Original Research

Cardiac Resynchronization Therapy Decreases the Mitral Coaptation Point Displacement in Heart Failure Patients

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Background: In patients with left ventricular (LV) dysfunction the mitral leaflet coaptation point (CPMA) is displaced towards the LV apex. The aim of our study was to estimate the value of CPMA measurement as a simple index regarding the acute effects of cardiac resynchronization therapy (CRT), which is coming to be an established method of treatment for congestive heart failure (CHF).

Methods: We studied 20 patients with CHF (NYHA III-IV) and LV ejection fraction (LVEF) 22 ± 4%. All patients received CRT and an echocardiogram was performed within 24-48 hours. The echocardiographic indices LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD), LVEF, mitral annulus diameter (MAD), and the degree of intraventricular desynchronization, were measured at CRT off and CRT on. The CPMA, the distance between the coaptation point of the mitral leaflets and the mitral annulus, was measured from the apical 4-chamber view in end-systole at both CRT on and CRT off.

Results: CRT improved both the contractility and dimensional indices in CHF patients. CPMA decreased from 11.3 ± 2 mm at CRT off to 9.1 ± 1.8 mm after CRT on ($p<0.001$) and MAD from 38.9 ± 3.9 mm at CRT off to 37.5 ± 3.7 mm at CRT on ($p<0.002$). LVEF improved from 24.5 ± 5.7% at CRT off to 29.5 ± 5.1% at CRT on ($p<0.001$). There was an improvement in LV synchronization from 88 ± 7 ms at CRT off to 48 ± 3 ms at CRT on ($p<0.001$). CPMA was correlated with MAD ($r=0.52$, $p<0.05$ and $r=0.59$, $p<0.05$ at CRT off and CRT on, respectively). Moreover, the absolute change in CPMA was correlated with LVESD ($r=0.68$) and LVEDD ($r=0.65$), both $p<0.05$, with the time difference of the basal segments of the septal and lateral wall at CRT on ($r=0.68$, $p<0.01$), and inversely correlated with LVEF ($r=-0.55$, $p<0.05$).

Conclusion: In patients with severe LV systolic dysfunction and dilatation CRT was associated with an improvement in both CPMA and MAD.

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Cardiac resynchronization therapy (CRT) has emerged as a new treatment for a subgroup of patients with heart failure and an asynchronous contraction pattern.[1,2] The evaluation of left ventricular desynchronization in heart failure patients is based upon a consideration of the resting time delays of longitudinal peak systolic velocities in the left ventricle in specific myocardial wall regions and a subsequent analysis of relative differences.[1,2] Thus, it has been demonstrated that CRT improves hemodynamic function, heart failure symptoms, exercise capacity and quality of life and that it reduces morbidity and mortality.[3] A number of studies have shown that function improves without an increase in oxygen consumption, indicating increased efficiency.[4-6]

Under normal conditions, the coaptation point of the mitral valve leaflets at systole practically reaches the level of the

mitral annulus.[7,8] This point is displaced apically under abnormal conditions, such as morphologic abnormalities of the leaflets or dilatation of the left ventricle (LV); as a result the distance between the coaptation point of the leaflets and the level of the mitral annulus (CPMA) is increased.[7-9] We have shown that this is the result of the failure of one or both of the leaflets to reach the level of the atrioventricular ring at the point of its peak systolic movement and can be attributed to poor LV systolic function.[7,9]

Incomplete mitral leaflet closure has thus been associated with elevated left ventricular filling pressure[10] and is related to both the size and function of the LV.[9] This distance can be used as an index reflecting LV dysfunction.[9] It has not yet been clarified whether it can reflect changes of ventricular geometry and function induced by CRT. The underlying mechanisms of biventricular pacing effects remain under investigation. The purpose of this study was to investigate the acute effects of biventricular pacing on the mitral valve coaptation point as an index of LV function in patients with heart failure.

Methods

Patients

The study population consisted of 20 consecutive patients, 19 men, mean age 56 ± 25 years (range 21-82 years), who were under evaluation and treatment for symptomatic heart failure. Patients in New York Heart Association (NYHA) functional class III or IV and with LV ejection fraction (LVEF) <35%, LV end diastolic diameter (LVEDD) >55 mm, an interventricular conduction delay with a QRS duration >120 ms according to current indication, and in sinus rhythm, were enrolled in the study.

In 9 patients (45%) the cause of heart failure was coronary artery disease, defined as >70% narrowing of at least one major coronary artery, diagnosed by coronary arteriography. In 11 patients (55%) the diagnosis of dilated cardiomyopathy was established by excluding significant coronary disease (using coronary angiography) or valvular disease (using standard echocardiography).

At the time of enrolment, all patients were in a clinically stable condition on standard heart failure medication. The doses of the background medication had remained constant for the last one month. Medication was kept constant during the study. Patients with atrial fibrillation and significant primary valvular heart disease were excluded.

Methods

All patients underwent a baseline echocardiographic examination using a GE Vivid 7 system (2.5 MHz transducer) within 24-48 hours after implantation of the biventricular pacemaker. At frame rates close to 100 frames per second c-TVI data were recorded in the apical 4-chamber view. The offline evaluation of the data was performed using Echo-PAC-PC, version 3.0x, GE Vingmed Ultrasound. Heart rate during the examination was measured simultaneously by electrocardiographic recording. The following measurements were performed sequentially, in the same session, a) during simultaneous biventricular pacing (CRT on), and b) shortly after reprogramming the pulse generator to AAI mode at the same basic rate (CRT off). Both a and b refer to 10-minute periods of CRT on and off. AV delay period was not altered. The order of the studies was randomized and the echocardiographer was blinded to the mode of pacing.

CPMA was measured from the apical 4-chamber view in end-systole and was evaluated at both CRT on and CRT off (Figures 1A, 1B). The degree of mitral regurgitation was not specifically studied. The echocardiographic indices LV end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD), as well as mitral annulus diameter (MAD), were also measured at CRT off and at CRT on, according to the recommendations of the American Society of Echocardiography. The left ventricular ejection fraction (LVEF) was estimated by Simpson's rule under both conditions.[11] Additionally, the systolic and diastolic velocities at the level of the mitral annulus in the septal and lateral wall, were measured by tissue Doppler in the apical 4-chamber view. The delay between the peak systolic velocities of the septum and lateral wall was also evaluated at both CRT off and CRT on, indicating the degree of intraventricular desynchronization. The systolic and diastolic velocity measurements at the level of the mitral annulus were repeated offline by the same observer and by a second echocardiographer in order to calculate intra- and inter-observer variability.

Statistics

All values were expressed as mean ± SD and a p-value <0.05 was considered statistically significant. Differences between CRT on and CRT off were tested for significance using the paired samples t-test. Parametric and non-parametric tests (Pearson and Spearman correlations) were applied to correlate CPMA changes produced by cardiac resynchronization thera-

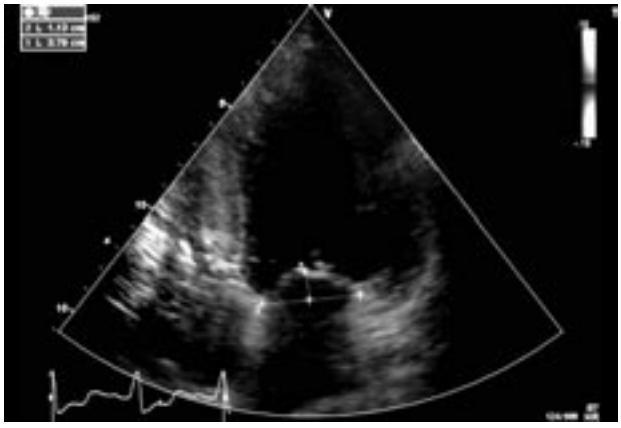

Figure 1A. Two-dimensional 4-chamber view, showing the mitral annulus plane and its distance from the mitral leaflets coaptation point (CPMA) in a patient with CRT off (value: 11.3 mm).

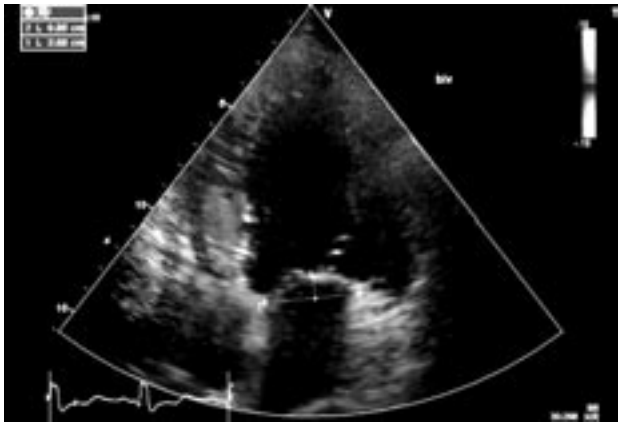

Figure 1B. Two-dimensional 4-chamber view, showing the mitral annulus plane and its distance from the mitral leaflets coaptation point (CPMA) in the same patient with CRT on (value: 8.6 mm).

py with functional and geometric parameters. Intra-observer agreement was calculated by Spearman correlation.

Results

In 9 patients the sequence of cardiac resynchronization was on/off and in the remainder it was the opposite.

Intra-observer and inter-observer variability

We observed good intra-observer agreement (correlation between two measurements by same observer) for the systolic and diastolic velocity measurements at the level of the mitral annulus at CRT off (r=0.90) and CRT on (r=0.93) (both p<0.001). The inter-observer agreement was 90%.

Effect of CRT on LV function and mitral valve indices

The echocardiographic variables of all the patients and the results of CRT (CRT on and off) are shown in Table 1. During CRT on the LVEF improved significantly, while CPMA and MAD both decreased. The tissue Doppler systolic and diastolic velocities in the septal and lateral wall at the level of mitral annulus also improved.

Synchronization measurements

There was an improvement in LV synchronization (time difference) from 88 ± 7 ms at CRT off to 48 ± 3 ms at CRT on (p<0.001).

Correlations

As expected,[9] CPMA was correlated with MAD (r=0.52,

Table 1. Changes in left ventricular and mitral valve indices in relation to cardiac resynchronization therapy.

	CRT off	CRT on	p value
LVEF (%)	24.5 ± 5.7	29.5 ± 5.1	<0.001
CPMA (mm)	11.3 ± 2	9.1 ± 1.8	<0.001
MAD (mm)	38.9 ± 3.9	37.5 ± 3.7	<0.001
TDIF (ms)	88 ± 7	48 ± 3	<0.001
SepSw (cm/s)	3.2 ± 1	4.5 ± 1.2	<0.001
SepEa (cm/s)	3 ± 1.4	3.7 ± 1.6	<0.003
LatSw (cm/s)	3.1 ± 1.9	4.6 ± 2.4	<0.001
LatEa (cm/s)	2.7 ± 1.6	3.6 ± 2.1	<0.012

CPMA – coaptation point mitral annulus distance; CRT – cardiac resynchronization therapy; LatEa – lateral wall diastolic wave velocity; LatSw – lateral wall systolic wave velocity; LVEF – left ventricular ejection fraction; MAD – mitral annulus diameter; SepEa – septal wall diastolic wave velocity; SepSw – septal wall systolic wave velocity; TDIF – time difference.

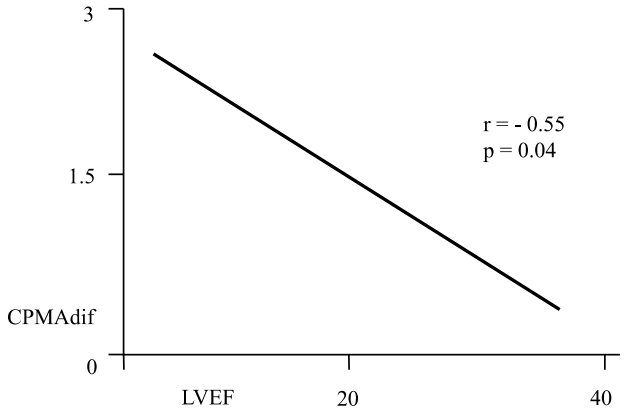

Figure 2. Diagram showing the inverse correlation between the change in the mitral leaflets coaptation point (CPMA) and baseline left ventricular ejection fraction (LVEF). The smaller the baseline LVEF, the greater the improvement in CPMA (CPMAdif) after cardiac resynchronization therapy.

$p<0.05$ and $r=0.59$, $p<0.05$, at CRT off and CRT on, respectively). The absolute difference in CPMA between CRT on and CRT off was correlated with the baseline degree of LV dilatation at both end-systole and end-diastole (LVESD $r=0.67$, LVEDD $r=0.65$, both $p<0.05$), and was inversely correlated with baseline LVEF ($r=-0.55$, $p<0.05$) (Figure 2). The change in CPMA was also correlated with the time difference of the basal segments of the anterior and lateral wall at CRT on ($r=0.68$, $p<0.01$) (Table 2).

The improvement in time difference between CRT on and CRT off was correlated with baseline CRT time difference (at CRT off) ($r=0.89$, $p<0.001$), signifying that the benefit of resynchronization therapy was greater in patients with greater intraventricular desynchronization.

Two groups of patients, classified according to their primary disorder, i.e. coronary artery disease or dilated cardiomyopathy, were evaluated at baseline using the unpaired samples t-test. The results did not reveal any statistically significant differences, except in the systolic wave in the septal wall on tissue Doppler at CRT off, which was higher in patients with coronary artery disease ($p=0.032$). The improvement at CRT on was similar in the two groups (Table 3).

Discussion

Kaul et al[8] conclusively showed that incomplete mitral leaflet closure was related to reduced LV function. In a previously published study[9] we have demonstrated that the distance between the mitral leaflet coaptation point and the mitral annular plane is correlated with LV and mitral annulus size. We found that patients with coronary artery disease and localized akinetic areas exhibit the same CPMA value, when compared to patients with global left ventricular dysfunction,[7-9] and that CPMA as a measure of incomplete mitral leaflet closure was related to both the size and function of the left ventricle. It was similar in two patient subgroups, with and without mitral regurgitation.[8,9] Additionally, we found no correlation of CPMA with the degree of mitral regurgitation.[9]

This finding supports the hypothesis that incomplete mitral leaflet closure is a result of dilatation and poor function, and not of outward pulling of the papillary muscle in systole.[9] Otsuji et al[10] studied dogs with experimental segmental mitral regurgitation. They found that the LV sphericity index, but not LVEF, was a predictor of mitral regurgitation severity. The same authors also found that incomplete mitral leaflet closure area, which corresponds to the CPMA that we used, increased with chronic regurgitation concomitantly with an increase in left ventricular dimension and a decrease in ejection fraction; however, these changes were not significantly correlated. In a recent editorial Kaul stressed that as the rate of rise of the systolic LV-left atrium pressure gradient decreased, the distance between the mitral leaflet coaptation point and the mitral annular plane in systole increased.[12]

In patients with heart failure and mechanical LV dyssynchrony that is usually identified by intraventricular conduction delay, i.e. left bundle branch block, resynchronization by biventricular pacing is the treatment of choice,[1,2] especially if the patient's clinical condition deteriorates despite optimal medical therapy. Resynchronization has also been found to reduce the spatial and temporal heterogeneity of contraction. In addition, it improves the synchrony of left and right ventricle (interventricular synchrony) and the synchrony of different segments of the left ventricle (intraventricular synchrony).[1,2,4,5] Furthermore, oxygen consumption seems to be distributed more homogeneously during CRT. These findings support the hypothesis that CRT rebalances the loading condition of the heart.[1,6]

It is known that congestive heart failure is accompanied by increased LV filling pressures. Dyssynchrony is known to cause a shortening of the LV filling time and a prolongation of the tension development time during the cardiac cycle. This leads to a re-

Table 2. Correlations between different echocardiographic indices with and without cardiac resynchronization therapy (CRT).

		SepSW	SepEa	SepSW CRT	SepEa CRT	LatSw	LatEa	LatSw CRT	LatEa CRT	EF	EF CRT	EF DIF	CPMA CRT	CPMA	CPMA CRT	MAD	MAD DIF	MAD	LVESD	LVEDD
SepSW	r	1	0.22	0.72	0.19	0.31	0.3	0.32	0.1	0.08	0.09	0.55	0.22	-0.1	0.01	0.07		0.28	-0.13	-0.06
	p		0.53	**0.01**	0.58	0.37	0.39	0.36	0.76	0.81	0.78	0.09	0.53	0.77	0.97	0.83	0.59	0.42	0.72	0.86
SepEa	r	0.22	1	0.16	0.94	0.04	0.6	0.2	0.68	0.08	-0.28	0	0.31	0.16	0.33	0.32	0.31	0.03	0	0.04
	p	0.53		0.64	**0.00**	0.91	0.06	0.56	**0.02**	0.81	0.42	0.99	0.37	0.63	0.34	0.35	0.37	0.92	0.98	0.9
SepSW CRT	r	0.72	0.16	1	0.02	0.28	0.04	0.32	-0.13	0.48	0.52	0.55	0.29	0.01	0.16	0.28	0.51	0.61	-0.19	-0.11
	p	**0.01**	0.64		0.93	0.43	0.89	0.35	0.7	0.15	0.11	0.09	0.4	0.96	0.64	0.42	0.12	0.06	0.6	0.77
SepEa CRT	r	0.19	0.94	0.02	1	0.21	0.72	0.35	0.77	-0	-0.42	-0.11	0.3	0.05	0.21	0.29	0.23	-0.07	-0.12	-0.06
	p	0.58	**0.0**	0.93		0.54	**0.01**	0.31	**0.00**	0.9	0.22	0.76	0.38	0.87	0.54	0.4	0.5	0.84	0.74	0.86
LatSw	r	0.31	0.04	0.28	0.21	1	0.72	0.93	0.5	0.73	0	0.06	-0.12	0.25	0.19	0.57	0.6	0.21	-0.62	-0.57
	p	0.37	0.91	0.43	0.54		**0.01**	**0.00**	0.13	**0.01**	0.98	0.85	0.72	0.47	0.59	0.08	0.06	0.55	0.07	0.1
LatEa	r	0.3	0.6	0.04	0.72	0.72	1	0.71	0.94	0.32	-0.29	0.01	-0.05	0.39	0.37	0.52	0.5	0.08	-0.5	-0.49
	p	0.39	0.06	0.89	**0.01**	**0.01**		**0.02**	**0.00**	0.36	0.41	0.96	0.88	0.25	0.29	0.12	0.13	0.81	0.16	0.17
LatSw CRT	r	0.32	0.2	0.32	0.35	0.93	0.71	1	0.5	0.62	-0.21	-0.13	0.08	0.33	0.38	0.63	0.64	0.16	-0.31	-0.25
	p	0.36	0.56	0.35	0.31	**0.00**	**0.02**		0.13	**0.05**	0.56	0.71	0.81	0.34	0.27	**0.04**	**0.04**	0.64	0.4	0.5
LatEa CRT	r	0.1	0.68	-0.13	0.77	0.5	0.94	0.5	1	0.19	-0.3	-0.06	-0.15	0.46	0.38	0.48	0.42	-0.01	-0.5	-0.51
	p	0.76	**0.02**	0.7	**0.00**	0.13	**0.00**	0.13		0.59	0.38	0.85	0.66	0.17	0.26	0.15	0.21	0.96	0.16	0.15
EF	r	0.08	-0.1	0.48	-0.04	0.73	0.32	0.62	0.19	1	0.74	-0.4	-0.55	0.21	-0.11	0.26	0.36	0.12	-0.68	-0.72
	p	0.81	0.81	0.15	0.9	**0.01**	0.36	**0.05**	0.59		0.9	**0.03**	**0.04**	0.42	0.66	0.32	0.15	0.65	**0.00**	**0.00**
EFCRT	r	0.09	-0.3	0.52	-0.42	0	-0.29	-0.2	-0.3	0.74	1	0.15	-0.21	0.12	-0.01	0.1	0.3	0.33	-0.31	-0.49
	p	0.78	0.42	0.11	0.22	0.98	0.41	0.56	0.38	0.9		0.44	0.43	0.63	0.95	0.7	0.24	0.2	0.2	**0.01**
EFDIFF	r	0.55	0	0.55	-0.11	0.06	0.01	-0.13	-0.06	-0.4	0.15	1	0.3	-0.08	0.1	0.22	0.27	0.13	0.21	0.29
	p	0.09	0.99	0.09	0.76	0.85	0.96	0.71	0.85	**0.03**	0.44		0.25	0.74	0.68	0.4	0.29	0.62	0.38	0.15

↓

CPMA DIF	r	0.22	0.31	0.29	0.3	-0.12	-0.05	0.08	-0.15	-0.55	-0.21	0.3	1	-0.16	0.46	-0.1	-0	0.27	0.67	0.65
	p	0.53	0.37	0.4	0.38	0.72	0.88	0.81	0.66	**0.04**	0.43	0.25		0.53	0.06	0.7	0.93	0.3	**0.00**	**0.00**
CPMA CRT	r	-0.1	0.16	0.01	0.05	0.25	0.39	0.33	0.46	0.21	0.12	-0.08	-0.16	1	0.79	0.39	0.59	0.28	0.06	0.05
	p	0.77	0.63	0.96	0.87	0.47	0.25	0.34	0.17	0.42	0.63	0.74	0.53		**0.00**	0.12	**0.01**	0.28	0.81	0.84
CPMA	r	0.01	0.33	0.16	0.21	0.19	0.37	0.38	0.38	-0.1	-0.01	0.1	0.46	0.79	1	0.29	0.51	0.42	0.48	0.45
	p	0.97	0.34	0.64	0.54	0.59	0.29	0.27	0.26	0.66	0.95	0.68	0.06	**0.00**		0.27	**0.04**	0.1	0.06	0.08
MAD CRT	r	0.07	0.32	0.28	0.29	0.57	0.52	0.63	0.48	0.2	0.1	0.22	-0.1	0.39	0.29	1	0.86	-0.02	-0.01	-0.02
	p	0.83	0.35	0.42	0.4	0.08	0.12	**0.04**	0.15	0.32	0.7	0.4	0.7	0.12	0.27		**0.00**	0.94	0.95	0.91
MAD	r	0.19	0.31	0.51	0.23	0.6	0.5	0.64	0.42	0.36	0.3	0.27	-0.02	0.59	0.51	0.86	1	0.41	0.04	-0.05
	p	0.59	0.37	0.12	0.5	0.06	0.13	**0.04**	0.21	0.15	0.24	0.29	0.93	**0.01**	**0.04**	**0.00**		0.11	0.87	0.83
MAD DIF	r	0.28	0.03	0.61	-0.07	0.21	0.08	0.16	-0.01	0.12	0.33	0.13	0.27	0.28	0.42	-0.02	0.41	1	-0.01	-0.08
	p	0.42	0.92	0.06	0.84	0.55	0.81	0.64	0.96	0.65	0.2	0.62	0.3	0.28	0.1	0.94	0.11		0.94	0.75
LVESD	r	-0.13	0	-0.19	-0.12	-0.62	-0.5	-0.31	-0.5	0.68	-0.31	0.21	0.67	0.06	0.48	-0.01	-0	-0.01	1	0.95
	p	0.72	0.98	0.6	0.74	0.07	0.16	0.4	0.16	**0.00**	0.2	0.38	**0.00**	0.81	0.06	0.95	0.87	0.94		1.09
LVEDD	r	-0.06	0.04	-0.11	-0.06	-0.57	-0.49	-0.25	-0.51	-0.7	-0.49	0.29	0.65	0.05	0.45	-0.02	-0.1	-0.08	0.95	1
	p	0.86	0.9	0.77	0.86	0.1	0.17	0.5	0.15	**0.00**	**0.01**	0.15	**0.00**	0.84	0.08	0.91	0.83	0.75	1.09	

Significant p-values are marked in **bold type**.

CPMA – coaptation point mitral annulus distance; CRT – cardiac resynchronization therapy; DIF – difference; EF – ejection fraction; LatEa – lateral wall diastolic wave velocity; LatSw – lateral wall systolic wave velocity; LVEF – left ventricular ejection fraction; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end systolic diameter; MAD – mitral annulus diameter; SepEa – septal wall diastolic wave velocity; SepSw – septal wall systolic wave velocity.

Table 3. Comparison of different indexes in patients with heart failure and dilated cardiomyopathy (DCM) or coronary artery disease (CAD). Values were tested using the independent samples t-test. The only significant difference was in the septal wall systolic wave velocity.

	DCM/CAD	N	Mean ± SD	p
SepSw CRT off	DCM	11	3.98±0.81	0.032
	CAD	9	2.58 ± 0.89	
SepEa CRT off	DCM	11	2.66 ± 1.27	0.430
	CAD	9	3.40 ± 1.54	
SepSw CRT on	DCM	11	5.22 ± 1.20	0.057
	CAD	9	3.8 ± 0.56	
SepEa CRT on	DCM	11	3.34 ± 1.70	0.506
	CAD	9	4.06 ± 1.56	
LatSw CRT off	DCM	11	4.22 ± 2.13	0.069
	CAD	9	2.09 ± 0.78	
LatEa CRT off	DCM	11	3.00 ± 2.06	0.654
	CAD	9	2.50 ± 1.24	
LatSw CRT on	DCM	11	5.88 ± 2.85	0.091
	CAD	9	3.36 ± 0.68	
LatEa CRT on	DCM	11	3.39 ± 2.49	0.813
	CAD	9	3.74 ± 2.03	
EF CRT off	DCM	11	24.88 ± 5.44	0.710
	CAD	9	24.00 ± 6.58	
EF CRT on	DCM	11	29.58 ± 5.16	0.967
	CAD	9	29.50 ± 5.50	
EF DIF	DCM	11	5.58 ± 3.48	0.671
	CAD	9	5.00 ± 3.33	
CPMA DIF	DCM	11	2.27 ± 1.54	0.674
	CAD	9	2.00 ± 0.81	
CPMA CRT on	DCM	11	9.42 ± 1.40	0.457
	CAD	9	8.71 ± 2.29	
CPMA CRT off	DCM	11	11.70 ± 2.24	0.350
	CAD	9	10.71 ± 1.71	
MAD CRT on	DCM	11	37.67 ± 3.32	0.848
	CAD	9	37.29 ± 4.50	
MAD CRT off	DCM	11	39.55 ± 3.17	0.447
	CAD	9	38.00 ± 4.80	
MAD DIF	DCM	11	1.90 ± 2.02	0.512
	CAD	9	1.29 ± 1.39	

CPMA – coaptation point mitral annulus distance; CRT – cardiac resynchronization therapy; DIF – difference; EF – ejection fraction; LatEa – lateral wall diastolic wave velocity; LatSw – lateral wall systolic wave velocity; MAD – mitral annulus diameter; SepEa – septal wall diastolic wave velocity; SepSw – septal wall systolic wave velocity.

duction in diastole and obviously to an increase in left ventricular end diastolic pressure.[6] Cardiac resynchronization therapy decreases both LV filling pressures and wall stress.

In our study we found that CRT improved not only the LVEF but also the MAD and CPMA, probably reflecting the changes in the LV end-diastolic pressure and the rate of rise of LV-left atrium pressure gradient. Furthermore, the fact the improvement in CPMA was positively correlated with the improvement in intraventricular synchronization underlines that the effects of CRT on the mitral coaptation point are dependent on the degree of synchronization. We also found that the improvement in CPMA after CRT was greater in patients with lower values of baseline LVEF.

A possible limitation of our observational study could be the fact that we did not measure the potential improvement in mitral regurgitation after CRT, neither semi-quantitatively nor by measuring the effective regurgitant orifice, as demonstrated by several other studies.[13-15] We focused mainly on the acute effects that resynchronization therapy exerts on the coaptation point of the mitral leaflets, irrespectively of mitral regurgitation. Of course, the acute hemodynamic variations found in heart failure patients should also be

taken into account. Nevertheless, we tried to minimize that aspect as the doses of the background medication were kept constant for the previous one month and during the study. In addition, patients with atrial fibrillation and significant primary valvular heart disease were excluded from our study.

In conclusion, in patients with severe LV systolic dysfunction and LV dilatation biventricular pacing is related with an acute improvement in both CPMA and MAD, which is strongly correlated with the degree of resynchronization as estimated by tissue Doppler imaging. CPMA measurement could be used as a simple and practical index for estimating the acute effects of CRT in heart failure patients. Long-term follow up of these patients in a double blind study will be needed to demonstrate the effects of CRT on hospitalization and survival in relation to CPMA and a decrease in MAD.

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