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Clinical performance of a new point-of-care cardiac troponin I assay compared to three laboratory troponin assays ☆

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ABSTRACT

Background: Studies of cardiac markers in diagnosing acute myocardial infarction (AMI) have mostly been performed using central laboratory platforms. The AQT90 FLEX TnI (troponin I) assay is designed for quantitative point of care testing (POCT). This study evaluated clinical performance in diagnosing AMI of the AQT90 FLEX TnI POCT assay compared with central laboratory troponin assays.
Methods: The study included 458 chest pain patients. Blood samples were obtained on admission and after 6–9 h. Blood was analyzed using the following assays: AQT90 FLEX TnI, Access AccuTnI, Abbott AxSYM ADV, Roche cTnT, Roche CKMBmass. Patients were diagnosed with AMI according to the new universal definition of AMI.
Results: The performance of the AQT90 FLEX TnI assay on admission was equivalent to the Abbott AxSYM ADV cTnI but inferior to the AccuTnI. After 6–9 h both laboratory based assays were superior. The AQT90 FLEX TnI had a negative predictive value (NPV) of 90 and 96% (admission; 6–9 h). No statistical differences were seen in receiver operating characteristics analysis.
Conclusions: The AQT90 FLEX TnI POCT assay was marginally inferior to the two laboratory based assays of cTnI in diagnosing AMI. A high (NPV) may make this assay suitable as a rule out marker.

1. Introduction

Measurement of cardiac troponins I and T (cTnI and cTnT) in blood is currently the recommendation for the biochemical identification of patients with myocardial cell injury and AMI [1,2]. It has recently been shown that the new assays of cTnI and cTnT may be even more sensitive than the previous assays of cTnT (4th generation) early in acute coronary syndrome (ACS) [3–6]. The introduction of new sensitive assays has led to increased interest in exploring the value of cTnI and cTnT in the acute setting and in particular as point-of care test (POCT) assays.

The cTnI assay developed for the AQT90 FLEX platform (Radiometer Medical ApS, Denmark) is a POCT assay designed to provide a high clinical performance together with a fast turn around time (TAT) with an analytical run time of approximately 18 min. AQT90 FLEX is a random-access point-of-care analyzer intended for the quantitative determination of cardiac, coagulation, and sepsis markers in whole blood or plasma [7].

Current guidelines recommend that that the 99th percentile of the upper reference limit (URL) should be used as a cut-off for the diagnosis of acute myocardial infarction (AMI) [2,8], given a coefficient of variation (CV) of ≤10% at the 99th percentile URL.

The aim of this study was to evaluate the clinical performances of a new POCT assay, the cardiac specific AQT90 FLEX TnI, and to compare it with two sensitive laboratory assays of cTnI, i.e. the Beckman Coulter AccuTnI assay and the Abbott AxSYM ADV assay, as well as the Roche cTnT (4th generation) laboratory assay.

2. Patients and methods

2.1. Patient specimens

The study population comprised 458 subjects who were admitted with chest pain and suspected of ACS. The study population included 293 males (64%) and 165 females (36%). Patients were referred by a general practitioner or the ambulance service. They were subsequently admitted and included by the physician on duty. Patients admitted more than once during the investigation period were only included on their first admission. Twelve lead electrocardiogram (ECG-12) was performed in all patients.

2.2. Routine diagnostic procedures

At the emergency department (ED) and in the coronary care unit (CCU), routine procedures comprised establishing time of onset of

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symptoms as accurately as possible (i.e. description of chest pain, pulmonary edema, severe dyspnea, syncope), a general patient history, clinical examination, ECG-12, and the laboratory tests described below.

2.3. Electrocardiogram

An ECG was taken on admission to the ED, on arrival at the CCU, and at least once daily thereafter.

2.4. Medical therapy

All patients were transferred to the CCU with a standard regimen for patients suspected of ACS: On arrival, 300 mg of aspirin was administered to all patients (thereafter 75 mg o.d.). If the ECG showed ST-depressions, T-wave inversions, or other signs that increased the likelihood of ACS, the physician on duty administered low molecular weight heparin (LMWH) (enoxaparin 1 mg/kg bodyweight b.d.) as well as clopidogrel (300 mg bolus, 75 mg o.d.). Otherwise, results of cTnT analysis were awaited. If ACS was diagnosed by elevated cTnT, or if the patient otherwise was considered unstable, treatment with the above-mentioned drugs and in many cases statins and beta-blockers were instituted.

2.5. Cardiac biomarkers

Cardiac troponin I (cTnI) was analyzed from lithium-heparinised plasma with three different assays:

AQT90 FLEX TnI immunoassay (Radiometer Medical ApS, Denmark). TnI assay is a one-step sandwich immunofluorometric assay based on the use of three monoclonal antibodies, two for capture and one for detection. The capture antibodies are targeting epitopes 41–49 in the stable mid-fragment, and 190–196 in the C-terminal end. The tracer antibody targets epitopes 137–149. During 15 min of incubation time, the tracer and capture antibodies form a complex with the analyte present in the sample. The measured signal is converted to a concentration using the calibration curve stored in the memory of the instrument. The limit of detection has been determined to be 0.0095 μg/L. The reportable range of the assay is 0.010–50 μg/L. The upper 99th percentile URL has been determined to be ≤0.023 μg/L. The concentration giving the coefficient of variation (CV) of 10% of the AQT90 FLEX TnI assay is 0.039 μg/L [9].

Access AccuTnI assay (Beckman Coulter) determined on the Access platform. For the AccuTnI assay, the upper 99th percentile URL is 0.04 μg/L for healthy subjects regardless of age [10] and the lowest concentration measurable with a 10% CV is 0.014 μg/L [11].

Abbott cTnI ADV assay (Abbott Diagnostics, Chicago, Il, USA) determined on the AxSYM platform. The reportable range of the assay is 0.02–50 μg/L. The upper 99th percentile URL is 0.08 μg/L. The lowest concentration with CV ≤10% is 0.16.μg/L [12].

Cardiac troponin T (cTnT) and creatine kinase MB mass (CKMBmass) was determined from serum on Elecsys 2010 (Roche Diagnostics, Mannheim, Germany). For cTnT (4th generation assay), the upper 99th percentile URL is <0.01 μg/L and the lowest concentration exhibiting CV <10% is 0.03 μg/L [13]. Upper reference value for CKMBmass is 4.7 (females) and 6.7 μg/L (males), respectively, with a CV of 2.3% at 5.7 μg/L [8].

2.6. Blood sampling

Blood sampling was scheduled according to the department's routine procedures where blood samples for cTnT and CKMBmass were obtained on arrival, after 6–9 h, and after 12–24 h according to consensus report and guidelines [2,14]. All patients had at least two blood samples taken to exclude/verify the AMI diagnosis.

On arrival, patients also had blood samples drawn for the evaluation of electrolytes, renal parameters and lipid metabolism.

Samples were centrifuged at 4000×*g* for 10 min. The plasma was stored at −80 °C until analysis. Blood samples were collected from February 2003 to October 2004 and analyses were performed in January 2009. The total processing time from obtainment of samples to storage did not exceed 2.5 h. Frozen samples were mixed after thawing and re-centrifuged before analysis. The AQT90 FLEXT TnI assay is stable for at least one freeze/thaw cycle and samples did not undergo repeat cycles. All analyses, including measurements with the AQT90 FLEXT TnI, were performed by trained laboratory staff.

2.7. Definition of AMI

Patients were classified as having AMI according to the new universal definition of AMI [2]. These included detection of rise and/or fall of cTnT >0.03 μg/L together with signs indicative of ischemia (clinical symptoms, ECG).

2.8. Exclusion criteria

Patients were excluded, if they had suffered a documented MI within the last week before admission or were admitted with ST-segment elevation MI (STEMI).

2.9. Statistics

Comparison between groups was performed by using Fischer's exact test. Medians and ranges were used for descriptive purposes. ROC analysis was performed by the method of Hanley and McNeil. McNemar test was used for testing differences in proportions. The level of significance chosen was 0.05. The statistical analyses were performed using MedCalc statistical software package (MedCalc, Belgium).

2.10. Ethics

The study was approved by the Ethical Committee of North Jutland and Viborg Counties. Patients gave informed consent.

3. Results

Of the 458 patients referred with chest-pain, 104 patients (23%) had a final diagnosis of AMI according to the above mentioned criteria. Of these, two patients (1.9%) developed ST segment elevations in the ECG and subsequently went to acute revascularization. The median time fron symptoms onset to the first blood sample was 2.2 h.

Table 1 shows baseline characteristics of the population.

Three assays of cTnI were compared (AQT90 FLEX TnI — designed for quantitative POC testing; Access AccuTnI and AxSYM ADV — designed for automated laboratory platforms). Table 2 shows the respective sensitivities and specificities for the MI diagnosis as well as area under the curve (AUC) (obtained in ROC analysis) of the assays investigated. The diagnostic cut-off values for the assays were: AQT90 FLEX TnI: 0.039 μg/L; Access AccuTnI: 0.04 μg/L; Abbott AxSYM ADV: 0.16 μg/L; Roche cTnT: 0.03 μg/L; Roche CKMBmass: 4.7/6.7 μg/L (females/males). Results are shown for the first and second sample, respectively.

On admission, the AQT90 FLEX TnI assay displayed a sensitivity of 58% (CI 95%: 47–69) and a specificity of 94% (CI 95%: 91–96%). For the second sample, the sensitivity and specificity increased to 85% (CI 95%: 75–92%) and 91% (CI 95%: 87–94%), respectively. The AUCs for