

What's new in the Fourth Universal Definition of Myocardial infarction?

When myocardial infarction (MI) was redefined in 2000 it was stated that myocardial injury detected by abnormal cardiac biomarkers in the setting of acute myocardial ischaemia should be labelled as myocardial infarction. Since then, this principle has remained a fundamental component of the Universal Definition of Myocardial Infarction including the Fourth Universal Definition of Myocardial Infarction Consensus Document.

Even though myocardial injury is a prerequisite for the diagnosis of MI it is also an entity in itself and is now considered a separate condition. Myocardial injury is said to be present when blood levels of cardiac troponin (cTn) are increased above the 99th percentile upper reference limit (URL). The injury may be acute, as evidenced by a newly detected dynamic rising and/or falling pattern of cTn values above the 99th percentile URL, or chronic, in the setting of persistently elevated cTn levels.

There are numerous situations such as infection, sepsis, and kidney disease that can cause myocardial injury which is diagnosed when patients demonstrate elevated cTn values. For example, a patient admitted with chest trauma following a motor vehicle accident may demonstrate a typical rising and falling set of cTn values as a result of a myocardial injury. A substantial number of patients with chronic renal failure demonstrate low grade, persistently elevated cTn values which imply a negative long-term prognosis for these individuals. It is thought that the persistently elevated cTn levels are the result of a number of factors including ongoing, low-grade myocardial injury.

Myocardial injury may also be related to coronary revascularization procedures. Both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) can lead to elevation of cTn values that may be related to the procedure itself or secondary to complications from the procedure.

The presence of an acute myocardial injury in the setting of acute myocardial ischaemia meets the clinical definition of MI. There are five different subtypes of MI that are based on pathological, clinical, and prognostic differences and require different treatment strategies.

Type 1 MI is the traditional clinical picture of a heart attack. The underlying pathophysiology involves atherosclerotic plaque disruption complicated by intraluminal thrombosis resulting in decreased oxygen and nutrient delivery to heart muscle. Depending on the ECG findings, Type 1 MI can be classified as either an ST elevation MI (STEMI) or a non-ST elevation MI (NSTEMI) in order to direct appropriate, guideline established therapy.

In Type 2 MI, oxygen deprivation is not caused by atherosclerotic plaque rupture in a coronary artery but rather by an acute stressor such as an acute gastrointestinal bleed with a precipitous drop in haemoglobin, or a sustained tachyarrhythmia with clinical manifestations of myocardial ischaemia. Each of these settings and many others may result in a supply/demand imbalance of myocardial oxygen and nutrient supply leading to ischaemia and a myocardial injury. However, individual ischaemic thresholds may vary substantially from one patient to

another depending on the magnitude of the stressor, the presence of non-cardiac comorbidities, the extent of underlying coronary artery disease (CAD), and cardiac structural abnormalities. Coronary atherosclerosis is commonly seen in patients with Type 2 MI who undergo coronary angiography. However, atherosclerotic plaque rupture with accompanying thrombosis is not seen.

Patients with Type 2 MI are treated by managing the underlying illness that has led to the ischaemic imbalance of oxygen supply and demand. Therapy may include volume adjustment, blood pressure management, blood transfusion, heart rate control, and respiratory support. Depending on the clinical situation, a coronary angiographic evaluation may be indicated once a patient is stable in order to assess the likelihood of clinically important CAD. Patients with atherosclerotic CAD should be managed according to current guidelines.

Type 2 MI and myocardial injury are frequently encountered in clinical practice and both entities are associated with poor outcome. Both Type 1 and Type 2 acute MI require a rising and/or falling pattern of cTn values. Acute myocardial injury may also manifest such a pattern. However, in patients with chronic myocardial injury related to structural heart disease the cTn values may be elevated and stable without the rising and falling pattern. Type 2 MI and non-ischaemic myocardial injury may coexist in the same patient.

The detection of cardiac biomarkers in blood is fundamental for establishing the diagnosis of MI. However, patients can manifest a typical presentation of myocardial ischaemia/infarction including presumed new ischaemic ECG changes or ventricular fibrillation and die before it is possible to obtain blood for cardiac biomarker determination. Such patients are designated as having a Type 3 MI, when suspicion for an acute myocardial ischaemic event is high, even when cardiac biomarker evidence of MI is lacking.

Percutaneous coronary intervention-related increases of cTn values establish a diagnosis of procedure-related myocardial injury, but cTn elevation alone does not meet the diagnosis of Type 4a MI. The Type 4a MI also requires an elevation of cTn values >5 times the 99th percentile URL in patients with normal baseline values or in patients with elevated pre-procedure cTn in whom the cTn levels are stable ($\leq 20\%$ variation) or falling. In addition, evidence of new myocardial ischaemia is required, either recognized from ECG changes, findings on imaging procedures, or as a result of a procedure-related complication that leads to reduced coronary blood flow. Other subcategories of PCI-related MI are stent/scaffold thrombosis, Type 4b MI, as documented

