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The Efficacy of Including His-Purkinje Conduction System Pacing (HP-CSP) In Synchronized Pacing Compared With Biventricular Pacing In Patients after Long-Term Cardiac Resynchronization Therapy (CRT)

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Abstract

Background: The benefit obtained from Cardiac Resynchronization Therapy (CRT) gradually decreases as HF progresses. It is still unknown that His-Purkinje Conduction System Pacing (HP-CSP) could maintain the benefit from CRT. We prospectively assessed the efficacy of an HP-CSP upgrade in a group of patients undergoing long-term CRT.

Methods: We compared thirteen patients who were prospectively upgraded to HP-CSP (upgrade group) and fourteen patients who were maintained on BiVP (replacement group) in the CRT replacement procedure in this study. Pacing parameters, echocardiograms, electrocardiograms and the New York Heart Association (NYHA) classification were assessed at baseline, before replacement and during follow-up.

Results: The QRS duration was significantly shorter after the upgrade in the HP-CSP upgrade group (169.5±33.8ms to 123.6±15.3ms, P=0.0008) and the replacement group (123.6±15.3 vs 160.2±25.2ms; P=0.0001). During the approximately 1-year follow-up, LVESV showed more decreased in HP-CSP upgrade group than replacement group (94.7±65.5ms vs 156.5±78.2ms, P=0.04) and LVEF showed significantly improved in HP-CSP upgrade group compared with replacement group (45.7±13.9ms vs 36.3±11.2ms, P=0.06). 10 of 13 patients (76.9%) were clinical responders after the HP-CSP upgrade compared with the baseline, while only 4 of 14 patients (28.6%) maintained a response in the replacement group.

Conclusions: Including HP-CSP in synchronized pacing configurations may improve the cardiac function of patients who did not acquire sufficient benefit from traditional CRT, and an upgraded to HP-CSP could be considered to maintain the efficacy of CRT in the patients after long-term CRT.

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Introduction

CRT is an effective method for treating HF patients with electrical dyssynchrony. The benefit obtained from CRT gradually decreases as HF progresses [1]. CRT decreased HF risk by approximately 20% in three years, while the risk of HF increased two-fold over the long-term follow-up (6-7 years) [1]. Exploration of how to maximize the synchrony provided by the device is ongoing, not only in patients who do not respond to CRT but also in patients who benefit from CRT and seek further benefit. Successful HP-CSP has significant beneficial effects on LV reverse remodeling and clinical outcomes both in patients with CRT indications and in some BiVP nonresponders and provides an alternate method to facilitate CRT [2-4]. However, in patients who require device replacement due to battery depletion after long-term CRT, whether including HP-CSP could provide further benefit through additional synchrony is still unknown.

In this study, we included a series of patients who had received CRT at least five years prior and needed replacement due to battery depletion. We hypothesized that the addition or replacement of HP-CSP in the synchronized pacing configuration could achieve better clinical benefits in patients than retaining traditional biventricular pacing, and we prospectively assessed the feasibility, safety, and clinical outcomes of these patients.

Material and Methods

Study population

A cohort of 27 consecutive patients who had previously undergone CRT and needed to have the device replaced due to battery depletion in our institution. HP-CSP upgrades were advised to all patients, especially those with HF clinical manifestations or HF progression based on echocardiography parameters. Finally, 13 patients (6 men and 7 women) underwent HP-CSP (upgrade group). Two patients did not have a pathway to facilitate the new implant lead due to superior vena cava obstruction, and the others did not have an intention to implant a new pacing lead maintained with BiVP. These 14 patients were considered the compared group (replacement group) (Figure 1). All patients were on optimal guideline-directed medical therapy. Each patient who received an HP-CSP upgrade or device replacement signed an informed consent form. The study was approved by the hospital ethics committee.

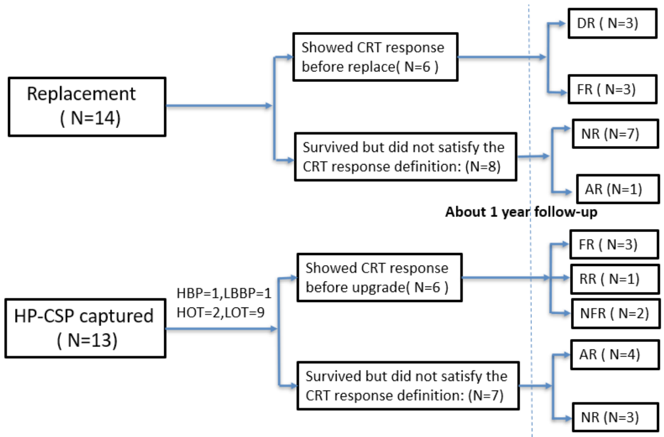


Figure 1: Flowchart of patients and CRT response results. HP-CSP: His-Purkinje conduction system pacing; HOT: His-optimized CRT; HBP: His-bundle pacing; LBBP: left bundle branch pacing; LOT: LBB-optimized CRT.

Table 1: Pacing characteristics.

Upgrade group	Device type	LV Pacing Port	RV Pacing Port	RA Pacing Port	Optimized program between two pacing ports	LBBP Stimulus–peak LVAT (Single HP-CSP)	QRS duration (ms)				Complications
							Intrinsic	Pre-upgrade	Single HP-CSP	Opti-mized	
1	CRT-D	HIS	RV apex	atrium	Single HBP	200	108	206	144	144	No
2	CRT-P	LV-ep	RV apex	LBB	20*	75	110	112	113	112	No
3	CRT-P	LV-ep	RV apex	HIS	50*	78	203	150	143	107	No
4	CRT-P	LBB	RV apex	atrium	Single LBB	90	152	134	110	110	No
5	CRT-P	LV-ep	LBB	atrium	LOT 0	84	180	142	142	122	No
6	CRT-P	LV-ep	LBB	atrium	LOT 40	82	192	136	134	120	No
7	CRT-P	LV-ep	LBB	atrium	LOT 20	85	191	158	140	136	No
8	CRT-D	LV-ep	LBB	atrium	LOT 0	86	207	178	164	154	No
9	CRT-D	LV-ep	LBB	atrium	LOT 20	160	182	172	138	135	No
10	CRT-D	LV-en	LBB	atrium	LOT 0	102	198	148	126	112	No
11	CRT-P	LV-ep	RV	HIS	20*	128	183	180	126	118	No
12	CRT-P	LBB	RV	atrium	LOT 40	76	164	130	115	105	No
13	CRT-D	LV-ep	RV apex	LBB	30*	85	134	160	152	132	No
Mean±SD						102.4± 38.0	169.5± 33.8	154.3± 25.2	134.4± 15.9	123.6± 15.3	

Replace group	Device type	LV Pacing Port	RV Pacing Port	RA Pacing Port	Optimized program between two pacing ports	QRS duration (ms)		Complications
						Intrinsic	Paced	
1	CRT-P	LV-ep	Mid-septum	atrium	LV>RV 10	134	130	No
2	CRT-D	LV-ep	RV apex	atrium	RV>LV 20	170	191	No

3	CRT-D	LV-ep	Mid-septum	atrium	LV>RV 50	134	122	No
4	CRT-D	LV-ep	RV apex	atrium	LV>RV 5	158	168	No
5	CRT-P	LV-ep	Mid-septum	atrium	LV=RV	190	168	No
6	CRT-D	LV-ep	RV apex	atrium	LV>RV 40	192	158	No
7	CRT-D	LV-ep	Mid-septum	atrium	LV>RV 40	178	196	No
8	CRT-P	LV-en	Mid-septum	atrium	LV>RV 20	184	168	No
9	CRT-D	LV-ep	RV apex	Mid-septum	30*	154	152	No
10	CRT-P	LV-ep	RV apex	atrium	LV>RV 20	189	126	No
11	CRT-P	LV-ep	Mid-septum	atrium	LV=RV	156	142	No
12	CRT-D	LV-ep	RV apex	atrium	LV>RV 40	164	151	No
13	CRT-D	LV-ep	Mid-septum	atrium	LV=RV	180	169	No
14	CRT-P	LV-ep	RV apex	Mid-septum	LV>RV 20	218	202	No
Mean±SD						171.5±23.4	160.2±25.2	

CRT: cardiac resynchronization therapy; CRT-D: CRT-defibrillator; CRT-P: CRT-pacemaker; LV: left ventricular; LBB: left bundle branch; LV-ep: left ventricular epicardium; LV-en: left ventricular endocardium; RV: right ventricular; RA: right atrium; LOT: LBB-optimized CRT; LBBP: left bundle branch pacing; LVAT: left ventricular activation time; BiVP: biventricular pacing; H-PSP: His-Purkinje system pacing.
*atrial port was connected to the His or LBB, and the interval between two pacing ports was programmed as the AV interval.

AR, CRT only showed a response after replacement or upgrade. DR, CRT only showed a response at an early stage of follow-up, and the effectiveness dissipated as the disease progressed. FR, CRT showed an enhanced response compared with that at the time before replacement, which showed a response. NFR, CRT showed a response, but there was no further response after replacement or upgrade. NR, CRT did not show obvious responses during the follow-up period. RR, CRT showed a response at an early stage of follow-up, and the effectiveness dissipated as the disease progressed, while a reshowed response was observed after replacement or upgrade.

Implantation technique

Intracardiac electrograms along with 12-lead surface electrocardiograms were continuously recorded during the procedure. The technique for HBP and LBBP was described in detail in previous reports [10,11]. In some patients, when the pacing lead could not achieve appropriate HBP, LBBP was attempted. HBP was confirmed by the previously established criteria [10]. The following criteria were used to confirm left conduction system capture [8,11]. 1) right bundle branch block configuration in lead V1 with terminal R-wave during unipolar tip pacing, with the paced QRS becoming narrow; 2). Left Bundle Branch (LBB) capture supported by abrupt shortening of the stimulus to the peak LV activation time with increasing output and then remaining short and constant at high and low outputs or by demonstration of output-dependent nonselective LBBP and selective LBBP at near-threshold outputs. 3) The position of the lead tip was under the subendocardium of the IVS; and/or. 4) Recording of LBB or Purkinje potentials during escape rhythm or premature beats (often seen when the LBBP lead is advanced near the LV septum) or during His corrective pacing. Patients who met criteria 1 and 2 and at least one of the latter two criteria were considered to have achieved LBB capture.

In the 12 patients undergoing a lead upgrade in CRT Defibrillator (CRTD) or Crt Pacemaker (CRTP) replacement, the original left lead was preserved or discarded due to the lead parameters and the QRS morphology provided by an additional HP-CSP lead. The appropriate interventricular (VV) delay and AV delay were programmed for the shortest QRS duration (QRSd). The connection method of the HP-CSP lead and the programmed setting are summarized in Table 1 for each patient.

Data collection and clinical follow-up

The time from first implantation to the second operation was reviewed and collected every 6 months after device replacement. Baseline demographics, medical history and New York Heart Association (NYHA) functional class were collected. The parameters included LVEF, LV End-Diastolic Dimension (LVEDD), LV End-Systolic Dimension (LVESD), LV End-Diastolic Volume (LVEDV) and LV End-Systolic Volume (LVESV), which were measured using Simpson's biplane and the M-mode method. The paced QRSd was measured from the end of the pacing stimulus to the end of the QRS complex. The short LV activation time (LVAT) was estimated by measuring the time from the intracardiac pacing spike to the R wave peak of the QRS complex in leads V5 and V6. Implantation-related complications and lead parameters, including unipolar tip pacing threshold, R-wave amplitude, impedance, and pacing percentage, were collected. Information regarding rehospitalization due to infection, embolism, stroke, perforation, death or heart failure was collected during the follow-up.

The CRT response was evaluated in combination with the clinical and echocardiographic responses [12]. A positive clinical response was defined as the patient 1) surviving and not being hospitalized for HF and 2) demonstrating improvement in NYHA class. Echocardiographic response was defined as 1) a reduction in LVESV≥15% or 2) an increase in LVEF≥10%. A CRT response was defined as satisfying ≥ two of the criteria mentioned above (including at least one echocardiographic response). Because the continuous efficacy of CRT pacing therapy may be affected by the progression of the disease in a relatively long-duration follow-up (at least 5 years), the CRT response was divided into six circumstances after the second operation. First, CRT only showed a response at an early stage of follow-up, and the effectiveness dissipated as the disease progressed (DR). Second, CRT did not show an obvious response throughout the entire follow-up period (NR). Third, CRT showed a response at an early stage of follow-up, and the effectiveness faded as the disease progressed, while a reshowed response was observed after replacement (RR). Fourth, CRT only showed a response after replacement or upgrade (AR). Fifth, CRT yielded an enhanced response compared with that achieved prior to replacement, which showed a response (FR). Sixth, CRT yielded a response, but there was no further response after replacement (NFR).

Statistical analyses

Continuous variables are reported as the mean±SD. Paired comparisons were performed using Student's t test if the data were normally distributed and the Wilcoxon signed-rank test if the data were nonparametric. Paired categorical data were compared using McNemar's test. P≤0.05 was considered significant.

Results

Implantation results and patient characteristics

Table 2 shows the patients' clinical characteristics. There were no significant differences between the two groups. All patients received optimized medical therapy, including β-blockers, aldosterone receptor antagonists, and angiotensin-converting enzyme inhibitors (or angiotensin receptor antagonists). The two patients who underwent the LV endocardium lead implantation were all administered anticoagulation therapy after implantation. The mean duration of pacing therapy before the second operation was 6 years, and the follow-up time ranged from 10–29 months.

Table 2: Baseline characteristics of the patients.

Paramaters		Upgrade Group (N=12)	Replace Group (N=10)	P value
Male		6 (46.2%)	9 (64.3%)	0.45
Age		66.4±11.7	63.0±7.0	0.37
Comorbidities				
Hypertension		2 (15.4%)	1 (0.7%)	0.60
Diabetes		7 (53.8%)	3 (21.4%)	0.12
Renal dysfunction		2 (15.4%)	3 (21.4%)	1.00
ICM		3 (23.1%)	5 (35.7%)	0.68
AF		5 (38.5%)	7 (50.0%)	0.70
Medication				
β-blocker		13 (100%)	14 (100%)	1.00
ACEI/ARB		13 (100%)	14 (100%)	1.00
Diuretics		11 (84.6%)	13 (92.9%)	0.60
Indication				
HF+LBBB		10 (76.9%)	10 (71.4%)	1.00
HF+HPD		3 (23.1%)	4 (28.6%)	1.00
QRSd (ms)	Intrinsic	169.5±33.8	171.5±23.4	0.86
	Pre-replace	154.3±25.2	160.2±25.2	0.55
NYHA Class (Pre-PM)		3.2±0.7	2.9±0.8	0.19
Echocardiogram				
LVEF (%)	Pre-PM	35.0±11.7	39.9±7.4	0.20
	Pre-replace	41.0±14.4	37.5±13.3	0.52
LVESV (ml)	Pre-PM	143.6±48.9	145.5±39.8	0.91
	Pre-replace	121.3±78.7	144.6±75.6	0.44

Electrocardiogram manifestation and programmed optimization

Individual electrocardiographic responses to BiVP, HP-CSP only, and His-Purkinje system optimized CRT (HPSO-CRT) are shown in Table 1. Before the second operation, the QRS duration provided by BiVP decreased moderately compared with intrinsic QRS in both the HP-CSP upgrade and replacement groups (169.5±33.8 ms to 154.3±25.2 ms in the upgrade group, 171.5±23.4 ms to 160.2±25.2 ms in the replacement group).

In the HP-CSP upgrade group, compared with BiVP, HP-CSP resulted in a further decrease in the QRSd from 154.3±25.2 ms to 134.4±15.9 ms (P=0.002 versus baseline and P=0.003 versus BiVP). However, HPSO-CRT resulted in a more robust decrease in the QRSd to 123.6±15.3 ms (P<0.01 versus baseline, BiVP, or H-PSP) (Figure 2). After the second operation, the QRS duration was significantly reduced in the HP-CSP upgrade group compared with the replacement group (P=0.0001) (Figure 2).

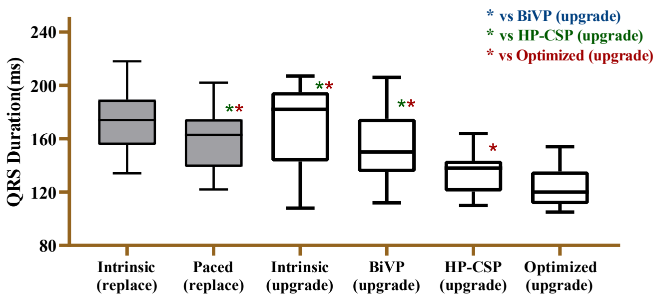


Figure 2: Flowchart of patients and CRT response results.
HP-CSP: His-Purkinje conduction system pacing; HOT: His-optimized CRT; HBP: His-bundle pacing; LBBP: left bundle branch pacing; LOT: LBB-optimized CRT.
Optimized vs HP-CSP: 123.6±15.3ms vs 134.4±15.9ms, P=0.003
Optimized vs BiVP: 123.6±15.3ms vs 154.3±25.2ms, P<0.0001
Optimized vs Intrinsic(Upgrade): 123.6±15.3ms vs 169.5±33.8, P=0.0008
HP-CSP vs BiVP: 134.4±15.9ms vs 154.3±25.2ms, P=0.003
HP-CSP vs Intrinsic(Upgrade): 134.4±15.9ms vs 169.5±33.8ms, P=0.002
BiVP vs Intrinsic(Upgrade): 154.3±25.2ms vs 169.5±33.8ms, P=0.21
Replace group:
Paced vs Intrinsic(Replace): 160.2±25.2ms vs 171.5±23.4ms, P=0.07
Upgrade group vs Replace group:
Paced vs BiVP: 160.2±25.2ms vs 154.3±25.2ms, P=0.55
Paced vs HP-CSP: 160.2±25.2ms vs 134.4±15.9ms, P=0.004
Paced vs Optimized: 160.2±25.2ms vs 123.6±15.3ms, P=0.0001.

Devices were programmed in DDD mode with the AV and VV delay optimized for the shortest QRSd post-implantation. In the upgrade group, two patients underwent HP-CSP only, which yielded a satisfactory QRS complex. Patient 1, due to a long S-QRS interval, only HBP alone could result in a satisfactory QRS morphology (Figure 3, Patient 1). Patient 4 was treated with a pacing configuration involving a right ventricular (RV) lead and LBBP, and the best QRS morphology could only be obtained with LBBP alone (Figure 3, Patient 3). There was no obvious difference in QRSd between LBBP only and LBBP in combination with an LV or RV lead in patient 2. In the other patients, a configuration involving an additional LV lead with HP-CSP, including 2 His-optimized CRT (HOT-CRT) and 8 LBB-optimized CRT (LOT-CRT), further decreased the QRSd (Table 1). In device programming, HP-CSP lead pacing with additional LV lead pacing more often yielded satisfactory QRSd or morphology (Figure 4 patient 10 in upgrade group). HP-CSP combined with LV endocardial pacing could acquire better QRS duration than upgrade to endocardial pacing (Figure 4).

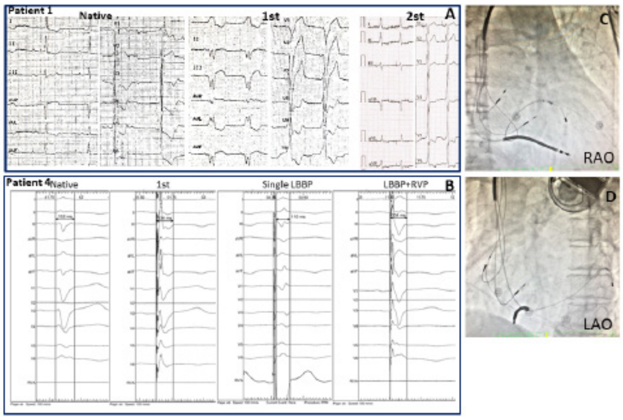


Figure 3: ECG manifestations for patient 1 and patient 4 in the upgrade group.

(A) The native ECG of patient 1 with HF and AVB showing a narrow QRS complex with second-degree atrioventricular block. The 1st CRT implantation resulted in a relatively wide QRS complex, and after upgrading to HBP, the QRS complex significantly narrowed. A long pacing signal QRS duration was noted on the ECG following the 2nd implantation, while an additional LV pacing lead was reserved, and the best QRSd could only be obtained under programmed HBP. **(B)** The intracardiac electrograms of patient 4 showed that single LBBP further narrowed the QRS complex compared with the 1st implantation, and the best QRSd could only be obtained under programmed LBBP. **(C)** and **(D)**, Final implantation images of patient 1 (RAO 30° and LAO 45°, respectively).

The mean HP-CSP capture threshold at the time of implantation was 1.30± 0.51 V at 0.5 ms, and it was 1.10± 0.44 V at 0.5 ms after an average of 9 months. The impendence was 715.3± 229.4 Ω and 465.5± 61.4 Ω at implantation and after an average of 9 months, respectively. The R-wave amplitudes were 8.16± 5.67 mV and 8.76± 6.23 mV at implantation and after an average of 9 months, respectively (Table 3). The overall pacing percentage was more than 90% in the cohort.

Both the HBP and LBBP capture thresholds remained stable during follow-up. Echocardiography showed that the pacing lead was positioned at the subendocardium of the IVS in all patients. No perforation into the LV cavity or pericardial effusion was observed. During the follow-up, the patients in both groups did not acquire an infection related to the operation, and no TIAs or strokes occurred in the two patients who underwent the implantation of LV-en lead.

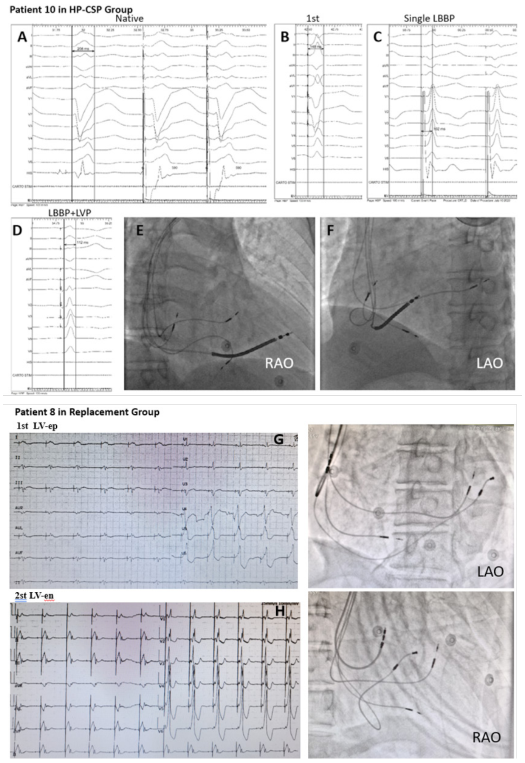


Figure 4: Implantation images and ECG manifestations for two patients with LV endocardial pacing (patient 10 in the upgrade group and patient 8 in the replacement group).

(A) The native ECG of patient 10 in the upgrade group with HF and LBBB showed that His pacing could not correct the LBBB. **(B)** The QRS complex was narrowed in the 1st CRT implantation compared with that in the native QRS complex. **(C)** After upgrading to LBBP, the QRSd significantly decreased to 126 ms, with a relatively long LAT of 102 ms. **(D)** Additional endocardial LV lead pacing combined with LBBP further narrowed the QRS complex to 112 ms. **(E)** and **(F)**, Final implantation image of patient 10. The position of the LV lead was the left ventricular endocardium (RAO 30° and LAO 45°, respectively). **(G)** and **(H)**, There was no obvious improvement in the QRS duration after replacement of the endocardial LV lead pacing (native=184 ms vs 1st =176 ms vs 2 st =168 ms). **(I)** and **(J)**, Final implantation image of patient 9 in the replacement group. The epicardial LV lead was preserved and given insulated treatment due to the adhesion with the coronary sinus veins (RAO 30° and LAO 45°, respectively).

Table 3: Parameters of the HP-CSP lead.

Patient No.	Threshold (V/0.5 ms)		Independence (Ω)		R-wave amplitude (mv)	
	At implantation	Average 9-month	At implantation	Average 9-month	At implantation	Average 9-month
1	2.0	1.25	925	437	5.2	-
2	2.0	2.0	533	409	4.4	2.2
3	1.3	1.7	446	390	4.3	3.9
4	0.8	0.5	893	399	8.4	-
5	0.9	0.9	925	585	11.2	13
6	1.5	0.9	647	507	19.6	16.4
7	1.0	1.0	463	475	12.3	4.9
8	1.2	1.0	589	418	2.5	2.7
9	0.8	0.75	821	532	4.1	6.6
10	0.8	0.5	1193	494	12.5	16.9
11	2.1	1.25	510	399	1.4	1.3
12	0.8	1.0	814	513	16	12.5

13	1.8	1.5	540	494	4.2	16
Mean±SD	1.30±0.51	1.10±0.44	715.3±229.4	465.5±61.4	8.16±5.67	8.76±6.23

CRT response between two groups

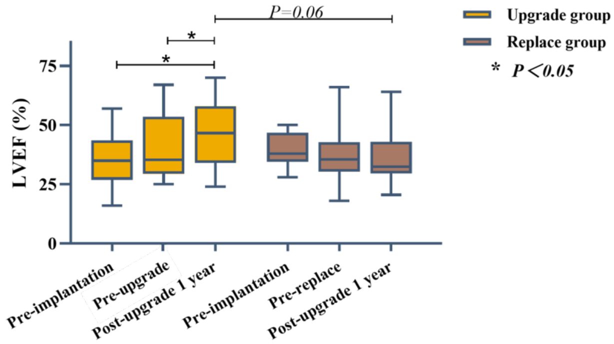
The NYHA and echocardiographic measurements are summarized in Supplemental Table 2. After the HP-CSP upgrade, compared with pre-PM values, the LVESV decreased from 143.6±48.9 ml to 94.7±65.5 ml (P=0.03), and the LVEF improved from 35.0±11.7% to 45.7±13.9% (P=0.02). Ten patients showed a CRT response compared with that at baseline (76.9%). Six patients showed a CRT response at the first implantation, and three patients showed a further response during follow-up. One patient (patients 3) who experienced a gradual decline in CRT benefit again exhibited an increase in cardiac function after the HP-CSP upgrade. Two patients who had shown a CRT response before upgrading showed no significant improvement in echocardiographic parameters after upgrading. In seven nonresponsive patients, four patients who did not show a response to previous CRT showed a response after upgrading. Three patients who did not show a response to previous CRT still did not show a response after upgrading.

In the replacement group, compared with the pre-PM group, the LVESV changed from 145.5±39.8 ml to 156.5±78.2 ml, and the LVEF changed from 39.9±7.4% to 36.3±11.2%. Four patients showed CRT response after replacement. Among the three patients who showed a significant response, two underwent atrioventricular node ablation, and the other was programmed for optimization based on the ORS morphology. One patient showed continuously deteriorative of the cardiac function. In eight nonresponsive patients, only one patient showed response after replacement. Four patients showed a CRT response compared with that at baseline (28.5%).

In the comparison between groups (Figure 6), LVESV showed more decreased in HP-CSP upgrade group than replacement group (94.7±65.5 ml vs 156.5±78.2 ml, P=0.04) and LVEF showed significantly improved in HP-CSP upgrade group compared with replacement group (45.7±13.9 vs 36.3±11.2, P=0.06).

Discussion

We present our initial clinical experience of adding HP-CSP to or adding HP-CSP in the configuration of synchronized pacing in a consecutive series of patients who had received CRT at least five years prior and needed replacement due to battery depletion. We hypothesized that electrical resynchronization measured by narrowing of the QRS complex can be accomplished more effectively by HP-CSP or HP-CSP combined with sequential LV pacing than by traditional CRT. In this nonrandomized controlled study, upgrade HP-CSP showed better results both in within-group comparison and between-group comparisons. This suggests that the degree of QRS narrowing achieved by fused LV pacing, in addition to the optimization of intrinsic His-Purkinje conduction, which is likely to provide additional hemodynamic and clinical benefits compared with traditional BiVP. The additional procedure that HP-CSP upgrade may provide better resistance to progression of heart failure in patients after long period CRT. For patients in whom traditional CRT may not provide sufficient synchronization or the benefit obtained from CRT gradually decreases as HF progresses, HP-CSP upgrade may be considered.



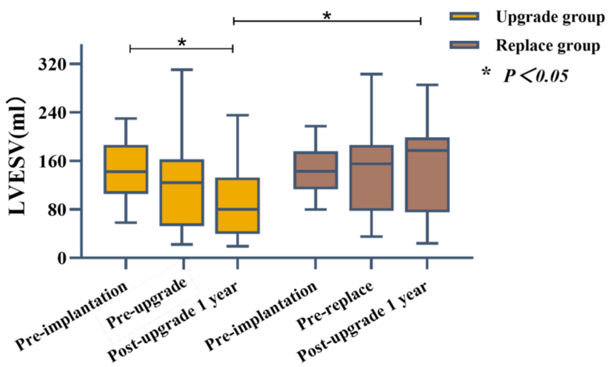


Figure 6: Comparison of echocardiographic parameters between two groups.

Upgrade group:

LVEF: Upgrade 1 year vs preupgrade (BVP): P=0.01; preupgrade (BVP) vs pre-PM: P=0.18; upgrade 1 year vs pre-PM: P=0.02

LVESV: Upgrade 1 year vs preupgrade (BVP): P=0.12; preupgrade (BVP) vs pre-PM: P=0.32; upgrade 1 year vs pre-PM: P=0.03

Replace group:

LVEF: Replace 1 year vs Prereplace (BVP): P=0.74; Prereplace (BVP) vs Pre-PM: P=0.52; replace 1 year vs Pre-PM: P=0.32

LVESV: Replace 1 year vs Prereplace (BVP): P=0.51; Prereplace (BVP) vs Pre-PM: P=0.95; replace 1 year vs Pre-PM: P=0.55

Comparison between groups:

LVEF: Upgrade 1 year vs Replace 1 year: P=0.06

LVESV: Upgrade 1 year vs Replace1 year: P=0.04

Effectiveness of resynchronization therapy utilizing His-Purkinje conduction system pacing compared with traditional BiV pacing

Currently, CRT is an effective method for treating HF patients with electrical dyssynchrony. Despite numerous research efforts to enhance the response rate of CRT through techniques such as echo-guided optimization and optimal LV lead positioning, 30% of CRT patients still remain nonresponsive. Additionally, the benefit obtained from CRT gradually decreases as HF progresses. Recently, HBP and LBBP have been proposed as alternatives to BiVP to accomplish CRT. The application of HBP and LBBP alone can improve cardiac function by resynchronization in HF patients with complete left bundle branch block (CLBBB) [6,7,13]. However, some patients who do not respond to BiVP may respond to HBP or LBBP [14]. Some small-sample control studies have shown that HP-CSP can improve clinical cardiac function more effectively than traditional CRT [8]. A randomized crossover study by [15]. Revealed an equivalent 6-month response rate using typical clinical measures when comparing HBP with BiVP. To expand the application of His pacing in patients with conduction system injury, [9].Optimized CRT by sequential HBP followed by LV pacing to maximize electrical resynchronization. His-optimized CRT improved clinical and echocardiographic outcomes in advanced HF patients requiring CRT [9].

In our study, expect the show that HP-CSP combined with LV pacing (including HOT CRT and LOT CRT) could acquire better electrical resynchronization (further decreasing the QRSd to 123.6±15.3 ms) and cardiac function than Biv pacing, some patients with preserved LVEF also acquire better results. Although these patients acquire obvious benefit after the first BiVP therapy, their QRS duration and morphology are still different from those of normal QRS. We prospectively added HP-CSP pacing of these patients (patients 2, 4 ,6 and 12 in the upgrade group), expecting that utilizing the His-Purkinje conduction system would yield better mechanical synchronization. The results showed that three patients showed further QRS narrowing and exhibited an enhanced response in both echocardiographic parameters and NYHA (Figure 5). These findings may suggest that even if patients had achieved a certain amount of benefit from BiVP, mechanical synchronization may be further improved by utilizing the His-Purkinje conduction system. This efficiency could also be expressed that upgrade group was relevant with more RR results (CRT showed a response at an early stage of follow-up, and the effectiveness dissipated as the disease progressed, while a re-showed response was observed after replacement or upgrade) than replacement group which was relevant with more DR results (CRT only showed a response at an early stage of follow-up, and the effectiveness dissipated as the disease progressed).

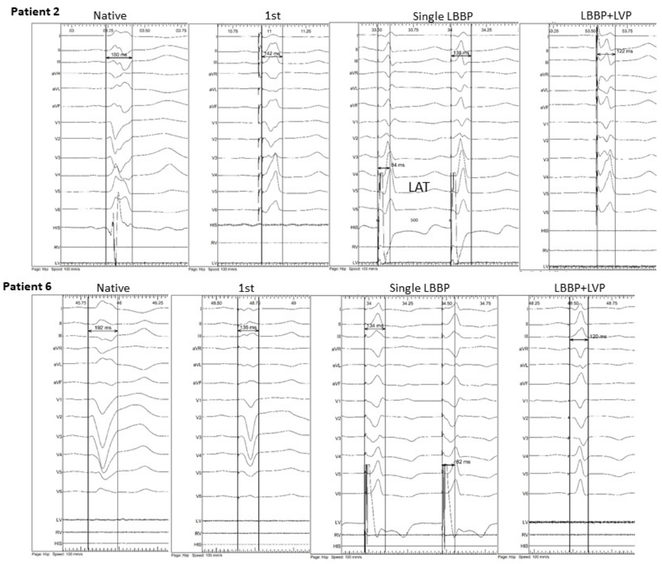


Figure 5: ECG manifestations for patient 2 and patient 6 in the upgrade group.
The ECG changes of two patients who had CRT response with preserved LVEF before the second operation, and after the upgrade to HP-CSP, the cardiac function further benefited. The native ECG of patient 2 and 6 with HF and wide QRS complex. The QRS complex was more narrow in the 1st CRT implantation than in the native QRS complex. After upgrading to LBBP, the QRSd markedly decreased. Additional LV lead pacing combined with LBBP further narrowed the QRS complex.

Consideration of synthetic and individualized resynchronization therapy strategies in HF patients

The benefit of utilizing the native His-Purkinje conduction system to excite cardiac tissue is appealing, as it can result in true cardiac resynchronization [16]. The damage of the His-Purkinje system differs by individual in patients with HF and wide QRS complexes who require CRT. In patients with advanced cardiomyopathy, LBBB and intraventricular conduction defects (IVCDs) may coexist. Some patients who cannot undergo ideal HBP or LBBP due to severe damage to the conduction system still need the traditional left pacing electrode to optimize the QRS duration or mechanical synchrony [9]. Using a single approach (HBP, LBBP or HOT-CRT) to address the various defects of the ventricular myocardium seems unfeasible. As we explored reutilization of the conduction system, an individualized pacing strategy involving the addition or replacement of HP-CSP in the synchronized pacing configuration could achieve the maximum clinical benefit in patients requiring CRT.

In some patients in our study, it was difficult to obtain proximal LBBP rather than left posterior fascicular or more distal conduction tissue-related pacing that could only correct part of the asynchrony of the ventricular myocardium. Implanting a left pacing lead through the CS and optimizing the programmed interventricular (VV) delay individually could achieve an ideal QRSd and morphology compared with single LBBP (Table 1). Although QRS narrowing has not been the strongest predictor of CRT response, electrical resynchronization reflected by QRS narrowing is valuable in the prediction of CRT response[17]. HBP and LBBP are associated with dramatic QRS narrowing and left ventricular resynchronization comparable to CRT, resulting in improved clinical outcomes. In our study, the strategy optimized the QRS complex on ECG through a combination of LBBP and LV pacing and achieved obviously improved clinical outcomes.

We conclude that there are 3 aspects of the CRT procedure that takes full advantage of HP-CSP. First, the LBBB could be corrected by HBP or proximal LBBP, and the QRS was nearly the same as the normal QRS complex or a related short LVAT. In this condition, if the parameters were acceptable, HBP or LBBP alone was enough to maintain good synchronization, the additional pacing lead was only needed as a reserve, and the pacing often fell into the ventricular refractory period and had no influence on cardiac contraction. Second, HBP or proximal LBBP usually cannot correct an LBBB to an acceptable level, and the relatively distal LBB, the left anterior fascicle (LAF) or the left posterior fascicle (LPF) can activate part of the ventricular myocardium through the conduction system, rendering the QRS complex relatively narrow. However, a conduction delay can still be seen in the latter half of the QRS complex. In this condition, an additional LV pacing lead would help to further narrow the QRS complex and improve QRS morphology, which suggests that it may provide more favorable hemodynamics. HOT-CRT could also be considered in this condition. With the two optimized programmed ventricular pacing modes, relatively advanced HP-CSP combined with LVP would yield better QRS morphology. Third, regardless of whether the proximal or distal LBB was unable to narrow the QRS, which usually suggests severe damage to the conduction system, traditional BiVP is the only potential alternative. This scheme involves using surviving conduction system tissue to control the myocardium combined with pacing myocardium, which cannot be activated through conduction tissue. This approach may maximize the acquired synchronicity in cardiac contractions, and its feasibility and effectiveness were demonstrated in our study.

Limitations

First, undergoing long-term BiVP therapy and surviving to have the opportunity to undergo an HP-CSP upgrade is does not often occur in a single center, so this study included only a small number of cases. The conclusions need to be validated by more cases or centers for a longer follow-up period so that mortality, hospitalization rates, and other outcomes can be assessed. Second, the high success rates of HP-CSP achieved by experienced operators need to be replicated in prospective studies. Third, the strategy of a pacing configuration involving HP-CSP between the LV and RV still needs to be explored to determine the optimal patient group and achieve the best hemodynamics. In our experience, some patients are limited to the use of LV pacing leads, and HP-CSP combined with RV pacing could further decrease the QRSd. However, in this study, additional RV pacing did not narrow the QRS complex. Finally, the use of QRS narrowing to judge the CRT response is limited, especially in patients with severe damage to the conduction system. Sometimes, the QRSd decreased to the same degree but with different QRS morphologies under different VV interval parameters, rendering program optimization confusing.

Conclusions

Including HP-CSP in synchronized pacing configurations may improve the cardiac function of patients who did not obtain sufficient benefit from traditional CRT and may be considered to maintain the efficacy of resynchronization pacing therapy in device replacement. An individual implantation strategy should be considered to maximize the utilization of HP-CSP for CRT.

Trial registration: None

Author contributions

Bing Zhu: Conceptualization, Methodology. Guohua Zhang: Software, Methodology. Songcai Xie: Writing- Original draft preparation, Writing- Reviewing and Editing, Methodology. Ying Luan: Writing- Reviewing and Editing. Wei Cao: Writing- Reviewing and Editing. Jian Xu:

Writing- Reviewing and Editing. Shuo Zhang: Writing- Reviewing and Editing. JinWei Tian:Funding acquisition, Supervision; Fan Wang: Supervision, Writing- Original draft preparation, Writing- Reviewing and Editing. Shufeng Li: Supervision, Funding acquisition, Project administration, Writing- Reviewing and Editing.

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