Cardiovascular disorders diagnosis and management

By

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The diagnosis of myocardial infarction

Myocardial infarction (MI) can be defined pathologically as myocardial necrosis due to prolonged ischaemia and may be recognised clinically through some combination of clinical features, electrocardiographic (ECG) findings and elevated values of biochemical markers or by imaging. After the onset of myocardial ischaemia, histological cell death takes from possibly as little as 20 minutes up to 4 hours or longer, and the entire process leading to a healed infarction takes at least 5–6 weeks.

The diagnosis of MI has in past decades been based on WHO criteria, which comprise a typical history of chest pain, the presence of diagnostic ECG abnormalities, and a rise in biochemical markers. The presence of two or more of these three defined the diagnosis. This long-established definition has been overtaken by the advent of more sensitive biochemical markers, and in particular the troponins.

Biochemical tests in myocardial infarction and ischaemia

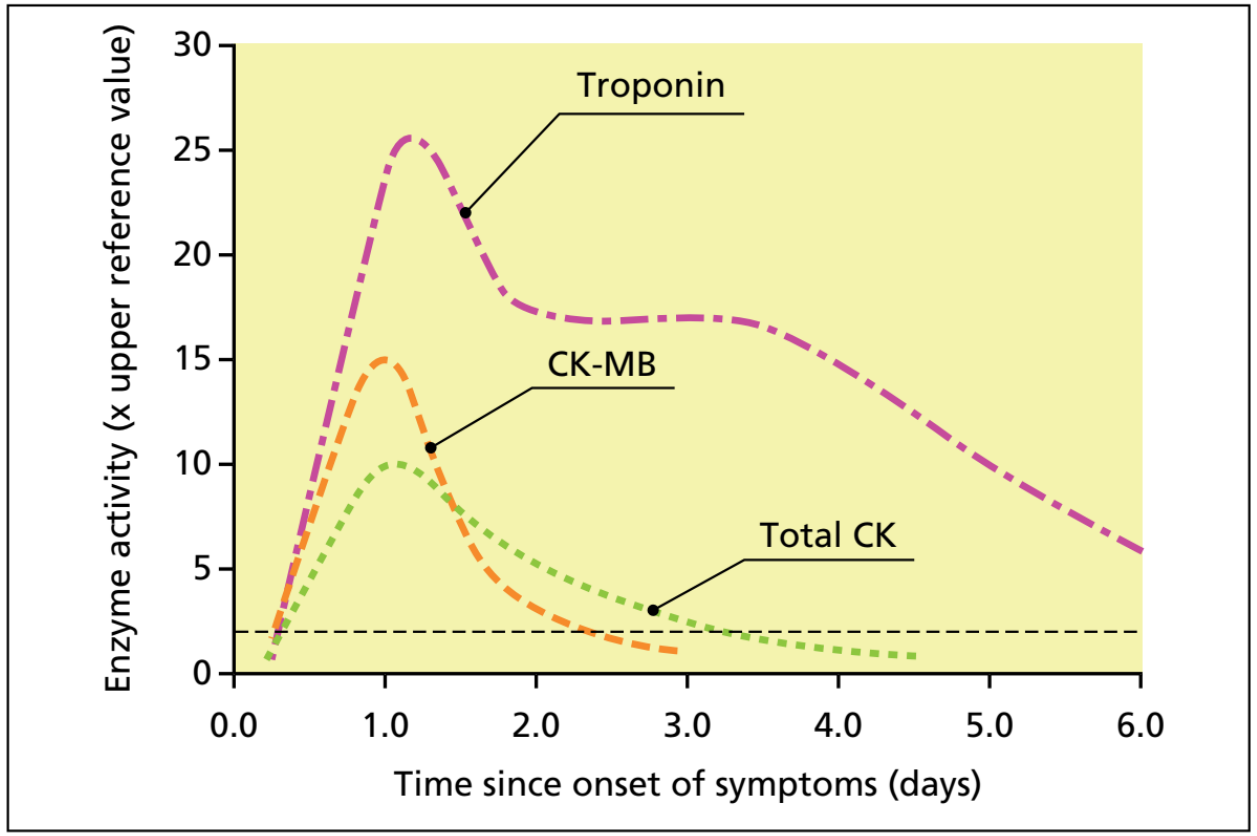
After MI, a number of intracellular proteins are released from the damaged cells. The proteins of major diagnostic interest include:

- troponin I and troponin T;
- enzymes, such as creatine kinase (CK), CK-MB, aspartate aminotransferase (AST) and lactate dehydrogenase (LDH);
- myoglobin.

The troponins and CK will be considered in detail because they are the most widely established biochemical indices of myocardial damage, although troponins have essentially taken the place of the enzymes in recent years. CK is, however, still used in some countries, and retains a use in the investigation of muscle disorders. Myoglobin is also a sensitive index of myocardial damage, and it rises very rapidly after the event. However it is nonspecific because it is raised following any form of muscle damage. It is not in wide laboratory use, but has a role in point of care analysers in the emergency setting. A negative result on an appropriately timed sample can be used to rule out myocardial damage and thereby determine early patient management. A positive result requires further investigation.

Time-course of changes.

After an MI, the time-course of plasma biochemical markers always follows the same general pattern (Figure). After an initial ‘ ’ phase, they rise rapidly to a peak between 18 and 36 h, and then return to normal at rates that depend on the half-life of each marker in plasma. The biphasic response of troponins with a rapid rise and prolonged elevation, and the rapid rise and fall of CK and CK-MB activity should be particularly noted. In patients treated by angioplasty or with thrombolytic agents, the general pattern of plasma marker changes shown in Figure is slightly modified, with a ‘washout’ of markers from the infarcted area, causing levels to rise rapidly to reach an early peak at 10–18 h.



Patterns of biochemical markers in the first few days after an uncomplicated MI.

Table 12.2 Time-course of plasma biochemical marker elevation after MI.

Enzyme	Abnormal activity detectable (h)	Peak value of abnormality (h)	Duration of abnormality (days)
Troponin T or I	4–6	12–24	3–10
CK-MB isoenzyme	3–10	12–24	1.5–3
Total CK	5–12	18–30	2–5
‘Heart-specific’ LDH	8–16	30–48	5–14

Optimal times for blood sampling

A sample taken on admission with an appropriate clinical history, if sufficiently elevated, will make the required diagnosis, but if not elevated will not rule out the diagnosis if insufficient time has elapsed for a significant rise in CK or troponin to have occurred (Table 12.2). Detection of a rise and/or fall in measurements is ideally required for the diagnosis of an acute MI, so testing should be repeated after 3–6 hours. It is likely that hospitals will have a local protocol for the initial diagnosis and management of patients suspected of MI, and this should be consulted. Except for the occasional patient seen for the first time 2 days or more after the episode, in whom troponin measurements might still be useful, it is very rarely of any value to take samples for plasma markers after 48 h from the onset of symptoms that suggest a diagnosis of MI.

Troponin

The troponin complex is exclusively present in striated muscle fibres and regulates the calcium-interactions of actin and myosin.

Creatine kinase

There are three principal CK isoenzymes, each comprising two polypeptide chains, either B or M; these give the dimers BB, MB and MM.

- Skeletal muscle has a very high total CK content; over 98% normally comprises CK-MM and less than 2% CK-MB. CK-MB may rise to 5–15% in some patients with muscle disease, and also in athletes in training.

- Cardiac muscle also has a high CK content. It comprises 70–80% CK-MM and 20–30% CK-MB. As a general rule, cardiac muscle is the only tissue with more than 5% CK-MB. Before troponin analyses were widely available, CK-MB measurement was useful in confirming the cardiac origin of a raised CK.
- Other organs, such as brain, contain less CK, often CK-BB. However, CK-BB rarely appears in plasma and is not of diagnostic importance. Plasma normally contains more than 95% of its CK as CK-MM.

CK is used in the diagnosis of some muscle diseases. It used to be used in the diagnosis of MI, but this is no longer recommended because of its lack of specificity. Increases, sometimes large, may occur after trauma or surgical operations, IM injections, in comatose patients, in diabetic ketoacidosis, acute renal failure and hypothyroidism, and after prolonged muscular exercise, especially in unfit individuals.

CK-MB isoenzyme

CK-MB is a more sensitive and specific test for myocardial damage than total CK. Its use has been largely overtaken by the widespread availability of troponin measurement. CK-MB (preferably by a mass measurement method) may be a more suitable alternative to troponin in less well-resourced settings and countries.

The diagnosis of heart failure

Heart failure is a complex clinical condition in which the heart's ability to pump is compromised by one or more of a number of underlying conditions, commonly ischaemic heart disease, but also heart valve abnormalities. The prognosis is poor if untreated, with a 2-year survival rate of under 50%.

The diagnosis of heart failure can be difficult, especially because the usual presenting symptoms such as breathlessness or ankle swelling are common and can be due to many different conditions. Physical examination is neither sensitive nor specific for heart failure, even in expert hands, with incorrect diagnoses in up to 50% of patients. The definitive diagnosis is best made by echocardiography, but access to this may be limited or delayed.

B-type natriuretic peptide (BNP) is a neurohormone secreted by cardiac myocytes in response to volume expansion and pressure overload, and plays a role in circulatory homeostasis. In heart failure the level of BNP increases, enabling differentiation of cardiac and pulmonary causes of breathlessness. It has an evolving role in the diagnosis of heart failure in both primary care and the emergency setting because it costs considerably less than echocardiography, and the result can be available much more rapidly.

Laboratory and point of care assays for BNP and for the inactive peptide N-terminal-proBNP (NT-proBNP) are available and provide qualitatively similar information.

Their accuracy is greatest in patients with more severe disease and poorest in those already receiving treatment. Levels rise with age, so age-related cut-offs should be used.

A number of other conditions can cause elevated BNP levels but, in a patient who is not on heart failure treatment, if levels are below the cut-off level then heart failure is highly unlikely and the patient should be investigated for other conditions. If the level is elevated the patient should proceed to further assessment, including echocardiography. The introduction of this strategy has the potential to speed up accurate diagnosis of heart failure, and to save money by restricting the use of echocardiography to those patients most likely to benefit from its use.

The diagnosis of thromboembolic disease

Laboratory investigations have a part to play in the investigation of possible thromboembolic disease. As the fibrinolytic system breaks down clots formed of cross- linked fibrin, degradation products are produced, including D-dimers. These are not detectable in the circulation under normal circumstances but are present in thromboembolic disease and in disseminated intravascular coagulation. Measurement of D-dimer levels is used in the diagnosis (or, more accurately, exclusion) of thromboembolic disease such as deep venous thrombosis (DVT) and pulmonary embolism (PE). In carefully selected patients at relatively low risk of DVT or PE, a normal result can effectively rule out these conditions, avoiding the need for more expensive and time-consuming imaging techniques. Careful clinical assessment is needed, because false-positive results are possible in non thrombotic pathologies such as neoplasia, recent surgery, MI and trauma.

Both laboratory and point of care tests are available for D-dimers and can help in the immediate management of patients presenting with symptoms or signs suggestive of DVT or PE, because a negative result offers reassurance. A positive result will require further investigation.

Thank you for your attention