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Original Research Article

Accuracy of delta high-sensitivity troponin I in diagnosing the severity of coronary artery disease with the SYNTAX score as the gold standard

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ABSTRACT

Background: The SYNTAX score is a comprehensive angiographic tool that quantifies the complexity and extent of coronary artery disease (CAD) based on the number, location, and severity of lesions in the coronary arteries. This study aimed to assess the accuracy of delta high-sensitivity troponin I in diagnosing the severity of coronary artery disease with the SYNTAX score as the gold standard.
Methods: This study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Bangladesh from July 2022 to June 2023. A total of 70 patients with significant delta hs-cTnI were divided into two groups: Group-A (n=36) with a delta hs-cTnI rise between >20 to 49%, and Group-B (n=34) with a delta hs-cTnI rise ≥50%. Coronary angiography was conducted, and the SYNTAX Score was calculated for both groups. Data analysis was performed using SPSS version 25.0.
Results:32.4% of patients with a high-rise of delta cTnI (≥50%) had a SYNTAX score >22, compared to none of the patients with a low-rise of cTnI 20-49% ($p<0.001$). The delta hs-cTnI showed a significantly moderate linear correlation with the SYNTAX score ($p=0.001$). The optimal cut-off value for high sensitivity, with minimal compromise in specificity, was 89.0, with an area under the curve of 0.847 ($p<0.001$), indicating that nearly 85% of severe CAD could be accurately diagnosed with a delta hs-cTnI value of 90.0 or higher in NSTEMI patients**.**
Conclusion: The study findings suggest that a delta hs-cTnI value of 90.0 or higher in NSTEMI patients can accurately diagnose nearly 85% of severe CAD.

Keywords: Accuracy, Delta high-sensitivity troponin I, CAD, Coronary artery disease, SYNTAX score

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death globally, responsible for approximately 32% of all global deaths.[1] Acute coronary syndrome (ACS) encompasses ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina. Annually, over 20 million patients present with symptoms suggestive of myocardial infarction (MI) in Europe and North America.[1]

The diagnosis of ACS is confirmed by a rise and/or fall of cardiac enzymes, along with supportive evidence such

as typical symptoms and suggestive electrocardiographic (ECG) changes. Measurement of high-sensitivity cardiac troponin I (hs-cTnI) or T assays plays a pivotal role in the early diagnosis of MI.[2]

Cardiac troponin (cTn) I or T assays are considered 'sensitive' if they can detect cTn in 20–50% of healthy individuals and 'high-sensitivity' if they detect cTn levels in >50% of healthy subjects, with a coefficient of variation of <10% at the 99th percentile upper reference limit.[2]

High-sensitivity troponin assays offer greater analytic precision at lower concentrations, enhancing clinical sensitivity for myocardial injury detection. They accurately recognize small changes in troponin concentration, indicating myocardial injury, within a short timeframe. The magnitude of absolute cTn change within 1 hour, 2 hours, or 3 hours correlates with the likelihood of MI presence.[3,4]

The "delta troponin" refers to the change in troponin concentration between two assays conducted within a specified time interval, with a significant delta troponin defined as a rise or fall of at least 20% from the initial value.

Current recommendations for early MI diagnosis suggest a ≥20% increase in troponin concentrations within 3–6 hours from baseline levels.[4] Coronary angiography with intervention is recommended for managing ACS patients.

Invasive treatment of NSTEMI occasionally reveals coronary arteries without significant stenosis. A study reported that 13% of NSTEMI patients had normal angiograms.[5] Previous research has shown a significant association between elevated troponin I levels and severe coronary artery disease, severe clinical presentation, and a high incidence of complex and culprit lesions on coronary angiography.[6,7]

Prognostic evaluation of NSTEMI includes clinical, laboratory, and anatomical criteria, with the SYNTAX score being one of the anatomical criteria used to grade the complexity of coronary lesions diagnosed by coronary angiography.

While few studies have assessed the relationship between the complexity of angiographic coronary lesions and hs-cTn, one study found that elevated troponin I levels more than 10-fold the maximum threshold of the normal range in NSTEMI patients strongly correlate with more complex and severe coronary artery disease.[8-10]

Several studies have consistently shown a positive relationship between increased hs-cTn and the prognosis of patients with ACS.[11] The objective of this study was to assess the accuracy of delta high-sensitivity troponin I in diagnosing the severity of coronary artery disease with the SYNTAX score as the gold standard.

METHODS

Study type

This cross-sectional study was conducted at the Department of Cardiology, Ibrahim Cardiac Hospital and Research Institute in Dhaka, Bangladesh.

Study duration

Spanning from July 2022 to June 2023.

Sampling size

In this study, 70 consecutive patients diagnosed with NSTEMI and admitted to the hospital were included using consecutive sampling.

Inclusion criteria

Inclusion criteria for participants were: patients aged 18 years or older, diagnosed with NSTEMI based on clinical presentation and elevated cardiac biomarkers, and admitted to the hospital during the study period.

Excluded criteria

Patients with significant comorbidities that could interfere with the study outcomes, those who did not consent to participate, and those without significant delta troponin elevation were excluded. Written informed consent was obtained from each patient after explaining the procedure.

Delta troponin was calculated, and patients without significant delta troponin elevation were excluded. Patient demographics and clinical history were recorded by the principal investigator. NSTEMI patients were divided into two groups based on delta hs-cTnI elevation >20-49% and ≥50% from baseline levels. Both groups underwent CAG within one to four days by interventional cardiologists. The SYNTAX score was used to assess both groups, with a low score defined as ≤22 and intermediate to high risk as >22.

Data collection

Data were collected through direct interviews with patients after obtaining consent from the researcher. Statistical analysis was performed using SPSS version 25. Measurement of hs-cTn was conducted using the dimension EXL platform by Siemens, USA, with a sensitivity of 4.0 pg/ml and specificity of 0.003% with cTn-T. Coronary angiography was performed using the Allura Xper FD biplane X-ray system.[10]

Statistical analysis

Data were analyzed using descriptive statistics, Chi-square ($\chi 2$) or Fisher's Exact Probability Test for

categorical data, and Student's t-test for continuous data. Correlation coefficients were determined using Pearson and Spearman correlation analyses. An optimal cut-off value was determined using a Receiver Operating Characteristic (ROC) curve. All tests were conducted at a 5% level of significance, with a p value<0.05 considered statistically significant.

RESULTS

The baseline characteristics of the patients are summarized in Table 1. The average age was similar between the groups, with group A having a mean age of 54.2 years and group B having a mean age of 55.7 years (p=0.524). Both groups had a higher proportion of males, 69.4% in group A and 64.7% in group B (p=0.673). The BMI distribution showed no significant difference between the groups, with the majority falling in the 25-29.9 kg/m² range.

Investigations revealed comparable results for hemoglobin, random blood sugar, HbA1c, serum total cholesterol, serum LD, serum HDL, serum triglycerides, serum creatinine, and eGFR. However, a significant difference was observed in delta hs-cTnI levels, with group B showing a much higher mean value (101.5±49.3 ng/l) compared to Group a (34.5±1.3 ng/l), p<0.001. Echocardiographic findings such as RWMA and EF showed no significant differences (Table 1).

Significant lesions in coronary vessels were observed with notable differences between the groups (Table 2). Lesions in the LCx were present in 73.5% of Group B compared to 41.7% of group A (p=0.007). Similarly, LAD lesions were more prevalent in Group B (82.4%) than in Group A (50.0%), p=0.004. Lesions in the LM and RCA did not show significant differences between the groups (Table 2). The severity of CAD is depicted in Figure 1, where Group B had a higher percentage of triple vessel disease (TVD) at 47.1% compared to 5.6% in group A. Single vessel disease (SVD) was more common in group A (38.9%) than in group B (23.5%), and double vessel disease (DVD) percentages were 38.9% for group A and 26.5% for group B (Figure 1).

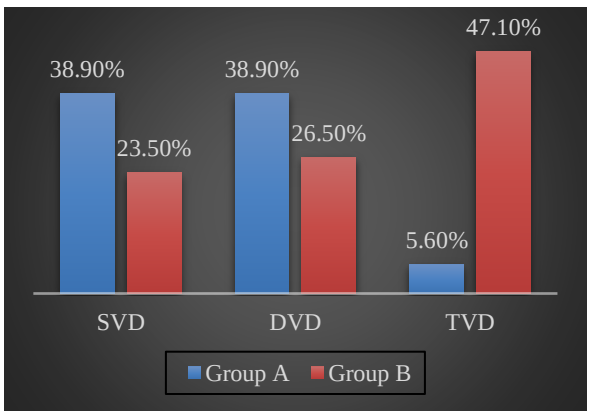

Figure 1: Severity of CAD.

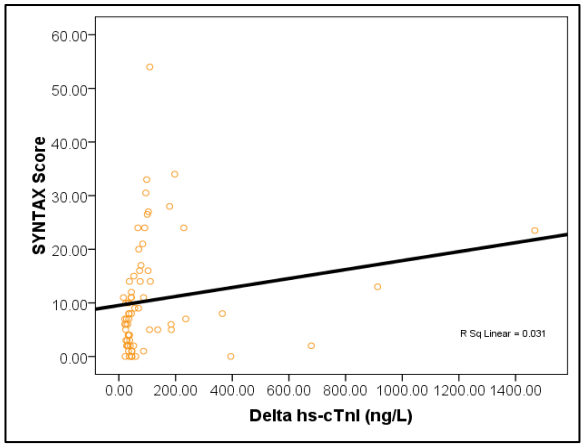

Figure 2: Correlation between delta hs-cTnI and SYNTAX score.

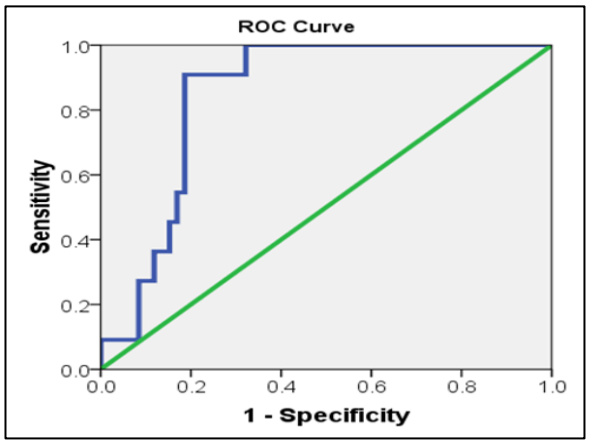

Figure 3: The area under the ROC curve.

Treatment procedures varied significantly between the groups (Table 3). PCI was performed in 58.3% of Group A and 50.0% of group B (p=0.484).

CABG was notably higher in group B (32.4%) with none in Group A (p<0.001). Medical management was slightly more common in group A (30.6%) compared to group B (17.6%), p=0.208 (Table 3).

The association between significant delta hs-cTnI and SYNTAX score is shown in table 4. All patients in group A had a SYNTAX score≤22, while 32.4% of group B had scores>22 (p<0.001) (Table 4).

The correlation between delta hs-cTnI and SYNTAX score is illustrated in figure 2, indicating a positive relationship (Figure 2). The area under the ROC curve for delta hs-cTnI was 0.847, indicating good diagnostic accuracy for severe CAD (Table 5).

The coordinates of the curve (Table 6) suggest that a delta hs-cTnI level of 63.0 ng/l or higher provides high sensitivity and acceptable specificity for diagnosing severe CAD (Table 6).

Finally, the accuracy of delta hs-cTnI in diagnosing severe CAD is shown in table 7. Patients with a delta hs-cTnI≥90 ng/l were more likely to have a SYNTAX score>22, demonstrating the marker's utility in predicting severe coronary artery disease (Table 7).

Table 1: Baseline characteristics (n=70).

Variables	Group		P value
	A (n=36)	B (n=34)	
Mean±SD age	54.2±11.3	55.7±8.9	0.524
Sex			
Male	25 (69.4%)	22 (64.7%)	0.673
Female	11 (30.6%)	12 (35.3%)	
BMI (kg/m^2)			
18.5-24.9	12 (33.3%)	7 (20.6%)	0.277
<18.5	1 (2.8%)	0 (0.0%)	
25-29.9	20 (55.6%)	20 (58.8%)	
30-39.9	3 (8.3%)	7 (20.6%)	
Investigation findings			
Hb (%)	12.1±2.0	11.9±1.7	0.775
RBS (mg/dl)	9.4±6.3	8.8±2.8	0.857
HbA1c (%)	8.1±1.8	8.3±2.3	0.681
STC (mg/dl)	184.9±44.2	192.5±59.7	0.543
S. LD (mg/dl)	113.1±35.5	109.5±51.8	0.728
S. HDL (mg/dl)	33.9 ±9.0	39. 9 18.1	0.087
S. TG (mg/dl)	223.1±132.6	200.4±91.9	0.411
SC (mg/dl)	1.1 ±0.4	1.3±1.1	0.384
eGFR (ml/1.73m^2)	78. 6 ±29.8	77.6±33.9	0.896
D. hs-cTnI (ng/L)	34.5 ±1.3	101.5±49.3	<0.001
Echocardiographic findings			
RWMA	15 (41.7)	14 (41.2)	0.967
EF (%)	56.7±7.0	53.8±8.9	0.138

Table 2: Significant lesions in vessels.

Lesions	Group		P value
	A (n=36)	B (n=34)	
LM (>50%)	2 (5.6%)	2 (5.9%)	0.671
RCA (>50%)	16 (44.4%)	19 (55.9%)	0.339
LCx (>50%)	15 (41.7%)	25 (73.5%)	0.007
LAD (>50%)	18 (50.0%)	28 (82.4%)	0.004

Table 3: Comparison of treatment procedures.

Treatment	Group		P value
	A (n=36)	B (n=34)	
PCI	21(58.3%)	17 (50.0%)	0.484
CABG	0 (0.0%)	11(32.4%)	<0.001
MM	11 (30.6%)	6 (17.6%)	0.208

Table 4: Association between significant delta hs-cTnI and SYNTAX score.

Score	Group		P value
	A (n=36)	B (n=34)	
>22	0 (0.0%)	11 (32.4%)	<0.001
≤22	36 (100.0%)	23 (67.6%)	

Table 5: Area under the curve (Description).

Test result variable (s): Delta hs-cTnI				
Area	**Std. error [a]**	**P value [b]**	**95% confidence interval of the area under the curve**	
			Lower bound	Upper bound
0.847	0.046	<0.001	0.758	0.937

Under the nonparametric assumption, b. Null hypothesis:true area=0.5.

Table 6: Coordinates of the curve.

Test result variable (s): Delta hs-cTnI		
Positive if≥	**Sensitivity**	**1-Specificity**
63.000	1	0.322
68.000	0.909	0.322
69.500	0.909	0.305
71.500	0.909	0.288
74.000	0.909	0.271
76.500	0.909	0.254
81.000	0.909	0.237
85.500	0.909	0.22
89.000	0.909	0.186
93.000	0.818	0.186
96.500	0.727	0.186
99.000	0.636	0.186
101.500	0.545	0.186
103.500	0.545	0.169
106.000	0.455	0.169

Table 7: Accuracy of delta hs-cTnI in diagnosing severe CAD.

Delta hs-cTnI (ng/l)	SYNTAX score		Total
	>22	≤22	
≥90	10	11	21
<90	1	48	49
Total	11	59	70

DISCUSSION

In this current study, the findings indicate a significant moderate, positive linear correlation of delta hs-cTnI levels (r=0.4, p=0.001) with the complexity of coronary lesions evaluated by the SYNTAX scoring system. Cardoso et al (2017) found a significant moderate,

positive linear correlation between hs-cTn levels and SYNTAX score (p<0.001, r=0.440). In the study by Altun et al, involving 287 patients, a linear correlation of hs-cTn levels with the complexity of coronary lesions measured by the SYNTAX score was also reported, but with lower statistical power (r=0.327) compared with our study (r=0.397) 8. In our study, before determining the accuracy of delta hs-cTnI in predicting severe CAD, an optimum cut-off value for delta hs-cTnI was determined using a receiver operating characteristic (ROC) curve.

The best cut-off value for high sensitivity without much compromise with specificity obtained was 89.0 with an area under the curve being 0.847 [(95% CI=0.758-0.937), p<0.001]. Although previous studies on the subject have compared troponin levels with the severity of coronary lesions, neither delta hs-cTn nor the SYNTAX score for evaluation of the severity of these lesions was used in these studies. One example was the Brazilian study by Faria RC et al.[12] The author compared the levels of troponin I with the severity of coronary lesions, which was measured by characteristics of the lesions in cardiac catheterization or changes in coronary circulation. In this study, although the author found no statistically significant correlation between increased troponin I levels and lesion severity or coronary circulation, the troponin levels were correlated with a higher number of obstructive lesions and the presence of thrombus.

The present study reported that patients with a high rise of delta hs-cTnI (≥50%) [Group B] had significantly more complex lesions in the major coronary arteries (LCx and LAD) than did patients with a low rise of hs-cTnI (≥20%-49%) [Group A]. The presence of significant lesions was observed to be significantly higher in Group-B than that in Group-A (p=0.017). The SYNTAX score (reflecting the complexity and severity of angiographic lesion) was also significantly higher in Group-B than in group-A (p<0.001) additionally, there were more TVDs in the former group than in the latter group (47.1 vs.5.6 %,). The SYNTAX score (reflecting the anatomical complexity and severity of CAD) demonstrated its significant presence in group B than in group A (p<0.001). About one-third (32.4%) of the patients in the group B had a SYNTAX score > 22 as compared to none of the patients in group A. The majority of the patients in either group had diabetes, hypertension, and dyslipidemia.

The prevalence of hypertension and dyslipidemia were significantly higher in group-B than that in Group-A (p=0.049 and p=0.058 respectively). Similar to the current study, hs-cTnI level and SYNTAX score, which reflected coronary complexity by coronary angiography, showed a favorable connection. Ndrepepa and associates in a larger case-control study included 904 patients with stable CAD (cases) and 412 patients with chest pain but without significant CAD on coronary angiogram (controls).[13] They showed that there was a close association between hs-Tn T level and severity of CAD as determined by the number of constricted coronary arteries or angiographic atherosclerotic burden in individuals with clinically stable CAD. The proportion of patients with a hs-cTnI level higher than or equal to the ninety-ninth percentile or upper reference limit increased from 17.7% in subjects with 1-vessel CAD to 35.5% in patients with 3-vessel CAD Based on these findings, Apple recently proposed considering high-sensitivity cardiac troponin a risk factor alongside conventional risk factors such as smoking, hypertension, and hyperlipidemia or as a denominator of cardiovascular risk.[14]

Tahhan and colleagues in an even larger cohort of patients (n=3087) with suspected or confirmed CAD demonstrated that elevated circulating levels of hs-cTnI are associated with the severity and progression of angiographic CAD and its adverse outcomes.[15] More specifically, their data showed that hs-cTnI is a powerful predictor of event mortality and morbidity, independent of CAD severity. Additionally, their research showed that patients in the highest quartile of hs-cTnI levels had an adjusted >4-fold greater risk of cardiovascular death during follow-up compared to those in the lowest quartile thus confirming the association between hs-cTnI levels and CAD severity in a much larger population. In Bangladesh Akteruzzaman et al, demonstrated that patients of unstable angina with raised serum troponin-I had more severe coronary lesions than those with low serum troponin-I.[16]

In this current study normal/insignificant lesions in coronary arteries were observed 10% of total subject & was significantly higher number of patients with a low rise of hs-cTnI (≥20%-49%) than did patients with a low rise of cTnI (≥20%-49%). Tahhan and colleagues (2018) investigated association between hs-cTnI and the severity and progression of CAD and found 11% of the population had normal angiograms.

Thus, the results of our study extend previous observations correlation of delta hs-cTnI levels (p=0.001) with the complexity of coronary lesions summarizing the results of the current study and those that have been compared and contrasted hitherto, it can be stated that greater than 50% rise of delta hs-cTnI is associate with more severe CAD. This work adds to the evidence that significant delta hs-cTnI may serve as a marker of the assumption of high-risk patient.

Despite the meticulous attention given by the researcher throughout the study, several limitations remain. The single-center design may constrain the generalizability of the findings to the broader community. Additionally, the small sample size in this prospective cohort study resulted in insufficient statistical power to assess clinical outcomes adequately. Moreover, the short-term follow-up period prevented an assessment of disease progression over time.

CONCLUSION

The study findings highlight the potential of a delta hs-cTnI value of 90.0 or higher in NSTEMI patients as a valuable diagnostic tool for identifying severe CAD, accurately diagnosing nearly 85% of cases. By combining this biomarker with the SYNTAX score, a comprehensive assessment of CAD severity can be achieved. This integrated approach may serve as a reliable gold standard for diagnosing the extent and severity of coronary artery disease, enhancing clinical decision-making and guiding appropriate interventions for patients with NSTEMI. This underscores the importance of incorporating both biochemical markers and clinical scoring systems for a more precise evaluation of CAD severity.

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