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Implementation of high sensitivity troponin into routine clinical practice - results of the extended CARdiac MArkers guideline uptake in Europe group (CARMAGUE) survey

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ABSTRACT

Background: Measurement of cardiac troponin (cTn) by a high sensitivity method is now the recommended strategy for the detection of myocardial injury. An international survey was undertaken to assess how this has been implemented.

Methods: A questionnaire based around 14 domains on cardiac biomarkers was distributed electronically with the aid of professional societies accessed by a web link within the invitation. Results were returned electronically then extracted into a relational database for analysis.

Results: Responses were obtained from 663 laboratories across 76 countries ranging from 1 to 69 largest country. The majority of responses (79.6%) came from the European area. Responses were grouped into broad geographic areas for analysis. Most responses came from hospitals providing a local and regional service of which the majority provided angioplasty. cTn measurement was the dominant biomarker. The majority of laboratories include creatine kinase (CK) in their cardiac profile and approximately 50% also offer the MB isoenzyme of CK. The majority of laboratories (91.9%) measure cTn by a high sensitivity method. Sex specific reference ranges were typically implemented for cardiac troponin I but not for cardiac troponin T. The preferred unit of measurement was nanograms/L. A structured decision-making pathway utilising high sensitivity cTn measurement was used by 83.3% of laboratories who responded. Single sample rule out is common but the majority used serial sampling strategy based on measurement on admission and three hours.

Conclusions: Measurement of cTn by a high sensitivity method is now well established internationally, the use of rapid diagnostic protocols lags behind.

Abbreviations: cTn, Cardiac troponin; hs-cTn, High sensitivity cardiac troponin; CK, Creatine kinase; CK-MB, Creatine kinase MB isoenzyme; UDMI, Universal Definition of Myocardial Infarction; EFLM, European Federation of Clinical Chemistry and Laboratory Medicine; IFCC, International Federation of Clinical Chemistry, and Laboratory Medicine; ACVC, Association for Acute Cardio Vascular Care; AACC, American Association for Clinical Chemistry; ADLM, Association for Diagnostic and Laboratory Medicine; IQA, Internal quality assurance; EQA, External quality assurance.

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1. Introduction

The measurement of cardiac Troponin (cTn) by high sensitivity methods (hs cTn) is now the preferred biomarker for the detection of acute myocardial injury. Troponin measurements are integrated in the Universal Definition of Myocardial Infarction (UDMI) [1] and endorsed in the guidelines of cardiac societies internationally [2]. Previous European surveys have shown the switch to cTn and confirmed the near universal uptake of high sensitivity methods [3–7]. Laboratories either currently use high sensitivity methods or intend to switch to them. Internationally, the barriers to introduction/ have proved to be either regulatory, most noticeably in the United States, or financial, where introduction of cTn measurement is seen as more expensive than measurement of other cardiac biomarkers such as creatine kinase (CK) or its MB isoenzyme (CK-MB). The most important attribute of hs cTn assays is the ability to support very rapid confirmation and exclusion of acute myocardial injury. In the most recent audit we have therefore concentrated on assessing the use and implementation of hs cTn assays.

2. Methods

We conducted an international online survey on the use of cardiac biomarkers for the diagnosis of myocardial infarction. The basic questionnaire design was agreed by the authors and then implemented through a web based system. The survey was designed for use by a group including clinical laboratory staff, Emergency Department staff and cardiologists. Only the responses from laboratory staff are reported here. The basic design was a set of pages which comprised 16 separate topics covering biomarker use, methodology and clinical application. The survey consisted of fourteen unique question stems with the number of stems shown varying from five to fourteen depending on participant responses. Questions covered cardiac biomarker repertoire and the clinical strategies currently in use in the organisations polled. A full description of the survey methodology is included as supplementary appendix 1 together with a survey map in supplementary appendix 2. The survey included questions to ensure data consistency by asking the same question in a different way as well as structuring responses to minimise incorrect data being supplied.

The invitation to participate in the survey was distributed electronically by email and by direct advertising. The survey was distributed to members of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM), the International Federation of Clinical Chemistry, and Laboratory Medicine (IFCC), the Association for Acute Cardio Vascular Care (ACVC) and American Association for Clinical Chemistry (AACC, now the Association for Diagnostic and Laboratory Medicine) via society mailing lists and newsletters as well as personal contacts.

The survey was initially launched in Europe in February 2022 and then in the USA in July 2023. The survey was hosted by the University of Edinburgh in English and was conducted in line with local ethical standards. The survey was openly available online and distribution outside of the above societies was encouraged by participants.

The University of Edinburgh uses an external company, Jisc Online Surveys, through which the survey was created, hosted and accessed by external users. Administrative access to the survey (the person who can alter, distribute and view the results of the survey) was held by one of the research group (MTHL) and accessed using a unique login and password linked to his University of Edinburgh staff account. Each survey was given a unique web URL which is how it was accessed by participants. Participants had to agree to the anonymous storage and use of survey responses in accordance with General Data Protection and Regulation (GDPR) guidance prior to participation in the survey. Anonymised data responses were held by Jisc and accessed via a secure account. To analyse the data, it was downloaded from Jisc into a secure desktop (one which requires a password to access) approved by the University.

Data was extracted as an excel file and transferred to a relational database (Microsoft access) for coding and interrogation. Data interrogation included checking that responses to the same category of question were consistent as a means of internal quality assurance. In particular, crosschecking between questions on page 5, 7 and 11 of the questionnaire (supplementary appendix 1). Statistical analysis was performed using the Analyse-It add in for Excel. Nonparametric statistics were used throughout. Absolute numbers are reported and percentages used for proportions to compare responses. Chi Square test or Fisher Exact test were used as applicable for statistical comparisons of tables.

3. Results

3.1. Response rate and hospital type

Responses were obtained from the 663 laboratories across 76 countries. In terms of numbers of laboratories responding per country, 48 countries had >=3 responding laboratories and 21 had >=10. A detailed breakdown by country is shown in Supplementary Table 1. Assessing absolute response rate is difficult as a number of laboratories have now formed laboratory networks covering more than one hospital with a standardised approach to analytes and equipment. Hence, for Finland one response may cover six hospitals. Results were aggregated by geographic regions into Europe, Asia, Africa, South America and Australasia. North America was divided into United States of America and Canada as there is a different regulatory approach that would significantly affected uptake and use of high sensitivity troponin as is noted in previous surveys. Analysis of results was by considering the survey responses overall, then comparing Europe with the rest of the world. As there were only 8 responses from Canada and 2 responses from Australasia, these were combined with the European data for some of the analysis as clinical, laboratory practices and regulatory practices are aligned with European models. Mexico was combined with responses from South America and the Caribbean. 79.6 % of responses came from the European area. Results were consistent in response when cross correlated.

482/663 (72.7 %) of responses were from hospitals providing both regional (tertiary referral) and local care with 181/663 (27.3 %) providing local care only. As can be seen from supplementary Fig. 1, the pattern of responses was different between Europe and the Americas and Africa and Asia. Although overall the distribution of responses was the same with the majority coming from hospitals with combined regional and local care, pairwise comparison showed that proportionally more centres in Europe and the Americas ($p = ns$ for Europe vs USA or South America, $p = 0.007$ Europe vs Africa plus Asia) responded from regional and local care compared to Africa and Asia. The provision of angioplasty was more common in centres providing both regional and local care. Overall this was available in 313/482 (64.9 %) of centres providing regional and local care compared to 43/181 (23.8 %) of those providing local care only ($p < 0.0001$). For Europe 402 undertook regional and local care of which, 257/402 (63.9 %) undertook angioplasty compared to 34/136 (25.0 %) of those providing local care only ($p < 0.0001$). By region, a similar distribution of angioplasty provision was seen (regional and local vs local, $p < 0.0001$ Supplementary Table 2 and supplementary Fig. 2).

3.2. Cardiac biomarker service

The provision of different cardiac biomarkers was remarkably consistent across all respondents. Cardiac troponin was provided by 649/663 (97.9 %) overall, varying by region from 95.8 % to 100 %. The distribution of provision of biomarkers overall and by region is shown in Fig. 1 below. The distribution between regions was not statistically significantly different. The range of markers offered over time for survey results from Europe alone is shown in Fig. 2 (upper figure) and comparison of previous studies with the current survey is shown in the lower

figure. Both sets of results show a significantly different distribution ($p < 0.0001$ for trend, both figures). There is an increase in the number of laboratories offering creatine kinase (CK) and myoglobin as part of their cardiac profile. Both sets of results however show that although there is an increase in laboratories offering the CK MB isoenzyme (CK-MB) this has not changed significantly since 2013 (p value for trend not significant).

Although a range of other biomarkers are offered, cardiac troponin remains the primary biomarker of choice in Europe (including Canada and Australasia) in 513/538 (95.4 %) and overall 623/663 (94.3 %). Laboratories not offering cardiac troponin as the main marker offer CK, CK-MB and myoglobin. This data is shown in Supplementary Fig. 3.

Examining the countries that do not offer troponin in the European area, they are those with a less well-developed economy although one laboratory in Germany reported offering CK-MB as its main biomarker. In the rest of the world surprisingly one laboratory in the United States reported offering CK as its main marker. There is discordance between the range of cardiac biomarkers offered and the main biomarker. For Europe (including Canada and Australasia), 527/538 have troponin but only 513 offer this as the main marker. In the remaining 14, troponin is available but as a secondary test. In the remaining 11 laboratories, CK or CK-MB only is available. In the rest of the world, of the 13 not offering troponin as a primary marker, 11 offer it as a secondary marker (including the one US hospital offering CK as the primary cardiac biomarker).

Data on the type of troponin assays was available for 522/538 (no data reported for 16) for Europe/Australasia/Canada and for 644/663 overall (no data reported for 19). In the laboratory, measurement was by a high sensitivity method (592/644, 91.9 %) with 29 (4.5 %) using a conventional sensitive assay and 23 (3.6 %) using point of care testing (POCT) but there were marked differences between different regions. POCT was used more extensively in Asia and Africa ($p < 0.0001$) and conventional sensitive troponin was used more commonly in all of the other regions except Europe/Australasia/Canada ($p < 0.0001$). The survey specifically asked what was the main method used in the Emergency Department (ED). Here POCT was more commonly used but this increase was only significant ($p = 0.0002$) outside Europe/Australasia/Canada and was most marked in Africa (Fig. 3). Data on whether a high sensitivity POCT was used was not captured.

592/644 (91.9 %) laboratories used a high sensitivity cardiac troponin assay. Data on the implementation of sex specific reference ranges was obtained from 542 respondents (5 did not respond, 45 did not know). Of the 542 who responded, 8 did not specify which type of troponin (cTnT or cTnI) they measured leaving 534 responses which could be analysed. 293/534 (54.9 %) had implemented sex specific reference ranges. There was a marked discrepancy between laboratories utilising hs-cTnT 71/234 (30.3 % implementation) compared to hs-cTnI 219/300 (73.0 % implementation). Differences in implementation of sex specific reference ranges between hs-cTnT and hs-cTnI were highly

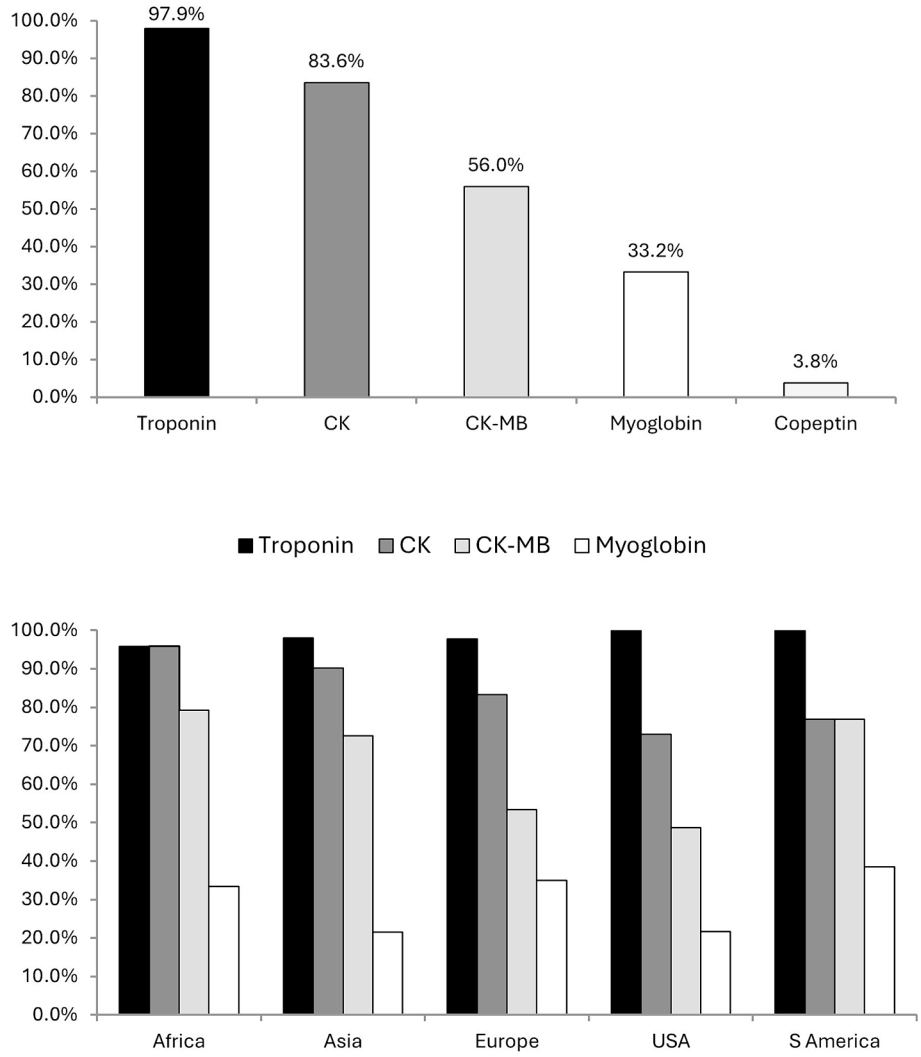

Fig. 1. Biomarkers offered overall (upper panel) and by region (lower panel). CK = creatine kinase, CK-MB = creatine kinase MB isoenzyme, USA = United States of America, S. America = South America.

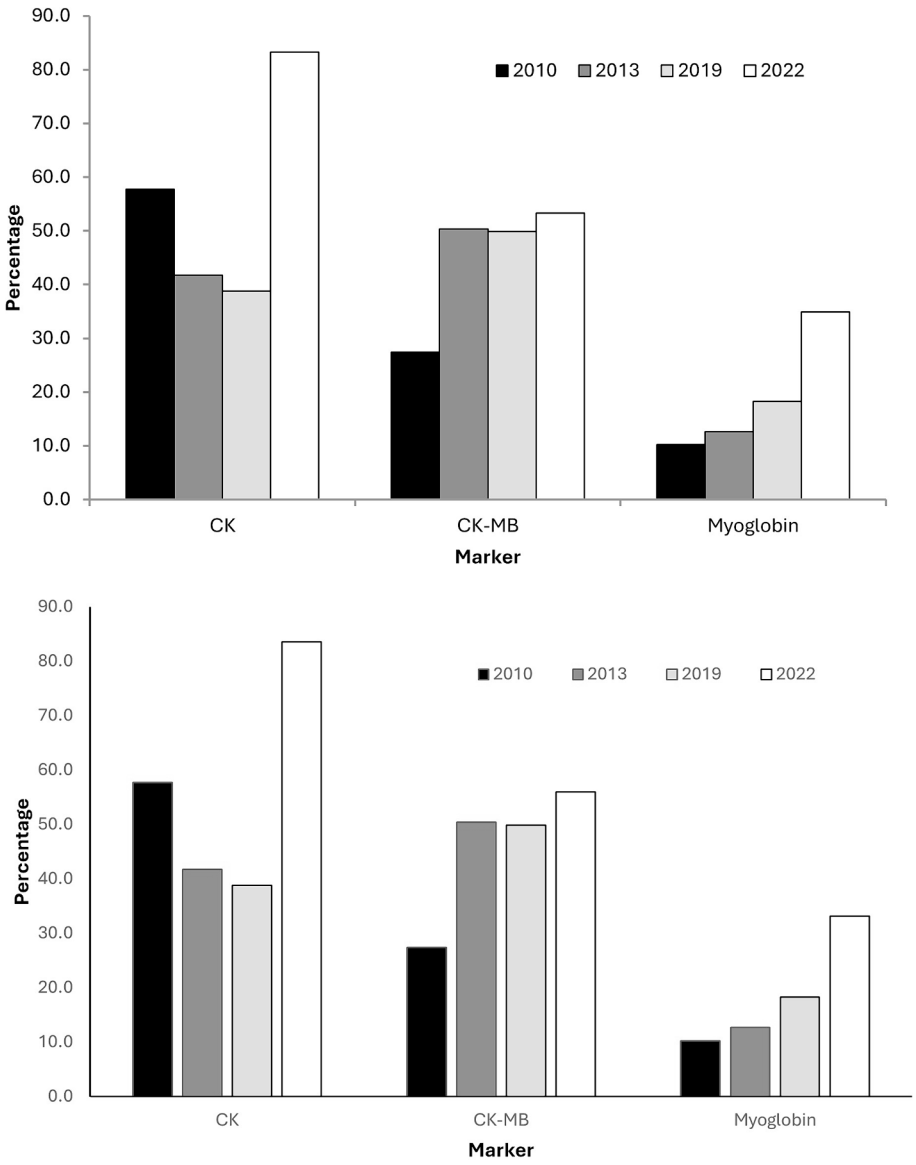

Fig. 2. Trends in biomarkers offered as part of the cardiac profile for Europe (upper panel) and compared with all data (lower panel). CK = creatine kinase, CK-MB = creatine kinase MB isoenzyme.

significant overall ($p < 0.0001$) and for Europe/Australasia/Canada ($p < 0.0001$) and the rest of the world ($p = 0.026$). 451 laboratories supplied data on the units they used (141 did not respond). The majority, 428 (94.9 %) reported in nanograms/L with the remainder reporting micrograms/L. Only limited data was available on the values used for the 99th percentile with meaningful data only available for hs-cTnT and the Abbott hs-cTnI assay. For those reporting sex specific 99th percentiles, there was a broad spread of values for the hs-cTnT assay with peaks at 16 ng/L and 22 ng/L in males ($n = 30$) and 9 ng in females ($n = 24$). In contrast, for hs-cTnI the male range was 34–36 ng/L in 79 % of respondents ($n = 93$) and the female range 15–17 ng/L in 80 % of respondents ($n = 93$). For hs-cTnT the non-sex-specific 99th percentile was 14 ng/L in 64.5 % ($n = 214$) but with a very broad spread of values. This data is shown in supplementary figures 4–8.

3.3. Turnaround time and clinical decision pathways

613/663 reported laboratory turnaround time (TAT) data (defined as time from sample receipt to result report) of which 568/592 reported the TAT for hs-cTn. This data is summarised in Table 1. The majority of laboratories report a TAT of 30–59 min. 351/663 (52.9 %) used a structured pathway, 123/663 (18.6 %) did not and 189/663 (28.5 %) were unaware if the pathway in use in the hospital.

A range of biomarkers and techniques were in use (Table 2) but the majority (83.5 %) were based on high sensitivity troponin.

The pathway used was based on a published or validated algorithm in 88.6 % of the respondents (88.4 % Europe, 89.7 % outside Europe). Of the 351 who responded 246/283 (86.9 %) in Europe used a hs-cTn based pathway. This compared with 269/317(84.9 %) of respondents in the previous survey (ns). 47/68 (69.1 %) of the non-European countries used hs-cTn based pathways. This was not statistically significantly different (Fisher) from the European data although Australasia and Canada used exclusively hs-cTn based pathway but the numbers are small. Of the 293 using hs-cTn based pathways, in Europe, a single sample rule out strategy was used in 152/246 (61.8 %) respondents compared to 56/269 (20.8 %) in the 2019 survey ($p < 0.0001$). In the rest of the world 29/47 (61.7 %) used single sample rule out. Most protocols stipulate a minimum interval between onset of chest pain and sample draw for interpretation of troponin results. Overall, the minimum time required from chest pain onset to time when a definitive

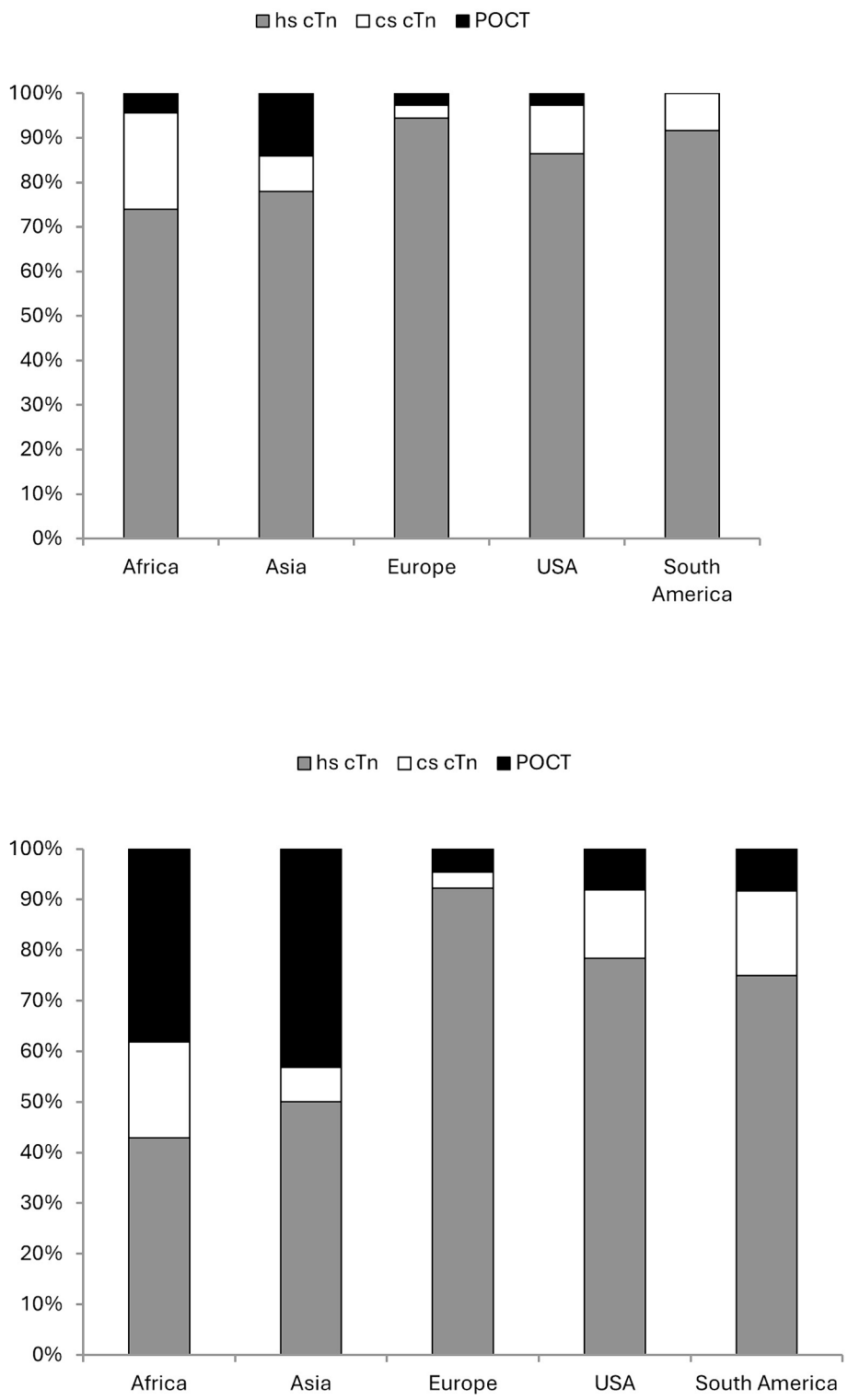

Fig. 3. The distribution of troponin methods by geographic area in the main laboratory (left panel) and used by the Emergency Department (right panel). USA = United States of America.

interpretation of a troponin result can be performed was documented in 204 and for those that utilised single sample rule out in 181. Although the modal answer was 3 h there was a great deal of variability with some laboratories not stipulating a minimum time from onset of chest pain before first definitive interpretive result. The responses are summarised in Table 3 below.

The choice of rule out cut off was only available for a small number of respondents. For hs-cTnT, a value of 5 ng/L (58 1 %) or 14 ng/L (27.4 %) was used and for hs-cTnI (Abbott) the dominant value was 5 ng/L (54.2 %). This data is shown in supplementary figures 9 and 10. Rapid serial sampling based on measurement at 0–1 h or 0–2 h occurred in 98/246 (39.8 %) of pathways in the current survey compared to 56/269 (20.8 %) in 2019 ($p < 0.0001$). However, a majority are still using a 0–3 h pathway. The use of a delta value was reported in 183/293 (62.5 %), this is 61 % in Europe and 70.2 % in non-European countries with 44.3 % using an absolute delta, 35.5 % a relative delta with 20.2 % not stating what type was used.

Table 1
Turnaround time for all cardiac biomarkers and for high sensitivity cardiac troponin only.

TAT- minutes	All biomarkers, n (%)	hs cTn only, n (%)
<30 min	121 (19.7)	106 (18.7)
30—59 min	406 (66.2)	381 (67.1)
60—89 min	61 (10.0)	60 (10.6)
90—119 min	16 (2.6)	15 (2.6)
≥120 min	9 (1.5)	6 (1.1)
Total	613	568

Table 2
Biomarkers and strategies reported in a structured decision-making pathway for management of chest pain.

Biomarker	n (%)
Contemporary troponin	9 (2.6)
Creatine-kinase MB	6 (1.7)
Don't know	3 (0.9)
High-sensitivity troponin	293 (83.3)
Multiple (including troponin)	31(8.8)
Myoglobin	2 (0.6)
No biomarker used	2 (0.6)
Point of care troponin	5 (1.4)

In the 293 respondents using hs-cTn as part of a structured diagnostic pathway (Table 2), 151 reported that follow-up strategy for troponin values between the rule-in and rule out cut-offs (often referred to as the grey zone or indeterminate values). 40 did not have a follow-up strategy and 102 were unaware of the subsequent investigations. Imaging occurred in 37 (24.5 %), hospital admission in 95 (62.9 %) and repeat troponin testing in 94 (62.3 %). Repeat troponin testing was reported at 1 (8.5 %), 2 (25.5 %), 3 (43.6 %), 6 (18.1 %) and 12 (2.1 %) hours and was unspecified in 2.1 %.

In the 649 laboratories measuring troponin, 607/649 (93.5 %) reported using internal quality assurance (IQA). 15 (2.3 %) did not and no data was available for 27. When laboratories using POCT (21) were excluded, the results were similar with 596/628 (94.9 %) using IQA. Comparing use of IQA by region, proportionately more countries in the Europe/Canada/Australasia group did not use IQA ($p = 0.0002$, chi-squared) but this result may be biased by results from one single European country. 561/649 (86.4 %) participated in external quality assessment (EQA) schemes, 53 (8.2 %) did not and no data was available in 35. Excluding POCT, the results were essentially similar with 554/628 (88.2 %) participating and 45 (7.2 %) not participating and no data in 29. Results were markedly different by geographic region ($p < 0.0001$, chi-squared) and with European countries being the worst participants in EQA schemes and 100 % participation from the US, Canada and Australasia. Significantly fewer participated in EQA than IQA ($p < 0.0001$, chi-squared).

Table 3
Minimum time from onset of symptoms to time of first definitive troponin result for all protocols (204/351) and for single sample rule out (181/351).

All		Europe		Non-European countries	
All protocols					
Chest pain duration	n (%)	Chest pain duration	N (%)	Chest pain duration	n (%)
1 h	45 (22.1)	1 h	40 (24.1)	1 h	5 (13.2)
2 h	32 (15.7)	2 h	27 (16.3)	2 h	5 (13.2)
3 h	67 (32.8)	3 h	51 (30.7)	3 h	16 (42.1)
6 h	24 (11.8)	6 h	17 (10.2)	6 h	7 (18.4)
No	34 (16.7)	No	30 (18.1)	No	4 (10.5)
Other	2 (1.0)	Other	1 (0.6)	Other	1 (2.6)
Total	204		166		38
Single sample rule out protocol					
Chest pain duration	n (%)	Chest pain duration	n (%)	Chest pain duration	n (%)
1 h	42 (23.2)	1 h	37 (24.3)	1 h	5 (17.2)
2 h	29 (16.0)	2 h	24 (15.8)	2 h	5 (17.2)
3 h	59 (32.6)	3 h	46 (30.3)	3 h	13 (44.8)
6 h	18 (9.9)	6 h	16 (10.5)	6 h	2 (6.9)
No	31 (17.1)	No	28 (18.4)	No	3 (10.3)
Other	2 (1.1)	Other	1 (0.7)	Other	1 (3.4)
Total	181		152		29

4. Discussion

The principal findings from this survey extend the data from the survey published in 2019 and confirms some of the previously noted trends. In addition, it provides some insight to allow comparison with clinical practices in the geographic regions although the data is limited. First, cardiac troponin measurement is now the accepted primary diagnostic test with measurement by high sensitivity methods. Second, a range of other cardiac biomarkers remain in routine clinical use. Third, the clinical application of high sensitivity troponin measurements that utilise the capacity for early diagnosis is not yet standardised or fully realised. Fourth and finally, there remains a lack of communication and engagement between the laboratory and the clinicians.

The use of troponin as the preferred cardiac biomarker was initially recommended in the redefinition of myocardial infarction and subsequently confirmed as the biomarker of choice by the universal definition of myocardial infarction and its subsequent amendments. In routine laboratory practice this recommendation has been fully implemented. The only exceptions occur where financial constraints occur, where measurement of CK has been retained. Such laboratories may also utilise the inexpensive measurement of CK-MB activity. As the cost economics of efficient patient management strongly favour the use of cardiac troponin in clinical management algorithms and the cost per test has now fallen significantly it is difficult to see why this occurs although economic factors and poor logistics may outweigh other benefits. Alternatively, local factors may mean that rapid diagnosis is not considered a priority due to lack of management options such as rapid access to angioplasty. In the previous survey the majority of laboratories were already using a high sensitivity assays or intending to change. In the current survey this trend has been confirmed. In addition, manufacturers are only retaining the previous generation of assays where they are unable to sell the high sensitivity versions. As pricing of the two versions of the assays are similar and the analytical and clinical advantages are now well documented, is expected (and recommended) that high sensitivity assays should be the only ones in routine clinical use. This is reflected by laboratory practice in Europe and probably accounts for the slower utilisation of high sensitivity assays notably in the United States where introduction was significantly delayed by regulation. Previously, other studies have noted variable uptake of high sensitivity assays and different patterns of utilisation [8,9] although this appears less marked in Europe.

In the current survey the utilisation of CK measurement was higher than previously documented. This value represents the changing questionnaire design. All laboratories retain measurement of CK or myoglobin for musculoskeletal disease and this is usually included within the cardiac marker group. Interestingly, the measurement of CK-MB remains significant and largely unchanged at around 50 % of the responding laboratories. This is despite recommendations that the measurement of CK-MB is no longer considered clinically appropriate [10]. Informal discussions with colleagues suggests retention of CK-MB

is not the choice of the laboratory but that of requesting clinicians and a dialogue with the object of clinician education with the objective of removing CK-MB should be facilitated by the laboratory.

The key value of high sensitivity troponin measurement is the ability to perform single sample rule out on first admission to the Emergency Department (ED). Studies have shown this can be achieved in up to 50 % of chest pain patients [11–13]. The current survey shows that there is a significant improvement in the use of single sample rule out strategies but implementation is by no means universal. Similarly, less than 50 % of hospitals are using rapid serial sampling (0–1 h or 0–2) whilst less than 50 % use an absolute delta value as recommended by current guidelines. Similarly, for cardiac troponin T which allows between hospital comparison, there is still significant utilisation of the 99th percentile as the rule out decision limit. This is consistent with other surveys of biomarker utilisation which show wide variation in practice [9,14].

In this study the specific question of clinical engagement and laboratory participation in protocol development was not specifically asked unlike in 2019. However, a number of respondents were unaware of the clinical services on offer in their own institution. The lack of knowledge of what diagnostic protocols were being used by the local clinicians suggest interdisciplinary communication a significant challenge and could also represent an opportunity of multidisciplinary exchanges that will benefit the patient. In the near future it is likely that the implementation of POCT systems will significantly expedite the application of rapid diagnostic algorithms in the ED. A key factor for implementation of such systems is close laboratory and clinician collaboration in order to maintain analytical quality. It is an absolute necessity to have close collaboration and awareness of the protocols used in clinical services over all the region.

5. Study limitations

In a survey of this kind, data is provided by those who are motivated to respond. It is notable that the survey received more responses from regional centres which also supplied the majority of angiographic services. The majority of the responses were from European laboratories but nevertheless this provides a reasonable snapshot of the current state and suggests those areas where educational intervention may be of benefit. Although some apparently inconsistent results were obtained these were very few and responses were accepted as representing the understanding of the participating laboratories, even if they seem apparently incorrect. A further factor to consider is the number of respondents from an individual country. Although the largest single response was from the UK, this only comprised 12.8 % of the total and comparison of pattern of answers with similar countries did not show any significant differences.

CRediT authorship contribution statement

Paul Collinson: Writing – original draft, Software, Project administration, Formal analysis, Data curation, Conceptualization. **Angelika Hammerer-Lercher:** Writing – review & editing, Formal analysis, Conceptualization. **Kristin Aakre:** Writing – review & editing, Conceptualization. **Damien Gruson:** Writing – review & editing, Conceptualization. **Janne Suvisaari:** Writing – review & editing, Methodology, Conceptualization. **Kari Pulkki:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Sanja Stankovic:** Writing – review & editing, Conceptualization. **Hansjorg Baum:** Writing – review & editing, Conceptualization. **Matthew T. Lowry:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Nicholas L Mills:** Writing – review & editing, Formal analysis, Conceptualization. **Paivi Laitinen:** Writing – review & editing, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [POC: Honoria Siemens Healthineers, Abbott Laboratories; Advisory Boards Radiometer, Psyros diagnostics, LumiraRx, Siemens Healthineers; Consultant to IFCC Committee on Clinical Applications of Cardiac Bio-Markers (C-CB). AHL: Honoraria Siemens Healthineers, Abbott Laboratories; Research support from Abbott Laboratories, Beckman Coulter and Siemens Healthineers. KA: Research Grants Siemens Healthineers, Roche Diagnostics; Consultancy CardiNor; Honoraria Siemens Healthineers, SNIBE; Advisory Boards Roche Diagnostics, Siemens Healthineers, SpinChip; Associate Editor Clinical Biochemistry, Chair International Federation of Clinical Chemistry Committee on Clinical Application of Cardiac Bio-Markers. DG: None. JS: None. KP: None. SS: Honoria Roche Diagnostics, Abbott Laboratories, SNIBE; President Serbian Society for Clinical Laboratory and Science (SCLM). HB: Grants Roche Diagnostics, Beckman Coulter. MTHL Clinical Research Training Fellowships (MR/W000598/1) from the Medical Research Council. NLM Chair Award (CH/F/21/90010), Programme Grant (RG/20/10/34966) and a Research Excellence Award (RE/18/5/34216) from the British Heart Foundation; Honoraria Abbott Laboratories, Siemens Healthineers, Roche Diagnostics; Advisory Boards Psyros Diagnostics, Roche Diagnostics, LumiraDx; Research Support Siemens Healthineers. PL. Chair Science Committee LabQuality Days.].

Data availability

Data will be made available on request.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2024.117900.

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