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Review Article

Importance and Sensitivity of Point-of-Care Cardiac Troponin Testing for the Diagnosis of Acute Coronary Syndrome and Acute Myocardial Infarction

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Abstract

Objective: To evaluate the importance and sensitivity of POC cTn testing for the diagnosis of ACS and AMI.
Methods: A literature review of papers indexed in the PubMed, Scopus, LILACS, and Cochrane databases was conducted in July 2020, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Group guidelines. For inclusion, the papers had to be original, be developed on humans, involve POC cTn testing, and address the diagnosis of AMI or ACS.
Results: Forty-three papers published between 1997 and 2020 were selected, providing data on a total of 51,410 individuals aged 18 to 98. The studies indicated the importance of POC cTn testing for diagnosing AMI and ACS, as well as its prognostic usefulness.
The POC tests were found to have good discriminatory power, showing median sensitivity, specificity, and negative and positive predictive values of 79.0%, 94.0%, 94.6%, and 62.5%, respectively. They were found to have an analytical performance equivalent to laboratory cTn tests, while having the advantage of providing results more quickly.
Conclusion: POC cTn testing is rapid, sensitive diagnostic tool for ACS and AMI.
Keywords: Point-of-care; cardiac troponin; myocardial infarction; acute coronary syndrome.

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1. Introduction

Approximately 6% of emergency hospital admissions are due to chest pain. Among these hospitalized patients, half are diagnosed with AMI (acute myocardial infarction).[1] One of the most common forms of cardiovascular disease is acute myocardial infarction (AMI), which constitutes the main cause of mortality and a national public health problem. When it is not diagnosed correctly and early enough, AMI can develop into acute coronary syndrome (ACS). [2]

One of the main reasons why patients seek help at hospital emergency units is ACS, which is also one of the main causes of death worldwide. It is more prevalent amongst older people, but the age at which it occurs has fallen in recent years in line with lifestyle and behavioral changes. [3]

In the last 20 years, creatine kinase (CK-MB), cardiac troponin (cTn), and myoglobin have been used as biomarkers to identify myocardial necrosis, and serve as the basis for the early diagnosis of AMI; cTn has high sensitivity and specificity for myocardial lesion, making it the gold standard biomarker for this purpose. [4]

In view of the need for increasingly early diagnosis, point-of-care (POC) testing has been used to speed up triage and reduce waiting times in emergency units. There is now a wide range of tests available on the market that could be used for the rapid diagnosis of AMI and ACS. [5] This systematic literature review is designed to evaluate the importance and sensitivity of POC cTn testing for the diagnosis of ACS and AMI via a systematic review of the scientific literature.

2. Methods

This literature review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. [6]

In July 2020, a single researcher did a literature review of the Pubmed, Scopus, LILACS, and Cochrane databases with the following keywords: point-of-care, troponin, cardiac troponin, immunoassay, unstable angina, acute myocardial infarction, and acute coronary syndrome. The snowball method was then used as a secondary research strategy, by which publications of interest were identified manually in the lists of references in the selected papers. All the references with an abstract available online were recorded on a spreadsheet.

The inclusion criteria for the papers were: (1) be an original work; (2) have been developed on humans; (3) involve POC cTn testing; and (4) address the diagnosis of AMI or ACS. Based on the titles and abstracts, the relevant publications were identified, which were then retrieved in full for review by two independent reviewers (A.R.S and L.C.O.). A third reviewer (J.F.N.N.) was consulted when necessary.

The data extracted from the papers were: (1) author/year of publication; (2) country of research; (3) age of participants; (4) sample size; (5) objectives; (6) POC tests used; (7) results; and (8) sensitivity, specificity, negative and positive predictive value, and area under the receiver operating characteristic curve (AUC) of the POC cTn test. Two authors (A.R.S. and L.C.O.) retrieved this information, using a special form. Divergences were resolved by consensus or, when not possible, by consulting a third author (J.F.N.N.).

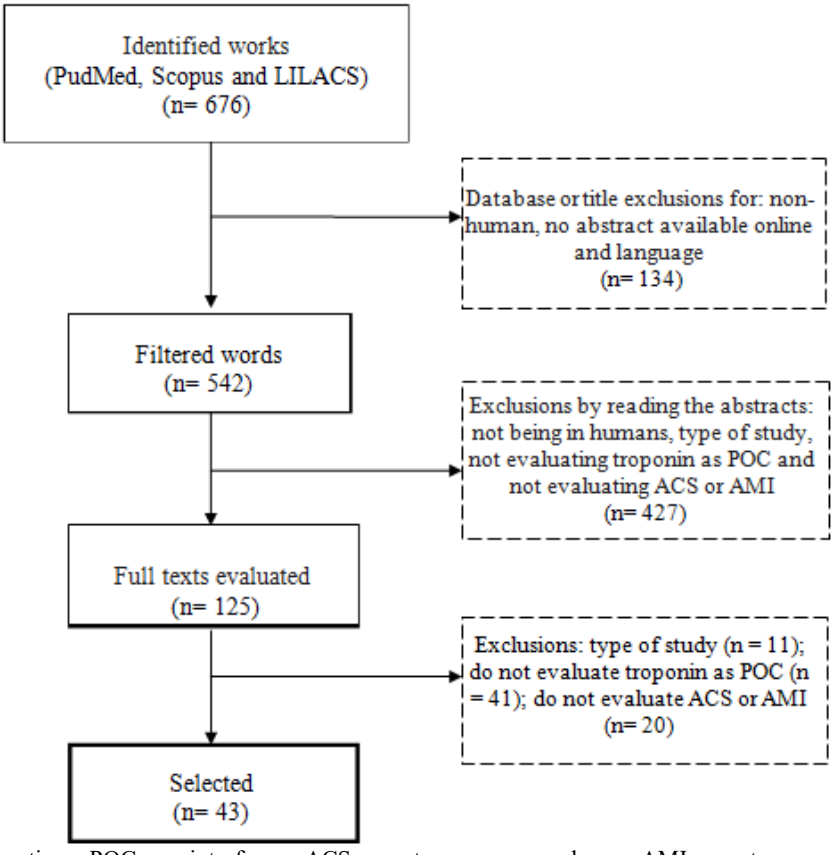
2.1 Evaluation of methodological quality

The methodological quality of the studies was assessed independently by two authors (A.R.S. and T.W.S.), through the Newcastle-Ottawa Scale (NOS). [17] The studies were classified as having a high (7–9 points), moderate (4–6 points) or low (< 3 points) quality. Discordant cases were debated until consensus, and a third author's (L.C.O) view was considered to reach an understanding.

2. Results

The initial search of the databases yielded 676 publications, of which 43 were selected: [1-5,7-47] (**Figure 1**). These papers, published between 1997 and 2020, contained data on 51,410 individuals aged between 18 and 98. The countries with the largest number of studies were Germany and the United States, and the prevailing methodology was the prospective, observational study. In addition, most of the studies were considered of high methodological quality (**Table 1**).

Figure 1: Flow chart of selection of papers*



Note: n=number of observations; POC = point of care; ACS = acute coronary syndrome; AMI = acute myocardial infarction.*Planned according to the PRISMA guidelines.

Table 1: Description of studies regarding authors, year of publication, origin, age of participants and sample size

ID	Author/year	Origin	Age (years)	N	Quality‡
1	Alghamdi *et al*, 2020 [1]	UK	18	446	High
2	Alghamdi *et al*, 2019 [18]	UK	18	700	High
3	Body *et al*, 2019 [29]	UK	57.6 (±15.6)*	868	High
4	Suzuki *et al*., 2018 [40]	Japan	70.0 (55.0-79.0)**	1,449	High
5	Gonçalvez *et al*., 2018 [2]	Brazil	UN	1,380	High
6	Cho *et al*., 2017 [43]	Korea	58.0 (±16.0)*	1,336	High
7	Greiser *et al*., 2017 [44]	Germany	26.0 (18.0-65.0)**	2,247 (cTn I) 2,259 (cTn T).	High
8	Slagman *et al*., 2017 [45]	Germany	61.0 (45.0-73.0)**	3,423 (M: 1,958; W: 1,465)	High
9	Tsai *et al*., 2017 [46]	Taiwan	75.4 (±6.6)*	146	Moderate
10	Wilke *et al*., 2017 [47]	Germany	71.0 (57.0-80.0)**	2,163	High
11	Andersson *et al*., 2015 [8]	Sweden	65.0 (±14.0)*	115	High
12	Asha *et al*.,2015 [9]	Australia	61.7 (±16.6)*	452	High
13	Ezekowitz *et al*., 2015 [10]	Canada	66.0 (53.0-78.0)**	601	High
14	Ezekowitz *et al*., 2014 [11]	Canada	70.0****	491	High
15	Palamalai *et al*., 2013 [12]	USA	58.0 (±16.0)*	169	Moderate
16	Schneider *et al*., 2013 [13]	Australia	66.0 (53.0-82.0)**	195	Moderate
17	Stengaard *et al*., 2013 [14]	Denmark	Group a. UAP: 63.0 (59.0-66.0)** b. AMI: 70.0 (67.0-71.0)** c. ACS: 65.0 (64.0-66.0)**	985 (a: 31; b: 200; c: 754)	High
18	Collinson *et al*.,2012 [15]	UK	53.0 (44.0-64.0)**	1,125	High
19	Diercks *et al*.,2012 [16]	USA	57.0 (48.0-67.0)**	858 (M: 476; W: 382)	High
20	Lee-Lewandrowsli *et al*., 2011 [17]	USA	M: 61.7 *** W: 68.6***	204	High
21	Sorensen *et al*., 2011 [19]	Denmark	Group a. Prehospital cTn T test: 66.0 (55.0-78.0)** b. No Prehospital cTn T test: 67.0 (55.0-79.0)**	4,905 (a: 958; b: 3,947)	High
22	Tomonaga *et al*., 2011 [20]	Switzerland	Group a. C: 65.0 (±16.0)* b. POC: 64.0 (±17.0)*	369 (a: 151; b: 218)	High
23	Macdonald *et al*., 2008 [21]	Australia	58.0 (±14.6)*	100 (M: 61; W: 39)	High
24	Straface *et al*., 2008 [22]	USA	58.4 (±18.2)*	5,241	High
25	Aplle *et al*., 2007 [23]	USA	Group a. pre-POC: 54.0*** b. post-POC: 51.0***	545 (a: 371; b: 374)	High
26	Cramer *et al*., 2007 [24]	Netherlands	64.0 (±14.0)*	358 (M: 208; W: 150)	High
27	Mockel *et al*., 2007 [25]	Germany	60.5 (±14.1)*	429	High
28	Aplle *et al*., 2006 [26]	USA	58.0 (19.0–96.0)**	369 (M: 207; W: 162)	High
29	Borrayo-Sánchez *et al*., 2006 [27]	México	55.0 (±18.0)*	48 (M: 25; W: 23)	Moderate
30	Di Serio *et al*., 2006 [28]	Italy	M: 52.0 (±14.0)* W: 56.0 (±11.0)*	100 (M: 63; W: 37)	Moderate
31	Ordónez-Llanos *et al*., 2006 [30]	Germany	63.0 (±14.6)*	1,410	High
32	Soria *et al*., 2006 [31]	México	54.1 (±2.6)*	40 (M: 22; W: 18)	Moderate
33	Hindle *et al*., 2005 [32]	Canada	UN	235	High
34	Seino *et al*., 2004 [33]	Japan	68.8 (±15.0)*	129 (M: 70; W: 59)	High
35	Agewall, 2003 [34]	Sweden	67.0 (±1.3)*	187 (M: 103; W: 84)	Moderate
36	Caragher *et al*., 2002 [35]	USA	UN	205	High
37	McCord *et al*., 2001 [36]	USA	64.0 (±1.3)*	817	High
38	Apple *et al*., 2000 [37]	UK	M: 28.0 (20.0-51.0)** W: 37.0 (20.0-62.0)**	166 (M: 68; W: 98)	Moderate
39	Heeschen *et al*,1999 [38]	Germany	59.4 (±9.1)*	412 (M: 269; W: 143)	High
40	Ohman *et al*., 1999 [39]	Canada	63.0 (53.0–71.0)**	12,666	High
41	Scuchert *et al*., 1999 [40]	Germany	69.0 (±13.0)*	195 (M: 93; W: 102)	High
42	Sylvén *et al*., 1998 [41]	Sweden	68.0 (±13.0)*	151	High
43	Baxter *et al*.,1997 [42]	USA	59.0 (26.0-98.0)**	721	High

Note: ID= number of identification; N= sample size; UN= uninformed; cTn= cardiac troponin; M= men; W= woman; USA= United States of America; UAP= Unstable Angina Pectoris; AMI= Acute Myocardial Infarction; ACS= Acute Coronary Syndrome; UK= United Kingdom; C= control; POC= point of care.

‡Newcastle-Ottawa Scale, 2013.; *Mean/Standard deviation; **Median/Interquartile ranger; ***Mean; ****Median.

The most cited POC cTn tests were AQT90 FLEX (Radiometer; 7 papers = 17.5%) and Stratus CS (Dade Behring; 6 papers = 15.0%). The studies generally indicated the importance of POC cTn testing for diagnosing AMI and ACS, as well as its prognostic usefulness, with this kind of test alone being considered sufficient for diagnostic accuracy, without the need for laboratory tests. The analytical performance of the POC tests was found to be equivalent to that of laboratory cTn tests, with the added advantage of providing the results more quickly (**Table 2**).

Table 2: Description of studies regarding objectives, POC cardiac Troponin test and results

ID	Objectives	POC cTn test	Results
1	The ultimate goal has been to produce assays that would measure cTn in the majority of normal healthy individuals.	UN	Biomarker testing specifically the measurement of cTn dominates the management of patients with suspected ACS. POCT now needs to not only match the analytical capability of laboratory methods for high sensitivity troponin but also be integrated within the decision matrix to demonstrate benefit.
2	To evaluate the diagnostic accuracy of a different POC cTnI assay with serial sampling over 3 hours, both with T- MACS and when used alone.	-Alere Triage Cardio 3 Cut-point: 0.01 µg / L	We obtained written consent from 446 patients to participate in the study. A total of 432 patients had a POC blood sample available for analysis at presentation only. In total, 396 patients had POC blood samples at presentation, and 347 patients had both blood samples at presentation and 3 hours later, relevant clinical data (including T- MACS variables) and follow- up data available. In these patients, the prevalence of adjudicated AMI was 14.9% 59/396), and the prevalence of MACE was 17.4% (69/396) at 30 days.
3	Search and evaluate the diagnostic accuracy of T-MACS decision aid algorithm to 'discard' the ACS when used in the prehospital environment with troponin at the place of care essay.	- Roche cobas h 232 TnT Cut-point:UN	Will aim to achieve clinical we will aim to achieve clinical implementation within 2 years. Clearly, this will involve additional work to demonstrate the feasibility and acceptability' of T-MACS in the ambulance; new clinical and training Regimes and to robustly communicate the clinical and cost effectiveness of the strategy. The recent update to NICE Guideline CG95 incorporated a novel diagnostic strategy (originally developed by our group) for in-hospital use based on data from observational studies with a similar design. Given that precedent, we anticipate that our findings will generate the evidence required by NICE to issue a recommendation for the clinical use of T-MACS with a POC troponin assay in the prehospital environment.
4	We evaluate the accuracy of Manchester's diagnosis with troponin alone acute coronary syndromes (t-Macs) assist in the decision POc ctn assay.	- i-STAT, abbott Cut-point: 20 ng/L	A total of 634 patients underwent POC i-Stat testing at 3 hours, of which 97 (15.3%) had ACS including 82 (12.9%) with AMI. Based on a single i-Stat POC cTnI measurement at the time of arrival in the ED, the area under the ROC curve (AUC) for T-MACS was 0.86 (95% CI 0.82 to 0.90). Accounting for the 3-hour POC cTnI concentration increased the AUC to 0.92 (95% CI 0.89 to 0.95).
5	To examine the usefulness of POC cTn in diagnosing ACS and to understand the limitations of a POC cTn I/T based diagnoses.	- AQT-90 FLEX (Radiometer) Cut-point: cTn T >0.017 ng/mL; cTn I >0.023 ng/mL.	One hundred and twenty patients were diagnosed with ACS. The POC cTn I/T levels were higher in the ACS group. When sampled >3 hours after the onset of symptoms, the POC cTn I level is considered to be suitable for use in diagnosing ACS. However, when sampled 3 hours after the onset of symptoms, careful interpretation of POC cTn is therefore required to rule out ACS.
6	To investigate the performance of markers eligible in a chest pain protocol, using POC. To evaluate if a POC for multiple cardiac biomarkers can be used for predicting severity and mortality in AMI patients.	- UN - Triage (Alere) Cut-point: 0.05 ng/mL	A multivariate regression model showed as predictors for AMI the variables ECG, previous AMI, levels of both miog at the third hour, and cTnI at the sixth hour after admission. A total of 329 patients were diagnosed with AMI. When three POC were positive, the percentage of involvement of the left main ACS was increased 10 fold (p <0.001). The risk increased more than 3 times with 2 positive POC compared to none (p= 0.005).
7	To determine the 99th percentile of two POC and compare with central laboratory tests.	- AQT-90 FLEX (Radiometer) Cut-point: 10 ng/L	The 99th percentile of cTn I in the POC was determined at 19 ng/L. Compared to central laboratory test the POC the analytical performance was equivalent.
8	A POC cTn T was compared to a cTn T central laboratory test to determine of diagnostic of ACS.	- AQT-90 FLEX (Radiometer) Cut-point: 30 ng/L	Of all patients, 3.6% had a diagnosis of NSTE AMI. For the hs cTn T assay, 28.4% of all values were at or below the limit of detection as compared to 75.7% of the POC cTn T values. The diagnostic performance was very similar for both assays.
9	To compare POC cardiac biomarker test results and suggest a clinical guideline.	Triage CardioProfilER (Alere) Cut-point: >0.4 ng/mL	Of the assessed patients, 43.8% (15/35) had UA. cTn I had the best results than the tests focusing on cTn I with CPK-MB and MCB.
10	To compare the performance of two POC cTn assays with that of a central laboratory hs method.	- AQT-90 FLEX (Radiometer) Cut-point: cTn T >17 ng/L; cTn I >23 ng/L.	POC and hs assays showed a comparable diagnostic performance in patients admitted with suspected ACS in relation to the release diagnosis, supporting the use of POC testing in this setting.

11	To evaluate a hs cTn and to compare with a POC cTn.	- Cobas h232 (Roche). Cut-point: 0.03 µg/L	The sensitivity for hs cTn T to find AMI or the combination of AMI and UA was 100 and 83.0%, respectively. The specificity of hs cTn T was lower compared with the POC method in population with acute chest pain (75.0%). Both hs cTn and POC cTn could become useful in primary care for patients <65 years.
12	To determine outcomes in patients suspected of an ACS who had POC cTn I compared with laboratory cTn I testing.	- AQT-90 FLEX (Radiometer) Cut-point: ≤14 ng/L	Thirty patients (13.1%) randomised to POC had at least one outcome compared with 29 (13.0%) control (p= 0.98). There were discrepancies between the results of POC and laboratory analysers. But, wasn't found difference in adverse outcome when POC cTn was used.
13	To randomize a POC cTn in ambulances to find out if cTn accelerates the time for the diagnosis.	- Triage (Alere) Cut-point: >0.03 ng/mL	The first cTn was available in 38 minutes in POC and 139 minutes in usual care. In POC, the cTn was >0.01 ng/mL in 17.4% and >0.03 ng/mL in 9.8%. The time from first medical contact to discharge from ED or admission to hospital was shorter in patients with POC cTn.
14	To test cTn and BNP before hospital guidance in patients with ACS.	- Triage (Alere) Cut-point: >0.03 ng/mL	cTn before hospital arrival was >0.03 ng/mL in 13.4% and >0.1 ng/mL in 3.6%. The prespecified threshold cTn >0.03 ng/mL was exceeded by 1 patient (12.5%) in the UA, 9 (31.0%) in the ACS, 2 (20.0%) in the AHF, and 14 (9.5%) in the other group. BNP before hospital arrival was 100 pg/mL in 36.4%, and 400 pg/mL in 11.6% of all patients. The prespecified BNP threshold of 400 pg/mL was exceeded by 3 patients (10.3%) in the ACS, 7 (63.6%) in the AHF, and 13 (8.7%) in the other group.
15	To evaluate the diagnostic performance of four POC cTn I assays compared to a central laboratory cTn I for detecting myocardial injury and AMI.	- AQT-90 FLEX (Radiometer) Cut-point: 9 ng/L - PATHFAST (Mitsubishi) cut-point:8 ng/L - GEM Immuno (Instrumentation Laboratory). Cut-point:1.3 ng/L - i-STAT (Abbott) Cut-point:20 ng/L	Nineteen of 169 patients had an AMI. Clinical sensitivity varied considerably between assays and across time points within each assay, comparable to the laboratory assays. The analytical variability that exists between POC cTn I assays demonstrates substantial diagnostic differences for ruling in and ruling out AMI.
16	To evaluate a decreased cut-off of POC cTn tests in the detection of cardiac injury.	- i-STAT (Abbott) Cut-point: ≥0.04 µg/L - AQT-90 FLEX (Radiometer) Cut-point: 0.0095 µg/L	Clinical review showed POC tests missed 6 of 13 patients with confirmed AMI (sensitivity= 46.0%) and that a lower cut-off allowed them to detect all (for the i-STAT) or most (4 of 6 for the AQT) of them.
17	To evaluate the feasibility of prehospital POC cTn T, its ability to identify patients with AMI and to predict mortality.	- Cardiac T (Roche) Cut-point: 50 ng/L	The was performed POC cTn T measurements in 985 subjects of whom, 200 (20%) had an AMI. Adjusted survival analysis showed an association between elevated prehospital POC cTn T level above the detection level of 50 ng/L and mortality.
18	To assess the impact of triple marker testing and the diagnostic efficiencies of different biomarker strategies.	- Stratus CS (Dade Behring) Cut-point: 0.03 mg/L.	Measurement of cTn I was the most diagnostically efficient than CPK-MB and miogl. Measurement of cTn I alone is sufficient for diagnosis.
19	To determine the diagnostic accuracy of a POC cTn I within 3 hours for patients presenting within 8 hours of symptom.	- Cardio3 (Biosite) Cut-point: 0.05 ng/mL	AMI was diagnosed in 82 patients (9.6%). There was no significant improvement in diagnostic accuracy associated with adding 6-hour serial testing to the 3-hour sample.
20	To compare 2 POC strategies (POC multimarker and POC cTn T), central laboratory cTn T assay in patients evaluated for AMI.	- Inverness (Biosite) Cut-point: 0.05 mg/L - i-STAT (Abbott) Cut-point: 0.08 g/L	The cTn T alone (i-STAT) was more sensitive for AMI than the multimarker POC panel (Inverness) with equal or better specificity. When compared with a POCT cTn I, the cTn T wasn't more sensitive. The POC cTn I alone also had the same sensitivity as the multimarker panel.
21	To investigate the prehospital cTn T testing in the diagnosis in patients with chest pain.	- TROP T (Roche). Cut-point: 0.10 ng/mL.	A diagnosis of AMI was established in 208 of 258 patients with increased cTn T. The prehospital test identified 30.0% of these patients, whereas the first in-hospital test detected 79.0%. The prehospital implementation of quantitative tests, with lower detection limits, could identify most patients with AMI.
22	To analyze the diagnostic accuracy of POC.	- Cardiac Reader (Roche) Cut-point: 0.1 ng/ml.	POC confers substantial benefit in primary care by correctly diagnosing significantly more patients.
23	To determine the use a biomarker of miog, CPK-MB and cTn I to identify patients with suspected ACS suitable for discharge.	- Triage Cardiac (Biosite) Cut-point: 0.05 ng/mL	The study group comprised 100 patients and six had a cTn-positive ACS. The Triage panel at 2 h after presentation predicted 12-h cTn T elevation and 30-day events. The majority of patients were ultimately suitable for discharge.

24	To compare a POC multimarker with a single and serial cTn I protocol in patients with chest pain.	- Triage Cardiac (Biosite) Cut-point: 0.4 µg/L	The diagnosis of AMI was based on a doubling miog and at least a 50.0% increase in the CPK-MB; a doubling of miog together with any detectable cTn I; or a cTn I ≥0.4 ng/mL. Using these new criteria, 145/148 cases were positive for AMI. Twelve confirmed non-AMI cases were positive by the new protocol, with 10 of 12 confirmed by the core laboratory as positive for cTn I. This rapid multimarker protocol seems superior to a cTnI only.
25	To determine the impact of POC cTn I regarding assay TAT, patient LOS, financial matrixes and outcomes compared to central laboratory testing.	- Stratus CS (Dade Behring) Cut- point: 0.1 µg/L.	The mean length of stay was significantly lower for the PostCS compared to the PreCS patient group: 2.4 vs 2.2 days (p= 0.05). The TAT from blood draw to reporting of results to healthcare providers was significantly lower in the PostCS group: 19.5 vs. 76 min (p <0.001). The direct charge of reagents to the laboratory for testing of cTn I was lower in the PreCS group. The groups with normal baseline cTn I concentrations had a greater survival rate compared to both patient groups with an increased cTn I.
26	To test the usefulness of a POC as compared to a laboratory method of cTn to predict adverse cardiac outcome.	- Cardiac Reader (Roche) Cut-point: 0.05 µg/L.	Discordance between cTn I and cTn T occurred in 11.4% (41/358) of cases. The rate of death or AMI was 25% (10/40) among patients with discordant cTn results as compared to 7.5% (17/228) among those with concordant negative results (p<0.001). Patients with a discordant reading were at high risk of adverse cardiac outcome, which was only identified by the laboratory cTn I. Markedly, the use of the rapid assay saved time at the expense of clinical sensitivity.
27	To define the role of Lp-PLA 2 in combination with cTn I, NT-proBNP, hs CRP and D-dimer in patients with ACS.	- Stratus CS (Dade Behring) Cut-point: 0.01 g/L	The primary end-point was death, AMI, unstable AP, admission for AHF, percutaneous coronary intervention, coronary artery bypass grafting, life threatening arrhythmia or resuscitation. In the remaining lower risk group with an incidence of 10.3%, further separation was performed using cTn I (cut-off 0.14g/L; RR= 3.1, 95% CI: 1.7–5.5) in patients with negative cTn I. In the patients with suspected ACS the cTn I and the Lp-PLA2 are effective independent markers for risk stratification.
28	To evaluate the use of a POC cTn I assay in ACS patients.	- i-STAT (Abbott) Cut-point: 0.04 g/L..	AMI was diagnosed in 8.1% of patients. Patients with symptoms suggestive of ACS and with an increased POC cTn I at presentation have a significant increase in risk over 60 days for ACS and cardiac events. Thus, the POC cTn I can be added to the list of assays for risk stratification.
29	To measure the diagnostic value of cTn I, miog and CPK-MB in preadmission to the hospital.	- Cardiac STATus (Spectral) Cut-point: 0.03 µg/L.	The cTn I, miog, and CPK-MB have high diagnostic value in ACS from the time of prehospital admission.
30	To identify patients with myocardial necrosis in the pre-hospital phase, NSTE, through the measurement of POC cTn.	- i-STAT (i-STAT Corporation) Cut-point: 0.015 mg /L	The median ambulance TAT was 12 min and the median hospital TAT was 40 min. The hs of the i-STAT cTn I method integrated with telemedicine procedures could play an important role in the management of ACS patients related to the pre-hospital phase.
31	To examine the predictive value of cardiac markers for adverse events measured by a POC.	- Cardiac T (Roche) Cut-point: 0.05 g/L	If the cTn T, measured either by the POC or a conventional laboratory analyzer, was >0.05 g/L, then the chance of a cardiac event was doubled (18.0% vs 9.0%). Serial cTn T measurement did not add any further value to the predictive power of the admission cTn T.
32	To validate the diagnostic usefulness of cTn I in patients with chest pain.	- Cardiac STATus MR (Dade International) Cut-point: 1.5 ng/mL	The rapid qualitative determination of cTn I is the highest clinical use test predictive value for early diagnosis and timely AMI.
33	To examine the utility of POC cTn I in patients with possible ACS.	- Cardiac STATus (Spectral) Cut-point: 0.15 µg/L	Of the 235 patients, 8 had AMI and 11 AMI NSTE. cTn I testing was positive in all cases of AMI. There were 3 positive cTn I and 33 raised CK levels in patients without ACS. Qualitative cTn I testing appears hs and more specific.
34	To compared the diagnostic efficacy of a newly developed whole blood panel test for H-FABP with the rapid cTn T test.	- TROP T (Roche) Cut-point: UN	Thirty-one patients (24.0%) had a diagnosis of AMI. When using the novel rapid H-FABP test, cardiac emergency triage to exclude non-AMI patients should be effectively organized within 3h of onset.
35	To examine the proportion of patients with a negative quantitative cTn T test who would fulfil the new AMI criteria, and to evaluate the clinical utility of cTn I.	- Stratus CS (Dade Behring) Cut-point: 0.006 µg/L - Cardiac reader (Roche). Cut-point: 0.04 ng/mL	Fifteen patients (8.0%) fulfilled the criteria of AMI, despite a negative cTn T (Cardiac reader; Roche). The undiagnosed AMI were very small. cTn I appeared to be a reliable method in patients with suspected myocardial cell necrosis.
36	To evaluate the diagnostic accuracy and practicality of cardiac biomarkers in the diagnosis of ACS.	- Stratus CS (Dade Behring) Cut-point: 0.10 g/L.	Of 205 patients, 32 (16%) had an FAD of ACS-positive; 173 (84%) had an FAD of ACS-negative. Of the ACS-negative patients, 17 (8%) had indeterminate cTn I results by POC. The mean time-to-result for the ACPP was 87 min and for the POC was 39 min. The sensitivity of the cTn I assay integral to this system was responsible for the high diagnostic accuracy.
37	To evaluate whether a multimarker strategy with POC measurement of miog, CPK-MB, and cTnI could exclude AMI.	- Triage Cardiac (Biosite) Cut-point: 0.19 ng/mL	Sensitivity and NPV for POC combination of miog and cTn I by 90 minutes was 96.9% and 99.6%, respectively. Median time from sampling to reporting of results was 71 minutes for the central laboratory vs. 24 minutes for the POC device (P <0.001). AMI can be excluded rapidly by use of POC of miog and cTn I in the first 90 minutes.

38	To evaluate the POC for cardiac markers for the diagnosis of AMI	- Alpha Dx (First Medical) Cut-point: 0.09 mg/L.	The POC can be used for ruling in and ruling out AMI.
39	To evaluate a POC testing.	- Stratus CS (Dade Behring) Cut-point: 0.03 mg/L	With Stratus CS, sensitivity for the detection of patients with AMI was 63% at arrival and 98% after 4 h. During 30 days, death or AMI occurred in 25.5% of these cTn I-positive vs 2.9% of cTn I-negative patients. The POC provided better analytical performance and comparable or better prognostic information than the old used test.
40	To assess whether a POC cTn T at enrollment could risk-stratify patients.	- Cardiac T (Boehringer Mannheim) Cut-point: 0.02 g/L	Patients with an elevated cTn T result at enrollment (8.9%) had significantly higher mortality at 30 days (15.7% vs 6.2% for negative patients; p <0.001). In a multivariable regression model, a positive cTn T result added independently to the prediction of 30-day mortality (p <0.001).
41	To evaluated the use cTn T as an objective marker to verify AMI.	- TROP (Boehringer Mannheim) Cut-point: 0.18 ng/mL	During follow-up, patients with a positive prehospital cTn T test result had cardiac events more often (9 of 11) than patients with a negative result (26 of 147; P <0.0001).
42	To compare the diagnostic efficacy of AMI of two rapid tests, one with both CPK-MB and miog and the other with cTn T.	- TROP T (Boerhinger Mannheim) Cut-point: 1.13 g/L	There was no difference in diagnostic performance between tests. The two tests have similar and reliable diagnostic capacities 12 hours after the onset of symptoms.
43	To evaluate the performance of a new POC cTn T in patients with symptoms of ACI.	- Cardiac T (Boehringer Mannheim) Cut-point: 0.2 g/L	Of 721 patients, 102 were diagnosed as having AMI. The sensitivity of this POC cTn T for detecting AMI is comparable to that of current serum assays and offers the advantage of providing rapid bedside results.

Note: ID= number of identification; cTn= cardiac troponin; POC= point of care; AMI= Acute Myocardial Infarction; hs= high sensitivity; UA= Unstable Angina; NT-proBNP= N-terminal pro-B-type natriuretic peptide; miog= mioglobin; CK= creatine kinase; CPK-MB= creatine kinase MB; ACS= Acute Coronary Syndrome; TAT= turnaround time; LOS= length of stay; ACI= Acute Coronary Ischemia; NPV= negative predictive value; FAD= final assigned diagnosis;; NSTE= non ST-elevation; BNP= B-type natriuretic peptide; AHF= Acute Heart Failure; ED= Emergency Department; Lp-PLA 2= lipoprotein-associated phospholipase A 2;T-MACS=Troponin- only Manchester Acute Coronary Syndromes; MACE= major adverse cardiac events; NICE= National Institute for Health and Care Excellence; CG 95= Clinical guideline;

As shown in **Table 3**, the area under the curve AUC of most of the studies varied between 0.786 and 0.960, confirming the good discriminatory power of the POC cTn tests. The median sensitivity, specificity, and negative and positive predictive values were 79.0% (interquartile interval [IQI]: 59.0-95.0%), 94.0% (IQI: 89.0-96.3%), 94.6% (IQI: 86.7-98.1%), and 62.5% (IQI: 50.0-80.8%), respectively (**data not shown**).

Table 3: Description of studies regarding sensitivity, specificity, negative and positive predictive value, and areas under the curve of POC cardiac troponin test

ID	Groups or time	Sensitivity	NPV	Specificity	PPV	AUC
1	Alere TriageCardio 3	88.9	95	65.3	-	0.97
2	Roche Cobas h232	-	-	-	-	-
3	i-STAT, Abbott	63.9	94.8	93.1	92.5	-
4	cTn I	-	-	-		0.833
	cTn T	-	-	-	-	0.786
8	-	-	-	-	-	0.896
9	-	14.0	79.0	99.0	50.0	0.567
	cTn T				83.0	
	EGRF ≥60	80.0	-	88.0	-	0.870
	≤30 EGRF <60	84.0	-	64.0	-	0.820
10	EGRF <30	100	-	22.0	-	0.890
	cTn I					
	EGRF ≥60	79.0	-	95.0	-	0.890
	≤30 EGRF <60	63.0	-	89.0	-	0.800
	EGRF <30	83.0	-	76.0	-	0.830
11	-	67.0	99.0	98.0	50.0	-
13	-	44.0	87.2	96.0	73.3	-
14	-	31.0	88.1	89.7	34.6	-
15	GEM	95.0	99.0	79.0	36.0	-
	i-SAT	74.0	96.0	88.0	44.0	-
	PATHFAST	95.0	93.0	78.0	32.0	-
	AQT-90	68.0	96.0	89.0	43.0	-
17	0-60 min	27.0	84.0	95.0	58.0	-
	60-120 min	38.0	81.0	97.0	80.0	-
	>120 min	52.0	89.0	94.0	69.0	-
18	Initial	-	-	-	-	0.960
	90 min	-	-	-	-	0.950
19	Peak value	84.1	98.2	93.4	57.5	0.950
	Initial	66.7	96.0	95.9	65.8	0.920
	1.5 h	79.2	97.5	94.4	62.6	0.940
	3 h	84.7	98.1	93.4	60.4	0.950
	6 h	87.5	98.4	92.6	58.3	0.950

20	-	63.0	95.0	94.0	58.0	-
21	-	59.0	95.0	93.0	-	0.82
23	2-12 h	100	99.0	-	-	-
	30 days	86.0	97.0	-	-	-
24	-	98.0	99.9	99.8	92.4	-
29	-	100	100	94.0	89.0	-
32	A	95.0	95.0	95.0	95.0	-
	B	64.0	64.0	90.0	90.0	-
	C	25.0	86.0	95.0	50.0	-
	D	50.0	95.0	95.0	50.0	-
34	≤3 h	50.0	86.7	96.3	80.0	-
	3 to <6 h	0	78.9	93.8	0	-
	6 to <12 h	60.0	84.6	100	100	-
	≥12 h	100	100	87.5	76.0	-
	Total	67.7	90.3	94.9	80.8	-
35	>0.4 µg/L	73.3%	-	100%	-	-
	>0.2 µg/L	100%	-	95.3%	-	-
	>0.07 µg/L	100%	-	54.1%	-	-
36	-	100	-	100	-	-
37	-	-	-	-	-	0.860
38	-	93.0	-	94.0	-	0.919
39	-	-	-	92.6	-	0.859
41	-	98.0	-	88.0	-	-
42	Initial					
	>0.1 µg/L	77.0	93.0	-	-	-
	>0.2 µg/L	96.0	87.0	-	-	-
	6 h					
	>0.1 µg/L	96.0	98.0	-	-	-
	>0.2 µg/L	91.0	91.0	-	-	-
43	Initial	19.6	88.1	98.1	62.5	-
	3 h	59.0	93.6	97.7	80.8	-
	6 h	69.7	94.6	96.6	78.5	-

Note: ID= number of identification; NPV= negative predictive value; PPV= positive predictive value; AUC= area under the curve; cTn= cardiac troponin; group A: Patients admitted with clinical symptoms of acute myocardial infarction; group B:Patients with high probability and coronary risk factors; group C: Patients with low probability of coronary risk; group D: Group control; eGRF=estimated glomerular filtration rate.

3. Discussion

Given that individuals suspected of having AMI or ACS should be diagnosed early and accurately, we evaluated the importance and sensitivity of POC cTN testing. This kind of testing could be extremely beneficial in the primary care setting, ensuring the correct diagnosis of more patients suspected of having ACS or AMI before they reach hospital, and serving as an effective, efficient tool for this purpose. Its benefits may extend to the hospital setting, influencing the procedures and treatments given and helping to bring about better outcomes.

However, some limitations of this systematic review should be considered. Although the net was cast wide in the search for papers and carefully evaluate many were subsequently discarded as they failed to meet the inclusion criteria. It may be that some publications of relevance were overlooked in this process. Also, as we based the search on published data, there could be a publication bias at play, as in all systematic reviews.

Some of the strengths of the study include the selection of the papers and the extraction of the data by two authors, increasing the likelihood of publications of interest being identified and data of interest being identified/ extracted effectively. Furthermore, the study was carried out according to the PRISMA guidelines (2009), which indicate a set of evidence-based items that are necessary for the systematization of reviews of this nature. Another point worth stressing is that although a variety of POC tests were analyzed, with different cutoff points, they all provided results quickly and proved perfectly applicable to the diagnosis of ACS or AMI.

All the studies indicated the importance of POC cTn testing for diagnosing AMI and ACS. Specifically, Wilke *et al* [47] found that POC and laboratory tests for cTn both had comparable diagnostic power, and suggested the value of using POC testing.

Using POC cTn testing in isolation, without recourse to laboratory tests, was found to be a good strategy, proving more practical and speeding up the diagnostic process. However, Apple *et al* [22] reported the need for and superiority of POC testing for multiple biomarkers, not just cTn.

The sensitivity of POC cTn assays is very clinically important. The values found were favorable but variable, the differences being related to multiple factors, as well as the number of participants in each study and the different protocols employed.

The POC tests presented median sensitivity and specificity values, negative and positive predictive values, and lower limits of detection in the quantitative cTn tests, identifying most of the patients with AMI. However, when the cutoff point of the test was lowered, the positive predictive values were found to be higher, enabling the detection of all the patients with AMI by the i-STAT POC test and four out of six by the AQT90 test .[13]

One of the advantages of using POC cTn testing, as reported in the research papers, was for prognosis, as pointed out, for example, by Cho *et al* [43].

When three POC cTn test results came out positive, the percentage of ACS was 10 times higher (p <0.001). Meanwhile, an over threefold increase in risk was found with two positive POC results, compared to none (p= 0.005).

The analytical performance of the POC cTn tests was found to be equivalent to the laboratory tests, with the added advantage of offering quick bedside results. [11,13,41]

According to McCord *et al* [36], the median time between sampling and results being given was 71 minutes for analyses in a central laboratory versus 24 minutes for POC devices (p <0.001). Gonçalves *et al* [2] indicate the importance of cTn testing early after onset of symptoms and hospitalization for the efficient diagnosis and treatment of AMI.

4. Conclusion

With high sensitivity and specificity for myocardial lesion, POC cTn testing has become an important tool in the diagnosis of ACS and AMI. POC tests give results more quickly than laboratory tests, but with the same sensitivity, providing an accurate diagnosis in a short enough time to help in medical decision-making processes, and leading to shorter hospital stays for patients. Consequently, they could help hospitals reduce costs both at the triage stage in emergency units and with reduced hospital stays.

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