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Association of echocardiographic diastolic tricuspid regurgitation with other echocardiographic parameters, survival scores and functional capacity in patients with advanced functional mitral regurgitation

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ABSTRACT

Aims: Functional mitral regurgitation (FMR) is an important condition associated with advanced heart failure and poor prognosis. The aim of this study was to investigate the effects of diastolic (presystolic) tricuspid regurgitation (DTR) on right ventricular function, survival rates and functional capacity in patients with advanced FMR. The relationship between DTR and right ventricular systolic function and the predictive factors involved in its development were also evaluated.

Methods: The study included 64 patients with advanced FMR who were evaluated for mitraclip therapy between June 2014 and February 2015. Demographic characteristics, cardiovascular risk factors, New York Heart Association (NYHA) functional classification and laboratory data were recorded. Left and right ventricular parameters were examined by echocardiography, and the diagnosis of DTR was made by color Doppler method. Estimated survival rates were evaluated using the Seattle Heart Failure Model Score (SHFSM) with 1- and 5-year projections.

Results: DTR was detected in 14 (22%) of the patients included in the study. The majority (85.7%) of the patients in the group with DTR were in NYHA III-IV stage and had low functional capacity. DTR showed significant assocation with right ventricular fractional area change (RV FAC), right ventricular peak systolic myocardial velocity (RV Sm), TAPSE, tricuspid regurgitation, ejection fraction, pulmonary artery systolic pressure, and pulmonary vascular resistance ($p<0.05$). In addition, DTR group had lower estimated survival rates compared to SHFSM (1-year estimated survival 64%, 5-year estimated survival 35%; $p<0.001$). In Binary Logistic Regression Analysis, RV FAC and RV Sm values were found to be independent predictors for the development of DTR.

Conclusion: DTR is an important echocardiographic parameter that indicates poor prognosis in patients with advanced FMR. This study demonstrated that DTR is associated with right ventricular dysfunction and decreased estimated survival rates. Early diagnosis of DTR may provide an important contribution to clinical management and prognostic evaluation in this patient group.

Keywords: Functional mitral regurgitation, diastolic tricuspid regurgitation, survival rate, functional capacity

INTRODUCTION

Functional mitral regurgitation (FMR) is a pathology observed in structurally normal mitral valves that develops due to left ventricular (LV) remodeling in patients with ischemic and non-ischemic dilated cardiomyopathy (DCMP). FMR, occurring in 55-75% of patients with DCMP, is associated with hemodynamic deterioration and increased mortality.[1-3] Mechanisms such as LV dilatation and papillary muscle dysfunction lead to incomplete closure of the mitral valves, causing blood to backflow from the LV into the left atrium during systole.[3]

Diastolic (presystolic) tricuspid regurgitation (DTR) is an echocardiographic finding that occurs when the pressure difference between the right atrium and right ventricle (RV) reverses at the end of diastole.[4] It is usually associated with conditions such as advanced heart failure, aortic valve pathologies and atrioventricular conduction blocks.[5-7] There are limited number of studies in the literature on the pathophysiopathology of DTR and its relationship with right ventricular function in patients with congestive heart failure (CHF). Although it is known that RV dysfunction is

associated with poor prognosis, the effects of RV dysfunction on survival have not been sufficiently elucidated.[8]

This study aims to investigate the effects of DTR on right ventricular function, survival scores and functional capacity in patients with advanced FMR. In addition, we aimed to evaluate the predictive factors involved in the development of DTR and its relationship with RV systolic function. Determining the effects of DTR on prognosis may provide important information to improve clinical management and evaluation processes in this patient group.

METHODS

This study was produced from the specialisation thesis titled 'the relationship of echocardiographic diastolic tricuspid regurgitation with other echocardiographic parameters, survival scores and functional capacity in patients with advanced functional mitral regurgitation' written in Kartal in 2015. Institutional approval was obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study included 64 patients with advanced FMR who were evaluated for mitraclip therapy at İstanbul Koşuyolu Yüksek İhtisas Training and Research Hospital between June 2014 and February 2015. Demographic data (age, gender, height, weight), cardiovascular risk factors (hypertension, diabetes, hyperlipidemia, smoking), past medical history and medications were recorded. The functional status of the patients was determined according to the New York Heart Association (NYHA) classification. FMR was found in all patients included in the study and patients with degenerative mitral valve pathology were excluded. In addition, patients with one or more of the following criteria were excluded:

- Patients with acute coronary syndrome in the last 3 months,
- Those with congenital heart disease,
- Hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia or infiltrative cardiomyopathy,
- Patients with an ICD, CRT or pacemaker device,
- Those with a mechanical prosthetic valve in the mitral or tricuspid position,
- Isolated right heart failure due to primary pulmonary hypertension,
- Those with any degree of atrioventricular block,
- Those with severe pulmonary insufficiency.

Echocardiographic Evaluation

All echocardiographic examinations were performed with the Vivid 7 Pro (GE Vingmed Ultrasound AS, Horten, Norway) in the left lateral decubitus position and during superficial respiration. Left and right ventricular parameters were measured in accordance with the American Society of Echocardiography (ASE) guidelines.[9] DTR was defined as a low velocity jet into the right atrium at the end of diastole using color Doppler.

Laboratory Investigations

Complete blood count, biochemistry panel, liver and renal function tests were evaluated on the same day. In addition, arrhythmia, signs of myocardial infarction and atrioventricular conduction disturbances were investigated by 12-lead electrocardiography (ECG).

Statistical Analysis

All statistical analyses of the data was performed with SPSS 15.0 (Statistical Package for Social Sciences) software. Continuous variables were expressed as mean±standard deviation and categorical variables as percentages. Student's t-test and Mann-Whitney U test were used for intergroup comparisons. Pearson and Spearman methods were preferred for correlation analysis. Independent predictors were determined by multivariate logistic regression analysis. The $p<0.05$ criterion was used for statistical significance.

RESULTS

The mean age of the 64 patients included in the study was 58.20±14.06 years, 50% had ischemic and 50% had DCMP. 53.1% of the participants were in NYHA III-IV stage and 46.9% were in NYHA I-II stage. Hypertension (54.7%), smoking (53.1%) and diabetes mellitus (34.4%) were the most common cardiovascular risk factors, while demographic parameters such as gender and body mass index were not significantly different between the groups (**Table 1**). DTR was detected in 22% (n=14) of the patients included in the study. Patients with DTR were generally in more advanced NYHA stages and a clinically worse functional capacity was observed in these patients.

Table 1. Demographic data and clinical characteristics of the patients

Parameter	Total (n=64)	DTR (n=14)	Non DTR (n=50)	p
Age (year)	58.20±14.06	56.5±16	58.6±13.6	0.62
Body-mass index (kg/m²)	26.61±4.57	26.3±5.5	26.7±4.3	0.76
Gender (male) (%)	%65.6	%71.4	%62.0	0.53
Hypertension (n,%)	35 (54.7)	7 (50)	28 (56)	0.76
Diabetes (n, %)	22 (34.4)	6 (42)	16 (47)	0.53
Smoking (n,%)	34 (53.1)	10 (71)	24 (48)	0.13
NYHA class (n,%)				
- NYHA I-II	30 (46.9)	2 (14)	28 (56)	<0.001
- NYHA III-IV	34 (53.1)	12 (86)	22 (44)	<0.001
CMP (ischemic)	32 (50)	7 (50)	25 (50)	1

DTR: Diastolic (presystolic) tricuspid regurgitation, NYHA: New York Heart Association, CMP: Cardiomyopathy

On echocardiographic examination, the presence of RV DTR resulted in significant deterioration in RV function parameters. In patients with DTR, the mean RV ejection fraction (EF) was around 22%, TAPSE 1.24 mm, RV Sm 8.6 cm/sec and FAC 21%. In patients without DTR, these parameters were 27.8%, 1.59 mm, 11 cm/sec and 32%,

respectively. Tricuspid regurfitation was also higher in DTR group as expected. In addition, pulmonary parameters such as PAPs and PVR were significantly higher in patients with DTR. There was no difference between groups regarding RV diameters, left atrium diameter, LV deceleration time, and left atrial volume index (**Table 2**).

Table 2. Echocardiographic parameters and univariate analysis results

	Non-DTR (n=50)	DTR (n=14)	p
LVEF (%)	27.80±7.08	22.14±6.41	0.009
EDD (mm)	6.64±0.83	6.64±0.74	0.99
ESD (mm)	5.54±0.90	5.57±0.73	0.90
LAd (mm)	4.82±0.57	5.02±0.64	0.268
LV DT (msn)	151.30±51.70	123.71±37.70	0.068
LAVi	36.89±11.14	40.15±9.13	0.320
TAPSE (mm)	1.59±0.51	1.24±0.35	0.020
RV Sm	11.04±2.72	8.67±1.56	0.003
RV FAC (%)	32.42±9.31	21.28±5.48	0.001
TR	2.12±0.92	3.07±0.73	0.001
PAPs (mmHg)	39.87±16.08	57.50±11.88	0.000
PVR (wood)	3.06±1.33	4.94±2.11	0.000

DTR: Diastolic (presystolic) tricuspid regurgitation, EDD: End-diastolic diameter, ESD: End-systolic diameter, LAd: Left atrium diameter, LAVi: Left atrial volume index, LV DT: Left ventricular deceleration time, LVEF: Left ventricular ejection fraction, RV Sm: Right ventricular peak systolic myocardial velocity, PAPs: Pulmonart artery systolic pressure, PVR: Pulmonary vascular resistance, RV FAC: Right venticular fractional area change, TR: Tricuspid regurgitation, TAPSE: Tricuspid annular plane systolic excursion

In binary logistic regression analysis, RV FAC and RV Sm values were found to be independent predictors for the development of DTR (**Table 3**). In addition, PVR and PAPs were also found to be independent predictors of DTR.

Table 3. Binary logistic regression analysis of independent echocardiographic markers of DTR

Variables	B	S.E.	Wald	Df	Sig.	Exp (B)
EF (%)	-0.107	0.101	1.125	1	0.289	0.898
RV Sm	-0.957	0.461	4.307	1	0.038	0.384
TAPSE (mm)	4.441	2.546	3.041	1	0.081	84.828
FAC (%)	-0.213	0.088	5.904	1	0.015	0.808
TR	2.302	-	-	3	0.508	-
PABs (mmHg)	0.096	0.056	2.944	1	0.086	1.101
PVR (wood)	0.594	0.404	2.163	1	0.141	1.811

DTR: Diastolic (presystolic) tricuspid regurgitation, EF: Ejection fraction, PAPs: Pulmonart artery systolic pressure, PVR: Pulmonary vascular resistance, RV Sm: Right ventricular peak systolic myocardial velocity, TAPSE: Tricuspid annular plane systolic excursion, TR: Tircuspid regurgitation

Patients with DTR show a significant decrease in 1-year and 5-year survival rates. While the 1-year and 5-year survival rates were 64% and 35%, respectively, in patients with DTR, these rates were 85% and 60%, respectively, in patients without DTR (**Table 4**).

Table 4. Survival rates and survival scores

Parameter	DTR (n=14)	Non DTR (n=50)	p
1-year survival (%)	64.0%	85.0%	<0.001
5-year survival (%)	35.0%	60.0%	<0.001

DTR: Diastolic (presystolic) tricuspid regurgitation

DISCUSSION

The aim of this study was to evaluate the effects of DTR on RV function, survival rates and clinical prognosis in patients with advanced FMR. The most important finding of our study showed that DTR had a significant negative impact on RV function, which significantly decreased the survival rates of patients. In particular, parameters such as RV EF, TAPSE, RV Sm and FAC were significantly reduced in the presence of DTR. These findings suggest that impaired RV function is a key factor in the development and progression of DTR. The presence of DTR was also found to be an important indicator associated with poor prognosis in survival prediction models such as the SHFSM.

DTR causes significant adverse effects on RV function, which may adversely affect the prognosis of patients. In our study, RV EF, TAPSE, RV Sm and FAC values were significantly lower in patients with DTR. The decrease in these parameters suggests that impaired RV function is a key factor in the development and progression of DTR. Szymanski et al.[10] associated the development of DTR with severe pulmonary hypertension and RV dysfunction, emphasizing that these parameters are important factors in the pathophysiology of DTR.

Given this evidence, DTR may have clinically important consequences in patients with advanced FMR. In our study, the presence of DTR had significant adverse effects on the survival rates of patients. Patients with DTR had significantly lower 1-and 5-year survival rates compared with patients without DTR.

There are many studies supporting our findings. According to a meta-analysis by Truong et al.[11] impaired RV function had a significant effect on the prediction of all-cause mortality in patients with FMR. According to a study by Doldi et al.[12] the presence of RV dysfunction in patients with primary mitral regurgitation was associated with a lower rate of symptomatic improvement and a higher 2-year mortality rate after mitra clip therapy. In addition, many studies have shown that RV function has a prognostic effect in pulmonary hypertension, congenital heart disease, pulmonary embolism, heart failure, cardiomyopathies, and valvular heart disease.[13-18]

An important feature of our study is that we comprehensively examined the effects of DTR on RV function in patients with advanced FMR. Compared to previous studies, this study provides a more detailed picture of the effects of DTR on patients by using multiple echocardiographic parameters to assess RV function. Furthermore, the use of survival prediction models such as the SHFSM to analyze the effects of DTR on survival rates and prognosis gave our study a deeper clinical meaning. The identification of parameters such as RV function and pulmonary pressure as independent predictors of DTR in multivariate analysis is one of the methodological strengths of our study and contributes to the prognostic value of DTR.

Limitations

Our study also has many limitations. The first one is that it is a single-center study, which may limit the generalizability of the findings. Furthermore, the relatively small number of patients makes validation difficult, especially in larger and heterogeneous groups. Our study examined RV function using echocardiographic parameters only and did not include further invasive testing or long-term follow-up data. This prevented us from assessing patients' response to treatment and the long-term effects of DTR. Furthermore, larger and longer-term studies examining the clinical management of DTR and its effects on treatment response are needed.

CONCLUSION

As a result, this study shows that DTR in patients with advanced FMR is associated with their RV function, pulmonary pressure and survival rates. Early recognition of DTR is critical for treatment and clinical monitoring in this patient group. RV dysfunction and pulmonary hypertension have been found to play an important role in the development of DTR and may adversely affect the prognosis of patients. These findings suggest that the effects of DTR on prognosis should be investigated in more detail in larger and long-term studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was produced from the specialisation thesis titled 'the relationship of echocardiographic diastolic tricuspid regurgitation with other echocardiographic parameters, survival scores and functional capacity in patients with advanced functional mitral regurgitation' written in Kartal in 2015.

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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