

**ABSTRACT** Background: Limited data exits on echocardiographic determinants of functional tricuspid regurgitation in Indian population with rheumatic valvular heart disease.

Aim: To characterize echocardiographic patterns in patients with more than mild functional tricuspid regurgitation and rheumatic valvular heart disease.

Methods: Hospital-based prospective observational study. Forty patients with rheumatic heart disease and functional tricuspid regurgitation underwent comprehensive echocardiographic assessment of right and left heart geometry as well as function.

Results and conclusions: Patients were distributed equally among moderate and severe tricuspid regurgitation groups. Mitral valve was most commonly involved, majority were in atrial fibrillation (62.5%). Patients with more than mild functional tricuspid regurgitation had statistically significant increases in right ventricular and atrial dimensions (p<0.001 moderate vs severe groups). Tricuspid regurgitation was also associated with pulmonary hypertension, tricuspid annulus dilatation and tethering of its leaflets. Left heart geometry and function had no bearing on functional tricuspid regurgitation. Study findings have therapeutic implications.

### Introduction

Functional tricuspid regurgitation is a consequence of deformation of the tricuspid valve apparatus that occurs as a result of alteration of right ventricular function and geometry in patients with advanced left heart disease, pulmonary hypertension, congenital heart disease and cardiomyopathies. Functional tricuspid regurgitation is associated with significant morbidity and mortality. <sup>1, 2</sup> In recent times, there has been a considerable interest on the mechanisms and determinants of functional tricuspid regurgitation. <sup>3-5</sup> Nevertheless, data pertaining to those with rheumatic valvular heart disease are scarce. Therefore, this study was done with an aim to characterize echocardiographic patterns in patients with more than mild functional tricuspid regurgitation and rheumatic valvular heart disease.

# Materials and methods

The study was a single center observational study done in the echocardiography lab of the Cardiology department of the Christian medical college hospital, a tertiary care hospital in India.

Inclusion criteria: patients aged 18 years and above, clinically suspected to have rheumatic valvular heart disease and referred for echocardiography.

Exclusion criteria: organic tricuspid valve disease, echocardiographic window that was suboptimal for quantitative assessments, prior tricuspid valve repair or replacement, permanent pacemaker implantation, cardiac tamponade, congenital heart disease and pregnancy.

Outcome variables and assessment: All enrolled patients underwent comprehensive echocardiography and Doppler evaluations in a systematic manner using a Philips iE 33 Ultrasound machine (Philips Medical Systems, Andover, MA, USA) using a 1-5 Mhz sector array probe. All examinations were stored for off-line analyses. Data sets were analyzed using dedicated software (4D Cardio-View<sup>™</sup>, Image Arena platform, Tomtec imaging systems, Munich, Germany). Patients were grouped as moderate and severe functional tricuspid regurgitation based on standard cut offs for percent regurgitation jet area and vena contracta. Other variables measured included right ventricular geometry and function, tricuspid annulus dimensions, tricuspid tethering area and height (area and height enclosed by the leaflets and annulus plane during systole), right atrial geometry, left ventricular geometry and function, and hemodynamics. Systolic pulmonary artery pressure was estimated from the peak regurgitation jet velocity using Bernoulli equation and adding the estimated right atrial pressure. Values were averaged over five cycles for patients in atrial fibrillation.

The study was conducted in accordance with the Declaration of Helsinki and within the framework of Good Clinical Practice. The study was approved by the institution's Ethics committee.

# Statistical analysis

All continuous variables were expressed as mean  $\pm$  standard deviation or as median (interquartile range) according to their distribution. Continuous variables that had a normal distribution were compared using independent samples T test, and variables with a non parametric distribution were compared using a Mann Whitney U test. Pearson correlation coefficient was used to analyze correlation between continuous variables. A 'p' value less than 0.05 was considered statistically significant for all tests. Data analysis was performed using IBM SPSS software version 18 (IBM SPSS Inc., Illinois, Chicago, USA).

# Results

A total of 40 patients were included in the analysis and distributed equally between moderate and severe func-

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tional tricuspid regurgitation groups. Mean age group of the study population was 41  $\pm$  12, majority were females. Twenty five patients had atrial fibrillation and majority had predominant involvement of the mitral valve (table 1). Nearly all patients were in NYHA class II.

### Table 1. Basal clinical characteristics

	Total (n=40) Moderate functional TR group (n=20)		Severe functional TR group (n=20)	
Age, years	41 ± 12	42 ± 13	41 ± 11	
Females, n (%)	28 (70)	16 (80)	12 (60)	
Atrial fibrillation, n (%)	25 (62.5)	12 (60)	13 (65)	
NYHA, n (%)				
2	39 (97.5)	20	0	
3	1 (2.5)	19	1	
Clinical diagnosis, n (%)				
Mitral valve alone	33 (82.5)	19 (95)	14 (70)	
Mitral + aortic valve	7 (17.5)	1 (5)	6 (30)	
Mitral stenosis				
Mild	3 (7.5)	3 (15)	0	
Moderate	7 (17.5)	3 (15)	4 (20)	
Severe	29 (72.5)	13 (65)	16 (80)	
Mitral regurgitation				
Mild	11 (27.5)	3 (15)	8 (40)	
Moderate	7 (17.5)	5 (25)	2 (10)	
Severe	5 (12.5)	3 (15)	2 (10)	
Aortic stenosis				
Mild	1 (2.5)	1 (5)	-	
Moderate	-	-	-	
Severe	2 (5)	-	2 (10)	
Aortic regurgitation				
Mild	6 (15)	1 (5)	5 (25)	
Moderate	1 (2.5)	-	1 (5)	
Severe	-	-	-	
Body surface area, m <sup>2</sup>	1.42 ± 0.15	1.42 ± 0.15	1.42 ± 0.16	
Heart rate, beats per minute	90 ± 18	93 ± 17	88 ± 19	

Values are expressed as mean ± SD or as number (percentages). NYHA stands for New York Health Association

# Right ventricular geometry and function

Patients with severe functional tricuspid regurgitation had statistically significant increase in basal, mid and longitudinal dimensions of the right ventricle when compared to the moderate group, who had values within the normal limits (table 2). Severe group had mildly diminished fractional area change, but the TAPSE values were within normal limits.

### Right atrial geometry

Right atrial dimensions were increased in both the groups, but significantly more in the severe functional TR group (table 2).

Table	2.	Echocardiographic	characteristics	of	the	study
popul	atio	on				

	Cut-off values <sup>6,7</sup> for abnor- mality	All (n=40)	Mod- erate func- tional TR (n=20)	Severe func- tional TR (n=20)	P val- ues*
Right Ventricle					
Mid dimenion, cm		3.4 ± 0.8	3.0 ± 8	3.9 ± 0.6	
Basal dimen- sion, cm	>3.5	4.6 ± 0.9	3.9 ± 0.6	5.2 ± 0.9	0.001
Longitudinal dimension, cm	>4.2 >8.6	6.6 ± 0.7	6.2 ± 0.6	7.1 ± 0.7	<0.001
End diastolic area, cm²	>25 >14	22.5 ± 8.5	17.5 ± 3.9	27.5 ± 8.9	<0.001
End systolic area, cm²	<35	14.5 ± 6.4	10.8 ± 3.0	18.3 ± 6.8	0.07
Fractional area change, % Right atrium		36.1 ± 8.0	38.4 ± 6.9	33.9 ± 8.6	
Major dimen- sion, cm	>5.3	5.9 ± 1.1	5.4 ± 1.0	6.4 ± 1.0	0.001
Minor dimen- sion, cm	>4.4	4.6 ± 1.1	4.0 ± 0.6	5.2 ± 1.1	<0.001
End-systolic area, cm <sup>2</sup>	>18	23.6 ± 7.6	19.4 ± 2.7	28.0 ± 8.9	<0.001
Iricuspid an- nulus		32+	27+	36+	
End systolic diameter, cm		0.6	0.3	0.5	-0.001
End diastolic diameter, cm	- >3.3	3.7 ± 0.6	3.2 ± 0.3	4.1 ± 0.4	< 0.001
Tethering area, cm <sup>2</sup>	-	1.7 ± 0.9	1.09 ± 0.39	2.23 ± 0.88	<0.001 <0.001
Tethering height, cm	<1.6	0.9 ± 0.3	0.65 ± 0.18	1.12 ± 0.29	0.08
TAPSE, cm		1.8 ± 0.4	1.9 ± 0.3	$1.7 \pm 0.5$	
Estimated sys- tolic pulmonary artery pressure, mmHg		67 ± 26	55 ± 16	79 ± 28	0.002
	>35-40				
Estimated mean pul- monary artery pressure, mmHg		41 ± 6	39 ± 6	43 ± 5	0.01
Lett ventricle	<52	58.0 ± 4.0	58 ± 3.0	58 ± 4.0	
tion, %	- 52	6.6 ±	6.6 ± 0.7	6.7 ±	0.99
Longitudinal dimension, cm	>150	85.3	90.5	74.2	0.82
End-diastolic volume	(maies)	(65-9- 98.9)	(75.6- 101.4)	(57.3- 93.2)	0.06
End-systolic	>61 (males)	33.1	35.5	32.3	0.07
		(27.3- 41.5)	(32.2- 42.5)	(23.8- 39)	

Values are expressed as mean  $\pm$  SD, median (interquartile range) or as number (percentages). \* P values for comparison between moderate and severe groups. TAPSE stands for tricuspid annular plane systolic excursion. TR stands for tricuspid regurgitation.

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### Tricuspid annulus geometry

Functional tricuspid regurgitation was found to be associated with significant tricuspid annular dilatation and deformation resulting in tethering of the tricuspid valve leaflets (table 2). End diastolic tricuspid annulus diameter and tethering area correlated significantly with vena contracta (r=0.50, p=0.001) and percent regurgitant jet area (r=0.57, p<0.001). (Figure 1)





### Pulmonary artery pressure

Functional tricuspid regurgitation was associated with increase in the estimated mean pulmonary artery pressures (table 2).

### Left ventricular geometry and function

Left ventricular geometry and function were within normal limits and was not associated with functional tricuspid regurgitation (table 2).

### Discussion

This observational study demonstrated that moderate and severe functional tricuspid regurgitation was associated with dilatation of right ventricle and atrium, dilatation and deformation of tricuspid annulus and pulmonary hypertension. Left ventricular geometry and function was not associated with functional tricuspid regurgitation.

Normal functioning of tricuspid valve requires co-ordination of its components comprising of valve leaflets, annulus, chordae, papillary muscles, right atrial and ventricular myocardium. Abnormalities of any of the above components can result in regurgitation. Functional tricuspid regurgitation is a consequence of pulmonary hypertension which results in elevated right ventricular pressures. Pressure overload leads to right ventricular dilatation and displacement of papillary muscles which in turn results in annular dilatation and inadequate leaflet co-aptation.

Prior studies have focussed on determinants of functional tricuspid regurgitation. Kim et al <sup>8</sup> identified right ventricular end systolic eccentricity index, end diastolic tricuspid annulus dimension and tricuspid valve tethering height as independent predictors of functional tricuspid regurgitation. In another retrospective study by Fukuda et al <sup>9</sup>, right atrial area, right ventricular spherical index and tricuspid valve tethering height predicted functional tricuspid regurgitation severity. Zhou et al <sup>10</sup> found significant association between annulus dilatation and atrial fibrillation. Most of these studies included predominantly non rheumatic pa-

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tients, nevertheless pathological process underlying functional regurgitation is likely to be the same. Similarly, our study showed right ventricular and atrial geometry, tricuspid valve deformations and pulmonary hypertension to be associated with more than mild functional tricuspid regurgitation. Left ventricular function and geometry did not appear to have any consequence on the degree of functional regurgitation. Similarly right ventricular function also did not significantly impact functional tricuspid regurgitation.

Findings of this study have implications for clinical practice and therapeutic options. Current guidelines recommend tricuspid annuloplasty if tricuspid annulus diameter is greater than 4 cm. Severe functional tricuspid regurgitation patients in this study too had an annulus dimension greater 4cm. However, some patients had severe tethering of the leaflets and annuloplasty alone may not be enough to address regurgitation sufficiently. Such patients may require techniques such as anterior tricuspid leaflet augmentation or in severe cases of tethering, tricuspid valve replacement.

Present study had some limitations including small sample size and lack of normal controls for analysis. The study demonstrated right sided heart chamber abnormalities in functional tricuspid regurgitation patients, however further pathogenetic and large scale observational studies with long term follow up are needed to fully understand the mechanisms and progression of functional tricuspid regurgitation.

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