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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

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ABSTRACT

Background: Primary percutaneous intervention (PCI) is the favored reperfusion strategy to achieve normal cardiac blood flow.

Objective: To study if the level of NT-pro BNP before primary PCI can be used as an independent predictor for successful reperfusion in cases presented with STEMI after primary PCI.

Patients and Methods: This study included 40 cases subjected to Emergency Departments of Ain Shams University and Misr University for Sciences and Technology (MUST) Hospitals from September 2021 to June 2022, diagnosed with STEMI and had been revascularized by primary PCI. Serum samples for NT-pro BNP were collected before primary PCI and correlated with the TIMI flow, MBG grades, and ST resolution post primary PCI.

Results: Our study demonstrated a higher baseline NT-pro BNP level that was significantly correlated with increased risk of poor myocardial reperfusion following primary PCI expressed by ST resolution less than 50%, TIMI flow grade < 3 as well as MBG < 3 and was also associated with increased incidence of No Reflow.

Conclusion: Initial NT-pro BNP level in STEMI cases correlates with myocardial reperfusion following primary PCI besides its early marker for risk stratification of STEMI patients. High-risk patients are in need of more aggressive complementary treatment strategies to improve microvascular perfusion and optimization of medical treatment.

Keywords: N terminal - pro B- type natriuretic peptide, ST elevation, Myocardial infarction, Primary percutaneous intervention, Myocardial reperfusion.

INTRODUCTION

Primary PCI is the optimal reperfusion technique in cases with STEMI within 12 hours of the beginning of symptoms, by a skilled team [(1)]. Fibrinolytic treatment is advised in patients without contraindications within 12 hours of symptom onset if prompt primary PCI is not possible following ST segment elevation myocardial infarction (STEMI) diagnosis [(2,3)].

Creatinine Kinase (CK), cardiac troponin, and CK-Myocardial Band (CK-MB) levels rise when STEMI occurs. N-Terminal-Pro-B-Type Natriuretic Peptide (BNP) is one of the cardiac biomarkers [(4, 5)]. The stretch of cardiac myocytes is the primary stimulation for pro BNP release in the heart [(6)]. In addition to myocardial strain and hormones, hypoxia and NT-pro BNP are other factors that may contribute to the monitored alterations in peptide plasma concentration in acute coronary syndrome [(7)].

The present study aimed to study if the level of NT-pro BNP before primary PCI can be used as an independent predictor for successful reperfusion in cases presented with STEMI after primary PCI.

PATIENTS AND METHODS

This is a prospective interventional study that was performed in Coronary Care Unit and Catheterization Lab Units of the Cardiology Department at Ain Shams University and MUST Hospitals, between September 2021 and June 2022.

This study was conducted on 40 cases who were diagnosed with STEMI and received primary PCI.

Inclusion Criteria:

Patients aged >18, who were presented with chest pain associated with ECG changes fulfilling criteria for diagnosis of STEMI within 48 hours of symptom onset or after 48 hours if they had persistent symptoms suggestive of ongoing myocardial ischemia or hemodynamic instability.

Exclusion Criteria:

Patients who presented after 48 h from the onset of chest pain and with STEMI without evidence of ongoing ischemia, patients underwent thrombolytic reperfusion therapy, patients resuscitated from cardiac arrest, patients known to have heart failure with decreased ejection fraction (EF), patients with congenital or valvular heart diseases, patients with pulmonary embolism, pulmonary hypertension or chronic lung diseases, patients with cardiac infiltrative, inflammatory or infectious diseases, patients with hyper dynamic circulation (sepsis, anemia, liver cirrhosis etc.), patients with severe renal impairment and patients with intracranial pathologies.

Diagnosis:

The patients were diagnosed as ST segment elevation according to the 2017 European Society of Cardiology guidelines.

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Pre-procedural parameters:

All cases were subjected to the following:

a) Full history taking focusing on demographics and risk factors for Coronary Artery Disease (CAD).
b) Clinical examination focusing on Killip class on admission.
c) Twelve lead surface ECGs.
d) Maximum ST segment elevation at the time of presentation in mm was recorded & ST segment resolution 90 minutes post PCI was recorded.
e) Laboratory investigations including CBC, serial cardiac enzymes, serum creatinine level, serum NT-Pro BNP level with Human NT-pro BNP ELISA Kit Elecsys pro BNP II.

Procedural Parameters:

a) All patients received full anti ischemic treatment according to the 2017 ESC guidelines of STEMI and then primary PCI was performed by an expert team [(1)].
b) Full angiographic and interventional details were obtained including route of access used, door to balloon time, total procedure time, the infarct related artery, site of occlusion, number of vessels affected, number of stents used, size of balloon and stents used, using glycoprotein IIb/ IIIa (GP IIb/IIIa) inhibitors, thrombolysis in myocardial infarction (TIMI) flow grade [(8)], myocardial blush grade (MBG) [(9)], occurrence of no reflow phenomenon or not and contrast volume used.

Post-procedural parameters:

a) All patients received full anti ischemic treatment according to the 2017 ESC guidelines of STEMI [(1)].
b) Echocardiography was performed on discharge to all patients commenting on the left ventricular function by the modified Simpson's method [(10)].

Ethical approval:

The study was approved by scientific and ethical committee of Faculty of Medicine, Ain Shams University. All study participants provided written informed permission after being informed of our research's goals. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduct of this study.

Statistical analysis

The Statistical Package for Social Science (IBM SPSS) version 23 was used to analyse the data. When the quantitative data were parametric, data displayed as means, standard deviations (SD), and ranges when data were non-parametric, they displayed as medians and interquartile ranges (IQR). As a result, the p-value was insignificant: $P > 0.05$, $P \leq 0.05$ as significant, and $P < 0.01$ as highly significant.

RESULTS

There was no statistical significance between any of the demographic data or history data and the ST resolution (Table 1).

Table (1): Relation of ST resolution with the demographic data and history of the studied patients

		STE resolution		Test value	P- value
		Less than 50%	More than 50%		
		No.= 14	No.= 26		
Age (Years)	Mean ± SD	54.93 ± 7.91	53.69 ± 13.98	0.305•	0.762
	Range	43 – 67	21 – 86		
Sex	Female	3 (21.4%)	3 (11.5%)	0.698*	0.403
	Male	11 (78.6%)	23 (88.5%)		
Smoking Status	No	6 (42.9%)	7 (26.9%)	1.053*	0.305
	Yes	8 (57.1%)	19 (73.1%)		
DM	No	8 (57.1%)	18 (69.2%)	0.584*	0.445
	Yes	6 (42.9%)	8 (30.8%)		
HTN	No	7 (50.0%)	17 (65.4%)	0.897*	0.343
	Yes	7 (50.0%)	9 (34.6%)		
Dyslipidemia	No	6 (42.9%)	14 (53.8%)	0.440*	0.507
	Yes	8 (57.1%)	12 (46.2%)		
Family Hx of IHD	No	11 (78.6%)	22 (84.6%)	0.230*	0.631
	Yes	3 (21.4%)	4 (15.4%)		
Prior MI	No	11 (78.6%)	24 (92.3%)	1.570*	0.210
	Yes	3 (21.4%)	2 (7.7%)		
CKD	No	13 (92.9%)	23 (88.5%)	0.195*	0.658
	Yes	1 (7.1%)	3 (11.5%)		

*: Chi-square test; •: Independent t-test

Patients with poor myocardial reperfusion (ST resolution < 50%) had longer duration of symptoms compared to those with complete ST resolution (Median (IQR) 10 vs 2.5, P= 0.039). There was no statistical relevance between the Killip class, the type of STEMI or the P2Y12 inhibitor taken before the PCI and the ST resolution (Table 2).

Table (2): Relation of ST resolution with the presentation of the studied patients

		ST resolution		Test value	P- value
		Less than 50%	More than 50%		
		No.= 14	No.= 26		
Duration of symptoms (hrs)	Median (IQR)	10 (4 – 24)	2.5 (2 – 6)	-2.060≠	0.039
	Range	1 – 72	0.25 – 48		
Killip Class	I	9 (64.3%)	22 (84.6%)	4.233*	0.237
	II	2 (14.3%)	2 (7.7%)		
	III	0 (0.0%)	1 (3.8%)		
	IV	3 (21.4%)	1 (3.8%)		
Type of STEMI	Non-Anterior STEMI	6 (42.9%)	11 (42.3%)	0.001*	0.973
	Anterior STEMI	8 (57.1%)	15 (57.7%)		
P2Y12 Inhibitor	Clopidogrel	1 (7.1%)	9 (34.6%)	3.663*	0.056
	Ticagrelor	13 (92.9%)	17(65.4%)		

*: Chi-square test; ≠: Mann-Whitney test Hrs: hours, IQE: inter-quartile range.

Table showed that there was a highly marked relation between the ST resolution and the myocardial reperfusion evaluated angiographically by the TIMI flow grade and the MBG. The higher the TIMI flow grade and the MBG, the more the ST resolution. Also, patients with ST resolution <50% had increased incidence of No reflow and longer procedure time.

Table (3): Relation between the ST resolution and the primary PCI data

		STE resolution		Test value	P- value
		Less than 50%	More than 50%		
		No.= 14	No.= 26		
Use of balloon post stent dilatation	Negative	6 (42.9%)	19 (73.1%)	3.546*	0.060
	Positive	8 (57.1%)	7 (26.9%)		
TIMI flow post stenting	I	6 (42.9%)	0 (0.0%)	18.628*	0.000
	II	5 (35.7%)	4 (15.4%)		
	III	3 (21.4%)	22 (84.6%)		
MBG post stenting	0	5 (35.7%)	1 (3.8%)	13.501*	0.004
	I	5 (35.7%)	3 (11.5%)		
	II	2 (14.3%)	7 (26.9%)		
	III	2 (14.3%)	15 (57.7%)		
No reflow	Negative	6 (42.9%)	25 (96.2%)	14.824*	0.000
	Positive	8 (57.1%)	1 (3.8%)		
GP IIb/IIIa Inhibitor	Negative	2 (14.3%)	14 (53.8%)	5.934*	0.015
	Positive	12 (85.7%)	12 (46.2%)		
	Range	70 – 250	50 – 250		
Total procedure time (min)	Mean±SD	76.79 ± 33.89	44.81 ± 20.66	3.716•	0.001

*: Chi-square test; •: Independent t-test DES: drug eluting stent, MBG: myocardial blush grade, GP: glycoprotein, IQR: inter-quartile range

The ROC curve showed that the best cut off point for NT-pro BNP to predict the ST resolution was ≤ 73 with high sensitivity and specificity (73.08% and 100% respectively) and an area under the curve (AUC) of 92.9%.

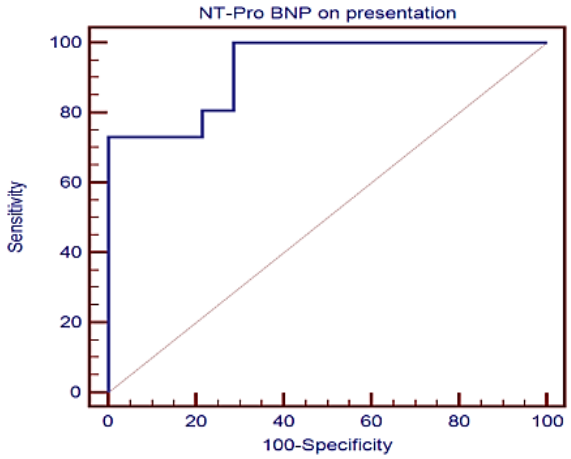

Figure (1): Receiver operating characteristic curve (ROC) for NT-pro BNP on presentation to differentiate between patients with >50% and < 50% resolution.

	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
NT-Pro BNP on presentation	≤73	0.929	73.08	100.00	100.0	66.7

There was a remarkable association between baseline NT-pro BNP level and the duration of symptoms, the amount of contrast used, the total procedure time, the level of HS (highly sensitive) Troponin and EF. Higher baseline NT-pro BNP was related with longer duration of symptoms, longer procedure time, larger amount of contrast, higher level of HS-Troponin and lower ejection fraction (Table 4).

Table (4): Correlation between the baseline NT-pro BNP level and other parameters.

	NT-Pro BNP on presentation	
	r	P- value
Duration of symptoms (hrs)	**0.625****	**0.000**
Door to balloon time (min)	0.228	0.157
Amount of contrast used (cc)	**0.401***	**0.010**
Total procedure time (min)	**0.462****	**0.003**
HS-Troponin	**0.395***	**0.012**
EF (%)	**-0.474****	**0.002**

Hrs: hours, Min: minutes, Hb: hemoglobin, TLC: total leucocytic count, PLT: platelet count, HS: highly sensitive

Table (5) showed that the patients with higher baseline NT-pro BNP were more frequently females and non-smokers.

Table (5): Relation between NT-pro BNP level and the demographic data and history of the studied patients

		NT-Pro BNP on presentation		Test value	P- value
		Median (IQR)	Range		
Sex	Female	1245.5 (730 – 3897)	57 – 9476	-2.027	0.043
	Male	69.5 (48 – 864)	24.5 – 6164		
Smoking Status	No	760 (73 – 1838)	48.7 – 9476	-2.108	0.035
	Yes	58 (45 – 864)	24.5 – 6164		
DM	No	62 (48 – 864)	27 – 9476	-0.993	0.321
	Yes	450.5 (64 – 1731)	24.5 – 6164		
HTN	No	68.5 (49.35 – 823.5)	32 – 4932	-0.759	0.448
	Yes	450.5 (49 – 1784.5)	24.5 – 9476		
Dyslipidemia	No	79 (51.6 – 823.5)	27 – 9476	-0.054	0.957
	Yes	94.5 (48.35 – 1784.5)	24.5 – 4932		
Family Hx of IHD	No	171 (50 – 1731)	24.5 – 9476	-1.157	0.247
	Yes	73 (45 – 106)	32 – 523		
Prior MI	No	83 (50 – 864)	24.5 – 9476	-0.716	0.474
	Yes	2083 (43 – 3897)	35.8 – 6164		
CKD	No	78 (48.35 – 1148.5)	24.5 – 9476	-1.105•	0.269
	Yes	745 (393.5 – 3462)	57 – 6164		

Median (IQR), range: non-parametric test, •: Mann-Whitney test.

Increased baseline TIMI flow grade 3, MBG 3, and NT-pro BNP levels were both related with inadequate myocardial reperfusion. Additionally, it was linked to a higher rate of No reflow (Table 6).

Table (6): Relation between baseline NT-pro BNP level and primary PCI data.

		NT-Pro BNP on presentation		Test value	P- value
		Median (IQR)	Range		
Use of balloon post stent dilatation	Negative	58 (48 – 523)	24.5 – 6164	-2.068•	0.039
	Positive	864 (64 – 3082)	27 – 9476		
TIMI flow grade post stenting	I	2814 (1224 – 4932)	106 – 6164	16.586≠	0.000
	II	864 (523 – 2083)	48 – 9476		
	III	57 (45 – 94)	24.5 – 3082		
MBG post stenting	0	2814 (1224 – 4932)	48.7 – 6164	14.164≠	0.003
	I	812 (314.5 – 2623)	73 – 9476		
	II	58 (48 – 83)	35.8 – 1838		
	III	57 (45 – 171)	24.5 – 3082		
No reflow	Negative	64 (45 – 730)	24.5 – 6164	-3.223•	0.001
	Positive	1838 (1224 – 3897)	53 – 9476		
ST resolution	Less than 50%	1960.5 (523 – 3897)	83 – 9476	-4.424•	0.000
	More than 50%	55.1 (45 – 171)	24.5 – 1073		

Median (IQR), range: non-parametric test, •: Mann-Whitney test.

•: Mann-Whitney test; ≠: Kruskall-Wallis test DES: drug eluting stent, GP: glycoprotein, IQR: inter-quantile range.

DISCUSSION

Following an acute MI, it has been assumed that the NT-pro BNP, a well-established marker for heart failure and neurohumoral activation, liberates from the myocardium [(11)]. According to recent research, the amount of natriuretic peptide or its pro-hormone may indicate the degree of CAD, the size of the myocardium that is at risk, and the likelihood that an angiogram would be successful following reperfusion in patients with STEMI [(12, 13-16)].

Out of the 40 patients, 26 patients (65%) had more than 50% ST resolution while 14 patients (35%) had less than 50% ST resolution in the ECG 90 minutes following primary PCI. In our study we have showed that a higher baseline NT-pro BNP concentration is significantly related to increased risk of poor myocardial reperfusion following primary PCI expressed by ST resolution less than 50%, TIMI flow grade less than 3 as well as MBG less than 3 and is also related to higher incidence of No Reflow. This comes in line with previous reports by **Lorgis *et al.* [(17)], Fabris *et al.* [(18)], Shavadia *et al.* [(19)]** and **Qin *et al.* [(20)].**

According to studies, 30% of STEMI patients who undergo PCI do not experience successful myocardial reperfusion. The injured myocardium is not well reversed after the coronary event, which results in delayed blood flow or no reflow. This would obviously increase NT-pro BNP levels and increase the likelihood of Major Adverse Cardiovascular Events (MACE) [(21)]. **Shavadia *et al.* [(19)]** have found that only one biomarker (higher pre-PCI NT-pro BNP levels) was connected to a congestive heart failure, notably higher 90-day risk of death, and cardiogenic shock. This also agrees with the findings of **Qin *et al.* [(20)]** and **Mathbout *et al.* [(22)]** who revealed that NT-pro BNP was a crucial predictor of MACE in cases with STEMI. These findings suggest that early risk stratification of cases at high risk for poor myocardial reperfusion including NT-pro BNP measurement is very important.

The current findings showed that that higher levels of initial NT-pro BNP correlated with increased risk of poor myocardial reperfusion. This allows for the potential for early risk categorization of STEMI patients based on NT-pro BNP level even in the ambulance setting. These high-risk cases would benefit from adjunctive measures and more aggressive secondary preventive therapies that would help enhance the myocardial reperfusion and therefore decrease the risk of LV dysfunction and occurrence of MACE.

Apart from the measures that may be used to improve myocardial reperfusion, also stratification risk would allow early administration of anti-failure medications such as beta blockers and ACE inhibitors especially angiotensin receptor neprilysin inhibitor (ARNI). **Zhang *et al.* [(23)]** have found that early sacubitril/valsartan delivery within 24 hours of primary PCI in STEMI cases reduced the frequency of acute heart failure and was linked to a lower rate of hospital readmission within six months. It implies that using sacubitril/valsartan, particularly if begun quickly after an acute MI, is generally safe and beneficial.

CONCLUSION

NT-pro BNP level before primary PCI in STEMI cases correlates with the myocardial reperfusion. Higher NT-pro BNP level was correlated with higher risk of poor myocardial reperfusion shown as TIMI flow < 3, MBG < 3 and ST resolution 90 mins

post PCI < 50%. Higher NT pro BNP level was related with higher incidence of No reflow phenomenon. We concluded that NT pro BNP level pre-PCI may be utilized to predict the myocardial reperfusion following primary PCI in STEMI patients. Our study showed that the best cut off point for NT-pro BNP to predict the ST resolution was ≤ 73 pg/ml with a sensitivity of 73.08% and a specificity of 100%.

RECOMMENDATIONS

The potential application of NT-pro BNP as an early marker for risk stratification of cardiac reperfusion in STEMI cases following initial PCI. The assessment of the predictive value of NT-pro BNP before PCI with reference to the occurrence of MACE should be the focus of larger research with longer follow-up periods. To improve myocardial perfusion in high-risk individuals with high NT-pro BNP levels, further strategies are required. Larger multicenter, adequately randomized, controlled studies should be directed to investigate the prognostic value of NT-pro BNP before primary PCI in prediction of poor myocardial reperfusion. Further studies should be directed towards more aggressive complementary treatment strategies to improve microvascular perfusion after primary PCI and to prevent the incidence of No reflow.

LIMITATIONS:

Due to the fact that this was a single-center, non-randomized trial with a small patient population and no long-term follow-up, our findings should only be regarded as hypothesis generating.

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