

ORIGINAL ARTICLE

Association of N-Terminal Pro Brain Natriuretic Peptide with Ventricular EctopyShazadi Ambreen¹, Humaira Fayyaz², Azmat Hayyat³**ABSTRACT**

Objective: This study aimed to determine the association of premature ventricular contractions burden of less than 20% with NT-pro BNP levels in patients with preserved left ventricular function.

Study Design: Case control analytical study.

Place and Duration of Study: It was conducted in physiology department of Islamic International Medical College (IIMC) in collaboration with Armed Forces Institute of Cardiology (AFIC) during the period of 18th April 2016 to 20th March 2018.

Materials and Methods: The study comprised a total of fifty participants which included 40 diagnosed patients of premature ventricular contractions (PVCs) and 10 healthy subjects (with no PVCs). PVCs burden was calculated by Holter monitoring report and echocardiography was done to determine left ventricular ejection fraction. Patients with burden >20% and Ejection fraction <50% were excluded. In all these patients NT-proBNP levels were measured and statistical analysis was done using SPSS version 25. Student's t-test and Pearson correlation tests were applied to see its association with PVCs burden.

Results: Ventricular ectopic burden <20% has NT-proBNP higher than controls but the increase is insignificant with p value of 0.056. Pearson correlation test showed no correlation of Premature ventricular contractions <20% with NT-pro BNP levels with r value of 0.1.

Conclusion: It can be concluded that the patients with PVCs burden less than 20% has no correlation with NT-pro BNP so they should not be considered as high risk patients.

Key Words: *Cardiomyopathy, NT-ProBNP, PVCs, PVCs Burden, Ventricular Ectopy.*

Introduction

Ventricular ectopy or premature ventricular contraction is defined as an extra heartbeat, originating from the ventricles and comes before the normal heart beat.¹ Premature ventricular contractions (PVCs) is common with an estimated prevalence of 1% to 4% in the general population.²

The mechanisms for ventricular ectopy production include re-entry, triggered activity and automaticity.³ Occurrence of re-entry takes place due to presence of one way block and an area of slow conduction. During ventricular activation slow conduction area

activates the blocked area after ventricular recovery, resulting in an ectopic beat.⁴ In the triggered activity, the preceding action potential produce after depolarizations which results in ectopic beat. Automaticity points to presence of an ectopic focus of pacemaker cells in the ventricle with sub threshold potential for firing. Basic rhythm of heart raises these cells to potential resulting in an extra beat.^{3,1}

Frequent ventricular ectopic beats have a high risk of developing dilated type cardiomyopathy.⁵ Rapid pacing due to PVCs results in LV dyssynchrony resulting in LV dilatation and ultimately reduced ejection fraction.⁶ During this process changes in neurohormonal pathway occurs which bring about release of bioactive peptides.⁷ ProBNP splits into BNP (32 amino acid) and N-Terminal proBNP (76 amino acid). ProBNP is mainly synthesized and secreted by cardiac myocytes in response to myocardial wall stretch.⁸ NT-proBNP levels are found to be raised in patients of left ventricular dysfunction and ventricular dilatation.⁹ In comparison of diagnostic significance of BNP with NT-proBNP, for left ventricular dysfunction, both are equivalent, but in some groups NT-proBNP is found to be superior.^{10,9}

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PVCs were long considered benign until they were found to be associated with risk of developing PVCs induced cardiomyopathy.¹¹ High PVCs burden is associated with development of cardiomyopathy but sometimes high burden patients do not develop cardiomyopathy and patients with the burden of 4% can develop cardiomyopathy. Currently no risk profile defines a group of patients at high risk of PVCs induced cardiomyopathy.¹² Role of NT-proBNP as a biochemical marker to predict cardiomyopathy needs to be studied.

This study aimed to determine the association of moderate ventricular ectopic burden (less than 20%) with N-Terminal proBNP levels in patients with preserved left ventricular function, thus assessing it's importance as a determinant to stratify high risk patients.

Materials and Methods

A case control study was conducted in Physiology department of Islamic International Medical College Rawalpindi, in collaboration with Electrophysiology department of Armed Forces Institute of Cardiology (AFIC) from 18th April 2016 to 20th March 2018 after approval from ethical review committee (ERC). A total of 50 patients were taken among which 40 were diagnosed patients of premature ventricular contractions with PVCs burden ≤20%. Patients were diagnosed on 24 hours Holter monitoring report and their PVCs burden was calculated by dividing total number of PVCs by total analyzed beats in 24 hours. Echocardiography was done in all the patients to assess their heart status. Inclusion criteria were specified as, age between 18-60 years, LV ejection fraction less than 50% and patients with PVCs burden less than 20. Patients with PVCs burden >20% and ejection fraction <50% were excluded from the study. Patients out of age range of 18-60 years were excluded from the study. Ten age matched healthy subjects with no PVCs were taken as controls. In all these patients, venipuncture technique was used to collect the blood sample. NT-proBNP levels were measured in all blood samples using ELISA kit and statistical analysis was done by using SPSS version 25. Data was normally distributed so parametric tests were applied. Pearson correlation test was applied to determine the correlation of NT-proBNP with moderate PVCs burden (burden <20%) and Student's t-test was applied to compare mean NT-proBNP

levels of PVCs patients with control subjects (having no PVCs).

Results

Baseline characteristics are shown in Table I which shows 47±6 years as the mean age of the PVCs patients. Among the total of 40 patients 18 were females and 22 were males.

Table I: Baseline Characteristics of Participants

Baseline and Clinical characteristics		PVCs Patients	Control	Total(n)
Age(years)		47±6	45±4	
Gender	Male	22	6	28
	Female	18	4	22
Total(n)		40	10	50

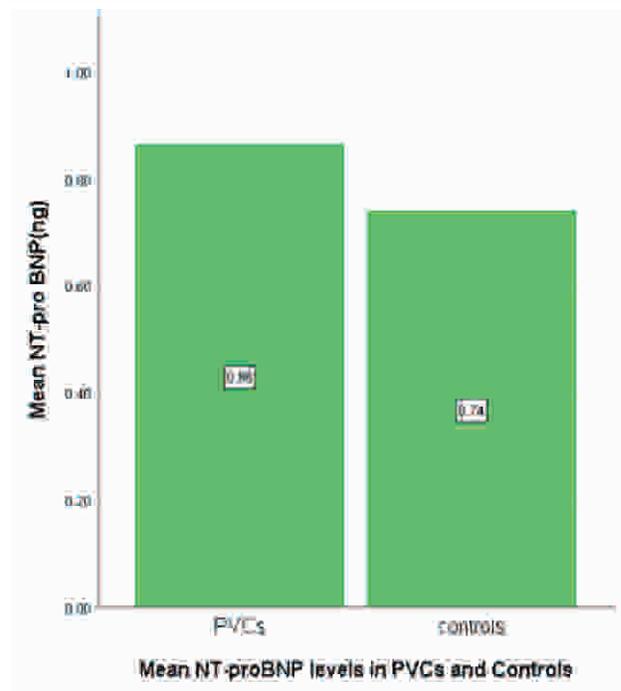


Fig 1: Comparison of Mean NT-Pro BNP in PVC's Patients and Controls

Figure 1 Mean NT-proBNP levels in PVCs patients are 0.86±0.47ng and in control group 0.74±0.49ng which shows that NT-proBNP levels are high in PVCs as compared to controls but the increase is insignificant with p value of 0.56. p value ≤0.05 was considered to be significant.

Table II shows correlation of PVCs burden <20% with NT-proBNP. Pearson correlation test was applied and r value of 0.1 shows no correlation of ventricular ectopic burden < 20% with N-Terminal pro BNP levels.

Table II: Correlation of Ventricular Ectopic Burden <20% with NT-ProBNP Levels

Ventricular Ectopy <20%	NT-pro BNP levels (ng/ml)	
	r value	p value
	0.1	0.6

r is Pearson correlation coefficient

P value<0.05 was considered to be significant.

Discussion

The current study was aimed to evaluate the association of NT-proBNP with PVCs burden less than 20% in patients with preserved LV function left (Left ventricular ejection fraction <50%). Levels of NT-pro BNP were not significantly raised in PVCs patients as compared to control groups. Hence the results suggest no correlation of NT-proBNP with PVCs burden less than 20%.

A study by Skranes et al, illustrates the association of N-Terminal pro BNP with PVCs which contradicts the present study findings. The contradiction may be due to the reason that current study is done on patients with PVCs burden less than 20% while that study was done on frequent PVCs (PVCs>24%) patients. That study also differed from the current study as it was done in community based population.¹³ In another study conducted on animals (dogs), NT-proBNP and Interleukin 6 (IL-6) were measured in all PVCs burden (25%, 33% and 50%). In all these PVCs burden of 25%, 33% and 50%, PVCs induced cardiomyopathy (LVEF<50%) was present among 11.1%, 44% and 100% of animals but no increase in NT-proBNP or IL 6 was observed in any of these burdens.¹⁴ This finding is in line with present study.

Another study aimed to identify the risk factors shows that the individuals with low socioeconomic status, increased waist hip ratio, body height>median and sokolow-Lyon Index have higher frequency of PVCs. At the same time the study demonstrates that the patients with higher NT-proBNP levels have frequent PVCs (PVCs burden>24%).¹⁵ But the present study showed no association of NT-pro BNP with PVCs which could be due to the fact that present study determined the NT-proBNP levels in patients of mild to moderate PVC burden (PVCs<20%) rather than frequent PVCs burden.¹⁵

Sajadieh et al conducted a study on middle aged and elderly patients which demonstrates that in the absence of any known cardiac disease, the NT-proBNP levels are higher in patients with frequent

PVCs as compared to those with no PVCs.¹⁶

In present study myocardial wall stress was not measured as this facility was not available in the center.

Conclusion

It is concluded from the present study that NT-proBNP levels are not raised in PVCs patients with burden of less than 20% as well as no correlation of NT-proBNP is found with PVCs in burden of less than 20%. Thus declining its importance as a determinant to stratify the patients at high risk

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