**Preventive Care in Nursing and Midwifery Journal**
**2021; 11(4): 1-7**

# *Association of Troponin-I Level on Admission with 6-month Clinical Consequences in Acute Coronary Syndrome Patients: A Preventive Approach in Patient Care*

Hassan Ahangar[1], Atefeh Heydari[2], Mehran Tahrekhani[3], Maryam Mohammadi[3], Mohammad Abdi[4], Ahmad Jalilvand[5*]

[1]Assistant Professor, Department of cardiology, Mousavi hospital, school of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran
[2]MD, Zanjan University of Medical Sciences, Zanjan, Iran
[3]MScN, RN, Department of Nursing Education, Abhar School of Nursing, Zanjan University of Medical Sciences, Zanjan, Iran
[4]Department of Emergency and Critical Care, Zanjan University of Medical Sciences, Zanjan, Iran, Department of Medical Education, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[*5]Associated Professor, Pathologist, Department of Pathology, Mousavi hospital, school of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

***Corresponding Author Address:*** Gavazang Road, Above Shahid Sabouti Boulevard, Ayatollah Mousavi Hospital, Zanjan, Iran

***Tel:*** 0098-9122413801

***Email:*** ahmad.jalilvand@zums.ac.ir

**Received**: 2 Nov 2020 **Accepted**: 6 June 2021

## Abstract

***Background:*** Cardiovascular diseases are the leading cause of mortality worldwide. Therefore, it is important to predict the future consequences of the disease in patients who have recovered.

***Objectives:*** We sought to determine the relationship between troponin-I level and 6-month clinical consequences (i.e., re-infarction, death, re-angiography and coronary artery bypass grafting) in patients with acute coronary syndrome (ACS).

***Methods:*** This prospective cross-sectional study was performed among 60 patients with ACS admitted to Ayatollah Mousavi Hospital in Zanjan, Iran. The participants were chosen using the convenience sampling method. Troponin-I level in these patients was initially evaluated. Afterwards, they were followed up for six months in terms of clinical consequences. A checklist was prepared to collect the required data. The receiver operating characteristic (ROC) analysis was conducted to determine the predictive power of high-sensitivity troponin I for the mentioned consequences. Iodine index was calculated to determine the cutoff point for this enzyme in order to predict the consequences.

***Results*****:** In general**,** 66.2% of the participants were male and the mean age was 60.46 ± 12.78 years. We found that 21.2% of the participants experienced one of the four clinical consequences in the follow-up period of 6 months. The sub-curved surface was calculated to be 0.705 for the prediction of consequences. The cutoff point for the prediction of consequences was 32.5; the negative predictive value for the cutoff point was 32.5, which was equal to 89.8%.

***Conclusion:*** Troponin-I has an acceptable predictive power to identify 6-month consequences of ACS. Moreover, considering the negative predictive value of troponin-I, it is recommended to use this biomarker in patients with ACS. In addition, healthcare providers should pay more attention to the follow-up of patients after discharge and design preventive programs.

***Keywords: troponin-I, acute coronary syndrome, sensitivity, specificity, preventive***

## Introduction

Cardiovascular diseases are the main cause of mortality [1]. Statistics show that one-third of deaths in the United States are due to cardiovascular diseases [2]. Several factors lead to cardiovascular diseases, including cigarette

smoking, low physical activity, nutrition, obesity, high blood cholesterol, diabetes and hyperlipidemia [2]. Cardiovascular diseases reduce the quality of life and increase medical costs and unemployment days for patients [3]. It also increases the workload of healthcare providers, especially nurses [4].

Cardiovascular diseases can be attributed to acute coronary syndrome (ACS), which is caused by ischemia of the heart muscle and includes unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) [5,6]. Acute coronary syndrome is identified based on clinical symptoms, acute changes in electrocardiogram (ECG) diagnosis and cardiac enzymes [7,8]. Acute coronary syndrome is caused by the sudden rupture of atheroma plaque and exposure to substances that promote platelet activity and production of thrombin. As a result, blood thrombosis in coronary arteries leads to an insufficient blood supply to the heart muscle [9].

Considering the vital function of the heart, rapid and accurate diagnosis of patients with ACS can be effective in the rapid treatment of these patients [10]. One method for the rapid diagnosis of ACS is the use of laboratory biomarkers [11]. Biomarkers play a marked role in the diagnosis and management of ACS patients. One of the biomarkers involved in the diagnosis of ACS is troponin-I, whose amount is elevated in the blood by damage to heart muscle cells [10]. Regardless of the patient's final diagnosis, troponin-I level is an important predictor of death [12]. Studies have shown that even in patients with no ACS, this biomarker increases significantly [12,13].

Considering the high significance of ACS and the adverse consequences it creates over time, especially during the first six months of the disease onset, the probability of occurrence of such consequences during this period is of particular importance. So far, most research has focused on laboratory aspects, but patient follow-up and attention to consequences with a preventive perspective have been disregarded [3-7]. Therefore, because these patients are very high-risk, it is necessary for healthcare providers, especially nurses and physicians, to examine these patients for Cardiac biomarkers upon arrival. In addition, patient education should be put at the forefront of healthcare providers' agenda to reduce the possible consequences. Thus, this study was conducted to determine the predictive power of troponin-I in predicting adverse clinical consequences of patients with ACS over a 6-month follow-up period.

## Methods

This was a prospective cross-sectional study of ACS admitted to the Angiography Ward of Ayatollah Mousavi Hospital in Zanjan. The participants were chosen using the convenience sampling method from March until October 2018. The study was conducted after obtaining the approval of the Center for the Development of Clinical Research at Ayatollah Mousavi Hospital and after receiving a code of ethics. Among all the patients with cardiovascular problems, 160 patients (with an age range of 40-75 years) were enrolled. The inclusion criteria comprised of clinical diagnosis of ACS (not a troponin-I test), being hospitalized for the first time, not having a previous history of MI or heart diseases, being under 70 years of age (due to high mortality over 70 years) and willingness to participate in the study. The exclusion criteria consisted of patients with a diagnosis other than ACS during hospitalization and impossibility to follow up the patient during the study period.

The sample size was calculated using the following formula based on the study by Danne et al [14].

$$n = \frac{Z^{2}_{1-\alpha/2} \times P(1-P)}{\delta^{2}}$$

(P=0.59, $\alpha$ = 0.05, $\delta = 1.3$ , n$\cong$ 160)

Troponin-I level with high sensitivity of these patients was measured on admission and 6 hours afterwards by using the Immuno-Chemiluminescence method with the ARCHITECT 2000i device (Abbott, USA). Then, the patients were followed up for a 6-month period via phone call**,** and their clinical consequences, including re-infarction, need for coronary artery bypass grafting (CABG), re-angiography and death were recorded. It should be noted that the gold standard for the diagnosis was patients' angiography, such that patients with

a definitive diagnosis of coronary artery disease were classified as the gold standard, and the patient's angiographic data was recorded. In this study, a checklist was prepared, which included patients' demographic data including age, gender, risk factors, arrhythmia, re-admission, laboratory test results, troponin-I level and clinical consequences, namely need for re-angiography, recurrence of infarction in 6 months, need for CABG and death.

This study was extracted from a General Medicine thesis. Before conducting the study, approval of the Ethics Committee of Zanjan University of Medical Sciences (code of ethics IR.ZUMS.REC.1396.292) was obtained, informed consent was granted by the participants and they were ensured of the confidentiality of their information.

Statistical analysis

After assigning appropriate codes to data, they were analyzed using SPSS, version 20. Descriptive statistics included frequency (percentage) for qualitative variables and mean (SD) or median (IQR= Interquartile range) for quantitative variables. In order to determine the cutoff point, receiver operating characteristic curves (ROC) were used in which, in addition to measuring the sub-curved surface, a cutoff point was determined based on iodine value. This value (also known as iodine adsorption value or iodine number or iodine index, commonly abbreviated as IV) in chemistry is the mass of iodine in grams that is consumed by 100 grams of a chemical substance [13]. Sensitivity, specificity and negative and positive predictive values were calculated using this cutoff point. Chi-square test was run to compare the two sex groups in terms of troponin-I level. Using the mentioned statistical methods, the cutoff point of this study was obtained and compared with those of other studies and the differences were assessed.

## Results

According to the results, the majority of the participants were male (66.2%). The mean (SD) age of the participants was 60.46 (12.78) years (Table 1). The median serum troponin-I level (IQR= interquartile range) was 25.40 (428.00-850.43 pg/mL). The disease consequences, including death, re-infarction, indication of re-angiography and CABG, over the course of 6-month follow-up are indicated in Table 2.

***Table 1: Demographic and clinical information of the patients in terms of gender, age, arrhythmia, readmission, risk factors and laboratory test results***

| Risk Factors | | | Descriptive Indicators | |
|---|---|---|---|---|
| | | | N | % |
| **Gender** | Male | | 106 | 66/25 |
| | Female | | 54 | 33/75 |
| **Risk Factors** | c/s* | | 27 | 16.9 |
| | HTN** | | 34 | 21.2 |
| | HLP*** | | 4 | 2.5 |
| | DM**** | | 18 | 11.2 |
| | DM + HTN + c/s | | 2 | 1.2 |
| | c/s + HTN | | 6 | 3.8 |
| | DM + c/s +HLP | | 2 | 1.2 |
| | HTN + HLP | | 5 | 3.1 |
| | HTN + DM | | 13 | 8.1 |
| | DM + HTN + HLP | | 5 | 3.1 |
| | c/s + DM | | 2 | 1.2 |
| | c/s + HLP | | 2 | 1.2 |
| | DM + HLP | | 1 | .6 |
| | Total | | 121 | 75.6 |
| **Arrhythmia** | Yes | AF | 8 | 5.00 |
| | | VF | 7 | 4.4 |
| | No | | 145 | 90.6 |
| **Re-admission** | Yes | | 25 | 15.63 |
| | No | | 135 | 84.37 |

| Risk Factors | | Dispersion Indicators | |
|---|---|---|---|
| | | Mean | SD |
| **Age** | | 60.46 | 12.78 |
| **Laboratory Test Result** | CTnI***** | 7.90 | 1.90 |
| | HDL | 35.50 | 1.16 |
| | LDL | 90.87 | 36.28 |
| | TG | 130.13 | 81.45 |
| | BS | 157.13 | 81.94 |
| | Vit-D | 55.05 | 2.08 |

***Coronary syndrome **Hypertension ***hyperlipidemia ****diabetic mellitus *****cardiac troponin-I**

***Table 2: The frequency of disease consequences during the 6 months of follow***-up

| Consequence | Death N (%) | Re-infarction N (%) | CABG N (%) | Re- angiography N (%) |
|---|---|---|---|---|
| **Yes** | 2(%1/25) | 2(%1/25) | 8(%5) | 22(%13/8) |
| **No** | 158(%98/75) | 158(%98/75) | 152(%95) | 138(%86/3) |

The results showed that the median serum troponin-I level related to IQR in patients with consequences was equal to 91.85 (14.75-4029.75). However, it was measured as 19.00 (6.85-194.50) in patients without consequences. In ROC analysis, the area under the curve (AUC) for the ROC curve (with 95% confidence interval) was equal to 0.705 (0.606-0.805).

In this study, there was no significant difference between men and women in terms of troponin-I in the under the curve (AUC) method (P=0.11). The cutoff point was 32.5 for the prediction of consequences (with the sensitivity of 0.735, specificity of 0.627 and iodine index of 0.362). The negative predictive value based on the cutoff point of 32.5% was found to be 89.8%, and the positive predictive value according to the same cutoff point was 34.7%. The results are presented in Figure 1 and Table 3.

***Table 3: Different cutoff points and sensitivity and specificity rates for troponin-I among patients with acute coronary syndrome***

| Cutoff points | Sensitivity | Specificity | Cutoff points | Sensitivity | Specificity |
|---|---|---|---|---|---|
| 12.5000 | .824 | 0.444 | 32.5000 | .735 | 0.627 |
| 13.5000 | .794 | 0.444 | 37.5000 | .706 | 0.627 |
| 14.5000 | .765 | 0.468 | 50.0000 | .706 | 0.643 |
| 15.8000 | .735 | 0.468 | 61.0000 | .676 | 0.643 |
| 17.3000 | .735 | 0.476 | 64.0000 | .647 | 0.643 |
| 18.5000 | .735 | 0.492 | 68.0000 | .618 | 0.643 |
| 19.5000 | .735 | 0.508 | 71.0000 | .618 | 0.651 |
| 20.3500 | .735 | 0.524 | 74.7000 | .618 | 0.659 |
| 21.8500 | .735 | 0.532 | 78.7000 | .618 | 0.667 |
| 24.0000 | .735 | 0.556 | 81.5000 | .618 | 0.675 |
| 25.4000 | .735 | 0.563 | 83.5000 | .588 | 0.675 |
| 25.9000 | .735 | 0.571 | 84.5000 | .559 | 0.675 |
| 27.5000 | .735 | 0.587 | 85.5000 | .559 | 0.683 |
| 29.5000 | .735 | 0.595 | 87.0000 | .529 | 0.683 |

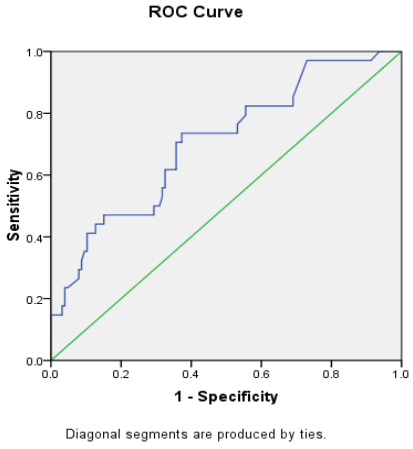


***Figure 1: Cutoff point using receiver operating characteristic (ROC)***

**Discussion**

We investigated the association between serum troponin-I level and the consequences of ACS patients in terms of re-infarction, death, the need for re-angiography and CABG. The results indicated a significant relationship between serum troponin-I level and the consequences of 6-month follow-up. In detail, serum troponin-I level was significantly higher in patients who experienced the consequences.

According to a study conducted by Clare et al. in 2011, this enzyme had a very high predictive power of 0.960 and a sensitivity of 96% to differentiate MI from damage caused by other organs. This predictive level was much higher than the predictive value in the present study.[16] A large part of this difference can be due to the consequences that were intended to predict in the two studies. As Clare claims, this enzyme is used to identify early myocardial infarction, Which is released from the heart muscle itself.. However, in our study, the goal was to predict later consequences that did not directly play a role in elevating the level of this enzyme at the beginning of the study and following initial infarction.

Shah et al. reported a negative predictive value of 99.6% of this enzyme for the rejection of myocardial infarction in ACS patients, which was 89.8% higher than the negative predictive value in our study. This diversity of finding is also related to the difference in the prediction of consequences in the two studies [15].

In the study by Shah, MI rejection was based on the results of high-sensitivity cardiac troponin-I at the time of ACS event, which was naturally unexpected due to the specificity of the enzyme for the heart tissue. However, in our study, 6-month consequences of ACS, which included MI, re-angiography, death, and CABG, were evaluated. As a result, this amount of negative predictive value can be considered valuable [16]. Another reason for this discrepancy is the difference in the choice of cutoff point to calculate the negative predictive value. In our study, as mentioned above, the cutoff point was considered 32.5, while in the study by Shah, this cutoff point was 5. Selecting a lower cutoff point usually results in a higher negative predictive value calculation, since considering a lower threshold will ensure more certainty for predicting or differentiating less heart muscle tissue damage. The results of our study also confirm the accuracy of this improvement, in that in the case of a cutoff point of 5, the negative predictive value increased from 89.8% to 95.7%.

The results of this study showed that more than 75% of the patients had various risk factors such as hypertension, diabetes, coronary artery problems and hyperlipidemia. Various studies have shown that these risk factors cause ACS in these patients [17,18].

In the present study, we showed that troponin-I has an acceptable predictive power for short-term consequences after MI. Meanwhile, this study

proposed an optimal cutoff point of 32.5 for the short-term consequences of MI. This cutoff point displays that although in our laboratory results the range of 19-100 pg/mL of troponin-I with high sensitivity was borderline and was regarded negative and ineffective in early diagnosis, it was found effective in determining the disease prognosis. Paying attention to high levels of this biomarker can be a signal for medical staff such as doctors, nurses and cardiac rehabilitation to pay more attention to the consequences in these high-risk patients. Therefore, following up these patients and providing preventive care to reduce consequences in the form of care, treatment, education and social support programs are recommended.

Limitations

One of the limitations of this study was the small sample size. It was not possible for us to carry out the study on more samples due to the lack of facilities and high laboratory expenses. Another limitation of this study was the lack of assessment of the predictive power of the enzyme for the four consequences under investigation separately due to the low level of troponin-I for each of these consequences

## Conclusion

Considering the high mortality rate of heart diseases and the need to diagnose the disease in the early stages and even before it, the use of biomarkers with high sensitivity is required. Therefore, it is recommended that troponin-I biomarker be considered in laboratory tests in hospitals and clinical centers to identify and predict consequences due to heart disease. Considering the relationship between high troponin-I level on admission and clinical consequences, healthcare providers are recommended to pay more attention to the follow-up of these patients after discharge and to design preventive programs.

## Acknowledgments

This article is part of the approved doctorate general practitioner's thesis (ID: A-11-1073-2) based on the ethics code IR.ZUMS.REC.1396.292 at Zanjan University of Medical Sciences.All authors of this thesis appreciate Zanjan University of Medical Sciences, Zanjan, Iran, as well as the Center for the Development of Clinical Research in Ayatollah Mousavi Hospital.Meanwhile, we sincerely appreciate the staff of Ayatollah Mousavi Hospital and all the patients who accompanied us todo this study.

## Conflict of interest

None declared.

## Funding:

The study was supported by Zanjan University of Medical Sciences.

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