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Prognostic Value of Cardiac Troponin I and T on Admission in Mortality of Multiple Trauma Patients Admitted to the Emergency Department: a Prospective Follow-up Study

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ABSTRACT

Introduction: The relationship between increased levels of cardiac troponins and morbidity and mortality of traumatic patients is not still well recognized. **Aim:** The aim of this study was to investigate the prognostic value of cardiac troponin I and T on admission in mortality of multiple trauma patients admitted to the emergency department. **Methods:** In this prospective follow-up study, the cardiac troponin I and T levels were measured in patients with multiple trauma referring to the emergency department (ED) between March 2014 and February 2015 at Imam Khomeini Hospital, Sari, Iran. Patients were followed prospectively until discharge from hospital or death. **Results:** The levels of cardiac troponins I and T in patients with multiple trauma were significantly associated with their mortality, especially at the level of 0.5 and 1.2 µg/dl ($p < 0.05$). Multivariate regression analysis showed association of level of cardiac troponin I and T with patients' mortality, after controlling for patients' age, vital signs and GCS on admission. The sensitivity and specificity of troponin I at levels greater than 0.4 µg/dl in predict mortality in this study were as 65.5% and 55.3%, while the values for troponin T were 65.1% and 54.9%, respectively. **Conclusion:** Elevated cardiac troponin I and T levels provide excellent prognostic information regarding mortality in patients with multiple-trauma, independent of age, hemodynamic variables and GCS score.

Keywords: Cardiac troponin I, Cardiac troponin T, Multiple trauma, Survival rate, Mortality.

1. INTRODUCTION

Cardiac troponins I and T are regulatory proteins that control myosin and actin calcium-mediated reactions. These biomarkers have the highest sensitivity and specificity to assess the damage to the cardiac cells (1). High sensitivity and specificity, availability and quick measurement have led to the use of these two biomarkers as the gold standard to determine cardiac ischemia following a myocardial infarction (MI), worldwide (2). Although these biomarkers are usually used to assess myocardial damage in patients suffering cardiac diseases, however, it has been shown that their levels also increase in different critically ill patients in the intensive care unit (ICU) (3, 4). Such patients may include the critically ill patients with sepsis, pulmonary embolism, stroke, renal failure and chronic obstructive pulmonary

disease (COPD) (5-8). According to previous studies, the prevalence of increased cardiac troponins level in the general population admitted to the ICU varies between 15% and 70% (9-13). It has been showed increases in cardiac troponin levels in more than 70% of critically ill patients admitted to the ICU, without any cardiac problems and cardiac ischemia (14).

Multiple trauma represents injuries related to the trauma of more than one body cavities or organs, which is considered as the main causes of mortality and morbidity. It has been also shown in this group of patients that the cardiac troponin levels will increase. However, most of these studies were limited to patients with blunt chest trauma who were suspected of cardiac contusion. On the other hand, it has been indicated that in non-traumatic patients with

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high cardiac troponin levels, these markers are significantly capable of predicting the patients' morbidity and mortality as an independent factor (15-17). However, the relationship between increasing levels of cardiac troponins and morbidity and mortality as well as the value of these biomarkers in predicting clinical outcome of traumatic patients is not still well recognized (17-19).

2. AIM

According to above mentioned issues and the lack of sufficient information about the relationship between cardiac troponin and the mortality rate of patients with multiple trauma, the aim of this study was to evaluate the prognostic value of cardiac troponin I and T on admission in mortality of multiple trauma patients admitted to the emergency department.

3. METHODS

The present prospective follow-up study was carried out on multiple trauma patients presenting to emergency department (ED) of Imam Khomeini Hospital, Sari, Mazandaran, Iran, The duration of the study was one year, through out March 2014 to February 2015. Protocol of this study was approved by the Ethics Committee of Mazandaran University of Medical Sciences. To maintain confidentiality of patients' medical profile data and adhering to ethical practice, the researchers keenly adhered to the principles introduced in the declaration of Helsinki during the study period. Information regarding the study method was given to the participants and written informed consent in the case of conscious patients was obtained from the patients themselves, and in the case of unconscious patients, from the proper surrogate decision maker. All consecutive patients with multiple trauma and hemodynamic instability, who had referred to the ED, were enrolled to the study. Patients with age ≥ 65 years and patients that their trauma occurred more than 24 hours previously were excluded from the study. The patients' Glasgow Coma Scale (GCS), heart rate, respiratory rate, oxygen saturation and mean systolic blood pressure were recorded upon ED admission. Also for all patients, immediately after admission to ED, a blood sampling was performed for cardiac troponin I and T testing. Troponins level were measured using a 3rd-generation immunoassay (Roche Modular analyzer).

A senior emergency medicine resident was responsible for gathering data of the patients by completing a predesigned checklist including baseline characteristics (including mechanism of trauma, age, sex, GCS, systolic blood pressure, heart and respiratory rate and O₂ saturation). All patients were followed prospectively from entry the study until hospital discharge or death.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software version 21. For reporting quantitative variables, mean and standard deviation (SD) were used and for qualitative variables, frequency and percentage were reported. Central tendency and dispersion indices were used to describe the data. The Chi-square test, and if necessary, the Fisher's exact test were

used for examining the qualitative data, while the t-test was used for quantitative data. Univariate and multivariate analysis were used to determine the relationship. In addition, the Multivariate Regression statistical analysis was applied to determine the independent predictive role of studied factors. The P-value < 0.05 was considered statistically significant.

4. RESULTS

In this study, from 1095 patients with multiple trauma referred to the ED of Imam Khomeini hospital, 400 patients meet the inclusion criteria. The patients included 333 male (83.3%) and 67 female patients (16.7%). The mean and SD of patients' age was 42.41 ± 20.44 years. The mortality rate in this study was 16.7%. The average age of deceased patients was significantly higher than the patients survived (63.50 ± 12.02 years vs. 38.20 ± 19.40 years, $P = 0.001$). Also, the highest mortality rate was significantly higher in men than in women (95.5% vs 4.5%, $P < 0.0001$).

The mean and SD of patients' GCS score upon admission to ED was 12 ± 1 . The lower mean of GCS score upon admission was significantly associated with mortality (10 ± 0.5 in died patients and 12 ± 1 in survivors, $P = 0.015$). The mean and SD of systolic blood pressure, heart rate and respiratory rate of patients upon admission to ED was 86 ± 3.73 mmHg, 110 ± 14 bits per minute and 20 ± 3 breaths per minute, respectively. Also, the mean oxygen saturation (O₂ sat) was $93.10 \pm 3.26\%$. Among the vital signs upon arrival, only the respiratory rate had a significant correlation with the patients' mortality. The respiratory rate on admission in deceased patients was 25 ± 4 , while it was 20 ± 4 in survived patients ($P < 0.0001$). Other clinical symptoms were not significantly associated with the patients' mortality. The mechanism of blunt abdominal injury included motor vehicle accident in 260 patients (65%), motorcycle accident in 60 patients (15%), falling in 47 patients (11.7%) and pedestrian injuries in 33 patients (8.3%), which showed no significant difference between died and survived patients. The sensitivity and specificity value of cardiac troponin I at the cut off point of > 0.4 $\mu\text{g}/\text{dl}$ in predicting mortality of patients with multiple trauma and hemodynamic instability in this study were 65.5% (CI95% 55.4-74.3) and 55.3% (CI95% 50.3-61.2), respectively. Also, at the cut off point > 0.12 $\mu\text{g}/\text{dl}$, the sensitivity and specificity value of cardiac troponin I in predicting patients mortality were 76.4% (CI95% 68.3-81.4) and 65.8% (CI95% 62.1-69.2), respectively (Table 1).

The sensitivity and specificity value of cardiac troponin T at the cut off point > 0.4 $\mu\text{g}/\text{dl}$ in predicting mortality of patients with multiple trauma and hemodynamic instability in this study were 65.1% (CI95% 55.1-73.9) and 54.9% (CI95% 49.3-60.2), respectively. Also, at the cut off point > 0.12 $\mu\text{g}/\text{dl}$, the sensitivity and specificity value of cardiac troponin T in predicting patients mortality were 76.1% (CI95% 68.0-81.1) and 64.8% (CI95% 61.0-68.1), respectively (Table 1). Multivariate regression analysis showed association between the levels of cardiac troponin I and T with patients' mortality, after controlling for

Troponin I level (µg/dl)	Survived patients	Died patients	Total	P-Value
< 0.4	148 (44.5%)	11 (16.5%)	159 (40.3%)	0.044
0.5-1.2	172 (51.6%)	48 (71.6%)	220 (55%)	0.049
> 1.2	13 (3.9%)	8 (11.9%)	21 (5.3%)	0.031
Troponin T level (µg/dl)	Survived patients	Died patients	Total	P-Value
< 0.4	150 (45%)	11 (16.4%)	161 (39.7%)	0.045
0.5-1.2	168 (50.5%)	48 (71.7%)	216 (54%)	0.05
> 1.2	15 (4.5%)	8 (11%)	23 (5.7%)	0.042

Table 1. Cardiac troponin I and T levels between patients who died and those who survived

patients' age, vital signs and GCS on admission (OR=0.6; CI 95%: 0.4-1.0).

5. DISCUSSION

In the present study, the levels of cardiac troponins I and T in patients with multiple trauma were significantly associated with mortality, and increased troponin levels, especially a slight increase between 0.5 and 1.2 µg/dl had been associated with increased mortality. Cardiac troponins I and T are regulatory proteins that control calcium-mediated reactions of myosin and actin. These biomarkers have the highest sensitivity and specificity rates to assess the damage to the heart cells (1). High sensitivity and specificity, availability and quick measurement have turned these two biomarkers a golden standard method to determine cardiac ischemia following MI around the world (2). Although these biomarkers are used only in patients with heart disease, however, it has been shown that their levels also increase in different critically ill patients in the intensive care unit (ICU) admissions (3-4). Such patients may include the critically ill patients with sepsis, pulmonary embolism, stroke, renal failure and chronic obstructive pulmonary disease (COPD) (5-7). According to previous studies, the prevalence of cardiac troponins increase in the general population admitted to the ICU has been varied between 15% and 70% (8-9, 12). Also, in critically ill patients admitted to the ICU with sepsis or septic shock, the prevalence has been estimated between 31% and 80% (10-11, 13). One of these studies is Ammann et al. research who showed that the cardiac troponin levels had increased in more than 70% of critically ill patients admitted to the ICU who have no heart problems and even have not cardiac reduced blood flow (14). Also, in a study by T. Reynolds et al. on critically ill patients diagnosed with sepsis and septic shock, the troponin levels more than 0.04 µg/dl were associated with higher mortality in patients admitted to the ICU. The authors have known higher associated morbidity rate of patients with mild increased levels of cardiac troponins (0.05-1.2µg/dl) independent of other prognostic factors such as age, the cause of hospitalization in ICU, severity of disease, mechanical ventilation and serum creatinine concentration (15). In addition, in Lim et al. study, the elevation of cardiac troponins in patients admitted to the ICU was associated with higher mortality rate (16). In a study by Stein R et al. increased troponin levels were associated with mortality rate in critically ill non-cardiac patients' independent from other risk factors. Thus, the mortality rate in patients with normal troponin lev-

el was 5%, while in patients with troponin, it has been elevated with an average 28% increase. This indicates a statistically significant difference. The overall mortality rate in this study was reported 13%, while in some studies; increased cardiac troponins have been associated with mortality (17). But, this relationship was not independent of disease severity and mortality APACHE 2 scoring. Thus, troponin increase with an increase in the APACHE 2 score was associated with higher hospital mortality rate of critically ill patients (18). In the study by Daniel A et al. increased troponin levels greater than 0.7µg/dl were considered positive and was associated with higher mortality of critically ill patients (non-cardiac) referred to emergency, especially in people over 65 years. However, in predicting a 28-day mortality of patients has not been an independent factor (19). In a study by Yan T et al., in evaluation of non-cardiac critically ill patients admitted to the emergency department, increased cardiac troponin levels were associated with higher mortality, and the troponin levels cutoff point was specified 0.05 Nanograms per liter. Also, in this study, the predictive role of cardiac troponins in association with the APACHE 2 score has been reported better than any of them alone (20). Most of these studies were limited to patients who had chest blunt trauma and were suspected of cardiac contusion. In a study by Ali Karakus et al., 100 multiple trauma patients who also had chest trauma were evaluated in terms of cardiac troponin levels. Their troponin levels were significantly high and had a significant relationship with higher mortality rate. Thus, the researchers of this study have considered follow-up in patients with chest trauma as an important issue. Meanwhile, it has been found that increased levels of cardiac troponin have a significant relationship with morbidity and mortality rates of non-cardiac critically ill patients (21). However, the value of these biomarkers in predicting clinical outcome in trauma patients is not still well recognized. Also, the clinical significant correlation between cardiac troponin and mortality rate is not well known (22). It is unclear how increased cardiac troponin, especially in cases of slight increase in critically ill patients who apparently have no cardiac ischemia or ACS, should be managed and treated due to the wide range of disease processes (20, 22).

It is not clear whether cardiac troponin increase is due to an underlying disease or results from subclinical myocardial damage, which also impacts on the patient's clinical outcome. Some consider this increase associated with myocardial injury in critically ill patients, even

though it is lower than the diagnostic value of myocardial infarction, which is associated with higher mortality rate and longer stay in ICU (23). It is not well defined in patients with multiple trauma that the elevation of cardiac troponins is due to the severity of the disease and physiological stress or results from a mechanical trauma to the chest (24, 25). In this regard, Martin M et al have considered troponin increase in trauma patients related to the severity of injuries and physiological stress. Even in the case of a small intervention, selective use of beta-blockers in some patients has been known associated with a reduction in mortality rate (25). However, sufficient studies have not been yet done on how to deal with the increased levels of troponin. In addition, whether management of treating with these increasing levels can affect the prognosis and outcomes of the patients still seem not well defined.

6. CONCLUSION

This study showed that in patients with multiple trauma, increased levels of cardiac troponins I and T upon admission to the ED are associated with higher mortality. This relationship is independent of patients' age, vital signs and GCS score on arrival to the ED.

- **Author's contributions:** Study conception and design: SHM, FB and ASY. Acquisition of data: SHM, FJ, IGK, FB, TA, SMP, MS, SJM and ASY. Statistical analysis and interpretation of data: SJM. Drafting of the manuscript: SHM, FJ, IGK, FB, TA, SMP, MS, SJM and ASY. Critical revision of the manuscript for important intellectual content: SHM, FJ, IGK, FB, TA, SMP, MS, SJM and ASY.
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