Predictive values of left ventricular mechanical dyssynchrony for CRT response in heart failure patients with different pathophysiology

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Background. **Cardiac resynchronization therapy (CRT) patients with different pathophysiology may influence mechanical dyssynchrony and get different ventricular resynchronization and clinical outcomes.**

Methods. **Ninety-two dilated cardiomyopathy (DCM) and fifty ischemic cardiomyopathy (ICM) patients with gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) were included in this retrospective study. Patients were classified based on the concordance between the left ventricular (LV) lead and the latest contraction or relaxation position. If the LV lead was located on or adjacent to both the latest contraction and relaxation position, the patient was categorized into the both match group; if the LV lead was located on or adjacent to the latest contraction or relaxation position, the patient was classified into the one match group; if the LV lead was located on or adjacent to neither the latest contraction nor relaxation position, the patient was categorized to the neither group. CRT response was defined as $\geq 5\%$ improvement of LV ejection fraction at the 6-month follow-up. Variables with $P < .05$ in the univariate analysis were included in the stepwise multivariate model.**

Results. **During the follow-up period, 58.7% (54 of 92) for DCM patients and 54% (27 of 50) for ICM patients were CRT responders. The univariate analysis and stepwise multivariate analysis showed that QRS duration, systolic phase bandwidth (PBW), diastolic PBW, diastolic phase histogram standard deviation (PSD), and left ventricular mechanical dyssynchrony (LVMD) concordance were independent predictors of CRT response in DCM patients; diabetes**

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mellitus and left ventricular end-systolic volume were significantly associated with CRT response in ICM patients. The intra-group comparison revealed that the CRT response rate was significantly different in the both match group of DCM (N = 18, 94%) and ICM (N = 24, 62%) patients (P = .016). However, there was no significant difference between DCM and ICM in the one match and neither group. For the inter-group comparison, Kruskal-Wallis H-test revealed that CRT response was significantly different in all the groups of DCM patients (P < .001), but not in ICM patients (P = .383).

Conclusions. **Compared with ICM patients, systolic PBW, diastolic PBW and PSD have better predictive and prognostic values for the CRT response in DCM patients. Placing the LV lead in or adjacent to the latest contraction and relaxation position can improve the clinical outcomes of DCM patients, but it does not apply to ICM patients. (J Nucl Cardiol 2022;29:2637–48.)**

Key Words: CRT • SPECT • Dilated cardiomyopathy • Ischemic cardiomyopathy • Left ventricular mechanical dyssynchrony

Abbreviations	
CRT	Cardiac resynchronization therapy
DCM	Dilated cardiomyopathy
ICM	Ischemic cardiomyopathy
LV	Left ventricular
LVEDV	Left ventricular end-diastolic volume
LVEF	Left ventricular ejection fraction
LVESV	Left ventricular end-systolic volume
LVMD	Left ventricular mechanical dyssynchrony
MPI	Myocardial perfusion imaging
PBW	Phase bandwidth
PSD	Phase histogram standard deviation

See related editorial, pp. 2649–2651

INTRODUCTION

There are 30% to 40% of cardiac resynchronization therapy (CRT) recipients who do not benefit from CRT.[1,2] LV mechanical dyssynchrony (LVMD) parameters measured by phase analysis from gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) provide repeatable and reproducible information about the presence of intraventricular synchronism.[3,4] They have been found to be independent predictors for CRT patient selection[5,6] and have been proven to have prognostic value.[7,8] Moreover, the concordance of LV lead on or adjacent to the late contracting viable segments measured by gated SPECT MPI was associated with CRT response and heart failure rehospitalization and all-cause mortality.[9]

In dilated cardiomyopathy (DCM) patients, systolic and diastolic LVMD were independent predictors for CRT response; and pacing the LV lead in the segments with the latest contraction and relaxation would improve the CRT response rate.[10] For ischemic cardiomyopathy (ICM) patients, the systolic phase bandwidth (PBW) as an LVMD parameter has been identified as an independent predictor of ventricular arrhythmia after CRT implantation.[6] However, comparative studies on the predictive value of LVMD for CRT in HF patients with different pathophysiology are still limited. The purpose of this study was to compare the predictive and prognostic values of LVMD measured by gated SPECT MPI and the concordance of LV lead with the sites of the latest contraction or relaxation position in DCM and ICM patients.

METHODS

Patient Population

CRT recipients were consecutively enrolled in a retrospective database at the First Affiliated Nanjing Medical University Hospital from May 2009 to August 2020. Study subjects selected retrospectively had DCM: a presence of LV dilation and LV systolic dysfunction in the absence of other etiological factors that might cause LV dysfunction by echocardiography according to the recent criteria or CAD that causes global systolic dysfunction;[11] or ICM: epicardial coronary artery stenosis greater than 50% or previous history of coronary revascularization or myocardial infarction.[12] A total of 92 DCM and 50 ICM patients who met the above criteria were included in the study, as shown in Figure 1. All patients met standard indications for CRT at the time of implantation: LVEF $<$ 35%, QRS duration $\geq$ 120 milliseconds with sinus rhythm, New York Heart Association (NYHA) functional class greater or equal to II, and optimal medical therapy for at least 3 months before CRT implantation. Exclusion criteria were as follows: atrial fibrillation, right bundle branch block, pregnancy or breastfeeding, and those being upgraded from right ventricular pacing. This study was approved by the Institutional Ethical Committee of the First Affiliated Hospital of Nanjing Medical University.

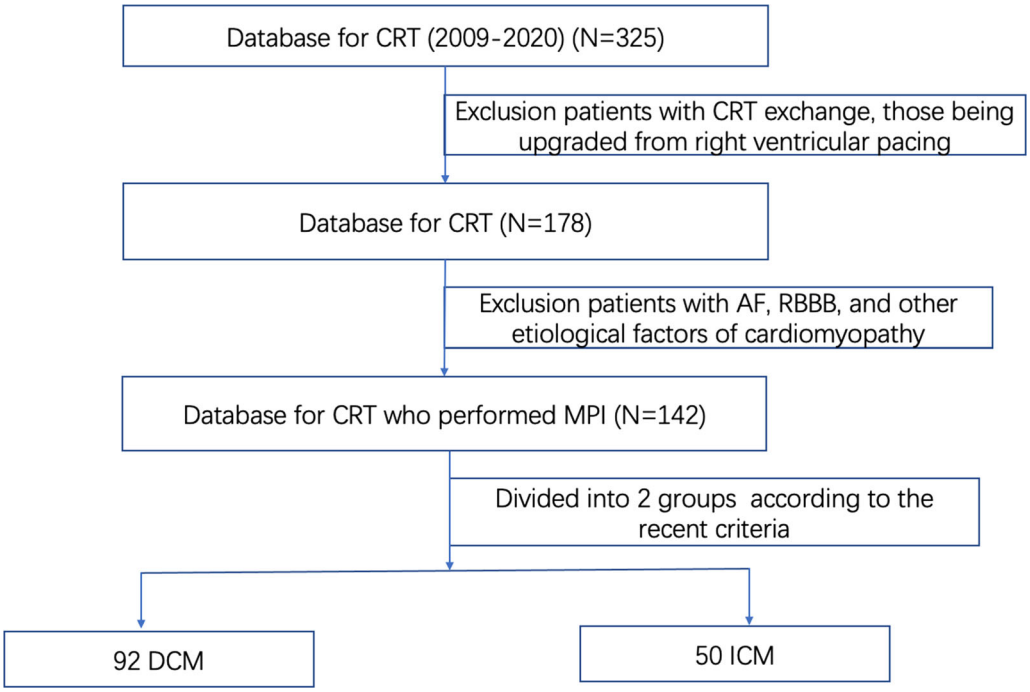

Figure 1. Study flow chart. *CRT*, cardiac resynchronization therapy; *AF*, atrial fibrillation; *RBBB*, right bundle branch block; *MPI*, myocardial Perfusion Imaging; *DCM*, dilated cardiomyopathy; *ICM*, ischemic cardiomyopathy.

Echocardiography

Echocardiography was performed at baseline before CRT implantation and at the 6-month CRT clinical follow-up. LV function was assessed twice by two experienced ultrasound experts, who were blinded to the clinical data before and 6 months after CRT implantation, and the mean value was used as the final record. LVEF was calculated using the 2-dimensional modified biplane Simpson method. Echocardiographic response to CRT was defined as an increase in LVEF by 5% or more.

SPECT MPI Assessment

Gated SPECT MPI was performed around 60 minutes after injection using 20-30mCi of 99mTc-sestamibi. All the images were acquired in a dual-headed camera (CardioMD, Philips Medical Systems) with a standard protocol with 20% energy window around 140 KeV, 180° orbit, 32 steps with 25 seconds per step, 8-bin gating, and 64 planar projections per gate. Image reconstruction and reorientation were performed by Emory Reconstruction Toolbox (ERToolbox; Atlanta, GA) using the OSEM method with 3 iterations and 10 subsets and filtered by a Butterworth low-pass filter with an order of 10 subsets and a cutoff frequency of 0.3 cycles/cm.

The resulting short-axis images were sent to an interactive tool for automatized accessing LV contour parameters by an automatic myocardial sampling algorithm that searched the maximal count circumferential profiles in each cardiac frame. Furthermore, the onset of mechanical contraction and relaxation throughout the cardiac cycle were obtained by multi-harmonic Fourier approximations.[13] Then, the LVMD was represented by phase distribution of systolic and diastolic dyssynchrony for the entire left ventricle, and quantitative parameters of LVMD were calculated as phase standard deviation (PSD) and phase bandwidth (PBW).[13,14]

CRT Implantation and LV Lead Position

The right atrial and ventricular leads were positioned under fluoroscopic guidance by a transvenous approach. The LV lead location was determined by coronary venous angiography cine images in the left anterior oblique (LAO) and right anterior oblique (RAO), and then correlated to the 13-segment polar map of the systolic and diastolic dyssynchrony.[12,15] LV lead located on or adjacent segment of the latest contraction or relaxation segment was classified as

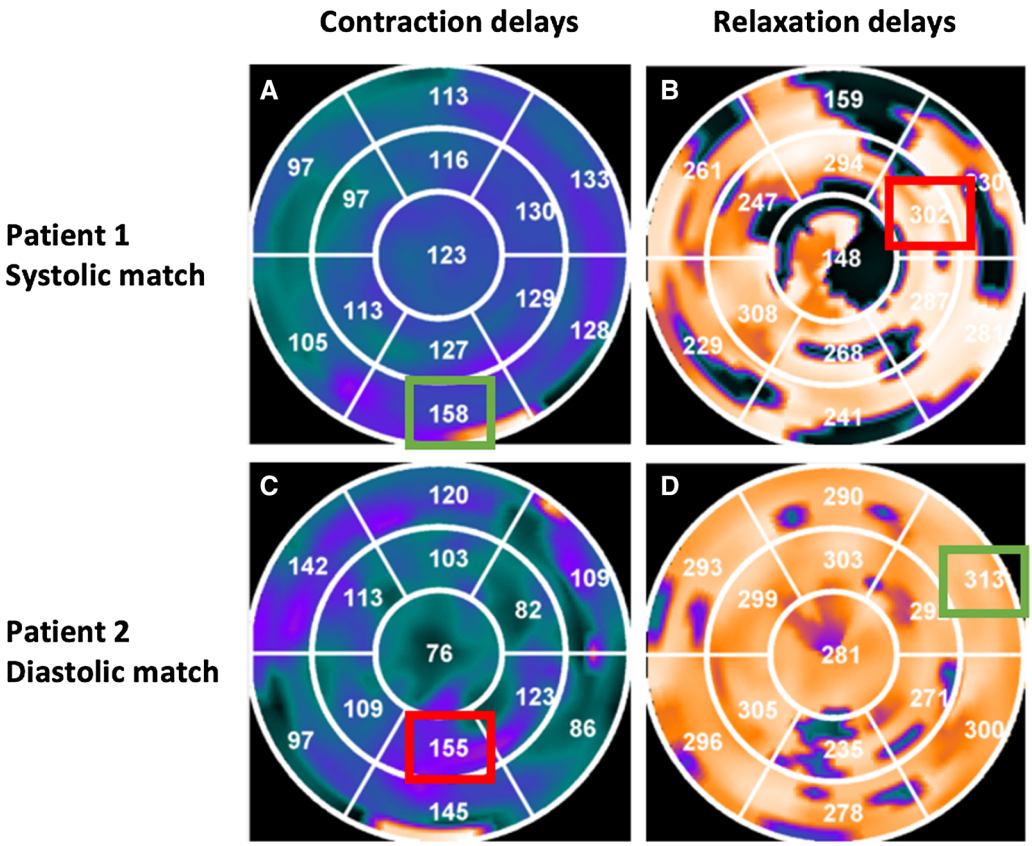

Figure 2. Illustrative examples of systolic match and diastolic match. Polar maps of patient 1 with ICM showing the LV lead located on the latest contraction segment (green in **A**), not on or adjacent to the latest relaxation segment (red box in **B**). This patient is classified as systolic match. The LV lead of Patient 2 is located on the latest relaxation segment (green box in **D**) and not on or adjacent to the latest contraction segment (red box in **C**).

being concordant to systolic phase or diastolic phase (one match), respectively, as depicted in two ICM examples in Figure 2.

Statistical Analysis

The differences between the DCM and ICM were compared by the unpaired *t*-test for continuous variables, expressed as mean ± standard deviation, and Chi-square test for categorical variables expressed in number and percentage. The systolic and diastolic LVMD within all patients, DCM patients, and ICM patients were compared by paired *t*-test. Univariate binary logistic regression analysis was performed on all clinically relevant variables to estimate potential predictors for CRT response. Due to the collinearity between LVMD parameters, and in order to avoid model overfitting, they were entered one by one with those selected variables that were found significant in the univariate analysis in a stepwise fashion into the multivariate logistic regression to obtain the optimal models. Kruskal-Wallis *H*-test was be used to analyze the difference of CRT response rate among three groups in DCM and ICM patients, respectively. Differences in survival over time were analyzed by the log-rank Kaplan-Meier survival analysis. $P < .05$ was considered to be statistically significant. Statistical analysis was performed by the Python Statsmodels package[16] and IBM SPSS Statistics software version 26 (SPSS Inc, Chicago, Illinois).

RESULTS

A total of 142 patients (DCM, 92; ICM, 50) who underwent SPECT MPI before CRT implantation were included in this study. The baseline characteristics of the included patients are shown in Table 1. For all patients, the age was 64.6 ± 14.5 years, and 71.1% (N = 101) patients were male. The baseline QRS duration (157.9 ± 23.3), medical therapy records, and LV functions were also shown in the baseline table. The

differences between systolic and diastolic LVMD in all patients, DCM patients, and ICM patients were significant (all $P < .001$).

In the univariate analysis for DCM patients, QRS duration (95%CI 1.0-1.05, $P = .014$), NT-proBNP (95%CI 0.0-0.61, $P = .026$), non-sustained ventricular tachycardia (NS-VT) (95%CI 0.1-0.64, $P = .004$), Scar burden (95%CI 0.93-1.0, $P = .029$), all LVMD parameters (systolic PSD, 95%CI 0.96-1.0, $P = .017$; systolic PBW, 95%CI 0.99-1.0, $P = .009$; diastolic PSD, 95%CI 0.95-0.99, $P = .003$; diastolic PBW, 95%CI 0.99-1.0, $P = .003$), LVMD concordance (95%CI 0.13-0.5, $P < .001$), and LV lead in scarred myocardium (95%CI 1.09-8.18, $P = .033$) were statistically significant predictors of CRT response. However, for ICM patients, only diabetes mellitus (DM) (95%CI 0.05-0.62, $P = .007$), QRS duration (95%CI 1.0-1.07, $P = .044$), NS-VT (95%CI 0.08-0.94, $P = .039$), LVEDV (95%CI 0.98-1.0, $P = .009$), LVESV (95%CI 0.98-1.0, $P = .009$) were

Table 1. Baseline characteristics and left ventricular parameters of the enrolled patients

Variables	All (N = 142)	DCM (N = 92, 64.8%)	ICM (N = 50, 35.2%)	*P* value
Age (year)	64.6 ± 14.5	60.3 ± 11.9	72.5 ± 15.3	0
Male (N, %)	101 (71.1%)	68 (73.9%)	33 (66.0%)	.424
Hypertension	65 (45.8%)	33 (35.9%)	32 (64.0%)	.002
DM	38 (26.8%)	20 (21.7%)	18 (36.0%)	.102
QRS duration (ms)	157.9 ± 23.3	155.6 ± 24.3	162.0 ± 20.7	.124
NT-proBNP	3841.6 ± 4441.7	3765.2 ± 3761.2	3982.2 ± 5474.4	.783
NS-VT	85 (59.9%)	56 (60.9%)	29 (58.0%)	.878
NYHA				.319
II	60 (42.3%)	38 (41.3%)	22 (44.0%)	
III	66 (46.5%)	46 (50.0%)	20 (40.0%)	
IV	16 (11.3%)	8 (8.7%)	8 (16.0%)	
Medication				
ACE inhibitors	79 (55.6%)	57 (62.0%)	22 (44.0%)	.06
ARB	28 (19.7%)	20 (21.7%)	8 (16.0%)	.548
Diuretics	134 (94.4%)	88 (95.7%)	46 (92.0%)	.603
β-Blocker	135 (95.1%)	89 (96.7%)	46 (92.0%)	.401
LVEF by echo	29.2 ± 7.2	28.8 ± 6.9	30.0 ± 7.7	.348
LVEDV	289.8 ± 129.6	310.8 ± 139.7	251.1 ± 97.4	.008
LVESV	238.7 ± 118.9	259.0 ± 126.6	201.5 ± 92.2	.006
Scar burden	27.7 ± 13.6	26.4 ± 12.0	30.1 ± 15.9	.128
Systolic PSD	43.8 ± 22.4	42.5 ± 21.9	46.2 ± 23.1	.356
Systolic PBW	163.9 ± 91.8	152.0 ± 87.0	185.8 ± 96.2	.036
Diastolic PSD	54.4 ± 23.2	53.3 ± 23.9	56.3 ± 21.9	.458
Diastolic PBW	191.4 ± 90.0	179.3 ± 89.7	213.6 ± 86.1	.03
LV lead in scarred myocardium	1.8 ± 0.4	1.8 ± 0.4	1.9 ± 0.3	.027
Diastolic match	103 (72.5%)	63 (68.5%)	40 (80.0%)	.203
Systolic match	60 (42.3%)	30 (32.6%)	30 (60.0%)	.003
LVMD concordance				.004
Both match	42 (29.6%)	18 (19.6%)	24 (48.0%)	
One match	79 (55.7%)	57 (61.9%)	22 (44.0%)	
Neither match	21 (14.8%)	17 (18.5%)	4 (8.0%)	

Data are expressed as mean ± SD or number (percentage)
DM, diabetes mellitus; *NT-proBNP*, N-terminal pro-natriuretic brain natriuretic peptide; *NS-VT*, non-sustained ventricular tachycardia; *NYHA*, New York Heart Association; *ACE inhibitors*, angiotensin-converting enzyme inhibitors; *ARB*, angiotensin II receptor blocker; *LVEF*, left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *PSD*, phase standard deviation; *PBW*, phase bandwidth; *LV*, left ventricular; *LVMD*, left ventricular mechanical dyssynchrony

statistically significant predictors of CRT response, as shown in Table 2.

In the multivariate models for DCM patients, QRS duration, NT-proBNP, 3 LVMD parameters (systolic PBW: 95% CI 0.98-1.00, $P = .041$; diastolic PSD: 95% CI 0.94-1.00, $P = .041$; diastolic PBW: 95% CI 0.98-1.00, $P = .028$) and LVMD concordance ($P < .003$ for all) were significantly independent predictors of CRT response. For ICM patients, DM and LVESV were significant independent predictors of CRT response; however, all LVMD parameters and LVMD concordance were not significant. The results of the multivariate analysis are shown in Tables 3, 4, 5 and 6.

Patients were divided into three groups based on the latest contraction or relaxation segment at the LV lead location: patients whose LV lead were concordant or adjacent to the latest contraction and relaxation segment (both match: DCM, N = 18; ICM, N = 24), and patients whose LV lead were concordant or adjacent to the latest contraction or relaxation segment (one match: DCM, N = 57; ICM, N = 22), and patients whose LV lead were neither concordant nor adjacent to the latest contraction or relaxation segment (neither: DCM, N = 17; ICM, N = 4). The intra-group comparison revealed that the CRT response rate of DCM patients (94%, N = 18) was much higher than ICM patients (62%, N = 24) in both match group ($P = .016$). There was no significant difference in the one match group ($P = .363$) and neither group ($P = .521$) between DCM and ICM patients, as shown in Figure 3. For the inter-group comparison, Kruskal-Wallis *H*-test revealed that CRT response was significantly different in the three groups of DCM patients ($P < .001$), but not in ICM patients ($P = .383$).

During the mean follow-up time of 39 ± 24 months (IQR 19-55), 10 (10.87%) DCM patients and 9 (18%) ICM patients died. Kaplan-Meier survival curves

Table 2. Univariate logistic regression analyses of DCM and ICM patients

	DCM			ICM		
Variables	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Age	1	0.96-1.03	.962	1.03	0.97-1.1	.294
Male	0.81	0.31-2.1	.66	1.07	0.33-3.45	.914
Hypertension	0.77	0.32-1.82	.546	0.44	0.13-1.47	.182
DM	1.07	0.39-2.94	.894	0.17	0.05-0.62	.007
QRS duration	1.02	1.0-1.05	.014	1.03	1.0-1.07	.044
NT-proBNP	0.02	0.0-0.61	.026	0.15	0.0-9.53	.371
NS-VT	0.25	0.1-0.64	.004	0.28	0.08-0.94	.039
NYHA						
II			.037			.191
III	1.68	0.34-8.35	.526	2.14	0.41-11.16	.366
IV	0.504	0.108-2.361	.385	0.66	0.13-3.47	.630
LVEF by echo	0.97	0.92-1.04	.404	1.02	0.94-1.09	.678
LVEDV	1	1.0-1.0	.438	0.99	0.98-1.0	.009
LVESV	1	1.0-1.0	.422	0.99	0.98-1.0	.009
Scar burden	0.96	0.93-1.0	.029	0.97	0.93-1.0	.075
Systolic PSD	0.98	0.96-1.0	.017	0.98	0.95-1.0	.064
Systolic PBW	0.99	0.99-1.0	.009	1	0.99-1.0	.107
Diastolic PSD	0.97	0.95-0.99	.003	0.97	0.95-1.0	.056
Diastolic PBW	0.99	0.99-1.0	.003	1	0.99-1.0	.171
LVMD concordance						
Both match			.000			.364
One match	127.50	10.48-1551.48	.000	5.00	0.45-55.63	.190
Neither match	11.93	2.49-57.28	.002	3.00	0.27-33.49	.372
LV lead in scarred myocardium	2.99	1.09-8.18	.033	3.9	0.38-40.37	.254

ACEI, angiotensin-converting enzyme inhibitors; *ARB*, angiotensin II receptor blocker; *CAD*, coronary artery disease; *MI*, myocardial infarction; *EDE*, end-diastolic eccentricity; *ESE*, end-systolic eccentricity; *LVEF*, left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *EDVi*, end-diastolic volume index; *ESVi*, end-systolic volume index; *PSD*, phase standard deviation; *PBW*, phase bandwidth

Table 3. Stepwise multivariate analysis for DCM and ICM patients including systolic PSD

	DCM			ICM		
Variables	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
DM				0.17	0.04-0.73	.017
QRS duration	1.03	1.00-1.06	.049			
NS-VT	0.48	0.13-1.77	.272			
NT-proBNP	1.00	1.00-1.00	.0			
LVESV				0.99	0.98-1.00	.019
NYHA (II)			.388			
NYHA (III)	1.40	0.15-12.70	.765			
NYHA (IV)	0.53	0.08-3.88	.539			
LVMD concordance (both match)			.001			
LVMD concordance (one match)	531.97	12.73-22233	.001			
LVMD concordance (neither match)	19.34	3.07-121.85	.02			
LV lead in scarred myocardium	2.54	0.53-12.09	.243			
Systolic PSD	0.97	0.94-1.00	.063	1.00	0.97-1.03	.990

Table 4. Stepwise multivariate analysis for DCM and ICM patients including systolic PBW

	DCM			ICM		
Variables	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
DM				0.16	0.04-0.69	.014
QRS duration	1.03	1.00-1.06	.043			
NS-VT	0.55	0.15-2.04	.371			
NT-proBNP	1.00	1.00-1.00	.011			
LVESV				0.98	0.98-1.00	.014
NYHA (II)			.403			
NYHA (III)	1.38	0.15-12.72	.776			
NYHA (IV)	0.54	0.07-3.98	.547			
LVMD concordance (both match)			.001			
LVMD concordance (one match)	635.05	12.08-28642	.001			
LVMD concordance (neither match)	20.76	3.23-133.30	.001			
LV lead in scarred myocardium	2.48	0.50-12.40	.268			
Systolic PBW	0.99	0.98-1.00	.041	1.00	0.99-1.01	.689

showed significantly longer survival in DCM patients with the concordance between LV lead with the latest contraction and relaxation position ($P = .050$), as shown in Figure 4. However, there is no significant difference of survival time in ICM patients based on the concordance between LV lead and the latest contraction or relaxation position, as shown in Figure 5.

DISCUSSION

The main finding of the present study was that systolic PBW, diastolic PSD and PBW were strong predictors of CRT response only in DCM patients. Furthermore, Kaplan-Meier analysis showed that the concordance of LV lead to the latest contraction and relaxation position were independent predictors of death from any cause and had significantly longer survival than LV lead only located in one latest position or none in DCM patients. Whether it is DCM or ICM, it is

Table 5. Stepwise multivariate analysis for DCM and ICM patients including diastolic PSD

	DCM			ICM		
Variables	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
DM				0.18	0.04-0.80	.024
QRS duration	1.07	1.00-1.05	.068			
NS-VT	0.45	0.12-1.66	.231			
NT-proBNP	1.00	1.00-1.00	.013			
LVESV				0.99	0.98-1.00	.017
NYHA (II)			.373			
NYHA (III)	1.69	0.19-14.98	.638			
NYHA (IV)	0.61	0.08-4.26	.622			
LVMD concordance (both match)			.001			
LVMD concordance (one match)	571.74	11.57-28252	.001			
LVMD concordance (neither match)	18.07	2.88-113.28	.002			
LV lead in scarred myocardium	2.49	0.51-12.9	.257			
Diastolic PSD	0.97	0.94-1.00	.041	1.00	0.97-1.03	.882

Table 6. Stepwise multivariate analysis for DCM patients including diastolic PBW

	DCM			ICM		
Variables	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
DM				0.16	0.04-0.67	.013
QRS duration	1.03	1.00-1.06	.051			
NS-VT	0.50	0.13-1.86	.304			
NT-proBNP	1.00	1.00-1.00	.013			
LVESV				0.99	0.98-1.00	.013
NYHA (II)			.460			
NYHA (III)	1.59	0.17-14.81	.683			
NYHA (IV)	0.64	0.09-4.79	.666			
LVMD concordance (both match)			.001			
LVMD concordance (one match)	659.19	13.59-31972	.001			
LVMD concordance (neither match)	19.85	3.14-125.31	.011			
LV lead in scarred myocardium	2.07	0.41-10.54	.380			
Diastolic PSD	0.99	0.98-1.00	.028	1.00	0.99-1.01	.621

necessary to avoid placing the LV lead in a non-latest contraction or relaxation position whenever possible.

Predictive Value of LVMD for CRT Patient Selection

Research on selecting appropriate patients for CRT with LVMD measured by gated SPECT MPI has been widely studied. In a study of 42 CRT patients, the receiver operating characteristic curve analysis showed that the optimal cutoff value of PSD and PBW were 43° (sensitivity and specificity of 70%) and 135° (sensitivity and specificity of 74%), respectively.[5] In a study with 324 consecutive patients with non-ICM CRT patients, it was demonstrated that systolic PSD, adjust to age, hypertension, diabetes, aspirin, beta-blockers, diuretics, QRS, and EF, was an independent predictor of all-cause mortality (HR 1.97, 95% CI 1.06-3.66, P = .033).[17] However, in a multi-center VISION-CRT clinical trial (N = 195), it was found that the systolic LVMD did not

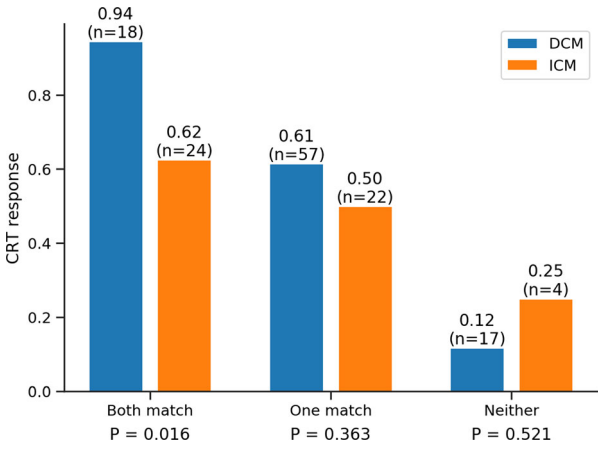

Figure 3. CRT response rate in DCM or ICM patients among different groups.

have a predictive value for CRT response, but they did not discuss it based on different pathology.[18] Peix et al[19] further analyzed part of the data from this clinical trial and found that CRT recipients with more dyssynchrony at baseline had significant improvement in non-ischemic patients with non-compaction myocardium, whose PSD was reduced from $89.5 \pm 14.2°$ to $63.7 \pm 20.5°$ (P = .028).

For DCM patients, Henneman et al[5] demonstrated that baseline systolic LVMD could be used to predict CRT response by the cutoff value of 43° for PSD with 74% sensitivity and specificity and 135° for PBW with 70% sensitivity and specificity. Wang et al[10] found that both systolic and diastolic LVMD had predictive value for CRT patient selection in 84 DCM patients (systolic PSD: 95% CI 0.92-1.00, P = .043; systolic PBW: 95% CI 0.99-1.00, P = .038; diastolic PSD: 95% CI 0.94-1.00, P = .032; diastolic PBW: 95% CI 0.99-1.00, P = .024). Similar results were found in our study that systolic PBW (95% CI 0.98-1.00, P = .041), diastolic PBW (95% CI 0.98-1.00, P = .028), and diastolic PSD (95% CI 0.94-1.00, P = .041) were independent significant predictors for CRT patient selection, except for systolic PSD (95% CI 0.94-1.00, P = .063), but its P value is still very close to .05.

For ICM patients, the presence of transmural scar tissue, which may affect the measurement of LVMD,[20] often resulted in non-response to CRT.[21] However, few studies have been done on the predictive value of LVMD for CRT in ICM patients. A study found that the difference between stress LVMD and rest LVMD was an independent predictor instead of rest LVMD for all-cause mortality in ICM patients;[22] however, not all CRT patients receive stress gated SPECT MPI. Our study demonstrated that both systolic and diastolic LVMD were not independent predictive factors for CRT response in ICM patients. This might be due to the presence of hibernating myocardium or severely scarred and dysfunctional myocardium, which requires further evaluation.[22]

LVMD to Guide CRT Lead Placement

The optimal LV lead position has been suggested to be the latest or adjacent to the latest segment mechanical activation.[9] In a study with 90 CRT patients, the patients with a concordant LV lead position (the LV lead placed in the site of the latest mechanical activation measured by SPECT MPI) had significant improvement in LV volumes and LV systolic function than the patients with a discordant LV lead position (79% vs. 26%, $P < .01$).[23]

For DCM patients, the CRT response could be increased when the LV lead is placed in the latest contraction and relaxation segment,[10] which was proved in our study among 92 DCM patients. A study with 64 CRT patients found that systolic PSD and PBW were significant factors to differentiate wide QRS duration ($\geq$ 150 ms) with narrow QRS duration (120-150 ms) among 47 DCM patients, and there were no similar results in ICM patients (N = 17).[24] In our study, both systolic and diastolic LVMD concordance between the latest activation segments and LV lead position were not independent predictive factors for CRT response in ICM patients. This finding was not surprising because the latest mechanical activation might be affected by the scar location due to the delayed electrical activation/conduction that might interfere with myocardial scar.[24] Furthermore, It showed a weak predictive value for CRT response in ICM patients by the concordance of the LV lead with the latest contraction or relaxation position, which was totally different compared with DCM.

LVMD in Different Pathophysiology of Heart Failure

Compared with DCM patients, poor predictive performance in ICM patients is due to the global scar burden, multiple scar segments, and regional ischemia, which may affect the remodeling response to biventricular pacing.[12] The contractility of myocardial scar tissue is impaired. Due to its electrophysiological inertia, it destroys the depolarizing waves from the adjacent myocardium, thereby prolonging the activation time of the ventricles.[12] In addition, the presence of scar tissue means that the availability of recruitable contractile cardiomyocytes is reduced to bolster myocardial pump and LV hemodynamics.[12] Therefore, placing the LV lead on or adjacent to a scar or ischemia may have a

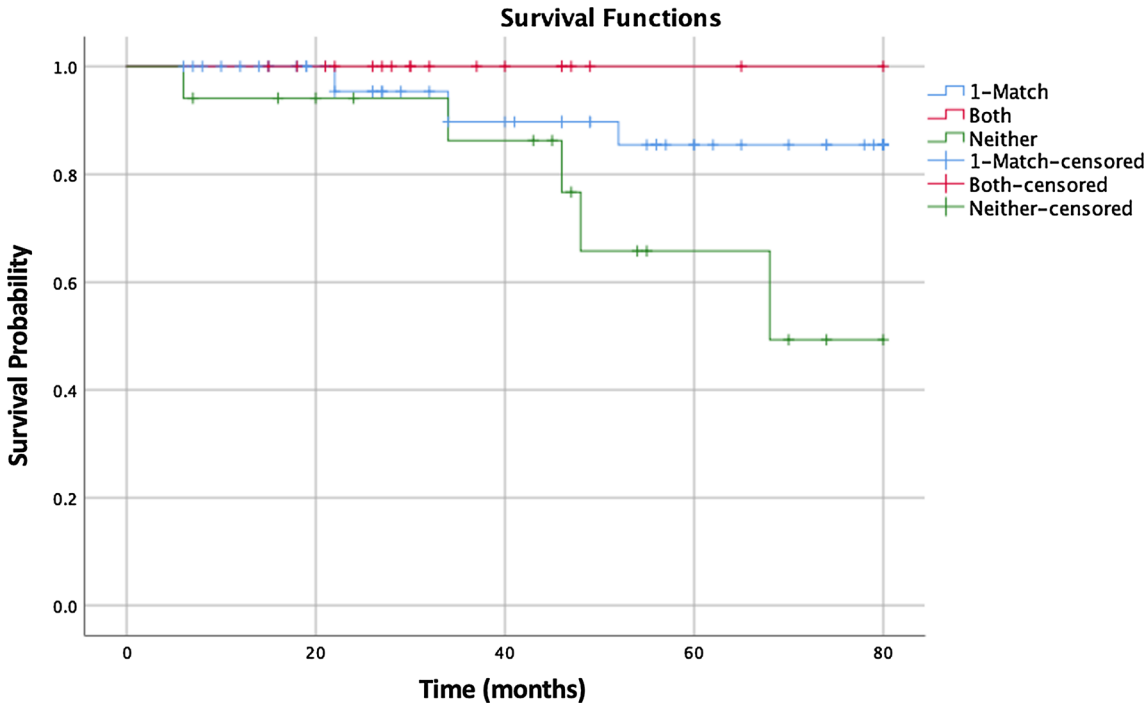

Figure 4. Kaplan-Meier event-free survival curve of DCM patients (log-rank Chi-Square = 5.98, *P* = .050).

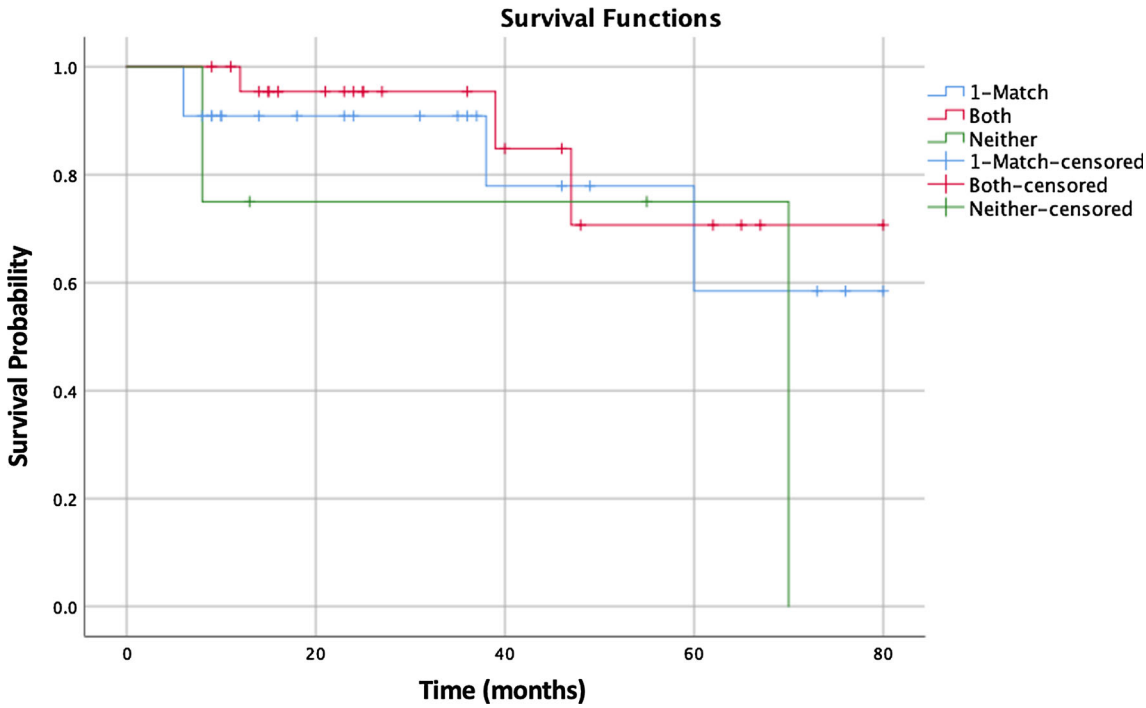

Figure 5. Kaplan-Meier event-free survival curve of ICM patients (log-rank Chi-Square = 1.33, *P* = .514).

poor effect. These results indicate that routine ischemia assessment before CRT device implantation may help identify CRT responders and help guide the placement of LV lead.

Study Limitations

The main study limitation was the small number of retrospective patients, which limited the statistical analysis and the generalizability of our findings. Using two different imaging modalities to identify the latest contraction or relaxation segments by SPECT MPI and the location of LV lead by coronary venography limited the granularity that can describe the location and consistency of LV lead. However, this definition method has gained wide acceptance.[12,25,26]

NEW KNOWLEDGE GAINED

The role of systolic and diastolic LVMD for CRT patient selection and guide LV lead placement is still unclear. This study demonstrates that systolic PBW, diastolic PBW and PSD, concordance between LV lead with the latest contraction or relaxation segment were independent predictive variables for CRT patient selection in DCM patients. In particular, in our sample, the same conclusion was not found in ICM patients.

CONCLUSIONS

Compared with ICM patients, systolic PBW, diastolic PBW and PSD have better predictive and prognostic values for the CRT response in DCM patients. Placing the LV lead on or adjacent to the latest contraction and relaxation position can improve the clinical outcomes of DCM patients, but it does not apply to ICM patients.

Disclosure

All authors declare that there are no conflicts of interest.

Author contributions

ZH—Contribution: Conception and design; analysis and interpretation of data; drafting of the manuscript and revising it critically for important intellectual content. DL—Contribution: Revising it critically for important intellectual content. CC—Contribution: Revising it critically for important intellectual content. H-YQ—Contribution: Revising it critically for important intellectual content. ZZ—Contribution: Revising it critically for important intellectual content. XH—Contribution: Revising it critically for important intellectual content. JZ—Contribution: Revising it critically for important intellectual content. M-LC—Contribution: Revising it critically for important intellectual content. CW—Contribution: Acquisition, analysis, and interpretation of data; revising the manuscript critically for important intellectual content. WZ—Contribution: Conception and design; analysis and interpretation of data; revising the manuscript critically for important intellectual content; and final approval of the manuscript submitted.

Declarations

Ethical approval

The study was approved by the scientific councils of the participating county scientific councils and complied with the Declaration of Helsinki. Written informed consent was obtained from all participants, and patient anonymity was maintained during data analysis.

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