

N-terminal-pro-brain natriuretic peptide, a surrogate biomarker of combined clinical and hemodynamic outcomes following percutaneous transvenous mitral commissurotomy



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Aim: To examine the relationship between plasma levels of N-terminal-proB type natriuretic peptide (NT-proBNP) and various echocardiographic and hemodynamic parameters in patients with mitral stenosis undergoing percutaneous transvenous mitral commissurotomy (PTMC).

Materials and methods: The study population consisted of 100 patients with rheumatic mitral stenosis who underwent PTMC. NT-proBNP levels in these patients were measured before PTMC and 48 hours after PTMC. These levels were then correlated with various echocardiographic and hemodynamic parameters measured before and after PTMC.

Results: Eighty-one percent of the study population were women, and the most common presenting symptom was dyspnea which was present in 94% of the patients. Dyspnea New York Heart Association class correlated significantly with baseline NT-proBNP levels ($r = 0.63$; $p < 0.01$). The plasma NT-proBNP levels in these patients increased as echocardiogram signs of left atrial enlargement and right ventricular hypertrophy developed ($r = 0.59$, $p < 0.01$). Patients in atrial fibrillation had significantly higher NT-proBNP levels than patients in sinus rhythm. Baseline NT-proBNP levels correlated significantly with left atrial volume ($r = 0.38$; $p < 0.01$), left atrial volume index ($r = 0.45$; $p < 0.01$), systolic pulmonary artery pressures ($r = 0.42$; $p < 0.01$), and mean pulmonary artery pressures ($r = 0.41$; $p < 0.01$). All patients who underwent successful PTMC showed a significant decrease in NT-proBNP (decreased from a mean 763.8 pg/mL to 348.6 pg/mL) along with a significant improvement in all echocardiographic and hemodynamic parameters ($p < 0.01$). The percent change in NT-proBNP correlated significantly with the percent improvement noted with left atrial volume ($r = 0.39$; $p < 0.01$), left atrial volume index ($r = 0.41$; $p < 0.01$), systolic ($r = 0.32$, $p < 0.01$), and mean pulmonary artery pressures ($r = 0.31$, $p < 0.01$).

Conclusions: The decrease in NT-proBNP levels following PTMC reflects an improvement in clinical and hemodynamic status; hence, it is reasonable to suggest that NT-proBNP is helpful in evaluating the response to PTMC.

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Introduction

Rheumatic heart disease (RHD) is a permanent sequelae of rheumatic fever (RF). The prevalence of RF and RHD has decreased in developed countries, but they still remain a major health hazard in developing countries. The incidence of RF is equal in both genders, but rheumatic mitral stenosis (MS) is two times more common in women [1].

Rheumatic fever affects all the valves microscopically, but clinically significant disease is observed mostly in the mitral valve [1]. Mitral stenosis being a mechanical obstruction to the forward flow of blood, the only definitive therapy is a mechanical relief in this obstruction. Three procedures are effective in providing such therapy, which are percutaneous transvenous mitral commissurotomy (PTMC), surgical mitral commissurotomy, and mitral valve replacement. A successful PTMC results in improvement in mitral valve area (MVA), thereby causing a decrease in left atrial (LA) pressures, decrease in pulmonary artery (PA) pressures, and increase in left ventricular end diastolic pressure.

Brain natriuretic peptide (BNP), a cardiac neurohormone secreted predominantly by ventricles and to some extent by atria, has a regulatory and modulatory role in the cardiovascular system by its diuretic, natriuretic, and vasodilator actions. N-terminal-pro B type natriuretic peptide (NT-proBNP) is part of prepro-BNP, which is secreted in a proportion equivalent to BNP. It is more stable than BNP due to its long half-life, therefore higher levels of NT-proBNP are observed. The diagnostic and prognostic role of NT-proBNP in left ventricular dysfunction of various etiologies has been extensively studied [2–4]. It has also been shown in studies that plasma NT-proBNP levels increase in diseases like primary pulmonary hypertension, cor-pulmonale, and pulmonary embolism which affect the pulmonary bed and right heart [5,6].

The prognostic role of various NPs in valvular heart diseases has been extensively studied [7–9]. It was noted that various NPs were elevated in patients of MS, and few of them correlated with the severity of MS [7]. Following a successful PTMC, a decrease in various NPs is expected and few studies have evaluated this change [10,11]. Although NT-pro-atrial-NPs are increased

Abbreviations

NT-proBNP	N-terminal-pro B type natriuretic peptide
PTMC	Percutaneous transvenous mitral commissurotomy
RHD	Rheumatic heart disease
RF	Rheumatic fever
MS	Mitral stenosis
MVA	Mitral valve area
LA	left atrium
PA	Pulmonary artery
BNP	Brain natriuretic peptide
NPs	natriuretic peptides
LAVI	Left atrial volume index
LVEDP	left atrial end diastolic pressure
AF	Atrial fibrillation
NYHA	New York Heart Association

in patients of MS along with BNP and NT-proBNP, due to the ease of laboratory tests and reproducibility usually only BNP or NT-proBNP is used. Plasma NT-proBNP levels are affected in MS and they correlate with the severity of MS [12–17]. Only a few studies have evaluated the change in NT-proBNP levels in patients of severe MS following PTMC [18–23].

The reversible nature of the pulmonary hypertension in MS may be an explanation for the decrease in NT-proBNP levels after PTMC. The decrease in pressures in the LA and right side of the heart following PTMC cause a decrease in wall stress which contributes to the decreased NT-proBNP levels. This present study is designed to examine the relationship between plasma levels of NT-proBNP and various echocardiographic and hemodynamic parameters in patients with MS undergoing PTMC.

Materials and methods

The study population consisted of 100 patients with rheumatic severe MS who underwent PTMC at department of Cardiology, Sri Venkateswara Institute of Medical Sciences, Tirupati, India between June 2012 and November 2013. The protocol was approved by the Institutional Ethics Committee and all patients gave a written informed consent. All patients with severe MS [2-dimensional (2D) MVA = 1.5 cm²] who were candidates for PTMC, as per ACC/AHA/ESC guidelines, were included in this study [24,25]. Inclusion criteria were patients with symptomatic severe MS with favorable valve morphology,

asymptomatic patients with severe MS who had more than moderate PA hypertension (>50 mmHg), and those at high risk for thromboembolic events. All patients with systolic or diastolic left ventricular dysfunction, systemic hypertension, cardiomyopathy, chronic diseases of the respiratory tract, those with concurrent more than mild mitral regurgitation (MR), aortic stenosis and/or regurgitation, left ventricular hypertrophy confirmed with echocardiography, renal failure, hepatic failure, and those developing severe MR following PTMC requiring immediate surgical intervention were excluded from the study.

Transthoracic, M-mode, 2D, and Doppler echocardiography were performed and LA volume, left atrial volume index (LAVI), mitral valve gradient, 2D-MVA, and PA pressures were measured on the day before and 48 hours after PTMC using Philips IE-33 machine, Holland. All patients underwent transesophageal echocardiography 24 hours before PTMC in order to exclude the presence of LA thrombus and to assess valve morphology.

Hemodynamic measurements (LA pressure, LVEDP, systolic and mean PA pressures, mean and end diastolic pressure gradient across the mitral valve) were recorded before and immediately after PTMC.

Mitral valve commissurotomy was performed with an Accura balloon catheter (Vascular concepts, Essex, UK) using the Inoue technique [26].

A 2-mL blood sample was collected with venipuncture into heparinised tubes 30 minutes before PTMC and 48 hours after PTMC. NT-proBNP levels were measured using Roche CARDIAC proBNP test kit (code 04659449190, Roche Diagnostics Ltd., Germany) and Cobas h 232 Point Of Care system. The reaction time for the assay is about 10–15 minutes and the detection range of the assay is 60–9000 pg/mL of NT-proBNP.

Statistical analysis

Data collected was tabulated on a Microsoft Excel spread sheet and analyzed with IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. Paired *t* test was used for intragroup comparisons. Correlation coefficient was used to assess the linear relation between two variables. As the plasma NT-proBNP levels were widely distributed, logarithmic (log) transformed values were used for correlation tests. The relation between NT-proBNP levels and dyspnea New York Heart Association (NYHA) class were assessed using Spearman's

correlation test. The relationship between NT-proBNP levels and electrocardiogram (ECG) changes were assessed using Spearman's correlation test. The relation between log NT-proBNP levels and echocardiographic and hemodynamic parameters were assessed using the Pearson correlation test. The percentage decrease in NT-proBNP levels and percentage change in various variables were assessed using the Pearson correlation test. A value of $p < 0.05$ was considered significant.

Results

Baseline characteristics of the study population

Most of the study population were women. The men to women ratio was 19:81. The mean age of the study population was 37.5 ± 11 years ranging between 13 and 63 years with the majority being below 40 years (62%) of age. The patients height ranged from 128 to 176 cm, with the mean height being 150.4 ± 9 cm. The body surface area of the patients ranged between 0.88 and 1.86 m² and the mean body surface area was 1.43 ± 0.18 m².

Most of the patients were diagnosed with severe MS during their first evaluation. The most common presenting complaint was dyspnea, which was present in 94% of the patients. Two percent of patients presented with predominant palpitations which were due to atrial fibrillation (AF) with a fast ventricular rate and 2% presented with hemoptysis.

History suggestive of RF in the past was present in only 21% of the patients, among whom one patient had a history of chorea. Thirteen percent

Table 1. Demographic data; dyspnea New York Heart Association class and N-terminal-pro B type natriuretic peptide.

Demographic data (population size $n = 100$)			
Men/women = 19/81			
Variable		Range	Mean \pm SD
Age (y)		13–63	37.5 ± 11
Height (cm)		128–176	150.4 ± 9
Weight (kg)		22–75	47.1 ± 10.7
Body surface area (m ²)		0.88–1.86	1.43 ± 0.18
Dyspnea NYHA class	No. of patients	NT-proBNP pg/ml (mean \pm SD)	NT-proBNP pg/mL (range)
Class I	2	97	87–107
Class II	57	461.2 ± 355.6	80–2207
Class III	40	1186.3 ± 666.5	210–6635
Class IV	1	8013	

$r = 0.63$; $p < 0.01$

NT-proBNP = N-terminal brain natriuretic peptide; NYHA = New York Heart Association; SD = standard deviation.

of the patients had undergone PTMC in the past, and a repeat PTMC was performed in view of severe mitral restenosis. History of a cerebrovascular accident was present in 3% of the patients. All three patients were diagnosed with severe MS during their evaluation for cerebrovascular accident (Table 1).

Dyspnea NYHA class and NT-proBNP level

It was observed that as the dyspnea NYHA class worsened, the mean NT-proBNP levels increased and there was a significant correlation between dyspnea NYHA class and NT-proBNP levels ($r = 0.63, p < 0.01$). The mean NT-proBNP level in clinically stable patients (NYHA class I, II) was 443.9 pg/mL and the mean NT-proBNP level in patients with pulmonary edema (NYHA class III, IV) was 1380 pg/mL (Table 1).

ECG findings and NT-proBNP level

In patients of MS who were in sinus rhythm (SR), those with evidence of right ventricular (RV) hypertrophy, along with LA enlargement

on ECG had higher levels of NT-proBNP than those with only LA enlargement. Patients in AF, despite their ventricular rate (fast/controlled), had higher BNP levels compared with those in SR. Mean NT-proBNP levels in patients with AF was 2358.6 pg/mL. A significant correlation was noted between these ECG changes and NT-proBNP levels ($r = 0.59, p < 0.01$) (Table 2).

Correlation of NT-proBNP levels with various echocardiographic and hemodynamic parameters at baseline (pre-PTMC)

Owing to the wide dispersion of data for NT-proBNP, log NT-proBNP was calculated. The relationship between log NT-proBNP levels and various echocardiographic and hemodynamic parameters were assessed using the Pearson correlation test. On correlation with various echocardiographic parameters, it was observed that log NT-proBNP correlated significantly with LA volume ($r = 0.38; p < 0.01$) and LAVI ($r = 0.45; p < 0.01$). On correlation with various hemodynamic parameters, it was observed that

Table 2. Electrocardiogram and N-terminal brain natriuretic peptide levels.

ECG	No. of patients	NT-proBNP pg/mL (mean ± SD)	NT-proBNP pg/mL (range)
SR, LAE	50	477.7 ± 362	100–1516
SR, LAE, Rt axis	18	659.3 ± 501.7	80–1796
SR, LAE, Rt axis, RBBB/RVH ± strain	19	1275.5 ± 784.9	253–8013
AF with CVR/FVR	13	2358.6 ± 1764.4	1030–6635

$r = 0.59; p < 0.01$

AF = atrial fibrillation; CVR = controlled ventricular rate; ECG = electrocardiogram; FVR = fast ventricular rate; LAE = left atrial enlargement; NT-proBNP = N-terminal brain natriuretic peptide; RBBB = right bundle branch block; Rt = right; RVH = right ventricular hypertrophy; SD = standard deviation; SR = sinus rhythm.

Table 3. Correlation of various parameters with N-terminal brain natriuretic peptide before percutaneous transvenous mitral commissurotomy.

Parameter	Pre-PTMC	Correlation coefficient (r value)	p
<i>Echocardiographic parameters</i>			
2D MVA (cm ²)	0.98 ± 0.15	0.19	0.07
LA diameter (cm)	4.2 ± 0.5	0.21	0.04
LA volume (cm ³)	69.1 ± 19.2	0.38	<0.01
LA volume index (cm ³ /m ²)	48.6 ± 14.4	0.45	<0.01
<i>Hemodynamic parameters</i>			
a wave (mmHg)	26.3 ± 7.3	0.18	0.1
v wave (mmHg)	28.5 ± 9.6	0.28	<0.01
Mean AP (mmHg)	21.4 ± 6.8	0.22	0.03
LV EDP (mmHg)	6.5 ± 2.6	0.03	0.75
Systolic PA pressure (mmHg)	53.7 ± 21.7	0.42	<0.01
Mean PA pressure (mmHg)	35 ± 15	0.41	<0.01
a-EDP gr (mmHg)	19.7 ± 7	0.01	0.94
m-EDP gr (mmHg)	15.3 ± 6.9	0.21	0.04
NT pro BNP (pg/mL)	763.8 ± 640.7		

a-EDP = left atrial a wave-left ventricular end diastolic pressure; AP = atrial pressures; LA = left atrium; LVEDP = left ventricular end diastolic pressure; MVA = mitral valve area; m-EDP = mean left atrial pressure-left ventricular end diastolic pressure; NT-pro BNP = N-terminal brain natriuretic peptide; PA = pulmonary artery; PTMC = percutaneous transvenous mitral commissurotomy.

Table 4. Changes in echocardiographic and hemodynamic parameters and N-terminal brain natriuretic peptide following percutaneous transvenous mitral commissurotomy.

Variables		Pre	Post	Diff	p
<i>Echocardiographic parameters</i>					
2D MVA (cm ²)	Mean range	0.98 ± 0.15 0.5-1	1.90 ± 0.30 1.1-2	0.95 ± 0.23 0.4-1.4	<0.01
LA diameter (cm)	Mean range	4.2 ± 0.5 2.9-5.8	3.8 ± 0.5 2.4-5	0.4 ± 0.3 0.2-1	<0.01
LA volume (cm ³)	Mean range	69.1 ± 19.2 35.5-132.5	55.1 ± 18 23.7-120.8	13.9 ± 7.6 3.4-34.7	<0.01
LA volume index (cm ³ /m ²)	Mean range	48.6 ± 14.4 27.2-92.7	38.8 ± 12.9 16.8-78.4	9.8 ± 5.4 0.4-26.8	<0.01
<i>Hemodynamic parameters</i>					
a wave (mmHg)	Mean range	26.3 ± 7.3 12-43	15.6 ± 6.4 6-38	10.8 ± 5.4 1-28	<0.01
v wave (mmHg)	Mean range	28.5 ± 9.6 10-56	16.2 ± 6.9 4-40	12.2 ± 6.1 3-34	<0.01
Mean AP (mmHg)	Mean range	21.4 ± 6.8 12-79	11.4 ± 4.8 6-60	10 ± 4.3 2-29	<0.01
LV EDP (mmHg)	Mean range	6.5 ± 2.6 2-16	9.3 ± 2.6 4-17	2.8 ± 1.3 1-6	<0.01
PA peak (mmHg)	Mean range	53.7 ± 21.7 23-134	39.1 ± 16 12-97	14.6 ± 11.7 2-53	<0.01
D2 peak PA (mmHg)	Mean range	53.7 ± 21.7 23-134	31.6 ± 13 12-70	22.1 ± 15.9 4-63	<0.01
PA mean (mmHg)	Mean range	35 ± 15 12-79	24.5 ± 10.5 6-60	10.5 ± 8.6 2-29	<0.01
a-EDP gr (mmHg)	Mean range	19.7 ± 7 4-37	6.4 ± 5.3 2-26	13.4 ± 5.8 3-28	<0.01
m-EDP gr (mmHg)	Mean range	15.3 ± 6.9 5-43	2.4 ± 2.3 0-16	12.7 ± 5 5-27	<0.01
NT-proBNP (pg/ml)	Mean range	763.8 ± 640.7 80-8013	348.6 ± 301.5 60-5599	377.6 ± 359.2 10-5790	<0.01

a-EDP = mitral end diastolic gradient (LA a wave - LV EDP); AP = atrial pressure; D2 peak PA = pulmonary artery systolic pressures after 48 hours; LA = left atrium; LVEDP = left ventricular end diastolic pressure; m-EDP = mean mitral pressure gradient (LA mean pressure-LV EDP); MVA: mitral valve area; NT-proBNP: N-terminal brain natriuretic peptide; PA = pulmonary artery pressure.

Table 5. Difference in N-terminal brain natriuretic peptide following percutaneous transvenous mitral commissurotomy in patients with atrial fibrillation (n = 12) and sinus rhythm (n = 80).

Rhythm	NT-proBNP prePTMC pg/mL mean ± SD	NT pro BNP postPTMC pg/ml mean ± SD	Paired Student t test
AF (n = 12)	2468.1 ± 860.2	1131.2 ± 530.6	0.018
SR (n = 80)	701.6 ± 582.4	284.6 ± 244.6	<0.01

AF = atrial fibrillation; NT-pro BNP = N-terminal brain natriuretic peptide; SD = standard deviation; S = sinus rhythm.

log NT-proBNP showed significant correlation with systolic PA pressures ($r = 0.42$; $p < 0.01$) and the mean PA pressures ($r = 0.41$; $p < 0.01$) (Table 3).

Changes in echocardiographic parameters, hemodynamic parameters, and NT-proBNP levels following PTMC

Ninety-two patients underwent successful PTMC. Four patients developed moderate to severe MR and four others developed AF (lasting >24 hours) following PTMC (Table 4). In patients who underwent successful PTMC (n = 92), all echocardiographic and hemodynamic parameters

showed a significant improvement ($p < 0.01$). NT-proBNP levels decreased significantly following PTMC ($p < 0.01$). A significant decrease in NT-proBNP levels was observed both in patients with AF ($p < 0.05$) and also in those with SR ($p < 0.01$) (Table 5).

Correlation between change in various echocardiographic and hemodynamic parameters with change in NT-proBNP levels

The percent decrease in NT-proBNP levels correlated with percent decrease in LA volume ($r = 0.39$; $p < 0.01$), LAVI ($r = 0.41$; $p < 0.01$) on

Table 6. Correlation between percent improvement in various echocardiographic and hemodynamic parameters with percent decrease in brain natriuretic peptide.

Parameter	Correlation coefficient (r value)	p
<i>Echocardiographic parameters</i>		
2D MVA (cm ²)	−0.08	0.43
LA diameter (cm)	0.12	0.25
LA volume (cm ³)	0.39	<0.01
LA volume index (cm ³ /m ²)	0.41	<0.01
PA (D2 PAP) mmHg	0.33	<0.01
<i>Hemodynamic parameters</i>		
a wave (mmHg)	0.23	0.04
v wave (mmHg)	0.19	0.07
Mean AP (mmHg)	0.17	0.10
LV EDP (mmHg)	−0.11	0.29
PA peak (mmHg)	0.32	<0.01
PA mean (mmHg)	0.31	<0.01
a-EDP gr (mmHg)	0.21	0.07
m-EDP gr (mmHg)	0.14	0.17

a-EDP = mitral end diastolic gradient (LA a wave – LV EDP); AP = atrial pressure; D2 PAP = pulmonary artery systolic pressures after 48 hours; EDP = mean mitral pressure gradient (LA mean pressure – LV EDP); LA = left atrium; MVA: mitral valve area; NT-pro BNP = N-terminal brain natriuretic peptide; PA = pulmonary artery pressure.

transthoracic echocardiogram. It also correlated significantly with the percent decrease in systolic PA pressures ($r = 0.32$; $p < 0.01$) and mean PA pressures ($r = 0.31$; $p < 0.01$) observed immediately following PTMC and the decrease in systolic PA pressures after 48 hours ($r = 0.33$; $p < 0.01$). On multivariate analysis, the percent change in systolic PA pressures over 48 hours independently predicted the percent change in NT-proBNP levels (Table 6).

Complications

Four patients developed moderate to severe MR following PTMC which was commissural. These patients were managed medically and were followed-up. A significant increase in NT-proBNP levels were noted in these patients following PTMC ($p < 0.01$). Four other patients developed AF during or after PTMC lasting for more than 24 hours. An increase in NT-proBNP level was noted in these patients despite

improvement in all other echocardiographic and hemodynamic parameters. This increase was not statistically significant ($p = 0.06$) (Table 7).

Discussion

This present study is the largest to date ($n = 100$), evaluating the changes in NT-proBNP levels with changes in various echocardiographic and hemodynamic parameters following PTMC. History suggestive of RF in the past was present in only 21% of the study population, which is much less compared with most of the studies where the reported incidence of history of RF in patients of MS was around 50% [1]. This shows us the burden of RF with subclinical carditis in the Indian population.

Similar to other studies, we noticed an elevated NT-proBNP level in patients of MS [13–23]. The most common presenting symptom was dyspnea; it was present in 94% of the patients. Similar to Arat Ozkan et al. [14] and Seluck et al. [19], we observed that NT-proBNP levels correlated significantly with dyspnea NYHA class of the patients (Table 1). Clinical symptoms, especially dyspnea, usually depends on the pulmonary capillary wedge pressure and PA pressures. This explains an increase in NT-proBNP level with worsening NYHA class. Thus, NT-proBNP can be used as a tool for risk stratification and for monitoring disease progression in patients of MS.

In patients with MS, significantly higher levels of NT-proBNP were noted with development of right axis deviation, RV hypertrophy, and AF on ECG (Table 2). These ECG changes reflect the sequential pathophysiological changes noted during MS with increasing severity and chronicity. LA pressures increase with the severity of MS, which results in increased pulmonary capillary wedge pressure that in turn leads to increased PA pressures, and thus RV pressure overload, thereby explaining the increase in NT-proBNP levels. Atrial fibrillation, however, represents the chronicity of the disease and thereby a dilated atria, increased PA pressures, and RV strain. Atrial fibrillation by itself causes an increased LA wall stress, thereby causing a further increase in NT-proBNP levels. This finding was contrary to

Table 7. Change in N-terminal brain natriuretic peptide following the development of complications.

Complication	NT pro BNP prePTMC (pg/mL)	NT pro BNP postPTMC (pg/mL)	p
Mod–Sev MR ($n = 4$)	980	1977.3	0.006
AF (>24 h) ($n = 4$)	309.8	996	0.06

AF = atrial fibrillation; Mod = moderate; MR = mitral regurgitation; NT-pro BNP = N-terminal brain natriuretic peptide; PTMC = percutaneous transvenous mitral commissurotomy; Sev = severe; SR = sinus rhythm.

that observed by Shang et al. [18] and Chadha et al. [20], who did not observe any difference in BNP/NT-proBNP levels between patients in SR and AF, but these studies were underpowered in terms of study group size.

Similar to Shang et al. [18], Seluck et al. [19], Chadha et al. [20], and Esteves et al. [23], a significant correlation between baseline NT-proBNP levels and PA pressures (systolic and mean) was noted. In addition, a significant correlation between NT-proBNP levels and LA volume (LA volume and LAVI) on transthoracic echocardiogram was also noted (Table 3). The significant positive correlation between baseline NT-proBNP levels and PA pressure may reflect the response of myocytes to chronic elevations of pressures in RV in MS patients. Studies in patients with lone AF [27,28] demonstrated a significant correlation between BNP levels and LAVI, reflecting the production of BNP in a stretched LA. This explains the correlation noted between NT-proBNP levels and LA volume and LAVI. Similar observations were reported by Davutoglu et al. [15], who noticed that in patients with RHD, a higher LA diameter correlated with a higher NT-proBNP level.

A significant decrease in NT-proBNP levels was noted following successful PTMC (Table 4); this was similar to previous studies [18–23]. Unlike Shang et al. [18] and Chadha et al. [20], a significant decrease in NT-proBNP levels were noted after PTMC, even in patients with AF (Table 5). A successful PTMC results in a decrease of pressure in LA, pulmonary artery, RV, and also a decrease in LA volume, which explains an expected decrease in NT-proBNP levels following PTMC even in patients with AF.

Similar to Seluck et al. [19], a significant correlation between percent change in NT-proBNP levels after PTMC and percent change in systolic PA pressures (immediate and after 48 hours) were noted (Table 6). A significant correlation has also been noted with percent decrease in LA volume and LAVI. The reversible nature of pulmonary hypertension in patients with MS and the decrease in LA volume following PTMC are a reasonable explanation for observed decrease in NT-proBNP levels.

Change in NT-proBNP level with a change in LA volume was observed by Therkelsen et al. [27] and Sacher et al. [28] in patients of lone AF where following cardio version/ablation they noticed a decrease in LA volume and decrease in NT-proBNP level. This observation goes with our findings, that a significant positive correlation between NT-proBNP and LA volume exists and

a decrease in NT-proBNP level following PTMC correlates with decrease in LA volume.

Four patients developed moderate-severe MR following PTMC – a significant increase in NT-proBNP was noted in them (Table 7). A significant MR following PTMC results in persistently high LA and PA pressures in these patients. An additional volume overload develops in LA and left ventricle, which might result in augmented secretion of NT-proBNP, thereby resulting in a higher NT-proBNP level.

Four other patients developed AF (lasting >24 hours) following PTMC (Table 7). In these patients, despite improvement in all echocardiographic and hemodynamic parameters, an increase in NT-proBNP levels was noted. New onset AF causes an increased tension in LA wall thereby increasing NT-proBNP which is countered by a decrease in NT-proBNP following a successful PTMC, and hence the probable net result of an insignificant increase in NT-proBNP levels in this subset of patients.

There are a few limitations in our study. Only patients with severe MS were studied, hence changes in NT-proBNP levels with increasing severity of MS could not be determined. Serial measurements of NT-proBNP immediately following PTMC, at 24 hours after PTMC, and during follow-up after 1 month could have added further information to our findings. Repeat hemodynamic measurements after 48 hours of PTMC could not be done as it is an invasive procedure and hence echocardiographic measurements of PA pressures and gradients across mitral valve were taken into consideration.

In conclusion, plasma NT-proBNP levels were significantly elevated in patients with severe MS, and they correlated with NYHA functional class of these patients. The baseline NT-proBNP levels correlated with LA volume, LAVI, systolic PA pressures, and mean PA pressures. Along with all echocardiographic and hemodynamic parameters, NT-proBNP also showed a significant improvement following a successful PTMC. The decrease observed in NT-proBNP levels which is statistically significant is noted in patients with SR, and also in those with AF. The decrease in NT-proBNP levels following PTMC correlated with decrease in LA volume, LAVI, an immediate decrease in systolic and mean PA pressures, and also decrease in PA pressures over 2 days.

The decrease in NT-proBNP levels following PTMC reflects an improvement in clinical status and an improvement in various echocardiographic and hemodynamic parameters following

PTMC. Thus, it seems reasonable to suggest that NT-proBNP is helpful in evaluating the response to PTMC in patients of severe rheumatic MS.

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