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ORIGINAL ARTICLE

Evaluating the response to cardiac resynchronization therapy performed with a new ventricular morphology-based strategy for congenital heart disease

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Abstract

Background In cardiac resynchronization therapy (CRT) for patients with congenital heart disease (CHD) and a ventricular morphology other than a systemic left ventricle (LV), we previously proposed pacing sites that are different from those used for a systemic LV. The leads should be placed laterally on opposite sides of both ventricles in patients with short-axis dyssynchrony and a single ventricular physiology with two ventricles, whereas they should be placed at the farthest sites along the longitudinal direction in the right ventricle (RV) in patients with long-axis dyssynchrony of the RV. Moreover, in patients with interventricular dyssynchrony and a biventricular physiology with a systemic RV, they should be placed at sites that both ventricles can contract simultaneously. We retrospectively investigated 27 consecutive procedures in 24 patients with CHD who underwent CRT to evaluate the effectiveness of a new ventricular morphology-based CRT strategy. The responder rate was 63% (17/27). The reasons for a non-response to CRT in 10 cases were as follows: non-optimal lead positions during CRT, 4; no systemic ventricular conduction delay or heart failure symptoms before the CRT, 5; short follow-up periods after the CRT, 2; and an extremely dilated systemic RV, 1. The responder rate became 88% (14/16), after excluding the procedures without a ventricular conduction delay or heart failure symptoms and those with non-optimal lead positions. This new strategy for CRT can provide favorable results for CHD patients with a systemic ventricular conduction delay and heart failure.

Keywords Congenital heart disease · Cardiac resynchronization therapy · Ventricular morphology · Responder rate · Non-responder

Introduction

Cardiac resynchronization therapy (CRT) is a well-established treatment for adult patients with left ventricular (LV) systolic dysfunction without congenital heart disease (CHD), particularly for those with a left bundle branch block pattern [1]. However, few studies have reported the effectiveness of CRT in CHD patients with heart failure because of the diversity of the ventricular morphology [2–4]. Figure 1 shows the ventricular morphologies that we should consider when we perform CRT. In a biventricular physiology (BiV) with a systemic LV, the subpulmonary right ventricle (RV) is also as important as the diseased ventricle in patients with CHD. The three types of single ventricular physiologies (SV) are an LV, biventricular, and RV morphology. An LV-type SV usually has a rudimentary RV. The RV-type SV is classified as that with or without a rudimentary LV. Further, the BiV with a systemic RV is also an important issue.

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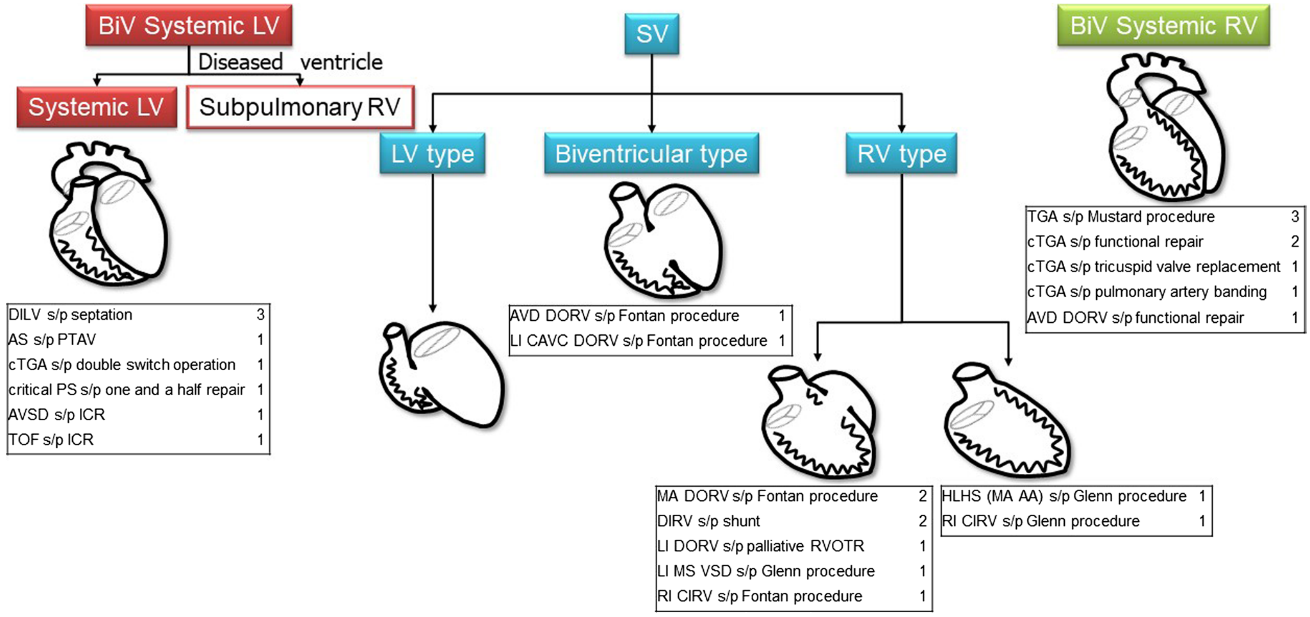

Fig. 1 Ventricular morphology relevant to cardiac resynchronization therapy. Detailed diagnoses of the 27 procedures are shown with a classification of the ventricular morphology. *AA(S)* aortic atresia (stenosis), *AVD* atrioventricular discordance, *AVSD* atrioventricular septum defect, *BiV* biventricular physiology, *CAVC* common atrioventricular canal defect, *CIRV* common inlet right ventricle, *(c)TGA*, (corrected) transposition of great arteries, *DIL(R)V* double inlet left (right) ventricle, *DORV* double-outlet right ventricle, *HLHS* hypoplastic left heart syndrome, *ICR* intracardiac repair, *L(R)I* left (right) isomerism, *LV* left ventricle, *MA(S)* mitral atresia (stenosis), *PTAV* percutaneous transluminal aortic valvuloplasty, *RV* right ventricle, *RVOTR* right ventricular outflow tract reconstruction, *s/p* status post, *SV* single ventricular physiology, *TOF* tetralogy of Fallot, *VSD* ventricular septal defect

We previously presented the following three unique types of dyssynchrony in a SV and BiV with a systemic RV: short-axis dyssynchrony in an SV with two ventricles, long-axis dyssynchrony of the RV in a systemic RV, and interventricular dyssynchrony in a BiV with a systemic RV (Fig. 2) [5, 6]. In addition, we proposed that the pacing sites should be determined depending on these cardiac dyssynchrony types.

In the case of intraventricular dyssynchrony within a systemic LV, we followed the same method used for general adult patients, wherein the RV apex and opposite side of the RV apex on the LV free wall were used for pacing

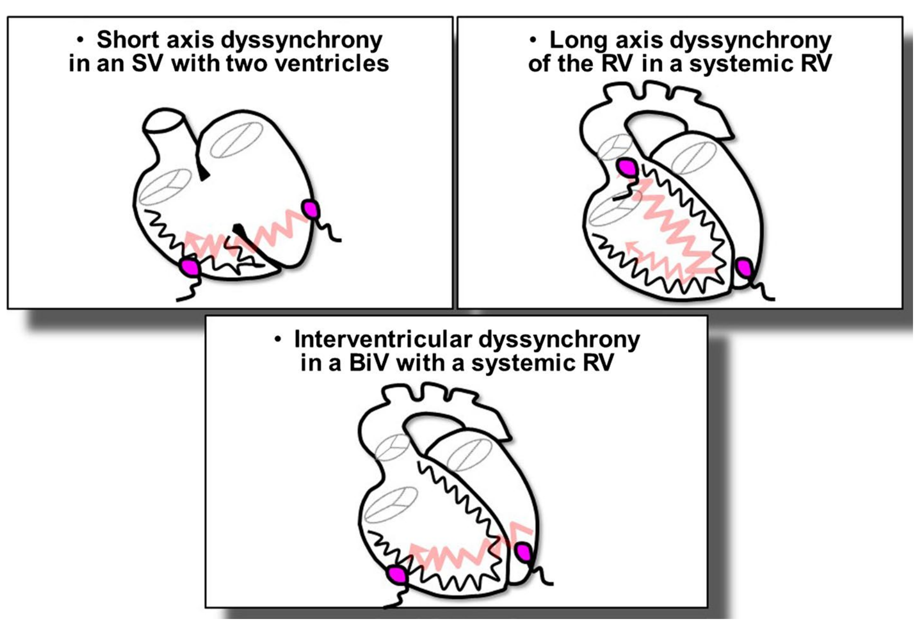

Fig. 2 Dyssynchrony types and pacing lead positions for cardiac resynchronization therapy. The dyssynchrony types and the ideal pacing lead positions for cardiac resynchronization therapy (CRT) are illustrated based on our previous papers [5, 6]. The arrows with a zigzag manner present the sequence of the ventricular conduction before the CRT, and the pink tadpole-shaped marks show the pacing lead position that we should consider for implantation. The abbreviations are as in Fig. 1

sites. However, in the other types of ventricular morphologies, we should consider different CRT pacing sites from those used for a systemic LV. Figure 3 shows the ideal pacing lead positions, depending on the ventricular morphologies and types of cardiac dyssynchrony. We proposed a new strategy that aimed to implant the pacing leads at ideal positions based on these ideas.

The purpose of this study was to assess the effectiveness of CRT in patients with CHD with this new strategy, investigate the cause of non-responders among these patients, and discuss the further steps that would improve the responder rate for CRT.

Materials and methods

Patients

Thirty-one consecutive procedures in 28 patients with CHD underwent CRT at the National Cerebral and Cardiovascular Center from July 2008 to December 2016. One patient with a diseased subpulmonary RV was excluded because it was not included our ventricular morphology-based CRT strategy. Three patients who died during perioperative period of other surgery at the same time as CRT implantation were also excluded. We retrospectively evaluated 27 procedures in 24 patients. Twelve patients with a systemic RV whose cases were reported previously were included [5, 6]. Three patients underwent a re-lead implantation after the initial CRT procedure.

Evaluation before the CRT

The evaluation before the CRT and determination of the pacing lead position before the CRT were performed by methods described previously [5].

In all 27 procedures, the patients underwent cardiac catheterization and ventriculography before the CRT. Cine angiographies were performed with 15 or 30 frames/s. An electrophysiological study was conducted for 23 procedures to examine the intracardiac electrograms and evaluate the acute effects of ventricular resynchronization caused by pacing from an electrode catheter that fused with the basic rhythm before the CRT; the study was not conducted in 2 patients with a BiV with systemic LV and 2 with a BiV with systemic RV. The acute effects were evaluated by the dP/dt max and ventriculography of the systemic ventricle.

Positions of the pacing leads

The pacing lead positions for CRT were decided on the basis of ventriculography results and intracardiac electrograms. First, we attempted to place the leads in an area that exhibited the most delayed motion by ventriculography. Next, we selected a position that showed the greatest delay from the QRS onset on the intracardiac electrograms. For patients who had none of the mechanical dyssynchrony patterns, the leads were positioned on the basis of the intracardiac electrograms [5].

To define the sRV pacing site, the RV free wall was divided into six regions according to the classification of the ventricular septum (Fig. 4a) [7]. Furthermore, the 17-segment model of the LV proposed by the American Heart

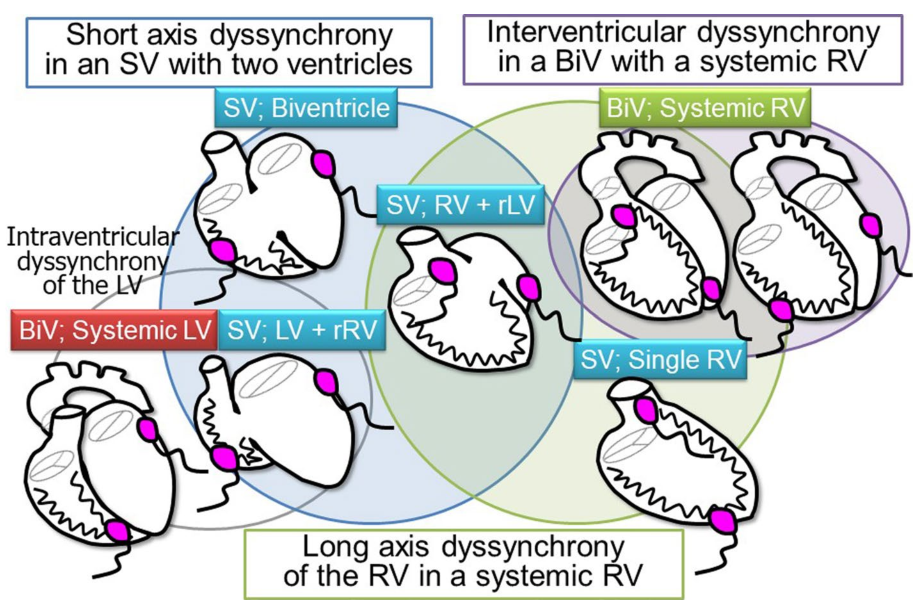

Fig. 3 The proposed pacing lead positions for cardiac resynchronization therapy based on the ventricular morphology with or without the three dyssynchrony types. The blue, green, and purple circles show the ventricular morphologies with short-axis dyssynchrony in the SV with two ventricles, long-axis dyssynchrony of the RV in a systemic RV, and interventricular dyssynchrony in a BiV with a systemic RV, respectively. *rLV* rudimentary LV, *rRV* rudimentary RV. The other abbreviations are as in Fig. 1

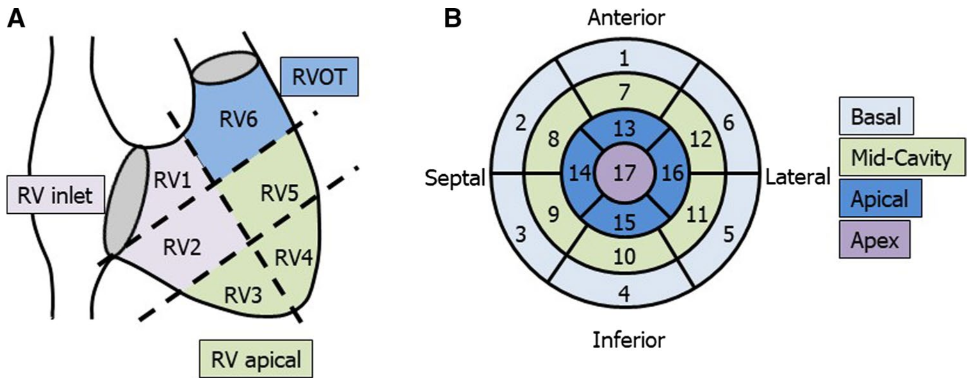

Fig. 4 Definition of the lead position. **a.** RV pacing site. The RV free wall was divided into six regions by first splitting it into anterior and inferior halves by drawing a line from the membranous portion to the apex and then dividing the base–apex length into thirds, following the classification of the ventricular septum. The basal and middle regions inferiorly correspond to the inlet portion of the RV (RV1 and RV2), and the two apical regions plus the anterior middle region match the antero-apical trabecular area (RV3, RV4, and RV5). The remaining antero-basal region corresponds to the outflow tract (RV6) [5, 7]. **b** LV pacing site. The 17-segment model of the LV proposed by the American Heart Association was used [8]. RVOT, right ventricular outflow tract. The other abbreviations are as in Fig. 1

Association was used to define the LV pacing site (Fig. 4b) [8].

We defined the pacing lead positions in Fig. 2 as being optimal [5, 6]. In patients with short-axis dyssynchrony in an SV with two ventricles, the pacing leads should be laterally placed on opposite sides of both ventricles. In patients with long-axis dyssynchrony of the RV, they should be placed at furthest sites along a longitudinal direction in the RV. In patients with interventricular dyssynchrony in a BiV with a systemic RV, these leads should be placed at sites that could contract both ventricles at the same time.

CRT

Of the 27 procedures studied, 16 (59%) had permanently paced ventricles before the CRT. Fifteen were paced with transthoracic epicardial leads and 1 with a transvenous endocardial lead. The pacing leads for CRT were implanted by the transthoracic epicardial approach in 24 procedures, five of which were implanted at the same time as other cardiac surgeries. In two procedures the leads were implanted by the transvenous approach (patients #3, 9 in Table 2). In another procedure, CRT was performed with a previously implanted transthoracic epicardial lead and newly implanted transvenous endocardial lead (patient #10 in Table 2). The pacing lead positions had been decided before the procedure as mentioned in the previous section. During CRT procedures, we implanted the lead within the area where had been already decided, searching the most delayed local ventricular potential from the QRS onset of the basic rhythm, and the stable pacing threshold. All procedures used dual-chamber pacemakers with CRT, but two procedures were performed under chronic atrial fibrillation and atrioventricular block with > 98% cumulative ventricular pacing. CRT was performed with ventricular pacing from two leads in 25 procedures, with fusion of the ventricular pacing from the two leads and the intrinsic QRS in five. Two procedures were performed with an implanted cathode and anode in the RV and LV with a single bipolar epicardial lead. The Ishikawa method [9] was used to optimize the atrioventricular delay in the patients with complete atrioventricular block assessable by echocardiography. For the five patients who underwent CRT to fuse the ventricular pacing with its own wide QRS rhythm, the atrioventricular delay was set as long as its own PR interval. The VV delay was set to make the QRS width in the electrocardiogram become narrower.

Definition of a responder

For the follow-up, ventriculography was performed 0.09–3.97 years (median 0.67 years) after the CRT implantation in 23 procedures. We defined a CRT responder as having a < − 15% change in the systemic ventricular end-systolic volume index (SyVESVI), as measured by cine angiography [10]. Among the responders, we defined super-responders when the change in the SyVESVI was < − 30% [10].

For the 4 procedures that the SyVESVI was unavailable after the CRT, a procedure should have met any of the following criteria to be regarded as a CRT responder: < − 5% change in the cardiothoracic ratio (CTR) or an improvement as per the New York Heart Association (NYHA) Functional Classification during the follow-up [5].

Patient characteristics and treatment outcomes

The following parameters were assessed to evaluate the patient characteristics: diagnosis of any cardiac defects, ventricular morphology (Fig. 1), lead position of the previous permanent pacemaker implanted before the CRT, NYHA Functional Classification, QRS duration, CTR (determined based on the chest radiography), brain natriuretic peptide levels, and α-human atrial natriuretic polypeptide (α-hANP) levels. Ventricular morphology of each patient was classified as in Fig. 1. The patients with a physiological single ventricle, such as those with a Fontan circulation, were classified with an SV, even when they had anatomically two ventricles. Furthermore, Simpson's rule was used to measure the ventricular volumes by cine angiography. The end-diastolic and end-systolic volumes were divided by the body surface area to obtain the end-diastolic and end-systolic volume indexes, and the ventricular ejection fraction was calculated. The systemic ventricular volume was defined as the LV + RV volume in patients with a BiV-type SV.

First, the responder rate was assessed in all procedures and in the procedures for the different ventricular morphologies. Second, the patient characteristics before the CRT and the changes in the QRS duration and systemic ventricular volume before and after the CRT were assessed to evaluate any variations between the responders and non-responders in terms of these parameters. Third, the patient characteristics in the non-responders were evaluated in detail to identify the reason for a non-response to the CRT. Finally, after the patient selection, the responder rate was re-assessed based on the reason for the non-response to the CRT.

Statistical analysis

The continuous values are presented as means ± standard deviations, unless otherwise specified. Skewed data are presented as the median and range. A two-tailed paired, unpaired Student test, or Wilcoxon signed rank-sum test was used for comparisons between responders and non-responders, and between the results before and after the CRT in the responders and non-responders, whichever was appropriate with regard to a normal distribution (Shapiro–Wilk test). JMP 13 statistical software (SAS Institute, Cary, NC, USA) was used to perform all statistical analyses. A p value of < 0.05 was considered statistically significant.

Results

Patient characteristics before the CRT

The patient characteristics before the CRT for the 27 procedures are shown in Table 1. Eight procedures (30%) were performed in patients with a BiV with a systemic LV. Eleven (40%) were performed in patients with an SV—two BiV

Table 1 Patient characteristics

	n	All	*N*	Responder	*n*	Non-responder	*p*
n		27		17 (63%)		10 (37%)	
Age at CRT (years)	27	20.4, 1.8–53.1	17	11.2, 1.8–47.3	10	27.9, 4.0–53.1	ns
Follow-up period after the CRT (years)	27	3.8 ± 2.8	17	3.6 ± 2.9	10	4.1 ± 2.8	ns
Before CRT							
Ventricular pacing		16 (59%)		10 (59%)		6 (60%)	ns
QRS duration (ms)	27	179 ± 40	17	176 ± 38	10	183 ± 47	ns
CTR (%)	26	57.2 ± 9.6	17	56.8 ± 9.2	9	58.1 ± 10.6	ns
BNP (pg/ml)	27	129.1, 13.2–969.7	17	104.7, 13.2–969.7	10	191.2, 21.4–767.1	ns
NYHA II or III		23 (85%)		14 (82%)		9 (90%)	ns
SyVEDVI (ml/m^2)[a]	27	129.1 ± 46.6	17	125.9 ± 42.3	10	134.4 ± 55.1	ns
SyVESVI (ml/m^2)[a]	27	87.1 ± 35.7	17	85.1 ± 31.2	10	90.5 ± 43.7	ns
SyVEF (%)[a]	27	31, 23–57	17	31, 23–52	10	30, 26–57	ns
Ventricular morphology							
BiV systemic LV		8		5		3	
SV		11		8		3	ns
BiV systemic RV		8		4		4	

The numbers in parentheses indicate the rate of each item in the responder and non-responder groups

CRT cardiac resynchronization therapy, *CTR* cardiothoracic ratio, *BNP* natriuretic peptide, *NYHA* New York Heart Association Functional Classification, *BiV* biventricular physiology, *LV* left ventricle, *RV* right ventricle, *SV* single ventricular physiology, *SyVEDVI* systemic ventricular end-diastolic volume index, *SyVESVI* systemic ventricular end-systolic volume index, *SyVEF* systemic ventricular ejection fraction

[a]SyVEDVI, SyVESVI, and SyVEF were measured by cine angiography using Simpson's rule

type; seven RV type with a rudimentary LV; and two RV type without a rudimentary LV. Eight procedures (30%) were performed in patients with a BiV with systemic RV. The detailed cardiac defects of each ventricular morphology are shown in Fig. 1.

Responder rate

Responders were found in 17 (63%) of 27 procedures (Fig. 5a). Cine angiography was performed in 23 procedures after the CRT, and 16 procedures were judged as responders by a $< -15\%$ SyVESVI change (Fig. 6c). In the other one procedure, an improvement as per the NYHA Classification during the follow-up was observed. There was no statistical difference between the types of ventricular morphologies in terms of responder rates, whereas the responder rate was 50% for the BiV with a systemic RV. Seven procedures had a super-response to CRT (Fig. 5a).

Comparison between responders and non-responders (Fig. 6)

Before the CRT, no differences were observed between the responders and non-responders in terms of the patient characteristics (Table 1). The QRS duration (before and after the CRT) significantly shortened in both the responders and non-responders, but no significant differences in the Δ QRS duration were found between the two groups (-51 ± 27 vs. -31 ± 43 ms, $p = \text{ns}$). In the responders, the SyVEDVI (Δ SyVEDVI, -22.9 ± 28.2 ml/m^2, $p = 0.0054$) and SyVESVI [Δ SyVESVI, -16.7 (-68, -9.4) ml/m^2, $p < 0.0001$] significantly decreased, and the SyVEF (Δ SyVEF, $8.8\% \pm 12.0\%$, $p = 0.0102$) increased after the CRT. However, no differences were observed in the SyVEDVI (Δ SyVEDVI, -3.2 ± 11.8 ml/m^2, $p = \text{ns}$), SyVESVI (Δ SyVESVI, 5.0 ± 13.2 ml/m^2, $p = \text{ns}$), and SyVEF (Δ SyVEF, $-0.2\% \pm 7.3\%$, $p = \text{ns}$) in the non-responders. The Δ QRS duration, Δ SyVEDVI, Δ SyVESVI, and Δ SyVEF did not differ between the ventricular morphologies (BiV with a systemic LV, SV, and BiV with a systemic RV) among the responders.

Reasons for the non-responders to CRT

The detailed patient characteristics in the 10 non-responders are shown in Table 2. To assess the reasons for the non-response to CRT, four patients had non-optimal pacing lead positions during the CRT (patients 2, 6, 7, and 9). Four patients had no systemic ventricular conduction delays (patients 1, 3, 7 and 10). Patient 8 had no heart failure symptoms (NYHA class I) before the CRT. The systemic RV in patient 4 was too dilated (RVEDVI = 243.5 ml/m^2) to prompt reverse remodeling of the RV, whereas the NYHA functional class improved from III to II after the CRT. Patients 5 and 10 had a short follow-up period after the CRT (0.1 and 0.5 years) to evaluate the chronic effects of CRT, and ventricular volume after CRT by cine angiography was not determined in these patients.

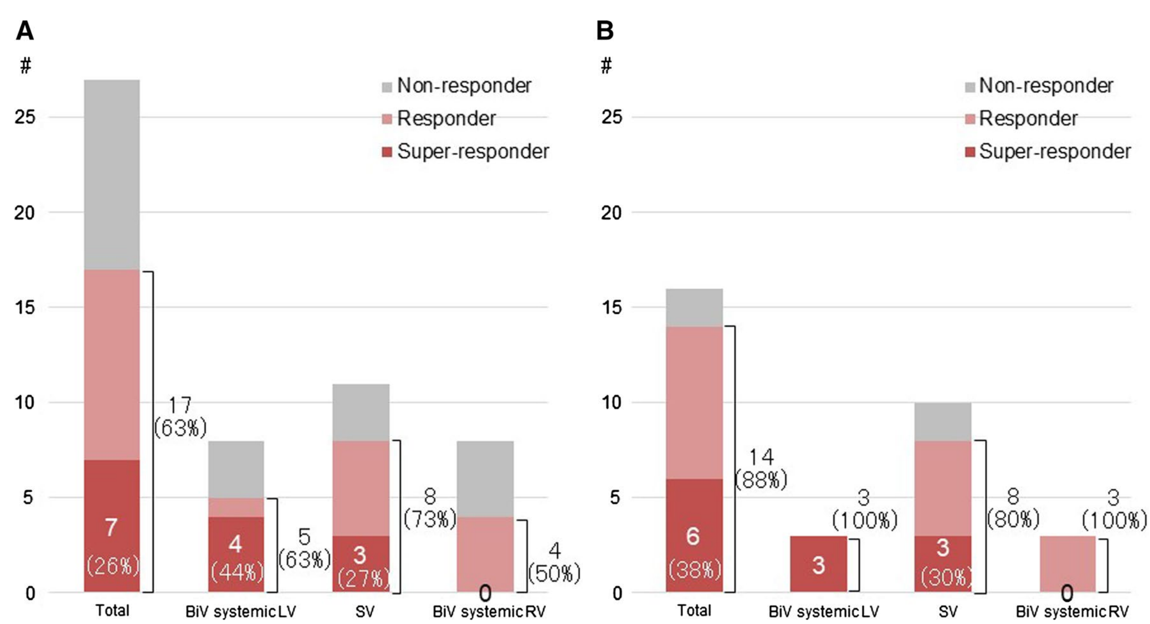

Fig. 5 Responder and super-responder rates. The responder and super-responder rates of the 27 (**a**), and 16 procedures after excluding those without systemic ventricular conduction delays or without heart failure symptoms before the CRT and non-optimal lead positions during the CRT (**b**). The abbreviations are as in Fig. 1

Heart and Vessels (2019) 34:1340–1350

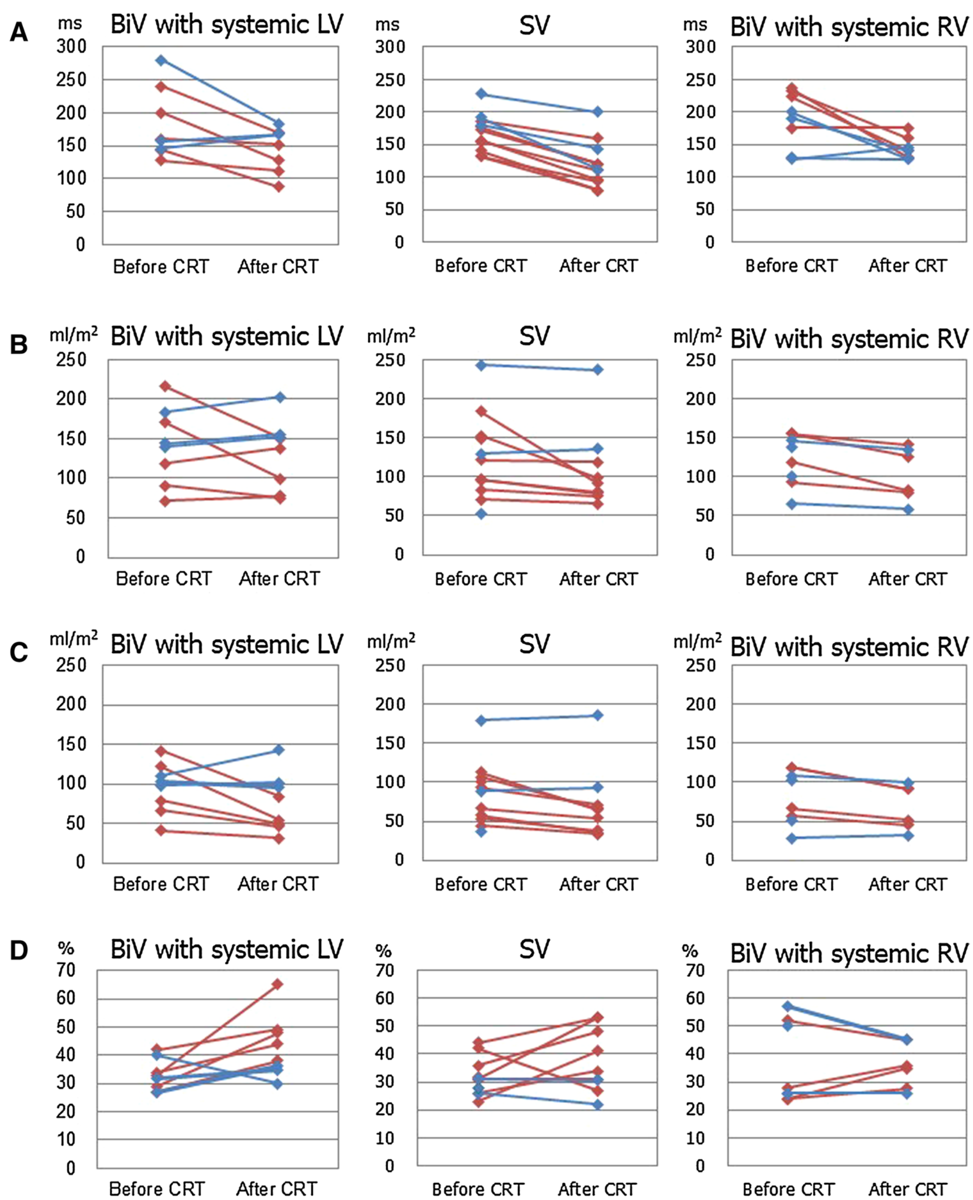

Fig. 6 Clinical data before and after CRT. The clinical data of the QRS duration (**a**), systemic ventricular volume end-diastolic volume index (SyVEDVI) (**b**), systemic ventricular volume end-systolic volume index (SyVESVI) (**c**), and systemic ventricular ejection fraction (SyVEF) (D) before and after the CRT are shown in patients with a BiV and a systemic LV, SV, and BiV and a systemic RV. The red indicates the responders, and the blue the non-responders. The abbreviations are as in Fig. 1

Responder rate after patient selection for CRT

Among the 27 procedures, no systemic ventricular conduction delay was observed in five procedures, and no heart failure symptoms were observed in two procedures (NYHA class I) before the CRT. In addition, the pacing lead positions during CRT were not optimal in five procedures. When we excluded 11 procedures without a systemic ventricular conduction delay or without the heart failure symptoms (NYHA class I) before the CRT and those with non-optimal lead positions during the CRT, the responder rate improved to 88% of 16 procedures, including six super-responders (Fig. 5b). Of the 11 excluded procedures, three were responders: one without a ventricular conduction delay before the CRT, one without heart failure symptoms, and one with a non-optimal lead position during the CRT. CRT was performed at the same time as the other cardiac surgeries in two of those three patients with a corrected transposition of the great arteries.

CRT response in the procedures which performed the other cardiac surgeries at the same time

Among five procedures at the same time as other cardiac surgeries, two were non-responders (patients 2 and 8 in Table 2) and three were responders. In two of three responders, the decrease in SyVESVI was most likely due to the surgical intervention, because one performed double-switch operation showed without a ventricular conduction delay before the CRT, and one performed tricuspid valve replacement

Table 2 Characteristics of the non-responders

Pt	1	2	3	4	5	6	7	8	9	10
Diagnosis	Critical PS, hypoplastic RV	DILV	AVSD	Lt iso, DORV, PA	MA, DORV	DIRV	cTGA	cTGA	cTGA s/p TVR	TGA
Operative status	One and a half repair	Septation	ICR	Palliative RVOTR	Fontan	BT shunt	PA banding	Functional repair	TVR	Mustard
Ventricular morphology	BiV with systemic LV	BiV with systemic LV	BiV with systemic LV	SV	SV	SV	BiV with systemic RV	BiV with systemic RV	BiV with systemic RV	BiV with systemic RV
Age at CRT (years)	26.6	28.5	46.3	4.1	27.4	38.4	4.0	9.4	35.7	53.1
Pacing lead position at CRT[a]	 RV2, LV13	 LV7, LV10	 RV3, LV5	 RV3, RV 6	 RV2, RV6	 RV2, RV4	 RV4, LV17	 RV2, LV17	 RV3, LV17	 RV2, LV17
Basic rhythm	RBBB	LBBB	RBBB	RV pacing (RV3)[a]	RV pacing (RV2)[a]	RV pacing (RV2)[a]	RV pacing (RV4)[a]	RV pacing (RV1)[a]	RBBB	RV pacing (RV2)[a] +own QRS
Before CRT										
QRS duration (ms)	157	280	146	180	192	228	130	200	190	128
CTR (%)	69.7	ND	56.3	72.2	46.2	71.6	55.3	44	52.4	55.6
BNP (pg/ml)	339	32.6	239.9	691.9	108.3	767.1	142.5	21.4	273.6	129.1
NYHA II or III	III	II	II	III	II	III	II	I	II	II
SyVEDVI (ml/m^2)	144.5	140.1	189.9	243.5	52.1	129.4	65.7	100	146.6	138.3
SyVESVI (ml/m^2)	97.8	102.7	110.4	179.4	37.7	89	28.4	50.1	107.9	101.7
SyVEF (%)	32	27	40	26	28	31.2	57	50	26	26
Follow-up period after CRT (years)	5.6	6.7	6.7	4.2	0.5	2.7	1.5	8.3	5.2	0.1
Δ QRS (ms)[b]	11	−96	22	−36	−80	−28	−2	−72	−50	18
Δ SyVESVI (%)[c]	3.6	−5.8	29.0	1.0	ND	1.0	13.0	ND	−8.1	ND

TVR tricuspid valve replacement

The other abbreviations are as in Fig. 1 and Table 1

[a]The pacing lead positions are shown in Fig. 4. The blue tadpole-shaped marks show the pacing lead positions. The solid and dotted lines show the transthoracic and transvenous leads, respectively

[b]ΔQRS (ms) = QRS duration after the CRT–QRS duration before the CRT

[c]SyVESVI (%) = (SyVESVI after the CRT–SyVESVI before the CRT)/SyVESVI before the CRT × 100

showed with a non-optimal lead position during the CRT. These two procedures were excluded when we evaluated the responder rate after patient selection for CRT. Other one responder which performed common atrioventricular valve replacement showed a favorable reaction in CRT with the improvement in a systemic ventricular conduction delay.

Discussion

The results of this study indicated that there was a 63% responder rate for CRT in patients with CHD when performed with a new strategy that aimed at implanting the pacing leads at ideal positions, depending on the ventricular morphologies and cardiac dyssynchrony types. Moreover, when we chose the patients with a ventricular conduction delay and with heart failure symptoms, which were higher than NYHA class II, and implanted the pacing leads at the optimal positions suggested, the responder rate improved to 88%.

Shortness of the QRS duration in the non-responders

The QRS duration significantly decreased after the CRT even in non-responders. CRT can somehow improve the electrical conduction dyssynchrony in most patients with CHD. However, this improvement in the electrical conduction synchronicity was not directly related to the ventricular volume reduction, which is reverse remodeling. In the report of adult CRT recipients without CHD, a larger decrease in the QRS duration after the CRT initiation showed greater echocardiographic reverse remodeling [11]. However, the same study revealed that approximately 40% of patients with a shortened QRS duration after the CRT had an unchanged or worsened clinical status, implying that the CRT should aim to improve the mechanical dyssynchrony rather than electrical dyssynchrony expressed by the QRS duration.

A new ventricular morphology-based strategy for patients with congenital heart disease

The mechanical dyssynchrony in patients with CHD is different from that in patients without CHD because of a heterogeneous ventricular morphology. We previously reported the unique patterns of mechanical dyssynchrony in CHD, based on the ventricular morphology (Fig. 2) [5, 6]. We believe that the choice of lead positions determined after taking these dyssynchrony patterns into account is necessary to improve the mechanical dyssynchrony in patients with CHD.

However, our strategy has technical limitations. In most patients, the transthoracic epicardial approach is needed to implant leads at the optimal position rather than the transvenous endocardial approach. Previous surgical procedures can often hinder an effective epicardial lead placement because of pericardial fibrosis, adhesions, or a high pacing threshold [12]. The risk of lead failures of epicardial leads due to fractures, insulation breaks, outgrowth, or exit block has gradually decreased over the years, but still remains higher than that of endocardial leads [13].

Improving the responder rate for CRT in patients with CHD

The major factors that affect the response to CRT, modified from a study on adult CRT recipients to fit patients with CHD, are the presence and location of the ventricular conduction delay, presence and location of mechanical dyssynchrony, condition of the myocardial damage, pacing lead positions, and device programming [14, 15]. The reasons for 9 of the 10 non-responders in the present study also matched those factors: non-optimal lead positions during CRT, no systemic ventricular conduction delay or heart failure symptoms before the CRT, and an extremely dilated systemic RV with extensive myocardial fibrosis. The chronic effects of CRT on the other one procedure (patient 5) were not evaluated because of a short follow-up period, which might turn out to be effective in the chronic phase.

To improve the effect of CRT in patients with CHD, we should choose the right patients and implant pacing leads in the optimal positions. These patients should be those with "clustered" ventricular mechanical dyssynchrony; a "clustered" contraction delay should be observed between the ventricle where we targeted an improvement by the CRT and other parts of the ventricle [16]. Stated differently, when we perform CRT for a diseased systemic ventricle, there must be a conduction delay within that systemic ventricle in order to achieve an effective CRT.

After the selection of the procedures with a conduction delay or heart failure symptoms before the CRT and that were suited for our new strategy of choosing the pacing lead positions, the response rate became 88% (14 of 16 procedures), which was a quite favorable result. Two non-responders after the selection had an extremely dilated RV and short follow-up periods (patients 4 and 5).

Study limitations

This study had several limitations. The sample size was small, and the basic cardiac anomalies were heterogeneous. In addition, the ventricular volumes were measured by cine angiography to evaluate all patients with one modality; however, magnetic resonance imaging is the mainstream of the volume measurements. In 4 of 27 procedures, cine angiography was not performed after the CRT, and the ventricular volume was not evaluated. As previously mentioned, implanting pacing leads at the ideal positions had technical limitations. Further, in this retrospective study, the patterns of the mechanical dyssynchrony were evaluated by cine angiography rather than by echocardiography. Even in adults without CHD, the detection of mechanical dyssynchrony by echocardiography is limited [17], and the echocardiographic results of dyssynchrony are not included in the criteria of CRT induction in the respective guidelines. Particularly, the mechanical dyssynchrony of the RVOT is difficult to evaluate by echocardiography because of its anterior position in the chest, heterogeneous anatomies, and misalignment of the remaining body of the RV [5]. Nevertheless, these results are valuable for assessing the effectiveness of CRT in patients with CHD with our new strategy.

Conclusion

The new strategy that aimed to implant the pacing leads in an ideal position depending on the ventricular morphology and cardiac dyssynchrony type in patients with CHD can provide favorable results when we choose patients with a systemic ventricular conduction delay and dysfunction. Further study is mandatory to identify the detailed factors of non-responders with this strategy.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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