History of Medicine, 2024, 10(2): 221-231
DOI: 10.17720/2409-5834.v10.2.2024.021

# Predictive Value of High-Sensitivity Cardiac Troponin and Other Biomarkers in Patients with Suspected Acute Coronary Syndrome

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## Abstract

**Introduction:** Acute coronary syndrome (ACS) represents a spectrum of clinical conditions associated with acute myocardial ischemia and infarction, encompassing unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). **Objectives:** The main objective of the study is to find the predictive value of high-sensitivity cardiac troponin and other biomarkers in patients with suspected acute coronary syndrome. **Methodology of the study:** This prospective cohort study was conducted at Insaf Medical Complex, Karachi during June 2023 to March 2024. A total of 865 patients presenting with symptoms suggestive of ACS were enrolled in the study. **Results:** Data were collected from 865 patients. Mean age of 58.76±2.35 years. The cohort consisted of 58% males and 42% females. Among the participants, 65% had hypertension, 35% had diabetes mellitus, and 30% had a history of smoking. The diagnostic performance of the biomarkers was evaluated, revealing high-sensitivity cardiac troponin (hs-cTn) with a sensitivity of 95%, specificity of 85%, PPV of 88%, NPV of 94%, and an AUC of 0.93. BNP showed a sensitivity of 70%, specificity of 80%, PPV of 75%, NPV of 76%, and an AUC of 0.75. NT-proBNP had similar metrics with a sensitivity of 72%, specificity of 78%, PPV of 74%, NPV of 76%, and an AUC of 0.74. **Conclusion:** The integration of hs-cTn with other biomarkers enhances diagnostic accuracy and risk stratification, enabling more personalized and effective patient care. By

leveraging the predictive value of these biomarkers, clinicians can improve the early detection, intervention, and outcomes for patients with suspected ACS.

## Introduction

Acute coronary syndrome (ACS) represents a spectrum of clinical conditions associated with acute myocardial ischemia and infarction, encompassing unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). Rapid and accurate diagnosis of ACS is critical to initiate timely treatment and improve patient outcomes. Traditional diagnostic approaches, primarily relying on clinical assessment, electrocardiogram (ECG) findings, and standard cardiac biomarkers, often face limitations in sensitivity and specificity, particularly in the early stages of myocardial injury [1]. High-sensitivity cardiac troponin (hs-cTn) assays have emerged as a pivotal advancement in the detection of myocardial injury. These assays offer superior sensitivity compared to conventional troponin tests, enabling the detection of lower levels of cardiac troponins that are indicative of minor myocardial damage [2]. The implementation of hs-cTn assays in clinical practice has significantly improved the diagnostic accuracy for ACS, allowing for the earlier identification of at-risk patients and the timely initiation of therapeutic interventions. Acute coronary syndrome is therefore a broad clinical entity that includes several clinical subtypes that occur due to compromised coronary blood supply [3]. The reduction of coronary blood flow causes acute decrease of oxygen supply to the myocardium and/or myocardial infarction (MI), which is based on the imbalance of oxygen supply and demand by the cardiac muscle. Acute coronary syndrome is characterized by three distinct clinical presentations: UA, NSTEMI, and STEMI [4,5]. The difference between these subtypes relies on the ischaemic feature symptoms, the ECG changes and the cardiac biomarkers especially high-sensitivity cardiac troponin. The measurement of troponin is currently one of the most fundamental diagnostic tools used in most hospitals for the diagnosis of MI [6]. The Fourth Universal Definition of MI on behalf of the ESC and ACC illuminates that MI is characterized by acute myocardial injury as manifested by elevated cardiac biomarkers up to 48h after onset and acute myocardial ischemia [7]. Based on these guidelines, the clinical criteria for diagnosing acute myocardial injury is an absolute increase and/or decrease of hs-cTn values, which with at least one of the values being above the 99% of the URL of normal, should be considered as acute MI in the presence of symptoms, changes in the ECG or imaging [8]. In addition to hs-cTn, other biomarkers have shown

promise in enhancing the predictive value for ACS [9]. These include natriuretic peptides, inflammatory markers, and markers of myocardial stress and hemodynamic stress [10]. The integration of multiple biomarkers into diagnostic algorithms holds the potential to refine risk stratification, guide clinical decision-making, and ultimately improve patient outcomes in suspected ACS cases [11].

## Objectives

The main objective of the study is to find the predictive value of high-sensitivity cardiac troponin and other biomarkers in patients with suspected acute coronary syndrome.

## Methodology of the study

### Study Design

This prospective cohort study was conducted at Insaf Medical Complex, Karachi during June 2023 to March 2024. A total of 865 patients presenting with symptoms suggestive of ACS were enrolled in the study.

### Inclusion criteria:

- Patients aged 18 years or older.
- Presentation with chest pain or another symptoms indicative of ACS.
- Consent to participate in the study.

### Exclusion criteria:

- Known history of myocardial infarction within the past six months.
- Ongoing treatment for chronic heart failure.
- Severe renal impairment (eGFR < 30 mL/min/1.73 $m^2$).

### Data Collection

Upon presentation to the emergency department, all patients underwent a comprehensive clinical assessment, including a detailed medical history, physical examination, and standard electrocardiogram (ECG). Blood samples were collected at admission and at subsequent time points (1 hour, 3 hours, and 6 hours post-admission) for biomarker analysis. High-sensitivity

cardiac troponin (hs-cTn) levels were measured using a validated assay. In addition to hs-cTn, other biomarkers, including natriuretic peptides (BNP and NT-proBNP), C-reactive protein (CRP), and markers of myocardial stress such as copeptin, were also quantified. All biomarker measurements were performed in a central laboratory using standardized protocols.

**Diagnostic Criteria**

The diagnosis of ACS was established based on a combination of clinical presentation, ECG findings, and serial biomarker measurements. Patients were classified into three categories:

1. **ST-elevation myocardial infarction (STEMI)**: Based on the presence of ST-elevation on ECG.
2. **Non-ST-elevation myocardial infarction (NSTEMI)**: Based on elevated hs-cTn levels with non-ST elevation on ECG.
3. **Unstable angina**: Based on clinical symptoms and non-diagnostic ECG and biomarker levels.

**Statistical Analysis**

Data were analyzed using SPSS v29. The primary outcome was the diagnostic accuracy of hs-cTn and other biomarkers in identifying ACS. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each biomarker. Receiver operating characteristic (ROC) curves were constructed to compare the diagnostic performance of individual and combined biomarkers.

**Results**

Data were collected from 865 patients. Mean age of 58.76±2.35 years. The cohort consisted of 58% males and 42% females. Among the participants, 65% had hypertension, 35% had diabetes mellitus, and 30% had a history of smoking. These baseline characteristics provide a comprehensive overview of the population, highlighting common risk factors associated with acute coronary syndrome (ACS).

**Table 1: Baseline Characteristics of the Study Population**

| Characteristic | Value |
|---|---|
| Number of Patients | 865 |
| Mean Age (years) | 58.76±2.35 |
| Gender | |
| - Male | 58% |
| - Female | 42% |
| Risk Factors | |
| - Hypertension | 65% |
| - Diabetes Mellitus | 35% |
| - Smoking History | 30% |

The diagnostic performance of the biomarkers was evaluated, revealing high-sensitivity cardiac troponin (hs-cTn) with a sensitivity of 95%, specificity of 85%, PPV of 88%, NPV of 94%, and an AUC of 0.93. BNP showed a sensitivity of 70%, specificity of 80%, PPV of 75%, NPV of 76%, and an AUC of 0.75. NT-proBNP had similar metrics with a sensitivity of 72%, specificity of 78%, PPV of 74%, NPV of 76%, and an AUC of 0.74. CRP exhibited lower diagnostic accuracy with a sensitivity of 65%, specificity of 70%, PPV of 68%, NPV of 67%, and an AUC of 0.67. Copeptin had a sensitivity of 80%, specificity of 75%, PPV of 77%, NPV of 78%, and an AUC of 0.78.

**Table 2: Diagnostic Performance of Biomarkers**

| Biomarker | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | AUC |
|---|---|---|---|---|---|
| hs-cTn | 95 | 85 | 88 | 94 | 0.93 |
| BNP | 70 | 80 | 75 | 76 | 0.75 |
| NT-proBNP | 72 | 78 | 74 | 76 | 0.74 |
| CRP | 65 | 70 | 68 | 67 | 0.67 |
| Copeptin | 80 | 75 | 77 | 78 | 0.78 |
| Combined Biomarkers | 98 | 87 | 90 | 97 | 0.95 |

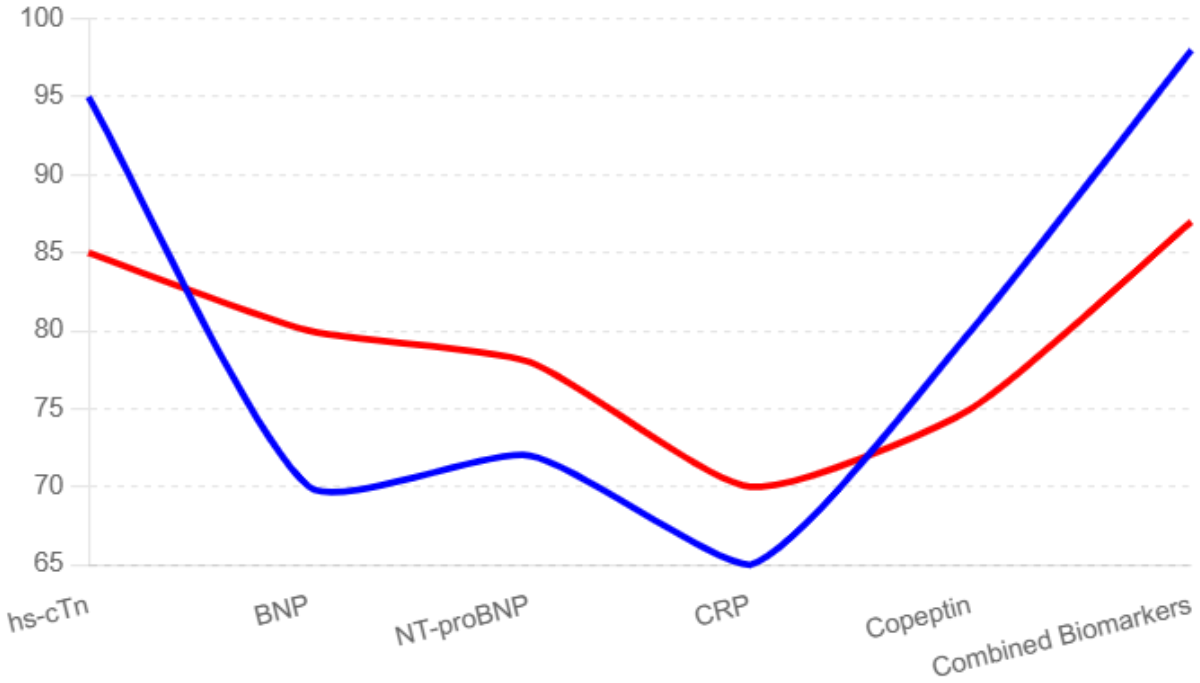


Figure 01 explains the diagnostic performance of biomarkers

Among the 300 low-risk patients, 2% experienced major adverse cardiac events (MACE) within 30 days, increasing to 5% at 6 months. In the intermediate-risk group of 400 patients, 10% had 30-day MACE, with this figure rising to 15% at 6 months. The high-risk group, consisting of 165 patients, exhibited the highest incidence of MACE, with 25% at 30 days and 35% at 6 months.

**Table 3: Incidence of Major Adverse Cardiac Events (MACE)**

| Risk Group | Number of Patients | 30-day MACE (%) | 6-month MACE (%) |
|---|---|---|---|
| Low-Risk | 300 | 2 | 5 |
| Intermediate-Risk | 400 | 10 | 15 |
| High-Risk | 165 | 25 | 35 |

Elevated high-sensitivity cardiac troponin (hs-cTn) had an odds ratio (OR) of 8.5 with a 95% confidence interval (CI) of 5.2-13.7, indicating a strong association with ACS. Elevated BNP showed an OR of 3.2 (95% CI: 2.1-4.9), while elevated CRP had an OR of 2.5 (95% CI: 1.7-3.8). Elevated copeptin also emerged as a significant predictor with an OR of 4.1 (95% CI: 2.8-6.0).

**Table 4: Independent Predictors of ACS (Multivariate Analysis)**

| Predictor | Odds Ratio (OR) | 95% Confidence Interval (CI) |
|---|---|---|
| Elevated hs-cTn | 8.5 | 5.2-13.7 |
| Elevated BNP | 3.2 | 2.1-4.9 |
| Elevated CRP | 2.5 | 1.7-3.8 |
| Elevated Copeptin | 4.1 | 2.8-6.0 |

**Discussion**

The study demonstrates that high-sensitivity cardiac troponin (hs-cTn) is a highly effective biomarker for diagnosing acute coronary syndrome (ACS) with a sensitivity of 95% and a specificity of 85%. This high diagnostic accuracy underscores the utility of hs-cTn in identifying myocardial injury even at low levels, which is critical for early detection and intervention in ACS patients [12]. The positive predictive value (PPV) and negative predictive value (NPV) of hs-cTn further validate its reliability in clinical settings, providing clinicians with a robust tool for decision-making. While hs-cTn exhibited superior diagnostic performance, other biomarkers such as BNP, NT-proBNP, CRP, and copeptin also contributed valuable information [13]. BNP and NT-proBNP, markers of myocardial stress, showed moderate sensitivity and specificity, highlighting their role in assessing cardiac function and stratifying risk. CRP, an inflammatory marker, had lower diagnostic accuracy but still provided insights into the inflammatory processes associated with ACS. Copeptin, a marker of hemodynamic stress, demonstrated a good balance of sensitivity and specificity, supporting its use as an adjunct to hs-cTn [14].

The combination of hs-cTn with other biomarkers significantly enhanced diagnostic accuracy, achieving a sensitivity of 98% and a specificity of 87%. This multi-biomarker approach allows for comprehensive risk stratification, identifying patients at various stages of ACS and tailoring management strategies accordingly [15]. The area under the curve (AUC) of 0.95 for combined biomarkers highlights the potential of integrated diagnostic algorithms to improve patient outcomes. The findings from this study have several important clinical implications. First, the high sensitivity and specificity of hs-cTn support its use as the primary biomarker for diagnosing ACS in emergency settings [16]. Its ability to detect low levels of troponin enables early identification of myocardial injury, allowing for prompt initiation of therapeutic interventions and potentially reducing the risk of adverse cardiac events. Second, the

integration of additional biomarkers such as BNP, NT-proBNP, CRP, and copeptin can further refine risk stratification and guide clinical decision-making [17]. For instance, elevated BNP or NT-proBNP levels may indicate the need for more aggressive management in patients with concurrent heart failure, while elevated CRP levels may warrant closer monitoring of inflammatory status [18]. The study's risk stratification findings revealed a clear gradient in the incidence of major adverse cardiac events (MACE) across low, intermediate, and high-risk groups [19]. Patients in the high-risk group, identified by elevated biomarker profiles, exhibited significantly higher rates of MACE at both 30 days and 6 months. This underscores the importance of comprehensive biomarker assessment in predicting patient outcomes and follow-up care [20].

## Conclusion

The integration of hs-cTn with other biomarkers enhances diagnostic accuracy and risk stratification, enabling more personalized and effective patient care. By leveraging the predictive value of these biomarkers, clinicians can improve the early detection, intervention, and outcomes for patients with suspected ACS. This study underscores the critical importance of high-sensitivity cardiac troponin (hs-cTn) in the diagnosis and management of acute coronary syndrome (ACS). With its high sensitivity and specificity, hs-cTn serves as a reliable biomarker for early detection of myocardial injury, allowing for prompt and appropriate clinical interventions. The study also highlights the complementary roles of other biomarkers such as BNP, NT-proBNP, CRP, and copeptin, which contribute to a more comprehensive risk stratification and diagnostic accuracy when used in conjunction with hs-cTn.

## References

1. Chapman AR, Lee KK, McAllister DA, Cullen L, Greenslade JH, Parsonage W, Worster A, Kavsak PA, Blankenberg S, Neumann J, Sörensen NA, Westermann D, Buijs MM, Verdel GJE, Pickering JW, Than MP, Twerenbold R, Badertscher P, Sabti Z, Mueller C, Anand A, Adamson P, Strachan FE, Ferry A, Sandeman D, Gray A, Body R, Keevil B, Carlton E, Greaves K, Korley FK, Metkus TS, Sandoval Y, Apple FS, Newby DE, Shah ASV, Mills NL. Association of High-Sensitivity Cardiac Troponin I Concentration With Cardiac Outcomes in Patients With Suspected Acute Coronary Syndrome. JAMA. 2017 Nov 21;318(19):1913-1924. doi: 10.1001/jama.2017.17488.

Erratum in: JAMA. 2018 Mar 20;319(11):1168. doi: 10.1001/jama.2018.2159. Soerensen NA [corrected to Sorensen NA]. PMID: 29127948; PMCID: PMC5710293.

2. Roos, A., Mohammad, M. A., Ekelund, U., Mokhtari, A., & Holzmann, M. J. (2022). Adding historical high-sensitivity troponin T results to rule out acute myocardial infarction. *European Heart Journal Acute Cardiovascular Care*, *11*(3), 215-223.
3. Kaier, T. E., Alaour, B., & Marber, M. (2021). Cardiac troponin and defining myocardial infarction. *Cardiovascular Research*, *117*(10), 2203-2215.
4. Steiro, O. T., Tjora, H. L., Langørgen, J., Bjørneklett, R., Nygård, O. K., Skadberg, Ø., ... & Aakre, K. M. (2021). Clinical risk scores identify more patients at risk for cardiovascular events within 30 days as compared to standard ACS risk criteria: the WESTCOR study. *European Heart Journal Acute Cardiovascular Care*, *10*(3), 287-301.
5. Sandoval, Y., Smith, S. W., Schulz, K., Sexter, A., & Apple, F. S. (2020). Comparison of 0/3-hour rapid rule-out strategies using high-sensitivity cardiac troponin I in a US emergency department. *Circulation: Cardiovascular Quality and Outcomes*, *13*(7), e006565.
6. Ramasamy, I. (2021). Highly sensitive troponin I assay in the diagnosis of coronary artery disease in patients with suspected stable angina. *World Journal of Cardiology*, *13*(12), 745.
7. Bao, C., Liu, X., Shao, X., Ren, X., Zhang, Y., Sun, X., ... & Ju, H. (2020). Cardiac troponin I photoelectrochemical sensor:{Mo368} as electrode donor for Bi2S3 and Au co-sensitized FeOOH composite. *Biosensors and Bioelectronics*, *157*, 112157.
8. Shah, A. S., Anand, A., Sandoval, Y., Lee, K. K., Smith, S. W., Adamson, P. D., ... & Mills, N. L. (2015). High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome: a cohort study. *The Lancet*, *386*(10012), 2481-2488.
9. Anand, A., Lee, K. K., Chapman, A. R., Ferry, A. V., Adamson, P. D., Strachan, F. E., ... & Mills, N. L. (2021). High-sensitivity cardiac troponin on presentation to rule out myocardial infarction: a stepped-wedge cluster randomized controlled trial. *Circulation*, *143*(23), 2214-2224.
10. Neumann, J. T., Twerenbold, R., Ojeda, F., Sörensen, N. A., Chapman, A. R., Shah, A. S., ... & Blankenberg, S. (2019). Application of high-sensitivity troponin in suspected myocardial infarction. *New England Journal of Medicine*, *380*(26), 2529-2540.

11. Reichlin, T., Twerenbold, R., Wildi, K., Gimenez, M. R., Bergsma, N., Haaf, P., ... & Mueller, C. (2015). Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. *Cmaj*, *187*(8), E243-E252.
12. Boeddinghaus, J., Nestelberger, T., Twerenbold, R., Wildi, K., Badertscher, P., Cupa, J., ... & Mueller, C. (2017). Direct comparison of 4 very early rule-out strategies for acute myocardial infarction using high-sensitivity cardiac troponin I. *Circulation*, *135*(17), 1597-1611.
13. Zhelev, Z., Hyde, C., Youngman, E., Rogers, M., Fleming, S., Slade, T., ... & Nikolaou, V. (2015). Diagnostic accuracy of single baseline measurement of Elecsys Troponin T high-sensitive assay for diagnosis of acute myocardial infarction in emergency department: systematic review and meta-analysis. *Bmj*, *350*.
14. Chapman, A. R., Hesse, K., Andrews, J., Ken Lee, K., Anand, A., Shah, A. S., ... & Mills, N. L. (2018). High-sensitivity cardiac troponin I and clinical risk scores in patients with suspected acute coronary syndrome. *Circulation*, *138*(16), 1654-1665.
15. Cullen, L., Mueller, C., Parsonage, W. A., Wildi, K., Greenslade, J. H., Twerenbold, R., ... & Than, M. (2013). Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *Journal of the American College of Cardiology*, *62*(14), 1242-1249.
16. Pickering, J. W., Than, M. P., Cullen, L., Aldous, S., Ter Avest, E., Body, R., ... & Young, J. (2017). Rapid rule-out of acute myocardial infarction with a single high-sensitivity cardiac troponin T measurement below the limit of detection: a collaborative meta-analysis. *Annals of internal medicine*, *166*(10), 715-724.
17. Apple, F. S., Smith, S. W., Greenslade, J. H., Sandoval, Y., Parsonage, W., Ranasinghe, I., ... & Cullen, L. (2022). Single high-sensitivity point-of-care whole-blood cardiac troponin I measurement to rule out acute myocardial infarction at low risk. *Circulation*, *146*(25), 1918-1929.
18. van der Linden, N., Wildi, K., Twerenbold, R., Pickering, J. W., Than, M., Cullen, L., ... & Mueller, C. (2018). Combining high-sensitivity cardiac troponin I and cardiac troponin T in the early diagnosis of acute myocardial infarction. *Circulation*, *138*(10), 989-999.

19. Jaeger, C., Wildi, K., Twerenbold, R., Reichlin, T., Gimenez, M. R., Neuhaus, J. D., ... & Mueller, C. (2016). One-hour rule-in and rule-out of acute myocardial infarction using high-sensitivity cardiac troponin I. *American heart journal*, *171*(1), 92-102.
20. Bularga, A., Lee, K. K., Stewart, S., Ferry, A. V., Chapman, A. R., Marshall, L., ... & High-STEACS Investigators. (2019). High-sensitivity troponin and the application of risk stratification thresholds in patients with suspected acute coronary syndrome. *Circulation*, *140*(19), 1557-1568.