FAST FACTS: The use of cardiac biomarkers in acute coronary syndrome (ACS) version 2

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CARDIAC BIOMARKERS

Cardiac biomarkers are endogenous substances released into the bloodstream indicating cardiac damage or myocardial stress including ischaemia and infarction. Cardiac biomarkers are used for diagnosis, risk stratification and management of patients with chest pain or signs of acute coronary syndrome (ACS).

Sudden or acute chest pain may present as angina which is due to partial or complete occlusion of a coronary artery, resulting in damage ranging from myocardial ischaemia to myocardial infarction (MI).

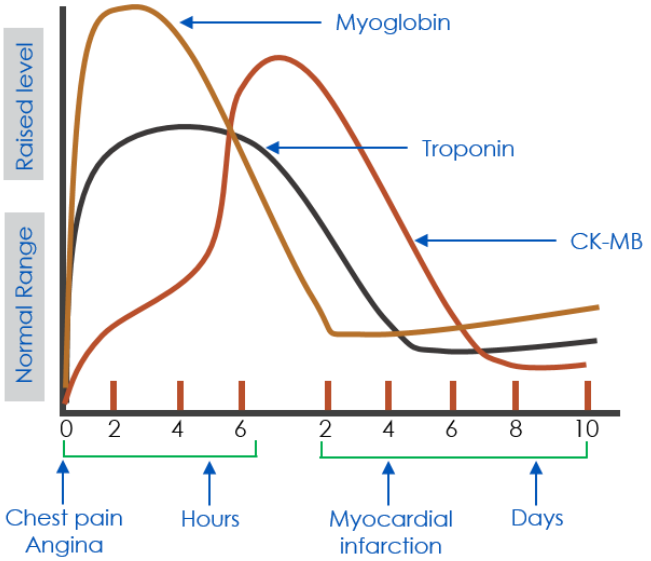
Acute coronary syndrome (ACS) includes:

- Unstable angina (UA)
- Non-ST elevation MI (NSTEMI)
- ST elevation MI (STEMI)

Early diagnosis, classification and appropriate treatment of ACS significantly decreases morbidity and mortality.

The rise, peak and fall of common biomarkers after cardiac injury is shown in Figure 1.

Acute myocardial infarction CK-MB



Marker	Rise	Peak	Fall
Troponin	3-12 h	24-48 h	5-14 days
Myoglobin	2 h	10 h	1-2 days
CK-MB	3-12 h	24 h	2-3 days

Figure 1: Cardiac markers in acute MI (adapted from https://labpedia.net (accessed 5 March 2025)

CARDIAC TROPONINS

According to the 2012 universal definition of acute MI, cardiac troponins (cTn) are the preferred biomarker for cardiomyocyte injury as it is considered the most cardiac-specific and sensitive of the currently available biomarkers. This is also endorsed by the American College of Cardiology (ACC), European Society of Cardiology (ESC), American Heart Association (AHA) and World Heart Federation.

High–sensitivity cardiac troponins (hs-cTn) allow for earlier identification of myocardial infarction, making earlier cTn assays, myoglobin and CK-MB redundant. It is recommended that hs-cTn become the standard of care for chest pain triage and its use eliminates the need for other biomarkers in ACS diagnosis and management, specifically myoglobin and CK-MB.

hs-cTn results must be used in conjunction with careful clinical examination, risk assessment and ECG interpretation for the diagnosis of ACS.

cTn levels are normal or slightly elevated in UA whereas there is at least one cTn value above the 99th percentile of healthy individuals in MI (NSTEMI or STEMI) along with clinical signs e.g ECG changes.
The limit of detection varies among the different hs- cTn assays ranging between 1 ng/L and 5 ng/L. Similarly, the 99th percentile varies among the different hs-cTn assays, ranging between 10 ng/L and 20 ng/L. Although analytical issues may arise with cTn, they are infrequent.

cTn is also the only marker identifying high-risk coronary patients who should be treated with glycoprotein IIb/IIIa antagonists and referred for invasive evaluation as soon as possible.

The 2023 ECS guidelines advise the 0/1-hour protocol if ACS is suspected with the 0/2-hour and 0/3-hour protocols as alternatives. hs-cTn is measured at baseline upon presentation and at 1, 2 or 3 hours respectively. The ESC 0/1-hour and 0/2-hour algorithms have been shown to have higher sensitivity and negative predictive values than the 0/3-hour algorithm for an index AMI even in patients with renal dysfunction, thereby reducing casualty waiting time. This is however not applicable to patients with known coronary artery disease.

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AMPATH LABORATORIES

MYOGLOBIN

Whilst serving as a marker of early cardiac damage, it is not cardiac specific and may increase due to concurrent skeletal muscle damage, which may confound the diagnosis of ACS.

CK-MB

Creatine Kinase (CK) is an enzyme released from damaged heart, muscle or brain cells. CK-MB, is an isoform of CK.

Common reasons for an increased CK-MB:

- Non-cardiac surgeries
- Trauma
- Skeletal muscle injury or chronic disease
- Exercise
- Renal failure

When there is concurrent skeletal muscle and myocardial injury, the percentage of CK-MB elevation is lowered by the high levels of total CK, reducing the sensitivity of CK-MB. Some have suggested using a ratio of CK-MB to total CK to improve specificity, but this significantly reduces the sensitivity. Spurious increases in CK-MB are also detected in patients with haemolysis, hyperbilirubinaemia and macrokinases (immunoglobulins linked to CK).

Increases in CK-MB not accompanied by increases in cTn values have been found not to be associated with adverse cardiac-related prognostic effects.

2014 AHA/ACC guidelines concluded that CK-MB is not useful for the diagnosis of ACS and therefore should not be included in a cardiac marker/chest pain panel for the following reasons:

- Less sensitive compared to cTn in detecting myocardial injury, periprocedural injury and MI
- Takes longer to appear in serum compared to cTn thereby delaying the detection of myocardial injury.
- Does not contribute to the diagnosis or risk stratification in patients with possible AMI.
- cTn performs better in diagnosing reinfarction.
- Incurs unnecessary costs.

CK-MB INDEX (CK-MB/CK)

The CK-MB index may be useful in the following scenarios:

Renal failure with an eGFR < 15 ml/min

cTn is elevated in dialysis patients without active myocardial injury due to decreased renal excretion and longer serum lifespan compared to CK-MB. hs-Troponin I is slightly advantageous over hs-Troponin T that has a slower renal clearance compared to troponin I. CK-MB is however still elevated in 30-50% of patients with this range of eGFR.

If the patient had a known or suspected ACS within the previous 2 weeks

cTn remains elevated for 5-14 days after a cardiac event and an elevated CK-MB index with its shorter lifespan may indicate a new ACS event as opposed to a resolving recent ACS event in which case cTn may still be elevated. However, research shows that elevated values of cTn values in the presence of an already elevated baseline level of cTn is easily observable (delta change). cTn are advantageous in the prompt rise, hence serial trends can be followed for reinfarction.

CK-MB may be used to estimate MI size

Peak hs-cTn levels however correlate with infarct size equally to peak CK-MB.

Detection of MI after percutaneous coronary intervention (PCI)

This remains controversial because uncomplicated successful interventions are often followed by a small cTn rise due to the increased sensitivity, and because of cTn kinetics i.e. abrupt rise followed by a prolonged elevation. This makes post-procedural levels difficult to interpret and has prompted some interventionalists to revert to using CK-MB, leading to significant underestimation of peri-procedural cardiomyocyte necrosis. However, obtaining a pre-PCI baseline cTn sample makes post-PCI increases easy to interpret and therefore prognosticate. The Universal Definition of MI (UDMI) also insists on having a baseline cTn value recorded prior to a cardiac procedure.