

ORIGINAL ARTICLE

Improved efficiency and cost reduction in the emergency department by replacing contemporary sensitive with high-sensitivity cardiac troponin immunoassay

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Summary. *Background:* Although unquestionable evidence has been provided that high-sensitive (HS) cardiac troponin (cTn) immunoassay outperform the former contemporary-sensitive techniques, some clinicians are still hesitant to implement HS methods in routine clinical practice. This study was hence planned to evaluate the impact of replacing a contemporary-sensitive with HS cTnI immunoassay on hospital and laboratory workload. *Methods:* Information on the total number of cTnI tests ordered, total number of blood samples collected, total number of CK-MB tests ordered, number of patients with the first HS-cTnI value below the limit of detection (LoD) and cumulative HS-cTnI values was extracted from the local hospital information system for the semesters before and after the HS method was introduced. *Results:* Although the total emergency department (ED) visits modestly increased after introducing HS-cTnI, the number of total cTnI tests declined by over 10%. A substantial reduction of single-sample test requests was noted, accompanied by a considerable decline of 3- and 4-sample collections (i.e., -61% and -73%, respectively). A high percentage of patients (27.5%) displayed HS-cTnI values <LoD at admission, thus allowing safe discharge. The introduction of HS cTnI immunoassay was effective to collapse the number of CK-MB test requested and also generated favorable return of investment for the part of laboratory budget concerning cTnI testing (-3.2% of total costs for cTnI and -99.8% of total costs for CK-MB). *Conclusion:* The results of this study show substantial organizational and economic benefits by replacing contemporary-sensitive with HS cTnI immunoassays. (www.actabiomedica.it)

Key words: cardiac troponin, high-sensitivity, myocardial infarction, acute coronary syndrome, emergency department

Introduction

The development and introduction into clinical practice of high-sensitivity (HS)-cardiac troponin (cTn) immunoassays have consistently modified the diagnostic approach to patients with suspected acute

coronary syndrome (ACS) during the last two decades (1). These novel immunoassays have remarkably amplified the diagnostic performance of cardiac biomarkers testing (especially in patients with non-ST elevation myocardial infarction; NSTEMI) and can also generate important clinical evidence of cardiac injury be-

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yond myocardial ischemia. Supported by reliable data (2-4), the fourth universal definition of myocardial infarction has endorsed and disseminated these concepts (5), so that the usage of HS-cTn immunoassays shall be considered virtually unavoidable now. Despite this evidence, some clinicians are still hesitant to replace the former so-called contemporary-sensitive methods with HS-cTn techniques, justifying this reluctance with concerns of overutilization, possible overdiagnosis of cardiac injuries, overcrowding of emergency departments (EDs), and excess of cardiac invasive testing. This translates into the reliable evidence that “contemporary-sensitive” or conventional (i.e., non-HS) cTn immunoassays, as well as myoglobin and creatine kinase MB (CK-MB) tests, are still largely used around the world (6-8).

With some differences due to the analytical characteristics of the assay, the hospital organization, and the clinicians’ background, the most common approach for diagnosing ischemic and non-ischemic myocardial injury encompasses a baseline measurement of cardiac biomarkers followed, when needed (i.e., values not diagnostic at the first measurement or non-diagnostic electrocardiogram), by serial sampling at different times points in order to detect suggestive changes in cTn and distinguishing thus an acute from a chronic cardiac damage (9, 10). Importantly, whether the “absolute delta” (i.e., the absolute variation of cTn troponin value between two time points), the “relative delta” approach (i.e., the percentage variation of cTn troponin value between two time points) or even an “integrated” approach (i.e., combining both modalities of calculating cTn variation, depending on the baseline value) would provide better diagnostic performance remains to be precisely defined (11).

In this study, we aimed to investigate the impact on hospital and laboratory workload consequent to the shift from a contemporary-sensitive toward a HS-cTnI immunoassay. For this purpose, we retrospectively analyzed data from two separate semesters in the local hospital, the first when a conventional cTnI assay has been used and the second few months after routine introduction of a HS-cTnI assay.

Materials and Methods

On April 16th, 2018, the University Hospital of Parma shifted from a contemporary-sensitive cTnI technique (Accu-TnI+3 -A98264. Beckman Coulter; Brea CA) toward a HS immunoassay (Access-HsTnI-B52700. Beckman Coulter; Brea CA). The specific characteristics of these assays have been previously described elsewhere (12, 13). Briefly, the values of the limit of blank (LoB), limit of detection (LoD) and 99th percentile of the upper reference limit (URL) of the former and new HS-cTnI immunoassays were 9 ng/L, 13 ng/L and 34 ng/L for AccuTnI+3 and 0.14 ng/L, 0.34 ng/L and 17.8 ng/L in men and 10.5 ng/L in women for Access-HsTnI, respectively. Despite the test exhibits much better analytical performance, the cut-off of 2.3 ng/L for LoD of the HS-cTnI was locally used for rule-out, as currently suggested by the manufacturer. After the introduction of Access HsTnI, CK-MB was contextually eliminated from the local “cardiac entry panel” so that its prescription remained only available at clinicians’ discretion. Several meetings, involving emergency physicians (EPs), cardiologists, laboratory professionals, and other hospital specialists, were organized in the three months before changing the cTnI immunoassay aimed at disseminating the knowledge on clinical use and interpretation of HS-cTnI.

The EPs were free to decide about timing for HS-cTnI sampling according to their clinical judgment, mostly based on available guidelines (14). Before the shift to HS-cTnI, blood sampling had been performed at 0, 3 and 6 hours. Although very rarely, further samples could still be collected when clinical suspicion remained high even after 6 hours from patient admission. This previous timing for sample collection was then maintained after introducing the HS-cTnI immunoassay. Nevertheless, in accordance with current guidelines (5), the EPs were instructed that in the vast majority of cases the 2nd sample (i.e., collected 3 hours from admission) shall be considered “diagnostic” (i.e., allowing safe diagnosis or rule out of AMI), thus making additional (later) testing almost unnecessary.

The months closer to the shift from the contemporary-sensitive to the HS-cTnI immunoassay were excluded from statistical analysis in order to allow a

sufficient period of customization with the new test. Therefore, all records of patients visited in the ED of the University Hospital of Parma for whom at least one cTnI test had been ordered between October 1st, 2017 and March 31st, 2018 (i.e., the semester before the immunoassay was changed), and between October 1st, 2018 and March 31st, 2019 (the semester after the immunoassay was changed) were extracted from the local hospital information system (LIS). The following data were analyzed throughout the study periods: (a) total number of cTnI tests ordered; (b) total number of blood samples collected; (c) total number of CK-MB tests ordered; (d) number of patients with the first HS-cTnI value below the limit of detection (LoD) who have been ruled out without additional tests, and (e) number of patients exhibiting either HS-cTnI values below LoD or comprised between the LoD and the URL, for whom a second HS-cTnI sampling was requested.

The statistical analysis was then carried out with Analyse-it (Analyse-it Software Ltd, Leeds, UK) and MedCalc statistical software (MedCalc Software, Ostend, Belgium). Due to the retrospective nature of the study and the maintenance of anonymity of all subjects, the consensus of the ethical committee was unnecessary. The study was performed in accordance with the Declaration of Helsinki and under the terms of relevant local legislation.

Results

The total number of ED visits during the two study periods is summarized in table 1. Although a modest increase of total ED visits occurred between the two semesters when contemporary-sensitive (first semester) or HS-cTnI (second semester) were used (+ 659; +1.1%), a considerable decrease were recorded in the total number of cTnI tests during the second semester (-779; -7.6%). This decline was even more evident when data were normalized for the number of total ED visits (see Table 2). Overall, the relative decrease of cTnI tests was 10% after introduction of HS-cTnI immunoassay in the second semester ($p < 0.001$).

The number of samples collected from each ED patient during the two different semesters (before and after introducing HS-cTnI), is shown in table 3. A substantial reduction of single-sample test requests was noted, accompanied by a considerable decline of 3- and 4-sample collections (i.e., -61% and -73%, respectively), thus reflecting a higher number of patients who could be ruled out with only two samplings in the semester after the HS-cTnI immunoassay was implemented. Out of the 6281 patients with a single HS-cTnI value, 1731 displayed a value <LoD at admission (27.5%), which together with low clinical risk would have permitted safely discharge, thus significantly contributing to reducing overcrowding in the ED. The val-

Table 1. Number of emergency department (ED) visits and cardiac troponin I (cTnI) tests during the two-study period, before (October 2017 to March 2018) and after (October 2018 to March 2019) introducing the high-sensitivity (HS) technique

Period	ED visits			cTnI tests in the ED		
	Before HS-cTnI	After HS-cTnI	Variation	Before HS-cTnI	After HS-cTnI	Variation
Year	2017	2018		2017	2018	
October	10112	10017	-0.4%	1642	1495	-8.9%
November	9356	9204	-1.6%	1625	1535	-5.7%
December	10020	9654	-3.6%	1730	1576	-9.0%
Year	2018	2019		2018	2019	
January	10120	10122	=	1861	1753	-6.0%
February	9011	9685	+7.5%	1548	1568	+1.2%
March	9750	10346	+6.1%	1825	1525	-16.5%
Total semester	58369	59028	+1.1%	10231	9452	-7.6%

HS-cTnI, high-sensitivity cardiac troponin I

Table 2. Percentage (%) of cardiac troponin requests on total emergency department (ED) visits before (October 2017 to March 2018) and after (October 2018 to March 2019) introducing the high-sensitivity (HS) technique

Period	Percentage (%) of cardiac troponin requests on total ED visits		Odds ratio (95% CI)
	Before HS-cTnI	After HS-cTnI	
Year	2017	2018	0.90 (95% CI, 0.84-0.98; p=0.010)
October	16.2	14.9	0.95 (95% CI, 0.88-1.03; p=0.210)
November	17.4	16.7	0.93 (95% CI, 0.87-1.01; p=0.078)
December	17.2	16.3	0.93 (95% CI, 0.87-0.99; p=0.047)
Year	2018	2019	
January	18.4	17.3	0.93 (95% CI, 0.86-1.01; p=0.070)
February	17.2	16.2	0.75 (95% CI, 0.67-0.81; p<0.001)
March	18.7	14.7	0.90 (95% CI, 0.84-0.98; p=0.010)
Total semester	17.5	16.0	0.90 (95% CI, 0.87-0.93; p<0.001)

HS-cTnI, high-sensitivity cardiac troponin I

Table 3. Number of blood sampling in emergency department patients in whom at least one cardiac troponin I (cTnI) test was requested

	Before HS-cTnI		After HS-cTnI		Odds Ratio (95% CI)
	N.	%	N.	%	
Only one sample	7572	74.0	6381	67.5	0.73 (95% CI, 0.69-0.78; p<0.001)
Two samples	1282	12.5	2562	27.1	2.60 (95% CI, 2.41-2.80; p<0.001)
Three samples	1210	11.8	467	4.9	0.39 (95% CI; 0.35-0.43; p<0.001)
Four samples	167	1.6	42	0.4	0.27 (95% CI, 0.19-0.38; p<0.001)
Total	10231	100	9452	100	-

HS-cTnI, high-sensitivity cardiac troponin I

Table 4. Distribution of high-sensitivity cardiac troponin I (HS-cTnI) values in emergency department patients in whom a second blood sample was requested

HS-cTnI value	Number	%
<LoD	403	15.7%
>LoD and <URL	1229	48.0%
- In women	- 460	- 17.9%
- In men	- 769	- 30.1%
>URL	930	36%
Total	2562	100%

LoD, limit of detection; URL, 99th percentile of the upper reference limit; HS-cTnI, high-sensitivity cardiac troponin I

ue of HS-cTnI in patients in whom a second test was requested is shown in table 4. Overall, 36% of these patients displayed a HS-cTnI value >URL, whilst 48% exhibited a value comprised between LOD and URL (17.9% women, 30.1% men) and 15.7% <LOD, respectively.

Despite the new HS-cTnI assay has a cost per test slightly higher than that of the former contemporary sensitive technique (1.02 versus 0.96€, based on the local tender), the lower number of tests led to a significant reduction in the cumulative cost of cTnI assessment in the local ED (from 9821 to 9603€; -2.2%), which decreased by further 100€ considering also the lower number of tubes collected after introducing the

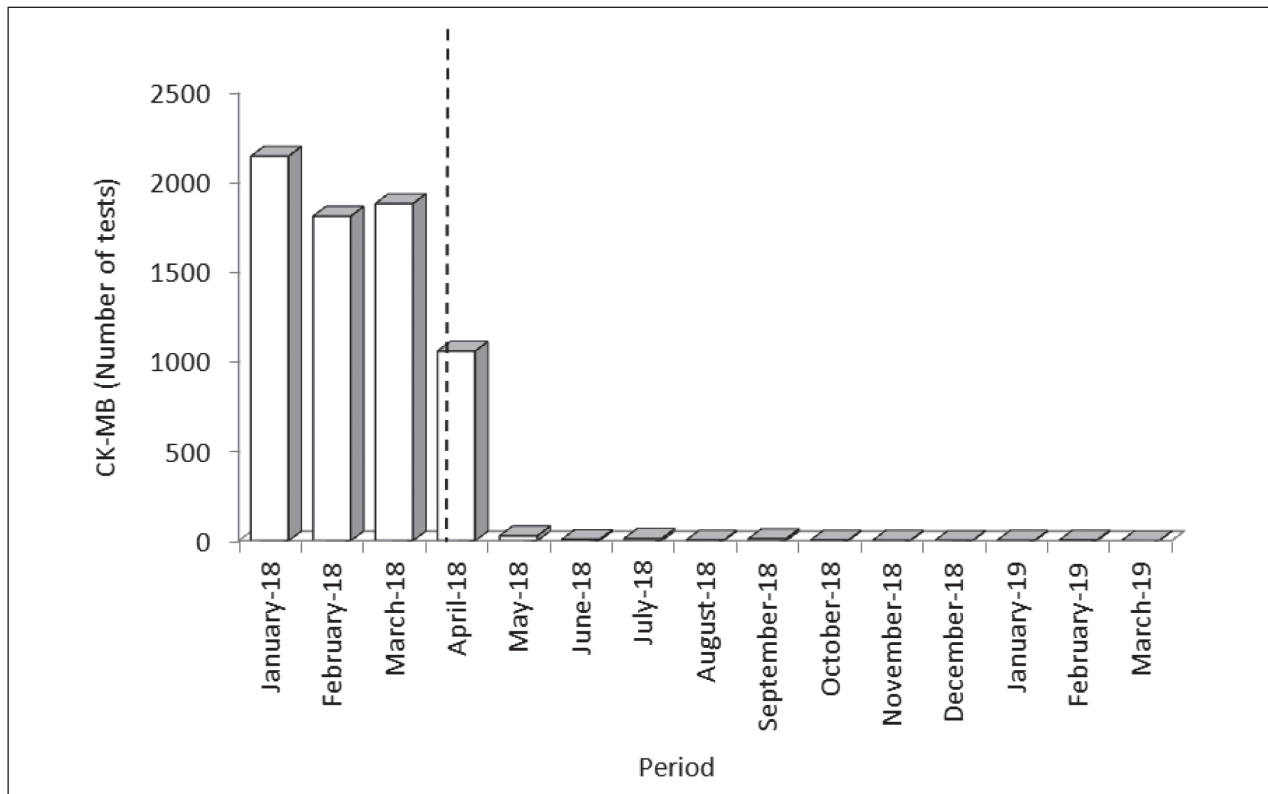


Figure 1. Graphical representation of the drop in creatine kinase MB (CK-MB) requests from the emergency department after shifting toward HS-cTnI. The dotted line defines the day of introduction of HS-cTnI immunoassay. CK-MB, creatine kinase MB

HS-cTnI immunoassay (i.e., final estimated saving, -3.2%). The trend of CK-MB test requests made in the ED is summarized in figure 1. A collapse can be observed in the overall number of requests, then stabilizing around 2 requests per month (between October 2018 and March 2019). In the period limited to the trimesters before and after the introduction of HS-cTnI, the overall number of requests for CK-MB declined by over 90% (OR, 0.098; 95% CI, 0.091-0.106; $p < 0.001$). From an economic point of view, these results entail remarkable savings since the overall budget for CK-MB can be estimated to decrease from 23811 to 40€ per year (-99.8%) in the local laboratory.

Discussion

Although the HS-cTn immunoassay have only been developed around 10 years ago, and despite an

overwhelming burden of recent data, several clinicians are still reluctant to accept the evidence supporting the analytical and clinical advantages of using HS-cTn immunoassays and remain hesitant to implement these methods into clinical pathways (15). Several factors have lead clinicians to use terms such as “troponin leak”, “false-positive” troponin elevation, or “troponinemia”. These terms are trivial and reflect only evidence of confusion and “fear of the unknown” so that they shall be avoided (16, 17).

In agreement with previous evidence (18-20), the results of our study confirm that, in a real-world setting, the better diagnostic accuracy of HS-cTnI may also improve ED efficiency and decrease the overall costs, which is an additional aspect in favor of introducing HS techniques for more timely and accurate management of patients admitted to the ED with symptoms suggestive of ACS. Another remarkable advantage was the possibility to persuade the local clinicians that us-

ing a HS-cTnI immunoassay, then CK-MB could be considered redundant or obsolete and could be safely abandoned. This paradigm shift has been unsuccessfully attempted many times before, when the contemporary-sensitive immunoassay was still in use (21), although it could only be concretized after introducing the HS method and the relative guidelines (5). Notably, the introduction of the HS cTnI immunoassay not only was effective to collapse the number of CK-MB test requests but also generated a favorable return on investment for cTnI testing. However, additional efforts shall be promoted among EPs to operate following the current guidelines for HS-cTnI testing and for harmonizing the practices, whereby the number of potentially inappropriate second blood sample collections remained extremely high (i.e., ~64%) even after introducing the HS-cTnI immunoassay.

Considering that the ED environment is worldwide increasingly overcrowded, further studies on a real-world clinical, economic, and organizational impact of the introduction of the new HS-cTn assays should be prioritized to give clinicians the best tools to rule out patients presenting to EDs with suspicion of ACS. This fact would help EPs to avoid that the increasing burden of ACS around the world would be translated into a “perfect storm” in the ED (22).

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