Guidelines and Recommendations

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Cardiac troponin measurement at the point of care: educational recommendations on analytical and clinical aspects by the IFCC Committee on Clinical Applications of Cardiac Bio-Markers (IFCC C-CB)

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Abstract: The International Federation of Clinical Chemistry and Laboarator Medicine (IFCC) Committee on Clinical Applications of Cardiac Bio-Markers (C-CB) has provided evidence-based educational resources to aid and improve the understanding of important analytical and clinical aspects of cardiac biomarkers. The present IFCC C-CB educational report focuses on recommendations for appropriate use, analytical performance, and gaps in clinical studies related to the use of cardiac troponin (cTn) by point of care (POC) measurement, often referred to as a point of care testing (POCT). The use of high-sensitivity (hs)-cTn POC devices in accelerated diagnostic protocols used in emergency departments or outpatient clinics investigating acute coronary syndrome has the potential for improved efficacy, reduction of length of stay and reduced costs in the health care system. POCT workflow integration includes location of the instrument, assignment of collection and testing responsibility to (non-lab) staff, instrument maintenance, in-service and recurrent training, quality control, proficiency assessments, discrepant result trapping, and troubleshooting and inventory management.

Keywords: cardiac troponin I; cardiac troponin T; educational recommendations; point of care testing.

Introduction

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Committee on Clinical Applications of Cardiac Bio-Markers (C-CB) has provided evidence-based educational resources to aid and improve the understanding of important analytical and clinical aspects of cardiac biomarkers. The present IFCC C-CB educational report focuses on recommendations for

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appropriate use, analytical performance, and gaps in clinical studies related to the use of cTn by point of care (POC) measurement, often referred to as a point of care testing (POCT). The focus is on hs-cTn POCT methods, as only these are suitable for the rapid algorithms discussed in the article.

Definition of point of care testing

Point of care testing is defined as diagnostic testing that is performed at or near to the site of the patient, performed by non-laboratory personnel, with the prompt result leading to a potential change in the care of that patient. This definition means, theoretically, any instrument can be used for POC testing. On the basis of this definition, pragmatically, POC testing can be divided into three classes of instrumentation.

1. Conventional instruments used in a laboratory space immediately adjacent to an acute patient care setting. These types of laboratories are typically referred to as, "hot labs" or "stat labs". Instrumentation is similar to that used in the main hospital central laboratory, although usually a different version of the main laboratory instrument system. There may be a particular need for specific types of utilities, such as power, water (usually deionized) and information technology. They are usually, but not always, staffed by laboratory professionals, and as such may or may not be considered POC. They act as satellite laboratories to the main central laboratory and function at the same level of training, accreditation and quality assurance. They are connected to both the laboratory information system (LIS) and hospital information system (HIS). Analytical evaluation and regulatory compliance are the same as the main laboratory and conform to the same guidelines.
2. Benchtop (or desktop) instruments suitable for either a central clinical laboratory or a smaller decentralized, dedicated workspace. This type of instrumentation does not need dedicated utilities beyond a conventional electrical supply and rarely a dedicated water source is required. Typically, they are not readily portable and not capable of autonomous operation as they require access to an external power supply to function. They are typically connected to a LIS and HIS.
3. Portable instruments which can be easily transported by one individual in person or on a cart/trolley. They are usually, but not inevitably, capable of fully autonomous function as they contain an internal power supply which may use rechargeable or non-rechargeable batteries. Such devices may be used at the patient bedside, deployed on a desktop or may be used for testing outside the hospital environment.

Only the desktop and portable instruments will be discussed further, as central laboratory instrumentation is already covered adequately by current guidelines.

POC testing for cardiac troponin

Current recommendations for the management of patients with suspected acute coronary syndrome (ACS), divides patients into two groups based on the initial electrocardiogram (ECG): (a) those with ST segment elevation myocardial infarction (STEMI) and (b) those where the initial diagnosis is unclear. Guideline recommended measurement of cTn by a high-sensitivity (hs) method is only used to guide management in patients without STEMI [1]. Even in patients presenting with suspected NSTEMI, only the highest ACS risk group, defined entirely by clinical criteria and the ECG, require immediate coronary intervention [1]. Most patients with a final diagnosis of ACS, rather than nonischemic chest pain, fall into medium or low risk ACS groups, with coronary intervention recommended within 24 h in the medium risk ACS group and 72 h in the low-risk ACS group. There is the opportunity to optimize the diagnosis by serial cTn sampling to distinguish acute cTn increases, a rising and/or falling concentration, or chronic, non-changing increased concentration. The focus of cTn testing in suspected NSTEMI is rapid exclusion of myocardial injury as a cause of ischemic symptoms to remove them from the emergency department (ED) and reduce the overcrowding associated with adverse outcomes [2].

The rationale for POC testing is based on:

1. Results are provided in a more, timely manner directly to the clinician responsible for immediate patient care.
2. Testing occurs close to the patient without the need for transfer of samples, allowing testing in a range of healthcare environments including ambulances and rural healthcare/clinics.

It is expected that this will have the following consequences.

1. More rapid decision making to produce more rapid inclusion of patients to appropriate clinical decision-making pathways, expediting and improving the quality of patient care, with improved outcome, shorter stay in acute and non-acute clinical areas, less crowded acute

care areas, shorter stay in the ED and better outcomes [3], although there is also evidence to the contrary [4]. There are caveats. Testing before clinical assessment may produce decision making driven by the cTn concentration rather than clinical pre-test probability. Rapid protocol driven decision making at the expense of clinical assessment may produce a reduction in the quality of care. Rapid decision making may result in a reduction in patient episode cost. This may not be achieved operationally. Hospital systems take time to turn over beds and increased need for personnel involved in bed turnover could paradoxically add cost. Finally, as for other POC tests, increased preanalytical and analytical errors are observed when capillary fingerstick samples are used [5]. Accordingly, there should be defined training about how to obtain samples properly, how to assess if they are adequate and when to not use the sample obtained. Doing this in a comprehensive manner with intermittent oversight of those involved will be important to maintaining appropriate quality control.

2. Clinically focused testing. A care model common to many ED's is panel-based testing in broad clinical categories. Most cTn testing is unselective, with more tests ordered for non-ACS than ACS conditions. A more selective approach to test ordering might be possible with timely test results, reducing inappropriate testing and raising pre-test probability. But a more bespoke testing strategy may be limited by the personnel available to perform the testing.

Role of POC testing for the measurement of cTn

The evidence base for the role of hs-cTn testing has been reviewed [6]. Its impact has been assessed both by modelling [7], meta-analysis [8], and in two recent randomized clinical trials [9, 10]. Implementation of rapid diagnostic, rule-out pathways based on hs-cTn baseline and two, early, serial measurements (0/1 h; 0/2 h) appears both safe and effective. The evidence base for POC cTn testing can be divided into two categories, clinical and methodological/analytical evaluation [11]. Clinical evaluation has largely focused on the ability to match hs-cTn central laboratory methods where diagnosis is based on the sex-specific 99th percentile and not rapid diagnostic rule out algorithms predicated on lower, sex independent cTn concentration decision cutoffs. It is apparent that analytical evaluation of putative hs-cTn POCT assays often does not meet hs-cTn criteria (Table 1).

Table 1: Specific requirements for evaluation of cardiac point of care testing.

Characteristic	Description	Method (citation)	Matrices examined
Limit of blank (LoB)	The highest apparent analyte concentration expected at 95% probability when blank samples containing zero analyte are tested	CLSI EP17-A2 [10]	cTn-free matrix
Limit of detection (LoD)	The lowest cTn concentration reliably distinguished from the LoB (i.e. with 95% confidence)	CLSI EP17-A2 [10]	Whole blood and plasma of primary sample
Limit of quantitation (LoQ)	LoQ is the lowest cTn value which can be measured with desired reproducibility. LoQ is lowest concentration cTn where the % CV=20%	Imprecision curve	Whole blood and plasma of primary sample
High sensitivity imprecision criteria (Part A)	Designation of a 'high-sensitivity' assay requires a % CV≤10% at both the 99th percentiles for both female and male URLs	Imprecision curve	Whole blood and plasma of primary sample
High sensitivity detection criteria (Part B)	Designation of a 'high-sensitivity' assay requires that a cTnI assay measure concentrations in ≥50% of healthy males and ≥50% healthy females above the assay's LoD	>400 healthy males and females and precision studies	
Linearity	The ability to provide results that are directly proportional to the quantity of cTn in a test sample	CLSI EP06-A [11]	Whole blood and plasma of primary sample
Imprecision	Closeness of agreement between independent test results of the same sample obtained under stipulated conditions	CLSI EP05-A3	Whole blood and plasma of primary sample

Table 1: (continued)

Characteristic	Description	Method (citation)	Matrices examined
Analytical specificity	The assay's ability to measure cTn in a testing matrix, that is independent of potential interfering substances/proteins that may be present	CLSI EP07-3rd ed CLSI EP37-1st ed	Whole blood and plasma of primary sample
High dose hook effect examination	A high dose hook effect is a state of antigen excess relative to the antibody probes, resulting in falsely lowered values	cTnI concentrations ranging from LoQ to 100 × 0 the upper measuring range of the assay ng/L	Whole blood and plasma of primary sample
Sample matrix comparison	Agreement of test results between plasma/serum and whole blood including capillary whole blood if being used. Matrices and sample types need to have the same actual cTn concentration	Passing-Bablok and Bland-Altman plots. Samples must span the concentration range with at least 150 across the decision points of the assay with 30 close to the relevant points (rule out very low, rule out low, rule out high, 99th male, 99th female)	Whole blood and plasma of primary sample
Hematocrit dependency assessment	Impact of red blood cell concentration, following haemolysis, in the sample for a measured cTnI concentration	CLSI EP09c	Whole blood and plasma of primary sample
Comparison hs-cTnI methods	Agreement between POC cTn testing method and a clinically validated hs-cTn method for cTnI or cTnT, as appropriate	Pools ranging from LoQ to linear limit compared for hscTn methods	Paired plasma samples

Adapted from [28].

Clinical trials/studies of conventional cTn POC testing

There have been randomized controlled trials (RCTs) and observational studies using cTn POC testing, summarized in Table 2. Six trials examined the impact of rapid provision of laboratory tests on clinical decision-making in the acute care environment using length of stay (LOS). None used hs-cTn POC assays. The results are not consistent with only 3 of 4 judged positive in terms of reduction of LOS. A common finding is reduction in turnaround times through use of POC testing does not necessarily translate to being clinically effective, more rapid process through the patient pathway with equivalent clinical outcome, unless the underlying patient flow has been optimized to the provision of test results. The provision of test results needs to be the time critical component of the patient pathway if clinical impact is to be achieved. An evidence-based review of POC testing in general supports this conclusion [12]. In a previous study where management was prespecified, although based on a protocol utilizing 12 h cTn testing followed by stress testing, provision of results by POC testing substantially reduced length of hospital stay in the rule out group [13]. An important factor was that the central laboratory testing and POC testing showed equivalent diagnostic sensitivity. In the multicenter Randomized Assessment of Treatment using Panel Assay of Cardiac markers (RATPAC) trial, there was a wide variety of outcomes concerning LOS [14, 15] but patient flow was not harmonized between the centers. It is apparent from the RATPAC study that appropriate trial design must pre-specify the management pathway in order to achieve improved patient flow in the target rule-out cohort.

Studies based on single sample rule out have shown a significant percentage of patients can be ruled out on admission testing alone; 30–50% for cTnI [16, 17] and approximately 40% for cTnT [18]. If this is combined with POC testing with a <15 min turnaround time, there is potential for significant improvement in patient flow. Currently, there have been no published studies that have specifically evaluated hs-cTn POC testing and the impact on patient flow in the hospital setting.

> Recommendation 1 – Clinical studies of cTn POC testing should be structured. In multicenter interventional studies, patient pathways should be harmonized to ensure coherent approaches to clinical decision making, informed by POC results.

Clinical validation of hs-cTn measurement by POC testing

There has been a previous retrospective study of single sample rule out using a research cTnI POC assay based on

Table 2: Randomised controlled clinical trials of point of care testing.

Type	Methodology	Cut off	Location(s)	Outcome(s)	Result(s)	Author
Single centre RCT	Roche cTnT CLT vs. cardiac reader POCT	0.2 µg/L	ED referrals to CCU	Length of stay in pre-specified rule out subgroup	Reduction of length of stay in POCT group	Collinson et al. [13]
Multicentre RCT (4 sites)	Abbott iSTAT cTnI		ED	Time to definitive care (discharge home or transfer to inpatient care)	Reduction in time to definitive care in 1/4 sites, no impact on time to transfer in 3/4, no impact on time to discharge in 2/4, increased time to discharge in 1/4	Ryan et al. [34]
Single centre RCT	Siemens stratus CS vs. siemens dimension RxL	0.1 µg/L	ED	Time to treatment Length of stay in the ED	Reduced time to treatment No reduction in ED stay	Renaud et al. [35]
Prospective observational study (3 sites)	Triage (biosite) cardiac panel vs. siemens dimension RxL	0.4 µg/L	ED	Retrospective review of diagnostic accuracy Length of stay	Improved diagnostic accuracy of a multimarker strategy Increased number of discharges before 24 h compared with historical data	Straface et al. [36]
Cluster RCT (2 sites)	Abbott iSTAT vs. Beckman coulter accu I	ns	ED	Length of ED stay	Not significant	Loten et al. [37]
Multicentre RCT (6 sites)	Siemens stratus CS vs. CLT (siemens cTnI ultra, Abbott cTnI, Beckman AccucTnI, roche cTnT)	0.7 µg/L	ED	Discharges before 4 h Length of hospital stay MACE	Increased discharges before 4 h with less admissions MACE equivalent in POCT and CLT groups	Goodacre et al. [14]
Cluster RCT (68 sites)	Roche cardiac reader POCT	0.1 µg/L	Rural primary care centres	Clinical diagnosis	Improved clinical diagnostic accuracy	Tomonaga et al. [38]
Single centre RCT	AQT flex cTnT vs. CLT hs-cTnT	14 ng/L	ED	MACE at 3 months	No significant differences	Asha et al. [39]

RCT, randomised controlled trial; cTnT, cardiac troponin T; CLT, central laboratory testing; POCT, Point of care testing; ED, emergency department; CCU, coronary care unit; cTnI, cardiac troponin I; MACE, major adverse cardiac events; ns, not stated.

stored plasma samples [19]. Further, three systems have been validated against the currently recommended rapid diagnostic algorithms [20–22]. Two studies were retrospective and utilized archived frozen plasma. In neither study was a prospective validation performed using whole blood with real time analysis and comparison with a predicate method. Evaluations using stored samples or even fresh plasma will have significant limitations which need to be acknowledged. Recently, investigators using the first novel POC hs-cTnI assay predicated on whole blood, have derived and validated a low cutoff concentration to identify patients at low risk of index MI at presentation and 30-days, with potential early patient discharge of up to 40% of patients presenting to EDs with symptoms of ischemia [22]. This study meets the appropriate clinical validation of hs-cTn measurement by POC testing, demonstration of clinical equivalence with laboratory-based hs cTn measurement when tested in the real world environment. Ideally testing would be performed by the staff who would use such instrumentation using the intended sample types under real world circumstances. This may not be totally practical but certainly the measurement should not be performed by laboratory trained staff but by the type of operators who might be expected to use the instrumentation in day-to-day patient management.

Finally, when comparing POC measurement with a central lab high sensitivity measurement, adjudication of the final diagnosis can be made using the central lab assay as long as it has been previously validated and adjudication uses the recommended 99th percentile for the assay. If not, an adjudication should be made by a third and different cTn method, preferably the same cTn (cTnT or cTnI) being studied by the POC assay being evaluated there may be a risk of bias when comparing a new method against the test used to establish the diagnosis but there is also a risk that treatment decisions may have been different if an independent assay is used for adjudication.

Recommendation 2 – Clinical validation studies of hs-cTn measurement by POC requires analysis to be performed by non-laboratory trained personnel, ideally those who will use such methods, on whole blood, in the clinical environment where routine use is being contemplated.

Analytical evaluation and monitoring of POCT testing for cardiac biomarkers

The analytical performance of cTn assays is guideline recommended and their evaluation should be performed to the same standards as evaluation of the equivalent cTn assay performed in a central laboratory.

Factors specific to the nature of POC testing technology, the expectation of the skill level required of the POC testing operator, and the environment in which the POC testing instrumentation will operate, means that additional factors need to be taken into consideration in evaluating POC testing instrumentation for cTn. For devices where the intended sample type is capillary (fingerstick) whole blood, the effects of capillary sampling on result variability and analytical outliers should be assessed, unless that information can be provided by the test manufacturer. A recent study has shown representative data comparing whole blood, plasma and capillary sampling on a POC hs-cTnI assay [23]. Preanalytical errors contribute significantly to POC testing [24] and hemolyzed samples are more common than is realized [25]. These types of studies are key to the proper implementation of POC cTn testing and may alter the suggested thresholds chosen for diagnosis.

> Recommendation 3 – Cardiac troponin POC testing should include evaluation of the factors affecting POC testing devices in general.

The general criteria for the evaluation of POC testing is summarized in Table 3, including recommendations for preanalytical issues, analytical validation, interference, implementation and quality assurance. A more comprehensive review of provision of POCT in general is to be found in recent publications [26].

> Recommendation 4 – Evaluation of cardiac biomarker POC testing should address analytical issues specific to the analysis of cTn assays.

The highlights for cTn POC testing are as follows.

1.1. Sample matrix: there are well-documented concentration differences between cTn measurements in serum, plasma, and whole blood.

1.2. Blood sampling methodology: although differences between arterial and venous blood are not well documented for cTn, discrepancies, if any, with capillary blood need to be addressed.

Table 3: General requireements for point of care testing.

Factor	Comments
1. Analytical validation	There are existing guidelines for the evaluation of assays. In principle, there is no difference between a reagent lot of a wet reagent and that of a POC cassette or cartridge-based reagent lot
1.1. Sample matrix	Assays which analytically use a serum/plasma separation step are the easiest to manage. Validation can be performed using serum/plasma samples providing equivalence between whole blood and serum/plasma can be demonstrated. Samples using whole blood without the separation step are more challenging. Although validation can be performed using serum/plasma samples, whole blood validation needs to be performed often beyond the simple demonstration of equivalent results when using a serum/plasma sample and a whole blood sample anticoagulated with the same anticoagulant. Analysis of whole blood should be followed by plasma analysis on the same sample to identify interference
1.2. Blood sampling methodology	POC testing applied to arterial or venous samples is the same as conventional central laboratory testing. The use of capillary sampling requires demonstration that the capillary samples and the conventionally drawn whole blood sample have analytically equivalent results over the appropriate range, with an appropriate number of samples
1.3. Hemolysis detection	This is a particular consideration when whole blood samples are used as the sample matrix without a plasma/serum separation step
2. Operational complexity	It is implicit in the rationale of POC testing that the equipment will be used in a non-laboratory environment. This means that certain factors normally considered as standard may not necessarily apply. These will include 2.1, 2.2.1, 2.1.2
2.1. Operator expertise and training	Anyone may be trained to use POC testing. The limitation will be the complexity of operation of the equipment. At one end of the skill spectrum accurate pipetting may be required. At the other end, the primary blood sample tube may be loaded onto the equipment. The greater the level of complexity, the greater the degree of training and operator expertise will be required. This will have a direct impact on the acceptability of the technology. The ideal POCT is “load and go” with walkaway operation, ideally loading a primary sample tube. There should be a well-defined training program with appropriate certification before routine POC testing begins by an operator. This should include participation in an ongoing QA program as a mandate for continued use of

Table 3: (continued)

Factor	Comments
	the POC testing system. When accurate sample timing is required, the staffing model should enable appropriate sample timing and not be in addition to existing duties
2.1.1. Staff grade required	This will be predicated by the degree of operator expertise required
2.1.2. Integration with existing working patterns	Ideally, POC testing responsibilities should not be additional to the duties undertaken by central laboratory staff. It is better if it is integrated within a more general role
3. Quality assurance strategy	3.1. Reagent batch QA 3.2. Real time instrument QA including instrument self-test and integrity test, reagent batch integrity (expiry date) and test IQA inbuilt to the reagent cartridge/test system 3.3. Operator QA
4. Operating environment	4.1. Ambient temperature. This will affect the ability of the instrumentation to perform in the expected operating environment 4.2. Reagent storage 4.2.1. Requirement for refrigerated storage 4.2.2. Reagent shelf life 4.2.3. Size and disposal of reagent packaging 4.3. Waste disposal 4.4. Power 4.5. Connectivity
5. Information technology requirements	Minimum requirements are: 5.1. Positive patient identification 5.2. Positive operator identification 5.3. Secure on-board result storage 5.4. Connectivity to secure long term data storage 5.5. Integration with the patient medical record
6. Regulatory environment	Common themes affecting the regulatory environment are: 7.1. Degree of risk of the test 7.2. Test complexity 7.3. Anticipated test environment

1.3. Hemolysis detection: this may be a particular problem with cTn assays using whole blood.

A schematic for the evaluation of cTn POC testing is summarized in Table 3. At present, a systematic comparison of venous whole blood or plasma and capillary (fingerstick) whole blood is only reported for two systems [23, 27, 28]. Early studies have shown both systematic bias and variability between venous plasma or whole blood and capillary whole blood cTn measurements may occur, though clinical concordance around common decision points is good. Use of venous and capillary samples interchangeably to trend values cannot be recommended until the relationship between venous and capillary cTn is better understood for individual assays.

Discordance between results can be established by paired analysis of consecutive blood samples on the central lab cTn assay (plasma and serum) and the POC whole blood cTn assay by central lab personnel before implementing the POC cTn testing using the intended sample type in routine clinical practice. Since different cTn assays will return different absolute concentrations, method comparison (lack of assay standardization) should focus on detecting differences in clinical performance and outcomes.

Quality assurance

It is known that external quality assurance routines are essential to monitor POC testing analyses [29]. The reasons probably include failure to adhere to calibration routines over time if the personnel running POC testing do not have proper laboratory training and are constantly dealing with the problems that occur concerning blood samples. Finally, on-going quality control testing using third party materials below and slightly above the 99th percentile may be challenging for some hs-cTn assays using plasma or whole blood as the matrix as there may be limitations with the third party material [30].

> Recommendation 5 – A quality assurance system needs to be in place that will ensure appropriate training and utilization of POC hs-cTn measurement. It should include quality control targeted at the decision levels used in routine patient management, as well as operator competency and real-time assessment of unknowing analytical performance.

The frequency that QC material should be measured is currently a matter for debate. There is an absence of published data. Pragmatically, testing should occur to verify the performance of every different lot as acceptance testing, but the frequency thereafter can be debated. POC tests include internal quality checks and if the cartridges are robust in a range of conditions testing could be as little as once monthly. If the quality system in place includes paired laboratory testing it could be argued that larger intervals could be used. An interesting approach using a risk-based assessment has been suggested for primary care and may have wider application [31].

Recommendation 6 – The POC system should include regular automatic system checks or there should be a regular maintenance procedure to verify instrument performance.

Modern instrumentation includes inbuilt system checks, but if these do not occur then a regular maintenance procedure to verify system performance should occur on a weekly basis.

Interpretation of POC cTn results

Results from a POC cTn assay and a central lab cTn assay, ideally being either all hs-cTnT or hs-cTn I assays, are viewed and flagged effectively as different biomarkers. Unless the hs-cTn POC and central laboratory assays have been calibrated and standardized to demonstrate analytical and diagnostic equivalence, which is currently unlikely, care will be required in interpretation. The POC and central laboratory assays are two different hs-cTn assays for which sex-specific 99th percentiles and delta values used in algorithms may significantly differ. The relevant change (delta) in cTn concentrations over time in a patient, that might indicate an acute, evolving myocardial injury, is dependent on the assay imprecision (% CV) at medical decision concentrations and the cTn release curve of the individual method (which are quite variable [32]). In addition, if a hospital or medical center utilizes different assays, for example a POC cTn assay in the ED and a different cTn assay in the hospital central laboratory, it will be impossible to keep check of the total %CV on the individual methods for a given cTn value. Hence the ability to follow the delta and appropriate interpretation will be lost, unless assay dependent analytics are used. Often the cause of a cTn increase above the sex-specific or overall 99th percentile upper reference limit (URL) from admitted patients is not clear and the delta value becomes a crucial piece in the diagnostic puzzle to differential acute form chronic myocardial injury. If the first blood sample were only analyzed by POC, the information concerning changing cTn concentrations will be invalid unless the same assay is used for the second sample measurement. POC and central lab results typically cannot be used interchangeably.

The cTn concentration that safely can exclude myocardial injury by any POC cTn assay should be determined. At present the Fourth Universal Definition of Myocardial infarction defines the presence of myocardial injury as above the sex-specific 99th percentile URL. If a patient sample has a cTn level above this threshold by POC testing, the very same sample should be analyzed by the central lab cTn assay if the patient is admitted. The only exception is if repeat testing is always by POC testing. If a POC device is used in a 0/1 h or 0/2 h algorithm in an acute care setting where there is also a central laboratory, the second sample should additionally be measured on the central lab hs-cTn assay if the patient is admitted. In that way there will be benefit from the fast rule-out from a baseline (the initial sample) and serial samples measured by POC when the initial assay result is appropriately low risk, but with the ability to assess a delta over time in the patients that require further testing in addition to the >2 h samples if admitted as an inpatient. This routine also provides an option to allow the central lab to monitor the quality of the POC assay results over time. By continuously comparing the POC assay result with the central lab cTn assay result, the central lab can be alerted if the results start to deviate. In addition, this will potentially allow identification of analytical problems such as heterophile antibodies or macro troponin where there is an unexplained deviation between POC and central laboratory measurement. There is however the possibility that measurement by POCT may be more robust in this regard [33].

Recommendation 7 – When several cTn assays are used within one institution the laboratory information system should use different labels, e.g. POC cTn and cTn, for requesting and reporting results. The relevant cut-off values must be communicated for each assay. Diagnoses using serial samplings must only be based on one assay and the institution should have a strategy for divergent between-assay results.

Conclusions

The use of hs-cTn POC devices in accelerated diagnostic protocols used in EDs or outpatient clinics investigating ACS may be implemented when the analytical robustness, clinical safety and cost efficacy of such devices has been demonstrated in scientifically sound analytical and clinical studies. In ischaemia, including chest pain, diagnosis is a relatively complex process. Successful realization of the time savings POCT can deliver requires clinical workflow optimization. Prior to implementation of POCT it is essential to map the clinical decision pathway.Unless the POCT workflow integrates well with patient management protocols, inefficiencies elsewhere will erode time savings, or perhaps even work against them. These include location of the instrument, assignment of collection and testing

responsibility to (non-lab) staff, instrument maintenance, in-service and recurrent training, QC, proficiency assessments, discrepant result trapping, and troubleshooting and inventory management.

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