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Original Article

Increasing Serum Troponin I and Early Prognosis in Patients with Chest Pain or Angina Equivalent Symptoms in the Emergency Department

HH Davarani, M AfzaliMoghadam, H Hosseinnejad, R Hamidian

Dept. of Emergency Medicine, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

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Abstract

Background: The purpose of this research was to determine the relation between negative or positive qualitative troponin I test and the short term prognosis of patients presenting to emergency department with chest pain or angina equivalent symptoms.

Methods: we assessed the qualitative rapid troponin I in patients with chest pain or angina equivalent symptoms after at least 4 hours and then we followed the patients in 72 hours after presentation for adverse events such as death, CCU admission, fatal arrhythmias and heart failure.

Results: After comparing qualitative troponin I test results and adverse events, we concluded that the troponin I was significantly more positive in patients with adverse events (i.e. CCU admission, fatal arrhythmias and heart failure) (P=0.031).

Conclusion: A single measurement of rapid qualitative troponin I test can be used as a prognostic factor in patients with chest pain or angina equivalent symptoms and also as a device for risk stratification of moderate and high risk patients.

Keywords: Troponin I, Chest pain, Angina, Acute coronary syndrome, Prognosis.

Introduction

Acute coronary syndrome, especially acute myocardial infarction (AMI), is one of the most common causes of global hospitalization with morbidity and mortality (1). Even if patients arrive at hospital alive, some expire at admission, some expire during hospitalization (because of arrhythmias or cardiogenic shock) and some expire after discharge due to re-occurrence of AMI or its adverse outcomes. The incidence of AMI (especially in young persons) is growing in the developing countries (2, 3) which in turn imposes immense socioeconomic damages for its adverse consequences (first 24-hours in-hospital mortality is 7% for ST elevated, 2.4% for non-ST elevated, and 11.8% for undetermined AMI; and corresponding 30-days mortality rate rise to 8.4%, 3.5% and 13.3% respectively (4)); therefore, it is invaluable to determine the high-risk patients as soon as possible for further monitoring and procedures. Besides, assessing patients with acute coronary symptoms like chest pain or its anginal equivalents is a time-consuming process; therefore, the above-mentioned triage helps saving patients' life through reducing that time.

In order to achieve this approach, it is wise to evaluate prognostic value of an emergency available and reliable test to stratify patients

***Corresponding Author:** Email: sdavaranii@yahoo.com

with chest pain (or its anginal equivalent). However ST-T segment changes in electrocardiogram suggest acute coronary diagnosis, but its sensitivity is as low as 50% and even up to 4% of patients are discharged inappropriately (5). Although, serial measurement of MB isoenzyme of creatine kinase (CK) has been widely used instead; it is a poor predictor for AMI outcome (6, 7). Measuring cardiac-specific protein, troponin, is proved to be superior predictor to conventional CK-MB (8, 9).

Cardiac troponin (I or T) is more sensitive and specific than creatine kinase MB in ACS diagnosis and its use will probably obviate the need for using other biomarkers. This so called "troponin-only" marker strategy will be more common (10).

In patients with ACS presented to emergency department, long term outcomes such as mortality and CHF was greater among them, whose "serum cardiac troponin I" was high at the time of primary presentation (11,12).

Besides, three major studies indicated that troponin isoforms predict long-term outcome of AMI; thus, those are useful for selecting invasive or medical therapy (13, 14). There are several subtypes of troponin (I and T) used for diagnosis of AMI; the qualitative troponin I test, however, is an available (due to its cost effectiveness) and reliable test for triage of acute coronary patients in emergency settings in the developing countries.

The present study was to determine the value of the result of troponin I rapid test in determining the 72-hour outcome of patients with chest pain (or its anginal equivalent).

Materials and Methods

Study population

This prospective cross-sectional survey was conducted in the Emergency Department of Rasul Akram Hospital (Tehran University of Medical Sciences, Tehran, Iran) from October 2005 to March 2006. Thus, all suspected patients with chest pain, or anginal equivalents including dyspnea, perspiration or nausea who referred to that emergency department were recruited after signing an "informed consent" form (n=296). Exclusion criteria were ST elevation on admission ECG, evidence of AMI within past 2 weeks and inability to provide informed consent. AMI was diagnosed in a clinical and paraclinical setting (based on European Society of Cardiology/American College of Cardiology definition of myocardial infarction (15). The patients' demographic (age, sex, active or current smoking a, opium usage, past medical history, drug history), clinical (systemic hypertension according to Joint National Committee sixth report(16), diabetes mellitus according to American Diabetes Association guideline (17) or a documented positive history, and dyslipidemia according to the updated Framingham guidance (18) or a documented positive history), electrocardiographic (Q wave, ST-T segment deviation, right and left bundle branch blocks (RBBB & LBBB)) and paraclinical (mean left ventricular ejection fraction (LVEF), cardiac valve involvement proven by echocardiography, and serum level troponin I >0.8 µg/L according to kit reference value, assessed by Spectral Cardiac STATus troponin I rapid test, Spectral Diagnostics, Canada) characteristics were recorded. According to Galvani et al. (19), blood sample was taken 4-6 hours after patient's admission.

We used a one step chromatographic immunoassay quantitative troponin I test device manufactured by ACON laboratories, Inc USA.

Risk stratification

In accordance with troponin I levels and ECG findings, patients were stratified to three subgroups: 1) high risk (troponin positive patients, with ischemic ECG findings. 2) moderate risk (troponin negative patients with ischemic ECG) and 3) low risk (troponin negative patients with normal ECG).

Event measurement

The early prognostic value of troponin I rapid test was evaluated for five major events during the first 72 hours after admission: patient's discharge, expiry, fatal arrhythmias, heart failure and CCU admission.

Statistical analysis

Frequency of variables was assessed. We used independent two sample *t* test to compare mean differences of variables. We also applied Chi-square test (with appropriate correction) to compare categorical variables. Logistic regression analysis was used for detecting variables related to categorized outcomes. All statistical calculations were done with SPSS ver. 15. *P* value <0.05 was considered significant.

Results

There were 410 patients referred to the emergency department with chest pain or its angina equivalent symptoms. After exclusion of 114 patients with ST elevation on admission ECG, totally 296 eligible were recruited, consisting of 148 male (50%) and 148 female (50%) patients with mean age 60 (±11.8) years. Compressing (212, 71.62%), stabbing (52, 17.56%) and vague (32, 10.81%) pain were the most common types of chest pain in descending order. Table 1 outlines the participants' medical and drug history. Concerning the ECG characteristics, Table 2 represents frequency of the corresponding changes in the study population.

The result of 72-hour outcome was as the follows: 104 patients (35.13%) discharged alive, 176 (59.45%) patients admitted in CCU, 8 patients (2.70%) had fatal arrhythmias and 8 patients (2.70%) suffered from heart failure. No patient expired after hospitalization.

The troponin I rapid test was positive in 40 patients (13.51%). The frequency of risk stratified groups was 40 patients (13.51%) for high risk, 144 patients (48.64%) for moderate risk and 112 patients (37.83%) for low risk subgroups.

The troponin I was significantly more positive in patients with adverse events (i.e. CCU admission, fatal arrhythmias and heart failure) (*P*=0.031). The mean serum concentration of CK-MB were significantly higher in positive troponin I (136 (±0.18)) versus negative troponin I (28 (±0.2)) patients (*P*=0.007); while it showed insignificant difference between discharged and adverse event groups (*P*>0.05).

When bivariate analysis suggested factors categorized age (<64 years), quality of pain, chest pain equivalents, past medical history, ECG characteristics, pulmonary edema, cardiomegaly and troponin I level as the probable influencing factors on patients' outcome, logistic regression analysis proposed that only age, ECG characteristics and troponin I level predicted prognosis (Table 3).

The distribution of patients' outcome within each risk-stratified group is delineated in table 4. Analysis indicated that there was a significant difference between low and moderate risk groups corresponding to the frequency of adverse events (*P*<0.001), but such discrepancy was not indicated between moderate and high risk groups (*P*=0.62).

Table 1: Frequency of patients with medical, drug history, ECG findings and chest pain referred to emergency department

	Frequency	Percent
Past medical history		
No history	56	18.91
Diabetes mellitus	60	20.27
Hypertension	72	24.32
Family history of AMI*	12	4.05
Smoking	28	9.45
CCU admission	68	22.97
Drug history		
No history	80	27.02
Beta blockers	68	22.97
ACEI†	68	22.97
Digoxin	24	8.10
Diuretic	16	5.40
Others	40	13.51
ECG characteristics		
Normal	132	44.59
Axial ST depression	32	10.81
Precordial ST depression	44	14.86
Axial T inversion	40	13.51
Precordial T inversion	48	16.21

*AMI, acute myocardial infarction; †ACEI, angiotensin converting enzyme inhibitor

Table 2: Variables predict categorized outcome of patients with chest pain referred to emergency department

Variable	*P* value	Odds ratio (confidence interval)
Categorized age (<64 years)	<0.001	3 (CI 95%: 1.7-5.2)
ECG characteristics	<0.001	8.9 (CI 95%: 5.1-15.6)
Troponin I level	0.001	2.4 (CI 95%: 1-5.42)

Discussion

Several studies have implied the importance of serum concentration of troponin isoforms for predicting adverse outcomes in acute coronary syndrome patients (20, 21). Patients with positive troponin rapid test at 6th hour were at higher risk (80%) of going to adverse outcome within 72 hours after admission; when other investigations propose an additional 7% risk of proven AMI or 4% risk for need of urgent revascularization within the 30 days after discharge in troponin positive patients (22, 23). Therefore, a 6th hour positive troponin I rapid test (with or without ECG characteristics indicating cardiac ischemia) is an early marker of important myocardial damage which reflects the probable necessity of coronary intervention (in high risk patients). In our study, logistic regression analysis put forward the troponin I as a predictor for cardiac ischemia prognosis.

Since nearly half of such patients have normal ECG, the role of troponin I rapid test is more emphasized as an emergency triage for patients

suffering from chest pain, in addition to its mentioned prognostic value. In the present study, positive troponin I rapid test was significantly more frequent in patients with adverse outcomes which is in agreement with other studies. Besides serum concentration of CK-MB was significantly higher in patients with positive troponin I that implicates the major myocardial damage, which in turn emphasizes probable need for coronary intervention. As seen, this difference is between troponin I negative and positive groups, not among five determined outcomes; therefore, it indicates that troponin I rapid test predicts the extent of myocardial damage better than the occurrence of clinical events.

Finally, we found out that the adverse outcomes took place significantly more in moderate and high risk groups than low risk group. This issue implicates that more vigilance should be considered in managing the moderate and high risk patients (according to troponin I levels). Nevertheless, surveys have shown that approximately 15% of patients with negative troponin I have ischemic ECG who should be considered for urgent elective coronary angiography soon after initiation of medical therapy.

Albeit troponin T seems more accurate in detecting the severity and extent of myocardial damage, most authorities now agree that both diagnostic and prognostic value of troponin T and troponin I are similar (24, 25). Thus, use of troponin I rapid test which is inexpensive in the developing countries seems rational. Since false positive troponin T or I are rarely reported in patients with chronic renal failure and true positive but irrelevant troponin T or I are observed in myocarditis, pulmonary embolism, interpretation of troponin test in conjunction with admission ECG or re-assessing troponin 12-16 hours after admission is recommended (26).

It is important to remember that cautious clinical assessment should not be substitute by troponin I rapid test. This cardiac marker is an invaluable accessory evaluation.

In conclusion, troponin I rapid test independently predicts 72-hour outcome of patients with ischemic chest pain. It is wise to use troponin I for risk stratification of moderate and high risk patients, because it is cost effective and reliable. Rapid bed side tests for cardiac troponin can help estimating the short term prognosis in patients with ACS in emergency departments. There is a more specific and sensitive test to assess the prognosis in patients with chest pain. Early assessment of "Growth differentiation factor 15 (GDF-15)" adds prognostic information about patients with chest pain in emergency setting according to a research and this can be studied more in future researches (27).

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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