Original Article

New Insights Into the Use of hs-cTnI and NT-proBNP in Chronic Coronary Syndromes

Moayed Basheer Hamid[1], Amal Abbas Hamoodi[2*], MS; Basil Oied Saleh[2], PhD; Ameen Abdulhasan Al-Alwany[3], MD

ABSTRACT

Background: A noninvasive method of determining the severity of coronary artery disease (CAD) is the use of cardiac biomarkers. This study aimed to investigate the use of serum levels of high-sensitivity cardiac troponin I (hs-cTnI) and N-terminal pro–B-type natriuretic peptide (NT-proBNP) in determining CAD severity.

Methods: This cross-sectional study included 125 participants categorized by coronary angiographic results into 3 groups: group I (no or < 50% stenosis), group II (1 or 2 vessels with ≥ 50% stenosis), and group III (left main stem or ≥ 3 vessels with ≥ 50% obstruction). Serum hs-cTnI and NT-proBNP levels were measured by enzyme-linked immunosorbent assay. Data were analyzed using SPSS version 25.0 and described as percentages, means, medians, and interquartile ranges (Q1–Q3). Receiver operating characteristic curves and relative quality were applied for both biomarkers.

Results: Median hs-cTnI and NT-proBNP levels were higher in group III than in groups I and II (P = .001). Both were higher in group II than in group I (P = .001). Receiver operating characteristic analysis showed that hs-cTnI and NT-proBNP effectively discriminated vascular obstruction severity with high sensitivity and specificity. Relative quality testing results showed a slight increase in predictive ability when the 2 biomarkers were combined.

Conclusions: Serum hs-cTnI and NT-proBNP levels, combined or separately, can be used to assess CAD severity concerning the number of diseased vessels, which may help improve risk stratification and management strategy selection. ***(Iranian Heart Journal 2026; 27(3): 20-26)***

KEYWORDS: cardiac biomarkers; noninvasive diagnosis; risk stratification; coronary stenosis

[1] Department of Medicine, College of Medicine, Al-Nahrain University, Baghdad, Iraq.
[2] Department of Biochemistry, College of Medicine, University of Baghdad, Baghdad, Iraq.
[3] Department of Medicine, University of Baghdad, College of Medicine, Baghdad, Iraq.

***Corresponding Author:** Amal Abbas Hamoodi, BS; Department of Biochemistry, College of Medicine, University of Baghdad, Baghdad, Iraq.
Email: aamal.abbas2209p@comed.uobaghdad.edu.iq **Tel:** +964 (780) 1612952

Received: May 13, 2025 **Accepted:** June 12, 2026

Coronary artery disease (CAD) is a leading cause of mortality worldwide.[1] Atherosclerosis, a chronic inflammatory disorder of the arterial wall that causes CAD in most patients,[2] is characterized by focal lipid-rich deposits of atheroma that do not cause symptoms until they compromise tissue perfusion, resulting in demand-led ischemia that manifests as chronic coronary syndromes or acute thrombotic vessel blockage from plaque ulceration or erosion, resulting in supply-led ischemia that manifests as acute coronary syndromes.[3] Conventional coronary angiography provides information only on the site and degree of luminal narrowing; it does not reflect the degree of atherosclerotic change within the arterial wall or the physiological implications of this narrowing. Furthermore, coronary angiography is an invasive procedure associated with potential complications.[4]

The severity of CAD and the risk of future cardiac events can be evaluated using various biomarkers, which reflect underlying pathologic processes and prognosis and guide treatment decisions; nonetheless, most of these markers are not routinely used in current clinical practice.[5] The cardiac-specific contractile proteins myosin and actin, as well as regulatory proteins known as troponins, make up heart muscle fibers. One of the constituents of the thin filament, the troponin complex, is crucial for controlling muscle contraction.[6] Troponin release occurs when myocardial cells are damaged because of insufficient oxygen supply caused by coronary artery narrowing or blockage. In acute coronary syndromes, plaque rupture and thrombus formation cause acute obstruction, leading to high troponin levels, while in chronic coronary syndromes, even without significant macrovascular obstruction, microvascular ischemia can elevate troponin levels.[7] Nevertheless, it is currently not advised to routinely test for high-sensitivity cardiac troponin I (hs-cTnI) when evaluating patients with chronic coronary syndromes.[8]

In heart failure, myocardial wall stress triggers the heart to produce B-type natriuretic peptide (BNP), a 108-amino-acid prohormone (proBNP). Upon release into the circulation, proBNP is cleaved in equal proportions into the physiologically inactive 76-amino-acid N-terminal fragment (NT-proBNP) and the physiologically active 32-amino-acid BNP, which is the C-terminal fragment. BNP has a variety of physiologic effects, including natriuresis/diuresis, peripheral vasodilation, and suppression of the sympathetic nervous system and the renin-angiotensin-aldosterone system.[9] Its levels can predict the severity of left ventricular dysfunction.[10] Experimental data indicate that myocardial ischemia causes cardiomyocytes to release BNP and NT-proBNP, regardless of ventricular wall stress.[11] Because myocardial ischemia depends on the location and extent of coronary obstruction, NT-proBNP may be used to predict the severity of coronary artery disease (CAD).[12]

The current study aimed to examine the clinical use of NT-proBNP and hs-cTnI in assessing CAD severity.

METHODS

The present cross-sectional study was carried out at Baghdad Teaching Hospital, Medical City Complex, Baghdad, Iraq, by the Department of Biochemistry, College of Medicine, University of Baghdad, between March 2024 and December 2024. It included participants older than 18 years undergoing elective coronary angiography for suspected CAD. A cardiologist performed the angiographic assessments while blinded to patient biomarker levels using left and right Judkins catheters (Boston Scientific).

Participants were subclassified according to the severity of coronary obstruction into 3 groups: group I included 48 participants with no coronary artery obstruction or minimal lesion (<50% stenosis); group II included 47 participants with significant obstruction (≥50% stenosis) in 1 or 2 coronary arteries; and group III included 30 participants with ≥50% stenosis in 3 coronary arteries or ≥50% stenosis in the left main coronary artery.

The sample size of each included group was calculated according to the proportionate stratified sampling equation,[13] and the power of the sample size was equal to or greater than 80% to identify a medium-to-large effect.[14]

This study was approved by the Scientific and Ethics Committees of the Department of Biochemistry, College of Medicine, University of Baghdad. Ethical approval was also obtained from Baghdad Teaching Hospital, Medical City Complex, and the Ministry of Health, Iraq.

Exclusion criteria included acute coronary syndromes; previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting; heart failure, myocarditis, or cardiomyopathy; pulmonary embolism; sepsis; stroke; chronic kidney disease; chronic liver disease; endocrine disorders; and cancer, based on history, physical examination, and laboratory results.

Five milliliters of blood was aspirated from the peripheral vein of each participant in the 3 groups and allowed to clot for 15 minutes and subsequently centrifuged for 10 minutes at 2500 rpm. The isolated serum was preserved at −45 °C until the day of laboratory testing, which included measurements of hs-cTnI (kit from Cloud-Clone Corp, USA) and NT-proBNP (kit from Elabscience Human NT-proBNP, USA), using the enzyme-linked immunosorbent assay sandwich technique by an ELISA reader (Huma Reader, Human Diagnostics, Germany) and washer (COMBIWASH). The principle of the ELISA technique with the biotin double-antibody sandwich method was employed for the evaluation of human hs-cTnI and NT-proBNP.

Statistical analyses were conducted using SPSS software version 25.0 (SPSS, Chicago). Mean (SD) was used to present normally distributed data, and analysis of variance was performed. Median and interquartile range (Q1–Q3) were utilized to present non-normally distributed data. The Mann-Whitney *U* test was drawn upon for comparisons between 2 groups, and the Kruskal-Wallis test was used for comparisons among 3 groups. The χ^2 test was applied to evaluate categorical variables, presented as numbers and percentages.

Receiver operating characteristic curves were used to assess the discriminative utility of biomarkers in differentiating across groups, Relative quality testing was utilized to compare the area under the curve for combined biomarkers vs individual biomarkers. The potential link between hs-cTnI and NT-proBNP and other factors was investigated using the Spearman rank correlation test. A difference was deemed statistically significant if the *P* value was below .05.

RESULTS

Table 1 shows the demographic analysis of the 3 study groups. Mean (SD) age and body mass index did not differ significantly among the 3 groups. Sex distribution revealed that males were significantly more frequent in groups II and III compared with group I. Smoking was significantly more common among patients in groups I and II than among those in group III. Hypertension was significantly more common in groups I and III than in group II. Table 2 presents the median (Q1–Q3) serum hs-cTnI and NT-proBNP levels of the 3 study groups. The median level of both biomarkers was significantly higher in group III than in groups I and II. Similarly, the median level of both biomarkers was significantly higher in group II than in group I.

The Spearman rank correlation test demonstrated a significant positive correlation between hs-cTnI and NT-proBNP in group I ($r = 0.757$; $P < .001$) and group II ($r = 0.57$; $P < .001$). No significant association was found between risk factors and the levels of these biomarkers, indicating the absence of confounding. In other words, the increase in biomarker levels was due to coronary obstruction rather than to the risk factors themselves.

Table 3 shows the results of receiver operating characteristic analysis. Both hs-cTnI and NT-proBNP demonstrated high discriminative ability in differentiating between groups based on CAD severity. The area under the curve for hs-cTnI was higher than that for NT-proBNP in the comparison between groups II and III, indicating that hs-cTnI had greater value in severity differentiation. In all comparisons, the combination of the 2 biomarkers slightly increased the predictive ability for coronary obstruction; in the comparison between groups II and III, the increase was 2.3%.

Table 1. Demographic and Clinical Characteristics of the Studied Groups

Parameter	Group I (n = 48)	Group II (n = 47)	Group III (n = 30)	*P*
Male	21 (43.75%)	34 (72.34%)	21 (70%)	.008**
Female	27 (56.5%)	13 (27.66%)	9 (30%)	
Age, mean (SD), y	53.71 (10.19)	55.23 (11.54)	58.60 (8.94)	.134*
BMI, mean (SD), kg/m²	32.15 (5.55)	31.88 (5.63)	30.15 (4.98)	.280*
Smoking	22 (45.83%)	23 (48.94%)	6 (20%)	.028**
Hypertension	21 (43.75%)	11 (23.4%)	15 (50%)	.034**
Diabetes mellitus	31 (64.58%)	20 (42.55%)	13 (43.33%)	.061

BMI: body mass index

Statistical tests: Analysis of variance for age and BMI; χ^2 test for categorical variables

Table 2. Biomarker Levels in the 3 Studied Groups

Parameter	Group I (n = 48)	Group II (n = 47)	Group III (n = 30)	*P**
hs-cTnI, median (IQR), pg/mL	94.37 (22.5–337.9)	94.37 (22.5–337.9)	484.76 (220–622.5)	.001
NT-proBNP, median (IQR), ng/mL	0.89 (0.66–1.47)	1.77 (0.96–4.94)	4.14 (1.27–5.49)	.001

*Nonparametric Kruskal-Wallis test

Table 3. ROC and AUC Analysis for Biomarkers

Group Comparison		AUC	Sensitivity, %	Specificity, %	95% CI	*P*	Cutoff Value	RQ
I vs II	hs-cTnI	0.924	83	96	0.872–0.976	< .001	224.3 pg/mL	1.019
	NT-proBNP	0.935	81	90	0.890–0.980	< .001	1.14 ng/mL	
	Combined	0.953						
I vs III	hs-cTnI	0.997	97	98	0.991–1.0	< .001	320.4 pg/mL	1.001
	NT-proBNP	0.992	97	96	0.985–1.0	< .001	1.35 ng/mL	
	combined	0.998						
II vs III	hs-cTnI	0.926	90	92	0.859–0.992	< .001	354.4 pg/mL	1.023
	NT-proBNP	0.878	80	79	0.802–0.954	< .001	2.4 ng/mL	
	Combined	0.947						

hs-cTnI: high-sensitivity cardiac troponin I; NT-proBNP: N-terminal pro–B-type natriuretic peptide

DISCUSSION

The age at presentation in this study was similar to that reported in the Middle East, where CAD occurs 12 years earlier than in Western countries.[15] Increasing age, albeit not statistically significant, was associated with multivessel CAD, similar to findings from a narrative review involving 75 articles.[16] Male participants were significantly predominant in groups II and III. Men are more likely than women to develop CAD, and they typically do so at a younger age. Additionally, compared with age-matched women, they had a higher risk of developing severe CAD.[17]

Severity of CAD was associated with risk factors such as hypertension, diabetes, smoking, and dyslipidemia in most studies[18] but not in the present study. One study stated that risk factors correlated with the occurrence of atherosclerosis but not with its severity.[19]

In the current study, smoking was less prevalent in group III than in the other groups. The association between smoking and the number of affected coronary arteries remains controversial. Five studies found a strong association between smoking and the number of affected arteries, whereas 6 studies found no association.[20] According to the ACUITY trial, smokers are more likely to require percutaneous coronary intervention and less likely to require coronary artery bypass grafting because of favorable coronary anatomy.[21] Compared with nonsmokers, smokers with CAD are at least 10 years younger.[22] A 2-fold increase in in-hospital mortality from all causes in smokers compared with nonsmokers was observed in the Million Women Study,[23] with an estimated decline in life expectancy of 10 years. From the aforementioned, a possible explanation is that smokers die before they reach triple-vessel CAD, or that older individuals may have a lower prevalence of smoking because of generational differences in smoking habits and increased health concerns as they age.

The results of the present study revealed a significant increase in hs-cTnI with a greater number of diseased arteries, which is in agreement with other studies that concluded a significant association of hs-cTnI with the presence of CAD in chronic coronary syndromes[24] and with angiographic severity.[25]

Increased myofibrillar troponin protolithic degradation may contribute to elevated cTnI levels in chronic coronary syndromes. This phenomenon may be explained by several mechanisms, including a local increase in intracellular Ca^{2+} concentration after ischemia, which increases the activity of the calcium-dependent protease calpain, leading to chronic proteolytic degradation of myofibrillar cTn. Alternatively, the development and release of membrane blebs containing troponin represent another pathologic process through which intact troponin may be released after ischemia without necrosis.[26]

In this study, plasma NT-proBNP levels were significantly increased with an increasing number of diseased arteries. This is consistent with findings from other studies that found a strong correlation between angiographic CAD severity and plasma NT-proBNP levels.[27] In individuals with chronic coronary syndromes, myocardial ischemia, irrespective of left ventricular dysfunction, may contribute to increased NT-proBNP levels. An elevation in BNP due to myocardial ischemia can be attributed to increased left ventricular wall stress and augmented gene production of NT-proBNP.[28] Still, natriuretic peptides and their receptors are prevalent in atherosclerotic plaques within human coronary arteries and are involved in cellular proliferation, migration, and vascular remodeling; atherosclerosis itself may increase BNP levels.[29] In contrast, among individuals undergoing elective angiography, Tarek Souaid et al[30] found no correlation between NT-proBNP and the degree of CAD.

CONCLUSIONS

Serum hs-cTnI levels were superior to NT-proBNP levels in assessing CAD severity in terms of the number of diseased vessels; however, both biomarkers, whether combined or separate, can be drawn upon. This may help improve risk stratification and management strategy selection.

Acknowledgments: The authors thank all study participants, including patients and medical and laboratory staff.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki ethical guidelines for human research. The Research Ethics Committee at the Department of Biochemistry, University of Baghdad, approved the study protocol from clinical and ethical perspectives (permission No. 430, February 26, 2024).

Funding: This study was self-funded.

Conflict of Interest: The authors declare no conflicts of interest.

REFERENCES

1. World Health Organization. World health sWORLD HEALTH ORGANIZATION - World health statistics 2024. ISBN 9789240094703. tatistics 2024. 2024. 1–96 p.

2. Björkegren JLM, Lusis AJ. Atherosclerosis : Recent Developments. 2023;185(10):1630–45.

3. Luo X, Lv Y, Bai X, Qi J, Weng X, Liu S, et al. Plaque Erosion: A Distinctive Pathological Mechanism of Acute Coronary Syndrome. Front Cardiovasc Med. 2021; 8(September):1–11.

4. Majeed SM, Bahjet Al Saffar H, AL- Marayati AN. Complication Following percutaneous coronary intervention via the femoral artery Experience in lraqi center for the Heart Disease and lbn Al-Bitar Hospital for cardiac surgery. J Fac Med Baghdad. 2016; 58(4):325–9.

5. Wallentin L, Eriksson N, Olszowka M, Grammer TB, Hagström E, Held C, et al. Plasma proteins associated with cardiovascular death in patients with chronic coronary heart disease: A retrospective study. PLoS Med. 2021; 18(1):1–22.

6. Sweeney HL, Hammers DW. Muscle contraction. Cold Spring Harb Perspect Biol. 2018; 10(2).

7. Wu AHB. Release of cardiac troponin from healthy and damaged myocardium. Front Lab Med [Internet]. 2017; 1(3):144–50. Available from: https://doi.org/10.1016/j.flm.2017.09.003

8. Tveit SH, Myhre PL, Hanssen TA, Forsdahl SH, Iqbal A, Omland T, et al. Cardiac troponin I and T for ruling out coronary artery disease in suspected chronic coronary syndrome. Sci Rep. 2022 Dec 1; 12(1).

9. Nishikimi T, Nakagawa Y. B-Type Natriuretic Peptide (BNP) Revisited—Is BNP Still a Biomarker for Heart Failure in the Angiotensin Receptor/Neprilysin Inhibitor Era? Biology (Basel). 2022; 11(7).

10. Nasser TH, El-Yassin HD, Yakoob S. B-Natriuretic Peptide Level as a Predictor for the Severity of LV Dysfunction. J Fac Med Baghdad. 2008; 49(4):438–48.

11. Kragelund C, Gustafsson I, Omland T, Grønning B, Køber L, Faber J, et al. Prognostic value of NH2-terminal pro B-type natriuretic peptide in patients with diabetes and stable coronary heart disease. Diabetes Care. 2006; 29(6):1411–3.

12. Kawabe M, Sato A, Hoshi T, Endo M, Yoshida I, Aonuma K. Incremental value of B-type natriuretic peptide for detection and risk reclassification of obstructive coronary artery disease on computed tomography angiography. J Cardiol [Internet]. 2017; 69(4):671–7. Available from: http://dx.doi.org/10.1016/j.jjcc.2016.06.008

13. Ahmed SK. How to choose a sampling technique and determine sample size for research: A simplified guide for researchers. Oral Oncol Reports [Internet]. 2024 Dec;12:100662. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2772906024005089

14. Edition T, Thompson SK, Wiley J, Wiley J. Estimating Proportions, Ratios, and Subpopulation Means. 2012; 57–66.

15. Almahmeed W, Samir Arnaout M, Chettaoui R, Ibrahim M, Ibrahim Kurdi M, Awad Taher M, et al. Coronary artery disease in Africa and the Middle East. Ther Clin Risk Manag. 2012; 8:65–72.

16. Lima Dos Santos CC, Matharoo AS, Pinzón Cueva E, Amin U, Perez Ramos AA, Mann NK, et al. The Influence of Sex, Age, and Race on Coronary Artery Disease: A Narrative Review. Cureus. 2023; 15(10).

17. Omidi N, Sadeghian S, Salarifar M, Jalali A, Abbasi SH, Yavari N, et al. Relationship between the severity of coronary artery disease and cardiovascular risk factors in acute coronary syndrome: Based on tehran heart center's data registry. J Tehran Univ Hear Cent. 2020; 15(4):171–6.

18. Charach L, Blatt A, Jonas M, Teodorovitz N, Haberman D, Gendelman G, et al. Using the Gensini score to estimate severity of STEMI, NSTEMI, unstable angina, and anginal syndrome. Med (United States). 2021; 100(41):E27331.

19. Aksu F, Ahmed S. Gensini Score's Severity and Its Relationship with Risk Factors for Coronary Artery Disease Among Patients Who Underwent Angiography in Somalia's Largest PCI Centre. Int J Gen Med. 2024; Volume 17(January):187–92.

20. Salehi N, Janjani P, Tadbiri H, Rozbahani M, Jalilian M. Effect of cigarette smoking on coronary arteries and pattern and severity of coronary artery disease: a review. J Int Med Res. 2021; 49(12).

21. Rgeeb AN, Alsalkh HA, Radhi AK, Amber K. Effect of Intravenous Abciximab on Coronary Flow Improvement After Re-vascularization in Primary Coronary Intervention and Short Term Impact. Med Arch (Sarajevo, Bosnia Herzegovina). 2020; 74(4):265–9.

22. Kodaira M, Miyata H, Numasawa Y, Ueda I, Maekawa Y, Sueyoshi K, et al. Effect of smoking status on clinical outcome and efficacy of clopidogrel in acute coronary syndrome. Circ J. 2016; 80(7):1590–9.

23. Pirie K, Peto R, Reeves GK, Green J, Beral V. The 21st century hazards of smoking and benefits of stopping: A prospective study of one million women in the UK. Lancet [Internet]. 2013;381(9861):133–41. Available from: http://dx.doi.org/10.1016/S0140-6736(12)61720-6

24. Myhre PL, Røsjø H, Sarvari SI, Ukkonen H, Rademakers F, Engvall JE, et al. Cardiac troponin T and NT-proBNP for detecting myocardial ischemia in suspected chronic coronary syndrome. Int J Cardiol. 2022; 361(April):14–7.

25. Askin L. Clinical Importance of High-Sensitivity Troponin T in Patients without Coronary Artery Disease. North Clin Istanbul. 2019;

26. Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: From myocardial infarction to chronic disease. Cardiovasc Res. 2017; 113(14):1708–18.

27. Fang Z, Zhou L, Bao Y, Ding W, Shi H, Luo X, et al. Association of NT-proBNP and multiple biomarkers with severity of angiographic coronary artery disease in diabetic and pre-diabetic chinese patients. PLoS One. 2011; 6(8).

28. Jehn S, Mahabadi AA, Pfohl C, Vogel L, Al-Rashid F, Luedike P, et al. BNP and NT-proBNP Thresholds for the Assessment of Prognosis in Patients Without Heart Failure. JACC Adv [Internet]. 2023;2(10):100688. Available from: https://doi.org/10.1016/j.jacadv.2023.100688

29. Zayed MA, Harring S, Abendschein D, Vemuri C, Lu D, Detering L, et al. Natriuretic Peptide Receptor-C is Up-Regulated in the Intima of Advanced Carotid Artery Atherosclerosis. J Med Surg Pathol. 2016; 131(3):139–48.

30. Souaid T, Hijazi Z, Barakett V, Sarkis A, Kadri Z, Batra G, et al. Association of GDF-15, hs-cTnT and NT-proBNP with coronary artery disease in patients undergoing elective angiography. Future Cardiol. 2022; 18(8):635–46.