Journal of Clinical Cardiology and Cardiology Research
2023 Volume 2, Issue 1
DOI: 10.59657/2837-4673.brs.23.004

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Research Article

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Which Type of Cardiomyopathy (Ischemic or Dilated) can be Attributed to more Alteration in Right Ventricular Dysfunction?

Running title: Right Ventricular Dysfunction and Type of Cardiomyopathy

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Abstract

Background: There are few studies in the literature comparing the RV function of the two entities of dilated cardiomyopathy (DCM) and ischemic cardiomyopathy (ICM). The aim of this study was to compare RV dysfunction among patients with ICM or DCM.

Methods: The study population consisted of 287 consecutive patients with heart failure referred for pre-CRT echocardiography evaluation at the Tehran Heart Center between January 2005 and December 2010. A complete transthoracic echocardiographic examination, which included 2-dimensional and Doppler echocardiography with colour flow mapping were performed using standard techniques. For assessing RV function, the two parameters of the tricuspid annular plane systolic excursion (TAPSE) and right ventricular peak mean systolic tissue velocity (RVSM) were measured.

Results: Comparing RV function on TAPSE measurement between the ischemic and dilated cardiomyopathy groups showed no significant differences between them that the mean of TAPSE was 15.05 ± 4.65 mm and 15.64 ± 4.90 mm, respectively. With respect to assessing RV function using peak mean systolic RVSM measurement, this parameter in the ischemic and dilated cardiomyopathy were also similar (3.795 ± 2.050 cm/s versus 4.551 ± 2.753 cm/s, p = 0.176).

Conclusion: There is no difference with regard to RV functional state between ICM and DCM.

Keywords: cardiomyopathy; ischemia; right ventricle; tricuspid

Introduction

The right ventricle (RV) systolic dysfunction has been shown as a powerful predictor of poor outcome in patients with congestive heart failure (CHF) [1,2]. In fact, the presence of RV systolic dysfunction is correlated with hemodynamic instability and adversely influences patient's survival. Some studies have shown that dilated cardiomyopathy (DCM) is characterized by more severe RV systolic dysfunction than ischemic cardiomyopathy (ICM) [3,4]. Even, it has been suggested that RV myocardial deformation at baseline and after CRT are more impaired in idiopathic compared with ischemic DCM patients [5]. Parcharidou et al [6]. found that the patients with ICM exhibited significantly lower systolic and diastolic velocities of tricuspid and mitral septal annular motion. According to their finding, heart failure could be accompanied by RV dysfunction, which is more pronounced in ICM than DCM patients. This discrepancy can be also influenced by other underlying defects such as presence of pulmonary hypertension, history of myocardial infarction, or severity of coronary involvement [7], and thus comparing level of RV dysfunction should be assessed with the presence of these concomitant indicators. The current study aimed to compare RV dysfunction between patients with ICM and DCM.

Methods

The study population consisted of 287 consecutive patients with heart failure and referred for pre-CRT echocardiography evaluation at the Tehran Heart Center, Tehran, Iran between January 2010 and December 2015. The main inclusion criteria were symptomatic heart failure, and left ventricular ejection fraction (LVEF) ≤35%. Those with prior CRT or pacemaker implantation, or implantable cardioverter-defibrillator were excluded from the study. The study protocol was approved by the research committee of the Tehran University of Medical Sciences and informed consent was obtained from all participants. At the time of baseline assessment, the patients were on maximal tolerated medical therapy, for at least for 3 months: 92.7% were on β-blockers, 91.3% on angiotensin-converting enzyme (ACE) inhibitors, 91.3% on diuretics, and 95.8% were on nitrates. At baseline, all patients were assessed clinically regarding demographics, topographic parameters, general risk profile, and drug history and ECG was also recorded for all of them. Ischemic cardiomyopathy was diagnosed as angiographic evidences of significant CAD (at least ≥ 70% in one epicardial coronary artery) with corresponding wall motion abnormality [8]. DCM was also defined as a heart muscle disease of unknown etiology that was diagnosed when other causes of cardiac failure such as coronary heart disease, amyloid or sarcoid heart disease, hemochromatosis were excluded [9].

For all patients, a complete routine transthoracic Echocardiographic examination, which included 2-dimensional and Doppler echocardiography with color flow mapping were performed using standard techniques. Echocardiography assessment was performed using a digital ultrasound machine commercially available (VIVID 7, Vingmed-General Electric, Horton, Norvey), using a 3.5 MHZ phased array transducer. The measurements were taken according to the guidelines of the American Society of Echocardiography. The patients underwent tissue Doppler imaging for RV function assessment 1 month before pacemaker implantation. For assessing RV function, the two parameters of the tricuspid annular plane systolic excursion (TAPSE) and peak mean systolic right ventricular tissue velocity (RVSM) were measured. We measured the TAPSE because this parameter has been proposed as a simple and reproducible method for quantitative assessment of RV ejection fraction [10]. On the other hand, the prognostic importance of TAPSE in the evaluation of RV function in patients with severe heart failure has been well-described, and it is recommended in the American guideline for echocardiographic quantification of RV function [11]. According to the previous studies, TAPSE ≤14 mm was considered as a marker of severe right ventricular dysfunction and a TAPSE ≤14 was chosen a priori as the cut-off to stratify the population into two groups according to baseline RV function [12,13]. Furthermore, according to the recent guideline of the Echocardiographic Assessment of the Right Heart in Adults, reported from the American Society of Echocardiography, the cut point of 16 for TAPSE can be used routinely as a simple method of estimating RV function, with a lower reference value for impaired RV systolic function of 16 mm [14]. Thus, we considered both cut-off points for the evaluation of RV function. Echocardiography with color-coded Doppler velocimetry was also employed to determine peak mean systolic RVSM. 3 heart cycles of the apical 4-chamber views were captured in conventional 2-dimensional and color tissue Doppler modes. The frame rate was greater than 100 milliseconds for tissue Doppler imaging. One basal segment of the RV free wall was used for all analyses. Offline analysis was conducted by an expert cardiologist. The peak mean systolic velocities (centimeters per second) were measured. The term *peak mean systolic velocity* was chosen, indicating that velocity measurements performed by pulsed wave Doppler myocardial imaging are higher than those performed by color Doppler imaging because pulsed wave Doppler myocardial imaging has an inherently higher temporal resolution and measures maximal instantaneous velocities, whereas color Doppler imaging, with its lower temporal resolution, uses autocorrelation techniques to measure regional mean velocities. The reproducibility of the data was published in our previous report [8].

The severity of TR was graded as mild when the Jet area-central jets occupied < 5cm^2 of the right atrial area, moderate when it occupied 5 to 10 cm^2, and severe when it occupied > 10 cm^2 [15,16]. The severity of MR was also graded as follows: mild, small central jet <4 cm^2 or <20% of left atrial area; moderate, signs of MR > mild present, but no criteria for severe MR; and severe, large central jet (usually > 10 cm^2 or > 40% of left atrial area) or variable size wall impinging jet swirling in LA [15].

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than

20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared using t test. Predictors exhibiting a statistically significant relation with TAPSE and RVSM measures in univariate analysis (p <0.1) were taken for multivariate linear regression analysis to investigate their independence as predictors. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. Statistical significance was determined as a p value of ≥ 0.05. All statistical analysis was performed using SPSS software (version 20.0, SPSS Inc., Chicago, Illinois).

Results

A total of 287 patients were recruited that among them, 129 were suffered from ICM and other from DCM. Baseline clinical features of the 287 patients enrolled in the study are summarized in Table I. The two groups were comparable for most of the clinical indices, including body mass index, systolic hypertension, current smoking, and cerebrovascular disease. However, patients with ICM were more frequently diabetics and hyperlipidemics. Male to female ratio was significantly higher in ischemic than dilated cardiomyopathy and the former group was older. Among all, 187 (65.2%) patients were in NYHA functional class III and 18.5% in NYHA class IV. No difference was found in NYHA class between the two groups. LV ejection fraction, mean heart rate, and mean pulmonary artery pressure were also comparable between the groups. The two groups were also similar in terms of MR and TR grading evidenced in echocardiography measurements.

Table 1: Baseline characteristics and clinical data in the two groups with ischemic or dilated cardiomyopathy

Characteristics	Ischemic cardiomyopathy (n=129)	Dilated cardiomyopathy (n=158)	P-value
Male gender, n (%)	111 (86.0)	102 (64.6)	< 0.001
Age (yr), mean/SD	59.36 ± 12.59	47.97 ± 17.82	< 0.001
Body mass index (kg/m^2), mean/SD	27.55 ± 4.22	26.73 ± 4.76	0.532
Diabetes mellitus, n (%)	50 (38.8)	36 (22.8)	0.036
Previous history of CAD, n (%)	129 (100)	19 (12.0)	< 0.001
Congestive heart failure, n (%)	11 (8.5)	19 (12.0)	0.516
Cerebrovascular disease, n (%)	3 (2.3)	1 (0.6)	0.312
Current smoking, n (%)	4 (3.1)	3 (1.9)	0.369
Hyperlipidemia, n (%)	20 (15.5)	10 (6.3)	0.030
Systolic hypertension, n (%)	13 (10.1)	11 (7.0)	0.435
Opium addiction, n (%)	5 (3.9)	3 (1.9)	0.370
Function class (NYHA):			
II	25 (19.4)	22 (14.0)	0.344
III	82 (63.5)	105 (66.4)	
IV	22 (17.1)	31 (19.6)	
Left ventricular ejection fraction (%)	22.13 ± 6.81	20.60 ± 7.15	0.068
Heart rate (/min), mean/SD	76.83 ± 16.18	80.56 ± 14.71	0.160
PAP (mmHg), mean/SD	42.14 ± 16.65	42.15 ± 13.59	0.996
Bundle branch block, n (%)			
Left BBB	101 (78.3)	134 (86.7)	0.537
Right BBB	19 (14.7)	16 (10.1)	
Atrial fibrillation, n (%)	5 (3.9)	9 (5.7)	0.772
MR grade, n (%)			
Normal	3 (2.3)	10 (6.3)	
Mild	54 (41.9)	64 (40.5)	0.853
Moderate	47 (36.4)	44 (27.8)	
Severe	25 (19.4)	40 (25.4)	
TR grade, n (%)			
Normal	15 (11.6)	21 (13.3)	
Mild	76 (58.9)	79 (50.0)	0.735
Moderate	27 (20.9)	34 (21.5)	
Severe	11 (8.6)	24 (15.2)	

Comparing RV function on TAPSE measurement between the ICM and DCM groups showed no significant differences between them that the mean of TAPSE was 15.05 ± 4.65 mm and 15.64 ± 4.90 mm, respectively (p = 0.331). Also, based on the two defined cut points for TAPSE for stratifying the patients' population into two groups (Table 2), no differences were observed in RV function between the patients with ICM and those with DCM. With respect to assessing RV dysfunction using peak mean systolic RVSM measurement, the peak mean systolic RVSM in the ischemic and dilated cardiomyopathy were also similar (3.795 ± 2.050 cm/s versus 4.551 ± 2.753 cm/s, p = 0.176). Multivariate linear regression model was fitted in order to assess differences in TAPSE index between the two study groups when adjusted for other variables as potential confounders (Table 3). The regression model showed also no difference in TAPSE index between the DCM and ICM groups.

Table 2: RV dysfunction in the two groups with ischemic or dilated cardiomyopathy

Characteristics	Ischemic cardiomyopathy (n=129)	Dilated cardiomyopathy (n=158)	P-value
TAPSE, mean/SD	15.05 ± 4.65	15.64 ± 4.90	0.331
TAPSE category, n (%)			
≤ 14	71 (55.0)	80 (50.6)	0.457
> 14	58 (45.0)	78 (49.4)	
TAPSE category, n (%)			
≤ 16	98 (76.0)	105 (66.5)	0.078
> 16	31 (24.0)	53 (33.5)	
peak mean systolic RVSM (cm/s)	3.795 ± 2.050	4.551 ± 2.753	0.176

Table 3: Relationship between the type of cardiomyopathy and RV dysfunction (TAPSE measure) in linear multivariable regression model

Item	Beta	Standard Error	P-value
Type of cardiomyopathy (ischemic vs. dilated)	0.226	3.646	0.653
Advanced age	0.057	0.146	0.712
Gender (male vs. female)	2.542	3.614	0.513
Functional class	-1.784	3.366	0.619
Left ventricular ejection fraction	0.001	0.319	0.998
Grade of mitral regurgitation	-2.458	2.601	0.388
Grade of tricuspid regurgitation	-3.444	2.327	0.199
Body mass index	0.086	0.561	0.884
Pulmonary artery pressure	0.103	0.162	0.553

Discussion

The present study compared RV function in patients with ICM and DCM and showed that the patients with ICM exhibited similar RV dysfunction assessed by TAPSE and peak mean RVSM parameters measurement compared with patients with DCM. This similarity was also confirmed in the multivariable analysis and independent of the influence of age, gender, body mass index, function class, history of diabetes mellitus, left ventricular ejection fraction and grading of mitral or tricuspid regurgitation. Some previous studies have shown that DCM is characterized by more severe RV systolic dysfunction than ICM [3,7]. Some abnormal changes in cardiovascular parameters result in the differences in the two types of cardiomyopathies. It has been indicated that the development of pulmonary hypertension is a sign of advanced disease resulting in RV dysfunction in ICM, while RV dysfunction occurred in DCM might be the result of the myopathic process affecting the myocardium of both ventricles, rather than of pulmonary hypertension [4,17]. This different underlying mechanism can describe the worse RV systolic and diastolic function in a group compared with another. Because in current study, the two groups were matched for pulmonary artery pressure as well as

left ventricular ejection fraction, this comparability might explain similarity in RV function in our study groups.

In this study, we used TAPSE index for assessing RV function in the cardiomyopathy groups. Most studies have focused on RV systolic dysfunction, and echocardiographic markers that have been identified as having an independent prognostic role in ICM or DCM are M-mode–derived TAPSE [18]. Moreover, the confounding effect of tricuspid regurgitation and its severity on RV function should not be ignored, because it has been clearly demonstrated that severe tricuspid regurgitation with severely dilated annulus can produce an irreversible deterioration of RV function [19]. So, because we tried to test our finding in a multivariable model with the presence of some above indicators, especially severity of tricuspid regurgitation, some probable underlying effectors on the measurement of TAPSE index confounding our result were unaffected.

In this assessment, the peak mean systolic RVSM in the ischemic and dilated cardiomyopathy were found to be 3.795 ± 2.050 cm/s versus 4.551 ± 2.753, respectively. It is concluded that color Doppler myocardial imaging velocities up to 20% less than pulsed tissue Doppler velocities, while color Doppler myocardial imaging measures peak mean systolic velocities for longitudinal shortening (3 references). According to our previous studies [20,21], in normal healthy adult hearts, the first and second peak mean systolic RVSM in basal RV free wall ranged 5.75-16.00 cm/s and 3.00-3.34 cm/s, respectively.

Conclusion

In conclusion, RV function might be similarly impaired in ischemic compared with dilated cardiomyopathy patients who were candidate for pre-CRT evaluation. Future longitudinal studies are warranted to understand the mechanisms of RV dysfunction as well as reversibility of RV dysfunction with CRT in the two types of cardiomyopathies.

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Cite this article: A Abbasi, M Sheikhvatan, Masoumeh L Tokaldany, M Rezvanfard, H Sadeghian. Et al. (2023). Which Type of Cardiomyopathy (Ischemic or Dilated) can be Attributed to more Alteration in Right Ventricular Dysfunction? *Journal of Clinical Cardiology and Cardiology Research*, BRS Publishers. 2(1); DOI: 10.59657/2837-4673.brs.23.004

Article History: **Received:** November 05, 2022; **Accepted:** November 28, 2022; **Published:** January 09, 2023