Troponin I and T are such large molecules that they cannot “leak” from a cardiac cell unless there has been irreparable cellular damage—that is, cell death.

On the other hand, troponin is often elevated in plasma in conditions other than overt ischemic heart disease (TABLE 1).^{4,5} In most cases, the mechanism of the increased plasma troponin level is not clearly understood, but clinical evidence of acute MI is otherwise lacking.

Creatine kinase still has a role

In some cases, CK and CK-MB may be helpful in determining the acuity of myocardial necrosis, but their use will vary by institution. These biomarkers typically rise 2 to 4 hours after the initial event and fall within 24 to 48 hours, whereas troponin levels stay elevated for days or weeks. Thus, the presence of troponin without CK and CK-MB in the right clinical context may indicate a past MI that is no longer acute.

■ INFARCTION: CELL DEATH DUE TO ISCHEMIA

MI is myocardial cell death due to prolonged ischemia. Under the microscope, it can be categorized as coagulation necrosis in which ghost-like cell structures remain after hypoxic insult (typical of most MIs) or contraction band necrosis with amorphous cells that cannot contract anymore, the latter often a hallmark of excessive catecholamine damage or reperfusion injury. Apoptosis occurs in the heart but is technically not considered necrosis and is thought not to be associated with elevated troponin levels.^{6,7}

In experiments in animals, cell death can occur as little as 20 minutes after coronary artery occlusion, although completion of infarction is thought to take 2 to 4 hours. The time to infarct completion may be longer in patients with collateral circulation or when the culprit coronary artery has intermittent (“stuttering”) occlusion. Preconditioning of

Acute pericarditis

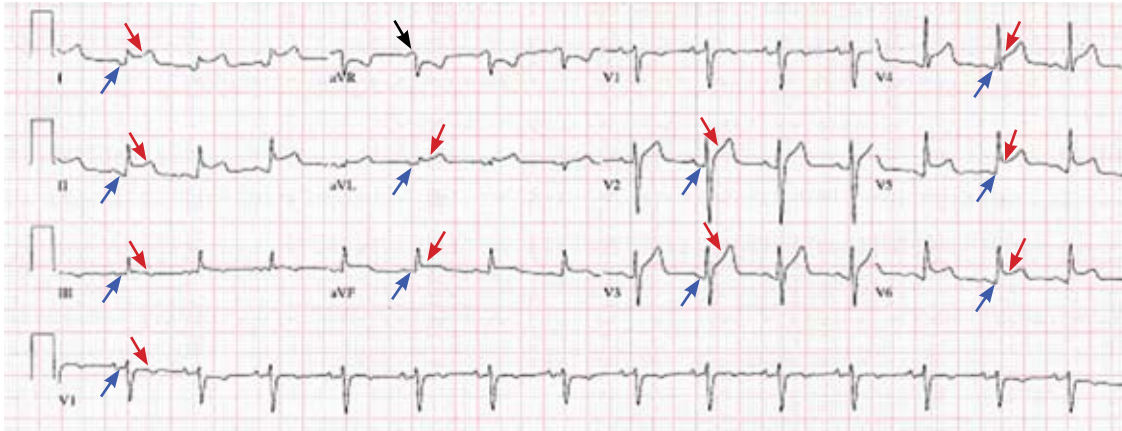


FIGURE 1. Acute pericarditis with elevation of the ST segment in all leads, often up-sloping (red arrows), and PR depression in all leads (blue arrows), except for PR elevation in aVR (black arrow).

myocardial cells with intermittent ischemia can also influence the timing of myocardial necrosis by protecting against cell death to some extent. Alteration in myocardial demand can influence the time required for completion of infarction either favorably or unfavorably; hence, reducing myocardial demand is beneficial in acute MI.

Three pathologic phases of MI

MI can be categorized pathologically as acute, healing, or healed.

Acute MI. In the first 6 hours after coronary artery occlusion, coagulation necrosis can be seen with no cellular infiltration. After 6 hours, polymorphonuclear leukocytes infiltrate the infarcted area, and this may continue for up to 7 days if coronary perfusion does not increase or myocardial demand does not decrease.

Healing MI is characterized by mononuclear cells and fibroblasts and the absence of polymorphonuclear leukocytes. The entire healing process takes 5 to 6 weeks and can be altered by coronary reperfusion.

Healed MI refers to scar tissue without cellular infiltration.

CLINICAL FEATURES VARY WIDELY

Sir William Osler said, “Variability is the law of life, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike and behave alike under the abnormal

conditions which we know as disease.”⁸

Just so, patients with acute MI display a wide variety of presentations, from no symptoms (about 25%) to severe, crushing chest pain. Discomfort may occur in the upper back, neck, jaw, teeth, arms, wrist, and epigastrium. Shortness of breath, diaphoresis, nausea, vomiting, and even syncope may occur. Unlike in acute aortic dissection, the discomfort is not usually maximal at its onset: it builds up in a crescendo manner. It is not usually changed by position, but can lessen in intensity upon standing. The discomfort in the chest is deep and visceral, and typically not well localized. A pressure sensation, air hunger, or “gas build-up” can be described. The only symptom may be shortness of breath or severe diaphoresis. The symptoms can last from minutes to hours and can be relieved by sublingual nitroglycerin. Atypical or less-prominent symptoms may make the diagnosis more difficult in the elderly, patients with diabetes mellitus, and women.

The physical examination during acute MI usually finds no clear-cut distinguishing features. The patient may appear pale and diaphoretic, and the skin cool to the touch. Heart sounds are generally soft. A fourth heart sound may be audible. Blood pressure may be low, but it can vary widely. Tachycardia, particularly sinus tachycardia, and pulmonary edema are poor prognostic signs.

In view of the wide variation in presentations, the history and physical findings

Variability is the law of life —Osler

TABLE 2

Electrocardiographic manifestations of acute myocardial ischemia*

ST elevation

New ST elevation at the J point in two contiguous leads

≥ 0.2 mV in leads V₂-V₃ (men)

≥ 0.15 mV in leads V₂-V₃ (women)

≥ 0.1 mV in other leads

ST depression and T-wave changes

New horizontal or down-sloping ST depression

≥ 0.05 mV in two contiguous leads; and/or

T inversion ≥ 0.1 mV in two contiguous leads with prominent R wave or R/S ratio > 1

*In absence of left ventricular hypertrophy and left bundle branch block

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TABLE 3

Common pitfalls in diagnosing MI by electrocardiography

False-positive findings

Benign early repolarization

Brugada syndrome

Cholecystitis

Failure to recognize normal limits for J-point displacement

Lead transposition or use of modified Mason-Likar configuration

Left bundle branch block

Metabolic disturbances such as hyperkalemia

Pericarditis or myocarditis

Pre-excitation

Pulmonary embolism

Subarachnoid hemorrhage

False-negative findings

Left bundle branch block

Left ventricular hypertrophy

Paced rhythm

Prior myocardial infarction with Q waves, persistent ST elevation, or both

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MI symptoms may be less prominent in elderly, female, or diabetic patients

can raise the suspicion of acute MI, but sequential electrocardiograms and measurements of biomarkers (troponin) are always necessary.

ELECTROCARDIOGRAPHY: NECESSARY BUT NOT SUFFICIENT

Electrocardiography is a key part of the diagnostic evaluation of suspected acute MI. As in the 2000 paper, the 2007 update reiterates the same classic changes that may be seen on an electrocardiogram. It should be ordered and reviewed promptly as soon as the diagnosis is suspected, and repeated frequently if the initial tracing is normal.

Although electrocardiography is necessary, it cannot distinguish myocardial ischemia from MI. In addition, electrocardiography alone cannot reliably be used to diagnose acute MI, as many conditions result in deviation of ST segments and may be misinterpreted as acute MI. Common examples include acute pericarditis (FIGURE 1), early repolarization, hyperkalemia, left ventricular hypertrophy, and bundle branch block.⁹

ST-elevation MI vs non-ST-elevation MI

Cases of acute myocardial ischemia and acute MI are traditionally divided by electrocardiography (TABLE 2) into those in which the ST segment is elevated (FIGURE 2) and those in which it is not (FIGURE 3). This dichotomy is useful clinically, as patients with ST-elevation MI are usually taken directly to the catheterization laboratory or given fibrinolytic therapy if they have no contraindications to it, whereas those with non-ST-elevation MI are brought to the catheterization laboratory less urgently, depending on various associated risk scores.

Changes in the ST segment can be very dynamic, making sequential tracings very useful. Rhythm disturbances and heart block are also more likely to be recorded when using sequential readings.

Pitfalls to electrocardiographic diagnosis

The electrocardiographic diagnosis of acute MI can be very straightforward or quite subtle,

Anterolateral ST-elevation MI

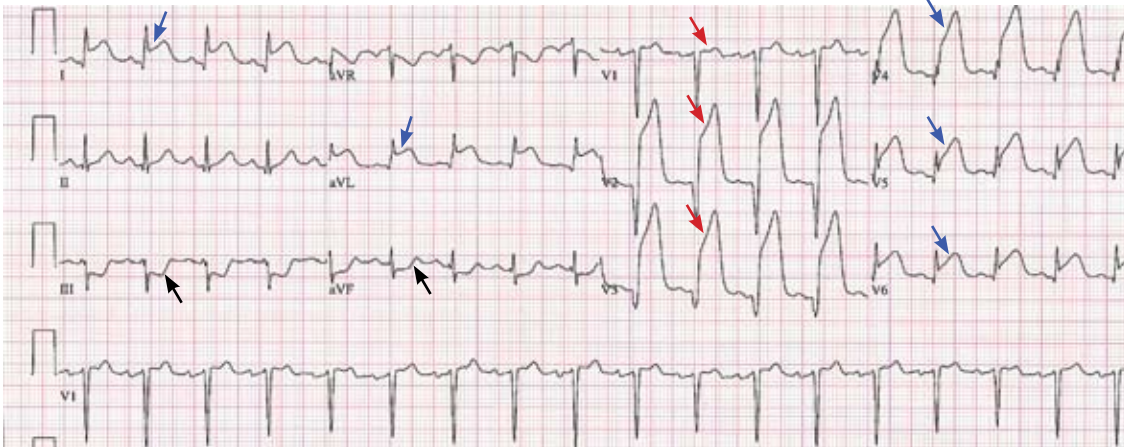


FIGURE 2. Anterolateral ST-elevation MI with ST elevation in V₁ through V₃ indicating infarction of the anteroseptal myocardium (red arrows), and in V₄ through V₆ and I and aVL indicating lateral wall involvement (blue arrows). Note the reciprocal ST depression in inferior leads, ie, III and aVF (black arrows).

Possible non-ST-elevation MI

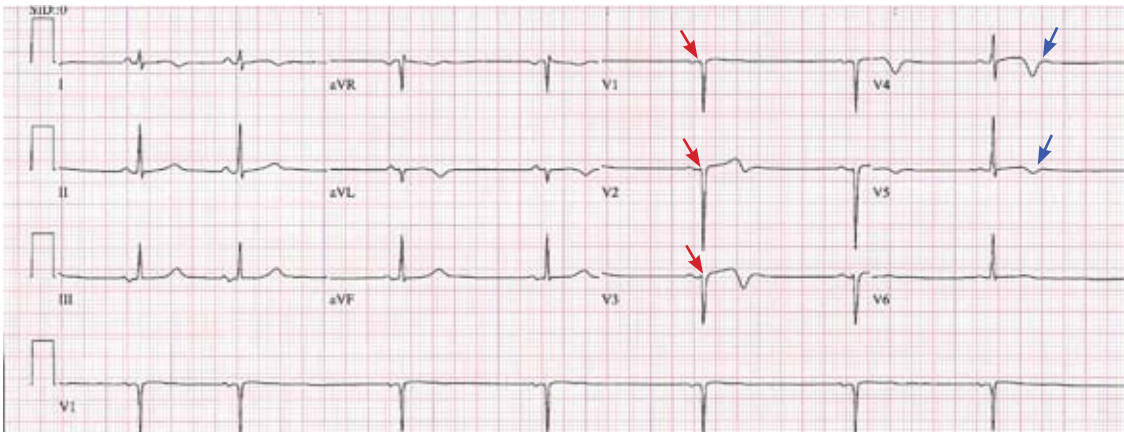


FIGURE 3A. Poor R wave progression (red arrows) with terminally symmetric T waves in leads V₁ through V₆ (blue arrows), which suggests possible myocardial injury; this patient had positive troponin consistent with non-ST-elevation MI.

ST changes can be very dynamic, making sequential tracings very useful

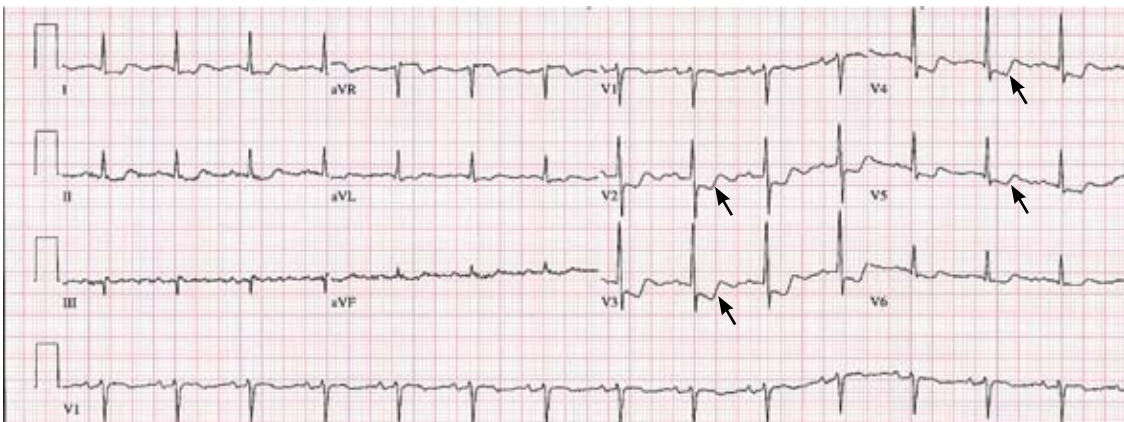


FIGURE 3B. ST depression across the precordium (V₁–V₆) suggestive of subendocardial injury (black arrows). An electrocardiogram 12 minutes later showed normalization of these changes; however, cardiac troponin was positive and consistent with non-ST-elevation MI.

Inferoposterior ST-elevation MI

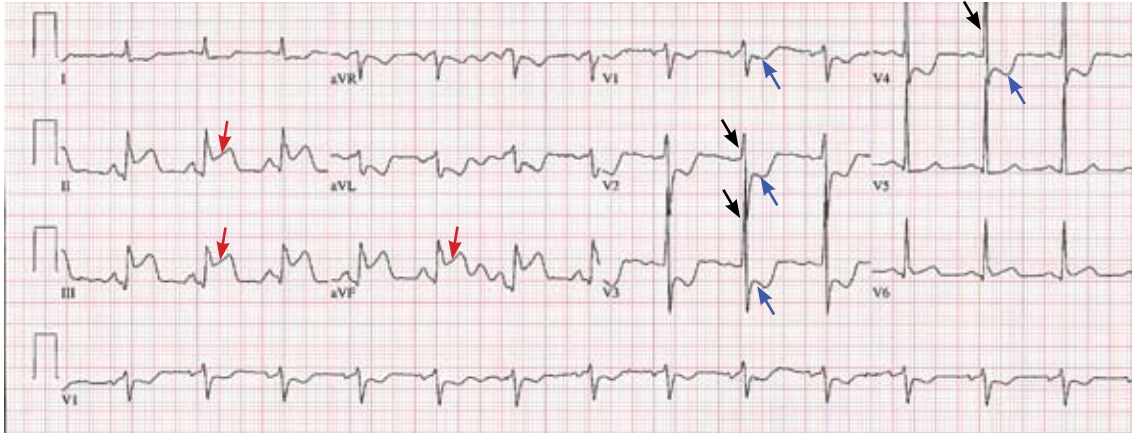


FIGURE 4. Inferoposterior ST-elevation MI with ST elevation in II, III, and aVF (red arrows) indicating injury in the inferior wall in addition to possible involvement of the posterior wall, as suggested by tall R waves (black arrows) with ST depression and T wave inversions (blue arrows) in V₁ and V₂.

Inferolateral ST-elevation MI

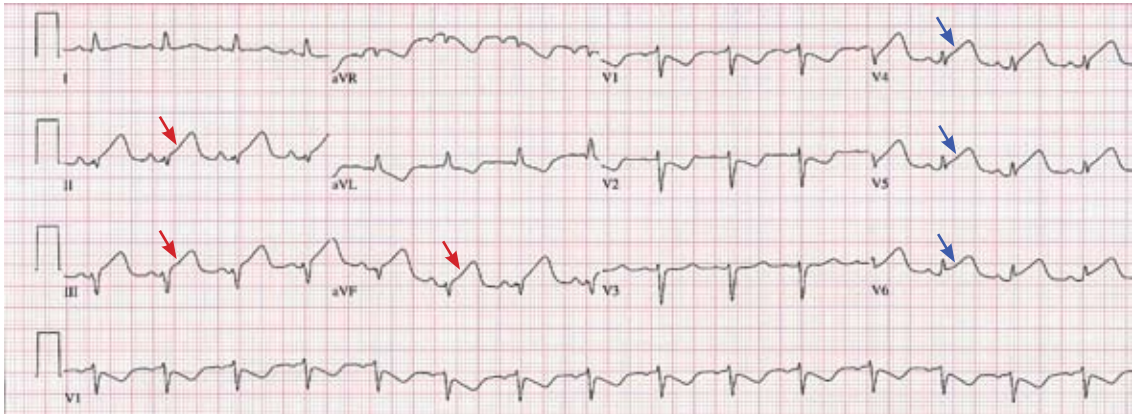


FIGURE 5. Inferolateral ST-elevation MI with ST elevation in II, III, and aVF (red arrows) indicating injury in the inferior wall in addition to ST elevation in V₄ through V₆ (blue arrows).

Posterior MI is frequently missed due to absence of ST elevation

and many pitfalls can confound the correct diagnosis (TABLE 3). When the diagnosis is in doubt, frequent sequential readings are very useful.

Prior MI. Q waves or QS complexes, when the Q wave is sufficiently wide (≥ 0.03 msec) or deep (≥ 1 mV), usually indicate a previous MI. However, many nuances that further raise or lower the suspicion for previous MI need to be considered. These are beyond the scope of this brief review but are available in the 2007 update.

Posterior MI (or inferobasal MI) is more difficult to identify than anterior MI and is frequently missed on electrocardiography due to the absence of ST elevation

on 12-lead readings. Changes on electrocardiography that raise the suspicion of posterior MI are prominent R waves in V₂ with accompanying ST-T depression. Patients with posterior MI are less likely to be taken directly to the catheterization laboratory unless ST elevations are seen due to concomitant infarction involving the inferior (FIGURE 4) or lateral (FIGURE 5) wall, or unless there is high suspicion for myocardial injury based on cardiac enzymes and information from the history and physical examination.

Right ventricular infarction often requires the use of right-sided leads, which may reveal ST elevation in V_{4R}.

**ECHOCARDIOGRAPHY
IF THE DIAGNOSIS IS IN DOUBT**

In many cases, acute MI is suspected on clinical grounds but electrocardiography does not verify an acute process. Troponin levels may not have had time to rise very much, if at all, or the results may not yet be known. Decisions to go to the catheterization laboratory or to do a computed tomographic scan of the chest to exclude aortic dissection must be made quickly.

Echocardiography is an excellent way to assess wall-motion abnormalities. In the absence of any wall-motion abnormality, a large ST-elevation MI is unlikely. A large wall-motion abnormality would verify the probability of ongoing acute MI and thus would help with rapid decision-making.

Furthermore, echocardiography can help determine the likelihood that the patient has aortic dissection or pulmonary embolism, either of which can mimic acute MI but requires very different treatment.

CLINICAL CLASSIFICATION OF ACUTE MI

The new classification scheme of the different types of MI is shown in **TABLE 4**.

The new classification scheme does not include myocardial necrosis from mechanical manipulation of the heart during open heart surgery, from cardioversion, or from toxic drugs.

As clinicians are aware, it is not unusual to see elevated biomarker levels in a host of conditions unrelated to acute myocardial ischemia or MI. The new classification of acute MI is most helpful in this regard. It will likely be even more helpful in guiding treatment and management when new ultrasensitive troponin assays are widely introduced into clinical practice.

The new classification also negotiates the controversy regarding elevated biomarker levels following percutaneous coronary intervention. In brief, elevation of biomarkers is not entirely avoidable even with a successful percutaneous coronary intervention, and furthermore, there is no scientific cutoff for biomarker elevations. So, by arbitrary convention, the troponin

TABLE 4

Clinical classification of MI

Type 1

Spontaneous myocardial infarction (MI) related to ischemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection

Type 2

MI secondary to ischemia due to either increased oxygen demand or decreased supply, eg, coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension, or hypotension

Type 3

Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, accompanied by presumably new ST elevation, new left bundle branch block, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained or at a time before the appearance of cardiac biomarkers in the blood

Type 4a

MI associated with percutaneous coronary intervention

Type 4b

MI associated with stent thrombosis as documented by angiography or at autopsy

Type 5

MI associated with coronary artery bypass grafting

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level must rise to more than three times the 99th percentile upper reference limit to make the diagnosis of type 4a MI. A separate type 4b MI is ascribed to angiographic or autopsy-proven stent thrombosis.

The new guidelines also suggest that troponin values be more than five times the 99th percentile of the normal reference range during the first 72 hours following coronary artery bypass graft surgery (CABG) when considering a CABG-related MI (type 5). Whenever new pathologic Q waves appear in territories other than those identified before the procedure, MI should be considered, especially if associated with elevated biomarkers, new wall-motion abnormalities, or hemodynamic instability.

Thus, the diagnosis of acute MI now has

widely accepted global criteria that distinguish various types of acute MI that occur under multiple circumstances. It is expected that describing the type of acute MI according to the new criteria will further enhance our understanding of the event, its proper management, and its prognosis. ■

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