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The clinical utility of CK-MB measurement in patients suspected of acute coronary syndrome

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ABSTRACT

Background: This study aims to assess the clinical utility of CK-MB measurement in patients suspected of acute coronary syndrome (ACS).
Methods: All CK-MB and troponin T measurements performed <1 h apart during the study period were obtained and analyzed for concordance. A total of 1214 cases with discordant biomarkers results were found. Retrospective review of electronic health records (EHRs) was performed to assess the clinical impact, if any, of the discordant biomarkers results.
Results: In 401 cases, CK-MB concentrations were increased whereas troponin T concentrations were negative at <0.01 ng/ml. In this group, clinical interpretations included, rhabdomyolysis, demand ischemia, and drug intoxication. No additional investigations for ACS were conducted in this group. Among the remaining 813 cases, troponin T concentrations were increased in the presence of a normal CK-MB result. In this group, the discordant normal CK-MB lowered suspicion for ACS in only 22 cases (2.7%). Most common interpretations for isolated positive troponin were demand ischemia and impaired renal function. In most cases, discordant CK-MB results were not considered a significant finding.
Conclusions: In the setting of suspected ACS, CK-MB has limited clinical impact when contemporary troponin assay results are available.

1. Introduction

Cardiac biomarkers play a critical role in the initial screening and diagnosis of acute coronary syndrome (ACS) particularly in patients with non-ST elevation myocardial infarction (NSTEMI). Creatine kinase isoform MB (CK-MB) has been the cornerstone of initial screening of patients with suspected ACS, however, troponins T and I became the preferred screening test for ACS without ST elevation due to their higher analytical sensitivity and specificity compared with CK-MB [1–4]. The joint guidelines from the American College of Cardiologists (ACC) and the American Heart Association (AHA) published in 2000 reflect this change that was later substantiated in a number of studies [5–7]. Troponin assays have since much improved in their analytical sensitivity and specificity, leading to improved diagnostic and prognostic value shown in several studies [8,9].

Contemporary troponin assays or high-sensitivity troponin assays are characterized by improved analytical sensitivity with greater degree of precision. According to consensus opinion, these assays should have coefficient of variance <10% at the 99th percentile value of population of interest [10,11]. Additionally, >50% of healthy individuals within the population of interest should have troponin concentrations below 99th percentile value but remain above the limit of detection [10,11].

With improvements in troponin assay, the most recent guideline from AHA/ACC published in 2014 states that with the advent use of contemporary troponin assays, CK-MB measurements do not provide additional value for the diagnosis of ACS (Class III, Level of evidence A) [12].

However, despite current evidence recommending the use of troponin as the sole biomarker in patients suspected of ACS, CK-MB testing remains widely used in the clinical assessment. While older guidelines listed both troponin and CK-MB as acceptable biomarkers in the diagnosis of ACS, high-sensitivity troponin assays rendered the clinical significance of CK-MB assay questionable at best.

Unfortunately, information regarding the qualitative changes in high-sensitivity troponin assay may not be readily available to clinicians, leading to reluctance in eliminating CK-MB testing in suspected ACS cases. Given currently available data, CK-MB testing is unlikely to add significant information and may increase the cost of medical care. Moreover, the discrepancy between troponin and CK-MB can lead to confusion in the interpretation of biomarker results, leading to less than optimal patient care.

In this study, we sought to assess the clinical utility of CK-MB assay results in patients with suspected ACS when used in conjunction with available high-sensitivity troponin T assay. Retrospective EHR review

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was performed to determine if CK-MB results added any clinically valuable information and influenced clinical decision-making.

2. Materials and methods

2.1. Study design

This is a retrospective review of electronic health record of patients suspected of ACS and who have undergone both troponin T and CK-MB testing during the same admission period. To reduce the effect of temporal changes, we selected cases with measurement of troponin T and CK-MB performed <1 h apart (Fig. 1). Additionally, we disregarded repetitive measurements performed within one week of admission. However, if measurements were performed >1 week apart, they were considered part of a separate event and were included in the review. For cases with discrepant troponin T and CK-MB results, clinical interpretations were collected following EHR review. The study population was from Parkland Memorial Hospital between August 2014 and January 2015. This study was approved by the institutional review board of the University of Texas Southwestern Medical Center, Dallas, TX.

2.2. Participants

Patients suspected of ACS and who have been tested for both CK-MB and troponin T during the same admission event between August 2014 and January 2015 were included into the study. Patients with discrepant CM-MB and troponin T results were included for final analysis and additional EHR review for clinical interpretation within 3 days of availability of discrepant CK-MB and troponin T results.

2.3. Assay systems

Both CK-MB and troponin T measurements were performed using the COBAS Immunoassay analyzer (Roche Diagnostics). Analysis was according to the manufacturer's protocol. Troponin T concentrations >0.01 ng/ml (99th percentile among general population) were interpreted as positive troponin, whereas, CK-MB index >3 and or absolute value >3 ng/ml in females or 5 ng/ml in males (which is the 97.5th percentile among general population), was interpreted as positive CK-MB. Gender specific reference intervals for CK-MB are obtained from the manufacturer (Roche) and verified by the clinical laboratory.

3. Results

A total of 8980 CK-MB and 26,041 troponin T measurements were performed during the study period. Cases were screened for discrepancy between CK-MB and troponin results as depicted in Fig. 1. Patients with discrepant biomarker results were identified for EHR review. Briefly, CK-MB measurements were matched with troponin measurements performed <1 h apart (76.2% of these cases were performed on the same sample). Repeat measurements within 1 week were excluded from the study, but if measurements were >1 week apart, this was regarded as a separate case and were included in the analysis. Finally,

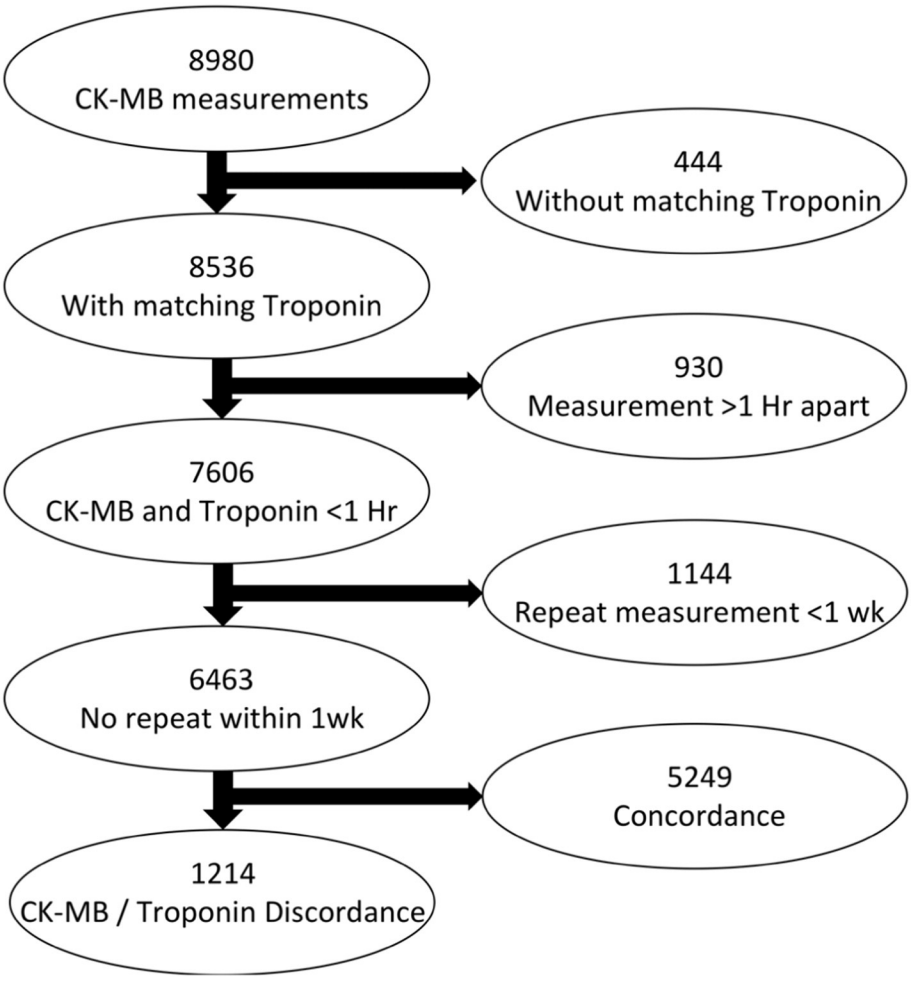

Fig. 1. Study inclusion criteria. CK-MB and troponin measurements performed within 1 h were reviewed for concordance. Repeat measurements were excluded if within less than 1 week. Final cases with discrepant CK-MB and troponin measurement were selected for electronic health record review.