Original Article

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Frequency of multi-vessel disease and its association with N Terminal-Pro Brain Natriuretic Peptide Levels among patients with First ST-Elevation Myocardial Infarction.

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Abstract

Background and Aims: To determine the frequency of multi-vessel disease among patients with First ST-Elevation Myocardial Infarction and to identify the cutoff value of N Terminal-Pro Brain Natriuretic Peptide (NT-proBNP) for diagnosis of multi-vessel disease.

Methodology: A descriptive cross-sectional study was conducted in the Department of Cardiology at a tertiary care hospital from September 2021 to February 2022. The study included 150 patients who presented to the emergency room with first ST-elevation myocardial infarction and preserved ejection fraction. NT-proBNP levels were tested within 12 hours of hospital admission. The severity of coronary artery disease was assessed by the number of vessels affected labeled, the luminal diameter narrowing and the syntax score.

Results: The mean age of participants was 60.60±11.1 years. 76% were men, 53.3% of the participants had hypertension, 44% had type 2 diabetes, and 14% were smokers. The mean BMI of the patients was 27.86±3.86. The mean ejection fraction of the patients was 50±4.5.Single-vessel disease was present in 47 (31%) and 103 (69%) had multi-vessel disease. The mean NT-proBNP level in single-vessel disease was 561.34 pg/mL, and in multi-vessel disease, it was 1640.65 pg/mL. Raised levels of NT-proBNP were significantly associated with the severity of coronary artery disease. (P-value <0.05). The optimal cut-off value of NTpro-BNP for ruling out multiple vessel disease was 947.50 pg/mL at 81% of sensitivity.

Conclusion: Pro-BNP is a valuable biomarker in assessing the severity of coronary artery disease in STEMI patients. Its levels have been shown to correlate with the degree of CAD severity including multi-vessel involvement.

Keywords: Acute Coronary Syndrome, NT-proBNP, coronary artery disease.

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Introduction

Inadequate blood and oxygen supply to the myocardium due to coronary artery stenosis generates a demand-supply imbalance and is the most common cause of myocardial ischemia in coronary artery disease (CAD). Blood flow is restricted by the formation of an atherosclerotic plaque in the coronary artery lumen.[1]

NT-proBNP, Troponin I, and Hs-CRP (High-sensitivity C-reactive Protein) are the three most well-known cardiac biomarkers related to the severity of coronary artery disease.[2] The neurohormone N terminal pro-B-type natriuretic peptide (NT-proBNP), which is elevated in acute myocardial infarction and angina pectoris, is synthesized and released by ventricular muscles.[3] The two basic sources of BNP and NT-proBNP release are wall stress and myocyte stretch. Among its various activities are sympathetic nerve activation, natriuresis, vasodilation, and inhibition of the renin-angiotensin-aldosterone system.[4]

BNP and NT proBNP have been shown to offer predictive information on acute coronary syndrome (ACS)[5], and they seem to be associated to the severity of CAD in these patients and have demonstrated an association with multivessel disease, poor TIMI flow, as well as are markers of coronary disease extension.[6]

Despite the worldwide use of NT-proBNP testing, prospective data that examine its role in the diagnosis of multivessel disease in ACS has been limited in our population.[7] So, we planned this

study to determine the prevalence of multi-vessel disease among patients with First ST-Elevation Myocardial Infarction as well as to determine NT-ProBrain Natriuretic Peptide cut-off value for the diagnosis of multi-vessel disease.

Materials and Method:

This descriptive cross-sectional study enrolled 150 consecutive patients, who presented to the emergency department with STEMI and underwent coronary artery angiography and primary angioplasty, for a period of six months from September 2021 - February 2022. The NT-proBNP levels were sent along with the baseline labs in the emergency department along with Troponin I and limited echocardiography was done to evaluate wall motion abnormality, left ventricular morphology, and systolic function pre-intervention and complete echocardiography (including diastolic dysfunction and RV systolic dysfunction) was done post-intervention, Those with preserved ejection fraction were then included in the study and those with reduced ejection fraction , more than grade 1 diastolic dysfunction and RV systolic dysfunction were excluded from the study. The hospital's ethical committee approved the research and informed consent was taken from the patients.

The inclusion criteria included both genders, male, and female, >18 years who presented to the emergency room with their first case of STEMI, which is indicated by a typical ST segment elevation >1mm in at least 2 or more contiguous leads accompanied by a characteristic chest pain lasting for more than 20 minutes.

When blood levels of cardiac troponin (cTn) rise above the 99th percentile upper reference limit (URL), myocardial damage is considered to be present. The injury may be acute, as evidenced by a newly detected dynamic rising and/or falling pattern of cTn values above the 99th percentile URL, or chronic, in the setting of persistently elevated cTn levels.[8]All patients who had a prior history of cardiomyopathy, renal failure, surgical history (having cardiopulmonary bypass) or having any valve surgery or any valvular disease, and those with a previous history of acute myocardial infarction, patients with left main disease and cardiogenic shock, electrocardiograms with pre-existing bundle branch block or displaying non-sinus rhythm and poor quality echocardiographic images were excluded from the study.

The levels of NT-proBNP were measured using an automated electrochemiluminescence immunoassay (ECLIA) on an Analyzer Axym from Abbott Diagnostic in line with established methods. The detection range of the test was 5-25,000 pg/ml, with a normal value of 194 pg/ml. The transthoracic echocardiogram was done using (GE Vivid 95), and the left ventricular ejection fraction was estimated using the modified biplane method.[9] The severity of coronary artery disease was assessed in multiple ways. First in terms of the number of vessels affected labeled as single vessel when one major coronary artery was involved and multi-vessel when ≥2 major coronary vessels were involved. According to the luminal diameter narrowing, ≥50% for the left main coronary artery and 70% for the major coronary arteries, also only those vessels were considered which had a diameter of ≥ 1.5mm.[10] Apart from this, the angiograms were also scored according to the syntax score system. For this, two interventional cardiologists were taken on board who were blinded to the patient characteristics and the study protocol. A senior cardiologist's opinion was sought when there was a discrepancy between the two results and then a consensus was reached. For the purpose of calculation, the software on the following website (http://www.syntaxscore.com) was used. Only coronary arteries with a diameter of 1.5mm having lesions causing ≥ 50% of stenosis were included in the calculation. According to the syntax score the patients were divided into 3 tertiles as follows; a low syntax group with a score of ≤22, an intermediate group with a score between 23 to 32, and a high syntax group with a score of ≥ 33 [11].

Sample size calculation and Data analysis

The sample size was calculated through Sample Size Calculator by Wan Nor Arifin (Available at https://wnarifin.github.io/ssc/ss1prop.html) by taking the prevalence of multivessel disease= 54%[12], margin of error=8%. The total calculated sample size was 150 patients. The statistical analysis of the collected data was carried out by using IBM SPSS Statistics version 26. Mean and standard deviation was computed for quantitative variables. Frequency and percentages were reported for qualitative variables. ANOVA was applied for mean comparison while the chi-square/Fisher exact test was applied to check the association of qualitative variables. Pearson's correlation coefficient was applied to determine the relationship between quantitative variables. The level of significance was considered at $p<0.05$.

Result: Among 150 participants, 76% (n=114) were men. The patients included had a mean age of 60.60 ± 11.1 years. Out of the total patients, 53.3% (n=80) were hypertensive whereas 44% (n=66) were diabetic and 14% (n=21) were smokers. Details of all demographics are mentioned in Table 1. Regarding the involvement of CAD, 31% (n=47) and 69% (n=103) patients had single-vessel disease and multi-vessel disease, respectively. The Association of CAD with demographics and risk factors are presented in Table 2. Troponin I (p=0.000) and NTpro-BNP (p=0.000) were significantly associated with the severity of coronary artery disease. The mean syntax score was 17.36 ± 3.5 for for single-vessel disease and 26.53 ± 5.2 was for multi-vessel disease.

The mean pro-BNP was 561.34 pg. /ml in single-vessel disease and 1640.65 pg/ml in multi-vessel disease. The Pro BNP and Syntax score showed a moderate, positive, and statistically significant relationship (r= 0.66, P <0.001) as presented in Figure 1. The optimal cut-off value of NTpro-BNP for ruling out multiple vessel disease was 947.50 pg/mL at 81% of sensitivity. The area under the receiver operating characteristic curve (ROC) of PRO BNP for diagnosing diagnosis of multi-vessel disease was 0.93 at 95% confidence interval (Figure 2).

Other predictive values for cut-off with different levels of sensitivity and specificity are mentioned in the table. 3.

Table 1: Patients' history and demographics

Patient's characteristics	frequency (percent)
Age(years); mean± std. dev	60.6 ± 11.1
Groups	
≤40 years	7(4.7)
41-59 years	61(40.7)

≥60 years	82(54.7)
Gender	
Male	114(76)
Female	36(24)
Trop-I (ng/mL); mean± std. dev	9.81±7.97
Groups	
<0.30 ng/mL	23(15.3)
0.30-10 ng/mL	72(48)
10-25 ng/mL	38(25.3)
>25 ng/mL	17(11.3)
Co-morbidities	
Hypertension	
Yes	80(53.3)
No	70(46.7)
Diabetes Mellitus	
Yes	66(44)
No	84(56)
Smoking Status	
Smoker	21(14)
Non-Smoker	129(86)
Type of MI	
Anterior	115(76.7)
Antero-lateral or lateral	15(10)
Inferior	20(13.3)
Coronary artery disease	
Single vessel disease	47(31.3)
Multi vessel disease	103(68.7)

Table 2: Association of CAD Severity with Demographic and Risk Factors

Patient's characteristics	Coronary artery disease frequency (percent)		p-value
	Single	Multi Vessel	
Age			
≤40 years	3(6.4)	4(3.9)	0.661
41-59 years	20(42.6)	41(39.8)	
≥60 years	24(51.1)	58(56.3)	
Gender			
Male	37(78.7)	77(74.8)	0.598
Female	10(21.3)	26(25.2)	
Troponin-I			
<0.30 ng/mL	18(38.3)	5(4.9)	<0.001*
0.30-10 ng/mL	16(34)	56(54.4)	
10-25 ng/mL	4(8.5)	34(33)	
>25 ng/mL	9(19.1)	8(7.8)	
NT Pro BNP			
<450 pg. /ml	17(36.2)	4(3.9)	<0.001*
450-1000 pg. /ml	11(23.4)	25(24.3)	
>1000 pg. /ml	19(40.4)	74(71.8)	
Co-morbidities			
Hypertension			
Yes	21(44.7)	59(57.3)	0.151
No	26(55.3)	44(42.7)	
Diabetes Mellitus			
Yes	20(42.6)	46(44.7)	0.809
No	27(57.4)	57(55.3)	
Smoking Status			
Smoker	3(6.4)	18(17.5)	0.069
Non-Smoker	44(93.6)	85(82.5)	
Type of MI			
Anterior	32(68.1)	83(80.6)	0.225
Antero-lateral or lateral	6(12.6)	9(8.7)	
Inferior	9(19.1)	11(10.7)	

Chi-square/fisher exact test was applied.
**Significant at 0.05 level.*

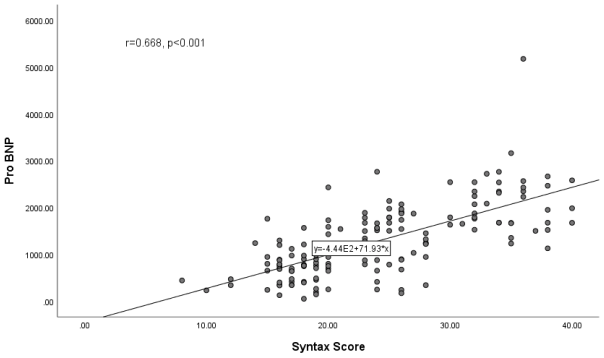

Figure.1. Relationship between Pro BNP and Syntax Score

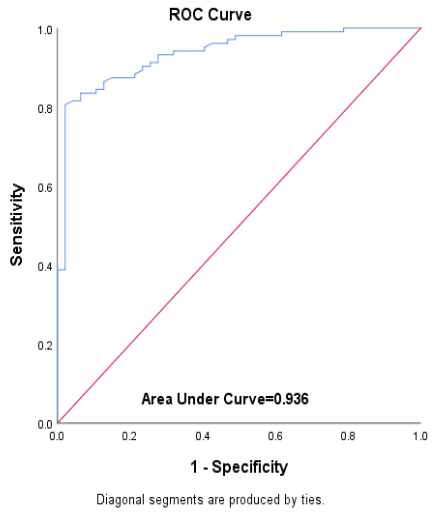

Figure.2. ROC Curve for detection of Pro BNP cut-off in diagnosis of multi vessel disease

Table No 3: ROC Coordinates of the Curve of different Pro-BNP cutoffs for diagnosis of multi-vessel disease

Coordinates of the Curve		
Positive if Greater Than or Equal To	**Sensitivity**	**1 - Specificity**
947.5000	.816	.064
962.0000	.816	.043
981.5000	.806	.021

Discussion:

The primary finding of the current study was that patients who presented with their first ST elevation myocardial infarction were more likely to have multi-vessel disease (68.7 %). Patients with low NT-proBNP values had single-vessel disease, whereas those with high NT-proBNP values had multivessel coronary artery disease. Early assessment at presentation in the emergency room helps with the stratification of risk in patients suffering from acute myocardial infarction as it is a critical predictor of outcome in these patients.[13] Another study reported that BNP and NT-proBNP are related to long-term prognosis in patients with predominant ST-segment elevation AMI.[14] A few studies have found that BNP levels in persons suffering from ACS can correlate with the CAD severity, degree as well as TIMI flow.[15]

When pro-BNP levels increase, it relates to a worsening of coronary artery disease. This is shown in one of the well-known studies, BIOMARCS.[16] when the left anterior descending artery is obstructed, Pro-BNP levels are greater than when the left circumflex and right coronary arteries have stenotic lesions. These elevated levels of Pro-BNP indicate multi-vessel involvement of the coronaries.[16] when a patient has an acute myocardial infarction, blood levels of natriuretic peptides (atrial natriuretic peptide, NT-ProBNP, and BNP) rise dramatically. 16 According to the findings of this investigation, the plasma NT-ProBNP level may be used to assess the degree of myocardial ischemia.[16] BNP levels are elevated in STEMI patients, unstable angina patients, and cases of myocardial infarction with non-ST elevation, displaying the extent of the severity of coronary vascular disease and aberrant coronary blood flow.[17] However, with respect to the cited study, our study was characterized by the absence of left ventricular dysfunction and enlargement, which are the main factors responsible for BNP increase.[18]

According to the findings of a meta-analysis, patients with acute coronary syndrome who had elevated BNP levels had an increased chance of dying or having a myocardial infarction.[19] Additionally, there is a notable rise in the likelihood of unfavorable consequences.[19] Another study showed that higher NT-proBNP levels were associated with cardiovascular and all-cause mortality in an unselected, large population of elderly patients in the primary care setting, independent of traditional risk factors, implying that NT-proBNP can help identify subjects at high risk for cardiac events.[20] Subjects with greater levels of NT-proBNP had a higher incidence of all-cause and cardiovascular mortality.[20] Another study explored in more depth and found Participants with stage 1 hypertension with elevated NT-proBNP had a higher risk of heart disease than those with stage 2 hypertension with lower NT-proBNP.[21] Similarly one more researcher found that NT-proBNP could predict worse outcomes in dysglycemic individuals with Chronic Coronary Syndrome and normal LVSF, implying that NT-proBNP could aid in risk stratification in this population.[22] The above studies differ from the present study as we did not control risk factors.

There are certain limitations of this study. It was an observational study with a small sample size and single center therefore, it is difficult to interpret concrete conclusions, also comprehensive echocardiography was not done prior to intervention. Further studies should be conducted in this regard to determine the sensitivity and specificity of NT-pro-BNP in predicting single and multi-vessel disease.

Conclusion:

The findings of this study support the utilization of Pro-BNP as a valuable marker in the risk stratification of patients with first ST–elevation myocardial infarction to assess the severity of coronary artery disease. Pro-BNP levels have been shown to correlate with the degree of CAD severity including multi-vessel involvement and can provide important prognostic information. Further research and validation studies are warranted to confirm the clinical utility of Pro-BNP in guiding optimal treatment strategies for STEMI patients.

Conflict of interest

The authors declared no conflict of interest.

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References:

1. Poznyak AV, Litvinova L, Poggio P, Moschetta D, Sukhorukov VN, Orekhov AN. From diabetes to atherosclerosis: Potential of metformin for management of cardiovascular disease. Int J Mol Sci 2022;23(17):9738. https://doi.org/10.3390/ijms23179738
2. Tasar O, Kocabay G, Cagdas M, Karabag Y. Correlation of B-type natriuretic peptide with severity of coronary artery disease assessed by SYNTAX score ii in ST elevation acute coronary syndrome patients. Intl J Cardiovas Acad. 2019;5(4):129. https://doi.org/10.4103/IJCA.IJCA_36_19
3. Diao Y, Yin M, Zhang B, Sun B. Predictive value of N-terminal pro-B-type natriuretic peptide (NT-pro BNP) combined with D-dimer for no-reflow phenomenon in patients with acute coronary syndrome after emergency of percutaneous coronary intervention. Bioengineered. 2021;12(1):8614-21. https://doi.org/10.1080/21655979.2021.1988361
4. Zhu Y, He H, Qiu H, Shen G, Wang Z, Li W. Prognostic Value of Systemic Immune-Inflammation Index and NT-proBNP in Patients with Acute ST-Elevation Myocardial Infarction. Clinical Interventions in Aging. 2023:397-407. https://doi.org/10.2147/CIA.S397614
5. Artha IM, Bakta IM, Manuaba IB, Wita IW, Rohman MS, Astawa IN, et al. The Effects of Percutaneous Coronary Intervention on Biomarkers and Quality of Life in Patients With Chronic Total Coronary Artery Obstruction. Cardiol Res. 2023;14(1):69-78. https://doi.org/10.14740/cr1455
6. Sarak T, Karadeniz M. The relationship between serum NT-proBNP levels and severity of coronary artery disease assessed by SYNTAX score in patients with acute myocardial infarction. Turk J Med Sci. 2019;49(5):1366-73. https://doi.org/10.3906/sag-1902-26
7. Goyal BM, Sharma SM, Walia M. B-type natriuretic peptide levels predict extent and severity of coronary artery disease in non-ST elevation acute coronary syndrome and normal left ventricular function. Indian heart J. 2014;66(2):183-7. https://doi.org/10.1016/j.ihj.2013.12.015
8. Thygesen K. What's new in the fourth universal definition of myocardial infarction? Circ. 2018; 138:e618–e651. https://doi.org/10.1161.
9. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Euro. Heart J.Cardiovasc.Imaging. 2015 Mar 1; 16(3):233-71. https://doi.org/10.1093/ehjci/jev014
10. Xiong QF, Fu XR, Ku LZ, Zhou D, Guo SP, Zhang WS. Diagnostic performance of coronary computed tomography angiography stenosis score for coronary stenosis. BMC Medical Imaging. 2024 Feb 9; 24(1):39.
11. Ho AB, Tran QB, bao Tran Q. The Role of N-Terminal-Pro-B-Type Natriuretic Peptide (NT-proBNP) and High-Sensitivity Troponin T (Hs-Troponin T) in the Evaluation of the Syntax Score in Patients With Acute Coronary Syndrome. Cureus. 2024 Mar 6; 16(3). DOI: 10.7759/cureus.55653
12) Varani E, Balducelli M, Aquilina M, Vecchi G, Hussien MN, Frassineti V, et al Single or multivessel percutaneous coronary intervention in ST-elevation myocardial infarction patients. Catheter Cardio Inte. 2008;72(7):927-33. https://doi.org/10.1002/ccd.21722
13) Zhang C, Jiang L, Xu L, Tian J, Liu J, Zhao X,wt al., Implications of N-terminal pro-B-type natriuretic peptide in patients with three-vessel disease. Eur Heart J. 2019;40(41):3397-405. https://doi.org/10.1093/eurheartj/ehz394
14) Tamara AF, Altoukhy S, AbdelHamid I. The Predictive Value of Estimation of N Terminal-Pro B-Type Natriuretic Peptide in Patients with ST Elevation Myocardial Infarction Undergoing Primary Percutaneous Intervention for the Outcome of Myocardial Reperfusion. The Egyptian J Hosp Med. 2023;90(1):1831-7. https://doi.org/10.21608/ejhm.2023.284343
15) Benmachiche M, Marques-Vidal P, Waeber G, Mean M. In-hospital mortality is associated with high NT-proBNP level. PLoS One. 2018; 13(11):e0207118. https://doi.org/10.1371/journal.pone.0207118
16) Oemrawsingh RM, Akkerhuis KM, de Mulder M, Umans VA, Kietselaer B, Schotborgh C, et al., High-Frequency Biomarker Measurements of Troponin, NT-proBNP, and C-Reactive Protein for Prediction of New Coronary Events After Acute Coronary Syndrome: BIOMArCS Study. Circ 2019;139(1):134-6. https://doi.org/10.1161/CIRCULATIONAHA.118.036349
17) Rudolf H, Mügge A, Trampisch HJ, Scharnagl H, März W, Kara K. NT-proBNP for risk prediction of cardiovascular events and all-cause mortality: The getABI-study. IJC Heart Vasc. 2020;29:100553. https://doi.org/10.1016/j.ijcha.2020.100553
18) Richards AM. N-terminal B-type natriuretic peptide in heart failure. Heart fail clin. 2018;14(1):27-39. https://doi.org/10.1016/j.hfc.2017.08.004
19) Fangauf SV, Belnap BH, Meyer T, Albus C, Binder L, Deter HC, et al. Associations of NT-proBNP and parameters of mental health in depressed coronary artery disease patients. Psychoneuroendocrinology. 2018;96:188-94. https://doi.org/10.1016/j.psyneuen.2018.06.001
20) Rudolf H, Mügge A, Trampisch HJ, Scharnagl H, März W, Kara K. NT-proBNP for risk prediction of cardiovascular events and all-cause mortality: The getABI-study. IJC Heart Vasc. 2020;29:100553. https://doi.org/10.1016/j.ijcha.2020.100553

21) Hussain A, Sun W, Deswal A, de Lemos JA, McEvoy JW, Hoogeveen RC, et al. Association of NT-ProBNP, blood pressure, and cardiovascular events: the ARIC study. J Am Coll Cardiol. 2021; 77(5):559-71. https://doi.org/10.1016/j.jacc.2020.11.063

22) Liu HH, Cao YX, Jin JL, Guo YL, Zhu CG, Wu NQ, et al. Prognostic value of NT-proBNP in patients with chronic coronary syndrome and normal left ventricular systolic function according to glucose status: a prospective cohort study. Cardiovasc Diabeto. 2021;20(1):84. https://doi.org/10.1186/s12933-021-01271-0