STUDY OF CHANGE IN N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS

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D.M. TRAINEE

A THESIS SUBMITTED FOR THE DEGREE OF DM CARDIOLOGY

DEPARTMENT OF CARDIOLOGY

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM

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DECLARATION

I, **Dr. Paidi Suresh Kumar,** hereby declare that the project in this book titled "**STUDY OF CHANGE IN N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS**" was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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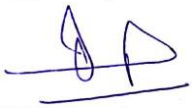
CERTIFICATE

I, hereby certify that the work in this dissertation titled "**STUDY OF CHANGE IN N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS**" is a certified record of original research work undertaken by Dr. Paidi Suresh Kumar done in the Department of Cardiology, in partial fulfillment of the requirement for the purpose of award of D.M. cardiology degree.



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TITLE

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CONTENTS

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Dr. Paidi Suresh Kumar

ABBREVIATIONS

ABBREVIATIONS

AF	-	Atrial fibrillation
AML	-	Anterior mitral leaflet
AR	-	Aortic regurgitation
AS	-	Aortic stenosis
BMV	-	Balloon mitral valvuloplasty
BMI	-	Body Mass Index
BNP	-	Brain natriuretic peptide
BSA	-	Body surface area
CMV	-	Closed mitral valvuloplasty
CO	-	Cardiac output
CI	-	Cardiac index
EF	-	Ejection fraction
Fr	-	French
GFR	-	Glomerular filtration rate
HR	-	Heart rate
LA	-	Left atrium
LAE	-	Left atrial enlargement
LAP	-	Left atrial pressure
LVEDP	-	Left ventricular end diastolic pressure
LVEF	-	Left ventricular ejection fraction
LVIDD	-	Left ventricular internal diameter in diastole
LVIDS	-	Left ventricular internal diameter in systole
MAP	-	Mean arterial pressure
MPAP	-	Mean pulmonary artery pressure
MR	-	Mitral regurgitation
MS	-	Mitral stenosis
MV	-	Mitral valve
MVA	-	Mitral valve area
MVG	-	Mitral valve gradient
MVR	-	Mitral valve replacement
NYHA	-	New York Heart Association

NP - Natriuretic Peptides
NT-proBNP - N-Terminal pro Brain natriuretic peptide
PA - Pulmonary artery
PAH - Pulmonary artery hypertension
PASP - Pulmonary artery systolic pressure
PADP - Pulmonary artery diastolic pressure
PAmP - Pulmonary artery mean pressure
PBMV - Percutaneous Balloon mitral valvuloplasty
PCWP - Pulmonary Capillary wedge pressure
PHT - Pressure half time
PML - Posterior mitral leaflet
PBMV - Percutaneous transvenous mitral commissurotomy
PVR - Pulmonary vascular resistance
RA - Right Atrium
RAD - Right axis deviation
RHD - Rheumatic heart disease
RVH - Right ventricular hypertrophy
RVSP - Right ventricular systolic pressure
RVEDP - Right ventricular end diastolic pressure
SD - Standard deviation
SR - Sinus rhythm
SVR - Systemic vascular resistance
TAPSE - Tricuspid annular plane systolic excursion
TEE - Transesophageal echocardiography
TMG - Transmitral gradient

SYNOPSIS

SYNOPSIS

Introduction: The change in serum levels of NT-proBNP (N-terminal pro-brain natriuretic peptide) is considered as reflection of hemodynamic alterations. The decrease in pressures in the left atrium (LA) and right side of the heart following PBMV cause a decrease in wall stress which contributes to the decreased NT-proBNP levels.

Aim: This present study is designed to assess the change in serum levels of NT-proBNP following PBMV (percutaneous balloon mitral valvuloplasty) and association between NT-proBNP reduction and various echocardiographic and hemodynamic parameters.

Methods: This is a Prospective Observational study consisted of 92 patients with rheumatic severe mitral stenosis (MS) who underwent PBMV. Serum NT-proBNP levels were measured 30minutes prior to the commencement of PBMV and 24 hours after PBMV. These values were correlated with various echocardiographic and hemodynamic parameters which were obtained before and after procedure.

Results: Eighty percent of the study population were women, and the common presenting symptom was dyspnea which was present in 100% of the patients. Baseline NT-proBNP levels in these patients significantly correlated with New York heart association (NYHA) functional class ($r = 0.377$; $p < 0.001$), left atrial diameter ($r = 0.207$; p 0.047), mean pulmonary artery pressures ($r = 0.338$; $p < 0.001$) and mean left atrial pressures ($r = 0.207$; p 0.048). Patients who were in atrial fibrillation had significantly higher NT-proBNP levels than patients in sinus rhythm (775 vs 481; $p <0.001$). All patients who underwent successful PBMV showed a significant decrease in NT-proBNP (decreased from a mean 580 pg/mL to 328 pg/mL) along with a significant improvement in various echocardiographic and hemodynamic parameters ($p < 0.001$). The change in NT-proBNP correlated significantly with the improvement with mean left atrial pressure ($r = 0.407$; p 0.020). Area under the ROC for NT-proBNP as a predictor of mitral valve area less than 1 cm^2 was 0.90 [95% CI 0.84-0.96]. When using a NT-proBNP cut-off value of more than 302 pg/ml, sensitivity was 90.1% and specificity was 61.9%. Area under ROC for change in NT-proBNP post PBMV as a predictor of mean left atrial pressure less

than 12 mm of Hg post PBMV was 0.93 [95% CI 0.88-0.98], when using change in NT-proBNP post PBMV, cut-off value of more than 238.5 pg/ml, sensitivity of 93.1% and specificity of 74.6%.

Conclusion: The decrease in serum NT-proBNP levels post procedure reflects procedural success as evidenced by correlation between reduction in NT-proBNP and improvement in echocardiographic and hemodynamic parameters, hence it is reasonable to consider serum NT-proBNP as a marker of successful PBMV.

Keywords: Mitral stenosis, N-terminal pro-brain natriuretic peptide, Percutaneous balloon mitral valvuloplasty.

INTRODUCTION

INTRODUCTION

Mitral stenosis (MS) first described by Vieussens in 1705, first disease to be diagnosed by echocardiography[1] and the first valve lesion to be treated by surgery[2] and percutaneous balloon mitral valvuloplasty (PBMV)[3]. It is highly prevalent in low and lower-middle income countries because of high prevalence of rheumatic fever. The first invasive therapeutic option, which should be considered in patients with mitral stenosis with favourable valve morphology, is percutaneous balloon mitral valvuloplasty (PBMV)[4]. The PBMV results in decreasing atrial and pulmonary pressure with increasing left ventricular preload[5].

Brain natriuretic peptide (BNP), a cardiac neurohormone secreted predominantly by ventricles and to some extent by atrium, has a regulatory and modulatory role in the cardiovascular system by its diuretic, natriuretic, and vasodilator actions[6]. Two previous reports demonstrated an association between elevated BNP levels and left atrial dimension, indicating BNP synthesis in atrial myocytes in response to an increase in left atrial pressure[7]. Atrial fibrosis and increased left atrial wall stress are the common pathophysiological changes associated with both MS and atrial fibrillation that may contribute to the elevated plasma levels of BNP. N-terminal pro-brain natriuretic peptide is part of prepro-BNP, which is secreted in a proportion equivalent to brain natriuretic peptide (BNP). It is more stable than BNP due to its longer half-life, therefore higher levels of NT-proBNP are observed.

The prognostic role of various natriuretic peptides (NP) in valvular heart diseases has been extensively studied. It was noted that various natriuretic peptides were elevated in patients with MS, and a few of them correlated with the severity of MS according to echocardiography (lower mitral valve area, higher peak mitral gradient and mean mitral gradient) and hemodynamics (higher pulmonary capillary wedge pressure and lower cardiac output) [8]. Following a successful PBMV, a decrease in various NPs is expected and a few studies have evaluated this change [9]. Although NT-pro-atrial-NPs are increased in patients of mitral stenosis along with BNP and NT-proBNP, due to the availability of laboratory tests and reproducibility usually only BNP or NT-proBNP is used.

Only few studies have evaluated the change in NT-proBNP levels in patients of severe MS following PBMV. The reversible nature of the pulmonary hypertension in MS may be an explanation for the decrease in NT-proBNP levels after PBMV. The decrease in pressures in the left atrium (LA) and right side of the heart following PBMV cause a decrease in stress on left atrium which contributes to the decreased NT-proBNP levels. 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 PBMV.

AIMS AND HYPOTHESIS

AIMS AND HYPOTHESIS

AIMS

- To assess the change in the serum level of NT-proBNP following PBMV in patients with rheumatic mitral stenosis.
- Determine the association between circulatory NT-pro-BNP reduction, post-PBMV echocardiography and hemodynamic parameters in overall cohort and also in subgroups (sinus rhythm, atrial fibrillation).
- Comparison between patients in sinus rhythm and atrial fibrillation with respect to change in parameters post procedure

HYPOTHESIS

- NT-pro-BNP reduces post PBMV and correlates with other Echocardiographic and hemodynamic parameters.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Rheumatic fever (RF)/rheumatic heart disease (RHD) is the result of autoimmune response to group A beta-hemolytic streptococcal pharyngitis leading to immune mediated inflammatory injury to cardiac valves. The inflammatory injury of the pericardium and myocardium is transient and self-limiting, without leaving any squeal. The valvular injury is the main cause of acute and long-term morbidity and mortality in patients with acute RF and RHD, respectively[13]. The risk of RF/RHD is primarily determined by the host, agent and environmental factors[14]. RF/RHD is considered to be a physical manifestation of poverty. The distribution of the burden of RF/RHD mirrors the distribution of human development index in given geographical region, state, and nation, as well as globally. The socioeconomic state, access, and quality of health-care services are important determinants of the burden of RF/RHD. The incidence of RF/RHD has practically disappeared in developed countries. However, RF/RHD continues to be a major cause of disease burden among children, adolescents, and young adults in low-income countries and even in high-income countries with socioeconomic inequalities. The burden of RF/RHD is likely to be variable among countries, within the country, within states depending upon the socioeconomic status and state of health systems. The major determinant of the persistent burden of RF/RHD in low income and lower-middle income countries are because of poor standards of living conditions, overcrowding, and lack of strong population-based surveillance system for pharyngitis, RF and RHD for effective implementation of primary and secondary preventive interventions

Although a worldwide decline in health-related burden of RHD was noted, the global burden of rheumatic heart disease continues to be significant although it is largely limited to poor and marginalized populations. The persistence of high rates of RHD in poor regions of the world where RHD remains endemic (defined as having high RHD-related mortality exceeding 0.15 deaths per 100,000 population among children 5–9 years of age). Overall, there were an estimated 38.0 million to 40.8 million cases of RHD globally in 2017, with the highest prevalence, disability, and mortality in Oceania, South Asia, and sub-Saharan Africa[15]. The prevalence ranged from 3.4 cases per 100,000 population in non-endemic countries to >1000 cases per 100,000 in endemic countries. There are a few reports of sporadic outbreaks of acute rheumatic fever (ARF) in the United States in the 1980s and 1990s and more recent reports from Australia and Italy[16].

Gender is an important biological determinant of susceptibility to diseases and their outcomes. The sex hormones are known to regulate both adaptive and innate immune responses. It is a well-established fact that autoimmune diseases have gender predilections. RHD is an autoimmune-mediated valvular injury, therefore, the autoimmune response may differ between genders, leading to differences in valvular damage and severity. The epidemiological studies of RF and RHD report no gender predilection for the incidence of RF; however, RHD is more prevalent in females[17].

RHD typically affects left-sided valves, with greater affinity and consequence for the mitral valve. Characteristic acute mitral valvulitis shows mitral annulus dilatation, chordal elongation, and anterior leaflet prolapse, with varying degrees of MR and rarely chordal rupture. Isolated aortic disease occurs in 2% of cases. Right-sided valve disease is not infrequent, typically affects the tricuspid valve (as primary valvulitis or as the result of deleterious hemodynamic consequences of left-sided valve disease), and rarely affects the pulmonic valve. Acute rheumatic valvulitis manifests as valvular regurgitation, but over time, chronic inflammation leads to valve stenosis from commissural fusion with or without associated regurgitation in a subset of patients. MS from commissural fusion, with variable degrees of involvement of other parts of the mitral valve apparatus, is the hallmark lesion of the later stages of RHD. The more malignant fulminant course of RHD, linked to recurrent bouts of ARF, occurs in the most endemic regions of the world[18].

MS limits blood flow from the left atrium to the left ventricle, and over time, the most common clinical manifestation of MS is exertional dyspnea and exercise intolerance, which worsens gradually. Some serious potential complications are associated with prolonged disease: while the stenosis progresses, pressure in the left atrium rises, resulting in left atrial enlargement and eventually atrial tachyarrhythmia: atrial fibrillation or flutter. These in turn can lead to thromboembolic events, most frequently to the cerebral circulation, resulting in cerebral ischemia and neurological damage. The elevated pressure in the left atrium can also result in pulmonary congestion and hypertension, which affect the right side of the heart, resulting in right ventricle dysfunction and tricuspid regurgitation. In turn, this may result in peripheral edema, ascites, and pleural effusions. Heart failure symptoms develop with progressive heart valve damage. It should also be considered that because of the slow, progressive nature of many valve lesions, patients may not recognize symptoms because they may have gradually limited their daily activity levels. Although chronic heart valve disease is often manifested in adolescents and young adults, advanced valve damage happens earlier in life in the most endemic regions. Patients may be diagnosed after a known ARF attack, however, a significant portion of RHD patients,

well over 50% in low and middle income countries, may present without any prior symptoms or memory of ARF. In these settings, RHD may present for the first time during pregnancy or after a complication such as acute heart failure, atrial arrhythmia, an embolic event, or infective endocarditis (IE). Most patients have heart failure symptoms at the time of clinical diagnosis through auscultation of pathological heart murmurs.

An electrocardiogram and chest radiograph can be helpful in the initial assessment of RHD patients. Although electrocardiography findings are not specific for RHD, they may demonstrate left atrial or right ventricular enlargement and ventricular strain. In more severe degrees of mitral valve damage, especially in older patients, atrial fibrillation may be present. The chest radiograph may show an enlarged left atrium or right ventricle and radiological signs of pulmonary venous congestion in more advanced cases[19].

The acceptable tool used to determine stenosis severity is the echocardiogram, based on European Association of Echocardiography /American Society of Echocardiography (EAE/ASE) definitions[20]. The severity of the stenosis is assessed by echocardiographic findings, with mitral valve area (MVA) as a main parameter and mean gradient and pulmonary artery pressure as supportive findings.

Table 1 : Grading of severity of mitral stenosis

Criteria for determining severity of mitral valve stenosis			
	Mild	Moderate	Severe
Mitral valve area (cm^2)	>1.5	1-1.5	<1
Mean Gradient (mm Hg)	5	5-10	>10
Pulmonary Artery Systolic Pressure (mm Hg)	30	30-50	>50

mm Hg- millimeters of mercury

As per 2020 ACC/AHA Guidelines for the Management of Valvular Heart Disease[4], stages of MS are defined by patient symptoms, valve anatomy, valve hemodynamics, and the consequences of valve obstruction on the left atrium (LA) and pulmonary circulation.

Table 2 : Stages of mitral stenosis

Stages	Definition	Valve Anatomy	Valve hemodynamics	Hemodynamic consequences	Symptoms
A	At risk of MS	Mild valve doming during diastole	Normal transmitral flow velocity	None	None

B	Progressive MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets. Planimetered MVA >1.5 cm^2	Increased transmitral flow velocities MVA >1.5 cm^2 Diastolic PHT <150ms	Mild to moderate LA Enlargement. Normal PASP at rest.	None
C	Asymptomatic severe MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets. Planimetered MVA ≤1.5 cm^2	MVA ≤1.5 cm^2 Diastolic PHT ≥150ms	Severe LA enlargement. Elevated PASP >50 mm Hg	None
D	Symptomatic severe MS	Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets. Planimetered MVA ≤1.5 cm^2	MVA ≤1.5 cm^2 Diastolic PHT ≥150ms	Severe LA enlargement. Elevated PASP >50 mm Hg.	Decreased exercise tolerence, exertional dyspnea

MS mitral stenosis, mm Hg millimetres of mercury, MVA mitral valve area, PHT pressure half time, PASP pulmonary artery systolic pressure, LA left atrium

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 (PBMV), surgical mitral commissurotomy, and mitral valve replacement. A successful PBMV results in improvement in mitral valve area, thereby causing a decrease in left atrial pressures, decrease in pulmonary artery (PA) pressures, and increase in left ventricular end diastolic pressure.

As per European society of cardiology (ESC) 2017 guidelines for management of valvular heart disease[38] indication for intervention in mitral stenosis-

- Should be limited to patients with clinically significant (moderate to severe) mitral stenosis (valve area <1.5 cm^2).
- May be considered in symptomatic patients with a valve area >1.5 cm^2 if symptoms cannot be explained by another cause and if the anatomy is favourable.

As per American college of cardiology (ACC)/ American heart association (AHA) 2020 guidelines for management of valvular heart disease[4] indication for intervention in mitral stenosis

- In symptomatic patients (NYHA class II, III, or IV) with severe rheumatic MS (mitral valve area ≤1.5 cm^2, Stage D) and favourable valve morphology.
- In asymptomatic patients with severe rheumatic MS (mitral valve area ≤1.5 cm^2, Stage C) and favourable valve morphology

Randomized trials have established the safety and efficacy of PBMV as compared with surgical closed or open commissurotomy in patients with a favourable valve morphology with less than 2+ MR in the absence of LA thrombus. Favourable valve morphology consists of

- Mobile and relatively thin valve leaflets
- Free of commissural calcium
- Absence of significant subvalvular fusion

An anatomic mitral morphology score can be used to determine suitability for PBMV and to evaluate the appearance of the commissures and degree of calcification.

Long-term follow-up has shown 70% to 80% of patients with an initial good result after PBMV to be free of recurrent symptoms at 10 years, and 30% to 40% are free of recurrent symptoms at 20 years[20].

Natriuretic Peptides

Various biomarkers have been examined for diagnosis and assessment of VHD severity and preoperative risk stratification. The list of such biomarkers is long and includes but is not limited to atrial natriuretic peptide (ANP), brain natriuretic peptide

(BNP), N-terminal-pro-BNP (NT-pro-BNP). For a biomarker to be used in assessment and management of VHDs, it must reflect atrial or ventricular wall stress and predict echocardiographic, clinical progression of the disease and provide prognostic information. Among the various biomarkers, natriuretic peptides have shown promising results in several studies.

Atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) are the two major hormones which are produced by cardiac myocytes in response to increased stress in the form of either pressure or volume overload. ANP is generally stored in the atrial muscles and released in response to stretch, whereas BNP is released predominantly by ventricles and to some extent by atria. This was supported by evidence for synthesis of BNP by atrial myocytes in response to chronic increase in wall stress and co-storage of BNP with ANP in atrial granules. BNP is a prohormone which is cleaved to produce its inactive form known as NT-pro-BNP. They both exert diuretic, natriuretic, and hypotensive effects by inhibition of renin-angiotensin system and sympathetic activity.

Head to head comparisons between BNP and NT-proBNP showed that NT-proBNP may be more discerning marker of early cardiac dysfunction and prognosis than BNP, particularly in structural heart disease patients [39]. The potential advantage may be due partly to sensitivity of NT-proBNP to renal dysfunction and less testing variability. Notably, as the normal values of NT-proBNP increase with age and in women, the absolute level of NT-proBNP must be interpreted with caution. This confounding effect of demographics becomes particularly crucial in patients with VHD for aging nature of target population and sex differences in prevalence. Altogether studies focusing on disease-specific use of NT-proBNP with age and sex and assessing a hard endpoint are necessary, as demonstrated in previous studies concerning BNP.

The normal plasma concentration of NT-pro-BNP tends to be higher than BNP by as much as 10-fold given the former has a longer half-life of 1-2 hours as compared to the half-life of BNP being approximately 22 minutes. The diagnostic and prognostic role of NT-proBNP in left ventricular dysfunction of various etiologies has been extensively studied. The best-established and widely used clinical application of BNP and NT-proBNP testing is for the emergent diagnosis of CHF in patients presenting with acute dyspnea. BNP and NT-proBNP, as the European Society of Cardiology recommended, are helpful in the diagnosis of HF and providing prognostic potential; as well at a low-normal concentration in untreated patients makes HF unlikely as the cause of symptoms[21].

According to heart failure association of ESC practical guidance on the use of natriuretic peptide concentrations 2019, cut-off values of BNP and NT-proBNP for the diagnosis of acute HF [40].

Table 3 : Cut-off values of BNP and NT-proBNP for the diagnosis of acute heart failure and in non-acute settings

	BNP (pg/ml)	NT-proBNP (pg/ml)
Rule out	<100	<300
Rule in	>400	<50 years- > 450 50-75 years- > 900 >75 years- >1800
Cut-off values of BNP and NT-proBNP in non-acute setting with mild symptoms		
	BNP (pg/ml)	NT-proBNP (pg/ml)
Rule in	>150	>600
Rule out	<35	<125

BNP- Brain natriuretic peptide, NT-proBNP- N terminal pro-brain natriuretic peptide

Elevated NPs levels can be also found in many circumstances involving LV dysfunction or hypertrophy; right ventricular (RV) dysfunction secondary to pulmonary diseases; cardiac inflammatory or infectious diseases; and endocrinology diseases and high output status without decreased left ventricular ejection fraction (EF), e.g., sepsis, renal failure, cirrhosis of liver, or intracranial pathologies. Even in the absence of significant clinical evidence of volume overload or LV dysfunction, markedly elevated NP levels can be found in patients with multiple comorbidities with certain degree of prognostic value[22].

In valvular heart diseases, BNP serum level was found to be related to functional class and prognosis, particularly in aortic stenosis (AS) and mitral regurgitation (MR). European guidelines for the diagnosis and management of VHD indicate using BNP in AS and MR but without definitive recommendations. In patients with chronic asymptomatic MR, several studies suggested the value of elevated BNP levels and a change in BNP as predictors of outcome. A cut-off BNP value ≥105 pg/ml determined in a derivation cohort was prospectively validated in a separate cohort and helped to identify asymptomatic patients at higher risk of developing heart failure, LV dysfunction or death on mid-term follow-up, and baseline low-plasma BNP had a high negative predictive value and might be helpful for the follow-up of asymptomatic organic MR patients[23].

For other types of VHD like aortic regurgitation, mitral stenosis, tricuspid regurgitation and multi-valvular heart disease, natriuretic peptides have been investigated only in small studies with controversial outcomes. Natriuretic peptides particularly NT-proBNP, in the prognosis of VHD remains a promising investigation but underexplored field.

Natriuretic Peptides in Mitral Stenosis

The diagnostic and prognostic value of natriuretic peptides in various valvular heart disease has been studied extensively. It has been noted various natriuretic peptides elevated in mitral stenosis patients, of which few of them correlated with severity of the disease.

In a study by Namik Kemal Eryol, et al., 2007, The relationship of BNP with mitral stenosis and other echocardiographic parameters were studied. The comparison of the 3 groups (mild, moderate, severe mitral stenosis) with one another revealed that the BNP level in the group with moderate MS was higher than that in the group with mild MS, however it was statistically insignificant (74.9 +/- 49.7 versus 49.9 +/- 40.5 pg/ml, $p > 0.05$). BNP level in the group with severe MS was significantly higher than that in the mild MS (144.3 +/- 83.9 versus 49.9 +/- 40.5 pg/ml, $p < 0.001$) and that in the moderate MS group (144.3 +/- 83.9 versus. 74.9 +/- 49.7 pg/ml, $p < 0.05$). When patients were taken together, as the area of the mitral valve decreased, the level of BNP underwent a corresponding increase (r 0.48, $p < 0.001$). They have ascertained that the level of plasma BNP and the degree of MS are significantly correlated, and as MS becomes more serious, the plasma BNP level rises[24].

In a study by Iltumur, et al., where 32 patients with MS (mean age 41.2 +/- 5.7 years) and 30 healthy individuals (mean age 40.3 +/- 4.9 years) were included in the study. In addition to NT-proBNP measurements, detailed transthoracic echocardiography was performed in all patients and healthy subjects. They Plasma levels of NT-proBNP were significantly higher in patients with MS than in controls (99.8 +/- 12.7 versus 48.5 +/- 10.5 pg/ml, $p <0.0001$). NT-proBNP levels showed a significantly greater increase in severe MS than in moderate MS (109.8 +/- 5.6 versus 88.3 +/- 7.6 pg/ml, $p <0.0001$). Although NT-proBNP levels did not correlate with left ventricular ejection fraction (LVEF) in patients with MS ($r = -0.33$; $p >0.05$), there was a positive correlation with pulmonary artery pressure ($r = 0.87$; $p <0.001$) and a negative correlation with mitral valve area (MVA) (r -0.89; $p <0.0001$)[25].

Natriuretic Peptides as an alternative to stress testing in asymptomatic patients

Current European Society of Cardiology (ESC) guidelines for management of valvular heart diseases (2017), recommend doing percutaneous mitral commissurotomy (PMC) for patients with clinically significant mitral stenosis (MS) (mitral valve area ≤1.5 cm^2) with suitable valve scores if patients are symptomatic. In asymptomatic patients, intervention is justified for those who become symptomatic on exercise testing and those who had low exercise capacity [achieve <5 Metabolic Equivalents (METs)]. Hence regular follow up for patients with significant mitral stenosis is crucial to take the proper decision of intervention in the proper time (either surgical replacement or alternatively balloon commissurotomy if the valve morphology is suitable). It is frequently encountered that rheumatic MS patients describe equivocal symptoms. Due to the long latent period between onset of the initial rheumatic valvular affection and development of significant mitral stenosis, it is difficult for the treating physician to truly identify patients with symptoms that could be attributed to either hemodynamically significant stenosis or non cardiac dyspnea. Some patients have a sedentary life style that may result in physical deconditioning and subsequently exertional symptoms. On the other hand, other patients who are considered asymptomatic adapt their level of exertion and thereby do not get symptoms. Symptomatic status is mainly subjective, and hence a better risk stratification objective tool is required to be implemented in regular follow up of rheumatic MS patients.

In a study by Kilickesmez, et al. In 2011 who found a correlation between NT pro-BNP level and exercise-induced augmentation of pulmonary artery pressure in patients with moderate to severe, asymptomatic or mildly symptomatic mitral stenosis. They studied 41 asymptomatic or mildly symptomatic moderate to severe mitral stenosis patients versus 21 age and sex-matched control healthy subjects. They found that the plasma concentrations of NT pro-BNP levels were significantly higher in patients with mitral stenosis than in control subjects before and after exercise ($P < 0.001$). The plasma levels of pre-exercise NT pro-BNP positively correlated with increasing right ventricular and LA diameter ($r = 0.339$, $P = 0.030$; $r = 0.481$, $P < 0.001$ respectively), exercise duration ($r = -0.365$, $P = 0.019$), resting heart rate ($r = 0.482$, $P = 0.001$), increasing rest and exercise pulmonary artery systolic pressure ($r = 0.530$, $p < 0.001$; $r = 0.505$, $P = 0.001$ respectively), and increasing post test mitral valve mean gradient ($r = 0.332$, $P = 0.034$). Positive correlation was observed between severity of post-exercise systolic pulmonary artery pressure and plasma NT pro-BNP levels. No statistically significant correlation was

found between pre-exercise NT pro-BNP with increasing left ventricle end diastolic diameter, rest mean mitral gradient, post-exercise heart rate, and decreasing mitral valve area. Post-exercise NT pro-BNP levels correlated significantly with the LA dimension ($r = 0.497$, $p = 0.044$), RV end diastolic diameter ($r = 0.344$, $P = 0.028$), exercise duration ($r = -0.331$, $P = 0.034$), heart rate ($r = 0.482$, $P = 0.001$), rest and post-exercise pulmonary artery systolic pressure ($r = 0.531$ $P < 0.001$; $r = 0.486$, $P = 0.001$, respectively), and mitral valve mean gradient ($r = 0.327$, $P = 0.037$). Analysis of the receiver-operating characteristic curve for NT pro-BNP as a predictor for the exercise induced pulmonary artery systolic pressure increase on exercise stress echocardiography showed an area under the curve of 0.78 (95% confidence interval 0.626–0.901, $P < 0.001$. Using an optimized cut-off level at 251 pg/mL derived from the receiver-operating characteristic curve for NT pro-BNP as a predictor for the exercise induced augmentation of peak PAP >60 mmHg, sensitivity was 89.4%, specificity was 70.0%. A multivariate regression analysis was performed for predictors of higher post-exercise pulmonary artery systolic pressure (PAP >60 mmHg) including age, gender, echocardiographic parameters, exercise time, heart rate, and pre and post-exercise levels of NT pro-BNP as variables. In this analysis, LA diameters and pre-test NTpro-BNP were independent predictors of higher post exercise PAP. These results suggest that increased plasma levels of pre-exercise NT pro-BNP is a predictor of pulmonary artery systolic pressure increase to >60 mmHg after exercise [26].

In a study by Ahmed El Zayat, et al., 2014 with an aim to evaluate the ability of a single baseline BNP level assessment to truly identify an important subset of asymptomatic clinically-significant rheumatic MS patients (with suitable valve scores for PBMV) whose exercise stress criteria (clinical and echo-Doppler) meet the ESC contemporary guidelines for intervention. 33 patients (group 1) who became symptomatic on exercise and had low exercise capacity were compared to 37 patients (group 2) who were asymptomatic on exercise and had reasonable exercise capacity. BNP level in group 1 was 92 ± 12 compared to 40 ± 10 pg/ml in group 2 ($P < 0.001$). Post PMC, BNP in group 1 significantly decreased (92 ± 12, compared to 31 ± 9 pg/dl, $P < 0.001$). There was a positive correlation between resting mitral valve area ($r = 0.327$, $P < 0.01$), left atrial dimension ($r = 0.285$, $P < 0.05$), resting mean transmitral gradient ($r = 0.319$, $P < 0.01$), baseline BNP level ($r = 0.635$, $P < 0.001$) and post-exercise elevation of SPAP >60 mmHg. Area under the ROC curve for BNP as a predictor of low exercise capacity and development of symptoms on exercise was 0.98 [CI 95% 0.96–1.0]. When using a cut-off

value of 55 pg/mL for BNP, sensitivity was 93.9% and specificity was 91.9% positive predictive value was 91.2% and negative predictive value was 94.4%[27].

NT-proBNP and Left Atrial Function in Mitral Stenosis

LA function has been conventionally divided into three phases

- Reservoir
- Conduit
- Pump

As a reservoir, the LA stores pulmonary venous return during left ventricular contraction and isovolumetric relaxation. As a conduit, the LA transfers blood passively into the LV. As a pump LA actively contracts during the final phase of diastole and contributes between 15 and 30% of LV stroke volume. As a continuum of the LV, especially during diastole, its size and function are very much influenced by the compliance of the LV. Various studies have observed negative correlations between NT-proBNP levels and LA reservoir and pump functions. In a study by Hoit et al. who examined LA mechanics during LV dysfunction and compared the compensatory response with a normal atrium versus a failing atrium (induced with rapid atrial pacing). With a normal atrium, reservoir function increased by 19% and booster pump function (atrial contraction) nearly doubled to maintain cardiac output despite a fall in LVEF from 57% to 32%. In contrast, with a failing atrium, reservoir function fell by 30%, conduit function increased by 33%, and atrial kick disappeared. Results showed that in conditions with the same LA sizes, the reservoir function of the LA could be diminished more significantly in pressure overload than volume overload, which means that pressure overload may have more pathologic effects on the atrial wall and its function[28].

LA pressure overload secondary to mitral stenosis leads to LA dilation, regardless of the severity of mitral stenosis, which in turn suggests that there are other factors beside the valvular obstacle that may influence LA dimensions, like intraatrial pressure variability, valvular compliance and resistance. Data derived from histopathological findings in atrial specimens obtained during surgery suggest there is an extensive interstitial fibrosis in both atria, associated with myocyte hypertrophy especially seen in patients in sinus rhythm, compared with patients with atrial fibrillation, where myocytolysis is the predominant histological change. Myocyte hypertrophy is a marker for cellular degeneration, associated with significant ultrastructural changes, such as myofibrillar destruction, a process that leads in time to a decrease and even to a loss of contractile function. During ventricular

systole, the left atrium has a reservoir function, collecting blood drained by the pulmonary veins that leads to LA filling and distension. In patients with mitral stenosis, elevated LA filling pressures lead to a decrease in pulmonary vein blood flow and, on the other side, to an increase in LA parietal tension, which in turn determines LA dilation and an alteration of the reservoir function. During early diastole, once the mitral valve opens, the LA acts as a conduit, allowing passive blood flow from the atrium to the left ventricle, this function being influenced by both LV diastolic relaxation and by mitral valvular resistance. In patients with mitral stenosis, although there is an increase in intra-atrial pressure and a decrease in LV intraventricular pressure, leading to a significant atrioventricular diastolic gradient, the passive blood flow during early diastole is restricted because of important valvular resistance. Thus, the LA conduit function is altered. LA booster pump function plays a very important role in maintaining an adequate cardiac output in patients with mitral stenosis, despite the valvular obstacle, therefore a loss of this function may lead to a worsening of heart failure. In patients with mitral stenosis both LA active emptying fraction significantly impaired, suggesting a failure of the LA pump secondary to LA dilation. Therefore, adaptative LA dilation as a response to LA pressure overload due to the valvular obstacle is correlated with a loss in LA contractility. Besides the aforementioned changes, the LA remodelling process has also functional consequences, leading to neurohormonal changes, where the increase in BNP and NT-proBNP was positively correlated with LA dimensions, and negatively correlated with mitral stenosis severity and LA reservoir and booster pump function. Interstitial fibrosis and cellular dissociation in patients with atrial dilation lead to electrical dispersion, a favourable substrate for initiating and maintaining reentry circuits which in turn are the main determinants for atrial fibrillation. Atrial fibrillation is the most common arrhythmia in patients with mitral stenosis, with atrial dilation is its main predictor, where an increase in LA dimensions is associated with the risk for developing atrial fibrillation[29].

NT-proBNP Assay Methods

First-generation assays for brain natriuretic peptide (BNP) were competitive radioimmunoassays that required extraction and purification of the plasma sample. Second-generation assays were based on monoclonal antibodies and radioisotope labels. These assays provided improved sensitivity and precision. Commercial versions of the monoclonal antibody assay first appeared in 1994 and initially required 12-36 hours to complete. Third-generation assays, which provided results in as little as 15 minutes, became available in 2000. These rapid assays used immunofluorescent methods. All of the commercially available assays for BNP and NT-proBNP for clinical use are rapid

immunoassays. The assay used in the Breathing Not Properly study, which first suggested clinically useful BNP cut-off values for diagnosing acute congestive heart failure (CHF), was the point-of-care Triage BNP Test. Other rapid-turnaround BNP assays are marketed, including the ADVIA Centaur BNP assay and the AxSYM BNP assay. Assays for the NT-proBNP fragment became available in late 2002. The Elecsys NT-proBNP assay was evaluated in the ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) study. Other NT-proBNP assays include the Dimension test, the Stratus CS Acute Care NT-proBNP assays and AQT90 FLEX NT-pro BNP immunoassay analyser [41].

MATERIALS AND METHODS

MATERIALS AND METHODS

This is a Prospective Observational study consisted of 92 patients with rheumatic severe MS who underwent PBMV at department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India between May 2019 and May 2021.

The protocol was approved by the Institutional Ethics Committee [SCT/IEC/1412]

Inclusion Criteria:

All Patients with severe MS (2-dimensional MVA < 1.5cm^2) who were candidates for PBMV, as per standard indications and guidelines of PBMV between the period may 2019 to may 2021 were included.

Exclusion criteria:

- Left ventricular ejection fraction (LVEF) less than 50%
- Coexistent valvular abnormality of more than moderate severity
- History of myocardial infarction or known coronary artery disease
- Chronic Renal dysfunction of stage 3 or higher
- Hepatic Failure
- Severe chronic obstructive pulmonary disease
- Mitral regurgitation of more than moderate severity,
- Thrombus in LA or LA appendage in TEE
- Patients with pulmonary oedema, congestive cardiac failure or in NYHA functional class IV.
- Those developing severe MR following PBMV requiring immediate surgical intervention were excluded from the study.

METHODOLOGY

The clinical, echocardiographic and hemodynamic parameters at the time of PBMV were analysed. All the patients prior to the procedure had detailed clinical and echocardiographic evaluation. The data collected included NYHA class and heart rhythm. Mitral valve structural pathology was assessed. Commissural calcification was assessed for the suitability of PBMV. Mitral valve area was determined by 2D echo planimetry and doppler pressure half time method. LA diameter measured in parasternal long axis (PLAX) view was taken. Mitral regurgitation was assessed by colour Doppler according to the degree of jet extension into the left atrium using Helmcke classification[10]. Maximum regurgitant jet area/ left atrial area from three orthogonal planes < 20% was defined as mild, 20-40% as moderate and > 40% as severe. Transmitral gradient was measured in apical four chamber view by continuous wave Doppler. Pulmonary artery hypertension was assessed by the right ventricular systolic pressure with peak tricuspid regurgitation jet velocity using modified Bernoulli's equation ($4v^2$ + Estimated right atrial pressure).

Prior to the procedure, transesophageal echocardiography was performed for every patient to rule out any clot in the left atrial body or the left atrial appendage. In addition transesophageal echocardiography provided additional information on the mitral valve structure and the severity of mitral regurgitation. The contraindications to the procedure were MR assessed by echocardiography of more than mild degree and left atrial (LA) thrombus on trans-esophageal echocardiography (TEE) performed prior to PBMV. Echocardiography was repeated within 24 hours after the procedure to evaluate mitral valve area, to assess the severity of mitral regurgitation and to detect the presence of iatrogenic atrial septal defect.

Hemodynamic data was obtained from the cardiac catheterization at the time of BMV. Right and left heart catheterization was performed and transseptal puncture was done using Brockenbrough needle. Mean left atrial pressure, left ventricular end diastolic pressure, pulmonary artery pressure, transmitral gradient, mitral valve area, cardiac output and the cardiac index were obtained and compared between the two groups.

BMV was done using Accura balloon (Vascular concepts, Essex, UK) using the Inoue technique [11]. Maximum balloon size was chosen using the formula[12].

Balloon size (mm) = (Patient's height (cm)/10) +10

A 2-mL blood sample was collected with venipuncture into heparinised tubes 30 minutes before commencement of PBMV and 24 hours after PBMV. NT-proBNP levels were measured using Point-of-care biomarker testing AQT90 FLEX immunoassay analyser. The reaction time for the assay is about 10–15 minutes and the detection range of the assay is 70–35000 pg/mL.

Procedural success was defined as increase in mitral valve area of at least 50% from the basal or a final valve area of >1.5 cm^2 with no major complications. Major complications included cardiac tamponade, systemic embolism, or death, increase in MR grade ≥3 or shunt across the iatrogenic septal defect ≥2.

STATISTICAL ANALYSIS

Data are expressed as mean ± standard deviation. Continuous variables were analysed using unpaired Student's t test and categorical variables using Chi-square and Fisher exact test. Comparison of variables before and after the procedure was carried out using paired t test. A p value <0.05 was considered to be significant. All analyses were performed using SPSS 26.

RESULTS

RESULTS

Baseline characteristics of the study population

Total 94 patients underwent PBMV during the study period of which 2 patients developed acute MR requiring emergency MVR, hence 2 patients were excluded and 92 patients were analysed. Most of the study population were women (74 out of 92 accounting to 80.4%) with women to men ratio (4.1:1) and age ranging between 13 and 68 years with the majority being below 50 years (79.34%) of age. Patient height ranged from 1.35-1.82 meters with mean height of 1.57 ± 0.09 meters. Patient weight ranged from 27-93.1 kgs with mean weight of 58.52 ± 12.15 kgs, BMI ranged from 13.35-32, with mean of 23.57 ± 4.41 kg/m^2 , BSA ranged from 1.01-2.14 m^2, mean of 1.59 ± 0.19m^2[Table 4].

Most of the patients had isolated Mitral stenosis. The most common presenting complaint was dyspnea, with 46 patients (50%) in NYHA FC-II and 46 patients (50%) in NYHA FC-III. 24% of the patients had undergone PBMV in the past while 15.2% and 1.09% patients undergone closed mitral valvuloplasty and open mitral valvuloplasty in the past, and a repeat PBMV was performed in view of severe mitral restenosis. Associated aortic valve disease present in 3.3% (mild Aortic regurgitation) and 1.09% (mild aortic stenosis) patients. In the present cohort 61 patients were in sinus rhythm (SR) and 31 patients were in atrial fibrillation (AF). Blood investigations showed mean haemoglobin 13.4 g/dl, mean serum creatinine of 0.87 mg/dl with mean GFR of 84.33 ml/min/1.73m^2 and mean NT-proBNP of 580 pg/ml [Table 4].

Table 4 : Baseline Characteristics of study cohort

	n(%), mean ± SD		**n(%), mean ± SD**
Total Patients	92	**Echocardiographic Parameters**	
Age	39.17 ± 12.43	Mitral Regurgitation	
Sex		No MR	16 (17.4%)
Male	18 (19.57%)	Trivial MR	21 (22.8%)
Female	74 (80.43%)	Mild MR	55 (57.8%)
Pregnancy	3 (3.3%)	Aortic Disease	
Height (m)	1.57 ± 0.009	Mild AR	3 (3.3%)
Weight (kg)	58.52 ± 12.15	Mild AS	1 (1.09%)
BMI (kg/m^2)	23.57 ± 4.41	LA Diameter (mm)	45.56 ± 5.61

BSA (m^2)	1.59 ± 0.19	Peak MVG (mm Hg)	27.39 ± 9.37
Prior Interventions		Mean MVG (mm Hg)	16.14 ± 5.93
Prior PBMV	22 (24%)	LVIDD (mm)	42.65 ± 5.49
Prior CMV	14 (15.2%)	LVIDS (mm)	26.80 ± 4.54
Prior OMV	1 (1.09%)	LVEF (%)	65.30 ± 6.03
Dyspnea		2D MVA (cm^2)	0.94 ± 0.20
NYHA II	46 (50%)	MVA PHT (cm^2)	0.97 ± 0.18
NYHA III	46 (50%)	HR	74.83 ± 13.23
		TAPSE	19.88 ± 1.56
		Hemodynamic Parameters	
		RA mean (mm of Hg)	6.58 ± 3.39
ECG		RVSP (mm of Hg)	50.70 ± 19.51
SR	61 (66.3%)	RVEDP (mm of Hg)	7.36 ± 2.27
AF	31 (33.7%)	PASP (mm of Hg)	50.63 ± 19.80
SR with LAE	29 (31.5%)	PADP (mm of Hg)	25.20 ± 8.09
SR with LAE, RAD and RVH	20 (21.7%)	PAmP (mm of Hg)	34.25 ± 11.99
		Mean LAP (mm of Hg)	24.35 ± 7.56
Blood Investigations		LVSP (mm of Hg)	120.27 ± 20.03
Hemoglobin (g/dl)	13.40 ±1.43	LVEDP (mm of Hg)	8.98 ± 2.68
Creatinine (mg/dl)	0.87 ± 0.19	MAP (mm of Hg)	87 ± 13.39
GFR	84.33 ± 28.29	MVG (mm of Hg)	15.96 ± 5.85
NT-proBNP (pg/ml)	580 ± 370	MVA (cm^2)	0.85 ± 0.17
		CO (L/min)	3.59 ± 0.65
		CI (L/min/m^2)	2.26 ± 0.36
		PVR (WU)	2.97 ± 3.09
		SVR (WU)	23.10 ± 5.86

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

Baseline 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 ($p < 0.001$). The mean NT-proBNP level in clinically stable patients (NYHA class II) was 390 pg/mL and the mean NT-proBNP level in patients with NYHA class III was 773 pg/mL [Table 5].

Table 5 : NYHA class and NT-proBNP level

NYHA class	n	NT-Pro BNP (pg/ml)		
		Mean	SD	Range
II	46	390	197	116-963
III	46	773	397	221-2490
P		**<0.001**		

NYHA- New York heart association functional class

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 [Table 6].

Table 6 : ECG findings and NT-proBNP

PRE-BMV		NT PROBNP (pg/ml)			
		Mean	SD	Range	n
Rhythm	**AF**	775	465	152-2490	31
	SR	481	265	116-1253	61
	SR with LAE	435	184	116-890	29
	SR LAE RVH RAD	544	314	198-1253	20

AF- Atrial fibrillation, LAE- Left atrial enlargement, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, SR- Sinus rhythm

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

The relationship between 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 NT-proBNP correlated significantly with LA diameter (r = 0.207; p 0.047). On correlation with various hemodynamic parameters, it was observed that baseline NT-proBNP showed significant correlation with pulmonary artery pressures and mean left atrial pressures [Table 7]

Table 7 : Correlation between various baseline parameters and NT-proBNP

Variable	r value	p	HEMODYNAMIC	r value	p
Age	0.079	0.454	**RA mean (mm of Hg)**	0.120	0.245
BMI	0.026	0.803	**RVSP (mm of Hg)**	0.336	**0.001**
Rhythm (SR/AF)	0.377	**<0.001**	**RVEDP (mm of Hg)**	0.150	0.105
NYHA	0.350	**<0.001**	**PASP (mm of Hg)**	0.340	**<0.001**
Hemoglobin	0.047	0.656	**PADP (mm of Hg)**	0.279	**0.007**
Creatinine	0.151	0.152	**PAmP (mm of Hg)**	0.338	**<0.001**
GFR	0.174	0.097	**Mean LAP (mm of Hg)**	0.207	**0.048**
Echocardiographic			**LVSP (mm of Hg)**	0.039	0.713
LA diameter (mm)	0.207	**0.047**	**LVEDP (mm of Hg)**	0.152	0.148
Peak MVG (mm of Hg)	0.017	0.873	**MAP (mm of Hg)**	0.113	0.285
Mean MVG (mm of Hg)	0.004	0.969	**MVG (mm of Hg)**	0.139	0.118
LVIDD (mm)	0.118	0.261	**MVA (cm^2)**	0.146	0.164
LVIDS (mm)	0.127	0.227	**CO (L/min)**	0.197	0.059
LVEF (%)	0.080	0.451	**CI ($L/min/m^2$)**	0.190	0.065
2D MVA (cm^2)	0.066	0.532	**PVR (WU)**	0.303	**0.003**
MVA PHT (cm^2)	0.101	0.351	**SVR (WU)**	0.174	0.098
HR (bpm)	0.137	0.193			
TAPSE (mm)	0.156	0.137			

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in

systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

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

Ninety-two patients underwent PBMV. PBMV was successful in 88 patients. In patients who underwent successful PBMV (n = 92), all echocardiographic and hemodynamic parameters showed a significant improvement. NT-proBNP levels decreased significantly following PBMV (580 ± 370 vs 328 ± 308; p < 0.001) [Table 8]. A significant decrease in NT-proBNP levels was observed both in patients with AF (775 ± 465 vs 499 ± 410; p < 0.001) [Table 13] and also in those with SR (481 ± 265 vs 240 ± 192; p < 0.001) [Table 14].

Table 8 : Changes in echocardiographic parameters, hemodynamic parameters, and NT-proBNP levels following PBMV.

Variable	**Pre**	**Post**	**Difference**	**p**
	Mean ± SD	Mean ± SD	Mean ± SD	
ECHO				
LA diameter (mm)	45.56 ± 5.61	43.20 ± 5.45	2.36 ± 3.54	**<0.001**
Peak MVG (mm of Hg)	27.39 ± 9.37	13.20 ± 4.02	14.18 ± 9.38	**<0.001**
Mean MVG (mm of Hg)	16.14 ± 5.93	5.73 ± 2.21	10.40 ± 5.78	**<0.001**
2D MVA (cm^2)	0.94 ± 0.20	1.56 ± 0.24	0.62 ± 0.28	**<0.001**
MVA PHT (cm^2)	0.97 ± 0.17	1.59 ± 0.23	0.62 ± 0.25	**<0.001**
HR	74.83 ± 13.23	71.78 ± 8.04	3.05 ± 13.70	**0.035**
HEMODYNAMIC				
RA mean (mm of Hg)	6.58 ± 3.39	5.59 ± 2.44	0.98 ± 1.98	**<0.001**

RVSP (mm of Hg)	50.70 ± 19.51	38.85 ± 13.69	11.87 ± 11.39	**<0.001**
RVEDP (mm of Hg)	7.36 ± 2.27	7.01 ± 2.19	0.35 ± 1.55	**0.029**
PASP (mm of Hg)	50.63 ± 19.80	38.92 ± 14.40	11.70 ± 11.01	**<0.001**
PADP (mm of Hg)	25.20 ± 8.09	16.76 ± 5.47	8.44 ± 5.80	**<0.001**
PAmP (mm of Hg)	34.25 ± 11.99	24.43 ± 8.55	9.81 ± 6.84	**<0.001**
Mean LAP (mm of Hg)	24.35 ± 7.56	15.01 ± 4.30	9.34 ± 6.30	**<0.001**
MVG (mm of Hg)	15.96 ± 5.85	4.88 ± 1.69	11.08 ± 5.14	**<0.001**
MVA (cm2)	0.85 ± 0.17	1.69 ± 0.36	0.83 ± 0.34	**<0.001**
CO (L/min)	3.59 ± 0.65	4.37 ± 0.83	0.77 ± 0.42	**<0.001**
CI (L/min/m2)	2.26 ± 0.36	2.76 ± 0.46	0.49 ± 0.28	**<0.001**
NT ProBNP (pg/ml)	580 ± 370	328 ± 308	253 ± 149	**<0.001**

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

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

The change in NT-proBNP levels correlated with change in LA diameter (r = 0.300; p 0.004) on transthoracic echocardiogram. It also correlated significantly with the change in right ventricular systolic pressure (r = 0.270; p 0.009), right ventricular diastolic pressure (r = 0.210; p 0.045), systolic PA pressures (r = 0.271; p 0.009), diastolic pulmonary artery pressure (r = 0.259; p 0.013), mean PA pressures (r = 0.274; p 0.008) and mean left atrial pressure (r = 0.356; p < 0.001) following PBMV [Table 9]. On multivariate analysis, the change in left atrial diameter and mean left atrial pressures predicted the change in NT-proBNP levels [Table 10].

Table 9 : Correlation between change in various echocardiographic and hemodynamic parameters with change in NT-proBNP levels

Variable	r value	p	Hemodynamic	r value	p
Age	0.009	0.935	**RA mean (mm of Hg)**	0.016	0.883
Rhythm (SR/AF)	0.11	0.292	**RVSP (mm of Hg)**	0.270	**0.009**
Echocardiographic			**RVEDP (mm of Hg)**	0.210	**0.045**
LA diameter (mm)	0.300	**0.004**	**PASP (mm of Hg)**	0.271	**0.009**
Peak MVG (mm of Hg)	0.067	0.524	**PADP (mm of Hg)**	0.259	**0.013**
Mean MVG (mm of Hg)	0.061	0.561	**PAmP (mm of Hg)**	0.274	**0.008**
LVIDD (mm)	0.073	0.492	**Mean LAP (mm of Hg)**	0.356	**<0.001**
LVIDS (mm)	0.143	0.173	**LVSP (mm of Hg)**	0.058	0.580
LVEF (%)	0.078	0.461	**LVEDP (mm of Hg)**	0.150	0.143
2D MVA (cm^2)	0.119	0.260	**MAP (mm of Hg)**	0.015	0.888
MVA PHT (cm^2)	0.163	0.121	**MVG (mm of Hg)**	0.143	0.173
HR	0.074	0.482	**MVA (cm^2)**	0.068	0.520
TAPSE (mm)	0.101	0.338	**CO (L/min)**	0.105	0.321
			CI ($L/min/m^2$)	0.152	0.147
			PVR (WU)	0.030	0.775
			SVR (WU)	0.090	0.394

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

Table 10 : Multivariate analysis- Predictors of change in NT-proBNP post PBMV

Variable	Correlation Coefficient (r value)	p
LA diameter (mm)	**0.402**	**0.022**
RVSP (mm of Hg)	0.217	0.406
PASP (mm of Hg)	0.161	0.527
PADP (mm of Hg)	0.112	0.577
PAmP (mm of Hg)	0.283	0.338
Mean LAP (mm of Hg)	**0.407**	**0.020**
PVR (WU)	0.203	0.101

LA- Left atrium, LAP- Left atrial pressure, PADP- Pulmonary artery diastolic pressure, PAmP- Pulmonary artery mean pressure, PASP- Pulmonary artery systolic pressure, PVR- Pulmonary vascular resistance, RVSP- Right ventricular systolic pressure.

Sub-Group Analysis

Out of 92 patients 61 patients were in sinus rhythm(SR) and 31 patients were in atrial fibrillation(AF), with mean age of 46.51 ± 9.58 in AF patients who were significantly older compared to sinus rhythm patients, and also most of the AF patients presented with NYHA FC-III(70.95%) where as SR patients in NYHA FC-II(60.65%). There is also significant difference in serum creatinine, GFR and echocardiographic parameters like left atrial diameter, mitral valve gradient, left ventricular dimensions and left ventricular ejection fraction and NT-Pro BNP [Table 11].

Table 11 : Comparison of Sinus Rhythm (SR) and Atrial Fibrillation (AF) patients

Variable	SR (n 61)	AF (n 31)	p
	mean ± SD	**mean ± SD**	
Age	35.44 ± 11.93	46.51 ± 9.58	**<0.001**
Sex **Male** **Female**	 25 (19.67%) 49 (80.33%)	 6 (19.35%) 12 (80.65%)	0.971
Height (m)	1.56 ± 0.08	1.58 ± 0.08	0.260
Weight (kg)	57.06 ± 12.13	61.38 ± 11.45	0.104

BMI (kg/m^2)	23.18 ± 4.41	24.33 ± 4.21	0.233
BSA (m^2)	1.55 ± 0.19	1.64 ± 0.17	**0.029**
Blood Investigations			
Hemoglobin (g/dl)	13.22 ± 1.51	13.75 ± 1.21	0.093
Creatinine (mg/dl)	0.83 ± 0.19	0.96 ± 0.16	**0.002**
GFR	91.66 ± 30.70	69.91 ± 14.79	**<0.001**
NT-proBNP (pg/ml)	481 ± 265	775 ± 465	**<0.001**
Echocardiographic Parameters			
LA Diameter (mm)	44.84 ± 5.46	47 ± 2.72	**0.041**
Peak MVG (mm of Hg)	24.26 ± 7.77	28.98 ± 9.77	**0.013**
Mean MVG (mm Hg)	14 ± 4.91	17.23 ± 6.15	**0.008**
LVIDD (mm)	41.13 ± 5.05	45.65 ± 5.14	**<0.001**
LVIDS (mm)	25.67 ± 3.98	29.03 ± 4.82	**<0.001**
LVEF (%)	66.20 ± 5.73	63.55 ± 6.32	**0.046**
2D MVA (cm^2)	0.97 ± 0.21	0.93 ± 0.20	0.375
MVA PHT (cm^2)	0.99 ± 0.19	0.96 ± 0.15	0.446
HR	73.63 ± 7.74	77.19 ± 20.07	0.225
TAPSE	19.96 ± 1.59	19.70 ± 1.50	0.452
Hemodynamic Parameters			
RA mean (mm of Hg)	6.30 ± 2.36	7.16 ± 4.82	0.252
RVSP (mm of Hg)	49.61 ± 19.81	51.26 ± 19.50	0.705
RVEDP (mm of Hg)	7 ± 2.57	7.56 ± 2.10	0.298
PASP (mm of Hg)	50.10 ± 20.97	50.90 ± 19.36	0.860
PADP (mm of Hg)	23.77 ± 6.64	25.93 ± 8.70	0.189
PAmP (mm of Hg)	33.23 ± 12.33	34.77 ± 11.88	0.568
Mean LAP (mm of Hg)	21.97 ± 5.30	25.57 ± 8.26	**0.013**
LVSP (mm of Hg)	125.94 ± 18.29	117.39 ± 20.41	0.054
LVEDP (mm of Hg)	8.93 ± 2.68	9.10 ± 2.72	0.775
MAP (mm of Hg)	83.92 ± 13.38	80.06 ± 11.36	0.173
MVG (mm of Hg)	14 ± 4.31	16.97 ± 6.31	**0.009**
MVA (cm^2)	0.89 ± 0.16	0.84 ± 0.18	0.178
CO (L/min)	3.64 ± 0.65	3.51 ± 0.66	0.369
CI (L/min/m^2)	2.33 ± 0.34	2.16 ± 0.39	0.064
PVR (WU)	2.70 ± 2.27	3.51 ± 4.27	0.237
SVR (WU)	22.09 ± 5.80	25.09 ± 7.55	0.058

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

NT-proBNP in AF group was significantly high (Range 152-2490) compared to SR group (Range 116-1253) and also most of the patients in AF group were in NYHA-III whereas most of the patients in SR group were in NYHA-II [Table 12]

Table 12 : NYHA and NT-proBNP in SR group and AF group

NYHA CLASS	**SR-n (61)**	**Pre NT PROBNP (pg/ml)**		
		Mean	**SD**	**Range**
II	37	383	205	116-963
III	24	634	278	221-1253
P		<0.001		
NYHA CLASS	**AF-n (31)**	**Pre NT PROBNP (pg/ml)**		
		Mean	**SD**	**Range**
II	9	407	186	152-602
III	22	925	463	377-2490
P		**0.003**		

NYHA- New York heart association functional class

Comparison of change in parameters pre and post PBMV in AF and SR group

Post PBMV most of the echocardiographic (LA diameter, mitral valve gradient, mitral valve area) and hemodynamic parameters improved significantly in both the groups[Table 13], [Table 14].

Table 13 : Comparison of change in parameters pre and post PBMV in AF group

Variable	**Pre**	**Post**	**Difference**	**p**
	Mean ± SD	Mean ± SD	Mean ± SD	

ECHOCARDIOGRAPHIC				
LA diameter (mm)	47 ± 5.72	44.5 ± 4.66	2.42 ± 3.85	**<0.001**
Peak MVG (mm of Hg)	28.98 ± 9.77	16.98 ± 3.35	12 ± 8.16	**<0.001**
Mean MVG (mm of Hg)	17.23 ± 6.15	8.42 ± 2.18	8.81 ± 4.88	**<0.001**
2D MVA (cm^2)	0.93 ± 0.2	1.61 ± 0.25	0.68 ± 0.32	**<0.001**
MVA PHT (cm^2)	0.96 ± 0.15	1.64 ± 0.22	0.69 ± 0.25	**<0.001**
HEMODYNAMIC				
RA mean (mm of Hg)	7.16 ± 4.82	5.77 ±2.64	1.39 ± 2.69	**0.01**
RVSP (mm of Hg)	51.26 ± 19.50	39.78 ± 15.40	11.48 ± 15	**<0.001**
PASP (mm of Hg)	50.90 ± 19.36	39.96 ± 17.25	10.94 ± 11.55	**<0.001**
PADP (mm of Hg)	25.93 ± 8.70	19.22 ± 6.46	6.71 ± 4.73	**<0.001**
PAmP (mm of Hg)	34.77 ± 11.88	26.38 ± 10.78	8.39 ± 6.40	**<0.001**
Mean LAP (mm of Hg)	25.57 ± 8.26	18.99 ± 4.28	6.94 ± 4.63	**<0.001**
MVG (mm of Hg)	16.97 ± 6.31	7.78 ± 1.51	9.19 ± 3.81	**<0.001**
MVA (cm2)	0.84 ± 0.18	1.69 ± 0.38	0.85 ± 0.36	**<0.001**
CO (L/min)	3.51 ± 0.66	4.19 ± 0.78	0.68 ± 0.28	**<0.001**
NT ProBNP (pg/ml)	775 ± 465	499 ± 410	276 ± 170.41	**<0.001**

CO- Cardiac output, HR- Heart rate, LA- Left atrium, LAP- Left atrial pressure, LVEF- Left ventricular ejection fraction, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVSP- Left ventricular systolic pressure, LVEDP- Left ventricular end diastolic pressure, MAP- Mean arterial pressure, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, MVG- Mitral valve gradient, PADP- Pulmonary artery diastolic pressure, PAmP- Pulmonary artery mean pressure, PASP- Pulmonary artery systolic pressure, RA- Right atrium, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, TAPSE- Tricuspid annular plane systolic excursion.

Table 14 : Comparison of change in parameters pre and post PBMV in SR group

Variable	**Pre**	**Post**	**Difference**	**p**
	Mean ± SD	Mean ± SD	Mean ± SD	

Echocardiographic				
LA diameter (mm)	44.84 ± 5.46	42.51 ± 5.73	2.33 ± 3.42	**<0.001**
Peak MVG (mm of Hg)	24.26 ± 7.77	8.96 ± 4.27	15.30 ± 9.83	**<0.001**
Mean MVG (mm of Hg)	14 ± 4.91	2.79 ± 0.9	11.21 ± 6.07	**<0.001**
2D MVA (cm^2)	0.97 ± 0.21	1.56 ± 0.23	0.59 ± 0.27	**<0.001**
MVA PHT (cm^2)	0.99 ± 0.19	1.57 ± 0.25	0.58 ± 0.26	**<0.001**
HEMODYNAMIC				
RA mean (mm of Hg)	6.3 ± 2.36	5.51 ± 2.36	0.79 ± 1.48	**<0.001**
RVSP (mm of Hg)	49.61 ± 19.81	37.58 ± 12.86	12.03 ± 11.18	**<0.001**
PASP (mm of Hg)	50.10 ± 20.97	38 ± 12.88	12.10 ± 10.80	**<0.001**
PADP (mm of Hg)	23.77 ± 6.64	14.44 ± 4.96	9.33 ± 6.13	**<0.001**
PAmP (mm of Hg)	33.23 ± 12.33	22.69 ± 7.26	10.54 ± 7.01	**<0.001**
Mean LAP (mm of Hg)	21.97 ± 5.30	11.4 ± 4.35	10.57 ± 6.72	**<0.001**
MVG (mm of Hg)	14 ± 4.31	2.2 ± 0.9	12.05 ± 5.49	**<0.001**
MVA (cm2)	0.89 ± 0.16	1.72 ± 0.36	0.83 ± 0.34	**<0.001**
CO (L/min)	3.64 ± 0.65	4.47 ± 0.86	0.83 ± 0.48	**<0.001**
NT ProBNP(pg/ml)	481 ± 265	240 ± 192	241 ± 136.71	**<0.001**

CO- Cardiac output, HR- Heart rate, LA- Left atrium, LAP- Left atrial pressure, LVEF- Left ventricular ejection fraction, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVSP- Left ventricular systolic pressure, LVEDP- Left ventricular end diastolic pressure, MAP- Mean arterial pressure, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, MVG- Mitral valve gradient, PADP- Pulmonary artery diastolic pressure, PAmP- Pulmonary artery mean pressure, PASP- Pulmonary artery systolic pressure, RA- Right atrium, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, TAPSE- Tricuspid annular plane systolic excursion.

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

The change in NT-proBNP levels correlated with change in LA diameter (r = 0.374; p 0.038) on transthoracic echocardiogram. It also correlated significantly with the change

in mean PA pressures (r = 0.356; p 0.049) and mean left atrial pressure (r = 0.532; p 0.002) following PBMV [Table 15]. On multivariate analysis, the change in mean left atrial pressures predicted the change in NT-proBNP levels [Table 16].

Table 15 : Correlation between change in various echocardiographic and hemodynamic parameters with change in NT-proBNP levels in AF patients

Variable	r value	p	HEMODYNAMIC	r value	p
Age	0.303	0.097	**RA mean (mm of Hg)**	0.172	0.355
ECHOCARDIOGRAPHIC			**RVSP (mm of Hg)**	0.319	0.080
LA diameter (mm)	0.374	**0.038**	**RVEDP (mm of Hg)**	0.197	0.288
Peak MVG (mm of Hg)	0.261	0.156	**PASP (mm of Hg)**	0.341	0.060
Mean MVG (mm of Hg)	0.065	0.730	**PADP (mm of Hg)**	0.334	0.066
LVIDD (mm)	0.075	0.690	**PAmP (mm of Hg)**	0.356	**0.049**
LVIDS (mm)	0.254	0.168	**Mean LAP (mm of Hg)**	0.532	**0.002**
LVEF (%)	0.214	0.247	**LVSP (mm of Hg)**	0.166	0.372
2D MVA (cm^2)	0.121	0.515	**LVEDP (mm of Hg)**	0.298	0.103
MVA PHT (cm^2)	0.039	0.835	**MAP (mm of Hg)**	0.036	0.849
HR	0.073	0.696	**MVG (mm of Hg)**	0.209	0.260
TAPSE (mm)	0.034	0.847	**MVA (cm^2)**	0.223	0.228
			CO (L/min)	0.066	0.723
			CI (L/min/m^2)	0.30	0.872
			PVR (WU)	0.416	**0.020**
			SVR (WU)	0.083	0.657

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary

artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

Table 16 : Multivariate analysis- Predictors of change in NT-proBNP post PBMV in AF patients

Variable	Correlation Coefficient (r value)	p
LA diameter (mm)	0.009	0.969
RVSP (mm of Hg)	0.091	0.805
PASP (mm of Hg)	0.134	0.704
PADP (mm of Hg)	0.014	0.959
PAmP (mm of Hg)	0.129	0.760
Mean LAP (mm of Hg)	**0.481**	**0.048**
PVR (WU)	0.265	0.164

LA- Left atrium, LAP- Left atrial pressure, PAmP- Pulmonary artery mean pressure, PASP- Pulmonary artery systolic pressure, PADP- Pulmonary artery diastolic pressure, PVR- Pulmonary vascular resistance, RVSP- Right ventricular systolic pressure.

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

The change in NT-proBNP levels correlated with change in LA diameter (r = 0.254; p < 0.048) on transthoracic echocardiogram. It also correlated significantly with the change in diastolic pulmonary pressure (r = 282; p 0.028), mean PA pressures (r = 0.267; p 0.037) and mean left atrial pressure (r = 0.371; p 0.003) following PBMV [Table 17]. On multivariate analysis, the change in mean left atrial pressures predicted the change in NT-proBNP levels [Table 18].

Table 17 : Correlation between change in various echocardiographic and hemodynamic parameters with change in NT-proBNP levels in SR patients

Variable	r value	p	HEMODYNAMIC	r value	p
Age	0.087	0.503	**RA mean (mm of Hg)**	0.193	0.136

ECHOCARDIOGRAPHIC			**RVSP (mm of Hg)**	0.245	0.057
LA diameter (mm)	0.254	**0.048**	**RVEDP (mm of Hg)**	0.220	0.088
Peak MVG (mm of Hg)	0.059	0.654	**PASP (mm of Hg)**	0.239	0.064
Mean MVG (mm of Hg)	0.030	0.820	**PADP (mm of Hg)**	0.282	**0.028**
LVIDD (mm)	0.163	0.210	**PAmP (mm of Hg)**	0.267	**0.037**
LVIDS (mm)	0.100	0.444	**Mean LAP (mm of Hg)**	0.371	**0.003**
LVEF (%)	0.001	0.993	**LVSP (mm of Hg)**	0.004	0.976
2D MVA (cm^2)	0.089	0.496	**LVEDP (mm of Hg)**	0.390	0.112
MVA PHT (cm^2)	0.211	0.102	**MAP (mm of Hg)**	0.013	0.919
HR	0.044	0.738	**MVG (mm of Hg)**	0.236	0.067
TAPSE (mm)	0.062	0.636	**MVA (cm^2)**	0.042	0.746
			CO (L/min)	0.206	0.111
			CI (L/min/m^2)	0.245	0.057
			PVR (WU)	0.064	0.622
			SVR (WU)	0.189	0.145

AF- Atrial fibrillation, AR- Aortic regurgitation, AS- Aortic stenosis, BMI- Body mass index, BSA- Body surface area, CI- Cardiac index, CO- Cardiac output, CMV- Closed mitral valvuloplasty, GFR- Glomerular filtration rate, HR- Heart rate, LA- Left atrium, LAE- Left atrial enlargement, LAP- Left atrial pressure, LVIDD- Left ventricular internal diameter in diastole, LVIDS- Left ventricular internal diameter in systole, LVEDP- Left ventricular end diastolic pressure, LVSP- Left ventricular systolic pressure, LVEF- Left ventricular ejection fraction, MAP- Mean arterial pressure, MVG- Mitral valve gradient, 2D MVA- two dimensional Mitral valve area, MVA PHT- Mitral valve area pressure half time, NT-proBNP- N-terminal pro brain natriuretic peptide, NYHA- New York heart association functional class, OMV- Open mitral valvuloplasty, PAmP- Pulmonary artery mean pressure, PADP- Pulmonary artery diastolic pressure, PASP- Pulmonary artery systolic pressure, PBMV- Percutaneous balloon mitral valvuloplasty, PVR- Pulmonary vascular resistance, RA- Right atrium, RAD- Right axis deviation, RVH- Right ventricular hypertrophy, RVEDP- Right ventricular end diastolic pressure, RVSP- Right ventricular systolic pressure, SR- Sinus rhythm, SVR- Systemic vascular resistance, TAPSE- Tricuspid annular plane systolic excursion, WU- Wood units.

Table 18 : Multivariate analysis- Predictors of change in NT-proBNP post PBMV in SR patients.

Variable	Correlation Coefficient (r value)	p

LA diameter (mm)	0.240	0.061
RVSP (mm of Hg)	0.392	0.479
PASP (mm of Hg)	0.473	0.434
PADP (mm of Hg)	0.288	0.328
PAmP (mm of Hg)	0.876	0.111
Mean LAP (mm of Hg)	**0.871**	**0.021**
PVR (WU)	0.377	0.139

LA- Left atrium, LAP- Left atrial pressure, PAmP- Pulmonary artery mean pressure, PASP- Pulmonary artery systolic pressure, PADP- Pulmonary artery diastolic pressure, PVR- Pulmonary vascular resistance, RVSP- Right ventricular systolic pressure.

Patients with Age less than 50 years

As shown in Table 19, total 73 (79.34%) patients were age more than 50 years there is no significant difference in baseline or post procedure parameters including NT-proBNP in both the groups.

Table 19 : Comparison between patients with age less than 50 years and more than 50 years

	<50 years	**>50 years**	**p**
n	73	19	
Sex **Male** **Female**	 13 60	 5 14	0.40
Mean age	35.02 ± 10.28 (13-49)	55.10 ± 4.44 (50-68)	
Rhythm **SR** **AF**	 54 19	 7 12	**0.002**
NYHA			0.197

FC-II **FC-III**	39 34	7 12	
MVA Pre	0.85 ± 0.18	0.89 ± 0.14	0.371
MVA Post	1.69 ± 0.35	1.72 ± 0.42	0.750
NT-proBNP pre	556.02 ± 372.50 (116-2490)	674.26 ± 354.81(152-1526)	0.217
NT-proBNP post	308.71 ± 319.67 (70-2270)	399.78 ± 252.90 (90-953)	0.253
d NT-proBNP	241.31 ± 155.47	274.47 ± 121.55	0.391

AF- Atrial fibrillation, MVA- Mitral valve area, NYHA- New York heart association functional class, NT-proBNP- N-terminal pro-brain natriuretic peptide, d NT-proBNP- change in NT-proBNP (delta NT-proBNP), SR- sinus rhythm.

GFR and NT-proBNP

As shown in Table 20, total 74 (80.43%) patients were with GFR more than 60 and 19.56% of patients with GFR less than 60, there is no significant difference in baseline and change in NT-proBNP post PBMV in both the groups.

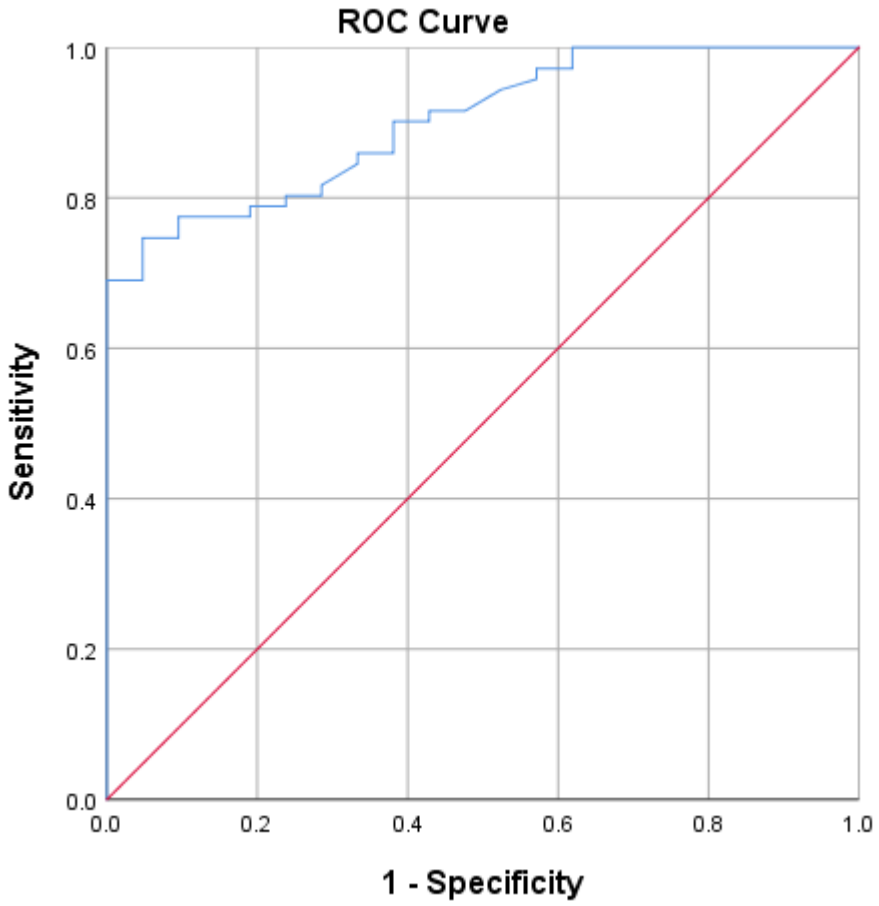
Table 20 : GFR and NT-proBNP

	GFR > 60 (n 74)	**GFR < 60 (n 18)**	**p**
NT-proBNP pre	563.59 ± 392.93	649.72 ± 253.12	0.379
d NT-proBNP	244.88 ± 158.50	286 ± 96.75	0.296

GFR-Glomerular filtration rate, d NT-proBNP- change in NT-proBNP (delta NT-proBNP)

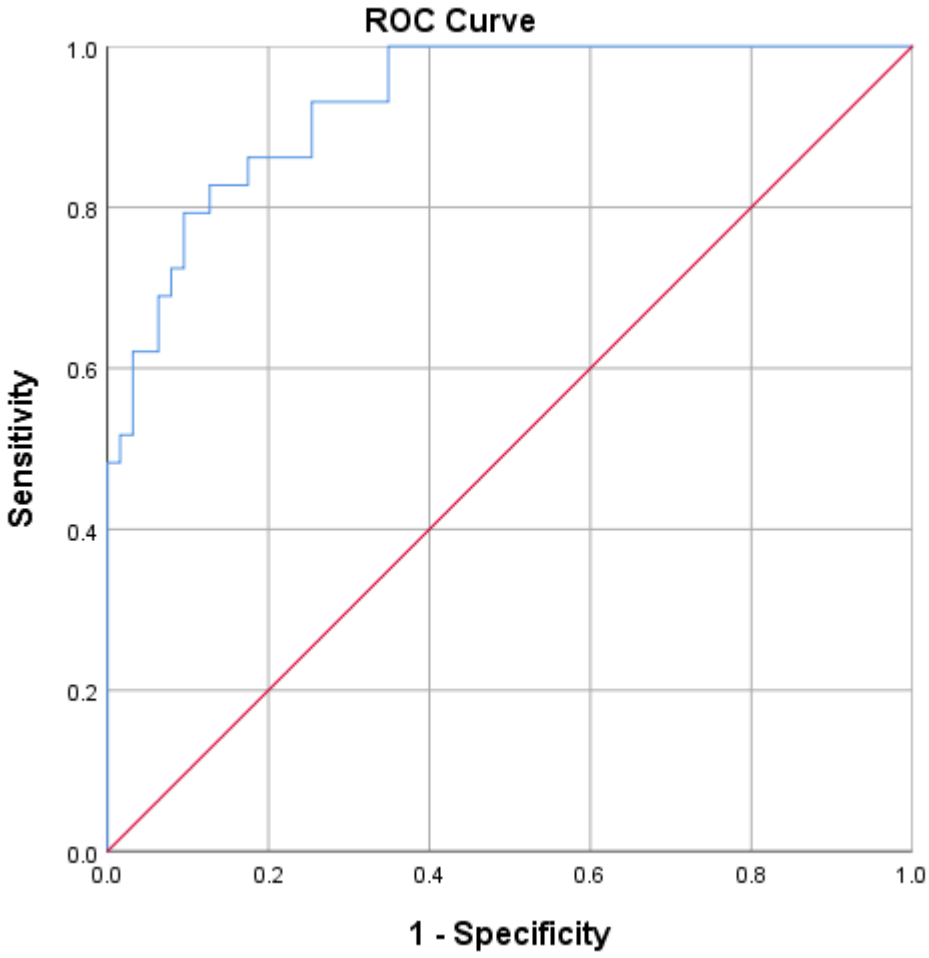
As shown in figure 1, analysis of receiver operating characteristic curve for NT-proBNP as a predictor of mitral valve area less than 1 cm^2 showed an area under curve of 0.90 [95% CI 0.84-0.96]. When using a NT-proBNP cut-off value of more than 302pg/ml, derived from the receiver operating curve as a predictor of mitral valve area less than 1 cm^2 with a sensitivity of 90.1% and specificity of 61.9%.

Figure 1 : ROC- NT-proBNP as a predictor of mitral valve area less than 1 cm^2



As shown in figure 2, analysis of receiver operating characteristic curve for change in NT-proBNP as a predictor of mean left atrial pressure less than 12 mm of Hg post PBMV, showed an area under curve of 0.93 [95% CI 0.88-0.98]. When using a change in NT-proBNP cut-off value of more than 238.5pg/ml, derived from the receiver operating curve as a predictor of mean left atrial pressure less than 12 mm of Hg post PBMV, with a sensitivity of 93.1% and specificity of 74.6%.

Figure 2 : ROC- change in NT-proBNP as a predictor of mean left atrial pressure less than 12 mm of Hg post PBMV.



Follow-up

Out of 92 patients 2 patients lost to follow up post procedure

Median follow-up time of remaining 90 patients was 15.5 months.

At the end of the follow-up period functional status of the patients was better than baseline, NYHA (2.5 vs 1.5), p = 0.048).

In 4 patients in whom PBMV was un-successful were in same functional class without any deterioration or improvement.

During the follow-up 1 patient died (due to non-cardiovascular cause) 11 months after PBMV, 1 patient had TIA and none required re-intervention.

DISCUSSION

DISCUSSION

This present study is the one of the larger studies to date, evaluating the changes in NT-proBNP levels with changes in various echocardiographic and hemodynamic parameters following PBMV.

According to previous findings from various studies that hormonal components (natriuretic peptides) secreted from atrial and ventricular cells in response to strain changes and wall motion abnormalities the current study aimed to assess the relationship between changes in NT-proBNP levels and echocardiographic parameters, hemodynamic parameters in mitral stenosis patients who are undergoing PBMV.

Baseline characteristics

The mean age of the study population 39.17 years [Table 4] with around 79.34% of patients with age less than 50 years [Table 19] which says that study cohort is relatively younger and it is similar to various studies on PBMV in mitral stenosis like Seluck et al. [31] and Morteza Safi et al [32]. It is quite obvious that the prerequisite for BMV is favourable valve morphology, whereas elderly patients tend to have greater degree of valve deformity with calcified thickened and relatively immobile valves often with significant sub-valvular disease making the valve unsuitable for PBMV.

In our present study 33.7% of patients are with atrial fibrillation with a mean age of 46.51 years which was significantly high compared to patients in SR in present study [Table 11], which can be explained by the proven facts from various studies[37] that age and left atrial diameter are the most consistent predictors of AF in patients with mitral stenosis. A longer disease period and inflammatory processes in older patients were suggested to be causative factors predisposing to AF[37].

Most of the patients in present cohort were females (4.1:1) [Table 4] which was similar with various studies [Table 21] related to rheumatic MS, and It is a well-established fact that autoimmune diseases have gender predilections. RHD is an autoimmune-mediated valvular injury, therefore, the autoimmune response may differ between genders, leading to differences in valvular damage and severity. The epidemiological studies of RF and RHD report no gender predilection for the incidence of RF, however, RHD is more prevalent in females[17].

Table : 21 Comparison of Sex Ratio

Author	n	Females : Males
MT Selcuk et al, TURKEY (2007)	60 (56 SR, 4 AF)	51:9 (5.7:1)
Chadha et al, INDIA (2008)	44 (25 SR, 19 AF)	27:17 (1.6:1)
Lelli et al, IRAN (2014)	45 (34 SR, 11 AF)	33:12 (2.75:1)
Morteza Safi et al, IRAN (2016)	25 (15 SR, 10 AF)	21:4 (5.25:1)
K.P. Ranganayakulu et al, INDIA (2016)	100 (87 SR, 13 AF)	81:19 (4.26:1)
Our Study	92 (61 SR, 31 AF)	74:18 (4.1:1)

AF- Atrial fibrillation, SR- Sinus rhythm, n- Total.

Major Findings

The present study demonstrates that

1. Rhythm (SR/AF), NYHA functional class, Echocardiographic parameter – Left atrial diameter, Hemodynamic parameters – Pulmonary artery pressure and mean left atrial pressure were correlated with basal NT-proBNP levels
2. Plasma NT-proBNP levels fell significantly after PBMV
3. Only factor that independently correlated with the change in NT-proBNP levels after PBMV was change in mean left atrial pressure
4. NT-proBNP cut-off value of more than 302pg/ml, derived from the receiver operating curve as a predictor of mitral valve area less than 1 cm^2 with a sensitivity of 90.1% and specificity of 61.9%.
5. Change in NT-proBNP cut-off value of more than 238.5pg/ml, derived from the receiver operating curve as a predictor of mean left atrial pressure less than 12 mm of Hg post PBMV, with a sensitivity of 93.1% and specificity of 74.6%.

The most common presenting symptom was dyspnea, it was present in all patients. Similar to studies by Arat Ozkan et al. [30], Seluck et al. [31] and Morteza Safi et al [32], we observed that NT-proBNP levels correlated significantly with dyspnea NYHA class of the patients [Table 5].

Clinical symptoms, especially dyspnea, usually depends on the pulmonary capillary wedge pressure and PA pressures. As the valve progressively narrows the resting diastolic mitral valve gradient increases which leads to increase in left atrial pressures and pulmonary capillary wedge pressure which in-turn leads to transudation of fluid into the lung interstitum and dyspnea at rest or with minimal exertion. 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 in patients with atrial fibrillation when compared with patients who are in sinus rhythm of equal severity of mitral valve stenosis [Table 7]. Interestingly similar to our observation study by Arat Ozkan et al. [30], showed that those with atrial fibrillation had significantly higher NT-proBNP levels compared to those with sinus rhythm.

In patients with mitral stenosis with development of right axis deviation, RV hypertrophy, and AF [Table 7] reflects the sequential pathophysiological changes like increased left atrial wall stress and atrial fibrosis 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. However these finding were contrary to that observed by Shang et al. [33] and Chadha et al. [34], 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.

Significant correlation between baseline NT-proBNP levels and measured LA diameter by transthoracic echocardiogram, and mean left atrial pressure on hemodynamic assessment [Table 8]. Studies in patients with lone AF [35] demonstrated a significant correlation between NT-proBNP levels and LA function, reflecting the production of NT-proBNP in a stretched LA. This explains the correlation noted between NT-proBNP levels and LA diameter and mean left atrial pressure. Similar observations were reported by Davutoglu et al. [36], who noticed that in patients with RHD, a higher LA diameter correlated with a higher NT-proBNP level. Atrial fibrosis and increased left atrial wall stress are the common pathophysiological changes associated with both mitral stenosis and atrial fibrillation that may contribute to the elevated neurohormonal levels (natriuretic peptide levels).

Similar to studies by Seluck et al. [31], Shang et al. [33] and Chadha et al. [34] a significant correlation between baseline NT-proBNP levels and PA pressures (systolic, diastolic and mean) was noted. The significant positive correlation between baseline NT-proBNP levels and PA pressure may reflect the response of myocytes to chronic elevations of afterload in right ventricle in Mitral stenosis patients. However in the state of mitral stenosis pulmonary artery hypertension does not always reflect only the overload of

right ventricle, it is overload of left atrium as well. Therefore we cannot disregard the contribution of left atrium to the elevated NT-proBNP levels. As in our study cohort is patients with mitral stenosis with preserved left ventricular function it is possible that the left atrium and right side of heart are responsible for elevated NT-proBNP levels rather than the left ventricle.

A significant decrease in NT-proBNP levels was noted following successful PBMV [Table 8] and this was similar to previous studies [Table 22] [31-34]. Unlike Shang et al. [33] and Chadha et al. [34], a significant decrease in NT-proBNP levels were noted after PBMV, even in patients with AF [Table 13]. A successful PBMV results in a decrease of pressure in LA, pulmonary artery, RV, and also improve in LA function, which explains an expected decrease in NT-proBNP levels following PBMV even in patients with AF.

Table 22 : Comparison between change in NT-proBNP post PBMV

Author	n	NT-proBNP
MT Selcuk et al, TURKEY (2007)	60 (56 SR, 4 AF)	293-214 (p<0.001)
Chadha et al, INDIA (2008)	44 (25 SR, 19 AF)	713-602 (p<0.01)
Morteza Safi et al, IRAN (2016)	25 (15 SR, 10 AF)	309.20-235.72 (p 0.009)
K.P. Ranganayakulu et al, INDIA (2016)	100 (87 SR, 13 AF)	763.8-348.6 (p<0.01)
Our Study	92 (61 SR, 31 AF)	580-328 (p<0.001)

AF- Atrial fibrillation, SR- Sinus rhythm, n- Total, NT-proBNP- N-terminal pro-brain natriuretic peptide.

On multivariate analysis there is significant correlation between change in NT-proBNP levels after PBMV and change in mean left atrial pressures were noted in overall cohort [Table 10] and also sub-group analysis of AF group [Table 16] and SR group [Table 18]. A significant correlation has also been noted with change in LA diameter in overall cohort. The improvement of LA function in MS patients following PBMV is a reasonable explanation for observed decrease in NT-proBNP levels. Change in NT-proBNP level with an improvement in LA function was observed in studies on AF post cardioversion [35] in patients of lone AF where following cardio version they noticed a improvement of LA function and decrease in NT-proBNP level. This observation goes with our findings, that a significant positive correlation between NT-proBNP and LA diameter/mean LA pressure exists and a decrease in NT-proBNP level following PBMV correlates with decrease in LA diameter/mean LA pressure.

Table 23 : Echocardiographic and hemodynamic parameters correlated with decrease in NT-proBNP post PBMV from various studies.

Author	N	
MT Selcuk et al, TURKEY (2007)	60 (56 SR, 4 AF)	PASP
Chadha et al, INDIA (2008)	44 (25 SR, 19 AF)	PAP
Lelli et al, IRAN (2014)	45 (34 SR, 11 AF)	Mean LAP Mean PAP
Morteza Safi et al, IRAN (2016)	25 (15 SR, 10 AF)	MPG
K.P. Ranganayakulu et al, INDIA (2016)	100 (87 SR, 13 AF)	LAVi PASP Mean PAP
Our Study	92 (61 SR, 31 AF)	Mean LAP LA diameter

AF- Atrial fibrillation, SR- Sinus rhythm, LA- Left atrium, LAP- Left atrial pressure, LAVi- Left atrial volume index, n- Total, NT-proBNP- N-terminal pro-brain natriuretic peptide, PAP- Pulmonary artery pressure, PASP- Pulmonary artery systolic pressure,

We did not find a significant correlation between NT-ProBNP levels and MVA [Table 7]. This may be due to presence of uniformly small valvular areas in our patients. NT-proBNP levels may elevate beyond a threshold of MS severity and not rise significantly with further reductions in mitral valve areas.

When echocardiographic and hemodynamic parameters of patients with atrial fibrillation compared to sinus rhythm patients we observed that [Table 11] in AF patients left atrial diameter, trans-mitral valve gradients and mean left atrial pressures were significantly high and left ventricular dimensions were significantly low, reflects the sequential pathophysiological changes of MS with increasing severity and chronicity.

There is no significant difference in change in NT-proBNP levels in patients with age less than 50 years compared to patients with age more than 50 years [Table 19] and also in patients with GFR more than 60 ml/min/1.73m^2 and patients with GFR less than 60ml/min/1.73m^2 [Table 20].

LIMITATIONS

LIMITATIONS

There are a few limitations in our study.

- Study population is relatively small
- Only patients with severe MS were studied, hence changes in NT-proBNP levels with increasing severity of MS could not be determined.
- Measurements of NT-proBNP during follow-up after would have added further information to our findings.
- We could not assess the right ventricular function accurately by the use of advanced imaging techniques which might give further information about right ventricular function.

CONCLUSION

CONCLUSION

In conclusion, plasma NT-proBNP levels were significantly elevated in patients with severe MS, Along with all echocardiographic and hemodynamic parameters, NT-proBNP also showed a significant improvement following a successful PBMV. The decrease observed in NT-proBNP levels which is statistically significant and is noted in patients with SR, as well as with AF. The decrease in NT-proBNP levels following PBMV correlated with decrease in LA diameter and mean LA pressure. The decrease in NT-proBNP levels following PBMV reflects an improvement in clinical status and an improvement in various echocardiographic and hemodynamic parameters following PBMV. Thus, it seems reasonable to suggest that NT-proBNP as a non-invasive marker in evaluating the response to PBMV in patients of severe rheumatic MS.

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APPENDIX

PROFORMA

TITLE OF THE STUDY:

STUDY OF CHANGE IN N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS

Name:

Age :

Sex:

BMV Date:

Parameters	Pre PBMV	Post PBMV
Clin & lab		
FC		
Rhythm		
ECHO data		
LA Size		
MVA (2D)		
MVA(PHT)		
MS Grad		
Wilkins		
Mobility		
Calcification		
Thickening		
SVP		
MC		

LC		
MR(0-4)		
LVID		
RVID		
LVEF		
RVSP		
TAPSE		
CATH Data		
PAP		
LA		
LV		
MG		
MVA		
INDEXED MVA		
CO		
CI		
PVR		
SVR		
DILATOR/BALLOON USED		
SIZE		
No. OF DILATATIONS		
MR SEVERITY		
NT-Pro BNP		

SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY TRIVANDRUM

PATIENT INFORMATION SHEET

TITLE: STUDY OF CHANGE IN N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS

Name of Investigators:
Dr. Paidi Suresh Kumar, Dr. Harikrishnan S, Dr. Sanjay G.

Dear Patient/Parent

We welcome you and thank you for your interest in this research project titled “STUDY OF CHANGE IN N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS”. Before your participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

PBMV is a procedure to treat mitral Stenosis and reduce symptoms such as chest pain, fatigue, shortness of breath, difficulty when exercising, dizziness and fainting. A plastic tube (introducer) is inserted into an artery in your groin (femoral artery). A balloon catheter is passed through the introducer sheath and directed to your mitral heart valve. The balloon is inflated to open your valve .This balloon catheter is removed. Your own diseased valve will not be cut or removed. In addition, x-rays and a transeosaphageal echo are performed during the procedure.

What does the present study involve?

Blood investigation results pre-procedure and post-procedure will be collected from the medical records.

How long does it take?

The hospital visit will be a routine consultation, and the tests done will be part of routine follow up. This may take up to 2-3 hours. Please be prepared to be in the hospital OPD during that time.

WHAT ARE THE RESPONSIBILITIES OF PARTICIPANTS?

Your decision to participate in this study is voluntary, your own personal choice. You may choose not to continue at any time, for any reason, without notice.

WHAT ARE THE EXPECTED RISKS FOR THE PARTICIPANTS?

The study involves collection of data from case records, pre and pkst procedure. There will be no risks for the participants because of participation in the study. They will be managed according to the hospital protocol. No specific intervention will be done.

WHAT ARE THE EXPECTED BENEFITS OF THE RESEARCH TO THE PARTICIPANTS?

The participants are evaluated in detail for any cardiac cause for functional impairment. A follow up examination and evaluation may be helpful in identification of any risk factors for poor outcomes or functional deterioration. It may be helpful in detecting patients who require early intervention or addition of medical therapy . The data derived from the study may be helpful in planning appropriate timing and surgical strategies for patients with similar conditions in the future.

WILL PARTICIPANTS BE COMPENSATED FOR PARTICIPATION IN THIS TRIAL?

You will not be paid for participation in the study.

WILL MY PARTICIPATION IN THIS STUDY BE KEPT CONFIDENTIAL?

All records of your study will be kept confidential. Your identity will not be revealed in any publication or release of results. Study records will be kept indefinitely for analysis and follow-up.

CAN I WITHDRAW FROM THE STUDY AT ANY TIME DURING THE STUDY PERIOD?

Yes, you can. Your decision will not affect your regular medical care.

IF THERE ARE ANY NEW FINDINGS / INFORMATION, WOULD I BE INFORMED?

Yes.

WHAT HAPPENS IN CASE OF A STUDY RELATED INJURY?

There will be no study related injury.

IS THERE ANY ALTERNATIVE TO THE TREATMENT MENTIONED?

Not applicable.

If you have any further questions, please ask: Dr. Paidi Suresh Kumar (Principal investigator), Senior Resident, Department of Cardiology (Email: sureshkumar55@sctimst.ac.in Ph. No: 9866311341)

For any clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234)

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൾ സയൻസസ് ആന്റ് ടെക്നോളജി,

തിരുവനന്തപുരം

രോഗികൾക്കുള്ള കാര്യവിവരണപത്രം

പഠനശീർഷകം

എൻ ടെർമിനൽ പ്രോബ്രെയിൻ നാട്രിയൂറെറ്റിക് പെപ്റ്റൈഡ് നിലവാരവും പെർക്യൂട്ടേനിയസ് ബലൂൺ മിട്രൽ വാൽവുലോപ്ലാസ്റ്റിക്ക് വിധേയരാകുന്ന രോഗികളുടെ നിലകളിൽ ഉണ്ടാകുന്ന വ്യതിയാനങ്ങളുടെ പഠനവും എക്കോകാർഡിയോഗ്രഫിയുടെയും രക്തചംക്രമ വ്യവസ്ഥയുടെയും ഘടകങ്ങളുടെ പാരസ്പര്യവും

ഗവേഷകരുടെ പേര്
ഡോ. പൈദീ സുരേഷ് കുമാർ,
ഡോ. ഹരികൃഷ്ണൻ എസ്,
ഡോ. സഞ്ജയ് ജി.

പ്രിയ സുഹൃത്ത്/രക്ഷകർത്താവ്,

എൻ ടെർമിനൽ പ്രോബ്രെയിൻ നാട്രിയൂറെറ്റിക് പെപ്റ്റൈഡ് നിലവാരവും പെർക്യൂട്ടേനിയസ് ബലൂൺ മിട്രൽ വാൽവുലോപ്ലാസ്റ്റിക്ക് വിധേയരാകുന്ന രോഗികളുടെ നിലകളിൽ ഉണ്ടാകുന്ന വ്യതിയാനങ്ങളുടെ പഠനവും എക്കോകാർഡിയോഗ്രഫിയുടെയും രക്തചംക്രമ വ്യവസ്ഥയുടെയും ഘടകങ്ങളുടെ പാരസ്പര്യവും എന്ന ഗവേഷണ പദ്ധതിയിൽ താത്പര്യം കാണിച്ചതിന് താങ്കളെ സ്വാഗതം ചെയ്യുകയും നന്ദി പ്രകാശിപ്പിക്കുകയും ചെയ്യുന്നു. ഗവേഷണ പഠനത്തിൽ പങ്കെടുക്കുന്നതിനുമുൻപ്, ഈ ഗവേഷണം എന്തിനാണ് നടത്തുന്നതെന്ന് താങ്കളറിയേണ്ടത് പ്രധാനമാണ്. ഗവേഷണത്തെപ്പറ്റി വ്യക്തമായി അറിയുന്നതിന് പ്രസക്തമായ എല്ലാ വിവരങ്ങളും ഈ പത്രികയിൽ നൽകിയിട്ടുണ്ട്. ഈ പദ്ധതി എങ്ങനെ നടപ്പാക്കുമെന്നതിന്റെ -സ്വഭാവം, ഉദ്ദേശം, നേട്ടങ്ങൾ, അപായങ്ങൾ, അസ്വസ്ഥതകൾ, മുൻകരുതലുകൾ എന്നിവയുടെ വിവരങ്ങൾ ഈ പത്രിക വിശദീകരിക്കുന്നു. താങ്കൾ ശ്രദ്ധാപൂർവ്വം ഉള്ളടക്കം വയിച്ച് മനസ്സിലാക്കുന്നത് പ്രധാനമാണ്. ഈ പത്രികയിൽ ചില ശാസ്ത്ര പദങ്ങൾ ഉണ്ടായേക്കാം, ആകയാൽ സമ്മതപത്രം ഒപ്പിടുന്നതിന് മുമ്പോ പദ്ധതിസമയത്ത് ആകെയോ, താങ്കൾക്കെന്തെങ്കിലും സംശയങ്ങളുണ്ടെങ്കിൽ, അഥവാ താങ്കൾക്ക് കൂടുതൽ വിവരങ്ങൾ ആവശ്യമെങ്കിൽ ഗവേഷകരോടോ അല്ലെങ്കിൽ ബന്ധപ്പെടുവാനായി താഴെപ്പറഞ്ഞിരിക്കുന്നവരോടോ ചോദിക്കാൻ താങ്കൾക്ക് സ്വാതന്ത്ര്യമുണ്ട്.

മിട്രൽ സ്റ്റെനോസിസ് ചികിത്സിക്കാനും നെഞ്ചുവേദന, ക്ഷീണം, ശ്വാസോഛ്വാസ തടസ്സം, വ്യായാമം ചെയ്യുമ്പോഴുള്ള ബുദ്ധിമുട്ടുകൾ, തലചുറ്റലും ബോധക്ഷയവും തുടങ്ങിയ ലക്ഷണങ്ങൾ കുറയ്ക്കാനും ഉപയോഗിക്കുന്ന ഒരു നടപടിയാണ് പിബിഎംവി. താങ്കളുടെ തുടയിലെ മഹാധമനിയിലേക്ക് ഒരു കുഴൽ (ഇൻട്രഡ്യൂസർ) കടത്തും. ഒരു ബലൂൺ കതീറ്റൽ ഇൻട്രൊഡ്യൂസറിന്റെ കവചത്തിലൂടെ

കടത്തിതാങ്കളുടെ മിട്രൽ ഹൃദയവാൽവിലേക്ക് കൊണ്ടുപോകും. താങ്കളുടെ വാൽവ് ബലൂൺ വീർപ്പിച്ച് തുറക്കും. എന്നിട്ട് ബലൂൺ കതീറ്റർ മാറ്റും. താങ്കളുടെ രോഗംബാധിച്ച വാൽവ് മുറിക്കുകയോ നീക്കം ചെയ്യുകയോ ചെയ്യില്ല. അതിനൊപ്പം നടപടിക്കിടയിൽ എക്സ്റെയും ട്രാൻസിസോഫേജിയൽ എക്കോയും നടത്തും.

ഇപ്പോഴത്തെ പഠനത്തിലുൾക്കൊള്ളുന്നതെന്താണ്?

ശസ്ത്രക്രിയാനടപടികൾക്ക് ഒരുദിവസം മുമ്പും ശേഷവും നടത്തിയ രക്തപരിശോധനാ വിവരങ്ങൾ ആശുപത്രിരേഖകളിൽ നിന്നു ശേഖരിക്കും

ഇതിനെത്ര സമയമെടുക്കും?

ആശുപത്രി സന്ദർശനം പതിവ് ചികിത്സയ്ക്കാണ്, പതിവ് തുടർചികിത്സയുടെ ഭാഗമാണ് പരിശോധനകൾ. ഇത് 2 മുതൽ 3 മണിക്കൂർ എടുത്തേക്കാം. ആശുപത്രിയുടെ ഒപിഡിയിൽ ആ സമയത്തുണ്ടാവാൻ ദയവായി തയാറാകുക.

പങ്കാളികളുടെ ഉത്തരവാദിത്വങ്ങളെന്തെല്ലാം?

പഠനത്തിൽ പങ്കെടുക്കാനുള്ള താങ്കളുടെ തീരുമാനം സ്വമേധയാ ആണ്. താങ്കളുടെ വ്യക്തിപരമായ തീരുമാനം. താങ്കൾക്ക് ഏതുസമയത്തും എന്തുകാരണത്താലും മുന്നറിയിപ്പില്ലാതെ പഠനത്തിൽ നിന്നും പിൻമാറാം

പങ്കാളികൾക്ക് പ്രതീക്ഷിക്കുന്ന അപായമെന്തെല്ലാം?

ചികിത്സാരേഖകളിൽനിന്നുള്ള വിവരശേഖരണവും ശസ്ത്രക്രിയയ്ക്കുമുമ്പും ശേഷവുമുള്ള വിവരങ്ങളും ശേഖരിക്കുകയാണ് പഠനത്തിൽ ഉൾക്കൊള്ളുന്നത്. പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് പങ്കാളിക്ക് അപായമൊന്നുമുണ്ടാകില്ല. അവ ആശുപത്രി പ്രവർത്തനചട്ടപ്രകാരം കൈകാര്യം ചെയ്യപ്പെടും. ഒരു പ്രത്യേക ഇടപെടലും നടത്തുന്നില്ല.

ഗവേഷണത്തിൽനിന്നും പങ്കാളികൾക്ക് പ്രതീക്ഷിക്കപ്പെടുന്ന നേട്ടങ്ങളെന്തെല്ലാം?

പങ്കാളികളിൽ പ്രവർത്തനപരമായ തകരാറുകൾക്ക് കാരണമായി ഹൃദയത്തിന്റെ എന്തെങ്കിലും തകരാറുണ്ടോയെന്ന് വിശദമായി വിലയിരുത്തപ്പെടും. തുടർപരിശോധനയും വിലയിരുത്തലും മോശം ഫലത്തിന്റെ അപായസാദ്ധതകളൾ അല്ലെങ്കിൽ പ്രവർത്തനപരമായ ശേഷികുറഞ്ഞുവരുന്നത് കണ്ടെത്താൻ സഹായകമാണ്. നേരത്തെയുള്ള ഇടപെടലുകളോ അധികമായ മരുന്നുചികിത്സയോ ആവശ്യമുള്ള രോഗികളെ കണ്ടെത്താനിത് സഹായകമാണ്. സമാനമായ അവസ്ഥയിലുള്ള രോഗികൾക്ക് വേണ്ടും വിധമുള്ള ചികിത്സ ആസൂത്രണം ചെയ്യാനും, ശസ്ത്രക്രിയാതന്ത്രവും വേണ്ടുന്ന സമയവും നിശ്ചയിക്കാനും പഠനഫലങ്ങൾ ഭാവിയിൽ സഹായകമായേക്കാം.

പങ്കാളികൾക്ക് പ്രതിഫലം നൽകുമോ?

ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതിന് താങ്കൾക്ക് പ്രതിഫലമൊന്നും നൽകില്ല

പഠനത്തിലുള്ള എന്റെ പങ്കാളിത്തം രഹസ്യമായി സൂക്ഷിക്കുമോ?

താങ്കളുടെ പഠനത്തിലെ രേഖകളെല്ലാം രഹസ്യമായി സൂക്ഷിക്കും. പ്രസിദ്ധീകരണങ്ങളിലോ, പഠനഫലം പുറത്തുവിടുമ്പോഴോ താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ വെളിവാക്കില്ല. പഠനരേഖകൾ അനന്തമായി വിലയിരുത്തലിനും തുടർചികിത്സയ്ക്കുമായി സൂക്ഷിക്കും.

പഠനകാലയളവിലെപ്പോഴും എനിക്ക് പഠനത്തിൽനിന്നും പിൻവാങ്ങാമോ?

താങ്കൾക്ക് കഴിയും. താങ്കളുടെ തീരുമാനം താങ്കളുടെ വൈദ്യ പരിചരണത്തെ ബാധിക്കില്ല.

പുതുതായി എന്തെങ്കിലും കണ്ടെത്തിയാലോ പുതിയവിവരങ്ങളുണ്ടെങ്കിലോ എന്നെ അറിയിക്കുമോ?

അറിയിക്കും

പഠനസംബന്ധിയായി പരുക്കുണ്ടായാലെന്ത് സംഭവിക്കും. ?

പഠന സംബന്ധിയായി ഒരു പരുക്കുമുണ്ടാകില്ല.

നിർദ്ദേശിതമായ ചികിത്സയ്ക്ക് പകരമെന്തെങ്കിലുമുണ്ടോ?

ബാധകമല്ല

താങ്കൾക്ക് കൂടുതലെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ചോദിക്കുക. ഡോ. പൈദി സുരേഷ് കുമാർ (പ്രധാന ഗവേഷകൻ), സീനിയർ റെസിഡന്റ്, കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്, ഇമെയിൽ. sureshkumar55@sctimst.ac.in, ഫോൺ. 9866311341
ഏന്തെങ്കിലുംവിശദീകരണങ്ങൾക്ക് ബന്ധപ്പെടുക. ഡോ. മാല രാമനാഥൻ, മെമ്പർസെക്രട്ടറി, SCTIMST-IEC, അഡീഷണൽ പ്രൊഫസർ AMCHSS, SCTIMST (ഫോൺ. 0471 2524234) ഇമെയിൽ iec.mem.sec@sctimst.ac.in

STUDY CONSENT FORM

TITLE OF THE STUDY: STUDY OF CHANGE IN N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS

Study number: All patients undergoing PBMV at SCTIMST will be included in study

Participant's name: Date of Birth / Age (in years):

I_____

son/daughter of _____

(Please tick boxes).

[ ] Declare that I have read the above information provided to me regarding the study: "STUDY OF CHANGE IN N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS." and have clarified any doubts that I had.

[ ] I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

[ ] I understand that the study staff and institutional ethics committee members may not need my permission to look at my health records even if I withdraw from the trial. I agree to this access.

[ ] I understand that my identity may not be revealed in any information released to third parties or published.

[ ] I voluntarily agree to take part in this study.

[ ] I received a copy of this signed consent form.

Name:

Signature:

Date:

Name of the witness:

Relation to Patient:

Date:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____

Name and Signature of Person Obtaining Consent

Dr. Paidi Suresh Kumar

Senior resident

Dept. of Cardiology SCTIMST

For any clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234.

പഠന സമ്മതപത്രം

പഠനശീർഷകം

പെർക്യൂട്ടേനിയസ് ബലൂൺ മിട്രൽ വാൽവുലോപ്ലാസ്റ്റിക്ക് വിധേയരാകുന്ന രോഗികളുടെ എൻ ടെർമിനൽ പ്രോബ്രെയിൻ നാട്രിയൂറെറ്റിക് പെപ്റ്റെഡ് നിലകളിൽ ഉാകുന്ന വ്യതിയാനങ്ങളുടെ പഠനവും എക്കോകാർഡിയോഗ്രഫിയുടെയും രക്തചംക്രമണ വ്യവസ്ഥയുടെയും ഘടകങ്ങളുടെ പാരസ്പര്യവും

പഠന നമ്പർ

SCTIMST യിൽ പിബിഎംവിക്ക് വിധേയരാകുന്ന എല്ലാവരെയും പഠനത്തിൽ ഉൾപ്പെടുത്തും.

പങ്കാളിയുടെ പേര് _____ **ജനനതീയതി/ വയസ്സ് (വർഷത്തിൽ)** :____

ഞാൻ..... പുത്രൻ/പുത്രി.....
(ദയവായി കോളങ്ങൾ അടയാളപ്പെടുത്തുക)

- മുകളിൽ, പെർക്യൂട്ടേനിയസ് ബലൂൺ മിട്രൽ വാൽവുലോപ്ലാസ്റ്റിക്ക് വിധേയരാകുന്ന രോഗികളുടെ എൻ ടെർമിനൽ പ്രോബ്രെയിൻ നാട്രിയൂറെറ്റിക് പെപ്റ്റെഡ് നിലകളിൽ ഉാകുന്ന വ്യതിയാനങ്ങളുടെ പഠനവും എക്കോകാർഡിയോഗ്രഫിയുടെയും രക്തചംക്രമണ വ്യവസ്ഥയുടെയും ഘടകങ്ങളുടെ പാരസ്പര്യവും എന്ന പഠന സംബന്ധിയായി എനിക്കു നൽകിയ വിവരങ്ങൾ വായിച്ചു എന്നു പ്രസ്താവിക്കുന്നു. എന്റെ എല്ലാ സംശയങ്ങളും പരിഹരിച്ചു.[ ]
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം പൂർണ്ണമായും സ്വമേധയാ ആണെന്നും അനുവാദം എനിക്ക് ഏതുസമയത്തും എന്റെ ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവലിക്കാൻ അവകാശമുണ്ടെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഞാൻ ഈ പഠനത്തിൽ നിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും സ്ഥാപനത്തിലെ നൈതിക കമ്മിറ്റി അംഗങ്ങൾക്കും എന്റെ ആരോഗ്യരേഖകൾ പരിശോധിക്കുന്നതിന് എന്റെ അനുവാദം ആവശ്യമില്ലെന്ന്ഞാൻ മനസ്സിലാക്കുന്നു. അതിനോട് ഞാൻ യോജിക്കുന്നു. [ ]
- എന്നെ തിരിച്ചറിയാനുതകുന്ന വിവരങ്ങൾ ഒന്നും മൂന്നാം കക്ഷികൾക്കു നൽകുകയോ പ്രസിദ്ധീകരിക്കുകയോ ചെയ്യില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഞാൻ സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിക്കുന്നു. [ ]
- ഒപ്പിട്ട സമ്മതപത്രത്തിന്റെ ഒരു പ്രതി എനിക്ക് ലഭിച്ചു [ ]

പങ്കെടുക്കുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേര്

ഒപ്പ്

പ്രധാന ഗവേഷകൻ

ഡോ. പൈദി സുരേഷ് കുമാർ

സീനിയർ റെസിഡന്റ്

കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്

വിശദീകരണത്തിന് ബന്ധപ്പെടുക. ഡോ. മാല രാമനാഥൻ, മെമ്പർസെക്രട്ടറി,
SCTIMST-IEC, അഡീഷണൽ പ്രൊഫസർ AMCHSS, SCTIMST (ഫോൺ. 0471 2524234)
ഇമെയിൽ

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1412/JULY-2019 12.08.2019

Dr. Paidi Suresh Kumar
Senior Resident, Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Paidi Suresh Kumar,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "STUDY OF CHANGE IN N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN PATIENTS UNDERGOING PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY AND CORRELATION WITH ECHOCARDIOGRAPHIC AND HEMODYNAMIC PARAMETERS (IEC/1412)" on 26th July, 2019.

The following documents were reviewed:

Original submission

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 04.07.2019 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

Revised submission

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 12.08.2019 with checklist*
2. *Copy of IEC Recommendation Letter dated 07.08.2019*
3. *TAC Approval Letter*
4. *IEC Application Form*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information and Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 26th July, 2019 at Noshir H Wadia Conference Hall, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
2.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
5.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

STUDY OF CHANGE IN NT-PROBNP LEVELS IN PATIENTS UNDERGOING PBMV

by suresh kumar

General metrics

96,272	14,745	1368	58 min 58 sec	1 hr 53 min
characters	words	sentences	reading time	speaking time

Score

This text scores better than 94% of all texts checked by Grammarly

Writing Issues

514	190	324
Issues left	Critical	Advanced

Plagiarism

37 sources

7% of your text matches 37 sources on the web or in archives of academic publications

MASTER CHART

Patient	Height in	Weight in	BMI (kg/m	BSA	Age (years	Sex	HISTORY	BMV date	FC	HB	CREATININ	GFR	Rhythm	LAE	RAD	RBBB/RVH	Pre LA size	Pre MVA 2	Pre MVA P	Pre MS gra	Pre MS gra	Pre HR (bp	Pre SVP	Pre MC	Pre LC	Pre MR
1	1.66	43	15.60459	1.408111	25	M		29.04.19	III	14.4	1.05	86.1	AF	1		1	47	0.75	0.8	16	9	67	PRESENT	FUSED	FUSED	MILD
2	1.54	69	29.09428	1.718042	42	F	BMV (199	06.05.19	II	12.8	0.86	72.4	SR				35	1.1	1	26	20	80		FUSED	FUSED	TRIVIAL
3	1.63	65	24.4646	1.715534	56	M	CMV (198	14.05.19	III	13.5	1.29	57.6	AF	1		1	49	1.2	0.9	31	15	70		FUSED	FUSED	MILD
4	1.6	76	29.6875	1.837873	57	F		20.05.19	II	15.5	1.2	46.3	AF	1			45	1.1	0.9	22	12	78		FUSED	FUSED	MILD
5	1.47	56.4	26.10024	1.517564	68	F		24.05.19	III	13.1	1.03	53.3	AF	1			47	1.03	0.9	32	19	65		FUSED	FUSED	MILD
6	1.58	70.4	28.20061	1.757776	51	F	CMV 1985	04.06.19	III	13.1	0.8	75.6	AF	1		1	43	1.2	1.1	18	10	60		FUSED	FUSED	MILD
7	1.675	48	17.10849	1.494434	27	M		10.06.19	II	16.6	1.08	89.6	SR	1			38	1.18	1.01	35	16	68		FUSED	FUSED	MILD
8	1.62	56	21.33821	1.587451	59	M	CMV(1988	24.06.19	II	14	1.02	76.5	AF	1			45	1.1	0.9	16	11	65		FUSED	FUSED	MILD
9	1.55	67.6	28.13736	1.706035	49	F	BMV (200	01.07.19	II	14.5	1.22	46.8	SR	1			47	1.16	0.9	22	14	88		FUSED	FUSED	TRIVIAL
10	1.39	47.2	24.42938	1.349979	24	F		01.07.19	III	13	0.68	106.3	SR	1			38	1.1	1.1	36	21	80		FUSED	FUSED	MILD
11	1.6	56	21.875	1.577621	34	F	CMV (200	08.07.19	II	12.2	0.76	87.1	SR	1	1	1	44	0.9	1	48	34	60		FUSED	FUSED	MILD
12	1.49	44.5	20.04414	1.357131	30	F		22.07.19	III	13.6	0.96	66.5	AF			1	35	0.7	0.8	45	26	67		FUSED	FUSED	TRIVIAL
13	1.53	53.4	22.81174	1.506486	33	F		22.07.19	II	12.2	1.01	63.1	SR				41	1.2	1.1	27	16	65		FUSED	FUSED	MILD
14	1.63	65	24.4646	1.715534	47	F	BMV (200	22.07.19	III	15.1	1.2	48.2	AF				42	1.2	1.3	25	12	65		FUSED	FUSED	MILD
15	1.545	67	28.06841	1.695705	54	F		03.08.19	III	14.8	1.07	53.4	AF				50	0.9	0.95	25	15	60		FUSED	FUSED	MILD
16	1.58	71.6	28.6813	1.772694	47	F	BMV (200	05.08.19	III	13.5	0.77	80.4	SR	1			50	1.01	1	26	11	65		FUSED	FUSED	NO
17	1.77	93.1	29.71688	2.13949	51	M		05.08.19	II	13.4	1.08	72.1	AF	1			60	1.1	1	24	10	72		FUSED	FUSED	MILD
18	1.58	60	24.03461	1.622755	27	F	7MONTHS	05.08.19	III	12.7	0.57	127.2	SR	1	1	1	48	0.6	0.75	30	18	85		FUSED	FUSED	NO
19	1.69	77.5	27.1349	1.907405	44	F		12.08.19	II	12.7	0.75	83.9	SR	1			52	1.06	1	22	12	68		FUSED	FUSED	TRIVIAL
20	1.67	54	19.36247	1.582719	29	F		12.08.19	II	12.4	0.82	82.4	SR	1			47	0.9	1	15	10	65		FUSED	FUSED	NO
21	1.57	44.3	17.97233	1.389954	37	F		13.08.19	III	11.9	0.7	94.2	AF	1			47	0.9	0.84	34	24	68		FUSED	FUSED	MILD
22	1.54	58	24.45606	1.575154	48	F		19.08.19	II	13.8	0.7	89.3	AF	1			44	1.1	1.1	33	22	60		FUSED	FUSED	MILD
23	1.68	73	25.86451	1.845716	54	F	BMV 1996	19.08.19	II	16.2	1.11	51.2	SR	1			45	0.85	0.9	25	14	75		FUSED	FUSED	NO
24	1.47	54	24.98959	1.484924	54	F		22.08.19	III	14.2	0.82	72.6	AF	1		1	46	1.1	1	16	10	70		FUSED	FUSED	TRIVIAL
25	1.65	45.8	16.82277	1.44885	25	M		02.09.19	II	15	0.94	97.8	SR	1		1	51	0.66	0.7	33	20	65	PRESENT	FUSED	FUSED	NO
26	1.5	48.9	21.73333	1.42741	48	F	CMV 1996	23.09.19	II	13.4	0.89	67.7	AF				40	0.78	0.94	25	12	66	PRESENT	FUSED	FUSED	NO
27	1.475	35.8	16.45504	1.211117	28	F	MOD AR	30.09.19	III	13	0.65	108.5	SR	1	1	1	43	0.4	0.4	45	23	75		FUSED	FUSED	NO
28	1.455	51.3	24.23212	1.439922	44	F	CMV 1990	14.10.19	III	14.8	1.15	51.3	SR	1			36	0.6	0.6	39	15	88	PRESENT	FUSED	FUSED	NO
29	1.54	37.3	15.72778	1.263175	13	F		22.10.19	II	11.1	0.63	131.5	SR	1	1	1	43	0.8	0.78	30	22	76		FUSED	FUSED	TRIVIAL
30	1.82	76.5	23.09504	1.966596	37	F		28.10.19	II	15.1	1.41	42	AF	1	1	1	42	0.9	0.97	23	17	66		PARTLY	FUSED	NO
31	1.58	65	26.03749	1.689017	60	M	CMV 1981	4.11.19	II	13.7	1.2	61.8	SR	1			44	0.9	1	20	11	69	PRESENT	FUSED	FUSED	MILD
32	1.56	70.6	29.01052	1.749095	22	F	RECURREN	4.11.19	II	11.5	0.77	93.7	SR	1	1	1	43	1.15	1.1	28	12	110	PRESENT	FUSED	FUSED	NO
33	1.445	53	25.38284	1.458548	49	F		19.11.19	II	12.7	1.01	58.3	SR				45	0.9	0.9	35	13	70		FUSED	FUSED	TRIVIAL
34	1.44	42.4	20.44753	1.302306	52	F	COPD	2.12.19	III	13.1	0.98	59.6	SR	1	1	1	43	0.9	1	37	20	80		FUSED	FUSED	NO
35	1.48	52.6	24.01388	1.470525	29	F		2.12.19	II	11.9	0.74	92.8	SR	1			46	1	1.1	16	10	65		FUSED	FUSED	MILD
36	1.56	60	24.65483	1.612452	27	F	Primi 31w	2.12.19	II	12.7	0.44	171.5	SR				31	1.1	1.2	28	20	82		FUSED	FUSED	NO
37	1.53	63	26.91273	1.636307	23	F	Primi 24w	16.12.19	II	13.4	0.48	160.3	SR	1			60	0.8	0.9	28	18	78		FUSED	FUSED	MILD
38	1.62	72.4	27.58726	1.804993	46	M	MOD AR, /	16.12.19	II	13.5	0.85	97	SR				38	1.4	1.5	18	8	80		FUSED	FUSED	MILD
39	1.57	53.4	21.66416	1.526052	28	M		16.12.19	II	15.3	1.08	81.4	SR	1			48	0.8	0.9	30	21	78		FUSED	FUSED	MILD
40	1.61	49.7	19.17364	1.49087	46	F		31.12.19	II	15	0.97	61.8	SR	1			46	1.1	1	25	15	70	PRESENT	FUSED	FUSED	TRIVIAL
41	1.51	37.8	16.57822	1.259166	58	F		31.12.19	II	14.4	0.87	66.9	SR	1			34	0.9	1	20	11	65	PRESENT	FUSED	FUSED	NO
42	1.61	69	26.61934	1.756654	35	F		06.01.20	II	12.4	0.75	87.9	SR	1		1	48	0.9	0.9	30	18	78	PRESENT	FUSED	FUSED	NO
43	1.56	32.5	13.3547	1.186732	31	F		13.01.20	III	11.3	0.66	104.5	SR			1	38	0.7	0.5	22	18	76	PRESENT	FUSED	FUSED	MILD
44	1.59	40	15.82216	1.32916	13	F		23.01.20	II	13.7	0.7	139.1	SR	1		1	45	1.1	1.3	24	15	80	PRESENT	FUSED	FUSED	TRIVIAL
45	1.81	87	26.55597	2.091451	33	M		03.02.20	II	15.7	1.19	70.4	SR	1		1 RBBB	51	0.8	1	20	13	84		FUSED	FUSED	MILD

Pre LVIDD	Pre LVISD	Pre EF (%)	Pre RVSP(m	Pre TAPSE	Post LA si	Post MVA	Post MVA	Post MS g	Post MS g	Post HR (b	Post SVP	Post MC	Post LC	Post MR	Post LVIDI	Post LVISI	Post EF (%	Post RVSP(m	Post TAPS	RA Pre A	RA Pre V	RA Pre M (mm of	RA Post A	RA Post V	RA Post M
46	29	57	33	20	45	1.6	1.75	16	7	60	PRESENT	SPLIT	PARTLY SP	MILD	46	29	57	28	18		4	3		4	3
42	27	60	36	22	35	1.43	1.55	13	8	77		SPLIT	FUSED	MILD	42	27	65	32	19	10	9	6	8	7	6
53	35	56	35	18	45	1.5	1.5	13	4	50		SPLIT	SPLIT	MILD	51	31	68	29	17		8	5		6	5
45	29	65	32	22	40	1.7	1.7	14	4	65		PARTLY SF	PARTLY SP	MILD	45	29	65	22	24		6	4		6	4
41	23	76	50	24	43	1.5	1.5	16	6	70		SPLIT	FUSED	MILD	40	23	66	20	22		6	6		4	4
44	31	56	65	20	40	1.6	1.7	15	7	75		PARTLY SF	SPLIT	MILD	45	31	56	40	19		17	15		16	10
39	27	60	35	22	33	1.6	1.6	12	6	76		SPLIT	SPLIT	MILD	45	26	73	25	18	8	6	5	6	5	5
40	23	65	35	20	42	1.5	1.45	11	5	68		SPLIT	SPLIT	MILD	40	23	66	25	19		4	5		8	6
39	23	63	41	19	45	1.9	2.02	12	3	80		SPLIT	PARTLY SP	MILD	35	23	63	30	18	8	6	5	7	4	4
40	23	65	45	22	38	1.6	1.68	15	7	75		SPLIT	PARTLY SP	MILD	40	23	65	34	19	25	12	12	10	6	4
44	29	68	50	20	42	1.5	1.55	18	8	72		SPLIT	PARTLY SP	MILD	44	29	68	40	18	7	5	4	5	4	3
53	34	67	81	19	35	1.6	1.86	17	7	76		SPLIT	SPLIT	MILD	49	30	65	34	19		5	4		5	4
41	29	58	50	21	40	1.6	1.9	13	3	70		SPLIT	PARTLY SP	MILD	40	29	60	35	22	8	6	5	5	3	3
46	30	62	48	18	44	1.3	1.2	15	8	76		SPLIT	SPLIT	MILD	46	24	66	31	23		8	4		9	6
46	32	58	31	19	46	1.9	1.8	16	4	70		SPLIT	SPLIT	TRIVIAL	45	31	59	25	19		8	6		6	4
44	29	60	40	20	45	1.6	1.75	14	7	76		PARTLY SF	PARTLY SP	TRIVIAL	44	29	60	35	20	9	7	5	8	6	5
54	35	67	55	18	55	1.8	1.9	17	9	70		SPLIT	SPLIT	MILD	64	35	67	40	21		30	25		20	15
28	19	68	85	23	45	1.2	1.3	21	12	81		SPLIT	SPLIT	TRIVIAL	31	18	70	63	17	13	16	13	13	15	12
48	33	63	60	18	50	1.9	2.1	16	6	76		SPLIT	SPLIT	MILD	49	33	63	24	20	4	5	6	5	7	6
43	26	69	38	19	45	1.8	1.9	14	7	70		SPLIT	SPLIT	MILD	43	26	69	23	21	6	5	5	4	5	4
44	23	56	43	18	47	1.7	1.6	9	4	70		SPLIT	SPLIT	MILD	44	23	66	35	19		12	10		12	10
45	27	69	50	21	42	1.55	1.5	12	6	75		SPLIT	SPLIT	MILD	45	27	69	40	20		5	6		4	5
40	23	65	48	20	43	1.65	1.7	19	7	65		SPLIT	SPLIT	MILD	44	26	68	24	20	9	2	10	6	8	7
41	29	58	90	17	46	1.84	1.8	16	4	60		SPLIT	SPLIT	MODERAT	46	29	65	63	18		14	10		12	8
45	29	65	35	20	48	1.35	1.4	19	9	75	PRESENT	SPLIT	SPLIT	MILD	45	29	65	38	19	10	7	6	6	8	5
35	21	70	44	19	40	1.4	1.52	10	5	70	PRESENT	FUSED	SPLIT	MILD	38	21	72	35	20		6	5		5	4
39	25	63	125	16	39	1.3	1.2	23	12	66		SPLIT	SPLIT	MILD	40	24	69	43	18	14	18	14	14	18	15
35	24	68	55	22	35	1.1	1	25	9	70	PRESENT	SPLIT	PARTLY SP	MILD	42	22	63	45	19	8	7	6	8	6	5
43	23	78	66	22	32	1.8	1.95	7	3	75		SPLIT	PARTLY SP	TRIVIAL	51	29	55	26	21	9	7	7	8	7	7
54	38	57	28	21	45	1.5	1.65	8	3	55		SPLIT	PARTLY SP	TRIVIAL	54	35	69	13	21		10	9		6	4
46	27	71	25	20	43	1.8	1.75	9	4	78	PRESENT	SPLIT	PARTLY SP	MILD	42	25	70	28	20	8	5	5	6	4	3
39	25	64	80	17	40	1.6	1.7	12	5	75	PRESENT	SPLIT	SPLIT	MILD	40	29	65	65	18	7	7	5	8	7	5
46	28	68	28	20	45	1.7	1.8	11	4	90		SPLIT	SPLIT	TRIVIAL	46	28	68	35	20	7	5	4	8	5	5
33	20	70	110	16	42	1.3	1.4	19	9	75		SPLIT	SPLIT	MILD	40	25	69	75	18	6	5	10	8	10	6
39	22	74	59	20	45	2.01	1.95	12	3	70		SPLIT	SPLIT	TRIVIAL	40	23	75	38	19	4	7	5	4	7	5
32	20	67	36	21	30	1.45	1.55	15	5	75		SPLIT	SPLIT	NO	36	20	72	30	20	4	6	5	4	6	5
38	25	52	52	22	58	1.4	1.4	18	8	70		SPLIT	SPLIT	MODERAT	38	20	75	35	21	4	3	5	4	5	4
49	28	73	39	21	35	1.8	1.75	14	7	65		SPLIT	SPLIT	MILD	48	29	73	35	20	5	5	5	6	7	5
40	25	64	54	20	45	1.85	1.7	15	5	70		SPLIT	SPLIT	MILD	40	25	64	35	22	8	9	7	8	9	7
39	21	77	40	21	45	1.2	1.1	18	6	68	PRESENT	SPLIT	SPLIT	TRIVIAL	40	21	77	25	22	8	4	3	8	6	4
26	15	75	42	22	34	1.4	1.5	13	6	69	PRESENT	PARTLY SF	SPLIT	NO	30	19	65	35	19	7	4	4	7	4	4
38	24	65	55	21	45	1.1	1.2	25	9	80	PRESENT	SPLIT	SPLIT	MILD	38	24	65	33	21	12	7	6	6	6	5
39	21	71	110	16	47	1.3	1.35	13	6	72	PRESENT	SPLIT	SPLIT	MODERAT	35	21	70	38	20	10	7	6	5	3	4
36	21	65	36	21	45	1.8	1.95	13	4	80	PRESENT	PARTLY SF	SPLIT	MILD	38	22	65	30	22	9	8	7	7	8	6
45	26	73	45	20	48	1.7	1.65	15	6	86		SPLIT	SPLIT	TRIVIAL	50	27	67	32	21	10	11	8	10	12	10

RVSP pre (	RVED pre	RVSP post	RVED post	PASP pre (	PADP pre	PAmP pre	PASP post	PADP post	PAmP pos	LA A pre (	LA V pre (	LA m pre (	LA A post	LA V post	LA m post	LVSP pre (	LVED pre(	LVSP post	LVED post	SBP pre (n	DBP pre (n	MAP pre(	SBP post (	DBP post (	MAP post
76	5	40	4	76	30	45	40	15	24		44	29		20	10	96	4	95	8	105	60	87	115	60	81
50	8	35	8	50	24	35	32	15	22	25	30	23	15	18	13	112	8	110	10	104	64	77	108	70	82
32	7	30	7	35	19	25	30	14	19		25	18		20	13	110	8	116	10	110	60	77	116	75	88
34	5	30	5	34	25	28	30	19	24		35	23		32	18	160	16	160	18	160	100	120	160	110	123
50	6	35	5	50	20	22	35	12	20		20	18		18	15	140	10	150	12	140	72	101	150	72	112
67	14	38	8	67	32	45	38	26	30		45	31		46	25	134	16	139	18	134	75	95	139	80	100
35	4	16	4	35	26	29	16	10	12	26	28	26	12	10	10	100	6	110	8	100	60	75	110	70	85
35	5	38	8	35	23	27	35	16	20		24	23		20	16	144	8	145	10	144	70	95	145	80	98
35	6	30	4	35	25	29	30	15	20	26	21	24	22	18	14	140	10	142	12	140	70	97	140	75	95
65	10	60	10	65	30	44	60	18	34	30	45	25	16	24	11	112	8	110	10	112	65	81	110	70	83
50	8	35	8	55	20	30	34	12	20	36	44	26	22	20	12	100	8	110	12	100	70	80	106	70	82
50	6	35	6	50	30	36	34	15	20		18	30		26	15	120	8	120	12	120	73	88	120	70	90
50	5	38	5	50	22	35	38	12	22	30	32	21	26	26	15	120	6	120	12	120	68	82	120	76	85
50	5	50	6	52	35	43	60	30	36		35	22		25	18	122	8	129	12	124	80	97	129	84	99
45	5	30	5	45	15	24	32	12	18		22	15		18	12	150	8	155	10	150	80	110	155	85	115
40	6	30	5	40	18	22	32	10	20	24	18	16	17	12	11	120	8	120	10	110	60	80	110	68	90
55	8	45	12	55	30	39	45	22	30		35	28		25	20	120	12	130	15	120	65	83	130	70	90
80	13	50	11	79	53	62	49	26	34	44	55	50	22	28	24	125	12	124	15	120	80	93	120	80	94
60	6	38	6	60	24	36	38	16	22	38	35	20	20	16	14	150	8	150	10	150	60	90	150	60	90
40	4	40	5	40	32	35	36	20	25	34	35	32	22	24	20	102	10	102	12	100	50	65	104	44	64
45	10	40	10	45	28	32	40	17	24		30	26		19	15	135	8	140	10	135	75	105	140	80	110
50	6	40	6	50	20	30	40	20	28		36	24		32	22	150	12	150	14	150	80	100	150	70	96
70	8	50	6	70	46	54	50	26	34	42	52	46	26	30	26	120	16	130	18	120	70	86	130	67	89
120	15	110	12	130	40	80	120	40	75		26	21		18	14	140	8	150	10	140	70	90	150	70	92
96	6	60	8	93	42	63	60	20	33	46	52	42	20	10	13	108	10	116	10	100	64	76	110	60	76
40	8	30	6	40	20	27	38	10	18		32	22		20	13	120	10	110	10	120	60	80	110	60	78
120	14	60	14	120	40	70	60	30	40	30	60	40	12	14	12	140	9	120	10	140	70	83	120	70	84
52	8	45	8	52	26	37	45	16	23	27	35	25	22	26	19	140	12	140	15	140	80	106	140	80	105
31	10	26	7	33	15	24	26	10	18	23	17	16	11	11	9	88	7	74	7	80	49	62	75	49	60
45	10	40	8	45	20	31	40	13	21		26	25	20	23	14	120	12	140	14	120	70	97	140	70	104
30	5	30	5	30	22	25	30	15	22	20	24	21	14	16	12	140	10	138	10	160	70	107	138	60	90
70	8	70	8	70	30	43	70	25	40	32	24	22	18	23	13	110	12	120	12	110	70	83	120	80	93
34	6	35	6	34	12	19	35	10	18	20	15	13	16	12	10	110	5	110	6	110	60	78	110	70	83
120	10	100	10	120	40	67	100	25	50	40	55	45	22	28	26	150	16	160	18	150	80	105	160	90	115
35	6	30	6	35	21	26	30	12	16	26	30	20	16	20	11	108	8	108	10	107	74	85	108	76	87
55	8	35	8	55	40	45	35	15	22	45	58	40	18	22	14	94	10	100	12	94	60	72	100	60	75
45	6	35	6	45	25	32	35	15	22	20	30	25	10	20	15	120	8	125	10	120	80	93	125	85	98
45	6	35	5	45	20	28	35	10	18	26	22	18	24	18	12	150	6	160	8	150	80	103	160	80	106
45	13	45	12	45	25	32	45	15	20	28	32	25	18	20	13	100	8	116	10	100	70	83	116	74	84
34	6	28	6	34	14	21	28	12	18	28	22	18	18	16	12	120	10	120	10	120	70	86	120	70	86
40	7	35	6	40	20	24	35	16	22	20	16	14	17	14	11	120	6	120	8	120	60	82	120	70	87
55	5	35	8	50	30	38	35	15	22	38	48	35	14	17	15	140	10	140	15	140	70	93	140	80	100
80	10	45	5	80	40	54	45	20	34	40	50	32	14	18	15	106	6	105	10	106	70	82	106	60	75
30	8	32	11	30	16	21	30	14	19	22	20	19	18	20	15	82	6	80	10	82	52	62	90	50	63
40	8	40	10	40	18	28	40	18	24	40	35	25	35	30	18	120	10	130	15	120	70	90	130	77	94

MG pre (m	MG post (r	MVA pre (	MVA post	CO pre (L/	CO post (L	CI pre (L/r	CI post (L/	PVR pre (v	PVR post (	SVR pre (v	SVR post (	DILATOR/	No. OF DIL	RESIDUAL	NT PROBN	NT PROBNP POST (p	Followup	NYHA	MVA 2D	MVA PHT	PMG	MMG	RVSP	MR	SURGERY	STROKE	MORTALIT
25	5	0.69	1.81	3.69	4.28	2.64	3.05	4.336043	3.271028	22.76423	18.2243	24	1 (20)	MILD	1253	795	25	II	1.4	1.6	14	6	36				
12	5	1.2	2.03	3.9	4.68	2.28	2.75	3.076923	1.923077	18.20513	16.23932	24	3 (22, 23, 2	MILD	258	184	25	I									
13	4	0.99	1.62	4.36	5.23	2.54	3.06	1.605505	1.147228	16.51376	15.86998	26	2 (25, 26)	MILD	652	356	25	II									
13	4	1	2.72	4.67	5.6	2.55	3.06	1.070664	1.071429	24.8394	21.25	26	2 (24, 25)	MILD	253	152	25	I									
12	6	0.9	1.5	3.6	4.37	2.38	2.89	1.111111	1.144165	26.38889	24.71396	24	2 (20, 21)	MILD	589	325	25	I									
15	7	0.89	2.03	4.12	4.94	2.35	2.82	3.398058	1.012146	19.41748	18.21862	26	2 (25, 26)	MILD	1526	953	24	II									
20	4	0.73	2.56	3.93	4.72	2.35	2.82	0.763359	0.423729	17.8117	16.94915	26	2 (24, 25)	MILD	256	70	24	I	1.78	1.8	7	4	23				
15	5	0.93	1.93	3.4	4.1	2.09	2.53	1.1764	0.9756	26.47059	22.43902	26	2 (23, 24)	MILD	153	90	24	II	1.3	1.2	11	4	28				
14	6	0.99	1.96	4	4.95	2.35	2.87	1.25	1.212121	23	18.38384	24	2 (21, 23)	MILD	356	125	24	II									
15	6	0.8	1.5	3.1	4.5	2.29	3.3	6.129032	5.111111	22.25806	17.55556	24	2 (20, 22)	MILD	956	574	4	II	1.6	1.65	20	8	15				
16	6	0.74	1.56	3.41	4.14	2.15	2.62	1.173021	1.932367	22.28739	19.08213	24	2 (21, 22)	MILD	306	112	23	I	1.4	1.3	11	5	42				
20	6	0.66	1.85	2.45	3.25	1.8	2.38	2.44898	1.538462	34.28571	26.46154	24	1 (22)	MILD	452	123	23	I	1.86	1.8	10	6	24				
15	4	0.79	2.39	3.67	4.41	2.44	2.94	3.814714	1.587302	20.98093	18.5941	24	2 (22, 24)	MILD	356	152	23	II	1.63	1.5	30	18	48	3			
15	7	0.9	2.03	3.74	4.49	2.18	2.62	5.614973	4.008909	24.86631	20.71269	24	2 (22)	MILD	596	352	23	II	1.45	1.5				2			
16	4	0.79	2.11	3.35	4.38	1.81	2.37	2.686567	1.369863	31.04478	25.34247	24	2 (22)	MILD	652	432	23	II									
12	3	0.75	1.8	4.8	5.23	2.77	3.02	1.25	1.720841	15.625	16.25239	24	3 (22, 23, 2	MILD	595	123	22	II	1.5	1.4	13	8	34	1			
16	8	1.1	1.98	4.43	5.91	2.14	2.85	2.48307	1.692047	13.09255	12.69036	24	2 (22, 24)	MILD	602	471	22	II	1.5	1.6	17	9	40	2			
35	9	0.79	1.6	3.81	4.58	2.35	2.82	3.149606	2.183406	20.99738	17.90393	24	3 (22, 23, 2	MODERAT	1125	689	22	II									
20	5	1	1.85	3.68	4.53	2.12	2.8	4.347826	1.766004	22.82609	18.54305	24	1 (22)	MILD	562	126	22	I	1.62	1.43	16	9	22	2			
22	6	0.92	1.83	4.62	5.95	2.68	3.45	0.649351	0.840336	12.98701	10.08403	24	1 (22)	MILD	452	162	**22**	**II**								**TIA 28.1.2021**	
18	4	0.85	1.7	3.84	4.61	2.78	3.34	1.5625	1.952278	24.73958	21.69197	24	2 (23, 23.5	MILD	956	632	22	II									
12	5	1.13	1.53	4.72	5.19	3.02	3.33	1.271186	1.156069	19.91525	17.53372	24	2 (22)	MILD	567	356	22	II									
30	8	0.95	1.62	4.94	6.1	2.7	3.33	1.619433	1.311475	15.38462	13.44262	24	4 (20, 21, 2	MILD	890	523	22	II	1.53	1.42	19	8	29	0			
13	4	1.06	1.54	2.46	3.26	1.68	2.23	23.98374	18.71166	32.52033	25.76687	26	2 (23, 24)	MILD	1056	752	**11**	**II**	**1**		**11**	**6**	**65**	**3**			**july 14 202**
28	6	0.5	1.3	3.06	3.8	2.12	2.63	6.862745	5.263158	22.87582	18.68421	24	4 (21, 22, 2	MODERAT	356	250	22	I									
12	4	0.77	1.44	2.84	3.38	2	2.35	1.760563	1.47929	26.40845	21.89349	24	2 (21, 22)	MODERAT	576	373	21	I	1.3		13	6		2			
33	7	0.41	1.23	2.05	3.45	1.7	2.87	14.63415	8.115942	39.02439	23.18841	24	3(20,22,23	MODERAT	653	254	21	I	1.2		22	9	38	2			
17	7	0.66	1.21	3.56	3.7	2.47	2.56	3.370787	1.081081	28.08989	27.02703	24	2 (21, 23)	MODERAT	452	152	13	II	1.6	1.4	24	10	30	2			
9	2	1.01	2	3.5	4.21	2.77	3.34	2.285714	2.137767	15.71429	12.58907	24	2 (20, 21)	MILD	298	70	20	I	1.7	1.6	13	4	34	1			
13	6	0.81	1.07	3.13	4	1.58	2.03	1.916933	1.75	28.11502	25	26	2 (24, 24)	MODERAT	576	325	20	II									
11	2	1.03	2.04	2.89	3.43	1.72	2.04	1.384083	2.915452	35.29412	25.36443	24	3(22, 23, 2	MILD	352	123	19	II									
15	9	0.81	1.69	4.5	5.18	2.58	2.97	4.666667	5.212355	17.33333	16.98842	24	2 (21, 23)	MILD	476	125	19	I	1.44	1.2	15	9	32	2			
14	7	1.1	1.6	3.68	6.55	2.53	4.51	1.630435	1.221374	20.1087	11.9084	24	2 (22, 24)	MILD	598	253	19	II									
29	8	0.89	1.34	3.79	4.55	2.91	3.5	5.804749	5.274725	25.06596	23.95604	24	2 (22, 23)	MODERAT	1253	759	18	I	1.5	1.45	10	4	35	2			
12	3	0.93	2.41	4.09	4.91	2.78	3.34	1.466993	1.01833	19.5599	16.70061	24	2 (21,22)	MILD	125	70	18	I									
25	4	0.64	1.5	3.94	4.73	2.44	2.94	1.269036	1.691332	17.00508	14.79915	24	2(21, 22)	MILD	259	104	18	II	1.6	1.7	40	15	62	1			
17	4	1.2	1.4	3.84	4.6	2.35	2.82	1.822917	1.521739	22.91667	20.43478	24	1 (22)	MODERAT	125	101	18	II									
12	4	1.3	1.8	5.17	6.61	2.89	3.69	1.934236	0.907716	18.95551	15.27988	24	2 (21, 22)	MILD	456	213	18	I									
17	3	0.8	1.5	3.77	5.23	2.4	3.33	1.856764	1.338432	20.15915	14.72275	24	3 (22, 23, 2	MILD	523	139	18	I									
10	4	0.68	1.03	2.82	3.41	1.74	2.1	1.06383	1.759531	29.43262	24.04692	24	2 (22, 23)	MODERAT	256	70	2	II									
10	3	1.01	1.41	2.38	2.89	1.87	2.27	4.201681	3.806228	32.77311	28.71972	24	2 (22, 23)	MODERAT	423	152	8	II									
25	9	0.7	1.2	3.09	3.96	1.76	2.26	0.970874	1.767677	28.15534	23.9899	24	2 (21, 24)	MODERAT	379	134	17	I	2	1.8	13	6	42	2			
21	8	0.68	1.13	2.5	3.4	2.1	2.9	8.8	5.588235	30.4	20.88235	24	2 (21, 23)	MODERAT	958	562	17	II									
12	4	1.1	1.9	3.38	3.8	2.48	2.79	0.591716	1.052632	16.27219	15	24	2(22, 24)	MILD	165	70	17	I	1.8	2.1	23	11	29	1			
25	5	0.8	1.7	3.97	5.18	1.89	2.47	0.755668	1.158301	20.65491	16.21622	26	2 (24, 26)	MILD	253	101	16	II									

46	1.52	62.2	26.92175	1.620562	45	F		03.02.20	III	13.9	1.01	59.3	SR	1			45	1.3	0.9	38	26	125		FUSED	FUSED	MILD
47	1.35	27	14.81481	1.006231	13	F		05.02.20	II	11.6	0.48	180	SR	1			45	0.88	1.1	26	17	90		FUSED	FUSED	MILD
48	1.56	59	24.24392	1.598958	24	F	BMV (201	10.02.20	III	9.1	0.59	125.2	SR	1		1	48	0.8	0.75	45	20	115		FUSED	FUSED	MILD
49	1.555	53	21.91871	1.513045	58	F		17.02.20	II	12.7	0.65	93.6	AF			1	40	0.7	1.1	14	7	72		FUSED	FUSED	MILD
50	1.605	72.9	28.29941	1.80281	39	F	MOD AS	18.02.20	II	12.4	0.92	68	SR	1			47	0.9	1.02	19	17	79	PRESENT	FUSED	FUSED	TRIVIAL
51	1.56	64.5	26.50394	1.671825	47	F	BMV 2013	02.03.20	II	14.8	0.9	67.1	AF	1			48	0.9	1	42	21	70	PRESENT	FUSED	FUSED	TRIVIAL
52	1.53	69.4	29.64672	1.717411	24	F	BMV 2018	11.05.20	III	11.9	0.62	118.3	SR	1			42	0.3	1.2	51	28	114	PRESENT	FUSED	FUSED	NO
53	1.57	68	27.58733	1.722079	45	F	CMV 1992	22.06.20	II	12.4	0.63	102.2	SR	1		1	48	1.2	1.06	19	16	110		SPLIT	FUSED	MILD
54	1.58	65	26.03749	1.689017	51	F		23.06.20	III	10.8	0.97	60.5	AF	1			47	1.1	1	16	11	70		FUSED	FUSED	MILD
55	1.56	55	22.60026	1.543805	47	F		26.06.20	II	15.3	0.66	96	SR	1			40	0.9	1	24	18	100		FUSED	SPLIT	MILD
56	1.485	69.7	31.60675	1.695619	40	F	CMV 1994	17.08.20	III	11.7	0.97	101.5	AF	1	1	1	44	0.51	0.55	15	10	57		FUSED	FUSED	TRIVIAL
57	1.55	40	16.64932	1.312335	55	F	OMV, ASC	17.08.20	III	13.7	1.01	56.9	AF		1	1 RBBB	40	0.8	0.9	27	19	70		FUSED	FUSED	MILD
58	1.59	62	24.52435	1.654791	44	F	CMV 1992	24.08.20	II	12	0.86	71.7	AF	1			55	0.9	1.2	25	10	55		FUSED	FUSED	MILD
59	1.71	71.7	24.52037	1.845467	27	M		24.08.20	III	16.3	1.02	87.6	AF	1			52	1.1	0.9	23	12	60		FUSED	FUSED	MILD
60	1.44	55	26.52392	1.48324	26	F		14.09.20	II	14.4	0.78	89.3	SR	1		1	39	0.6	0.9	40	22	70		FUSED	FUSED	TRIVIAL
61	1.48	54.5	24.8813	1.496849	41	F	BMV 2008	21.09.20	II	13.5	0.81	77.9	SR				42	0.8	1.1	22	17	75	PRESENT	FUSED	FUSED	MILD
62	1.528	64.3	27.54002	1.652022	57	F	CMV 1997	19.10.20	III	13.6	0.98	58.5	SR	1			47	1.1	1.2	21	11	61		FUSED	FUSED	MILD
63	1.56	54	22.18935	1.529706	43	F	BMV 2014	19.10.20	III	14.1	1.03	58.5	AF	1			57	1	1	25	12	65		FUSED	FUSED	MILD
64	1.56	46.5	19.1075	1.419507	31	F	BMV 2008	30.10.20	III	12.2	0.71	96	SR	1			48	0.9	1.1	25	14	69	PRESENT	FUSED	FUSED	MILD
65	1.56	68.5	28.1476	1.722885	44	F		30.10.20	III	13.8	0.96	68	AF	1		1	48	0.9	1	28	18	80		FUSED	FUSED	TRIVIAL
66	1.55	51.6	21.47763	1.490526	37	F		07.12.20	III	12.1	0.8	80.7	SR	1			46	0.9	1	44	24	78		FUSED	FUSED	MILD
67	1.46	58	27.20961	1.533696	44	F	CMV 1996	14.12.20	III	11.8	0.74	85.3	SR	1		1	50	1	0.9	24	12	77	PRESENT	FUSED	FUSED	TRIVIAL
68	1.72	47.2	15.95457	1.501703	32	F	CMV 1999	21.12.20	III	14.8	0.94	69	AF	1		1 RBBB	47	0.6	0.7	20	18	70		FUSED	FUSED	TRIVIAL
69	1.59	68	26.89767	1.733013	49	F		21.12.20	III	14.8	0.97	61	AF	1			55	0.9	1	32	17	90		FUSED	FUSED	MILD
70	1.42	60	29.756	1.538397	48	F	BMV 2001	28.12.20	III	10.2	1.05	59.2	SR	1			44	0.9	1.2	14	8	68		FUSED	FUSED	MILD
71	1.52	74	32.02909	1.76761	42	F	BMV 2007	4.1.21	III	14.1	0.92	68.7	AF	1	1		50	1.3	1	15	8	70		FUSED	FUSED	MILD
72	1.56	57.9	23.79191	1.583982	27	F		8.1.21	III	11.9	0.84	81.3	SR	1			50	0.9	1	25	14	66		FUSED	FUSED	MILD
73	1.52	52	22.50693	1.481741	45	F	BMV 2003	18.01.21	II	14.7	0.7	90.5	SR		1	1	38	1.04	1	21	9	105		FUSED	FUSED	TRIVIAL
74	1.55	57.3	23.85016	1.570695	32	F	BMV 2001	18.01.21	II	13.7	0.72	93.9	SR			1	39	1.2	1.2	34	24	87	PRESENT	FUSED	FUSED	MILD
75	1.69	80	28.01022	1.937926	50	M	CMV 1989	01.02.21	III	17.4	0.91	88.2	SR	1	1	1 RBBB	48	1	1.2	27	17	75		FUSED	FUSED	MILD
76	1.635	59.4	22.22035	1.642483	24	M	1 AS 1-2A	08.02.21	II	14.9	0.93	99.8	SR	1		1 RBBB	56	0.8	1	35	30	76		FUSED	FUSED	MILD
77	1.78	74.4	23.48188	1.917985	39	M	BMV 1998	08.02.21	II	13.4	0.85	100.3	SR	1			50	1.1	1	28	11	70		FUSED	FUSED	MILD
78	1.54	52	21.92613	1.491457	47	F	HYPOTHR(	08.02.21	III	12.8	1.3	43.9	SR				47	1.2	1.1	39	23	65	PRESENT	FUSED	FUSED	MILD
79	1.62	62	23.62445	1.670329	31	F	BMV 1999	15.02.21	III	12.6	0.64	108.2	SR				45	0.9	1.2	35	16	70	PRESENT	FUSED	FUSED	NO
80	1.56	73	29.99671	1.778576	40	F	BMV 2009	15.02.21	III	12.3	0.61	108.6	SR				43	1.1	1.3	22	14	65		FUSED	FUSED	MILD
81	1.56	58	23.833	1.58535	25	F		01.03.21	III	14.2	0.76	92.7	SR	1			40	0.9	0.98	21	16	70		FUSED	FUSED	MILD
82	1.58	65	26.03749	1.689017	52	F	BMV 1996	08.03.21	III	12.3	0.94	62.5	AF				43	1	0.9	23	11	70	PRESENT	FUSED	FUSED	MILD
83	1.55	59	24.55775	1.593825	48	F		12.03.21	III	13.8	0.8	76.6	AF				41	0.8	0.9	24	11	65		FUSED	FUSED	MILD
84	1.58	52	20.83	1.510703	25	F		22.03.21	II	12.8	0.76	92.7	SR	1			57	0.6	0.6	26	21	73	PRESENT	FUSED	FUSED	TRIVIAL
85	1.54	62	26.14269	1.628564	47	F		22.03.21	III	12	0.97	61.6	SR				47	1.1	0.9	58	38	70	PRESENT	FUSED	FUSED	MILD
86	1.55	36	14.98439	1.24499	27	F	RECURREN	29.03.21	II	12.5	0.67	179.1	SR				40	1.03	1	14	8	65		FUSED	FUSED	MILD
87	1.55	50	20.811	1.4672	50	F		09.04.21	III	12.3	1.02	57.4	SR	1		1	46	1.05	1.03	17	12	90		FUSED	FUSED	MILD
88	1.77	49.4	15.768	1.56	20	M	BMV 2017	12.04.21	II	12.9	0.92	104.9	SR	1			51	0.7	0.8	29	14	65	PRESENT	FUSED	FUSED	TRIVIAL
89	1.71	54	18.46	1.63	24	M	BMV 2009	19.04.21	II	13.7	1.06	85.8	SR	1			46	0.93	1	49	24	70	PRESENT	FUSED	SPLIT	TRIVIAL
90	1.7	52	17.78	1.56	16	M		22.04.21	III	14.8	0.85	120.2	SR	1		1	43	0.95	0.9	36	21	75		FUSED	FUSED	TRIVIAL
91	1.57	66	26.77	1.6965	44	F	BMV 2005	10.05.21	III	13.1	0.76	82.7	AF	1			53	1.2	1.3	15	10	86		PARTLY SP	FUSED	MILD
92	1.69	57.2	20.02	1.65	44	M		10.05.21	III	14.8	1.01	80.2	AF	1			55	1.2	0.8	23	15	80	PRESENT	PARTLY SP	PARTLY SP	MILD

41	26	67	76	21	45	1.32	1.4	13	6	78		SPLIT	SPLIT	TRIVIAL	43	29	60	38	20	10	11	10	10	12	10
41	26	67	57	20	45	1.25	1.4	13	6	73		SPLIT	SPLIT	MODERAT	40	26	67	25	22	10	9	8	10	9	8
35	20	74	57	20	46	1.2	1.3	10	6	80		SPLIT	SPLIT	MILD	35	20	74	40	18	5	6	5	5	6	5
50	32	60	50	21	40	1.9	2	9	3	85		SPLIT	SPLIT	MILD	50	32	63	50	17		12	8		11	8
40	21	80	67	20	45	1.8	1.7	19	6	75	PRESENT	SPLIT	SPLIT	MILD	40	22	78	45	18	5	6	6	5	6	6
48	34	56	30	19	46	1.75	1.8	9	4	80	PRESENT	SPLIT	SPLIT	NO	48	30	65	40	20		26	20		16	10
41	27	70	67	20	46	1.65	1.8	11	8	76	PRESENT	SPLIT	PARTLY SF	MILD	36	19	75	42	23	5	6	6	5	6	6
42	27	67	58	21	48	1.56	1.65	13	6	75		SPLIT	SPLIT	MILD	44	31	64	35	20	9	8	5	8	7	4
47	30	65	34	20	50	1.5	1.4	11	4	70		PARTLY SF	PARTLY SF	MILD	52	37	60	24	22		4	4		4	4
40	29	55	40	20	38	1.5	1.6	10	4	74		PARTLY SF	SPLIT	MILD	47	32	58	23	23	8	7	5	7	5	3
41	25	65	60	21	45	1.6	1.55	11	5	62		SPLIT	SPLIT	MILD	34	21	69	41	20		4	4		4	4
44	28	61	22	20	41	1.4	1.46	20	13	97		PARTLY SF	SPLIT	MODERAT	42	29	59	38	19		7	6		6	5
40	27	56	32	19	50	1.9	1.8	9	3	63		SPLIT	SPLIT	MILD	43	30	56	30	21		6	5		6	5
49	34	59	30	21	50	1.8	1.7	12	4	56		PARTLY SF	SPLIT	MILD	49	36	53	25	20		9	7		9	6
38	26	60	80	17	28	1.6	1.69	11	4	65		SPLIT	FUSED	MODERAT	41	27	59	35	22	8	6	5	6	5	4
48	29	62	40	19	35	1.1	1.1	10	5	60	PRESENT	SPLIT	FUSED	MILD	33	20	70	30	21	10	8	6	8	6	4
46	27	68	34	20	45	1.6	1.7	8	4	76		SPLIT	PARTLY SF	MILD	40	24	72	22	22	5	9	6	5	8	6
42	28	64	50	21	55	1.8	1.9	8	3	76		SPLIT	SPLIT	MILD	42	30	66	24	21		8	6		8	6
48	33	59	45	21	43	1.5	1.4	13	7	64	PRESENT	SPLIT	SPLIT	MODERAT	46	32	57	35	20	11	8	6	10	5	6
38	22	69	61	19	45	1.54	1.65	12	5	60		SPLIT	SPLIT	MILD	38	21	72	40	18		9	6		7	5
45	28	65	78	21	46	1.4	1.5	10	5	61		SPLIT	PARTLY SF	MODERAT	43	29	58	23	20	8	6	5	7	5	3
36	23	68	38	19	40	1.39	1.41	10	4	70	PRESENT	PARTLY SF	PARTLY SF	TRIVIAL	44	24	74	31	18	7	6	4	5	3	3
40	21	77	77	22	45	1.3	1.24	10	6	70		PARTLY SF	SPLIT	MILD	46	28	68	38	17		6	3		6	3
48	28	70	54	20	47	2.43	2	10	5	74		SPLIT	SPLIT	MODERAT	43	29	60	23	19		7	5		6	4
38	26	67	27	19	41	1.6	1.8	8	3	65		SPLIT	SPLIT	MILD	40	28	60	30	20	12	10	9	12	11	8
50	37	56	34	20	48	1.9	1.8	9	4	68		SPLIT	SPLIT	NO	48	28	69	25	21		8	4		8	3
42	28	68	30	19	50	1.6	1.53	12	5	75		SPLIT	SPLIT	MILD	46	27	70	28	20	11	8	7	9	6	6
44	29	60	30	21	44	1.55	1.5	8	3	80		PARTLY SF	SPLIT	MILD	41	26	64	20	21	10	7	3			3
45	28	68	46	22	34	1.3	1.29	10	6	64	PRESENT	SPLIT	SPLIT	MILD	42	29	56	20	20	9	8	6	8	6	5
45	30	63	37	22	40	1.35	1.4	10	5	60		SPLIT	SPLIT	MILD	40	27	61	32	19	8	6	5	12	8	6
40	23	62	45	20	50	1.3	1.4	15	6	65		SPLIT	SPLIT	MILD	35	22	67	50	18	9	10	7	8	8	6
50	27	78	50	18	45	1.7	1.8	11	5	74		SPLIT	SPLIT	MILD	48	29	68	33	19	9	7	8	9	6	8
41	24	72	66	19	40	1.4	1.48	18	8	72	PRESENT	SPLIT	SPLIT	MILD	40	25	69	46	18	12	9	10	10	9	9
32	18	60	47	18	37	1.45	1.4	13	6	75	PRESENT	SPLIT	SPLIT	NO	43	29	61	38	19	8	6	5	5	4	4
49	35	58	30	19	42	1.69	1.63	10	6	78		SPLIT	SPLIT	MILD	48	26	63	24	19	7	4	3	4	5	3
40	23	68	23	22	40	1.9	2	9	3	65		SPLIT	SPLIT	MILD	38	23	68	28	20	7	5	6	7	4	4
39	23	65	43	18	40	1.5	1.65	7	4	70	PRESENT	SPLIT	SPLIT	MILD	39	23	65	35	20		9	8		8	7
53	34	65	28	19	40	1.78	1.8	10	3	70		SPLIT	SPLIT	MODERAT	53	34	65	20	21		6	5		5	4
43	28	64	52	20	55	1.54	1.6	15	7	85	PRESENT	SPLIT	SPLIT	TRIVIAL	43	28	64	34	20	12	14	11	9	12	10
47	30	66	60	19	45	1.6	1.54	12	4	65	PRESENT	SPLIT	SPLIT	MILD	47	30	66	24	21	7	8	8	6	8	7
42	25	68	30	20	40	1.5	1.55	7	4	69		SPLIT	SPLIT	MILD	45	28	64	25	20	8	4	4	8	4	4
42	26	68	50	18	45	1.2	1.3	15	9	78		SPLIT	SPLIT	MODERAT	42	26	68	30	19	4	6	5	4	6	5
42	28	60	46	20	51	1.2	1.2	17	8	62	PRESENT	SPLIT	SPLIT	MILD	48	30	64	30	19	4	6	5	4	6	5
52	36	59	35	19	42	1.68	1.75	9	3	68	PRESENT	SPLIT	SPLIT	MILD	55	37	59	21	21	8	6	7	6	4	2
39	23	65	77	20	40	1.5	1.56	22	11	92		PARTLY SF	SPLIT	MILD	49	32	58	20	22	8	4	4	6	4	4
50	31	68	32	18	48	1.95	1.52	12	4	62		PARTLY SF	SPLIT	MILD	46	28	67	16	19		5	6		5	6
49	27	75	35	19	37	1.1	1.2	16	8	85	PRESENT	PARTLY SF	SPLIT	MILD	46	30	60	10	19		7	8		6	7

60	10	40	10	60	25	38	40	15	23	33	28	24	23	20	14	140	10	144	12	140	80	96	144	89	103
40	8	30	11	40	29	34	29	19	23	28	34	27	21	25	18	75	12	80	14	84	47	61	80	49	62
55	8	45	8	55	28	37	45	15	25	26	32	28	14	17	15	100	8	95	10	100	60	75	95	60	72
64	8	55	10	64	30	45	55	20	34		43	23		30	19	140	11	135	15	140	80	105	135	75	100
65	8	40	8	65	28	40	45	23	31	33	39	28	22	30	23	136	16	132	18	136	80	98	132	85	100
65	8	45	6	65	35	45	45	20	28		45	33		32	20	110	10	120	12	110	75	86	120	70	87
65	8	45	8	65	35	45	45	22	30	30	40	33	22	30	21	125	15	128	18	125	80	95	128	79	97
40	8	35	5	40	20	27	35	15	24	22	28	18	20	26	16	120	6	130	12	120	60	86	130	70	90
50	6	45	6	50	20	36	45	19	30		25	20		26	14	103	10	103	12	103	60	75	103	65	73
32	6	24	5	32	18	24	24	10	12	22	18	18	10	12	10	100	6	110	8	100	55	75	110	60	78
65	5	40	5	65	25	40	40	16	27		18	16		12	10	110	6	100	8	110	60	80	100	50	70
45	10	40	10	45	25	33	40	20	30		30	24		28	21	140	12	130	16	140	74	96	130	75	94
35	8	30	8	35	18	23	30	16	21		26	18		20	16	135	8	135	12	135	75	95	135	75	95
42	6	28	6	42	22	32	25	7	15		26	20		14	10	110	8	110	10	110	76	88	110	60	80
50	8	36	6	50	24	33	36	20	24	28	26	22	13	16	11	105	8	92	10	105	50	68	92	60	71
40	8	35	8	40	24	29	35	16	24	23	26	24	20	22	16	120	10	118	12	120	60	82	118	62	80
45	8	45	7	45	20	30	45	22	30	26	40	25	22	36	24	125	10	140	18	135	80	100	140	80	100
32	6	28	6	32	23	26	29	15	19		28	23		18	12	120	8	130	10	120	80	100	135	83	101
50	10	40	10	50	22	33	40	20	29	30	32	22	30	38	26	138	8	136	22	138	78	97	136	75	94
95	8	37	4	95	29	52	44	15	23		41	30		18	13	100	5	135	7	128	72	94	110	70	83
56	6	46	5	56	25	36	46	14	30	25	42	25	18	24	15	130	8	140	12	130	70	90	140	70	95
35	5	40	6	38	19	25	33	12	21	20	28	19	15	18	13	140	8	140	10	140	70	90	138	70	89
35	5	30	6	34	16	22	30	17	20		25	18		13	9	85	7	84	8	90	60	70	95	60	72
42	6	32	5	42	18	26	30	12	20		26	18		20	14	140	8	150	10	140	80	105	150	75	108
42	10	40	10	42	22	30	36	14	22	28	32	24	26	30	16	100	12	110	14	110	60	80	112	65	80
30	5	25	5	30	16	22	28	10	20		14	18		12	16	144	6	128	11	144	78	100	124	76	90
45	8	30	6	43	19	28	30	15	20	26	24	22	20	18	15	120	10	120	12	118	70	89	120	70	85
40	8	35	7	40	24	30	35	18	22	26	32	24	22	28	16	130	10	135	12	130	80	96	136	80	96
45	6	40	5	40	19	27	39	18	20	22	32	21	18	25	15	110	10	112	12	106	70	82	107	60	75
40	8	36	8	40	16	24	36	18	23	24	26	20	20	28	18	100	8	106	12	100	70	80	106	70	82
60	8	50	7	54	30	38	47	20	29	30	37	31	18	16	16	100	10	100	12	96	60	72	90	60	70
58	8	30	7	53	25	35	31	17	25	24	28	25	22	16	16	110	10	120	12	110	50	70	120	60	80
85	10	60	10	85	40	55	60	30	40	35	42	35	20	16	16	182	12	180	14	185	100	127	180	85	120
50	8	34	8	50	26	34	30	15	20	25	35	22	14	19	15	112	6	113	8	113	60	80	113	60	79
33	6	26	7	32	20	24	28	12	17	23	24	20	16	12	12	125	8	124	9	125	77	100	124	70	95
40	8	30	5	36	16	23	30	14	20	24	11	17	16	7	10	100	6	110	8	100	60	75	110	70	85
44	5	40	5	45	20	24	40	15	19		20	12		10	10	150	8	155	10	150	90	110	155	92	112
32	6	24	5	32	14	21	24	10	14		22	14		16	8	126	7	130	7	120	70	86	130	67	89
65	9	45	8	65	40	49	45	25	32	30	50	40	25	30	22	100	10	110	14	100	65	78	110	60	79
65	8	45	8	65	35	45	40	16	24	28	40	29	11	16	12	100	8	110	10	100	60	75	110	66	78
30	5	20	5	30	15	20	20	9	13	20	14	14	16	8	8	130	5	105	6	130	60	83	105	58	74
50	6	35	6	50	25	32	35	13	21	24	35	25	11	16	12	146	8	130	9	146	66	93	130	60	83
50	6	35	6	50	35	40	35	15	22	35	45	34	15	18	15	95	8	108	10	94	60	71	108	68	72
40	6	34	5	40	24	28	34	16	20	23	35	24	13	19	14	130	6	132	8	100	60	73	108	60	76
24	4	24	4	24	18	20	24	12	16	24	18	16	18	12	10	70	4	78	6	70	36	45	78	40	53
30	5	22	5	30	16	21	22	14	18		14	16		14	12	120	10	126	12	120	70	85	126	72	88
38	5	30	5	38	23	28	30	22	25		30	23		32	22	110	10	118	12	110	65	85	118	64	82

14	3	0.9	1.4	3.82	4.62	2.35	2.85	3.664921	1.948052	22.51309	20.12987	24	1 (24)	MODERAT	589	356		16	I								
13	4	0.58	1.1	2.29	2.94	2.29	2.94	3.056769	1.70068	23.1441	18.36735	24	3 (20, 21, 2	MODERAT	339	152		16	I								
20	5	0.75	1.2	3.74	4.49	2.35	2.82	2.406417	2.227171	18.71658	14.92205	24	3 (21, 22.5	MODERAT	648	253		16	II								
12	4	0.7	2	3.42	4.1	2.28	2.73	6.432749	3.658537	28.36257	22.43902	24	2 (21, 22)	MILD	425	189		16	I	1.4	1.49	29	10	60	2		
12	5	0.62	1.4	2.88	3.29	1.63	1.86	4.166667	2.431611	31.94444	28.57143	24	2 (23, 24)	MODERAT	324	150		16	I								
23	7	0.84	2.02	3.93	4.72	2.35	2.82	3.053435	1.694915	16.79389	16.31356	24	2 (22, 24)	MILD	152	70		15	II								
18	3	0.72	1.91	3.74	4.49	2.18	2.62	3.208556	2.004454	23.79679	20.26726	24	3 (21, 22.5	MILD	745	453		13	II								
12	4	1.16	1.78	3.16	4.49	1.83	2.61	2.848101	1.781737	25.63291	19.15367	24	1 (21)	MILD	198	70		12	II								
12	3	0.93	2.14	3.95	4.75	2.35	2.82	4.050633	3.368421	17.97468	14.52632	24	1 (24)	MILD	895	526											
12	3	0.99	1.6	3.97	4.15	2.64	2.76	1.511335	0.481928	17.63224	18.07229	24	2(21, 23)	MILD	562	254											
11	3	0.81	2.01	3.57	3.9	2.11	2.3	6.722689	4.358974	21.28852	16.92308	24	1(22)	MILD	1030	351		10	II								
12	5	0.6	1.01	2.69	2.87	2.05	2.19	3.345725	3.135889	33.45725	31.01045	24	2 (22, 23)	MILD	1040	729		10	II								
10	4	1.1	1.3	3.93	4	2.62	2.66	1.272265	1.25	22.90076	22.5	24	2 (22, 24)	MODERAT	363	304		10	II								
11	3	0.83	1.64	2.86	2.86	1.55	1.55	4.195804	1.748252	28.32168	25.87413	26	2 (23,25)	MILD	2490	2270		10	I								
14	4	0.9	1.7	3.68	4.16	2.55	2.89	2.98913	3.125	17.11957	16.10577	24	2 (21, 23)	MILD	250	70		9	I								
11	4	0.9	1.59	3.3	3.42	2.24	2.32	1.515152	2.339181	23.0303	22.22222	24	3 (21, 23, 2	MODERAT	205	154		9	I	1.54	1.32	13	7	13	1		
18	4	0.85	1.93	2.91	3.3	1.77	2.01	1.718213	1.818182	32.30241	28.48485	24	2(22, 23.5	MILD	353	130		8	I								
15	4	1.15	2.02	3.45	3.81	2.26	2.5	0.869565	1.83727	27.24638	24.93438	24, 26	2(22.5, 24,	MILD	769	528		8	II								
22	4	1.01	1.25	4.34	4.49	3.07	3.18	2.534562	0.668151	20.96774	19.59911	24	1(21)	MODERAT	403	583		7	II								
25	6	0.7	1.6	2.43	3.07	1.41	1.75	9.053498	3.257329	36.21399	25.40717	24	2(21)	MILD	623	508	INTERMIT	7	I								
11	3	0.86	1.9	3.51	4.21	2.35	2.82	3.133903	3.562945	24.21652	21.85273	24	2(22)	MILD	498	414	ENDOMET	6	II	1.58	1.3	16	10	20	2		
11	3	1.01	1.82	3.64	4.18	2.37	2.72	1.648352	1.913876	23.62637	20.57416	24	3(21, 23, 2	MILD	442	211		6	II								
11	3	0.81	1.77	3.28	3.93	2.18	2.62	1.219512	2.798982	20.42683	17.55725	24	4(21, 22, 2	MODERAT	917	192	JUGULAR I	5	II	1.5	1.6	7	4	33	1		
12	4	0.85	1.71	3.78	4.54	2.18	2.62	2.116402	1.321586	26.45503	22.90749	24	2(21, 22.5	MILD	455	219		6	II	1	1	31	13	42	3		
12	4	0.79	2.09	3.34	4.01	2.18	2.62	1.796407	1.496259	21.25749	17.95511	24	2(22, 24)	MILD	543	312		6	II	1.6	1.52	13	6	22	0		
12	5	1.15	2.09	4.35	4.9	2.47	2.78	0.91954	0.816327	22.06897	17.7551	24	3(22, 24, 2	MILD	377	372		5	I								
12	3	0.74	1.94	3.72	4.46	2.35	2.82	1.612903	1.121076	22.04301	17.713	24	4(20, 21, 2	MILD	630	165		5	I								
14	6	0.68	1.2	4.19	5.24	2.5	3.12	1.431981	1.145038	22.1957	17.74809	24	2(22)	MODERAT	116	70	HAD TRAN	5	II	1.54	1.7	8	3		2		
13	5	0.75	1.3	3.59	4.5	2.3	2.9	1.671309	1.111111	21.16992	15.55556	24, 26	6(22, 23, 2	MODERAT	204	132		5	II								
12	6	0.9	1.3	3.8	5.5	2	3.2	1.052632	0.909091	19.73684	13.81818	24	3(22, 23, 2	MODERAT	546	293		4	II								
19	6	0.67	1.71	3.06	3.74	1.86	2.28	2.287582	3.475936	21.24183	17.1123	24	2(22, 24)	MILD	794	356		4	I	1.8	1.3	15	6	50	1		
15	7	0.96	1.89	5.6	6.55	2.96	3.41	1.785714	1.374046	11.07143	10.99237	26	2(23, 25)	MILD	365	192		4	I	1.25	1.1	16	6	28	2		
21	4	0.57	1.67	3.38	3.48	2.25	2.3	5.91716	6.896552	34.61538	31.89655	24	1(22)	MILD	958	453		4	I								
16	7	0.97	1.83	4.1	4.6	2.39	2.68	2.926829	1.086957	18.29268	16.30435	26	2 (24, 25)	MILD	256	70		4	II								
16	5	0.97	2.06	3.79	4.6	2.19	2.65	1.055409	1.086957	25.59367	20	26	2(24, 25)	MILD	359	170		4	I								
11	5	0.7	1.7	3.9	4.3	2.65	2.85	1.538462	2.325581	17.69231	18.83721	24	2 (22, 23)	MILD	432	216		3	I	1.56	1.6	11	4	21	1		
10	4	0.9	1.3	3.67	4.41	2.18	2.62	3.269755	2.040816	27.79292	23.80952	24	2 (22, 23)	MODERAT	575	356		3	II								
11	5	0.8	1.3	3.47	4.17	2.18	2.62	2.017291	1.438849	23.34294	20.38369	24	3 (22, 23, 2	MODERAT	1020	523		3	II								
30	7	0.75	1.79	3.55	4.27	2.35	2.82	2.535211	2.34192	18.87324	16.15925	24	3 (21, 22, 2	MILD	963	653		3	II								
21	3	0.85	2.72	3.54	4.25	2.18	2.62	4.519774	2.823529	18.92655	16.70588	24	2 (22, 23)	MILD	1024	893		3	II								
10	3	1.07	1.89	3.81	3.96	2.97	3.09	1.574803	1.262626	20.73491	17.67677	24	2 (22)	MILD	183	93		3	I								
17	3	0.59	1.19	2.88	3.91	1.97	2.67	2.430556	2.30179	30.55556	19.94885	24	2 (21)	MODERAT	576	285		2	II	1.6	1.4	25	13	41	3		
26	5	0.609	1.56	3.97	5.85	2.55	3.75	1.511335	1.196581	16.62469	11.45299	24	2 (22)	MILD	652	224		2	I								
18	6	0.79	1.68	3.359	4.135	2.1	2.58	1.190831	1.451028	19.6487	17.89601	24	2 (22)	MILD	526	224		2	I								
11	5	0.988	2.15	3.892	5.723	2.483	3.652	1.027749	1.048401	10.53443	8.561943	24, 26	3(22, 24),	MILD	221	70		2	I								
6	2	1.18	2.04	2.891	3.561	1.71	2.107	1.729	2.075	22.184	23.027	22	2 (20, 22)	MILD	1256	878		1	I								
13	8	0.6746	1.12	2.432	3.26	1.47	1.97	2.055	0.92	31.66	23.006	24, 26	4 (22, 24, 2	MODERAT	1179	967		1	I								