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IM - COMMENTARY

High-sensitivity troponin allows accurate rapid diagnosis and discharge but it is not a substitute for a comprehensive patient evaluation

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High-sensitivity cardiac troponin (hscTn) assays are replacing the older generation methods for the detection of acute myocardial injury. The key advantage is the higher sensitivity and diagnostic accuracy of hscTn assays, leading to a more rapid confirmation or exclusion of acute myocardial infarction (AMI). The 2015 European Society of Cardiology (ESC) guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (NSTE-ACS) recommend the use of a 0 h/3 h algorithm, but 0 h/1 h rule-in and rule-out protocols have also been proposed [1]. The positive predictive value for MI is 75–80%, mainly due to the confounding effects of a few other cardiac conditions (dysrhythmias, heart failure, etc.) and many other non-cardiac diseases associated with increased hscTn (pulmonary embolism, infections, renal dysfunction, etc.). In a busy Accident & Emergency Department (A&E), where time and space come at a premium, but missing a diagnosis has awkward consequences, the negative predictive value for AMI is very important. This exceeds 98%, allowing the identification of candidates for early discharge and outpatient management [2–4]. In patients presenting to A&E > 3 h after symptom onset, one sample should be sufficient to exclude AMI, and several studies show that the diagnosis of AMI is unlikely in case of undetectable hscTn serum levels [5–9]. Still ruling out myocardial injury based on a single hscTn determination irrespective of the presentation time is controversial.

Fabbri et al., in this retrospective single-center cohort study including consecutive patients with suspected myocardial ischemia but no ECG abnormalities, conclude that a single 0-h hscTn < 5 ng/L, equal to the detection limit, may lead to a rapid and safe discharge, without unfavorable outcomes at short- and long-term follow-up [10]. At 30 day follow-up, no subject out of 326 with hscTn < 5 ng/L met the primary outcome of fatal or non-fatal AMI within 30 days (NPV 100%). In the group of 675 subjects (67.4%) with hscTn 5–14 ng/L, the 99th percentile cut-off, the primary outcome occurred in 12 subjects (1.8%, NPV of 98.2%). At 1 year, AMI occurred in 2 patients (0.6%) with hscTn < 0.5 ng/L and in 26 cases (3.9%) with hscTn 5–14 ng/L (NPV 99.4% vs. 96.1%, respectively; $P = 0.002$). These results reinforce the assumption derived from the previous studies that a single undetectable hscTn value, in conjunction with normal ECG and a low ischaemic risk (the GRACE risk score is lower in patients with hscTn < 5 ng/l than in those with hscTn 5–14 ng/L; 84.2 ± 32.3 vs 112.0 ± 25.3, $p < 0.001$) represents a useful diagnostic tool to guide decision making for early diagnosis or exclusion of AMI [11]. It is important to note that in this study, time from symptom onset to sampling time was greater than 2 h for almost all patients, although it is not clearly indicated in how many patients with undetectable values the delay exceeded 3 h. Theoretically, the delay to be considered should be the interval between symptom onset and hospital admission, available only in 72% of the cases in this study, since collection and shipping of blood samples should be performed as soon as possible. Similarly, with symptoms suggestive of myocardial ischemia, the delay in calling the emergency service for an ambulance or anyway in presenting to A&E should be minimized. The conclusions of this study cannot be extended to patients with very early presentation to hospital or stuttering symptoms or high GRACE scores for whom a two-sample strategy and a longer observation period are probably still more appropriate. Furthermore, the absence of hscTn should not be considered as a proof that the patient is free from coronary artery disease. The complete absence of cardiac adverse events at 12 months in a relatively small group does cancel the recommendation of the current ESC NSTEMI guidelines to perform, during admission or shortly after

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discharge, a cardiac stress imaging test in those patients with multiple risk factors for CAD or convincing symptoms, despite normal ECG and negative or borderline hscTn values [1]. Various trials show that normal dobutamine or dipyridamole stress echocardiograms have high NPV for MI, and are associated with excellent clinical outcomes. An alternative to overcome the operator dependency of the accuracy of these tests, now considered the test of choice in younger patients by the National Institute for Health and Care Excellences (NICE) guidelines, is coronary computed tomographic angiography (CCTA) [12]. Randomized trials show that CCTA in the A&E setting reduces length of stay, initial cost, and time to discharge, and a meta-analysis of nine trials reports an overall high negative predictive values to exclude ACS and excellent outcomes in patients presenting with low to intermediate pretest probability for MI [13].

Troponin has almost eliminated the use of CK-MB, now not available in many hospitals. There is no doubt that history is going to repeat itself, and hscTn will displace the current troponin assays due to the key advantage of a more rapid rise. This will lead to changes in the definitions of AMI and uncertainties in the best strategies to follow in NSTEMI patients.

Currently, according to the fourth universal definition of myocardial infarction, the presence of myocardial injury is defined as a cTn value above the 99th percentile upper limit of confidence, but the diagnosis of acute myocardial infarct (AMI) requires clinical, ECG or imaging concomitant changes. It will be difficult to compare the incidence of endpoints when events are discriminated using a stringent marker such as hscTn, possibly raised just by a short exertional ischemic episode, and certainly positive in all cases after coronary angioplasty. The evidence for a worse prognosis after PCI and CABG is limited to the increases of CK-MB of 8–10 times ULN, and, less convincingly, cTn 40–70 times ULN [14–18]. The risk is that naming periprocedural injury minimal enzymatic changes will raise unnecessary concerns, unduly penalize revascularization strategies vs conservative treatment, and drop attention towards true large clinically significant enzymatic leaks. Finally, the criteria of current guidelines indicating the need and optimal timing of angiography will require reassessment, probably raising the bar to perform early direct angiography only for patients with the most significant troponin increases.

Compliance with ethical standards

Conflict of interest The authors certify that they have no affiliation or financial involvement in any organization with a direct financial interest in the subject matter discussed in the manuscript.

Statement of human and animal rights All procedures performed in studies discussed in the manuscript were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study (commentary) formal consent is not required.

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