

Are all troponin assays equivalent in the emergency department?

A Eisenman, V Rusetski, D Avital, J Stoler, T Snitkovsky

ABSTRACT

Introduction: Cardiac-specific troponins (cTn) are recently-introduced, sensitive and specific markers of myocardial injury, and their absence should allow to safely exclude a coronary event. Various assays are commercially available but the relative advantage of each is not clear. Our objective was to compare the reliability of the two most commonly used troponin assays (cTnI and cTnT), in the emergency department (ED) for clinical decision when myocardial infarction (MI) or acute coronary syndrome (ACS) is suspected.

Methods: This prospective study included all patients arriving at the ED over a six-month period with chest pain or symptoms suggesting MI or ACS, in which diagnosis could not be confirmed due to absence of characteristic ECG features. All patients were tested with at least one of the two troponin assays available at the ED.

Results: Of the 54 included patients, ten (19%) were eventually diagnosed with MI/ACS. Qualitative assays for cTnI and cTnT identified the MI/ACS patients by both assays (respective positive predictive values of 0.5 and 0.7, and negative predictive values of 1.0 and 0.9). However, these assays were only partially correlated (R equals 0.49) and differed significantly. The quantitative assay for cTnI, but not for cTnT, discerned those who had MI/ACS (group A) from those who had other condition (group B) by their troponin levels (MI/ACS – 17.2 ± 23.8 ng/ml versus others – 0.37 ± 0.91 ng/ml, p is less than 0.001).

Conclusion: In the ED, bedside assays of troponins are invaluable tools for the clinician, and their use is cost-effective. However, in the recommended cutoffs levels, only troponin I but not troponin T allowed the safe discharge of patients not requiring acute hospital care.

Keywords: acute coronary syndrome, myocardial infarction, troponin I, troponin T

Singapore Med J 2005; 46(7):325-327

INTRODUCTION

Despite decades of investigation, the diagnosis of acute myocardial infarction (MI) is still quite complex, because the majority of patients with chest pain fall in the low or medium risk category and present with atypical symptoms and nonspecific electrocardiographical changes⁽¹⁾. While cardiac biochemical markers are important for diagnosis and for stratification of the risk, the ideal cardiac marker and the best diagnostic approach for patients presenting with chest pain in the emergency department (ED) remain elusive⁽¹⁾. Cardiac-specific troponins (cTn) are recently-introduced, sensitive and specific markers for the diagnosis of myocardial injury⁽¹⁻⁵⁾. cTn I (cTnI) and T (cTnT) are proteins integral to the function of cardiac muscle that are not present in normal serum, and therefore are very sensitive indicators of myocardial damage. The ability to assay their serum levels accurately and quickly has revolutionised the concepts of minor myocardial injury and infarction, and introduced powerful prognostic indicators of future adverse cardiac events⁽⁵⁾. Several commercial assays kits for cTnI and one for cTnT are available⁽²⁾, and some allow for bedside analysis⁽⁵⁾. Our objective was to compare the utility of two of these assays in the setting of a busy ED (150,000 visits/year) in order to evaluate the effectiveness of such tests for reliable clinical decisions when myocardial infarction or acute coronary syndrome (ACS) are suspected.

METHODS

This prospective study was conducted in the ED of a 600-bed regional hospital in Northern Israel. Included were all the patients arriving at the ED over a six-month period in 2002, with symptoms suggesting ACS but with normal or equivocal electrocardiograms. All had endured chest pains for more than four hours. The final diagnosis and outcome of these patients were obtained later from their hospital records. Clinical classification was according to the American Heart Association and the Acute Myocardial Infarction ACC/AHA Pocket Guidelines April 2000⁽⁶⁾.

Department of
Emergency
Medicine
The Western
Galilee Hospital
PO Box 21
Naharia
Israel 22100

A Eisenman, MD
Head Medical Section

V Rusetski, MD
Consultant

D Avital, RN, MA
Head of Nursing

J Stoler, MD
Director

Biochemistry
Laboratory

T Snitkovsky, PhD
Director

Correspondence to:
Dr Arie Eisenman
Tel: (972) 4910 7250
Fax: (972) 4910 7593
Email: eisenman@
naharia.health.gov.il

Without breaking these criteria, we further defined the criteria as follows for the needs of this study: 1. Unstable angina (UA): patients presenting typical chest pain for more than four hours without conclusive ischaemic ECG changes. 2. Acute coronary syndrome (ACS): patients presenting typical chest pain for more than four hours with ischaemic ECG changes: T wave inversion. 3. Acute MI: patients with or without typical chest pain for more than four hours with ischaemic ECG changes: ST-T elevation or depression, or significant new rise in cardiac enzymes or troponin. Only patients responding to the criteria of UA or ACS were included in the study. Patients with acute MI whose diagnosis was straightforward were excluded.

All included patients (n=54) were tested with at least one of the two available assays for troponin: 50 patients (92.5%) for cTnI, 52 (96.2%) for cTnT, and 48 (89%) for both. Troponin was assayed by one of the following commercial assays: Trop T (Cardiac T Quantitative Troponin®, Roche Diagnostics, Switzerland) for bedside assays, and Troponin I (AxSYM Troponin-I Assay®, Abbot Diagnostics Division, Germany). The cut-off values used were 0.3 ng/mL for troponin T and 0.4 ng/mL for troponin I, according to the respective manufacturer instructions. The data were analysed with the chi-square test for frequencies and with Student's t-test for parametric data. Data is presented as mean \pm standard deviation (SD), and the significance level was set at $p < 0.05$.

RESULTS

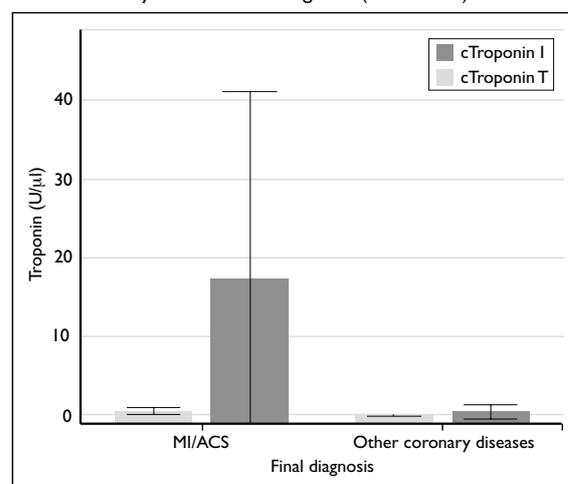
54 patients were included in the study. Of these, ten (19%) were eventually diagnosed with MI or ACS (group A). The remaining patients were diagnosed with conditions such as chest pain, chest wall pain, pneumonia, unstable angina, abdominal pain, pulmonary embolism, and acute respiratory failure (group B). 37% of the patients were discharged from the ED following evaluation.

The qualitative assays for cTnI and cTnT were performed (Table I). Individuals suffering from MI/ACS were identified by at least one of the two assays tested (respective positive predictive values of 0.5 and 0.7, and negative predictive values of 1.0 and 0.9). The assay for cTnT was somewhat more specific than that for cTnI (0.95 vs. 0.74), but the sensitivity of the cTnI assay was 1.0 (compared to 0.55), and identified no false negatives. None of the patients found by both assays to be negative to cTn has developed coronary syndromes. The two assays, however, correlated only partially (Spearman's $R = 0.49$). Indeed, the qualitative assays differed significantly,

Table I. Number of suspected MI/ACS patients and their qualitative troponin bedside assays.

	MI/ACS Group A	Others Group B	p-value
Troponin T assay			<0.0001
Positive	5	2	
Negative	4	37	
Troponin I assay			<0.0001
Positive	10	10	
Negative	0	28	

Fig. 1 Quantitative assay for cTn in ED patients with suspected MI, broken-down by their eventual diagnosis (mean \pm SD).



and of the 48 patients tested by both assays, cTnT identified only 5 out of 10 MI/ACS patients. Likewise, only 27 out of 37 true negatives were discerned by both assays.

Besides the qualitative value of the tests which allowed differentiating those who had coronary events from those who had not, the quantitative level of a positive troponin test could distinguish between those who had true MI/ACS versus other coronary diseases. Thus, while the quantitative assays for cTnI identified clear differences between the levels of the troponins in the two groups of patients (17.2 ± 23.8 ng/ml with MI/ACS vs 0.37 ± 0.91 ng/ml having other diagnoses, $p < 0.001$) (Fig. 1), the differentiation of the groups by the quantitative assay for cTnT was not statistically significant.

DISCUSSION

Myocardial salvage in cases of acute coronary event (MI/ACS) is time dependent, and the greatest potential benefit exists in the first few hours of ACS⁽⁷⁾. The rapid exclusion of ACS in the ED is essential, albeit not always straightforward. In this respect, testing for troponin in the ED has become a common practice for the investigation of chest pain.

MI is more likely in patients with elevated cTnI than in those with normal values⁽⁸⁾, and mortality of patients with elevated troponin I or T is significantly increased (odds ratio= 3:1) compared to that of patients with a negative test⁽⁹⁾. Clinical judgment supported by troponin tests was demonstrated to be more predictive than clinical judgment alone⁽⁹⁾. Indeed, in the setting of the ED, stratification of patients with unstable coronary artery disease by means of cTn is important for clinical management⁽²⁾ and helps to determine the need for hospitalisation and intensity of treatment⁽⁹⁾.

The assay for troponins is especially useful when other diagnostic tools, such as ECG, and the clinical picture are inconclusive. Both available assays, cTnI and cTnT, allow easy and quick quantitative and qualitative decisions in the laboratory or at the bedside. By applying defined threshold values, single testing for cTnI and cTnT within 12 hours after onset of symptoms is appropriate for risk stratification⁽¹⁰⁾. The reduction of clinical events by invasive treatment occurred only in patients with elevated cTn levels⁽²⁾. Still, the controversy whether there is a clinically significant difference between cTnT and cTnI in regard to predictive value and cardiac specificity remains unsettled⁽¹⁰⁾.

Our study found that in the setting of ED, where immediate diagnosis is required, cTnI assays fared better than those for cTnT. This finding concurs with other reports that demonstrated that although both markers identified myocardial damage in equal numbers of patients with clinically unstable angina⁽⁸⁾, cTnI was the most cardiac-specific in the diagnosis of acute MI⁽¹⁾. cTnI had the highest specificity and positive predictive value (99% and 98%) as compared with cTnT (96% and 93%), and it is higher than that of the mass of creatine kinase (CK) or its activity⁽³⁾. In an experimental study, the accuracy of detection of the extent of myocardial injury was higher with cTnI than with cTnT, CK and lactic dehydrogenase⁽⁵⁾. On the other hand, cTnT was more predictive for long-term adverse outcome and possessed maximal prognostic value for the 30-day outcome⁽¹⁰⁾.

In patients with acute MI without initial diagnostic electrocardiograms who presented to the ED within 24 hours of onset of their symptoms, the early diagnostic efficiency of cTnI was compared with that of cTnT, CK, CK-MB isoenzyme, and myoglobin. The sensitivities of all five biochemical markers for MI were poor at the time of ED presentation but

rose significantly with time. In the initial two hours, cTnT was significantly better than cTnI, but still of low sensitivity. Later, cTnI was significantly more specific for acute MI than cTnT, similar to CK-MB or myoglobin⁽¹¹⁾. Since the positive likelihood ratios for cTn-I, CK-MB, and myoglobin were superior to those of CK and cTn-T from six to 24 hours, it was concluded that the cTn are of benefit in identifying acute MI six hours or later after onset⁽¹¹⁾.

In conclusion, we found that in the setting of ED, while both qualitative assays of cTn have high negative and intermediate positive predictive values, the quantitative assay of cTnI has a stronger discriminating power than that of cTnT. This is especially important for deciding on discharge from the ED, with high degree of certainty, that the patients had not suffered a coronary event. Although validation on a larger scale of these findings is needed, emergency physicians should be aware of the differences that exist between various types of troponin essays while taking clinical decisions on patients with suspected ACS/MI.

REFERENCES

1. Chu WW, Dieter RS, Stone CK. A review of clinically relevant cardiac biochemical markers. *WMJ* 2002; 101:40-8.
2. Venge P, Lagerqvist B, Diderholm E, et al. Clinical performance of three cardiac troponin assays in patients with unstable coronary artery disease (a FRISC II substudy). *Am J Cardiol* 2002; 89:1035-41.
3. Sobki SH, Saadeddin SM, Habbab MA. Cardiac markers used in the detection of myocardial injury. *Saudi Med J* 2000; 21:843-6.
4. Bertinchant JP, Robert E, Polge A, et al. Release kinetics of cardiac troponin I and cardiac troponin T in effluents from isolated perfused rabbit hearts after graded experimental myocardial contusion. *J Trauma* 1999; 47:474-80.
5. Sarko J, Pollack CV Jr. Cardiac troponins. *J Emerg Med* 2002; 23:57-65.
6. Cannon CP, Battler A, Brindis RG, et al. American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes. A report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee). *J Am Coll Cardiol* 2001; 38:2114-30.
7. Hofgren C, Karlson BW, Herlitz J. Prodromal symptoms in subsets of patients hospitalized for suspected acute myocardial infarction. *Heart Lung* 1995; 24:3-10.
8. Ottani F, Galvani M, Ferrini D, et al. Direct comparison of early elevations of cardiac troponin T and I in patients with clinical unstable angina. *Am Heart J* 1999; 137:284-91.
9. Heidenreich PA, Alloggiamento T, Melsop K, et al. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. *J Am Coll Cardiol* 2001; 38:478-85.
10. Heesch C, Deu A, Langenbrink L, Goldmann BU, Hamm CW. Analytical and diagnostic performance of troponin assays in patients suspicious for acute coronary syndromes. *Clin Biochem* 2000; 33:359-68.
11. Tucker JF, Collins RA, Anderson AJ, et al. Early diagnostic efficiency of cardiac troponin I and troponin T for acute myocardial infarction. *Acad Emerg Med* 1997; 4:13-21.