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Point-of-care tests in suspected acute myocardial infarction: A systematic review ☆

Madeleine H.E. Bruins Slot [a,1], Geert J.M.G. van der Heijden [b,1], Saskia D. Stelpstra [a,1], Arno W. Hoes [a,1], Frans H. Rutten [a,*,1]

[a] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands
[b] Department of Social Dentistry of the University of Amsterdam. Gustav Mahlerlaan 3004, 1081 LA Amsterdam, The Netherlands

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ABSTRACT

Background: A review of cardiac point-of-care (POC) tests used to detect or exclude acute myocardial infarction (AMI) with a focus on test performance within 6 hours after the start of symptoms.
Methods: A systematic review of articles on the diagnostic accuracy of point of care (POC) tests in patients suspected of AMI from the PubMed database from January 1st 1990 to December 1st 2012.
Results: Our search yielded 42 studies evaluating POC tests. Troponin (Tn) was investigated in 29 studies, and creatine kinase-myocardial band isoenzyme (CK-MB), myoglobin, and heart-type fatty acid-binding protein (H-FABP) each in 13 studies. Eight studies used a multimarker approach. In 14 studies results were presented or could be recalculated for test results within 6 hours of symptom onset or with a median time from symptoms onset to testing of 3 hours. In this time frame the negative predictive value (NPV) ranged from 31 to 97% with single testing, and from 59 to 100% with a multi-marker approach. Just one study satisfied to all items used for methods appraisal.
Conclusions: The ideal POC test for the diagnosis of AMI within 6 hours after the onset of symptoms does not yet exist. Evaluated POC tests were in general of poor methodological quality and reported too many false negatives to be considered as save for the assessment of patients suspected of AMI. A POC test of high-sensitive troponin could possibly fill the gap in the early hours after symptom onset, especially in those with non-definitive electrocardiography.

1. Introduction

Diagnosing acute myocardial infarction (AMI) poses a dilemma for physicians, especially in the large group of patients with recent onset chest pain or discomfort suspected of cardiac origin with non-definitive electrocardiography (ECG) [1,2]. Missing the diagnosis has a great negative impact because the mortality of untreated AMI is high, while early treatment, including immediate revascularisation of those with definitive electrocardiographic abnormalities (e.g. ST-elevation myocardial infarction) can dramatically reduce the risk of mortality and improve prognosis. Establishing the diagnosis in patients with chest discomfort as early as possible is therefore key; however, it is difficult, especially in the out-of-hospital setting, and time consuming in the emergency department in those with non-definitive ECGs. Point-of-care (POC) tests of cardiac biomarkers of necrosis or ischaemia provide results within minutes, thus reducing turnaround time and allowing rapid provision of results that could help decision-making and patient management and thus safely minimize the time-frame of uncertainty about presence or absence of AMI, notably in cases with inconclusive findings on electrocardiography [3]. Recently, a POC panel assessment showed to increase successfully discharge home and reduce median length of stay in the emergency department [2]. A next step would be that POC biomarkers or a panel of such markers could safely exclude AMI or other life-threatening event even in the pre-hospital setting in cases with an inconclusive ECG [4].

For the definite diagnosis of AMI a combination is needed of symptoms suggestive of AMI and a rise and/or fall in levels of cardiac troponin I or T (cTnI or cTnT), or creatine kinase myocardial band isoenzyme (CK-MB) if troponin is not available [5,6]. A major limitation of standard troponin and CK-MB is their low sensitivity in detecting AMI in the early hours immediately after onset of symptoms, and as a result, standard troponin is not consistently elevated in AMI within the first 6 hours (see also Table 1). This is a major disadvantage because in Europe patients suspected of AMI already contact a primary care physician on average 1 to 3 hours after the start of symptoms [7,8], and patients presented straightaway at the hospital by self-referral or direct transport with an ambulance arrive after a median of 4 hours after symptom onset [9].

Thus, there is a need to timely but also efficiently and reliably rule out AMI, especially in patients with a low suspicion of AMI. POC tests containing early biomarkers for cardiac necrosis, ischaemia, or hemodynamic stress could be useful in this setting.

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* Corresponding author. Tel.: +31 6 88 7568051.
E-mail address: F.H.Rutten@umcutrecht.nl (F.H. Rutten).
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Table 1
Characteristics of biomarkers of potential value in suspected acute myocardial infarction.

Cardiac biomarker	Weight (kDa)	Cardiac specificity	Elevated after (hours)	Reaches peak at (hours)	Duration of elevation (days)
Troponin I	23.5	+++	4–10	16	4–7
Troponin T	37	+++	4–10	16	10–14
CK-MB	85	+++	3–4	16	2–3
Myoglobin	18	−	1–3	6	0.5–1
H-FABP	15	++	<2	6	1–1.5

CK-MB is creatine kinase myocardial band. H-FABP is heart-type fatty acid binding protein.

The aim of this systematic review is to provide an overview of published studies assessing the value of available POC tests of early (cardiac) biomarkers in detecting AMI, with a focus on the results within 6 hours after symptoms onset.

2. Methods

2.1. Literature search

We performed a systematic electronic search of the literature from 1 January 1990 until 1 December 2012 using the PubMed database. Search terms used were "acute myocardial infarction," "acute coronary syndrome" and synonyms such as "ischaemic heart disease" combined with "troponin," "high-sensitive troponin," "myoglobin," "creatine kinase myocardial band OR CK-MB" and "fatty acid-binding protein OR FABP." Additionally, to identify studies that used a POC test we used the search terms "point of care test OR bedside test OR office test OR near patient test." Box 1 shows the exact search terms used. We screened the title and abstract of all studies for relevance. Full-text publications were retrieved for original articles written in English. For all relevant publications the records retrieved with the "related articles" link in PubMed were screened and reference lists were checked for other relevant studies.

2.2. Selection of publications

We selected studies that used POC tests of biomarkers for the diagnosis of AMI and reporting diagnostic accuracy data. We excluded studies that reported only on prognosis and studies in which accuracy data of biomarkers were obtained by comparing confirmed AMI patients with healthy controls (a "diagnostic case–control study") (see Fig. 1). We systematically collected characteristics of the selected studies and their biomarkers on a standardized case record form. The collected items were as follows: number of patients included, patient domain, prevalence of the outcome and the type of reference test, time intervals of biomarker measurement, and diagnostic accuracy parameters of the biomarkers (see Table 2).

2.3. Methods appraisal

Each study was assessed by two authors (M.B.S. and S.S.) for quality based on the criteria as proposed by the QUADAS-2 checklist (Quality Assessment of Diagnostic Accuracy Studies) [10]. The following criteria were used: (1) use of a valid reference standard in accordance with international AMI guidelines; (2) performance of the same reference standard in all patients; (3) independent interpretation of the index and reference tests; (4) cut-off value for positive index test pre-specified and not derived from study data; (5) completeness of data, notably reporting of withdrawals from the study; (6) reporting of indistinct test results of the POC index tests. Information provided in the published articles for all criteria was scored as clear or unclear. When sufficient clear information was provided, criteria were scored as satisfied (no/yes) (see Table 3).

2.4. Definition of myocardial infarction

In the international guidelines, the definition of AMI is based on a typical rise of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit in combination with evidence of myocardial ischaemia, i.e. at least one of the following: symptoms of ischaemia, ECG changes indicative of new ischaemia (new ST-T changes or new left bundle branch block, development of pathological Q waves), imaging evidence of new loss of viable myocardium or new regional wall motion abnormality [5,6]. Until 2000, the widely accepted standard for diagnosing myocardial infarction was the WHO criteria [11]. These criteria consisted of a clinical history of chest pain (typical or atypical) with unequivocal ECG changes and/or unequivocal serum enzyme (typically CK and CK-MB) changes, where the pattern of rise and fall should be consistent with time of symptom onset. The major difference between both definitions of AMI is that troponin is much more sensitive than CK-MB, and thus able to detect smaller myocardial infarctions.

2.5. Data analysis

From each included study we aimed to extract the number of patients with a true-positive, false-positive, false-negative, and true-negative test result either through direct or through recalculations based on reported measures of accuracy in combination with the prevalence and sample size of a study. Sensitivity, specificity, and a test's positive predictive value (PPV) and negative predictive value (NPV) are provided in Table 2. Accuracy data were separately calculated for studies providing test results within the first 6 hours after onset of symptoms, or included patients with a mean duration of symptoms of 3 hours or less; however, these data are not presented in the tables.

We used SPSS V.17.0 for all analyses.

Box 1
Search terms used.

Pubmed Search	((((((((((((((troponin[Title/Abstract]) OR Tn[Title/Abstract]) OR TnT[Title/Abstract]) OR TnI[Title/Abstract]) OR myoglobin[Title/Abstract]) OR H-FABP[Title/Abstract]) OR FABP[Title/Abstract]) OR CK-MB[Title/Abstract]) OR ((((fatty[Title/Abstract]) AND acid[Title/Abstract]) AND binding[Title/Abstract]) AND protein[Title/Abstract])) OR (((fatty[Title/Abstract]) AND acid-binding[Title/Abstract]) AND protein[Title/Abstract])) OR ((((creatine[Title/Abstract]) AND kinase[Title/Abstract]) AND myocardial[Title/Abstract]) AND band[Title/Abstract])) OR (((creatine[Title/Abstract]) AND kinase-myocardial[Title/Abstract]) AND band[Title/Abstract]))))) AND ((((((((((point of care[Title/Abstract]) OR point-of-care[Title/Abstract]) OR office[Title/Abstract]) OR bedside[Title/Abstract]) OR near patient[Title/Abstract]) OR POC[Title/Abstract]) OR on-site[Title/Abstract]) OR rapid[Title/Abstract]) OR ultra-rapid[Title/Abstract])) AND (((((((test[Title/Abstract]) OR tests[Title/Abstract]) OR assay[Title/Abstract]) OR assays[Title/Abstract]) OR immunoassay[Title/Abstract]) OR immunoassays[Title/Abstract]) OR diagnosis[Title/Abstract]) OR testing[Title/Abstract]))) AND ((((((((acute[Title/Abstract]) AND coronary[Title/Abstract])) AND ((((syndrome[Title/Abstract]) OR syndromes[Title/Abstract]) OR ischemia[Title/Abstract]) OR ischaemia[Title/Abstract])))) OR ((myocardial[Title/Abstract]) AND ((((ischemia[Title/Abstract]) OR ischaemia[Title/Abstract]) OR infarction[Title/Abstract]) OR infarctions[Title/Abstract])))) OR (((heart[Title/Abstract]) AND ((disease[Title/Abstract]) OR diseases[Title/Abstract])) AND ((ischemic[Title/Abstract]) OR ischaemic[Title/Abstract])))) OR ((((attack[Title/Abstract]) OR attacks[Title/Abstract])) AND heart[Title/Abstract]))	402 hits