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NT-proBNP as a Predictive Biomarker for Contrast-Induced Nephropathy in ACS Patients Undergoing Coronary Angiogram – An Observational Study

Ravi Kumar Reddy[1], Jyotsna Maddury[1]

[1]Department of Cardiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

***Corresponding author:**
Dr. Jyotsna Maddury,
HOD, Department of Cardiology, Nizams Institute of Medical Sciences, Hyderabad, Telangana, India.

ravikumarmatlidoc@gmail.com

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ABSTRACT

Objectives: 1. To assess the value of baseline NTproBNP at admission and to determine the levels of serum creatinine at 48 hours and 72 hours after procedure for evidence of contrast-induced nephropathy (CIN) for patients undergoing CAG. 2. To evaluate the relationship between the values of NTproBNP and evidence of CIN.

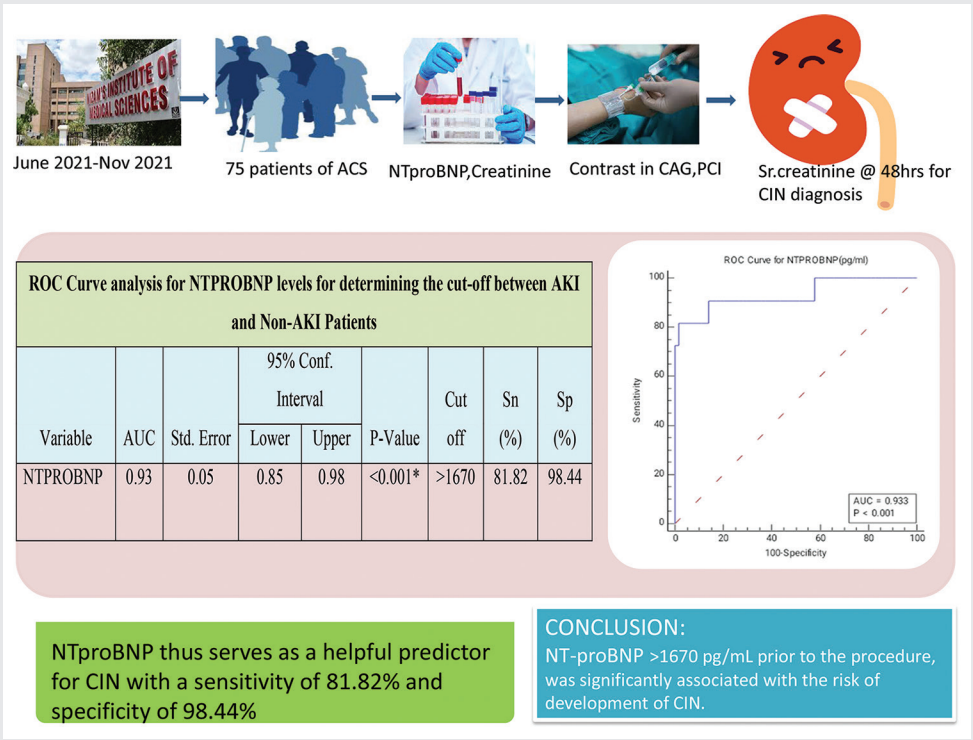
Materials and Methods: This is an observational study performed between June 2021-November 2021 at Nizams Institute of Medical Sciences in 75 patients diagnosed with ACS. we assessed the role of nt pro bnp as a predictive biomarker for diagnosis of contrast induced nephropathy in patients of ACS undergoing coronary angiography. Serum creatinine is repeated at 48 h post procedure and compared to baseline.

Results: Spearman's correlation test was used to assess the correlation between NT-proBNP values and ejection fraction on the 2D echo. The rho value (-0.69) was suggestive of a strong negative correlation. *P* value & lt; 0.001 making it statistically significant. Simple linear regression analysis was used to predict the NT-proBNP levels by ejection fraction percentage among study patients, it showed that, for every 1% decrease in ejection fraction, the NT-proBNP levels will significantly increase by 102.90 pg/mL at *P* and lt; 0.001. Wilcoxon Signed Rank test was used to compare the baseline serum creatinine values with 48/72 h serum creatinine values after undergoing angiography with contrast, incidence of acute kidney injury (AKI) as shown by the resulting *P* value was and lt; 0.001, thus statistically significant. The ROC curve analysis to establish the association between NT-proBNP as a marker for incidence of AKI (CIN) shows shows that, NT-proBNP cut off and gt;1670 pg/mL has a sensitivity of 81.82% and specifity of 98.44% and is statistically significant with *P* value and lt; 0.001.

Conclusion: It was observed that NT-proBNP >1670 pg/mL prior to the procedure, was significantly associated with the risk of development of contrast induced nephropathy. Measurement of serum NT-proBNP pre procedure aids in identifying at risk population for developing CIN.

Keywords: NT-proBNP, CIN, Coronary angiogram, Acute coronary syndrome, Biomarker

ABSTRACT IMAGE



INTRODUCTION

Coronary interventions require the usage of iodinated contrast, this in addition to the elderly patient population along with the procedural complexity has increased the incidence of renal dysfunction, known as contrast-induced nephropathy (CIN). The reported incidence of CIN in high-risk patients undergoing CAG lies between 10% and 20%.[1]

This increased incidence could be attributed to the patient factors including geriatric group of patients, history of diabetes and chronic kidney disease, or procedure related factors such as intra-arterial route of administration, use of high osmolar contrast agents, repeated exposure to contrast agents within 48 h, and volume of contrast used.[2] The prevention of CIN is of prime significance, with rising cases of CAGs and PCIs.

CIN is defined as an absolute increase in serum creatinine of ≥0.5 mg/dL (44.2 μmol/L) or a ≥25% relative increase in serum creatinine from the baseline value at 48–72 h after exposure to contrast agents in the absence of alternative causes for acute kidney injury (AKI).[3,4]

Risk-score models such as Mehran CIN score and BMC2 CIN score are being increasingly used bedside as a guide in predicting and preventing the said complication. These scores are lacking in quantitative biomarkers which predict multi-organ dysfunction. Such an objective test, in addition to these risk score models, performed at admission, before the coronary interventions would better aid in preventing CIN. N-terminal pro-brain natriuretic peptide (NT-proBNP) is one such biomarker which is easily available. It is associated with increasing age, heart failure, diabetes, renal disease, and geriatric patients which are risk factors for CIN.[5,6] There is evidence of measurement of serum BNP at admission aiding in identification of patients at risk of developing CIN after primary PCI.[7] The purpose of this study is to determine the value of baseline NT-proBNP as a predictive biomarker in development of CIN for patients undergoing CAG.

MATERIAL AND METHODS

The study included 75 patients more than 20 years age admitted in NIMS cardiology department from period June 2021 to November 2021 with chest pain and established diagnosis of ACS (STEMI, NSTEMI, UNSTABLE ANGINA) not more than 2 week old. Patients with pre-existing renal disease, cardiogenic shock, acute LVF, and age >65 years were excluded from the study. Patients were enrolled in the study after admission and taking a duly informed consent.

Serum creatinine and NT-proBNP levels are measured on the day of admission. Nephrotoxic drugs to be stopped on admission.

The formula used for maximum contrast dose: 5 × body weight [kg])/serum creatinine. Modification of Diet in Renal Disease equation was used in calculating Estimated Glomerular Filtration Rate (eGFR). Repeat serum creatinine is measured at 48 h after contrast administration.

The CI-AKI is defined as a relative increase of ≥25% or absolute increase of ≥0.5 mg/dL in creatinine concentrations within 48 h after coronary angiography.

Statistical analysis

Spearman's correlation test was used to assess the relationship between Ejection Fraction (EF) and NT-proBNP levels among study patients.

Simple linear regression analysis was performed to predict the NT-proBNP levels by EF percentage among study patients.

Mann–Whitney Test was used to compare the mean NT-proBNP, creatinine levels at different time intervals based on presence of DM/HTN/Smoking condition among patients.

Wilcoxon Signed–Rank test was used to compare the mean creatinine levels (in mg/dl) between baseline and 48/72 h time period.

ROC curve analysis was performed for NT-proBNP levels for determining the cutoff between AKI and Non-AKI Patients. The level of significance (*P*-value) was set at $P < 0.05$.

RESULTS

The study is an observational prospective study involving 75 patients belonging to the age group of 57.11 ± 8.25. All patients underwent diagnostic coronary angiography. The study included 72% males and 28% females. Of the total patient population, 32% of them are diabetic (24), 20% of them hypertensive (15), and 29.3% of them smokers. Spearman's correlation test was used to assess the correlation between NT-proBNP values and EF on the 2D echo. The rho value (−0.69) was suggestive of a strong negative correlation. $P < 0.001$ making it statistically significant [Table 1].

When simple linear regression analysis was used to predict the NT-proBNP levels by EF percentage among study patients, it showed that, for every 1% decrease in Ejection Fraction, the NT-proBNP levels will significantly increase by 102.90 pg/ml at $P < 0.001$ and this is accounted by 31% variation in ECHO and EF [Table 2].

Mann–Whitney test was used to compare the risk factors such as diabetes, smoking, hypertension and its probable association with the serum NT-proBNP values in our study and to verify if they contribute as confounding factors. However, the results show *P* value as not significant [Figure 1].

Thus, high values of NT-proBNP serve as a predictor and help in practicing target-guided adequate measures to prevent CIN, in the form of regulating contrast volume, drugs such as N-acetyl-cysteine, and hydration in the predicted at risk patient population [Figure 2].

Contrast volume used was 80 ml in approximately 53.3% of patient population and 60 ml in 36%. When Wilcoxon Signed–Rank test was used to compare the baseline serum creatinine values with 48/72 h serum creatinine values after undergoing angiography with contrast, incidence of AKI as shown by the resulting *P* value was < 0.001, thus statistically significant [Table 3].

The ROC curve analysis to establish the association between NT-proBNP as a marker for incidence of AKI (CIN) shows that, NT-proBNP cutoff >1670 pg/ml has a sensitivity of 81.82% and specify of 98.44% and is statistically significant with *P* value < 0.001 [Table 4 and Figure 3].

DISCUSSION

NT-proBNP is a neurohormone secreted in response to increased intracardiac volume and pressures, from the

Table 1: Comparison of mean creatinine levels (in mg/dl) between baseline and 48/72 h time period using Wilcoxon signed–rank test.

Time	*n*	Mean	SD	Mean diff.	*P*-value
Baseline	75	0.979	0.115	−0.139	<0.001*
48/72 h	75	1.118	0.261		

Table 2: Simple linear regression analysis to predict the NT-proBNP levels by EF percentage among study patients.

Ind. Variable	Unstandardized coefficients		*t*	*P*-value	R2
	B	SE			
Constant	5781.36	836.12	6.914	<0.001*	0.31
ECHO and EF	−102.90	17.78	−5.787	<0.001*	

EF: Ejection fraction, SE: Standard error

Table 3: Comparison of mean creatinine levels (in mg/dl) between baseline and 48/72 h time period using Wilcoxon signed–rank test.

Time	N	Mean	SD	Mean Diff	*P*-value
Baseline	75	0.979	0.115	−0.139	<0.001*
48/72 h	75	1.118	0.261		

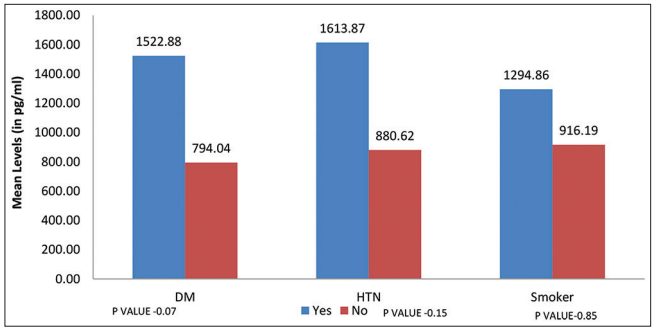


Figure 1: Mean NT-proBNP levels based on presence of DM/HTN/smoking condition among patients.

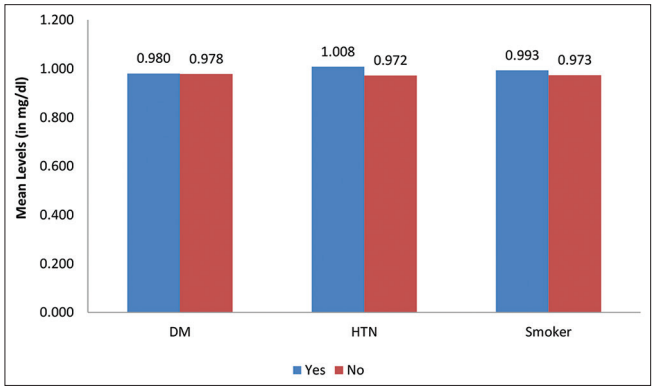


Figure 2: Mean creatinine levels at baseline based on presence of DM/HTN/smoking condition among patients.

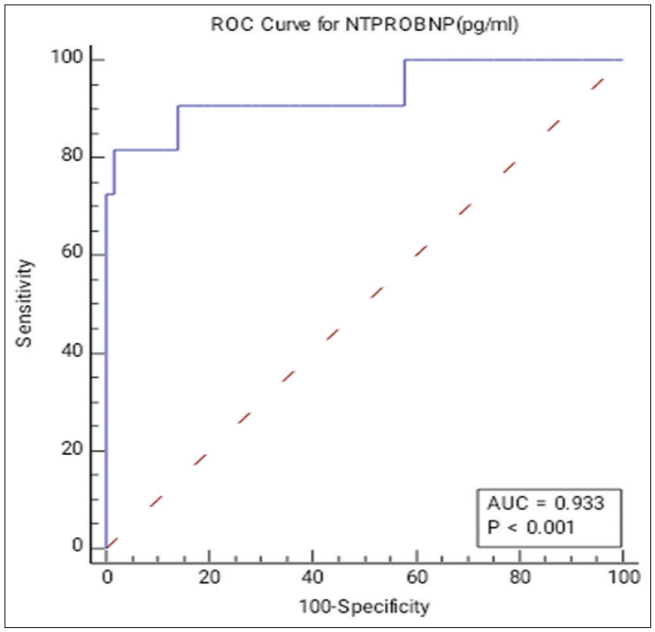


Figure 3: ROC curve for NT-proBNP (pg/ml).

myocardium. It is an established biomarker for the left ventricular dysfunction. Mann–Whitney test was used to compare risk factors such as diabetes, hypertension, smoking, and its association with the serum NT-proBNP values in our study and to verify if they contribute as confounding factors. However, the results show p value as not significant. Similar results were found in the study by Liu *et al.*, where contrast volume to creatinine clearance ratio was evaluated and compared to CIN incidence in patients undergoing PCI[6]

Serum creatinine levels, at both baseline and at 48/72 h when compared in the patient population with comorbidities like diabetes and hypertension and risk factor like smoking has shown to be statistically not significant as indicated by the p value obtained from the mann whitney test. The present study showed a significant association between the high values of NT-proBNP with an increased risk of CIN. Baseline NT-proBNP (before procedure) value of more than 1670 pg/mL, the cutoff value, was a strong and independent predictor of CIN.

A similar study was performed in patients undergoing cardiac surgeries; pre-operative NT-proBNP and its relation with development of post-operative AKI were assessed. In this study by Wang *et al.*, it was observed that post-operative AKI occurred in (34.0%) patients, with Stage 2 AKI in (3.4%) patients, Stage 3 AKI in (1.3%) patients, and new-onset dialysis was required in (0.7%) patients.[7]

The NT-proBNP concentrations were significantly correlated with all the stages of AKI ($P < 0.01$). Including NT-proBNP in pre-operative assessment has substantially improved in predicting post-operative AKI.[7]

Another study by Jarai *et al.*, including a total of 979 patients of ST-segment–elevation myocardial infarction that was enrolled in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction trial, also had compared the BNP levels done before primary percutaneous coronary intervention in predicting post-operative incidence of CI-AKI.[8]

The reason for this association is unclear; however, the potential mechanisms by which elevated NT-proBNP values were associated with incidence of AKI/CIN are hypothesized as follows:

1. Baseline high NT-proBNP values are related to associate risk factors that are independent risk factors for the development of CIN that includes advanced age, diabetes mellitus, hypertension, and smokers. It was observed that high values of NT-proBNP is seen in association with a higher risk of developing end-stage renal disease in diabetics[9]
2. Renal dysfunction patients have high NT-proBNP values. This may be attributed to either decreased renal clearance or decreased renal responsiveness to BNP.[10] Studies showed that NT-proBNP values increase with decreasing GFR in patients of cardiac dysfunction. This

Table 4: ROC Curve analysis for NT-proBNP levels for determining the cutoff between AKI and Non-AKI patients.

Variable	AUC	SE	95% Conf. Interval		*P*-value	Cut off	Sn (%)	Sp (%)
			Lower	Upper				
NT-proBNP	0.93	0.05	0.85	0.98	<0.001*	>1670	81.82	98.44

AKI: Acute kidney injury

decreased clearance ability of NT-proBNP is possibly due to impaired renal function.[11] However, our study excluded CKD patients

3. BNP decreases the effect of catecholamines and generates nitric oxide, which inhibits myocardial contractility, causing vasodilation and renal hypo-perfusion. CIN is a subtype of cardiorenal syndrome type 1. Definition of which is, worsening renal function attributed to acute heart failure that may exacerbate both cardiac and renal impairment.[12,13]

Recent studies focus on the inflammatory markers and its role in predicting the link between cardiac and renal diseases. The natriuretic peptides are established biomarkers in heart failure and since increased levels can be seen in renal impairment and heart failure, they probably also reflect renal injury.[14]

Thus, this biomarker useful in predicting both cardiac and renal impairment has the potential as a valuable diagnostic tool.

CONCLUSION

NT-proBNP >1670 pg/mL before the procedure was significantly associated with the risk of development of CIN. Measurement of serum NT-proBNP pre-procedure (coronary angiography) aids in identifying and predicting at risk population for developing AKI/CIN. NT-proBNP value pre procedure serves as a biomarker in predicting risk of development of CIN. We can practice target guided adequate measures (such as, hydration, decreasing contrast volume used and n-acetylcysteine injection) to prevent CIN in such patients with high ntprobnp values.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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