Diagnosis of Myocardial Infarction:
Implications For Your Practice

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The criteria for diagnosis of MI have changed with the widespread use of troponin assays. Troponin is a very sensitive biomarker for myocardial necrosis. Not all patients with elevated troponin have MI. Troponin elevation must occur in the settings of myocardial ischemia for this diagnosis to be made.

Cardiac biomarkers

The diagnosis of MI is contingent upon biochemical evidence of myocardial necrosis. Biomarkers used in the past included aspartate transaminase, lactate dehydrogenase and creatine kinase (CK). The World Health Organization's diagnosis of MI from the early 1980s required presence of ischemic chest pain, ECG changes and elevation of the myocardial isoenzyme of CK. Subsequently, readly available assays for troponin were developed.

Troponin is a regulatory protein that controls calcium-mediated actin-myosin interaction. The troponin complex consists of three subunits:

- troponin T, which binds to tropomyosin and facilitates contraction,
- troponin I, which binds to actin and inhibits actin-myosin interactions and
- troponin C, which binds to calcium ions.

The amino acid sequences of the skeletal and cardiac isoforms of cardiac troponin T and troponin I are sufficiently dissimilar and therefore detectable by monoclonal antibody-based assays. Troponin C is not used clinically because both cardiac and smooth muscle share troponin C. Troponin starts to rise within four to six hours of onset of myocardial necrosis because of rapid leak of the cytosolic pool (3% of troponin I) and this is subsequently followed by slow release and degradation of the bound troponin. The half-life of troponin is two hours. Troponin level peaks at 18 to 24 hours and declines over 10 to 14 days. Troponin I and T are very sensitive and specific biomarkers for myocardial necrosis (even if very minor). Any elevation of troponin which is > 99% above the upper reference range for that particular type of assay with a coefficient of variation of < 10% means that there has been some

Patient cases

Edna
An 84-year-old woman presents to the ED with shortness of breath. She is in atrial fibrillation with a ventricular rate of 130 bpm. She has 1 mm ST depression on the ECG during atrial fibrillation. Once she converts to sinus rhythm, there is only T wave flattening. Troponin I is elevated at 1.2 ug/L (normal < 0.15 ug/L).

John
A 74-year-old man presents with a left hemiparesis. He does not have any chest discomfort. ECG shows sinus rhythm with left axis deviation. Troponin is elevated at 2.0 ug/L.

Joan
A 56-year-old woman who is on hormone replacement therapy presents with shortness of breath and elevated jugular venous pressure. ECG shows T wave inversions in leads V1-3. Pulmonary embolism is confirmed on a CT angiogram. Troponin is elevated at 4.0 ug/L.

Do these patients have a MI?

For the correct answer, see page 21.

Table 1
New definition of MI

Two criteria must be fulfilled:
1. Rise and fall of cardiac biomarker, preferably troponin
2. Evidence of myocardial ischemia consisting of chest pain, ECG changes (ST elevation, at least 0.5 mm ST depression, 1 mm T wave inversion, new Q waves), or new wall motion abnormality

myocardial necrosis. However, this by itself does not make the diagnosis of MI.

New definition of MI

With widespread use of troponin assays in the ED and in acutely ill patients, it soon became apparent that although troponin is very sensitive at picking up any degree of myocardial necrosis, troponin elevation is not specific for acute coronary syndrome (ACS) (*i.e.*, thrombotic occlusion or subtotal occlusion of a coronary artery). A new definition of MI was developed by the joint European Society of Cardiology, World Heart Federation and the American College of Cardiology/American Heart Association (Table 1).[1]

The diagnosis of MI is contingent upon biochemical evidence of myocardial necrosis.

Troponin level has to rise above the upper normal range and in addition there has to be clinical evidence of myocardial ischemia consisting of chest pain and/or specific ECG changes and/or a new wall motion abnormality on an imaging test

Table 2
Types of MI

Type 1: MI due to primary coronary event such as plaque rupture
Type 2: MI due to increased myocardial oxygen demand or decreased supply: anemia, hypertension, coronary embolism, coronary spasm, arrhythmias
Type 3: Sudden unexpected cardiac death with evidence of infarction or autopsy/coronary angiography evidence of coronary thrombosis
Type 4: Related to percutaneous coronary intervention (PCI) (troponin 3 times the upper reference limit (URL))
- 4a: MI with PCI
- 4b: Stent thrombosis on angiography or autopsy

Type 5: Related to coronary artery bypass surgery (troponin 5 time the URL).
New Q waves or left bundle branch block or new graft/coronary occlusion or new wall motion abnormality

(radionuclide angiogram, contrast left ventriculogram, ECHO, or cardiac MRI). Specific types of MI (Table 2) are categorized by pathophysiology (type 1: coronary thrombosis; type 2: supply-demand mismatch) or specific settings (type 3: cardiac arrest; type 4: following percutaneous coronary intervention; type 5: following cardiac surgery). A common universal definition of MI is important for correct classification of patients in clinical trials, development of appropriate therapeutic strategies, insurance policies, advice on travel and driving restrictions, accurate population statistics and health policy decision-making.

Other causes of troponin elevation

There are many causes of myocardial necrosis and troponin elevation which are unrelated to coronary artery disease (CAD). Table 3 outlines the most common causes. Myocardial necrosis can occur in

Table 3

Causes of elevated troponin not related to acute coronary syndrome

Left or right ventricular strain:
- Heart failure
- Pulmonary embolism
- Arrhythmias
- Strenuous exercise

Myocardial injury not related to Coronary Artery Disease:
- Cardioversions/defibrillations/chest compressions
- Myocarditis, myopericarditis
- Myocardial contusion
- Drugs/toxins (chemotherapy)
- Myocardial infiltrative disorders

Sepsis or systemic inflammatory response syndrome:
- Pneumonia and other infections
- Shock/hypovolemia
- Burns

Central nervous system injury/high catecholamines:
- Takotsubo cardiomyopathy (stress related cardiomyopathy, apical ballooning)
- Subarachnoid hemorrhage
- Stroke

Renal failure

any condition associated with increased ventricular filling pressures, myocardial inflammation, direct cardiac injury or injury related to high catecholamine states. Some of these conditions are associated with ECG changes as well, but the diagnosis of MI is not made if there is no evidence of myocardial ischemia and there is an alternative explanation for the troponin elevation.

Implications of troponin elevation

Because troponin is such a sensitive biomarker for myocardial necrosis, the incidence of MI has increased from 50% to 200%.[2] Is this increased rate of MI clinically significant or is this just a benign "troponin leak?" Evidence suggests the former. Troponin elevation indicates a worse short-term and long-term prognosis both in patients with ACS and in those patients who do not have a MI. It is a marker of a sicker patient. The higher the troponin level, the greater the risk of dying.[2,3]

Management of patients with elevated troponin

Correct diagnosis of MI is essential. If the patient has troponin elevation but does not have a MI, treatment should be directed towards the main problem (*i.e.*, sepsis, stroke, arrhythmia, *etc.*). There is no indication for routine use of heparin, ASA or clopidogrel in patients with troponin elevation who do not have ACS. It is probably reasonable to monitor the rhythm of patients with non-ACS significant troponin elevation (*e.g.*, > 3.0 ug/L) for 24 hours.

If the patient has a type 1 MI, percutaneous coronary intervention or thrombolysis, as well as antithrombotic and antiplatelet therapy are indicated for ST elevation MI and ASA, clopidogrel, heparin and a β-blocker should be administered for non-ST elevation MI.

If the patient has a type 2 MI (supply-demand problem), they are likely to have underlying CAD. The underlying problem should be corrected (tachyarrhythmia, anemia, hypoxemia) and if the

More on patient cases

None of the patients presented have MI despite troponin elevation.

- **Edna** has atrial fibrillation with non-specific ST changes. She should be anticoagulated for prevention of stroke and started on rate controlling medication such as diltiazem or β-blocker
- **John** has a stroke and should not receive heparin
- **Joan** has right ventricular strain from pulmonary embolism and should be anticoagulated

None of these patients have primary coronary artery thrombosis (*i.e.*, type 1 MI).

patient does not have significant life-limiting comorbidities, risk stratification with a sestamibi scan or stress ECHO may be appropriate. β-blocker and secondary prevention strategies for vascular protection including ASA and statin may be indicated.

When the ECG changes are non-specific and it is unclear whether the patient with troponin elevation is having a MI, an ECHO may be helpful to assess for the presence of a new wall motion abnormality corresponding to a specific coronary arterial distribution.

Summary

The new definition of MI requires troponin elevation in the setting of myocardial ischemia as demonstrated by ischemic chest pain or ECG changes. Troponin is a biomarker that is highly sensitive and specific for myocardial necrosis but troponin elevation can occur in the absence of myocardial ischemia and an ACS. Troponin elevation is associated with a worse outcome but this is not necessarily due to a cardiac event (*i.e.*, ventricular fibrillation, heart failure). It is important to correctly identify the cause of troponin elevation, to avoid expensive and potentially harmful cardiac investigations in the absence of MI and to manage the underlying problem appropriately.

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Take-home message

- The diagnosis of MI requires troponin elevation in the setting of myocardial ischemia as manifested by chest pain, ECG changes or a new wall motion abnormality on an imaging test
- Troponin elevation indicates myocardial necrosis. This may be secondary to MI or several non-thrombotic cardiac and systemic diseases (most commonly acute pulmonary embolism, pericarditis, acute or severe heart failure, myocarditis, sepsis and/or shock)
- The degree of troponin elevation is inversely related to the prognosis: the higher the troponin elevation, the worse the prognosis
- Management of the patient with an elevated troponin will depend on the underlying cause. If the troponin elevation is not secondary to MI, there is no indication for acute antithrombotic therapy (heparin) or antiplatelet therapy

References

1. Thygesen K, Alpert JS, White HD, et al: Universal Definition Of Myocardial Infarction. J Am Coll Cardiol 2007; 50(22):2173-95.
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3. Blich M, Sebbag A, Attias J, et al: Cardiac Troponin I Elevation In Hospitalized Patients Without Acute Coronary Syndromes. Am J Cardiol 2008; 101(10):1384-8.