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Short review

Fourth Universal Definition of Myocardial infarction

Aleksandar Lazarević[1,2,3]

[1]University of Banja Luka, Faculty of Medicine, Banja Luka, Republic of Srpska, Bosnia and Herzegovina; [2]University Clinical Center of the Republic of Srpska, Division of Cardiovascular Diseases; [3]Cardio Internal Medicine Outpatient Clinic, Banja Luka.

Abstract *The fourth Universal Definition of Myocardial infarction was necessary for several reasons, including the superiority of highsensitive troponin (cTn) that changed evaluation of myocardial infarction. Even though myocardial injury is a prerequisite for the diagnosis of myocardial infarction in terms of myocardial ischemia, it is also an entity in itself. Two most important parts of this concepts include: 1. presence of myocardial injury and 2. evidence of the presence or absence of acute myocardial ischaemia. Presence of myocardial injury is defined with raised cTn concentrations above 99th percentile uper reference limit. A rising and/or falling patern of cTn values indicates acute myocardial injury, whereas chronic myocardial injury is characterized by continuing elevated cTn values (less than 20% variation). The Fourth universal definition of myocardial infarction retaines the five types of myocardial infarction, as described in the Third universal definition of myocardial infarction, though with modifications. The five types of myocardial infarction represent five separate situations that produce myocardial ischaemia and myocardial necrosis and have different pathological findings, clinical presentation, prognosis, and the treatment strategies.*

Key words *myocardial infarction, myocardial ischaemia, troponin, percutaneous coronary intervention, coronary artery bypass*

The Fourth Universal Definition of Myocardial Infarction was recently simultaneous published in the Journal of the American College of Cardiology,[1] Circulation,[2] European Heart Journal,[3] and Global Heart,[4] and was necessary for many reasons, including the superiority of high-sensitive cardiac troponin (cTn).

Although the clinical criteria for MI have not been changed, cTn assays changed the way in which the evaluation of MI proceeds. In the setting of myocardial ischaemia, myocardial injury detected by abnormal cTn levels represents a precondition for the diagnosis of MI.

Even though myocardial injury is a prerequisite for the diagnosis of myocardial infarction (MI) it is also an entity in itself and is now considered a separate condition.[5] The most important part of this concept includes: 1. Presence of myocardial injury and 2. Evidence of the presence or absence of acute myocardial ischaemia.

Presence of myocardial injury is defined with raised cTn concentrations above the 99th percentile upper reference limit (URL). The pattern of rising and/or falling values of cTn shows that the injury can be an acute one, when the cTn value is above 99th percentile URL. When cTn value is constantly elevated (less than 20% variation), we say it is a chronic injury.

Myocardial injury can be caused by different conditions like sepsis, infection and kidney diseases and other conditions in patients with raised cTn values. For example, a patient with Takotsubo syndrome may show a rising and falling pattern of cTn values resulting from myocardial injury. Negative prognosis refers to a significant number of patients suffering from chronic renal failure with low grade myocardial injury presented with low grade steadily raised cTn values.

However, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) procedures and/or complications related to the procedure can be the cause of elevated cTn values.

An acute myocardial injury with acute myocardial ischaemia corresponds to the clinical definition of MI. The Fourth Universal Definition of Myocardial infarction retains the five types of MI as described in the third Universal Definition of Myocardial Infarction, though with modifications.[6]

The five types of acute MI compose five separate situations that produce myocardial ischaemia and myocardial-cell death and have different pathological findings, clinical presentation, prognosis and treatment strategies.[7-9]

Type 1 MI is defined by an acute coronary atherosclerotic plaque rupture or erosion accompanied by intraluminal thrombosis. On the basis of ECG findings is classified as a ST elevation MI (STEMI) or a non-ST elevation MI (NSTEMI).

Type 2 MI includes patients with evidence of acute myocardial ischaemia who do not have atherosclerotic plaque rupture or erosion but instead have an imbalance of myocardial oxygen supply and demand. The causes of Type 2 MI may include cardiogenic shock, anaemia, arrhythmias, coronary spasm, coronary embolism, coronary dissection

Correspondence to: Aleksandar Lazarevic, MD, PhD, FESC, FACC, Cardio Internal Medicine Outpatient Clinic, Pave Radana 17, 78 000 Banja Luka, Bosnia and Herzegovina, Tel: +387-65-560011 Fax: +387-51-260333, E-mail: aleksandarlazarevicbl@gmail.com

and other causal factors. Patients with Type 1 MI usually need to be treated by urgent invasive approach, whereas patients with Type 2 MI may present with other causes of symptoms so that an early invasive approach is not recommended, it can even be harmful. In patients with Type 2 MI, illness that has led to the ischemic imbalance of oxygen supply and demand should be treated by blood transfusion, volume adjustment, heart rate control, respiratory support.

Type 3 MI includes patients demonstrating signs and symptoms of myocardial ischaemia, with sudden cardiac death before a blood sample can be obtained or patients with evidence of MI by autopsy.

Type 4 MI includes patients with coronary intervention (PCI) - related MI (Type 4a) arbitrarily defined by elevation of cTn values >5 times the 99th percentile URL in patients with normal baseline values.[10-11] In patients with elevated pre-procedure cTn in whom the cTn levels are stable (≤20% variation) or falling, the post-procedure cTn must rise by >20%. However, the absolute post-procedural value must still be at least five times the 99th percentile URL. Subtypes of PCI related MI also include stent/scaffold thrombosis (Type 4b), documented by angiography or autopsy or in-stent restenosis (Type 4c).

With CABG procedure, the following factors can cause procedural myocardial injury: myocardial preservation, direct traumatic injury to the myocardium and any possible ischemic injury. Therefore, cTn elevation values are expected after any CABG procedure.

To diagnose type 5 MI, use cTn value > 10 times the 99th percentile URL as the cut-point in the first 48 h following CABG, that occurs from a normal baseline cTn value (≥99th percentile URL), along with ECG, angiographic or imaging finding of new myocardial ischaemia.[11]

For both types 4 and 5, the serum marker of a MI must be supported by either ECG or imaging changes indicative of ischaemia. In the case of a CABG-related MI, this could also include evidence of coronary-graft occlusion.

A new section on Takotsubo syndrome is also included. With approximately 1-2% of patients with suspected STEMI, Takotsubo syndrome (TTS) can mimic MI. Emotion or physical stressors trigger TTS and above 90% of patients are women in their postmenopausal period. The rise and fall of cTn values support an acute myocardial injury; high catecholamine surges are known to primarily trigger cTn release from cardiomyocytes.

It is more and more recognized that some patients with MI do not have angiographic obstructive CAD. Clinically significant coronary arterial obstruction is defined as stenosis ≥50% of a major epicardial vessel luminal diameter. It is said that these patients have suffered from MI but they do not have coronary arterial narrowing. Such patients are described by the term MINOCA that is myocardial infarction with non-obstructive coronary arteries. It is more frequent in women and commonly presents NSTEMI rather than STEMI.

The Consensus Document on the Fourth Universal Definition of Myocardial Infarction also provides an extensive amount of detailed information about analytic issues of cTn, the use of ECG, and suggests the importance of imaging for diagnosing myocardial injury and MI in situations where diagnosis is ambiguous.

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Sažetak

Četvrta univerzalna definicija infarkta miokarda je bila potrebna iz više razloga, uključujući i superiornost visokosenzitivnog troponina (cTn) koji je promijenio evaluaciju infarkta miokarda. Iako je lezija miokarda preduslov za dijagnozu infarkta miokarda u uslovima ishemije miokarda, ona predstavlja i poseban entitet. Dva najvažnija dijela novog koncepta čine: 1. postojanje miokardne lezije i 2. dokaz postojanja ili nepostojanja ishemije miokarda. Miokardna lezija je definisana kao porast koncentracije cTn iznad 99. percentile gornje referentne granice. Lezija može biti akutna, ukoliko se registruje porast i pad koncentracije cTn, ili hronična, ukoliko je cTn konstantno povišen (sa manje od 20% varijacija koncentracije). Četvrta univerzalna definicija infarkta miokarda je zadržala podjelu na pet tipova infarkta miokarda, koja je bila opisana u Trećoj univerzalnoj definiciji infarkta miokarda, uz odgovarajuće modifikacije. Pet tipova infarkta miokarda predstavljaju pet odvojenih situacija koje dovode do ishemije miokarda i nekroze miocita i imaju različite patološke nalaze, kliničku prezentaciju, prognozu i strategiju liječenja.

Ključne reči: *myocardial Infarction, myocardial Ischemia, percutaneous coronary Intervention, troponin, sepsis, coronary artery bypass, diagnostic imaging, electrocardiography*