VIEWPOINT

Fourth Universal Definition of Myocardial Infarction: Will it change how we practice emergency medicine?

Cuarta Definición Universal del Infarto de Miocardio: ¿cambiará la práctica de la Medicina de Urgencias y Emergencias?

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Introduction

The recently published 4th Universal Definition of Myocardial Infarction (UDMI)[1] advocates for the use of high sensitivity cardiac troponin assays (hs-cTn) since there are now a large number available throughout the world[2]. It thus emphasizes some of the important concepts that one must embrace to use these assays effectively as it updates the prior 3rd definition from 2012[3]. Much of this information should directly affect the practice of the Emergency Medicine.

The 4th emphasizes to a greater extent than prior reports, the need to differentiate between acute myocardial infaction (AMI) and myocardial injury. The new UDMI highlights issues about hs-cTn measure-ments and reinforces the use of the 99th reference percentile value (p99th) as the limit for defining myocardial injury. It suggests the importance of correct interpretation of a change between serial determinations (Δ value) and recommends a cautious use of the so-called "rapid algorithms" for AMI diagnosis.

This article will briefly comment on the above mentioned issues but one should also note the new clinical sections on specific clinical situations like Takotsubo syndrome, AMI without significant coronary obstruction – ≥ 50% obstruction in a larger epicardial vessel– (abbreviated as MINOCA), chronic kidney disease and atrial fibrillation as well.

Myocardial damage, AMI type 1 or type 2

The 4th UDMI states that any concentration of cTn ≥ 99th defines the existence of myocardial damage (Figure 1). Concentrations of hs-cTn should be expressed in units (ng/L, pg/mL) to avoid possible confusion in their interpretation derived from expressing them in units (µg/L) that generate a high number of decimals. Regardless of its etiology, the existence of high cTn values implies a poor prognosis[4].

Myocardial damage can be acute or chronic. There is acute myocardial damage when cTn ≥ p99 is detected and the Δ value between serial measurements exceeds the fixed limit; both the p99 and the Δ values are specific to each method used to measure cTn. Expressing Δ values in absolute terms would have a higher diagnostic performance than expressing them as percentages; however, this circumstance must be validated for each cTn measuring method[5]. According to the UDMI, a percentage Δ value is significant if in serial determinations cTn exceeds an increase/decrease of 50% when any of the serial cTn measurements is < p99. However, if any of the serial cTn determinations is ≥ p99, the significant Δ value would be that of a Δ 20% change - to preserve diagnostic sensitivity at the expense of lower specificity. Chronic myocardial damage is considered to exist when cTn ≥ p99 concentrations are detected, but the significant Δ value is not exceeded. The 4th UDMI cites as examples of this situation the cTn values and the Δ value observed in chronic renal disease, structural heart disease or in advanced age.

In accordance the UDMI, myocardial ischemia is defined by symptoms, changes in the electrocardiogram, evidence of viable myocardium loss or regional alterations in myocardial contractility. AMI is diagnosed when myocardial ischemia is accompanied by cTn concentrations ≥ p99th and a value exceeding the limit defined for any given assay. When myocardial ischemia is due to atherothrombosis, AMI is of type 1. If the ischemia is secondary to an imbalance of the oxygen supply/requirement to the myocardium, the diagnosis is type 2 AMI. The 4th definition cites as examples of type 2 AMI as those associated with hypertensive crisis, sustained tachycardia or coronary vasospasm. The prognosis of type 1 and type 2 AMI is similar, but type 2 AMI does not have specific treatment beyond treating its triggering cause.

Finally, the new definition highlights that an acute myocardial damage other than AMI exists. It occurs when a cTn ≥ p99th and a significant Δ value are detected, but evidence of myocardial ischemia is not found. This kind of acute myocardial damage can be due to cardiac causes, such as myocarditis, heart failure or Takotsubo syndrome or non-cardiac causes that indi-

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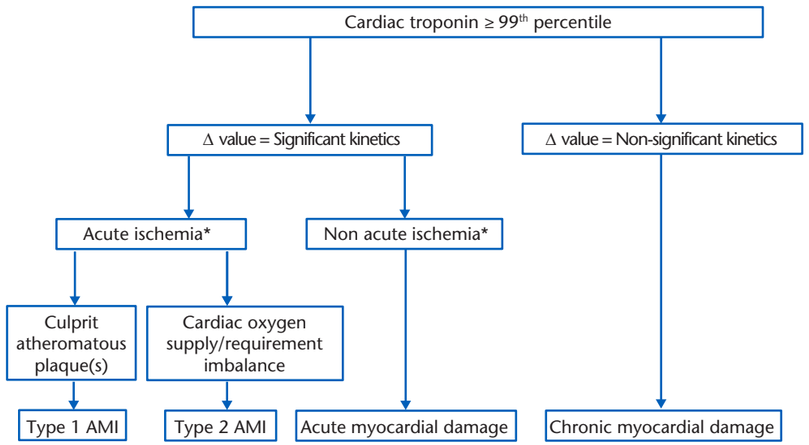

Figure 1. A model for interpreting elevated cardiac troponin (cTn) ≥ p99 values. Adapted from Fourth universal definition of myocardial infarction. Δ value: Change observed among serial cTn determinations. *Myocardial ischemia requires of the occurrence of suggestive signs or symptoms. AMI: Acute myocardial infarction

rectly affect the heart, such as pulmonary embolism or sepsis. However, it is acknowledged that there are groups of subjects - elderly, women or patients with diabetes-in whom the symptoms of myocardial ischemia can be atypical[6], making difficult to differentiate between acute myocardial damage without AMI and type 2 AMI. In this situation, the new guidelines suggest the use of imaging to clarify the diagnosis if there is substantial clinical suspicion. The lack of clear differences between the two clinical situations is one reason for the variability that exists in the reported frequency of type 2 AMI diagnosis, which varies from 1.6 to 29.6%[7].

Use and interpretation of cardiac troponin

The improved analytical quality of the still-in-use methods to measure cTn, denominated as contemporaries, as well as the progressive introduction into practice of the hs-cTn measures permits the accurate detection of very low cTn concentrations, including that of the p99th. The UDMI advocates for the use of hs-cTn assays. Regardless of the assays, the increased sensitivity of all the assays facilitate the evaluation of patients with possible AMI. This higher sensitivity will cause many differences in the triage of patients in the ED.

The diagnosis of AMI can be early and safely ruled-out when undetectable or very low hs-cTn concentrations are observed in patients[8,9]. However, this strategy is only appropriate for low-risk patients who consult at least 2 hours after the onset of symptoms[10]. This strategy, though, is only appropriate for low-risk patients who consult at least 2 hours after the onset of symptoms[10]. A very recent study, in patients consulting for chest pain in hospital emergency departments, found that up to 17.8% of them were diagnosed with myocardial damage by measuring cTn with a contemporary method with improved sensitivity, and that this percentage increased to 21.4% when hs-cTn was used[11]. Nevertheless, if the contemporary method of cTn had been of low sensitivity, the difference would have been greater than that of the aforementioned study. The increase in patients with hs-cTn ≥ p99 concentrations will lead to an increase in the diagnosis of AMI, since hs-cTn also allows for the detection of significant changes in Δ value that were not detectable with the previous methods[12]. Not all of these patients, however, will have an AMI. Many of the patients with clinical symptoms compatible with AMI, but with no increase in contemporary cTn, were diagnosed as unstable angina; measuring hs-cTn should be reclassified as AMI. The impact of this reclassification has been analyzed in a Spanish study[13]. However, as already mentioned, there are many different clinical situations of AMI with elevated cTn[14,15]. The key point is to determine whether there is adequate evidence of myocardial ischemia. Finally, the new definition of AMI recommends using p99 values of hs-cTn stratified by sex, unlike the algorithms recommended in the clinical guidelines of the European Society of Cardiology, which do not establish this recommendation[16]. The 4th UDMI also warns that in patients who consult late a significant Δ value may not be observed as the cTn is found on the plateau of the time-concentration curve. This circumstance has been observed in up to 26% of patients with AMI[17].

Other aspects of the 4th definition of UDMI

The 4th UDMI highlights the importance of scrupulously controlling the time intervals between the onset of symptoms and the first determination of cTn, and between its serial determinations. When cTn is measured using contemporary methods, it is recommended that it be measured at admission and at 3 and 6 hours later. When cTn is measured with high-sensitivity methods, the serial intervals are shortened, although there is no unanimous recommendation in this regard. Although it has been proposed that AMI be excluded with a single measure of hs-cTn on admission if it is very low or undetectable, the most frequent is to take a series of hs-cTn measurements on admission and within 1-2 hours afterwards. However, the 4th UDMI emphasizes that the use of these "rapid algorithms (serializations)" is not advisable in those patients who consult early (< 2 h from symptoms).

Conclusion

The updated 4th UDMI will affect the practice of Emergency Medicine. The distinction between myocardial damage and AMI, the need for careful interpretation of baseline and serial (Δ value) cTn values, particularly when measured with high sensitive methods and the possibility of using rapid diagnosis algorithms for ruling-out or ruling-in AMI will challenge the current practice. The knowledge and correct application of the concepts contained in the 4th UDMI will ensure its positive impact for physicians and patients.

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