
Rapid Cardiovascular Diagnostics

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Abstract

Rapid cardiovascular diagnostics have played an integral role in the development of the clinical utility of cardiac biomarkers. Rapid qualitative and quantitative tests are used as an alternative to clinical chemistry laboratories, where urgent testing for cardiac biomarkers has been unavailable. Biomarkers are clinically available for diagnosis and prognosis across the heart disease continuum. Early risk markers of plaque formation and destabilisation are non-urgent and can be performed routinely as part of the pathology laboratory repertoire. Rapid diagnostic tests are best suited for markers of ischaemia, necrosis and heart failure, where patients often present acutely to emergency medical services. This chapter reviews the evolution of rapid cardiovascular diagnostics both in the pre-hospital and emergency department setting, compared to the utility of centralised laboratory testing. Further, limitations to their use and improvements by novel technology are discussed.

Keywords: cardiovascular disease, cardiac markers, cardiac troponin, centralised laboratory testing, ischemia, natriuretic peptides, rapid tests

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the Western World with rates for coronary heart disease and stroke-related mortality exceeding that of any cancer. Patients who present to the emergency department (ED) with chest pain are often a complex clinical challenge. Classical electrocardiographic (ECG) changes of an acute cardiac episode occur in only 5–15% of ED presentations. Blood-borne biomarkers offer an alternative diagnostic mode and have been part of the clinical testing repertoire since the 1950s.

Cardiac biomarker testing can be performed in a spectrum of clinical settings. Normally, this occurs in a centralised laboratory, where blood is drawn from the patient and transported

either by hand or pneumatic delivery chutes (Figure 1). The samples are processed in the laboratory along with other patient samples received from inpatients, outpatient clinics or from primary care. The combination of samples and the utility of multidisciplinary pathology laboratories can result in a time delay from drawing the sample to obtaining the results in the clinical setting (Figure 2).

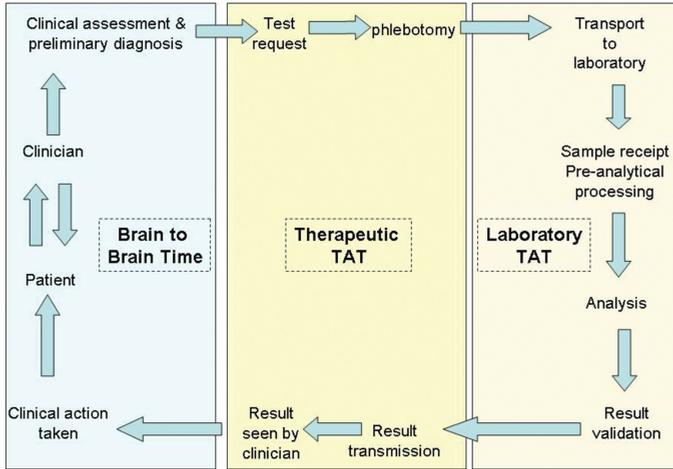


Figure 1. Cycle of delivery of diagnostic testing results. TAT, turnaround time.

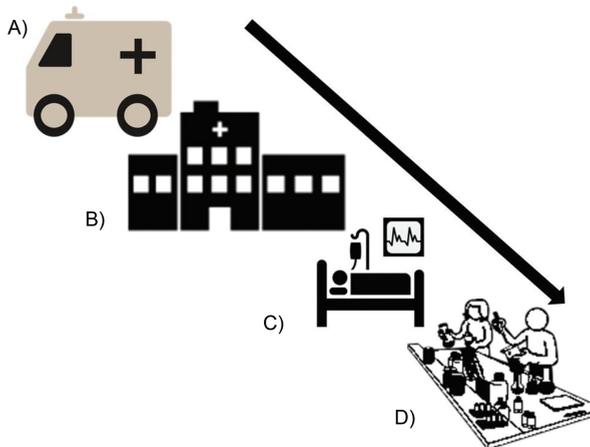


Figure 2. Cardiac biomarker testing. Testing can be performed in a number of settings including (A) pre-hospital by paramedical and ambulance personnel, (B) in a hot or STAT laboratory in the Emergency Department, (C) in the point of care setting such as the ED cubicle, patient bay or bedside or as is most conventional and (D) in a centralised clinical chemistry laboratory.

1.1. Point of care testing

The alternative to centralised laboratory testing is point of care testing (POCT). This has been known by many names and acronyms including near-patient testing; bedside testing; physicians' office testing; extra-laboratory, satellite 'hot lab'; decentralised laboratory; ancillary laboratory; or alternate site testing. Essentially, the aim of POCT analysis is to perform diagnostic laboratory tests with a shorter turnaround time (STAT) than that obtained by the central laboratory.

POCT is the *immediate* provision of a test *at the point of healthcare delivery* when the result will be used to make a decision and to take appropriate action, which leads to an improved health outcome [1]. POCT is not a novel concept, mentioned early in the foundation of medicine by Hippocrates (c. 460-370BC) and Galen (129-c.200AD). It was also described in the seventh century by the Byzantine physician Theophilus Protospatharius, a forerunner of modern Urology. Theophilus used uroscopy, the practice of visually examining patients urine with a urine flask and determining disease using the urine wheel; a colour chart of 20 urine flasks aligned in a circle and acts as a reference to link urine colour to particular diseases.

POCT can be useful for diagnosis (e.g. D-dimer or troponin in deep vein thrombosis and cardiac presentations), as a treatment guide or to monitor success of therapy (e.g. glucose/HbA1c in diabetes), in patient-related use (e.g. guidance and convenience of home INR and white cell count) and in physician-related factors (e.g. primary care natriuretic peptide testing to guide therapy in chronic heart failure). There are many advantages and disadvantages of using POCT over central laboratory services and these are given in **Table 1**.

Advantages	Disadvantages
Simpler sample collection (often finger prick)	Increased workload
Simpler pre-analytical handling	Increased error rate
Faster test results	Incompatibility if different laboratory methods used, e.g. clinical cut-off values
Reduces pathology access barriers	Increased cost
Increased patient satisfaction and user experience	Inadequate storage of results

Table 1. Advantages and disadvantages of point of care testing.

The most successful case in point for POCT is the use of glucose monitoring by finger prick testing. This has successfully revolutionised the management of diabetes both in the clinical scenario but more importantly in the patient's home. Other examples exist such as urine test strips for multiple analytes such as haemoglobin, reducing sugars, ketones, pH; human chorionic gonadotrophin (HCG) testing in home pregnancy testing kits; blood gas and electrolyte analysis; cholesterol testing in pharmacies, international normalised ratio (INR) for patients on warfarin anticoagulation therapy; rapid drugs of abuse screening in police custody

or the ED; procalcitonin and c-reactive protein for rapid detection of sepsis; and human immunodeficiency virus in salivary samples.

The driver for adopting successful POCT is a balance between meeting realistic clinical need with the appropriate technology at a sensible cost. The overwhelming utility for POCT is the rapid delivery of results. This is appropriate for acute conditions, such as cardiac or respiratory events, ectopic pregnancy and sepsis. The other need is for diagnosis outside of standard clinical areas, such as monitoring in the patients home, testing in specialised walk-in centres (HIV testing) or in social care (drugs of abuse).

1.2. Analytical actuary and precision of point of care testing

Methods employed for POCT need to demonstrate adequate analytical performance with acceptable accuracy and precision in comparison to centralised laboratory methods. Obtaining results faster is of very limited value if the coefficient of variation (CV) for the analyte is excessively large (e.g. 25%) compared to a central laboratory method with a CV of 5% at the same concentration. It is generally accepted that the performance of POCT is limited compared to central laboratory testing due to constraints such as the technology employed, knowledge and training of users who are often non-laboratory trained and inadequate quality assurance monitoring.

Performance has been well documented for blood gas analysis [2–5], cholesterol determination on eight POCT systems [6] and for INR [7] as determined on the popular CoaguCheck XS device, which was highly comparable ($r = 0.91$) to a laboratory-based method.

1.3. Effect of point of care testing on turnaround time

There have been many studies investigating the effect of POCT usage on turnaround time (TAT). TAT for activated partial thromboplastin time in a centralised laboratory can take 45–60 min to complete yet 5–10 min by POCT [8, 9]. Blood gas analysis can be reduced from 25 min to approximately 13 min [10]. Collinson and colleagues [11] demonstrated improved TAT with cardiac marker testing by POCT compared to central laboratory testing. Typical laboratory and POCT TAT for common parameters are given in **Table 2**.

Analyte	Laboratory TAT (min)	POCT TAT (min)	Δ TAT (min)
Urinalysis	40	4	-36
β HCG (pregnancy)	78	5	-73
Glucose	10	6	-4
Cardiac markers	110	17	-93

Table 2. Commonly achieved turnaround times (TAT) for central laboratory or point of care testing (POCT).

1.4. Impact on patient care

Having an analytically sound and faster method of determining an analyte is all well and good; however, the final piece of the jigsaw is the translation into improvement of patient management and outcome over and above that of the central laboratory.

Parvin et al. [12] investigated the effect of routine use of POCT by non-laboratory personnel in the ED on length of stay. A handheld device was used to determine Na, K, Cl, glucose and urea. There was no relevant decrease in length of stay in the ED. In a UK study of 1728 patients, changes in patient management are made earlier for those who received POCT haematology testing (74 min earlier) and biochemical testing (21 min earlier) reducing the time to decision affecting patient management [13]. However, such changes did not affect clinical outcome or length of stay in the ED.

Specifically, for cardiac markers, on the basis of 263 admissions with chest pain, Collinson et al. [11] have demonstrated that patients who received POCT had a reduced length of stay, both in the coronary care unit and overall hospital stay compared to those who received conventional biomarker testing provided by the central laboratory. This final important step has played a pivotal role in the adoption (or lack of) of rapid cardiovascular diagnostics by POCT and is the focus of the remainder of this chapter.

2. Cardiovascular disease epidemiology

CVD is the leading cause of global death. World Heart Federation statistics demonstrate that 17.1 million deaths globally each year are due to CVD, with 82% occurring in the developing world. Such numbers are often difficult to comprehend. One in every five deaths in the USA is due to CVD. Thirty-five per cent of UK people <65 years old die prematurely due to CVD daily. Data prediction suggests that 23 million people will die annually from CVD by the year 2030.

2.1. Acute chest pain

The largest category of patients admitted to UK hospitals is due to chest pain [14]. Patients with chest pain are diagnostically challenging. The majority present with either stable ischaemic heart disease (IHD) or no IHD [15]. Such admissions are either clinically inappropriate or are of short duration, lasting hours or a few days maximum. However, 2–7% of patients with acute myocardial infarction (AMI) are inappropriately discharged from the ED [16, 17]. Improvements to diagnosis have been made utilising risk scoring systems [18], computerised decision support [19, 20] and automated ECG interpretation [21]. Although clinical assessment is paramount in the assessment of chest pain, cardiac biomarker measurements are now routinely used to aid diagnosis.

2.2. Cardiac biomarkers: a historical perspective

Since the early 1950s, the measurement of serum enzymes in the plasma following myocyte cell necrosis initially by activity then as mass concentration progressively became commonplace in the routine clinical laboratory. The utility of cardiac biomarkers in AMI was first introduced in 1954, with subsequent identification of biomarkers of infarction and ischaemia (**Figure 3**). Classical enzymatic cardiac biomarkers, such as aspartate transaminase (AST), lactate dehydrogenase (LDH) and creatine kinase (CK) and its MB isoform (CK-MB), or the muscle protein, myoglobin, were the front-line routine diagnostic tests for the larger part of 20 years. These, however, all demonstrated poor clinical utility, due to specificity. The majority of these enzymes and proteins had similar distribution and concentrations in both cardiac muscle cells and skeletal muscle. CK-MB proved superior of all the early markers and became the gold standard test for the diagnosis of AMI.

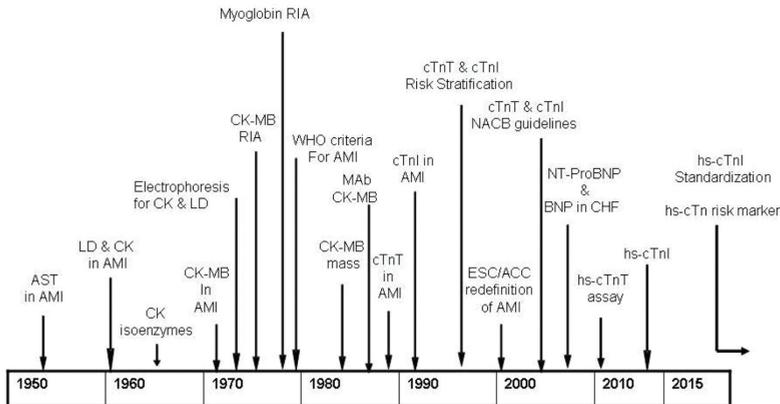


Figure 3. Historical chronology of biomarkers for the assessment of acute coronary syndrome. AMI, acute myocardial infarction; ACC, American College of Cardiology; AST, aspartate transaminase; BNP, B-type natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase-MB isoform; cTn, cardiac troponin; cTnI, cardiac troponin I; cTnT, cardiac troponin T; ESC, European Society of Cardiology; MAb, monoclonal antibody; NACB, National Academy of Clinical Biochemistry; NTproBNP, N-terminal pro-B-type natriuretic peptide; WHO, World Health Organisation. (Adapted with permission from Gaze and Collinson [22]).

Since the early 2000s, cardiac troponin T (cTnT) and I (cTnI) have become the universal gold standard test for the diagnosis of acute coronary syndrome (ACS) in those patients who present with chest pain and non-ST segment elevation on the ECG. ACS is a spectrum of disease ranging from unstable angina following an episode of cardiac ischemia to full thickness acute myocardial infarction (AMI) due to total occlusion of a coronary artery.

There have been numerous attempts to characterise the disease progression associated with CVD using different biomarkers targeting specific pathophysiological mechanisms. In patients who are asymptomatic, there are a number of biochemical tests that can be used to assess cardiovascular risk (**Table 3**). These are broadly categorised into those that assess plaque formation such as the lipid profile too assess vascular risk and metabolic markers associated

with obesity. As the pathological processes of atherosclerosis advances, markers are available to establish vulnerable culprit lesions in the coronary circuit. These markers of plaque destabilisation are associated with inflammation and cellular communication.

Plaque formation	Plaque destabilisation	Plaque rupture
Vascular risk markers	Inflammatory markers	Cardiac ischemia
Cholesterol [†] , HDL [†] , LDL [†] , IDL, VLDL, non-HDL cholesterol [†]	C-reactive protein [*]	Ischaemia-modified albumin
Cholesterol:HDL [*]	Pentraxin 3	Whole blood choline
Apolipoprotein A1 [*]	Oxidised LDL	Unbound free fatty acids
Apolipoprotein B100 [*]	Malondialdehyde	
Lp(a) [*]	Myeloperoxidase	
Homocysteine [*]	Isoprostanes	
	Xanthine oxidase	
Metabolic markers	Cytokines	Cytosolic proteins
Albumin [*]	Tumour necrosis factor alpha	CK-MB [*]
Insulin [*]	Interleukin 6	Myoglobin [*]
Ghrelin	Osteoprotegerin	Heart-type fatty acid-binding protein
Leptin		
Adiponectin		
Resistin		
	Chemokines	Structural proteins
	Monocyte chemoattractant factor	Cardiac troponin T [*]
		Cardiac troponin I [*]
		Myosin light chain
	Adhesion molecules	Extracellular matrix turnover and remodelling
	CD40 ligand	Matrix metalloproteinases (MMP)
	P selectin	Tissue inhibitors of MMP
	E selectin	Procollagen III aminopeptide
	L selectin	Procollagen type 1 COOH-terminal peptide
	Intercellular adhesion molecule-1	Procollagen type 1 NH ₂ -terminal peptide
	Vascular cell adhesion molecule-1	Basement membrane laminin
	Vascular endothelial growth factor	Tenascin C
	Placental growth factor	Galectin-3 [*]
	Hepatic growth factor	
	Endothelial growth factor	
		Biomechanical strain
		Atrial natriuretic peptide
		ProB-type natriuretic peptide [*]
		B-type natriuretic peptide [*]
		Interleukin 33/ST 2

Plaque formation	Plaque destabilisation	Plaque rupture
		Growth differentiation factor 15
		Neurohormonal activation
		Aldosterone*
		Copeptin (ADH)
		Adrenomedullin
		Apelin
		Endothelin
		Relaxin
		Urotensin

*Those in routine clinical use.

Table 3. Cardiovascular biomarkers for detection of the cardiovascular disease spectrum categorised into those that detect plaque formation, plaque destabilisation and plaque rupture.

When patients develop symptoms of chest pain, there are biomarkers available to establish a diagnosis of acute plaque rupture. In those who survive AMI and develop chronic heart failure, natriuretic peptides are used for diagnosis and more importantly monitoring of treatment response.

3. Methodology for measurement of cardiac biomarkers

POCT in general costs more per test than that for centralised laboratory diagnostics. Costs are associated with utilising more hardware per test. Single assay cartridges are often used and dedicated instruments are required for detection. Conversely, large platform analysers utilise common detection methods for a number of specific tests and use reagent packs of 100 tests or more. Cost is also proportionate to volume of tests. An instrument, for example, that produces only four cholesterol tests an hour is not suitable for a large routine laboratory setting, where workload for cholesterol determination runs into the hundreds on a daily basis.

Biomarkers produced upstream of plaque rupture and necrosis are associated with assessment of cardiovascular risk. Their primary utility is in low-risk ambulatory patients presenting to the primary care setting. There is no need for urgency in obtaining such results as the clinical presentation is not acute. Similarly, for patients with established Chronic Heart Failure (CHF) managed in primary care, STAT analysis of natriuretic peptides is not warranted. While POCT exist for the determination of high-sensitivity C-reactive protein (hs-CRP) and for B-type natriuretic peptide (BNP) and its NT-pro form (NTproBNP), their use has declined in popularity with the emergence of large high throughput analysers offering similar TAT, at relatively cheaper cost.

Many National and International societies have adopted a TAT of <60 min for cardiac biomarkers. In emergency departments with rapid chest pain protocols, a 30 min TAT is

desirable. Centralised pathology provision is possible with pneumatic air tube delivery of samples, STAT processing of samples and host communication with instruments to prioritize samples for 'urgent' analysis over more routine tests that could be performed later. A study in the USA of 159 hospitals, which audited 7020 cTn and 4368 CK-MB determinations, demonstrated TAT of 90 min for cardiac biomarkers [23].

Due to patents, a single manufacturer (Roche Diagnostics) produces assays for cTnT on both large-scale immunoassay analysers and at the point of care. Cardiac troponin I, however, is unlicensed and currently not standardised. A multitude of *in vitro* diagnostic manufacturers produce cTnI methods for both POCT and centralised laboratories. An in-depth review of the measurement of cTn has been published previously [24].

3.1. Point of care testing for cardiac troponin

A number of manufacturers produce POCT cartridges as 'strip tests', which are quantitative methods. These are akin to those used in pregnancy. The rapid stick tests provide a visual detection line to determine a positive result (**Figure 4**) but do not quantify the amount of protein present in the sample. The principle is immunochromatographic lateral flow technology and is common to all strip tests. Fundamentally they work in three steps:

1. *Sample application and separation*: Normally, anticoagulated whole blood is used for POCT to negate the need for clotting and centrifugation. The test actually takes place in the plasma component and requires separation of red blood cells by a capture fleece allowing the plasma to travel in the direction of flow by simple diffusion or by capillary flow in a lumen.
2. *Immunoreactive step*: Antibodies (Ab) against the protein of interest are immobilised on the test strip, which is often made of nitrocellulose. The plasma sample causes mobilisation of the antibodies from the nitrocellulose strip. The sample containing the protein (antigen) of interest combines with the capture and detection antibody to form an Ab-Antigen complex. The detection Ab reacts with a colour-producing substance such as the streptavidin-biotin combination.
3. *Detection step*: The intensity of the colour line produced is proportional to the amount of protein present in the sample. However, it is near impossible to determine differences in intensity with the naked eye.

The vast majority of the strip tests are not validated by the Food and Drug Administration (FDA) or CE marked for European *in vitro* diagnostic use. They are relatively cheap and of benefit in the Developing world, where cost to by technologically advanced readers and the need for power resources are simply not available or cost effective.

In the simulation in **Figure 4**, of note is the internal quality control. As each cartridge is effectively a single run, quality control of a reagent batch or lot number cannot guarantee validity of each individual test cartridge. In the scenario depicted in **Figure 4B–D**, all control lines are present, indicating that each test strip is valid. If a positive line occurs for any of the

protein markers in the absence of a control line, the cartridge is not valid and should be voided. The sample should then be repeated on a fresh cartridge.

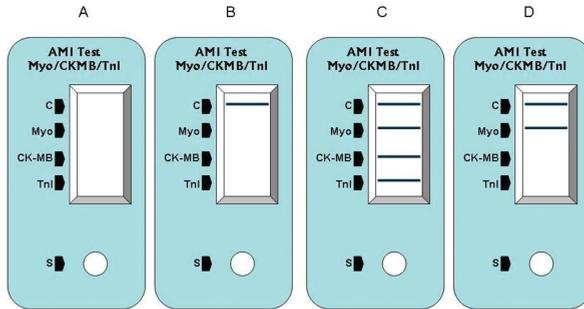


Figure 4. Simulation of a qualitative strip test for a triple panel of cardiac markers. (A) Sample of blood is placed in well at position S. (B) A control line (internal quality control) appears at C to indicate the test strip is valid. (C) A valid test strip positive for myoglobin, CK-MB and cTnI. (D) A valid test strip positive for myoglobin but negative for CK-MB and cTnI.



Figure 5. A variety of POCT platforms. (A) Cardiac Reader, Roche Diagnostics; (B) Stratus CS, Siemens Healthcare; (C) Triage, Alere; (D) Cobas h232, Roche Diagnostics; (E) iSTAT, Abbott Laboratories; (F) Meritas, Trinity Biotech; (G) LABGEOIB10, Samsung; (H) PATHFAST, Mitsubishi Chemical Europe and (I) AQT90, Radiometer.

There are a number of portable readers (**Figure 5**) that complement the strip technology in order to quantify the concentration of cTn in the sample. These include the Cardiac Reader and the newer Cobas h232 for cTnT from Roche Diagnostics; the Triage meter for cTnI and BNP (Alere); the Stratus CS for cTnI, myoglobin, CK-MB and NTproBNP, D-dimer and hs-CRP (Siemens Healthcare Diagnostics); the Pathfast for cTnI, myoglobin and CK-MB (Mitsubishi Chemical); the iSTAT for cTnI, CK-MB and BNP (Abbott Laboratories) and the AQT90 flex for cTnT, cTnI, CK-MB, myoglobin, NTproBNP, CRP and D-dimer (Radiometer).

The assay performance characteristics of the cTn POCT reader assays are given in **Table 4**. Since 1979, the WHO criterion for the diagnosis of AMI was the gold standard definition. This was based on the utility of CK-MB measurement, at five times the upper limit of normal. With the advent of cTn assays, which were, in their infancy, rather analytically insensitive, the equivalent value of cTn was adopted as the appropriate cut-off to define AMI. For cTnT, this was 0.1 µg/L. Originally, the cardiac reader reported cTnT values in the range 0.1–50 µg/L. Samples with values below 0.1 µg/L were reported as <0.1 µg/L. The equivalent laboratory-based assay underwent a number of developments to improve analytical performance. The third generation cTnT assay reported to 0.01 µg/L and the clinical cut-off value was 0.03 µg/L. This is lower than that reported by the Cardiac reader and samples in the range 0.03–0.09 µg/L would have been deemed positive in the centralised laboratory and negative by the Cardiac Reader.

Manufacturer/instrument /assay	Capture antibody epitope (aa residues)	Detection antibody epitope (aa residues)	Detection antibody tag
Abbott Laboratories i-STAT	41–49, 88–91	28–39, 62–78	ALP
Inverness Biosite Triage	NA	27–40	Fluorophore
Mitsubishi Chemical PATHFAST	41–49	71–116, 163–209	ALP
Radiometer AQT90	41–49, 190–196	137–149	Europium
Response Biomedical RAMP	85–92	26–38	Fluorophore
Roche Cardiac Reader cTnT	125–131	136–147	Gold particles
Siemens Stratus CS	27–32	41–56	ALP

aa, amino acid; ALP, alkaline phosphatase.

Table 4. POCT assay characteristics for cardiac troponin measurement.

3.2. Clinical application of POCT cardiac troponin testing

If the turnaround time cannot be realised by the central laboratory, POCT at satellite locations or near the patient can improve the diagnostic decision process. A number of studies have demonstrated a sufficient reduction in turnaround time from 87 to 25 min in order to meet international guidelines [11, 25–27]. The biggest disadvantage to POCT is the cost per assay compared to that of the central laboratory, making POCT an expensive alternative.

Multiple cardiac biomarker measurements have been advocated for the early diagnosis of AMI. The utility is based on the presence of a lag period in cardiac necrosis. Initially, when cells die, elevation of cTn may not be detectable until a significant amount of cellular damage has occurred. In the initial 3 h from chest pain onset, the measurement of myoglobin or

the CK-MB may be appropriate especially in the point of care setting and a protocol based on triple cardiac marker testing has been suggested [27] and validated [28]. However, the introduction of assays in the centralised laboratory capable of measuring troponin concentrations within the reference interval [29] and the detection of very early rises in cTn [30, 31] in the initial 3 h from presentation challenges this concept.

To date, there have been four randomised control trials of point of care testing [11, 32–34]. Two studies report outcomes [11, 34] with no difference in the number of adverse events in patients randomised to either POCT or central pathology laboratory testing. One study reported diagnostic accuracy, observing that POCT and central laboratory testing were equivalent [11]. In this study, a POCT cTnT method with the same decision limit as that in use by the central laboratory method of 0.1 µg/L. Although appropriate at the time of the study, the 0.1 µg/L decision limit is now considered too high for centralised cTnT determination. Further studies are required to assess the utility of POCT for cardiac troponin in comparison to high-sensitive methodology available in the central laboratory.

In the recent multicentre, Randomised Assessment of Treatment, using Panel Assay of Cardiac Markers (RATPAC) study performed in the UK, Goodacre et al. demonstrated that POCT increases successful discharge home of patients within 4 h of attendance and significantly reduced the median length of stay (8.8 h in POCT arm compared to 14.2 h in the central lab testing arm). There was no effect in overall bed use [35]. The use of POCT was associated with higher cost in the ED, coronary care and increased cardiac intervention costs but overall lower general inpatient costs [36].

3.3. POCT cardiac troponin in the pre-hospital setting

There are very limited data using point of care testing (POCT) for cTn in the pre-hospital setting. The majority utilised the initial rapid Trop T assay from Roche Diagnostics [37–39], which was far less sensitive than we are used to in current laboratory diagnostics. The cut-off for AMI was 0.1 µg/L which equates to 100 ng/L in new units. By contrast, the current hs-cTnT assay has a 99th percentile cut-off value of 14 ng/L. There are even less published data using POCT cTnI [40–42].

What is important to remember is that the current POCT technology for cTn is not suitably analytically sensitive enough when compared to laboratory-based immunoassay. To this end, they are reliable as rule in tests if patients are positive for cTn; however, their role as a rule out marker is questionable due to the equivalent high cut-off values employed.

In urban areas, where patients receive rapid response to emergency calls within minutes with subsequent rapid transfer, the value of POCT is questionable. However, if a suitable sensitive POCT could be developed, this may have major benefit in rural areas, where patients can be triaged to appropriate cardiac centres that offer immediate primary coronary interventional surgery. Furthermore, it is not common practice to draw venous blood samples in the pre-hospital setting by paramedical staff. There are a number of companies that are investing in new technology with the hope of delivering a sensitive POCT troponin test with the added benefit of possibly using finger-prick testing rather than venepuncture. The Samsung device

1B10 cTnI assay has been studied in the Scottish Ambulance Service. The pilot study demonstrated that patients with non-ST segment elevation myocardial infarction who demonstrated elevated cTnI in the pre-hospital setting benefited from disposition triage similar to those with ECG changes indicative of an ST elevation AMI. The pre-hospital cTnI measurement gives a documented actual time zero from pain up to 2 h earlier than in-hospital testing, leading to a reduction in time to second measurement if the initial sample was negative or detectable but below the 99th percentile cut-off for positive [43].

The demand for POCT by finger-prick testing is attractive across many disciplines and would be of benefit for self-monitoring at home by patients. This is already in common practice for diabetic patients but has practical implications for others such as those with CHF. However, a recent publication by Bond and Richards-Kortum has demonstrated vast differences in haematological parameters when using capillary blood sampling. The coefficient of variation for platelets was 19% when using capillary blood compared to 4–5% when using venous blood samples. Higher CVs were also obtained from lymphocytes, granulocytes and haemoglobin determination [44].

4. Conclusion

Point of care testing for cardiac biomarkers is only practical for the measurement of acute biomarkers of necrosis such as the cardiac troponins. Risk markers are not required urgently and therefore can be performed in a more cost-effective manner by centralised laboratory testing. Recent advances in centralised laboratory testing have resulted in more sensitive methods available with improved TAT. These cannot be met by the current POCT technology. Alternative detection methodologies are required for providing robust low concentration analysis of proteins in small sample volumes at relatively cheap cost.

5. Executive summary

- Cardiac disease is the largest cause of morbidity and mortality in the world.
- Cardiac troponins T and I are considered the gold standard diagnostic test for the detection of acute coronary syndromes.
- POCT for risk markers, such as lipids and C-reactive protein, is not cost effective.
- POCT technology for cTnT and cTnI cannot meet the current analytical performance of centralised laboratory testing.
- Novel technology is required to make POCT more sensitive analytically, which will have a major impact on clinical performance.

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