Research Article

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Comparison of high sensitive and conventional troponin assays in diagnosis of acute myocardial infarction
Akut Miyokard Enfarktüsü Tanısında Yüksek Sensitif Ve Konvansiyonel Troponin Testlerinin Karşılaştırılması

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Abstract

Introduction: We aimed to compare the positive predictive values (PPV) and negative predictive values (NPV) of four cardiac troponin assays in the diagnosis of AMI in Turkish population.

Methods: This study is an observational comparative study, which is performed between 2012 and 2013 (527 patients). Troponin levels were measured with chemiluminescence Cobas troponin T assay, immunofluorescence Triage troponin I assay, immunofluorometric Radiometer troponin I assay and immunochromatographic Toyo troponin I assay.

Results: Sensitivity and specificity of immunofluorometric assay (Radiometer) are 56.82% and 71.34%; immunochromatographic assay (Toyo) are 29.4% and 88.62%, immunofluorescence assay (Triage) are 47.13% and 76.12%, chemiluminescence assay (Roche) are 60.49 and 67.42%, respectively. PPV, NPV and positive likelihood ratios (LR+) of immunofluorometric assay (Radiometer) are 45.5%, 79.7% and 1.98, immunochromatographic assay (Toyo) are 51.5%, 75.4% and 2.58, immunofluorescence assay (Triage) are 46.5%, 76.6% and 1.97, chemiluminescence assay (Roche) are 45.8%, 78.9% and 1.86, respectively. In four assays, troponin levels were statistically significant higher in AMI positive group in comparison to negative group (p < 0.001 for all).

Conclusion: There was no statistically significant difference between these troponin methods in comparisons of PPV and NPV in the diagnosis of AMI, but low sensitivity of Triage and Toyo assays should be considered.

Keywords: Troponin assay; Acute myocardial infarction; High sensitive troponin; Conventional troponin; Diagnostic performance study.

Özet

Amaç: Türk popülasyonunda akut miyokard enfarktüsü (AME) tanıında dört kardiyak troponin testinin pozitif ve negatif prediktif değerlerini (PPD ve NPD) kıyaslaması amaçlanmıştı.

Metod: 527 hastadan 2012 ile 2013 yılları arasında gözleme dayalı karşılaştırma çalışması yapılmıştır. Troponin düzeyleri kemilüminesans Cobas troponin T testi, immunofluoresans Triage troponin I testi, immünfluormetrik Ridiometer troponin I testi ve immünkromatografik Toyo troponin I testi ile ölçülmüştür.

Bulgular: Sensitivite ve spesifite değerleri sırasıyla Roche immünfluormetrik test için %56.82 ve %76.12; Toyo immünfluormetrik test için %67.42'yi gerçekleştirmiştir.
immünkromatografik test için % 29.4 ve % 88.62; Triage immünfloresans test için % 47.13 ve % 76.12; Roche Cobas kemilüminesans test için ise % 60.49 ve % 67.42 olarak saptanmıştır. PPD, NPD ve pozitif olabilirlik oranı sırasıyla Radiometer immünflorometrik test için % 45.5, % 79.7 ve 1.98; Toyo immünkromatografik test için % 51.5, % 75.4 ve 2.58; Triage immünfloresans test için % 46.5, % 76.6 ve 1.97; Roche Cobas kemilüminesans test için % 45.8%, 78.9% and 1.86 olarak hesaplanmıştır. Dört metodun troponin değerleri AME pozitif hastalarda negatiflere göre istatistiksel olarak anlamlı yüksektir. (herbiri için p < 0.001).

Sonuç: AME tanısında tüm metodların PPD ve NPD kıyaslamasında istatistiksel olarak anlamlı bir fark bulunmuş olup, Triage ve Toyo metodlarının düşük sensitivite değerleri gözönünde bulundurulmalıdır.

Anahtar Kelimeler: Troponin testi; Akut miyokard enfarktüsü; Yüksek sensitif troponin; Konvansiyonel troponin; Tanısal performans çalışması.

Introduction

The advances in the biochemical research on discovering an ideal biomarker for the diagnosis of acute myocardial infarction (AMI) have led to the discovery of cardiac troponins as a gold standard marker of myocardial injury [1, 2]. By courtesy of advances in the immunoassay techniques, the 99th percentile cutoff value of cardiac troponins required for the diagnosis of AMI decreased with the latest available ultrasensitive cardiac troponin assays capable of measuring level as low as 0.005 ng/mL [3]. Troponins have both diagnostic as well as prognostic significance in myocardial necrosis, but the results should be interpreted in the context of clinical history, ECG findings, and cardiac imaging techniques like echocardiography to establish the correct diagnosis [4]. The monitoring of the cardiac troponins would help to differentiate acute myocardial infarction (AMI) from many other conditions such as cardiomyopathy, heart failure, renal failure, pulmonary embolism, etc [5, 6]. The development of high sensitive cardiac troponin assays has led to the exclusion of the diagnosis of AMI in emergency department (ED) with a single test on admission. The undetectable troponin (<0.003 ng/mL) with highly sensitive cardiac troponin assays at present have a high negative predictive value for AMI in patients with chest pain at ED.

In this study, we aimed to compare the positive predictive values (PPV) and negative predictive values (NPV) of four different cardiac troponin assays including a new conventional troponin assay (Turklab) in the diagnosis of AMI in Turkish population and to reveal diagnostic performance of this new conventional troponin assay (Turklab).

Methods

Subjects

This observational, comparative study was conducted in Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey, between February 2012 and 2013. The study patients were randomly selected from the patients who were admitted to emergency department with chest discomfort. Patients presenting with chest pain were screened for inclusion. Exclusion criteria were chest pain due to trauma, aged <18 years, no chest pain within 24 h of the index ED visit, chest pain lasting <1 min, no ECG or no troponin assay performed within 24 h of index ED visit, a clear alternative diagnosis at initial medical assessment, hemodynamic instability, advanced terminal disease, inability to communicate. We collected data from patients presenting within first 6 h of symptom onset. The patients presenting outside of the first 6 h of symptom onset were also excluded. Five hundred twenty seven patients admitted to the emergency department with symptoms of acute coronary syndrome were included in the study. Clinically, angiographically and echocardiographically confirmed AMI has been revealed in 163 patients. Two groups were constituted whether acute myocardial infarction diagnosis was made or not. Troponin measurements of the patients were performed via four different troponin assays within sixth hours of symptom onset. PPV and NPV of four different troponin assays in the diagnosis of AMI were compared. The study protocol was approved by the local ethics committee and written informed consent was taken from all patients. The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) and International Conference on Harmonization (ICH) guidelines.

Diagnosis of AMI

Symptoms and clinical characteristics considering of acute coronary syndrome such as chest pain, syncope, significant arrhythmia, significant changes of myocardial injury on ECG such as ST depression and elevation, wall motion abnormalities on echocardiography and angiographic criteria of AMI were used to the diagnosis...
of AMI. The angiographic criteria of AMI was accepted as the evidence of plaque rupture or erosion in an epicardial coronary vessel, complex lesions consisting of plaque rupture and/or thrombus formation and culprit lesions [7]. A complex lesion was defined as an acute or recent total occlusion (dye stasis at the site) or a patent vessel with a significant lesion that was usually eccentric with either overhanging edges, abrupt shoulders, ulcerations, and/or filling defects at or distal to the lesion indicating intracoronary thrombus [7]. A culprit lesion was considered as the only significant lesion on angiography (usually >70% diameter stenosis) and in multivessel disease, the culprit lesion was a significant lesion in a vessel that corresponded to the new electrocardiographic changes or wall motion abnormalities [7]. The diagnosis of AMI was made by the discretion of at least two cardiologist blinded to the laboratory measurements according to above criteria.

### Troponin assays and measurements

The troponin measurements were taken within sixth hours of symptom onset in accordance with current guidelines. Venous blood samples were collected by venipuncture in a serum separator tube and K3 EDTA tubes from all patients at the time of admission.

1. Roche high sensitive troponin T (hsTnT) assay (Roche Diagnostic, Basel, Switzerland): EDTA plasma was obtained after centrifugation for 10 min at 1500 g and hsTnT test is measured with Cobas e411 analyzer (Roche High-Sensitive Troponin T; Hoffman-La Roche Diagnostics, Basel, Switzerland) using the method of chemiluminescence. The assay employs two monoclonal antibodies specifically directed against human cardiac troponin T. The antibodies recognize two epitopes (amino acid position 125–131 and 136–147) located in the central part of the cardiac troponin T protein which consists of 288 amino acids. The measuring range for the Roche device is between 0.003 and 10 μg/L [8, 9].

2. Radiometer high sensitive troponin I (hsTnI) assay: EDTA whole blood sample was used for the measurement of hsTnI using the method of the AQT90 FLEX cTnI immunoassay (Radiometer Medical ApS, Copenhagen, Denmark). The assay is a one-step sandwich immunofluorometric assay based on the use of three monoclonal antibodies, two for the capture and one for the detection. The capture antibodies are targeting epitopes 137–149. During 15 min of incubation time, the tracer and capture antibodies form a complex with the analyte in the sample. The measured signal is converted to a concentration using the calibration curve stored in the memory of the instrument. The limit of the detection has been determined to be 0.0095 μg/L. The reportable range of the assay is 0.010–50 μg/L. The upper 99th percentile has been determined to be ≤ 0.023 μg/L [10].

3. Triage Conventional Troponin I (cTnI) Assay: Troponin I measurement was performed from EDTA whole blood sample using Triage Conventional Troponin I (cTnI) Assay (Alere San Diego Inc, California, USA). A single use immunofluorescence test device designed to determine the concentration of troponin I. The device evaluated, the Triage Cardiac Panel, is a self-calibrating fluorescence immunoassay system for the quantitative determination of myoglobin, CK-MB mass, and cardiac troponin I. Briefly, after addition of the whole blood sample, the cells are separated from the plasma via a filter in the device, and a certain amount of plasma reacts with fluorescent antibody conjugates within the reaction chamber, and the mixture flows down the device detection lane. Complexes of the analytes and fluorescent antibody conjugates are captured on discrete zones, producing binding assays that are specific for each analyte. The concentration of each analyte, directly proportional to the fluorescence detected, is measured by the Triage meter [11]. The reportable measuring range for the Triage (cTnI) assay device is between 0.01 and 10 μg/L [10].

4. Toyo Turklab Conventional Troponin I (cTnI) assay: EDTA whole blood sample was used to measure troponin I with Toyo test device (Turklab A.S, Izmir, Turkey) which is an immunochromatographic assay. There is capture reagent immobilized test area in which whole blood sample reacts with the particles coated with anti-cardiac troponin I antibodies. The measuring range for the Turklab (cTnI) assay device is between 0.5 and 25 μg/L.

Glucose, HDL, LDL, total cholesterol and triglycerides were measured from serum samples via Cobas systems (Roche Diagnostic Basel, Switzerland) by using commercial kits (Roche Diagnostic Basel, Switzerland).

Complete blood count (CBC) was made from EDTA whole blood samples with BC 6800 auto analyzer (Mindray Medical International Limited, Shenzhen, China). Two levels of internal quality controls were performed for all devices.
**Statistical analysis**

The statistical analyzes in this study were performed via the Number Cruncher Statistical System 2007 program package (NCSS statistical software, Utah, USA). For the evaluation of the data, descriptive statistical methods were used (mean, standard deviation, median, interquartile range). For the groups not showing normal distribution, Kruskal-Wallis test in the comparisons of the groups, Dunn’s multiple comparison test in the sub-group comparisons, Mann-Whitney U-test in the comparison of the two groups were used. For the groups showing normal distribution, independent t-test in the comparison of the two groups. Spearman correlation test to determine the relationships of the variables with each other were used. In the receiver operating characteristic (ROC) analysis, the area under the ROC curve was calculated for the troponin measurements. Cut off values were selected by youden index and z-test was used for comparing AUC of two diagnostic tests in a paired design. Sensitivity, specificity, positive predictive value, likelihood ratio (LR+) and cut-points were calculated. Results were evaluated as significant \( p < 0.05 \) level at 95% confidence interval.

**Results**

Demographic, clinical and laboratory characteristics of the patients are presented in Table 1. The presence of diabetes mellitus, hypertension, smoking and obesity did not differ between groups. The history of coronary intervention, coronary by-pass, known peripheral artery disease and cerebrovascular accident were not significant among two groups. The group without myocardial infarction was younger than the group with myocardial infarction. The group without myocardial infarction had significantly higher triglyceride levels (\( p = 0.003 \)) and higher hematocrit levels (\( p = 0.018 \)), but lower glucose levels (\( p = 0.027 \)) and lower white blood cell counts (\( p = 0.0001 \)) in comparison to the group with myocardial infarction. There was no difference between the groups in LDL-, HDL-, total cholesterol, creatinine levels and platelet counts (\( p > 0.05 \)) (Table 1). The diagnosis of myocardial infarction was confirmed by all of the four methods (Table 2). The male patients had higher troponin levels with all of the four methods compared. In this study, 41 patients in the group AMI (–) had ST elevations, 32 of which were associated with ST elevations not meeting AMI criteria such as minimal elevations, single lead or not contagious lead elevations, six of which had early repolarization, two was pericarditis and one has previously diagnosed chronic pericardial effusion.

In comparison of four troponin methods in different clinical scenarios, there were significant differences among non-cardiac chest pain, acute coronary syndrome (non-STEMI) and ST segment elevation myocardial infarction (STEMI) groups (\( p = 0.0001 \)) (Table 3). The troponin levels of the non-cardiac chest pain group were lower than other two groups (\( p = 0.0001 \)) and the troponin levels of the non-STEMI group were also lower than the STEMI group (\( p = 0.0001 \)) (Table 3). A positive correlation was observed among all of the four different troponin methods (\( p = 0.0001 \)). The four tests showed no significant difference in comparison with each other (\( p > 0.05 \)) (Table 4). Receiver operating curve (ROC) analysis and comparisons of area under the curve (AUC) values of four troponin methods has been presented in Tables 5 and 6, respectively.

Radiometer high sensitive troponin I (hsTnI) I assay had a sensitivity of 56.82%, a specificity of 71.34%, PPV of 45.5%, NPV of 79.7% and positive likelihood ratio (LR+) of 1.98. Triage Conventional Troponin I (cTnI) Assay had a sensitivity of 47.13%, a specificity of 76.12%, PPV of 46.5%, NPV of 76.6% and LR + of 1.97. Toyo Turklab Conventional Troponin I (cTnI) assay had a sensitivity of 29.4%, a specificity of 88.62%, PPV of 51.5%, NPV of 75.4% and LR + of 2.58. Roche high sensitive troponin T (hsTnT) assay had a sensitivity of 60.49%, a specificity of 67.42%, PPV of 45.8%, NPV of 78.9% and LR + of 1.86 (Table 7). There were no statistically significant differences between four different troponin assays in comparisons of PPV and NPV in the diagnosis of AMI but the sensitivity of Triage and Toyo Turklab methods were lower than Radiometer and Roche methods.

**Discussion**

According to the results of the present study, there were no statistically significant differences between four different troponin methods in comparison of PPV and NPV in the diagnosis of AMI. We have found sensitivity of Triage and Toyo Turklab methods to be lower than Radiometer and Roche methods. The strength of this study comes from the comparison of the power of frequently used troponin methods including Toyo Turklab Conventional Troponin I (cTnI) assay, which is a device recently developed in Turkey that can easily measure troponin I from EDTA whole blood sample, like Radiometer and Triage methods, in the diagnosis of AMI. According to our knowledge, this
is the first study comparing the power of Turklab conventional troponin I method with other frequently used troponin methods in the diagnosis of AMI.

The universal definition of AMI criteria for the diagnosis of AMI is pivotally centered on elevated troponins, in an ischemic setting, with ischemic symptoms or ischemic

Table 1: Demographic, clinical and laboratory characteristics of patients.

| Variables                                      | MI (−) n=360 | MI (+) n=163 | p-Value |
|------------------------------------------------|--------------|--------------|---------|
| Age (year)                                     | 50.52±13.48  | 55.66±14.51  | 0.0001  |
| Gender                                         |              |              |         |
| Female                                         | 105          | 47           | 28.83%  | 0.938  |
| Male                                           | 255          | 116          | 71.17%  |         |
| BMI (kg/m²)                                    | 27.6±4.06    | 27.54±4.5    | 0.884   |
| Heart rate (bpm)                               | 77.96±14.09  | 79.92±14.15  | 0.152   |
| Systolic blood pressure (mmHg)                 | 150.57±26.99 | 150.28±34.38 | 0.921   |
| Diastolic blood pressure (mmHg)                | 88.22±17.05  | 87.45±18.25  | 0.652   |
| History of coronary intervention               | 66           | 22           | 13.66%  | 0.138  |
| History of CABG                                | 24           | 7            | 4.35%   | 0.261  |
| History of CVA                                 | 3            | 3            | 1.86%   | 0.334  |
| Known peripheral artery disease                | 3            | 3            | 1.88%   | 0.331  |
| Known coronary artery disease                  | 91           | 26           | 16.25%  | 0.013  |
| Smoking                                        |              |              |         |
| No                                             | 105          | 46           | 29.11%  | 0.863  |
| Yes                                            | 145          | 71           | 44.94%  |         |
| Ex smoker                                      | 83           | 41           | 25.95%  |         |
| Duration of pain (min)                         | 7.8±1.8      | 7.6±1.5      | 0.353   |
| Left ventricular ejection fraction (%)         | 51.92±10.61  | 48.29±10.39  | 0.008   |
| DM                                             | 51           | 27           | 16.88%  | 0.536  |
| HT                                             | 89           | 47           | 33.57%  | 0.660  |
| Pain type                                      |              |              |         |
| Atypical                                       | 208          | 55           | 33.74%  | 0.0001 |
| Typical                                        | 150          | 108          | 66.26%  |         |
| Pain location                                  |              |              |         |
| Sternum                                        | 196          | 81           | 64.80%  | 0.0001 |
| Sternum, arm and raw                           | 31           | 40           | 32.00%  |         |
| Epigastric                                     | 12           | 3            | 2.40%   |         |
| Back                                           | 6            | 1            | 0.80%   |         |
| Nausea and vomiting                            | 61           | 62           | 39.49%  | 0.0001 |
| Sweating                                       | 54           | 39           | 24.84%  | 0.023  |
| Dizziness                                      | 18           | 6            | 3.82%   | 0.448  |
| Dyspnea                                        | 22           | 9            | 5.73%   | 0.711  |
| ECG                                            |              |              |         |
| Normal                                         | 261          | 72           | 44.17%  | 0.0001 |
| T wave inversion                               | 22           | 11           | 6.75%   |         |
| ST depression                                  | 17           | 6            | 3.68%   |         |
| ST elevation                                   | 41           | 65           | 39.88%  |         |
| Bundle branch block                            | 11           | 5            | 3.07%   |         |
| Combined                                       | 6            | 4            | 2.45%   |         |
| Triglyceride (mmol/L)                          | 2.09±1.38    | 1.72±1.06    | 0.003   |
| LDL cholesterol (mmol/L)                       | 3.33±0.99    | 3.48±0.95    | 0.102   |
| HDL cholesterol (mmol/L)                       | 1.14±0.33    | 1.15±0.30    | 0.848   |
| Total cholesterol (mmol/L)                     | 5.01±1.12    | 5.05±1.07    | 0.657   |
| Glucose (mmol/L)                               | 6.97±3.61    | 7.72±3.41    | 0.027   |
| Creatinine (µmol/L)                            | 78.68±21.21  | 85.74±74.26  | 0.076   |
| White blood cell count (10⁹/L)                 | 8.99±2.8     | 10.62±3.7    | 0.0001  |
| Hematocrit (%)                                 | 41.01±4.89   | 39.85±5.62   | 0.018   |
| Platelets (10⁹/L)                              | 257.52±64.22 | 251.17±62.76 | 0.295   |

Unpaired t and χ² tests were used for statistical analyses. Bold numbers indicate significant p-Values (<0.05). Values are presented as mean±SD or number or percentage of patients.
electrocardiographic changes, and a rise and/or fall in troponin levels [4]. The cut-point requires a troponin level greater than the 99th percentile of a healthy population as measured with an assay with an imprecision CV of ≤ 10%, and a definition of rise and/or fall is required to distinguish “normal” or chronic background troponin levels from acute changes [4]. The universal definition of AMI group recommended a 20% change from the baseline value to be diagnostic of re-infarction with the current troponin assays [4]. The high sensitivity assays provide rapid diagnosis of AMI and it is important that there is a rising and/or falling pattern of troponin levels to distinguish non-ischemic pathophysiology from AMI.

The development and standardization of high sensitive assays is also important. The first-generation assay for cardiac troponin T (cTnT) used bovine cTnT as the reference material and exhibited non-specific binding to human skeletal muscle troponin, but this problem was solved by refinement of the detection antibody in the second-generation assay and the use of recombinant human

cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay. Datas are presented as mean ± SD and median (interquartile range). Mann-Whitney U was test used for statistical analyses.

Table 3: Troponin levels of four methods in different clinical scenarios.

| Troponin method | Non-cardiac chest pain n=264 | Acute coronary syndrome n=121 | ST elevation MI n=105 | p-Value |
|-----------------|-------------------------------|-------------------------------|----------------------|---------|
|                 | Mean±SD  | Median (IQR) | Mean±SD  | Median (IQR) | Mean±SD  | Median (IQR) |         |         |
| Troponin T (hsTnT) Roche (μg/L) | 0.01±0.04 | (0.003–0.01) | 0.29±0.66 | (0.007–0.255) | 1.97±2.93 | (0.096–2.243) | 0.0001 |         |
| Troponin I (cTnI) Triage(μg/L) | 0.06±0.07 | 0.05 | 1.75±4.9 | 0.05 | 7.85±10.38 | 2.555 | 0.0001 |
| Troponin I (cTnI) Toyo Turklab(μg/L) | 0.51±0.3 | 0.5 | 1.43±3.13 | 0.5 | 7.12±9.09 | 2.95 | 0.0001 |
| Troponin I (hsTnI) Radiometer(μg/L) | 0.09±0.99 | 0.01 | 0.9±2.93 | 0.035 | 5.63±8.17 | 1.4 | 0.0001 |
|                  | Mean±SD  | Median (IQR) | Mean±SD  | Median (IQR) | Mean±SD  | Median (IQR) |         |         |
| Troponin T (hsTnT) Roche | R | 1 | 0.920 | 0.711 | 0.861 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (cTnI) Triage | R | 0.920 | 1 | 0.767 | 0.878 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (cTnI) Toyo Turklab | R | 0.711 | 0.767 | 1 | 0.807 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (hsTnI) Radiometer | R | 0.861 | 0.878 | 0.807 | 1 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |

cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay. Datas are presented as mean ± SD and median (interquartile range). Kruskal-Wallis test was used for statistical analyses.

Table 4: Results of Spearman correlation test among four troponin methods.

| Troponin methods | Troponin T (hsTnT) Roche | Troponin I (cTnI) Triage | Troponin I (cTnI) Toyo Turklab | Troponin I (hsTnI) Radiometer |
|------------------|--------------------------|--------------------------|-------------------------------|-------------------------------|
| Troponin T (hsTnT) Roche | R | 1 | 0.920 | 0.711 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (cTnI) Triage | R | 0.920 | 1 | 0.767 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (cTnI) Toyo Turklab | R | 0.711 | 0.767 | 1 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
| Troponin I (hsTnI) Radiometer | R | 0.861 | 0.878 | 0.807 |
|                  | p | 0.0001 | 0.0001 | 0.0001 |
cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay.
sensitivity and the specificity between the high-sensitivity and conventional assays were statistically significant (p < 0.01), the areas under the curves were similar for both tests carried out 3–6 h after presentation [13]. Our results are similar to this meta-analysis. The areas under the ROC curves were similar for four tests. In another meta-analysis by Sethi et al. which included in 8628 patients from fifteen studies, it was found that there was no statistically significant difference in the area under the curve between high sensitive troponin (95% CI: 0.920) and conventional troponin (95% CI: 0.929) at the 99th percentile (p = 0.62) [14]. Our results are also consistent with this meta-analysis.

Recently, Januzzi et al. has compared the performance of a commercially available sensitive Tn I (sTnI) and pre-commercial high sensitive TnI (hsTnI) method to conventional Tn (cTn) assays with coronary computed tomographic angiography (CTA) [15]. In comparison with cTn, 29% of ACS cases previously categorized as UAP were reclassified to acute myocardial infarction with sTnI or hsTnI. In patients with acute chest discomfort, use of sTnI and hsTnI methods led to significant improvement in the early diagnostic accuracy for ACS [15]. An hsTnI below limit of detection had 100% negative predictive value for ACS or significant coronary artery stenosis in those randomized to CTA in their study.

The high sensitivity cardiac troponin assays have improved sensitivity, but reduced specificity in comparison with the conventional troponin assays. With repeated measurements after 6 h of symptom onset, the area under the ROC curve values are similar for the four tests in our study. It has been reported that the elevation of high sensitive troponin levels predicts higher risk of mortality in patients with suspected ACS and normal conventional troponin assay results, and helps in the early identification of higher-risk patients in this setting [16]. Haaf et al. also reported that hsTnT is more accurate than hsTnI in the prediction of long-term mortality [17]. In PEACE study, it has been suggested that hsTnT concentrations were associated with cardiovascular death and heart failure but not with myocardial infarction [18], and hsTnI concentrations are

cTnT for standardization in the third-generation assay [12]. The fourth generation cTnT assay uses fragment antigen-binding (FAB) of two cTnT specific mouse monoclonal antibodies in a sandwich format. Nowadays, the fourth-generation cTnT assay has been considered the standard assay for the diagnosis of AMI.

In a meta-analysis, Al-Saleh et al. evaluated 9186 patients from 9 studies that assessed the use of hsTnT assays, and the mean sensitivity of these tests in the diagnosis of acute MI was found to be 0.94 [95% confidence interval (CI) 0.89–0.97], and the mean specificity of conventional tests was 0.72 (95% CI 0.63–0.79) but the mean specificity was 0.73 (95% CI 0.64–0.81) for the high sensitivity assays compared with 0.95 (95% CI 0.93–0.97) for the conventional assays, and these differences in the

![Table 5: Receiver operating curve (ROC) analysis of four troponin methods.](image)

| Troponin methods | AUC   | SE    | 95% CI       |
|------------------|-------|-------|--------------|
| Troponin T (hsTnT) Roche | 0.644 | 0.031 | 0.595–0.691  |
| Troponin I (cTnT) Triage | 0.603 | 0.032 | 0.553–0.651  |
| Troponin I (cTnI) Toyo Turklab | 0.593 | 0.032 | 0.543–0.641  |
| Troponin I (hsTnI) Radiometer | 0.643 | 0.031 | 0.594–0.689  |

cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay. AUC, Area under the receiver operating characteristics (ROC) curve; SE, standard error; CI, confidence Interval.

![Table 6: Comparisons of area under the ROC curve values.](image)

| Comparisons | p-Value |
|-------------|---------|
| Troponin I (hsTnI) Radiometer/Troponin I (cTnI) Triage | 0.092 |
| Troponin I (hsTnI) Radiometer/Troponin I (cTnI) Toyo Turklab | 0.057 |
| Troponin I (hsTnI) Radiometer/Troponin T (hsTnT) Roche | 0.951 |
| Troponin I (cTnI) Triage/Troponin I (cTnI) Toyo Turklab | 0.691 |
| Troponin I (cTnI) Triage/Troponin T (hsTnT) Roche | 0.105 |
| Troponin I (cTnI) Toyo Turklab/Troponin T (hsTnT) Roche | 0.077 |

cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay.

![Table 7: Diagnostic performances of four troponin kits in diagnosis of AMI.](image)

| Troponin methods | Cut off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | LR |
|------------------|---------|-----------------|-----------------|---------|---------|----|
| Troponin T (hsTnT) Roche (μg/L) | > 0.015 | 60.49           | 67.42           | 45.8    | 78.9    | 1.86 |
| Troponin I (cTnI) Triage(μg/L) | > 0.059 | 47.13           | 76.12           | 46.5    | 76.6    | 1.97 |
| Troponin I (cTnI) Toyo Turklab(μg/L) | > 0.5  | 29.41           | 88.62           | 51.5    | 75.4    | 2.58 |
| Troponin I (hsTnI) Radiometer (μg/L) | > 0.012 | 56.82           | 71.34           | 45.5    | 79.7    | 1.98 |

cTnI, Conventional troponin I assay; hsTnT, high sensitive troponin T assay; hsTnI, high sensitive troponin I assay, AMI, acute myocardial infarction; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.
also associated with cardiovascular risk, heart failure and mortality as independent from conventional risk markers and hsTnT in patients with stable CAD [19]. Correia et al. showed that high sensitivity troponin I predicts cardiovascular events similarly to conventional troponin T in the setting of non-ST-elevation ACS [20]. However, Ndrepepa et al. pointed out that the elevated levels of hsTnT in patients with stable or unstable angina presenting with undetectable cTnT are significantly associated with reduced survival [21]. They also took attention that the use of hsTnT instead of cTnT significantly improved risk stratification regarding long-term mortality but increased the proportion of patients with NSTEMI among patients with non ST elevation acute coronary syndrome [22].

Although the elevation of high sensitive troponin levels predicts higher risk of mortality in patients with suspected ACS [16, 21–23]. The lower specificity of high-sensitivity assays results in higher rates of false positive tests, so some patients are incorrectly considered as undergoing NSTEMI, and the use of high sensitive troponin assays leads to performing additional investigations, more coronary angiography and interventions [24, 25]. These additional investigations and interventions may pose the risk of the increased work load on emergency departments, cardiology referrals and cardiac catheterization laboratories, and bring additional costs to the health care system, and also cause increased anxiety to patients [25].

In other causes of cardiac injury including pulmonary embolism, myocarditis, pericarditis, congestive heart failure, septic shock, myocardial contusion, elevation of troponins has been shown to be associated with a bad outcome in most cases [26]. In cardiac contusion, the role of troponin measurement has been debated. The right ventricle is most commonly injured in blunt trauma, but the tissue volume of the right ventricle is reduced, which leads to concern that troponin levels will not adequately elevate with blunt myocardial contusion. Alone, an elevated troponin is inadequate to diagnose myocardial contusion but when it is combined with an abnormal electrocardiogram, patients are at risk for increased complications requiring intervention, but when a negative 6-h troponin is combined with a normal electrocardiogram and a hemodynamically stable patient, the negative predictive value for significant blunt myocardial contusion approaches 100% [27]. To date, the role of high sensitive troponin and conventional troponin assays in these circumstances has not been revealed well.

The present study does have several limitations. This was a single center study. The sample size in our study was relatively small. Long term follow up data were not available to reveal the clinical and prognostic importance of the results. The diagnosis of AMI was performed via coronary angiography and echocardiography. To use the tools showing the loss of myocardial viability such as positron emission tomography and thallium scintigraphy would have been better. Although it has recently been reported that triglyceride levels were higher in all age groups of AMI [28], in our study, triglyceride levels were significantly higher in AMI (−) group than AMI (+) one. This contrary result to current literature is probably due to play of chance. Few very high triglyceride levels may have caused this result. Despite all limitations, our study comparing the diagnostic power of four different troponin kits frequently used in the diagnosis of AMI provides important contribution to the establishment of correct diagnosis of AMI.

Conclusions

The performance of a new developed Toyo Turklab Conventional Troponin I (cTnI) assay was evaluated in this study in addition to three other troponin methods. There were no statistically significant differences between all four (Radiometer, Roche, Triage and Toyo Turklab) different troponin assays in comparison of PPV and NPV in the diagnosis of AMI, but low sensitivity of Triage and Toyo (Turklab) assays should be considered.

Conflict of interest statement: There is no conflict of interest.

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