A pilot study of cardiac troponin I in patients with acute myocardial infarction and unstable angina

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ABSTRACT

Objective: To assess the value of cardiac troponin I in the initial management of acute myocardial infarction and unstable angina, as well as the concordance between creatine phosphokinase-cardiac isoenzyme and cardiac troponin I.

Methods: We reviewed retrospectively the charts of 32 patients with acute myocardial infarction or unstable angina admitted to the Intensive Care Unit from the Emergency Room of King Khalid Military City Hospital, Hafar-Al-Batin, Kingdom of Saudi Arabia from April 1998 to September 2000. The time of admission to the intensive care unit, which corresponds to the beginning of thrombolytic therapy, the time when cardiac enzymes (creatine phosphokinase-cardiac isoenzyme and cardiac troponin I) are available as well as number of cardiac troponin I determinations before obtaining a significant positive result (>2ng/ml) and the delay between admission and the first significant positive result of cardiac troponin I, were evaluated.

Results: Sixteen patients had confirmed acute myocardial infarction based on the association of typical chest pain, electrocardiographic findings with ST segment elevation and significant increase of the ratio creatine phosphokinase-cardiac isoenzyme/creatine phosphokinase > 10%. Sixteen patients had unstable angina and out of the 16 patients (81.25%) with acute myocardial infarction, 13 received thrombolytic therapy which was initiated on the basis of typical clinical history and electrocardiographic features, before the availability of cardiac enzymes. Troponin I was available in only 13 cases. The number of tests performed in these patients was 32. The first positive result of cardiac troponin I was available within a mean time of 16.66 ± 20.8 hours from admission. The number of negative tests performed before obtaining a frank positive result was 9 in 12 patients. The number of positive tests after having obtained the first frank positive cardiac troponin I result was 10 in 12 patients. In all cases of cardiac troponin I, results were concordant with creatine phosphokinase-cardiac isoenzyme. In the 16 patients with unstable angina, only 11 patients had cardiac troponin I serum level. A total of 21 tests were performed. In 9 patients 14 cardiac troponin I tests were < 2 ng/ml. This was correlated with normal creatine phosphokinase-cardiac isoenzyme/creatine phosphokinase ratio. In 2 patients, 7 cardiac troponin I tests were positive. Both of them had significant increase of creatine phosphokinase-cardiac isoenzyme/creatine phosphokinase ratio and electrocardiographic features of myocardial ischemia and were referred for urgent coronary angiography.

Conclusion: Cardiac troponin I levels are not helpful in the initial management of patients with acute myocardial infarction. Thrombolytic therapy should be therefore instituted before the availability of cardiac troponin I results. However, cardiac troponin I results are concordant with creatine phosphokinase-cardiac isoenzyme in retrospective confirmation of the diagnosis of acute myocardial infarction a few hours after onset. In patients with unstable angina, cardiac troponin I should be used mainly for risk stratification.

Keywords: Acute myocardial infarction, troponin I.

Early diagnosis of acute myocardial infarction (AMI) is crucial for the survival of the patients. Furthermore, the effectiveness of thrombolytic therapy is closely correlated with the precocity of diagnosis. According to the World Health Organization (WHO), at least 2 criteria from the following should be present: (a) Clinical history of ischemic chest discomfort of more than 30 minutes duration, (b) The evolution of typical unequivocal electrocardiographic (ECG) changes in at least 2 leads of the 12-lead standard ECG, (c) The rise and fall of serum enzymes, indicative of muscle cell injury.[1] However, in clinical practice, as many as one 3rd of the patients with AMI, pass easily unrecognized either due to atypical chest pain or painless AMI.[2,3] In addition, nearly half of the patients with AMI do not exhibit ECG changes at initial presentation to the Emergency Room.[4] The aim of our study was to assess the clinical importance of cardiac troponin I (cTnI) in the initial management of AMI and unstable angina in our institution as well as the concordance between creatine phosphokinase-cardiac isoenzyme (CK-MB) and cTnI.

Methods. We retrospectively reviewed the charts of patients with AMI and unstable angina admitted to the Intensive Care Unit (ICU) from the Emergency Room of King Khalid Military City Hospital, Hafar Al Batin, Kingdom of Saudi Arabia (KSA) from April 1998 to September 2000. The time of admission to ICU which corresponded to the beginning of thrombolytic therapy, the time when cardiac enzymes (creatine phosphokinase MB and cTnI) were available as well as the number of cTnI determinations before obtaining a significant positive result (>2ng/ml) and the delay between admission and the first significant positive result of cTnI, were evaluated. Cardiac troponin I levels were determined by the troponin I Microparicle Enzyme Immunoassay (MEIA) of Abbott laboratories. The sensitivity, specificity, positive and negative predictive values for cTnI were calculated.

Results. Thirty-two charts were reviewed. The mean age of the patients was 50.22 ± 11.54 years (range: 33–95 years). Sixteen patients had confirmed AMI based on the association of typical chest pain, ECG findings with ST segment elevation, and significant increase of the ratio CK-MB/CK > 10%. Sixteen patients had unstable angina and out of the 16 patients with AMI (81.25%), 13 received thrombolytic therapy. Two patients had already installed necrosis and had conservative management with Aspirin, Heparin and Beta-blockers. One patient did not receive thrombolytic therapy due to over age (110 years) and associated medical problems. In all cases, thrombolytic therapy was initiated on the basis of typical clinical history and ECG features, before the availability of cardiac enzymes. Troponin I results were available in only 13 cases. The number of tests performed in these patients was 32. Twenty two tests were positive and 10 were negative. The first positive result of cTnI was available within a mean time of 16.66 ± 20.8 hours from admission. The number of negative tests performed before obtaining a frank positive result was 9 in 12 patients. The number of positive tests after having obtained the first frank positive cTnI result was 10 in 12 patients. In all cases cTnI values were concordant with CK-MB results. In 16 patients having unstable angina only 11 patients had cTnI serum level. A total of 21 tests were performed. In 9 patients 14 cTnI tests were <2ng/ml. This was correlated with normal CK-MB/CK ratio. In 2 patients, 7 cTnI tests were positive. Both had significant increase of CK-MB/CK ratio and ECG features of myocardial ischemia. They were referred to a specialized center for urgent coronarography. Sensitivity, specificity, positive and predictive negative values are shown in **Table 1.**

Discussion. Our study revealed that cTnI was not useful in acute management of patients with AMI, since in all cases, thrombolytic therapy was administered on the basis of typical clinical findings and according to the WHO criteria.[1] In our study cTnI was not more useful than CK-MB in the initial decision making. Early reperfusion with timely thrombolytic therapy was our major concern. Waiting for a positive result of cTnI would have delayed unreasonably life saving reperfusion therapy as suggested by a mean delay of 16.66 hours for positive cTnI, and would have resulted in more myocardial damage, and life threatening complications. Our study, though small and retrospective, was appropriate to bring strong evidence of the non usefulness of cTnI in the initial management of AMI. However, cTnI served for retrospective confirmation of AMI as well as CK-MB. In view of these findings, we can affirm that serial determination of cTnI as performed in our patients is not cost-effective. Indeed, the 9 early tests performed before obtaining the first positive result and the 10 positive tests obtained after the first

Table 1 - Performance of cardiac troponin I in diagnosing acute myocardial infarction.

Performance	%
Sensitivity	85.7
Specificity	81.8
Predictive positive value	85.7
Predictive negative value	81.8

positive result as well as the only negative test obtained in one patient resulted in 20 unnecessary tests with a global cost of 1000 SR. This represents 62.5% of the total cost of cTnI tests performed for AMI. Our findings are supported by recent clinical trials which have demonstrated that cTnI is released into the blood stream within hours following AMI or ischemic damage. Elevated levels of cTnI (above the values established for non AMI specimens) are detectable in serum within 4 to 6 hours after the onset of chest pain, and reach peak concentrations approximately 12 hours, and remain elevated for 3 to 10 days following AMI.[4-7] The temporal pattern of cTnI release following AMI extends across the diagnostic window of CK-MB.[8] According to the manufacturer, the clinical performance of cTnI measurement with the Abbott, troponin I micropraticle enzyme immunoassy showed a sensitivity of 93.9% and a specificity of 93.4%. The diagnostic cut-off for the AMI patients was determined to be 2ng/ml. It is important to mention that we had used this diagnostic cut-off. However, it is imperative that our laboratory establishes its own diagnostic cut-off in order to assure proper representation of our specific population and to reflect current practice and criteria for AMI diagnosis at our institution. In our study, sensitivity was 85.7% and specificity was 81.8%. These values were lower than the values reported by the manufacturer. This discrepancy should be confirmed or infirmed by a prospective study including a larger group of patients.

The assessment of cTnI in unstable angina was another aspect in our study. It is now admitted that troponin values allow risk stratification in unstable angina. Cardiac troponin I concentrations of more than 0.4ng/ml were identified in 41% of patients with unstable angina in the thrombolysis in myocardial ischemia (TIMI) III B trial,[9] mortality at 42 days was significantly higher among those positive for cTnI (3.7% versus 1%) and each one ng/ml increment in cTnI concentration at admission was associated with a significant increase in the risk ratio for death and AMI. In our study, 2 patients with unstable angina with high cTnI were referred to a Specialized Center for coronary angiography. However, they had at the same time a clinical history and ECG features compatible with myocardial ischemia. No referral was recorded on the basis of isolated abnormal cTnI value, and no discharge was allowed on the basis of

an isolated normal cTnI value. This fact emphasizes the need for prospective studies in order to correlate troponin concentrations with the severity of coronary artery disease, particularly with angiographic data.

In conclusion, the use of cTnI should be rational. In AMI, cTnI brings retrospective confirmation for the diagnosis in addition to the usual features. Thrombolytic therapy should not be delayed. It must be mainly based on clinical diagnosis according to WHO criteria, and before the availability of any lab results. In unstable angina, cTnI is expected to bring more information for risk stratification for coronary artery disease with consequent management strategies. According to sensitivity and specificity results, the revision of the diagnostic cut-off in our institution for our specific population is mandatory. A prospective study will be helpful to clarify these important issues.

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