

# Evaluation of Longitudinal Right Ventricular Mechanical Dyssynchrony before and Early after Cardiac Resynchronization Therapy: A Strain Imaging Study

Maryam Esmailzadeh, MD, FACC, FCAPSC<sup>1</sup>, Hoorak Poorzand, MD<sup>2</sup>,  
Majid Maleki, MD, FACC, FCAPSC<sup>1\*</sup>, Anita Sadeghpour, MD, FACC,  
FASE<sup>2</sup>, Mozghan Parsaee, MD<sup>2</sup>

<sup>1</sup>Iran Cardiovascular Research Institute, Department of Echocardiography, Tehran, Iran.

<sup>2</sup>Shaheed Rajaei Cardiovascular, Medical and Research Center, Tehran, Iran.

Received 29 September 2010; Accepted 20 October 2010

## Abstract

**Background:** The right ventricular (RV) dyssynchrony has not been studied extensively and the existing literature has established the effect of cardiac resynchronization therapy (CRT) on the left ventricular (LV) dyssynchrony, but there is a dearth of data on the effect of CRT on the forgotten ventricle. We sought to evaluate the presence of mechanical right ventricular dyssynchrony in patients with systolic heart failure, selected for CRT, and track the changes early afterward utilizing the longitudinal strain analysis.

**Methods:** Thirty-six patients with severe left ventricular systolic dysfunction, candidates for CRT, were enrolled in this study. Mechanical dyssynchrony was assessed using tissue Doppler echocardiography. The time interval between the onset of the QRS to the peak systolic longitudinal strain at the RV free wall and the septum was obtained. The RV mechanical delay was calculated as the absolute value of the difference in the time-to-peak measurements between the RV and septum. The RV dyssynchrony was defined as the calculated delay in strain imaging, which was  $\pm 2$  SD above the mean value for the control subjects (20 cases). The RV function was evaluated using the RV fractional area change (RVFAC), tricuspid annulus plane systolic excursion (TAPSE), and peak systolic strain values of the RV free wall. Four to 7 days after CRT implantation, echocardiographic reevaluations were done.

**Results:** The calculated cut-off value for the RV dyssynchrony was 41.5 msec, according to which the pre-CRT analysis specified two patient groups: Group 1 (16 cases) with RV dyssynchrony and Group 2 (20 patients) without RV dyssynchrony. Significant improvement in the RV dyssynchrony was noted in Group 1 after CRT ( $30 \pm 28.9$  msec vs.  $68.8 \pm 21$  msec;  $p$  value  $< 0.01$  vs.  $14 \pm 10$  msec vs.  $19 \pm 16.5$  msec;  $p$  value = 0.18 respectively). A significant correlation was found between the severity of the RV dyssynchrony and peak systolic strain in the RV free wall ( $r = -0.5$ ;  $p$  value  $< 0.05$ ). No significant relation was found between the RV dyssynchrony and right ventricle fractional area change (RVFAC), LV mechanical dyssynchrony, time-to-peak systolic strain in the RV free wall, QRS width, or morphology. In Group 1, the peak systolic strain increased insignificantly ( $p$  value = 0.15 for the basal segment;  $p$  value = 0.20 for the mid segment). A moderately significant correlation was found between the RV mechanical delay before CRT vs. the post-CRT values ( $r = 0.4$ ;  $p$  value = 0.01).

**Conclusion:** Early after CRT, the RV mechanical delay can improve and the significant improvement is seen in patients with baseline RV mechanical dyssynchrony.

*J Teh Univ Heart Ctr 2011;6(1):24-30*

**This paper should be cited as:** Esmailzadeh M, Poorzand H, Maleki M, Sadeghpour A, Parsaee M. Evaluation of longitudinal right ventricular mechanical dyssynchrony before and early after cardiac resynchronization therapy: a strain imaging study. *J Teh Univ Heart Ctr 2011;6(1):24-30.*

\*Corresponding Author: Majid Maleki, Professor of Cardiology, Echocardiography Research Center, Iran Cardiovascular Research Institute, Shaheed Rajaei Cardiovascular, Medical and Research Center, Tehran, Iran. 1996911151. Tel: +98 21 23921. Fax: +98 21 22055594. E-mail: majid33@yahoo.com.



**Keywords:** Heart ventricles • Cardiac resynchronization therapy • Heart-assist devices • Ventricular function, right

## Introduction

Echocardiography has an important role in the management of patients with systolic heart failure undergoing cardiac resynchronization therapy (CRT).<sup>1</sup> An echocardiographic evaluation of abnormalities in mechanical activation (dyssynchrony) improves case selection for CRT. Clinical trials have demonstrated the beneficial effects of CRT on the left ventricular (LV) systolic dysfunction and LV reverse remodeling, both of which have a great impact in reducing morbidity. Still, precious little is known about the effect of CRT on the right ventricle (RV) function, which by itself can have a key role in risk stratification in heart failure patients.<sup>2,3</sup>

The effect of CRT on the severity of the RV dyssynchrony and the relation between the RV dyssynchrony and CRT response are not fully known. Furthermore, a cut-off value validated for the RV dyssynchrony is yet to be introduced. The aim of this study was to evaluate the prevalence and severity of the RV dyssynchrony before and early after CRT via deformation indexes (strain imaging).

## Methods

The study population consisted of 36 patients with severe LV systolic heart failure, candidate for cardiac resynchronization device implantation. The inclusion criteria were based on the approved recommendations for CRT and comprised LV ejection fraction (LVEF)  $\leq 35\%$ , severe heart failure (New York Heart Association [NYHA] functional class III or IV), and a QRS duration  $\geq 120$  msec.<sup>4</sup>

The patient population was divided into two groups according to the presence of the RV mechanical dyssynchrony. In addition, a group of 20 normal subjects (60% men, mean  $\pm$  SD age of  $55.2 \pm 17.3$  years), who were age and gender matched to the patients with systolic heart failure, were also included.

Echocardiographic data acquisition was performed before CRT implantation and during the subsequent days, early after the procedure (4-7 days). All the patients underwent color-coded tissue Doppler study using a Vivid 7 digital ultrasound scanner (GE, Milwaukee, Wisconsin, USA). Color-coded tissue Doppler cine loops from three consecutive beats at the phase with the optimal image quality were recorded. The images were obtained from the apical views using a 3.5-MHz transducer at a depth of  $16 \pm 4$  cm. Gain was minimized to allow clear tissue signal with minimal background

noise. Frame rate was more than 120/sec. The timing of the aortic valve opening and closure was determined from the pulsed-wave Doppler of the LV outflow tract and was superimposed on the LV segments-related tissue velocity and strain waveforms. For the RV waveforms, the Doppler profile of the pulmonary artery was employed in the same manner. The region of interest was defined as  $5 \times 6$  mm, located in the basal and mid segments of the RV free wall and interventricular septum (four-chamber view), so as for the time interval from the onset of the Q wave on the surface ECG to the time-to-peak systolic velocity in tissue Doppler imaging and the time-to-peak systolic strain in strain imaging to be assessed.

The RV velocity and strain were not measured at the apical RV free wall due to difficulties with maintaining parallel alignment with the ultrasound beam at this sample volume location. In a similar manner, for the LV longitudinal dyssynchrony assessment, the interventricular septum in conjunction with the lateral, inferior, anterior, anteroseptal, and posterior regions was evaluated at the base and mid segments.

All the measurements were obtained in three representative cardiac cycles and averaged and corrected for the heart rate (corrected interval = measured interval/RR interval).<sup>1,2</sup>

The RV mechanical delay was determined as the difference in the time-to-peak values from the interventricular septum to the RV free wall.

The RV longitudinal dyssynchrony in strain imaging was defined as the difference in the time-to-peak strain between the RV free wall and the interventricular septum (diff-TTP $\epsilon$ RVS) was determined as a measurement more than two standard deviations above the means in the control group. The study population was divided into two groups according to the presence or absence of the RV mechanical dyssynchrony before CRT implantation: Group 1, patients with RV dyssynchrony, and Group 2, patients without RV dyssynchrony.

The tricuspid annular planar systolic excursion (TAPSE), tricuspid annulus peak S velocity in the Doppler tissue study, and RV fractional area change (RVFAC) were calculated as the RV function markers. The RV end-diastolic area (RVEDA) and RV end-systolic area (RVESA) were also measured by tracing the RV endocardial border on the apical four-chamber view, and the RVFAC was detected as a measure of the RV systolic function using the following equation:  $RVFAC = (RVEDA - RVESA)/RVEDA \times 100$ .<sup>6</sup>

The RV Dysfunction was defined as TAPSE  $< 20$  mm and/or a tricuspid annulus peak S velocity in the Doppler tissue

study of < 11.5 cm/sec.<sup>5</sup> The RV enlargement was defined as a mid RV size of > 3.3 cm.<sup>6</sup>

The mechanical dyssynchrony index (the Yu index, Ts-SD by TSI) was derived from calculating the standard deviation (SD) of the time-to-peak systolic velocity of twelve LV segments (in three-apical views). A cut-off value of  $\geq 33$  msec was used to signify mechanical dyssynchrony.<sup>7</sup>

The baseline evaluations having been obtained, the patients underwent implantation of a cardiac resynchronization device (InSync model 8040, Medtronic and Frondier II model 5596 St. Jude) along with three pacing leads: a standard right atrium (RA) lead, a specialized LV lead, and a standard RV lead. The three leads were inserted transvenously via the subclavian route (except for one patient). The atrial lead was positioned in the high right atrium. The LV pacing lead was placed in a tributary of the coronary sinus. The tip of the RV lead was positioned at the apical region in all the patients. Adequate pacing and sensing properties of all the leads were tested.

Early CRT response was defined as clinical improvement in NYHA class, which was measured by the use of a 6-minute walk test.

Four to seven days after CRT, all the patients underwent a repeated echocardiographic study.

The statistical analyses were conducted using SPSS (Statistical Package for Social Sciences version 15.0, SPSS Inc. Chicago, IL) software. The qualitative variables were expressed using percentages, while the quantitative data were defined using mean, standard deviation, and/or confidence intervals.

The ANOVA and paired-sample T-test and bivariate correlation tests were utilized for inferential statistics. Normal distribution of the quantitative data was checked using the Kolmogorov-Smirnov test. The level of significance was set at 0.05.

## Results

In total, 36 systolic heart failure patients with a mean  $\pm$  SD age of  $59.2 \pm 12.0$  years (range: 25-80 years) were included. Twenty-one (58.3 %) patients were male and 15 (41.7%) were female.

The etiology of heart failure was ischemic in 17 (47.2%)

patients, seven of whom had a history of coronary artery bypass surgery (19.4% of total 36 cases). The etiology in 19 patients was non-ischemic, 18 patients had dilated cardiomyopathy, and one case had LV non-compaction.

The LV pacing lead was placed in a tributary of the coronary sinus in 35 patients with the exception of one patient, in whom the epicardial lead was implanted due to technical difficulties (Table 1).

Twenty-eight (77.8%) patients had RV dysfunction at baseline (based on the TAPSE and/or S' value).

Table 1. Location of left ventricular related lead in each group of patient study

Location of LV lead	patients with RVMD (n=16)	patients without RVMD (n=20)
LCV	8 (50)	10 (50)
ALCV	1 (6.3)	5 (25)
PLCV	5 (31.3)	4 (20)
RVOT branch of CS	1 (6.3)	1 (5)
Epicardial	1 (6.3)	none

Data are presented as n (%)

LV, Left ventricle; RVMD, Right ventricle mechanical dyssynchrony; LCV, Left cardinal vein; ALCV, Anterolateral cardinal vein; PLCV, Posterolateral cardinal vein; RVOT, Right ventricular outflow tract; CS, Coronary sinus

The major baseline electrocardiographic abnormality was left bundle branch block (LBBB) in 19 (52.8%) patients and right bundle branch block (RBBB) in 2 (5.6%). The other ECG abnormalities were not specific, including non-specific ST-T changes or intraventricular conduction abnormalities, which did not fulfill the LBBB- or RBBB-related criteria. The QRS duration was  $143.7 \pm 16.9$  msec (range = 120 -180 msec). A 6-minute walk test was done before and early after CRT. The RV longitudinal dyssynchrony by strain imaging was calculated 41.5 msec [ $2 \times ([11.0] + 19.5 = 41.5)$  (Table 4)]. Accordingly, a mechanical delay of more than 41.5 msec was assumed as the RV mechanical dyssynchrony in this study. A significant improvement in the functional capacity was seen in 32 patients ( $227 \pm 40$  m vs.  $330 \pm 50$  m; p value < 0.05). In the other 4 (11.11%) patients, the walking distance decreased relative to the pre-CRT state and they were thus assumed to be non-responders to CRT. The cut-off value for the RV mechanical dyssynchrony was 41.5msec. Sixteen (44.4%) patients were identified as Group 1 based on this value (Table 2). No significant difference was noted with respect to the LV dyssynchrony, RV dysfunction and enlargement, etiology

Table 2. Characteristic of patients with (Group 1) and without (Group 2) RV mechanical dyssynchrony\*

	Number	RV Enlargement	RV dysfunction	LV Dyssynchrony Pre / Post	CRT Responder	Ischemic / Nonischemic
Group 1	16	9 (56.4)	13 (81)	5 (31) / 3 (18)	14	7 (48.3) / 9 (56.3)
Group 2	20	11 (55)	15 (75)	11 (55) / 7 (35)	18	10 (50) / 10 (50)

\*Data are presented as n (%)

RV, Right ventricle; LV Dyssynchrony; Pre / Post, Number and percentage of the patients with concomitant left ventricular dyssynchrony in each group, before and after CRT, CRT, Cardiac resynchronization therapy



Table 3. Baseline characteristic of study groups

	Control group	Patients with RVMD	Patients without RVMD	P value
Age (y)	55.2±17.3	61.6±10.2	57.2±13.1	0.13*
RR interval (msec)	871.2±140.2	795.0±96.2	814.6±107.5	0.14*
QRS width (msec)	NA	143.1±19.5	144.2±14.8	0.81†
LVEDV (ml)	69.5±8.0	222.1±80.2	223.9±81.4	<0.01‡
LVESV(ml)	29.8±4.0	180.0±85.3	171.3±67.9	<0.01‡
LVEF (%)	61.8±7.0	18.8±5.5	19±5.6.0	<0.01‡
Ts-SD (msec)	NA	32.8±14.2	41.8±17.7	0.12†

Data are presented as mean ± SD

RVMD, Right ventricle mechanical dyssynchrony; LVEDV, Left ventricular end diastolic volume; LVESV, Left ventricular end diastolic volume; LVEF, Left ventricular ejection fraction; Ts-SD, Standard deviation of the time-to-peak systolic velocity in the ejection phase (12-sites); NA, Not available

\*According to the ANOVA test

†According to the independent T test

‡Control group was different from patient groups according to the Tukey HSD test

Table 4. Baseline values of time to peak systolic tissue velocity, strain and mechanical delay in the study groups

	Control Group	Patients with RVMD	Patients without RVMD	P value
TTPsRV (cm/s)	175.0±38.3	188.1±30.1	184±19.3	0.42*
TTPsSep (cm/s)	169.0±48.4	207.8±50.3	203.5±32.3	0.01†
TTPeRV (%)	348.5±28.7	328.1±50.7	320.5±31.0	0.05*
TTPeSep (%)	329±26.3	301.9±55.8	319.5±32.9	0.12*
diffTTPsSep-RV (cm/s)	17.0±10.3	28.4±25.5	25.5±14.3	0.11*
diffTTPeSep-RV (%)	19.5±11.0	68.8±20.9	14.0±10.4	<0.01‡

Data are presented as mean ± SD

RVMD, Right ventricle mechanical dyssynchrony; TTPsRV, Time to peak systolic tissue velocity of right ventricular free wall; TTPsSep, Time to peak systolic tissue velocity of septum; TTPeRV, Time to peak right ventricle systolic strain; TTPeSep, Time to peak systolic strain of septum; diffTTPsSep-RV, The difference in time to peak systolic tissue velocity between septum and right ventricular free wall; diffTTPeSep-RV, The difference in time to peak systolic strain velocity between septum and right ventricular free wall

\*According to the ANOVA test

†Control group was different from the patient groups according to the Turkey HSD test

‡Group 1 was different from the other groups

for heart failure, and CRT response; and nor was there any significant difference in terms of the QRS width (p value = 0.8) and baseline LV dyssynchrony (p value = 0.1) between the groups (Table 3). Table 4 summarizes the time-to-peak and mechanical delay values at baseline in the cases.

There was a statistically significant decrease in the RV dyssynchrony after CRT in both basal and mid segments on the basis of the corrected time-to-peak systolic velocity (p value = 0.021, 95% confidence interval (CI): 0.05-0.53; p value = 0.035, 95% CI: 0.02-0.53, respectively) and corrected time-to-peak systolic strain (p value = 0.016, 95% CI: 0.10-0.91; p value = 0.038, 95% CI: 0.2-0.83, respectively) (Table 4). The interventricular mechanical delay significantly decreased after CRT in the basal and mid segments only according to the corrected time-to-peak systolic strain (p value = 0.012, 95% CI: 0.21-1.60; p value = 0.007, 95% CI: 0.26-1.60, respectively). The intra LV mechanical delay did not show any significant change after CRT according to the time-to-peak systolic velocity and strain values (p value > 0.05). There was a moderately significant decrease in the time-to-peak systolic strain of the RV free wall after CRT implantation in comparison with the pre-CRT values (r = 0.4; p value = 0.014). The differences

in the baseline mid RV size, RVFAC, and TAPSE were not statistically important (p value > 0.05) in the patients and did not significantly change after CRT (Table 5). The LVEF significantly increased after CRT in Group 2 (p value = 0.01) but not in the patients with baseline RV dyssynchrony (p value = 0.4). The Yu index decreased in both groups after CRT (p value = 0.06 in Group 1 vs. p value = 0.04). There was a significant invert correlation between the baseline RV dyssynchrony and LV dyssynchrony (r = -0.51; p value = 0.004). There was no significant difference between the time-to-peak values (RV and septum) at baseline, and they did not significantly change after CRT (Table 6). There was a significant decrease in the RV dyssynchrony after CRT in Group 1 (p value < 0.001) (Table 7).

In Group 1 patients, a moderate correlation was noted between the delay in time-to-peak RV strain but not in the time-to-peak systolic velocity and RV dysfunction (r = 0.52; p value = 0.038).

The peak systolic RV strain improved in both groups after CRT, albeit insignificantly (group 1: p value = 0.3 in the basal segment; p value = 0.8 in the mid segment; Group 2: p value = 0.8 in the basal segment; and p value = 0.8 in the mid segment). A significant correlation was found between

Table 5. Comparison of measurements before and after CRT between the study groups

	Patients with RVMD			Patients without RVMD			P value (Post CRT)
	Pre CRT	Post CRT	P value	Pre CRT	Post CRT	P value	
RR interval (msec)	795±96.2	790±119.5	0.82	814.6±107.5	788.3±97.0	0.31	0.72
RV size (mm)	31.1±4.9	30.9±3.7	0.94	30.5±2.3	31±3.4	0.73	0.61
RVFAC (%)	0.33±0.1	0.31±0.8	0.45	0.31±0.0	0.28±0.1	0.46	0.51
TAPSE (mm)	16.3±4.2	16.6±3.1	0.81	17.3±3.9	17.6±4.1	0.72	0.61
LVEDV (ml)	222.1±80.2	195±71.0	0.09	224±81.4	204.3±83.6	0.09	0.62
LVESV (ml)	180±85.3	152.5±73.0	0.22	171.3±67.9	157±77.0	0.11	0.82
LVEF (%)	18.8±5.5	24.2±19.0	0.42	19±5.6	22.7±8.0	0.01	0.83
Ts-SD (msec)	32.8±14.2	27±9.0	0.06	41.8±17.7	29.4±14.1	0.04	0.61

Data are presented as mean ± SD

RVMD, Right ventricle mechanical dyssynchrony; CRT, Cardiac resynchronization therapy; RV, Right ventricle; RVFAC, Right ventricular fractional area change; TAPSE, Tricuspid annulus plane systolic excursion; LVEDV, Left ventricular end diastolic volume; LVESV, Left ventricular end systolic volume; LVEF, Left ventricular ejection fraction; Ts-SD, standard deviation of the time-to-peak systolic velocity in the ejection phase (12-sites)

Table 6. Measurements before and after CRT and comparison between the groups; Time to peak values

	Patients with RVMD			Patients without RVMD			P value (Post CRT)
	Pre CRT	Post CRT	P value	Pre CRT	Post CRT	P value	
TTPsRV(cm/s)	188±30	191±31	0.62	184±19	199±42	0.13	0.83
TTPsSep (cm/s)	207±50	198±36	0.44	203±32	200±45	0.64	0.82
TTPeRV (%)	328±50	314±46	0.35	320±31	326±40	0.55	0.74
TTPeSep (%)	301±55	316±40	0.32	319±32	320±26	0.92	0.63

Data are presented as mean ± SD

RVMD, Right ventricle mechanical dyssynchrony; TTPsRV, Time to peak systolic tissue velocity of right ventricle; TTPsSep, Time to peak systolic tissue velocity of septum; TTPeRV, Time to peak right ventricle systolic strain; TTPeSep, Time to peak systolic strain of septum

Table 7. Comparison of peak systolic strain and the difference in time to peak systolic velocity and strain between septum and right ventricular free wall before and after CRT between the study groups

	Patients with RVMD			Patients without RVMD			P value (Post CRT)
	Pre CRT	Post CRT	P value	Pre CRT	Post CRT	P value	
diffTTPsSep-RV (cm/s)	28.4±25.5	20.6±22.6	0.22	25.5±14.3	16.5±15.0	<0.01	0.53
diffTTPeSep-RV (%)	68.8±21.0	30±28.9	<0.01	14±10.0	19±16.5	0.18	0.05
Peak Systolic strain (RVB) (%)	12.8±1.2	16.8±5.6	0.15	17.5±6.6	18.2±6.8	0.33	0.64
Peak Systolic strain (RVM) (%)	18.6±9.4	21.2±5.8	0.23	23.1±7.1	24.8±4.6	0.84	0.22

Data are presented as mean ± SD

RVMD, Right ventricle mechanical dyssynchrony; diffTTPsSep-RV, The difference in time to peak systolic tissue velocity between septum and right ventricular free wall; diffTTPeSep-RV, The difference in time to peak systolic strain between septum and right ventricular free wall; RVB, Right ventricular basal segment; RVM, Right ventricular middle segment

the peak systolic strain and RV dyssynchrony and ( $r = -0.5$ ;  $p$  value  $< 0.05$ ) but not with the time-to-peak RV systolic strain ( $r = -0.17$ ;  $p$  value = 0.3).

There was no correlation between the RV dyssynchrony and RVFAC ( $r = -0.13$ ;  $p$  value = 0.4) or between the RVFAC change and peak systolic strain ( $p$  value = 0.13). The location of the LV lead (LCV, ALCV, and PLCV) had no effect on the RV dyssynchrony (ANOVA test;  $p$  value = 0.59). There was no correlation between the QRS width and severity ( $p$  value = 0.8) and morphology ( $r = -0.18$ ;  $p$  value = 0.2) and RV dyssynchrony. Missing data precluded an evaluation of the correlation between the RV dyssynchrony and pulmonary pressure.

## Discussion

Assessment of the RV function remains difficult mainly because of its complex geometry and thin myocardial walls.<sup>8</sup> On the other hand, assessment of the RV function is important as the RV dysfunction is associated with worse clinical outcomes.<sup>2, 3, 9</sup> In several studies, longitudinal systolic strain and strain rate have been validated as reliable techniques for the evaluation of the RV function under various loading conditions.<sup>10, 11</sup> In an RV strain study on 70 subjects, who underwent right-heart catheterization, the RV strain correlated significantly with the invasive measures of the RV performance in patients with pulmonary hypertension and normal LV systolic function. However,



there was no correlation between the RV strain and pulmonary hemodynamics in patients with left-sided heart failure.<sup>12</sup>

Tissue Doppler imaging has been useful in the assessment of patients with pulmonary hypertension, showing a smaller peak longitudinal RV free wall strain with delayed time-to-peak values.<sup>13</sup> Further studies are needed to define the role for myocardial strain imaging in these patients.

The regional temporal delay noted between the basal segments of the RV free wall and interventricular septum may not reflect changes that occur elsewhere along the RV free wall. Even though regional changes in dyssynchrony might in fact not reflect changes in terms of global mechanics, the finding of basal dyssynchrony in itself is quite valid and useful.<sup>13, 14</sup> In our study in patients with RV dyssynchrony, mechanical activation in the RV free wall was more delayed (though not statistically significant), and both RV dyssynchrony and time-to-peak systolic strain decreased early after CRT with no significant change in the RV function and size.

The RV dyssynchrony has not been studied extensively, and a definite cut-off value is yet to be validated. In a study on young patients (mean age = 21 years) after atrial switch operation, the cut-off value for the RV dyssynchrony was 49 msec.<sup>15</sup> In another study on the arrhythmogenic RV dysplasia, a value more than 56 msec was obtained as the RV dyssynchrony.<sup>16</sup> It is deserving of note that the age of the control groups in the said studies did not match that of our cases. In our study, the method for obtaining this value was the same as those two studies, but we obtained 41.5 msec in the strain analysis of our age-matched control group.

We did not find a significant relation between the RVFAC and RV dyssynchrony early after CRT ( $r = -0.13$ ;  $p$  value = 0.4). This was in contrast to some other studies. In the RV dyssynchrony in the ARVD, a modest but significant correlation was found between the RVFAC and RV dyssynchrony ( $r = -0.38$ ,  $p$  value = 0.001) and between the RVEDA and RV dyssynchrony ( $r = -0.38$ ,  $p$  value = 0.001).<sup>16</sup> In another study on patients with varying degrees of pulmonary artery pressure, this significant relation was reported ( $r = -0.89$ ).<sup>11</sup>

We did not observe a significant change in the RV size early after CRT. In a study on the effect of CRT on the RV size, a significant reverse LV and RV remodeling was seen after six months ( $p$  value < 0.0001) and the RV reverse remodeling was only observed in patients with remarkable LV dyssynchrony at baseline; additionally, no significant RV reverse remodeling was noted immediately (one day) after CRT.<sup>17</sup>

We found a significant relation between the RV dyssynchrony and peak systolic RV strain ( $r = -0.5$ ;  $p$  value < 0.05). The peak systolic strain and TAPSE improved in both groups early after CRT, but the increase was insignificant. In a study on the RV function three months after CRT, no significant change in the TAPSE was found but there was

a significant increase in the peak systolic strain ( $p$  value = 0.001). These results were only detected in patients with septal RV lead position and not the apical one.<sup>2</sup> This is comparable to our study in that all the patients had an RV apical lead. A substantial proportion of normal subjects have tissue velocity-derived dyssynchrony indexes higher than the cut-off value proposed for predicting the beneficial effect of CRT. The strain-derived timing index appears to be more specific for dyssynchrony in patients with systolic dysfunction.<sup>18</sup> In our study, we preferentially selected strain modality for the evaluation of dyssynchrony. We preferred the longitudinal strain study over radial imaging because in the RV, the contraction occurs predominantly in the longitudinal plane.<sup>19</sup>

The RV dyssynchrony has been proved to be associated with disease severity as it is correlated with pulmonary hypertension severity, NYHA class, and number of hospitalization.<sup>20</sup>

The existing literature has established the effect of CRT on the LV dyssynchrony, but there is a dearth of data on the effect of CRT on the forgotten ventricle. We found a significant improvement in the RV dyssynchrony after CRT, which is more prominent in patients with baseline RV dyssynchrony. On the other hand, a significant relation was detected between the RV dyssynchrony and systolic strain, which is validated as a marker of the RV function. It seems that CRT can enhance the RV hemodynamic and thus improve the prognosis in systolic heart failure patients.

First and foremost amongst the limitations of the present study is the use of the longitudinal strain imaging, which is an angle-dependent method. Another limitation is the lack of a gold standard for assessing the baseline RV function. Although many studies have employed the TAPSE, RV Tei-index, and Doppler myocardial imaging to assess the RV function, more data are needed, particularly in correlating the echocardiographic data with the invasive measures of the RV function. Finally, we evaluated only the early effect of resynchronization on the RV.

## Conclusion

CRT can significantly improve the RV mechanical delay as early as a few days after the procedure and this improvement is remarkably seen in patients with baseline RV dyssynchrony. Our results showed that CRT improved the RV function (though insignificantly). Moreover, a significant correlation was found between the peak systolic strain and RV dyssynchrony.

## Acknowledgement

This study was supported by Iran Cardiovascular Research

Institute. We wish to thank all the nursing staff involved in the echocardiography and electrophysiology and pacing departments at Shaheed Rajaei Cardiovascular, Medical and Research Center.

## References

1. Gorcsan J, Abraham T, Agler DA, Bax JJ, Derumeaux G, Grimm RA, Martin R, Steinberg JS, Sutton MJ, Yu CM. Echocardiography for cardiac resynchronization therapy: recommendation for performance and reporting- a report from the American Society of Echocardiography Dyssynchrony Writing Group endorsed by the Heart Rhythm Society. *J Am Soc Echocardiogr* 2008;21:191-210.
2. Donal E, Thibault H, Bergerot C, Leroux PY, Cannesson M, Thivolet S, Barthelet M, Rivard L, Chevalier P, Ovize M, Daubert JC, Leclercq C, Mabo P, Derumeaux G. Right ventricular pump function after cardiac resynchronization therapy: a strain imaging study. *Arch Cardiovasc Dis* 2008;101:475-484.
3. Di Salvo TG, Mathier M, Semigran MJ, Dec GW. Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. *J Am Coll Cardiol* 1995;25:1143-1153.
4. Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, Tavazzi L, Smiseth OA. Diagnosis and treatment of chronic heart disease. Guidelines of the European Society of Cardiology. Revision 2005. *Kardiol Pol* 2005;63:509-543.
5. Bleeker GB, Steendijk P, Holman ER, Yu CM, Breithardt OA, Kaandorp TA, Schalij MJ, van der Wall EE, Nihoyannopoulos P, Bax JJ. Assessing right ventricular function: the role of echocardiography and complementary technologies. *Heart* 2006;92:i19-26.
6. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, Developed in Conjunction with the European Association of Echocardiography, a Branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440-1463.
7. Yu CM, Fung JW, Zhang Q, Chan CK, Chan YS, Lin H, Kum LC, Kong SL, Zhang Y, Sanderson JE. Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy. *Circulation* 2004;110:66-73.
8. Tulevski II, Romkes H, Dodge-Khatami A, van der Wall EE, Groenink M, van Veldhuisen DJ, Mulder BJ. Quantitative assessment of the pressure and volume overloaded right ventricle: imaging is a real challenge. *Int J Cardiovasc Imaging* 2002;18:41-51.
9. Chin KM, Kim NH, Rubin LJ. The right ventricle in pulmonary hypertension. *Coron Artery Dis* 2005;16:13-18.
10. Eyskens B, Ganame J, Claus P, Boshoff D, Gewillig M, Mertens L. Ultrasonic strain rate and strain imaging of the right ventricle in children before and after percutaneous closure of an atrial septal defect. *Am Soc Echocardiogr* 2006;19:994-1000.
11. López-Candales A, Dohi K, Bazaz R, Edelman K. Relation of right ventricular free wall mechanical delay to right ventricular dysfunction as determined by tissue Doppler imaging. *Am J Cardiol* 2005;96:602-606.
12. Rajagopalan N, Simon MA, Shah H, Mathier MA, López-Candales A. Utility of right ventricular tissue Doppler imaging: correlation with right heart catheterization. *Echocardiography* 2008;25:706-711.
13. López-Candales A, Rajagopalan N, Dohi K, Gulyasy B, Edelman K, Bazaz R. Abnormal right ventricular myocardial strain generation in mild pulmonary hypertension. *Echocardiography* 2007;24:615-622.
14. Chow PC, Liang XC, Lam W, Cheung E, Wong KT, Cheung YF. Mechanical right ventricular dyssynchrony. *Am J Cardiol* 2008;15:874-881.
15. Chow PC, Liang XC, Lam WW, Cheung EW, Wong KT, Cheung YF. Mechanical right ventricular dyssynchrony in patients with atrial switch operation for transposition of the great arteries. *Am J Cardiol* 2008;101:874-881.
16. Tops LF, Prakasa K, Tandri H, Dalal D, Jain R, Dimaano VL, Dombroski D, James C, Tichnell C, Daly A, Marcus F, Schalij MJ, Bax JJ, Bluemke D, Calkins H, Abraham TP. Prevalence and pathophysiologic attributes of ventricular dyssynchrony in arrhythmogenic right ventricular dysplasia/cardiomyopathy. *J Am Coll Cardiol* 2009;54:445-451.
17. Bleeker GB, Schalij MJ, Nihoyannopoulos P, Steendijk P, Molhoek SG, van Erven L, Bootsma M, Holman ER, van der Wall EE, Bax JJ. Left ventricular dyssynchrony predicts right ventricular remodeling after cardiac resynchronization therapy. *J Am Coll Cardiol* 2005;46:2264-2269.
18. Conca C, Faletta FF, Miyazaki C, Oh J, Mantovani A, Klersy C, Sorgente A, Pedrazzini GB, Pasotti E, Moccetti T, Auricchio A. Echocardiographic parameters of mechanical synchrony in healthy individuals. *Am J Cardiol* 2009;103:136-142.
19. Rushmer RF, Crystal DK, Wagner C. The functional anatomy of right ventricular contraction. *Circ Res* 1953:162-170.
20. López-Candales A, Dohi K, Rajagopalan N, Suffoletto M, Murali S, Gorcsan J, Edelman K. Right ventricular dyssynchrony in patients with pulmonary hypertension is associated with disease severity and functional class. *Cardiovasc Ultrasound* 2005;3:23.