Editorial

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High-sensitivity assay for cardiac troponins with POCT methods. The future is soon

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A well-known mantra highlights that “good, fast and cheap” in laboratory testing is a mission impossible. However, the recent history of cardiac troponin assays may deny this aphorism. In the last 10 years, the introduction of high-sensitivity cardiac troponin (hs-cTn) assays made it possible to progressively reduce the time to diagnosis of acute myocardial infarction (AMI) from 6 to 12 h to from 1 to 3 h [1, 2]. In particular, the 2020 ESC guidelines recommend the rapid 0/1-h algorithm (blood draw at admission at baseline and 1 h later) as the first clinical option because it provides the best balance between safety and efficacy by allowing the reduction of the length of stays in Emergency Departments (ED) of patients with suspect of Acute Coronary Syndromes (ACS) [3].

Until now, the successful clinical implementation of these rapid algorithms was restricted to clinical hospital laboratories, as current hs-cTn methods require the use of large automated platforms [3, 4]. Point-of-care-testing (POCT) for cTn assays with high-sensitivity performance may represent a formidable progress because they should assure a more rapid diagnostic turnaround-time, thus facilitating the valuable management of patients admitted to Emergency Departments with chest pain [3]. Furthermore, hs-cTn POCT assays may open the possibility of a “decentralized” diagnosis of myocardial injury and infarction, even in primary care and other remote clinical settings [5]. However, most commercially available POCT

methods for cTn, did not meet the criteria recommended to be considered an high-sensitivity assay [3, 4, 6]. Therefore, the obvious advantage of POCT methods, namely the shorter turnaround-time, was counterbalanced by lower sensitivity, lower diagnostic accuracy and lower negative predictive value [3].

However, very recent studies suggest that POCT methods for cTn could provide comparable analytical performance characteristics to those of central laboratory hs-cTn assays. In 2019, Sorensen et al. [7] reported the clinical results obtained with the PATHFAST POC hs-cTnI assay using the PATHFAST immunoanalyzer system, which is a POCT method with analytical performance compliant with an high-sensitivity assay. Diagnostic algorithms using rapid (0/1 h) and standard 0/3 h approaches were evaluated in a derivation data set with 669 patients and validated in an additional 610 patients and compared with those obtained with the Architect hs-cTnI method [7]. Moreover, in 2020 Boeddinghaus et al. [8] directly compared the diagnostic accuracy of POC-hs-cTnI-TriageTrue vs. the best-validated central laboratory assays using specific 0/1-h algorithms in 1,261 patients (178 with AMI, 14%). The POC-hs-cTnI-TriageTrue assay provided high diagnostic accuracy in patients with suspected AMI with a clinical performance comparable to that of the best-validated central laboratory assays [8].

In this issue of the *Journal*, Apple et al. [9] report the sex-specific 99th percentile URL values for males and females in heparinized plasma from the AACC universal sample bank (USB) using the Siemens point of care (POC) Atellica VTLi hs-cTnI immunoassay. The reference population (age range: 18–91 years, median: 39 years) included 693 subjects, 363 males and 330 females [9]. Of note, Authors excluded the possible outliers using some surrogate biomarkers, also including NT-proBNP, as recommended by international guidelines and some expert documents [10–13]. The calculated 99th percentile URL values were: overall, 23 ng/L [90% confidence interval (CI)] 20–32 ng/L; males, 27 ng/L (90% CI 21–37 ng/L); females, 18 ng/L (90% CI 9–78 ng/L) [9]. The percentages of subjects having measurable concentrations higher than LoD for the post exclusion subjects were: overall 83.7%,

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male 87.3%, female 79.7% with no statistical differences compared to the non-exclusion subjects [9]. The results of this study shows that the novel POC Atellica® VTLi hscTnI assay meets the designation of a ‘high-sensitivity’ assay according to the criteria recommended by current international guidelines [10].

As for the development of reliable POCT tests for the Pandemic COVID-19 disease [14], the progression toward reliable POCT methods for hs-cTn assay to reach the marriage between quickness and consistency was certainly not an easy task. As principles of Laboratory Medicine state, speed and accuracy should go hand in hand and the presumed advantages of rapid testing need to be balanced against the possible lower sensitivity (sometimes even specificity) [14].

As noted by the NICE guidelines [4], the major limitation of recent clinical studies on hs-cTnI POCT methods [7–9] is that troponin levels were tested in stored plasma samples rather than in whole blood samples used in clinical practice, the so-called “real life”. Very recently, Gopi et al. [15] investigated the agreement between plasma and whole blood hs-cTnI by using the PATHFAST hs-cTnI assay. Furthermore, these Authors compared the results of POCT method with those measured in the central laboratory with the hs-cTnT assay in 224 fresh samples collected from 191 patients presenting with suspected ACS. The results of this study indicate that whole blood can be used interchangeably with plasma for a more convenient and less time- and labor-consuming testing of hs-cTnI on the PATHFAST analyzer [15].

According to the NICE guidelines, therefore, we may conclude that further evidence on diagnostic performances of POCT hs-cTnI methods is needed before these tests can be recommended for the use in clinical practice [4]. However, taking as a whole, the most recently available data [7–9, 15] strongly suggest that for POCT high-sensitivity methods to measure cTn, “the future is soon”, even if some further steps should be taken before crossing the finish line.

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