What tests for suspected myocardial infarction?
Serum cardiac troponin I or creatine kinase?

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Research question
Can cardiac troponin I (cTnI) replace creatine mass kinase (CK-MB) as the serum biochemical marker for detection of acute myocardial infarction (MI)?

Type of article and design
Prospective study of a diagnostic test.

Relevance to family physicians
In 1992, ischemic heart disease accounted for 21% of deaths; half were attributable to acute MI. Reduction in mortality could be as high as 30% to 50% for patients receiving thrombolytic therapy within 6 hours of onset of chest pain and 7.5% for patients consulting between 6 and 12 hours after onset of symptoms. In the United States, only 30% of patients admitted to an intensive care unit for evaluation of chest pain were found to have a cardiac cause for their symptoms. We need strategies to improve diagnosis of acute MI and thus improve use of intensive care resources.

Panju et al reviewed predictors in the history and physical examination of acute MI and attached likelihood ratios to them. The most powerful features increasing the probability of MI and their associated likelihood ratios (LR) are new ST segment elevation (LR 5.7 to 53.9), new Q wave (LR 5.3 to 24.8), chest pain radiating to both left and right arms simultaneously (LR 7.1), presence of a third heart sound (LR 3.2), and hypotension (LR 3.1). The most powerful features decreasing the probability of MI are normal electrocardiograph (ECG) results (LR 0.1 to 0.3), pleuritic chest pain (LR 0.2), chest pain reproduced by palpation (LR 0.2 to 0.4), sharp or stabbing chest pain (LR 0.3), and positional chest pain (LR 0.3). Given this information, how can we arrive at a more precise diagnosis by replacing the traditional serum CK-MB with cTnI as a marker for acute MI?

Overview of study and outcomes
At an urban teaching hospital, 327 random consecutive patients were prospectively evaluated for acute MI. Diagnosis of MI was based on a modification of World Health Organization criteria that require at least two of the following: clinical history of typical chest pain for longer than 30 minutes, evidence of ischemic changes on ECG (ST segment depression, ST segment elevation, T wave inversion), and a rise in CK-MB mass concentration to >5.0 µg/L or a change of >25% between two CK-MB measurements. All patients were assessed by detailed clinical examination 24 to 72 hours after admission.

All patients had serial ECGs on admission and at least once daily thereafter. An experienced cardiologist, who was unaware of biochemical marker results, evaluated the ECGs. Serum CK-MB and cTnI were obtained on admission and every 6 to 8 hours for at least 24 to 48 hours. Upper limit of normal was 5 µg/L for CK-MB and 0.8 µg/L for cTnI. Patients diagnosed with acute MI were similar to those without MI in age, sex, history of coronary artery disease, hypertension, diabetes, chronic renal failure, tobacco use, alcohol use, and cocaine use.

Results
Of the 19% of patients diagnosed with acute MI, results of ECG were diagnostic for 79% and nondiagnostic for 21%. Cardiac troponin I demonstrated 100% diagnostic sensitivity and 100% negative predictive value.
accuracy for acute MI compared with 88.2% and 96.5% respectively, for CK-MB and 73.5% and 91.7% respectively, for total CK. Both cTnI and CK-MB were more diagnostically specific than total CK: 96.3% and 93.2% and 84.6% respectively. Cardiac troponin I demonstrated 75.6% positive predictive accuracy for acute MI compared with 78.9% for CK-MB and 58.1% for total CK. There was a significant correlation between increasing and peak cTnI and peak CK-MB concentration (P < .001) in 168 specimens examined for the 62 patients with acute MI. Six patients were diagnosed with non–Q wave MIs in which peak CK-MB concentrations were not increased (> 4.6 µg/L). Peak cTnI concentrations increased in all six patients (range 2.1 to 18.9 µg/L). Of the 327 patients, 150 (45.9%) had an accurate history for time of onset of chest pain, with a median time from symptom onset to arrival at an emergency department of 3.4 hours. Among these 150 patients were the 62 patients with acute MI. All three markers showed parallel increase over time and peaked between 12 and 18 hours after onset of chest pain. Compared with total CK and CK-MB, cTnI was significantly elevated (P < .01) at all periods > 6 hours and remained elevated longer than CK-MB and total CK more than 48 hours after onset of chest pain. Half-life calculations for cTnI demonstrated a significantly longer half-life for Q wave MIs (24.2 hours) compared with non–Q wave MIs (7.3 hours) (P < .01). Diagnostic sensitivity for detection of acute MI improved over the 24 hours after onset of chest pain for each marker, with cTnI demonstrating significantly (P < .02) improved sensitivity at > 12 hours. All three markers demonstrated poor early sensitivity at < 6 hours after onset of chest pain (40%). Sensitivity of cTnI was 100% at 12 to 24 hours. Diagnostic specificities during the first 12 hours after onset of acute MI were 95.4% at 0 to 6 hours and 95.2% at 6 to < 12 hours for cTnI; and 95.4% at 0 to 6 hours and 96.4% at 6 to < 12 hours for CK-MB. In comparison, specificity for total CK over the same time ranges was < 80%. New serial changes for both CK-MB and cTnI occurred in two patients who had reinfarction documented by new ST segment changes while they were hospitalized after initial presentation of acute MI. Being able to assess patients’ risk factors, however, would help us better estimate the utility of the test. For example, we cannot determine the risk of events in clinically high-risk subsets with negative troponin test results. All three markers demonstrated poor early sensitivity (40%), but we do not know whether there were additive effects in combining two or more markers.

**Application to clinical practice**

Data from this study illustrate that cTnI was significantly more sensitive than CK-MB in diagnosis of acute MI. There was no significant difference in sensitivity between cTnI and CK-MB. Total CK was less sensitive and less specific than either cTnI or CK-MB. As demonstrated in an earlier study, cTnI concentrations were superior in detecting minor myocardial injury when CK-MB is normal, as demonstrated in the six patients with non–Q wave MIs. Cardiac troponin I can remain elevated for 5 to 10 days after chest pain in patients with acute MI, which could make it particularly useful in family practice settings.

Obviously, troponin’s usefulness is based on its availability. Rapid testing (within 20 minutes) with cTnI might allow rapid and safe discharge of patients with acute chest pain from emergency departments because cTnI has 100% sensitivity and 81.9% specificity for diagnosis of acute MI. Having said this, we should add that a troponin test cannot replace clinical evaluation of patients with chest pain.

**Bottom line**

- The sensitivity of cTnI was significantly higher than that of CK-MB, indicating that cTnI testing is better at ruling out acute MI when results are negative. The difference in specificity between the two tests was not statistically significant.
- The early sensitivity (< 6 hours from onset of pain) observed for all three markers was low (< 40%), confirming a continuing need for serial biochemical measurements if history indicates likelihood of acute MI.
- This and previous studies have demonstrated the superiority of cTnI in detecting minor myocardial injury.
- Previous studies have demonstrated that cTnI is a valid predictor of prognosis in patients with acute coronary syndromes.
- Troponin is only one part of the workup of patients with chest pain and cannot replace clinical examination. It is a relatively new marker, so if your instinct still tells you that your patient has had an acute MI, despite reassuring test results, caution seems reasonable.
Points saillants

• La sensibilité de la mesure des troponines I et T (cTnI) était considérablement plus élevée que celle de la créatinine-kinase M B (ck-mb), indiquant que des résultats négatifs à l’épreuve du dosage de la cTnI étaient plus déterminants pour exclure un infarctus aigu du myocarde. La différence quant à la spécificité n’était pas statistiquement significative.

• La sensibilité précoce (<6 heures depuis l’apparition de la douleur) observée pour les trois indicateurs était faible (<40%), confirmant la nécessité de poursuivre les mesures biochimiques si l’anamnèse laisse présumer la probabilité d’un infarctus aigu du myocarde.

• La présente étude et des études antérieures ont démontré la supériorité de la cTnI dans la détection de lésions myocardiques mineures.

• Des études antérieures ont fait valoir que la mesure de la cTnI était un test prédictif valable dans le pronostic des patients présentant des syndromes coronariens aigus.

• La mesure de la troponine n’est qu’une composante de l’ensemble des interventions auprès de patients présentant une douleur thoracique et ne peut pas remplacer l’examen clinique. C’est un indicateur relativement nouveau et si votre instinct vous pousse toujours à croire que votre patient a subi un infarctus aigu du myocarde malgré des épreuves rassurantes, la prudence reste de mise.

References


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