

Original research article**A study on evaluate the utility of 3D vena contract a area in assessing the severity of MR****Dr. Ravikanth A**

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Abstract**Aim:** To study the levels of NT-pro BNP and its correlation with various echocardiographic parameters including 3D vena contract a width in patients with MR.**Methodology:** The study was done prospectively in the department of cardiology, Kamineni Academy of Medical Sciences, between September 2019-August 2020. 74 Patients diagnosed with primary mitral regurgitation and who were treated at KAMS during study period were included.**Results:** We observed that moderate to severe mitral regurgitation prevalence increases with age. Mitral regurgitation was almost equally distributed in both males (n = 36) and females (n= 38). In our study we observed that CRHD was the most common cause of organic mitral regurgitation. In echocardiography, increasing vena contract a width and increasing PISA correlated to increased levels of plasma NT-pro ANP and NT-pro BNP. No other correlation was found between measures on MRI, echocardiography and natriuretic peptides. We also observed that there was a significant correlation between 3D VC and 2D VC in all patients of mitral regurgitation with central jet and in patients of mild MR with eccentric jet. However, correlation is better in central jets compared to eccentric jets in moderate MR ($r = 0.956$ vs $r = 0.774$).**Conclusion:** This study showed that NT-proBNP measurement has the same sensitivity and specificity as echocardiographic indices and may be used as a hormonal factor for the evaluation of patients with mitral regurgitation in combination with echocardiography. Myocardial performance index combined with NT-proBNP measurement may be helpful in detection of subclinical impairments in left ventricle functions.**Keywords:** Mitral regurgitation, NT-pro BNP, Echocardiography, Natriuretic peptides**Introduction**

Mitral regurgitation (MR) is a common valvular disease that causes significant morbidity and mortality^[1]. Population studies have estimated the prevalence of MR to be 20%^[2]. Mitral regurgitation causes progressive systolic and diastolic left ventricular dysfunction which has negative impacts on prognosis of patients with MR². Understanding the degree of systolic, diastolic dysfunction and severity of regurgitation would be helpful to establish the best treatment strategy and improve patient survival^[3, 4]. Accurate assessment of ventricular function and severity of MR using echocardiography alone may be difficult and bring us to diagnostic dead end. The use of multiple echocardiographic indices and hormonal parameters in combination can provide an accurate assessment of MR severity and LV dysfunction in most cases^[5].

B- type natriuretic peptide and N-terminal pro BNP are synthesized and secreted in response to increase in wall stress by cardiac myocytes. Plasma levels of NT Pro BNP which are elevated in myocardial infarction and heart failure patients are independent prognostic factors in numerous studies. In contrast only a few studies have evaluated NT Pro BNP in valvular heart diseases^[10, 11]. The purpose of this study is to compare NT Pro BNP and echocardiographic indices in patients with MR.

Elevated plasma levels of neurohormones such as BNP (B- type natriuretic peptide) and NT Pro BNP (N-terminal pro BNP) have been shown to indicate early states of myocardial deterioration in various diseases^[6, 7]. In congestive heart failure, BNP and NT Pro BNP have been shown to correlate with haemodynamics and functional status and to predict outcome. Such findings raised hope that natriuretic peptides may also be useful in valvular heart diseases^[8, 9].

Accurate assessment of MR is important for clinical decision making and outcome prediction. The calculation of an effective regurgitant orifice area (EROA) by the proximal isovelocity surface area

(PISA) method is a important method for quantification of MR ^[12]. However it requires flow and geometric assumptions which has limited its clinical applications. Recently 3D echocardiography allowed for the direct measurement of the effective regurgitant orifice area by 3D guided planimetry of the vena contracta area ^[13]. This single measurement is not dependent on geometric and flow assumption. Therefore it can provide direct and more accurate quantification of MR than 2D measurements. The purpose of this study is to evaluate the utility of 3D Vena contracta area in assessing the severity of MR.

Aim of the Study

To study the levels of NT-proBNP and its correlation with various echocardiographic parameters including 3D vena contracta width in patients with MR.

Objectives

1. To compare the levels of NT- Pro BNP in patients of mild, moderate and severe MR.
2. To correlate the levels of NT- Pro BNP with the NYHA class in patients with MR.
3. To correlate the levels of NT Pro BNP with the echocardiographic indices, including 3D Vena Contracta area in patients with MR.
4. To compare 3D Vena Contracta area with 2D Vena Contracta width and PISA in patients with MR.

Methodology

The study was done prospectively in the department of cardiology, Kamineni Academy of Medical Sciences, between September 2019-August 2020.

Inclusion Criteria

1. 74 Patients diagnosed with primary mitral regurgitation and who were treated at SVIMS during study period were included.
2. Sinus rhythm on ECG with no conduction disturbances.

Exclusion Criteria

1. Mitral regurgitation due to ischemic heart disease or cardiomyopathy.
2. Mitral valve stenosis with a valve area < 2 cm².
3. Aortic valve disease (peak velocity across aortic valve > 2.5 m/s or more than mild aortic regurgitation).
4. LV hypertrophy (LV wall thickness > 12 mm).
5. Primary right heart disease.
6. Previous cardiac Surgery.
7. Uncontrolled arterial hypertension (BP>160/100mmg).
8. Moderate to severe respiratory diseases.
9. Atrial fibrillation.
10. Patients with poor echocardiographic acoustic window.

Patient history, physical examination, ECG, Echocardiography and plasma levels of NT-Pro BNP collected as per the proforma.

Measurement Of NT Pro BNP Levels

About 2 ml of blood sample for NT-Pro BNP was collected by venipuncture into heparinised tubes on diagnosis of Mitral regurgitation by echocardiography. NT-Pro BNP levels were measured by using Roche CARDIAC Pro BNP test kit (code 04659449190, Roche Diagnostics Ltd. Germany) with cobas h 232 POC (Point of Care) system.

Echocardiographic Examination

Transthoracic M-mode, Two-dimensional and Three-dimensional color Doppler echocardiographic examinations were performed by using the Philips IE-33 machine, Holland.

Two-Dimensional Echocardiography and Measurements

Two-dimensional echocardiography was performed with the use of a S5-1 probe. LV enddiastolic and end-systolic diameters (LVEDD and LVESD) were measured by the 2D method from parasternal long-axis view. Left ventricular end-diastolic volume (LVEDV) and LV endsystolic volumes (LVESV) were measured using the Simpson biplane method, and left ventricular ejection fraction (LVEF) was calculated using the modified Simpson biplane method. LA volume was assessed using the biplane area-length method from apical 4- and 2-chamber views.

Two-dimensional quantification of MR included the proximal isovelocity surface area (PISA) method, vena contracta width (VCW), and ratio of jet area to left atrial area. A narrow color flow sector width and the least depth were chosen to maximize image resolution.

Proximal isovelocity surface Area Method

Proximal flow convergence was acquired from magnified apical 4- chamber, 2-chamber, and long-axis views, with baseline shift of the Nyquist limit (30–40 cm/s) to optimize visualization of flow convergence. The ROA was calculated using the formula $ROA = 2 \pi \times r^2 \times V_{aliasing} / V_{max}$, where "r" was the maximal PISA radius (cm), $V_{aliasing}$ was aliasing velocity of the proximal flow convergence (cm/s), and V_{max} was maximal velocity of continuous-wave Doppler MR signal (cm/s). MR volume was calculated as $(ROA \times \text{regurgitant time-velocity integral})$. The severity of MR was graded on the basis of current ASE recommendations as mild ($<0.2 \text{ cm}^2$), moderate (0.2 to 0.39 cm^2), or severe ($\geq 0.40 \text{ cm}^2$).

Vena Contracta Width

The vena contracta was acquired from a magnified parasternal long-axis view with the central beam through the leaflet tips. Vena contracta width (VCW) was defined as the narrowest width of the proximal jet measured at or in the immediate vicinity of the MR orifice at the leaflet tips. The severity of MR was graded on the basis of current recommendations as mild ($<0.3 \text{ cm}$), moderate (0.3 to 0.69 cm) or severe ($\geq 0.7 \text{ cm}$).

Jet Area to Left Atrial Area Ratio

The color flow Doppler image of the MR jet was acquired from the apical 4- and 2-chamber views at a Nyquist limit of 50 to 60 cm/s. The ratio of MR jet area to left atrial area (JA/LAA) was calculated from the average of both views. The severity of MR was graded on the basis of current recommendations as mild ($<20\%$), moderate (20% to 39%) or severe ($\geq 40\%$).

Two-Dimensional Integrative Method

The 2D integrative method recommended by the ASE was used as the reference standard for MR grading. To categorize MR within a certain grade, at least 2 of 3 color Doppler methods listed above were assessed within the same grade with at least 1 supportive data (pulmonary vein flow; mitral inflow; density of continuous wave Doppler MR jet; left atrial enlargement).

Myocardial performance index

The Tei index is calculated from the ratio of time intervals (a-b/b) derived with the aid of pulsed Doppler echocardiography.

Doppler-derived dP/dt

An apical four chamber view was obtained and the mitral regurgitant jet was identified using color flow imaging.

Three-Dimensional Color Doppler Acquisition and Data Analysis

A full-volume 3D color Doppler acquisition was obtained with the use of the X3-1 (1–3 MHz) matrix array transducer from the apical window over 7 to 14 consecutive cardiac cycles with ECG gating and with the narrowest sector possible to maximize the frame rate, with nyquist velocities of 50 to 80 cm/s.

Statistical Analysis

Data collected was tabulated on Microsoft Excel spread sheet and analysed with IBM SPSS version 20 software. All results for continuous variables are expressed as mean $\pm$ SD. The Independent sample t-test was used for comparison of parametric variables, one-way ANOVA for comparison of values of echocardiographic indices and N-terminal pro BNP between three groups with MR. As the plasma NT-proBNP levels were not normally distributed, logarithmic (log) transformed values were used for correlation tests. The relation between log NT-proBNP levels and echocardiographic and hemodynamic parameters were assessed by the Pearson correlation test. The relation between NT-proBNP levels and dyspnea NYHA class were assessed using Spearman's correlation test.

Table 1: Baseline characteristics

	Group 1 (Mild) n = 20	Group 2 (Moderate) n = 28	Group 3 (Severe) n = 26
Men: Women	12:8	14:14	10:16
Age (years)	37.50 $\pm$ 13.22	46.96 $\pm$ 10.73	50.04 $\pm$ 11.60
BSA (m ²)	1.32 $\pm$ 0.07	1.43 $\pm$ 0.17	1.52 $\pm$ 0.16
LVEF (%)	60.40 $\pm$ 2.41	56.18 $\pm$ 4.23	56.73 $\pm$ 6.27
LVEDD (mm)	47.45 $\pm$ 6.05	51.29 $\pm$ 4.78	57.27 $\pm$ 3.55
LVESD (mm)	27.80 $\pm$ 3.96	32.82 $\pm$ 4.91	39.00 $\pm$ 2.89
LVEDV (ml)	100.75 $\pm$ 2.73	131.86 $\pm$ 23.15	140.50 $\pm$ 18.97
LVESV (ml)	44.20 $\pm$ 3.54	64.04 $\pm$ 9.02	68.62 $\pm$ 7.74
LVEDVI	75.90 $\pm$ 3.71	92.89 $\pm$ 22.99	92.85 $\pm$ 17.88
LVESVI	32.95 $\pm$ 2.91	44.86 $\pm$ 9.67	45.15 $\pm$ 7.95

LAVOLUME (ml)	39.65 +/- 3.37	57.57 +/- 6.71	65.54 +/- 6.15
LAVI	29.60 +/- 2.85	40.82 +/- 7.99	43.12 +/- 7.23
RVSP (mm of Hg)	19.10 +/- 4.96	41.29 +/- 8.69	50.88 +/- 6.97
dp/dt (mm of Hg)	1580.50 +/- 197.98	1230.89 +/- 195.34	1253.23 +/- 231.23
MPI	0.37 +/- 0.01	0.45 +/- 0.06	0.46 +/- 0.09
LAJETAREA (%)	17.00 +/- 1.68	32.89 +/- 3.73	42.23 +/- 2.21
PISA (cm ²)	0.16 +/- .017	0.34 +/- 0.03	0.41 +/- 0.02
2DVCWIDTH (mm)	2.69 +/- 0.17	6.04 +/- 0.51	7.19 +/- 0.19
3DVCWIDTH (mm)	2.69 +/- 0.14	6.48 +/- 0.79	7.56 +/- 0.28

The baseline characteristics of 74 patients with mild (n = 20), moderate (n = 28) and severe (n = 26) MR were listed in Table 1.

Age: Mean age of study population in mild MR was 37+/-13 years, moderate MR was 47+/-10 years, severe MR was 50+/-11 years.

Table 2: Diagnosis

CRHD was most common cause of MR seen in 37(57%) patients followed by MVP 23(31%) patients and Degenerative in 14(19%) patients.

Diagnosis	No. of patients	Percentage
CRHD	37	50.0
MVP	23	31.1
Degenerative	14	18.9

Comparison of Log NT-pro BNP levels in patients with mild, moderate and severe MR (Table 3)

Due to wide dispersion of data for NT-pro BNP levels, log NT-proBNP levels were calculated.

Annova test was used for comparison of NT-proBNP levels.

Log NT-proBNP levels in groups with mild MR, moderate MR and severe MR were 4.09 +/- 0.01, 4.78+/-0.79, 5.08+/-1.16 ($p<0.01$).

Table 3: Comparison of Log NT-pro BNP levels in patients with mild, moderate and severe MR

Diagnosis	Log NT-pro BNP levels	P-Value
Mild MR	4.09+/-0.01	$p<0.01$
Moderate MR	4.78+/-0.79	
Severe MR	5.08+/-1.16	

Comparison of Myocardial performance index in patients with mild, moderate and severe MR (Table 4)

ANNOVA test was used for comparison of MPI.

MPI in groups with mild MR, moderate MR and severe MR was 0.37 +/- 0.01, 0.45 +/-0.06, 0.46 +/-0.09 ($p<0.01$).

Table 4: Comparison of Myocardial performance index in patients with mild, moderate and severe MR

Diagnosis	MPI	P-Value
Mild MR	0.37+/-0.01	$p<0.01$
Moderate MR	0.45+/-0.06	
Severe MR	0.46+/-0.09	

Table 5: Correlation of NT-pro BNP levels with dyspnea NYHA class in patients with mitral regurgitation

Diagnosis	Log NT-pro BNP levels	P-Value
NYHA-I	4.48+/-0.06	$p<0.01$
NYHA-II	5.54+/-0.78	
NYHA-III	6.68+/-1.21	

It was observed that as the dyspnea NYHA class worsened, the mean NT-proBNP levels were increased and there was a significant correlation between dyspnea NYHA class and NT-proBNP levels ($r = 0.63$, $p<0.01$).

Table 6: Correlation of Log NT-pro BNP levels in severe MR patients with symptoms and without symptoms

Diagnosis	Log NT-pro BNP levels	P-Value
Severe MR without symptoms	4.09+/-1.21	$p<0.01$
Severe MR with symptoms	5.98+/-0.78	

It was observed that as the dyspnea NYHA class worsened the NT-proBNP levels increased and there was a significant correlation between dyspnea NYHA class and NT-proBNP levels in patients of severe MR.

Table 7: Correlation of log NT-pro BNP levels with echocardiographic indices

Parameter	r	P
LVEDV	0.793	< 0.01
LVESV	0.706	< 0.01
LVEDD	0.727	< 0.01
LVESD	0.617	< 0.01
LVEDVI	0.733	< 0.01
LVESVI	0.677	< 0.01
LA volume	0.735	< 0.01
LAVI	0.709	< 0.01
LVEF	-0.846	< 0.01
RVSP	0.665	< 0.01
MPI	0.945	< 0.01
dp/dt	-0.795	< 0.01
2D VC WIDTH	0.430	< 0.01
3D VC WIDTH	0.441	< 0.01
Pisa	0.440	< 0.01
LA Jet Area Ratio	0.249	0.33

NT-proBNP plasma levels were significantly correlated with MPI ($r = 0.945$, $p < 0.01$), and following echocardiographic indices: LVEDV ($r = 0.793$, $p < 0.01$), LVESV ($r = 0.706$, $p < 0.01$), LVEDVI ($r = 0.733$, $p < 0.01$), LVESVI ($r = 0.677$, $p < 0.01$), LVEDD ($r = 0.727$, $p < 0.01$), LVESD ($r = 0.617$, $p < 0.01$), RVSP ($r = 0.665$, $p < 0.01$), LA volume ($r = 0.735$, $p < 0.01$), LAVI ($r = 0.709$, $p < 0.01$), MR 2D VC ($r = 0.430$, $p < 0.01$), 3D VC ($r = 0.441$, $p < 0.01$) PISA ($r = 0.440$, $p < 0.01$) and negative correlation with LV ejection fraction ($r = -0.846$, $p < 0.01$), dp/dt ($r = -0.795$, $p < 0.01$), but there were no significant correlations between NT-proBNP plasma level and LA jet area ratio ($P = 0.33$).

Sensitivity and specificity of natriuretic peptide levels and echocardiographic parameters for patients with normal and abnormal MPI: (Table 8)

We categorized patients into two groups according to MPI cut off level of 0.45.

The area under the ROC curve for NT-pro BNP levels to predict MPI abnormality was shown in figure: 8 It was observed that a cut off value of NT-proBNP of 524 pg/ml predicted abnormal MPI.

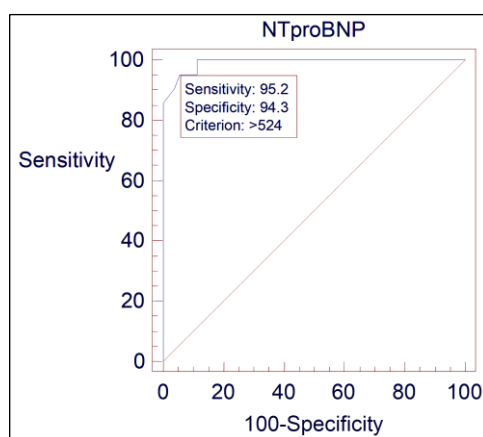


Fig 1

The areas under the ROC curve for NT-pro-BNP and echocardiographic measures were 0.991 (95% confidence interval [CI] 84.3-98.8) for NT-pro-BNP, 0.854 (95% CI 55.7-81.7) for LV end-systolic diameter, 0.887 (95% CI 68.0-90.6) for LV end-diastolic diameter, 0.914 (95% CI 72.4-93.3) for LV end-systolic volume, and 0.947 (95% CI 68.0-90.6) for LV end-diastolic volume, 0.918 (95% CI 70.2-91.9) for LA volume, and 0.971 (95% CI 81.8-97.9) for LV ejection fraction, 0.904 (95% CI 55.7-81.7) for RVSP, and 0.961 (95% CI 93.3-100.0) for dp/dt.

The sensitivity, specificity, and area under the ROC curve for abnormality of MPI by natriuretic peptide levels and echocardiographic measures are shown in Table 8.

Table 8

Variable	Cut point	Sensitivity (%)	Specificity (%)	AUC
NT-proBNP (pg/ml)	> 524	95.24	94.34	0.991
LVESV (ml)	>65	85.71	84.91	0.914
LVEDV (ml)	>127	95.24	81.13	0.947
LVEDD (mm)	>34	90.48	69.81	0.854
LVEDD (mm)	>54	85.73	81.13	0.887
LA Volume (ml)	> 61	90.48	83.02	0.918
LAVI	>37	85.71	66.04	0.832
dp/dt (mm of Hg/sec)	1185	85.76	94	0.961
LVEDVI	>90	76.19	83.02	0.862
LVEF (%)	55	90.48	92.45	0.971
LVESVI	>37	97.00	54.72	0.836
RVSP (mm of Hg)	>40	98.24	69.81	0.904

Correlation of 3D VC and PISA in MR (Table 9)

Table 9

Type of jet Correlation of 3D VC and PISA in mild MR		
	Correlation coefficient	P value
Central Jet	0.959	<0.05
Eccentric Jet	0.949	<0.05
Correlation of 3D VC and PISA in moderate MR		
	Correlation coefficient	P value
Central Jet	0.807	<0.05
Eccentric Jet	0.617	<0.05
Correlation of 3D VC and PISA in severe MR		
	Correlation coefficient	P value
Central Jet	0.817	<0.05
Eccentric Jet	0.572	<0.05

It was observed that there was a significant correlation between 3D VC and PISA levels in patients of mitral regurgitation. However correlation is better in MR with central jet compared to eccentric jet in moderate and severe MR ($r = 0.807, 0.817$ vs $r = 0.617, 0.572$).

Correlation of 3D VC and 2D VC in MR (Table 10)

Table 10

Type of jet Correlation of 3D VC and 2D VC in mild MR		
	Correlation coefficient	P value
Central Jet	0.959	<0.05
Eccentric Jet	0.949	<0.05
Correlation of 3D VC and 2D VC in moderate MR		
	Correlation coefficient	P value
Central Jet	0.956	<0.05
Eccentric Jet	0.774	<0.05
Correlation of 3D VC and 2D VC in severe MR		
	Correlation coefficient	P value
Central Jet	0.556	<0.05
Eccentric Jet	0.346	0.271

It was observed that there was a significant correlation between 3D VC and 2D VC in all patients of mitral regurgitation with central jet and in patients of mild MR with eccentric jet. However, correlation is better in central jets compared to eccentric jets in moderate MR ($r = 0.956$ vs $r = 0.774$), but there were no significant correlations between 3DVC and 2D VC in severe MR ($P = 0.27$).

Type of jet Correlation of 3D VC and 2D VC in mild MR		
	Correlation coefficient	P value
Central Jet	0.959	<0.05
Eccentric Jet	0.949	<0.05
Correlation of 3D VC and 2D VC in moderate MR		
	Correlation coefficient	P value
Central Jet	0.956	<0.05
Eccentric Jet	0.774	<0.05
Correlation of 3D VC and 2D VC in severe MR		

	Correlation coefficient	P value
Central Jet	0.556	<0.05
Eccentric Jet	0.346	0.271

Discussion

In the present study, we aimed to assess the relationship between the mitral regurgitation severity and NT-proBNP levels and correlation of 2D echocardiographic indices, 3D vena contracta with NT-proBNP levels. We also sought to evaluate whether inclusion of 3D vena contracta area in assessing severity of organic MR is superior to 2D echocardiographic assessment.

Similar to Nkomo VT *et al.* [14] we observed that moderate to severe mitral regurgitation prevalence increases with age. Mitral regurgitation was almost equally distributed in both males (n = 36) and females (n= 38). In our study we observed that CRHD was the most common cause of organic mitral regurgitation followed by MVP which was similar to that described by Kumar R *et al.* [15], Cinteza M *et al.* [16].

Timothy M. Sutton *et al.* [17] showed that plasma natriuretic peptides levels increase with the severity of MR and are higher in symptomatic compared to asymptomatic patients, even when LVEF is normal. Hellgren L *et al.* [18] observed that there was a correlation between increasing regurgitant fraction on MRI and increased levels of plasma NT-proANP and NT-proBNP. In echocardiography, increasing vena contracta width and increasing PISA correlated to increased levels of plasma NT-proANP and NT-proBNP. No other correlation was found between measures on MRI, echocardiography and natriuretic peptides. Davutoglu *et al.* [19] showed that plasma NT-proBNP is a potential marker of disease severity and correlates with symptoms in patients with chronic rheumatic valve disease. Shokoufeh Hajsadeghi *et al.* [20] showed that there is no statistically significant difference in BNP of the patients with mild, moderate or severe MR. In the present study, we observed that increase in plasma NT-proBNP levels was significantly associated with increase in severity of MR assessed by 2D and 3D echocardiography.

Ursula Klaar *et al.* [21] showed that low plasma natriuretic peptide levels, with their high negative predictive value, appear to be particularly helpful by identifying individuals at low risk. Serial measurements of BNP or NT-proBNP may help to improve the timing of intervention in MR.

Left ventricular ejection fraction is an important determinant in mitral valve surgery in patients with mitral regurgitation, but in some instances it is difficult to accurately measure LVEF because of abnormally shaped ventricles or poorly defined endocardium. Myocardial performance index, a Doppler-derived echocardiographic index, is independent of ventricular geometry, blood pressure and age. Since MPI incorporates both systolic and diastolic ventricular function, may provide a better assessment of the global LV function than LVEF. Similar to Shokoufeh Hajsadeghi *et al.* [20], Sayar N *et al.* [22] in the present study, we observed that MPI correlates positively with left ventricular volumes and dimensions both in systole and diastole, RVSP, LA volume.

When we have chosen cut point level of 0.45 for MPI based on Ono M *et al.* [23] we could define a cutoff value of 524 pg/ml for NT-proBNP serum level and some of the echocardiographic indices to differentiate normal and abnormal MPI.

Furthermore, calculation and comparison of area under ROC curves for NT-proBNP and echocardiographic measures such as LV end-diastolic volume, LV end-systolic volume, LV end-systolic dimension and LV end-diastolic dimension showed that there is no significant difference between these indices such that one may be chosen as the best one for prediction of MPI abnormality.

Results of this study suggest that natriuretic peptide testing may add to the information obtained by echocardiography in the assessment of MR in clinical practice. When echocardiographic assessment is technically difficult, low NT-pro BNP levels would suggest that MR is not severe. Measurement of natriuretic peptides may also be useful when it is not clear whether symptoms of dyspnea or fatigue are due to cardiac disease.

We also observed that there was a significant correlation between 3D VC and 2D VC in all patients of mitral regurgitation with central jet and in patients of mild MR with eccentric jet. However correlation is better in central jets compared to eccentric jets in moderate MR (r =0.956 vs r = 0.774) similar to Xin Zeng *et al.* [24]. Similar to Chaim Yosefy *et al.* [25] we observed that for eccentric jets, VC width by 2D echo was correlated less well with 3D VC, and 2D VC width underestimated regurgitant orifice area especially in moderate to severe MR patients. Accurate assessment of MR is important but still challenging in daily clinical practice.

Currently, various color Doppler 2D methods are used for MR quantification, however, each method has its limitations, based on technical issues or inaccurate geometric assumption. Besides the 2D methods, recent studies showed that planimetry of the VCA was highly feasible by using color Doppler 3D echocardiography, which provided a new approach for MR quantification by direct measurement of the ROA.

Conclusion

This study showed that NT-proBNP measurement has the same sensitivity and specificity as echocardiographic indices and may be used as a hormonal factor for the evaluation of patients with mitral

regurgitation in combination with echocardiography. Myocardial performance index combined with NT-proBNP measurement may be helpful in detection of subclinical impairments in left ventricle functions. Low plasma natriuretic peptide levels, with their high negative predictive value, appear to be particularly helpful in identifying individuals at low risk. Serial measurements of NT-proBNP may help to improve the timing of intervention in MR. Three-dimensional VCA may provide a single, directly visualized, and reliable measurement of ROA, independent of geometric and flow assumptions, which classifies MR severity comparable to current clinical practice using the ASE-recommended 2D integrative method. The 3D VCA method may improve accuracy of MR grading compared with the 2D PISA method by eliminating geometric assumptions.

Conflict of Interest: None.

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