Left bundle branch pacing vs ventricular septal pacing for cardiac resynchronization therapy

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BACKGROUND The outcomes of left bundle branch pacing (LBBP) and left ventricular septal pacing (LVSP) in patients with heart failure remain to be learned.

OBJECTIVE The objective of this study was to assess the echocardiographic and clinical outcomes of LBBP, LVSP, and deep septal pacing (DSP).

METHODS This retrospective study included patients who met the criteria for cardiac resynchronization therapy (CRT) and underwent attempted LBBP in 5 Mayo centers. Clinical, electrocardiographic, and echocardiographic data were collected at baseline and follow-up.

RESULTS A total of 91 consecutive patients were included in the study. A total of 52 patients had LBBP, 25 had LVSP, and 14 had DSP. The median follow-up duration was 307 (interquartile range 208, 508) days. There was significant left ventricular ejection fraction (LVEF) improvement in the LBBP and LVSP groups (from 35.9 ± 8.5% to 46.9 ± 10.0%, $P < .001$ in the LBBP group; from 33.1 ± 7.5% to 41.8 ± 10.8%, $P < .001$ in the LVSP group) but not in the DSP group. A unipolar paced right bundle branch block morphology during the procedure in lead V1 was associated with higher odds of CRT response. There was no significant difference in heart failure hospitalization and all-cause deaths between the LBBP and LVSP groups. The rate of heart failure hospitalization and all-cause deaths were increased in the DSP group compared with the LBBP group (hazard ratio 5.10, 95% confidence interval 1.14–22.78, $P = .033$; and hazard ratio 7.83, 95% confidence interval 1.38–44.32, $P = .020$, respectively).

CONCLUSION In patients undergoing CRT, LVSP had comparable CRT outcomes compared with LBBP.

KEYWORDS Cardiac resynchronization therapy; Deep septal pacing; Heart failure; Left bundle branch pacing; Left ventricular septal pacing

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Introduction

Biventricular pacing has been the standard pacing modality for cardiac resynchronization.[1] However, ventricular activation spreading between the right ventricular (RV) endocardium and left ventricular (LV) epicardium with biventricular pacing is not physiological. Conduction system pacing, including His bundle pacing (HBP) and left bundle branch pacing (LBBP), has emerged as a physiological pacing modality that activates the ventricles by recruiting the native conduction system. HBP is limited by higher pacing thresholds and higher rates of lead dislodgement. LBBP, which is performed by pacing distal to the His bundle, has demonstrated better clinical and echocardiographic outcomes compared with biventricular pacing in cardiac resynchronization therapy (CRT) candidates.[2,3] However, despite the increasing experience with ventricular septal lead placement, left bundle branch (LBB) capture is only achieved in around 50% to 80% of cases.[4–7]

LBB area pacing is defined as capture of the subendocardial area of the left side of the interventricular septum with or without LBB capture.[8–10] Deep septal pacing (DSP), defined as the inability to penetrate the septum to reach the LV subendocardium without a right bundle branch block

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KEY FINDINGS

- Left ventricular septal pacing had a comparable cardiac resynchronization effect as left bundle branch pacing with similar improvement in left ventricular ejection fraction, rates of heart failure hospitalization, and overall survival.
- Deep septal pacing had no significant effect on improving left ventricular ejection fraction and left ventricular reverse remodeling.
- A unipolar paced right bundle branch block morphology indicating left bundle branch pacing or left ventricular septal pacing was associated with a greater cardiac resynchronization therapy response.

(RBBB) pattern, which is mainly due to interventricular scar,[11] has been proposed as a potentially viable alternative.[8] Left ventricular septal pacing (LVSP) provides short-term hemodynamic and electrical resynchronization effects similar to biventricular pacing and possibly HBP.[12] However, the clinical outcomes of LVSP remain to be learned. Therefore, the objective of this study was to assess the comparative echocardiographic and clinical outcomes of LBBP, LVSP, and DSP in patients with heart failure and reduced ejection fraction (HFrEF).

Methods

Study design and patient selection

The research reported in this article adhered to the Helsinki Declaration guidelines. This retrospective study included adult patients who met the American College of Cardiology/American Heart Association/Heart Rhythm Society guideline indications for CRT and underwent attempted LBBP between October 1, 2018, and February 28, 2023.[13] CRT indications included (1) LVEF $\leq$35% and QRS duration $\geq$120 ms or (2) LVEF 36% to 50% and expected ventricular pacing burden $\geq$40%. Patients with HFrEF were on optimal medical therapy at least 3 months before CRT device implantation. Clinical, electrocardiographic, echocardiographic, device implantation, and interrogation data were manually collected from the electronic health records.

Study sites

The study included 5 Mayo Clinic sites: (1) Rochester, Minnesota; (2) Eau Claire, Wisconsin; (3) La Crosse, Wisconsin; (4) Jacksonville, Florida; and (5) Phoenix, Arizona. The study was approved by the Institutional Review Board of the Mayo Clinic. Only patients who had previously consented to use their records for research purposes were included.

Implantation procedure

LBBP was attempted in all patients using the SelectSecure 3830 pacing lead (Medtronic, Minneapolis, MN) and a delivery sheath as previously described.[14,15] The sheath and the lead were positioned against the basal RV septum, 1 or a few centimeters below the His bundle. The lead was screwed into the ventricular septum using clockwise rotation. While advancing the lead, the unipolar tip paced QRS morphology was closely monitored using a multichannel recording system. After several attempts to place the lead tip in the LV endocardium, DSP was considered a potentially viable alternative when LBBP and LVSP were not achievable. Fluoroscopic observation of contrast injection via the delivery sheath in 30° left anterior oblique was performed to assess the lead depth into the ventricular septum and to avoid lead perforation into the LV. The depth of the lead inside the ventricular septum using sheath angiography was reviewed by J.C. and F.M.E. Additional RV pacing lead or defibrillation lead was implanted at the operator's discretion.

Pacing group definitions

Based on the pacing lead tip–unipolar pacing, LBBP was defined by a terminal r/R-wave in lead V1 or RBBB with 1 of the following criteria of LBB capture: (1) short and constant left ventricular activation time (LVAT) at high and low output in lead V6 of $<$80 ms; (2) demonstrated LBB potential; or (3) QRS transition during the threshold test or programmed stimulation (from nonselective to selective LBBP).[8,16] LVSP was defined as unipolar-tip pacing with a RBBB morphology in lead V1 and absence of LBB capture.[8] DSP was defined as unipolar-tip pacing with absent terminal r/R-wave in lead V1 (QS or rS morphology in lead V1) (Figure 1).[8]

Follow-up and definition of outcomes

Baseline patient demographic, medication use, and electrocardiographic data were collected. The procedure time and fluoroscopy time were recorded during the procedure. The distance of the lead to the tricuspid valve annulus was measured at 30° right anterior oblique projection. Pacing thresholds, R-wave amplitudes, and lead impedances were measured at the end of the procedure. Patients returned for in-person follow-up in the device clinic at 3 months and, subsequently, by remote monitoring every 3 months. At follow-up, R-wave amplitude, pacing thresholds, and lead impedances were measured. All capture thresholds were defined using a pulse width of 0.4 ms. In patients who received CRT pacemaker or CRT defibrillator devices, LBB area pacing was programmed prior to the RV lead.

Echocardiographic parameters were collected from baseline and follow-up transthoracic echocardiography, including left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD), and left ventricular end-diastolic diameter (LVEDD). Response to CRT was defined as an absolute increase of $>$5% in LVEF after 3 months of device implantation.[17] Time to first heart failure (HF) hospitalization and overall survival were determined by a review of electronic health records. HF hospitalization was defined as an

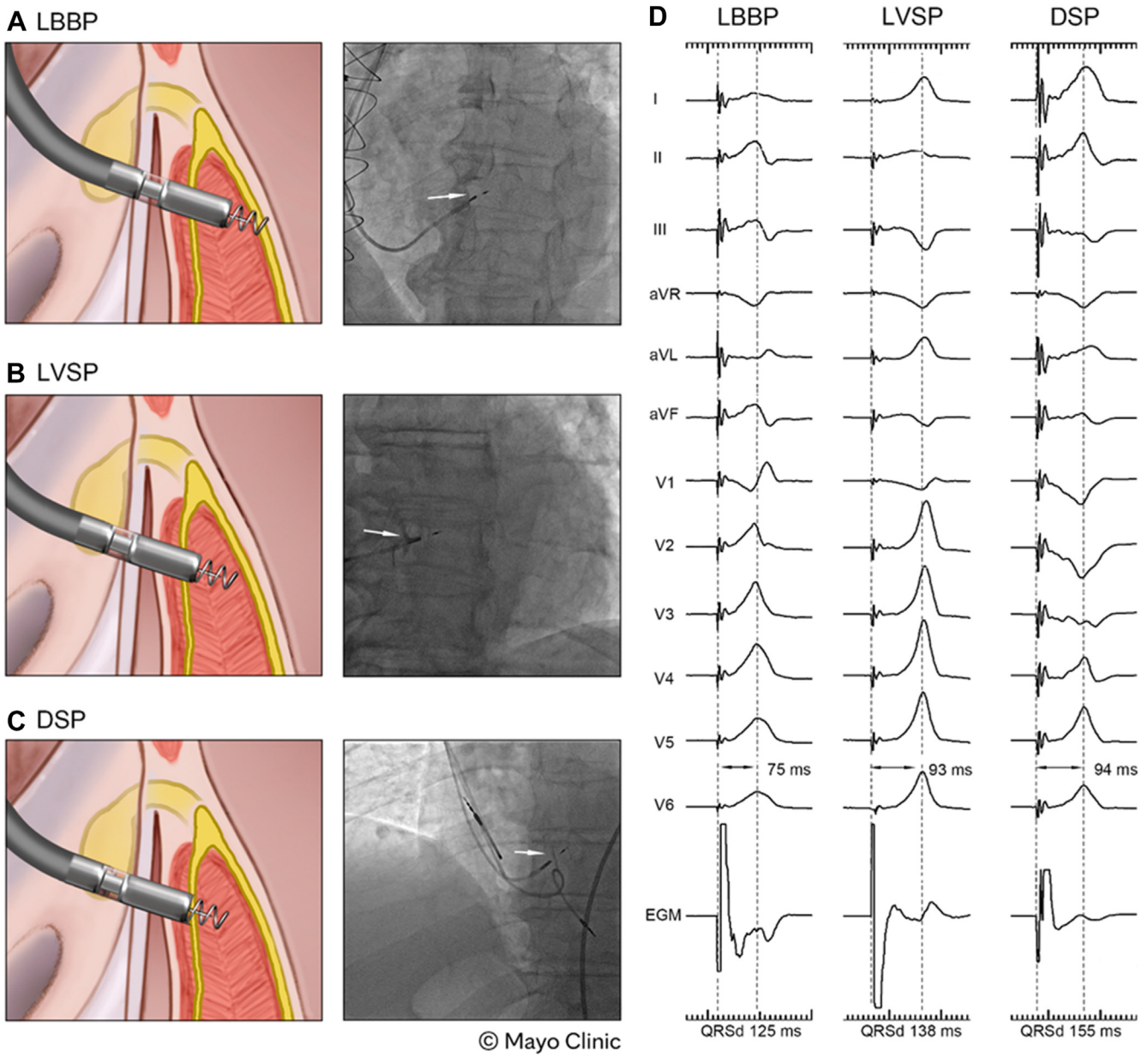


Figure 1 Examples of pacing electrocardiograms and sheath angiographies to delineate the depth of the lead in the septum. Examples of illustrations and fluoroscopy images with left anterior oblique projection showing the lead depth in the left bundle branch pacing (LBBP) group (A), left ventricular septal pacing (LVSP) group (B), and deep septal pacing (DSP) group (C). (D) Examples of electrocardiograms and ventricular electrograms (EGMs) by unipolar tip pacing in LBBP with left ventricular activation time (LVAT) of 75 ms and QRS duration of 125 ms, in LVSP with LVAT of 93 ms and QRS duration of 138 ms, and in DSP with LVAT of 94 ms and QRS duration of 155 ms. QRSd = QRS duration.

unplanned outpatient or emergency department visit or inpatient hospitalization in which the patient presented with signs and symptoms consistent with HF requiring intravenous diuretic therapy. The follow-up time was estimated from the date of the procedure to the date of the last clinical encounter.

Statistical analysis

Continuous variables were reported as mean ± SD or median (interquartile range). One-way analysis of variance or the Kruskal-Wallis test was used to compare the difference in continuous outcomes between the 3 groups as appropriate. Paired *t* test or Wilcoxon signed rank test was used to compare the difference in continuous outcomes within the same group before and after the procedure as appropriate. Categorical variables were reported as percentage and compared by using the chi-square test or Fisher exact test as appropriate. Bonferroni multiple comparisons were applied to pairwise comparisons. Freedom from HF hospitalization and overall survival outcomes were compared using Kaplan-Meier or Cox analyses. The data analysis was performed using SPSS software

Table 1 Baseline characteristics

	LBBP (n = 52)	LVSP (n = 25)	DSP (n = 14)	*P* value
Age, y	73.7 ± 10.4	71.7 ± 12.1	78.5 ± 8.9	.162
Female	18 (34.6)	8 (32.0)	4 (28.6)	.905
BMI, kg/m^2	29.2 ± 5.9	31.1 ± 7.2	27.1 ± 6.1	.153
Hypertension	35 (67.3)	19 (76.0)	9 (64.3)	.667
Coronary artery disease	35 (67.3)	21 (84.0)	11 (78.6)	.254
Atrial fibrillation	26 (50.0)	14 (56.0)	9 (64.3)	.616
ICM	23 (44.2)	15 (60.0)	8 (57.1)	.374
NICM	29 (55.8)	10 (40.0)	6 (42.9)	.374
Diabetes	20 (38.5)	15 (60.0)	4 (28.6)	.101
Sleep apnea	20 (38.5)	13 (52.0)	3 (21.4)	.168
CRT indication				
LVEF ≤35% + QRS duration ≥120 ms	20 (38.5)	14 (56.0)	4 (28.6)	.190
LVEF ≤50% + expected ventricular pacing ≥40%	32 (61.5)	11 (44.0)	10 (71.4)	.190
Electrocardiography				
LBBB	20 (38.5)	10 (40.0)	2 (14.3)	.166
RBBB	4 (7.7)	2 (8.0)	2 (14.3)	.759
IVCD	5 (9.6)	5 (20.0)	4 (28.6)	.179
Right ventricular pacing	13 (25.0)	6 (24.0)	4 (28.6)	.949
Echocardiography				
LVEF, %	35.9 ± 8.5	33.1 ± 7.5	40.9 ± 6.9	.018*
LVEDD, mm	56.4 ± 7.9	60.2 ± 7.6	59.4 ± 7.3	.129
LVESD, mm	45.5 ± 7.9	49.9 ± 8.3	45.3 ± 8.3	.094
Medications				
Beta-blocker	45 (86.5)	23 (92.0)	11 (78.6)	.499
ACE inhibitor/ARB	28 (53.8)	14 (56.0)	6 (42.9)	.712
Spironolactone	20 (38.5)	16 (64.0)	5 (35.7)	.081
Sacubitril-valsartan	13 (25.0)	11 (44.0)	3 (21.4)	.177
Diuretic	47 (90.4)	24 (88.0)	11 (78.6)	.527

Values are mean ± SD or n (%). *$P < .05$.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; DSP = deep septal pacing; ICM = ischemic cardiomyopathy; IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LBBP = left bundle branch pacing; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVSP = left ventricular septal pacing; NICM = nonischemic cardiomyopathy; RBBB = right bundle branch block.

version 28.0 (IBM, Armonk, NY). A 2-sided $P \leq .05$ was considered statistically significant.

Results

Baseline characteristics

A total of 91 consecutive patients with HFrEF underwent attempted LBBP. LBBP was achieved in 52 (57.1%) patients, LVSP in 25 (27.5%) patients, and DSP in 14 (15.4%) patients. The baseline characteristics of the study groups are summarized in Table 1. The mean age was 73.9 ± 10.8 years, and 30 (33.0%) patients were female. The mean LVEF was 35.9 ± 8.3%. There was no difference in QRS morphology (left bundle branch block [LBBB], RBBB, or intraventricular conduction delay) among the 3 groups. The LVSP group had a lower baseline LVEF than the other groups. The median follow-up duration was 307 (interquartile range 208–508) days. A total of 36 (39.6%) of patients had CRT defibrillator therapy, 20 (22.0%) patients had CRT pacemaker therapy, and 35 (38.5%) patients had single- or dual-chamber pacemakers. A total of 32 (35.2%) patients had a suboptimal or failed coronary sinus lead placement and received alternative LBBP. The median V-V interval in these patients was 70 (LBBP early interquartile range 0–80) ms.

Implant characteristics and pacing parameters

The paced QRS duration was the narrowest in the LBBP group (133.6 ± 19.4 ms in LBBP vs 141.2 ± 20.2 ms in LVSP vs 151.1 ±19.5 ms in DSP, $P = .011$) (Table 2). The average paced LVAT was 83.3 ± 20.5 ms and was significantly different among the 3 groups ($P < .001$). The examples of pacing electrograms and sheath angiographies to delineate the lead depth into the ventricular septum in the 3 groups are shown in Figure 1. The lead depths were comparable in the LBBP and LVSP groups (12.8 ± 3.8 mm vs 10.3 ± 3.7 mm, $P = .251$), while DSP leads penetrated shallower in the interventricular septum (6.7 ± 1.5 mm, $P = .034$) compared with LBBP leads. The lead distance from the annulus, procedure duration, and fluoroscopy time were similar among the 3 groups (Table 2).

Pacing thresholds at implantation and follow-up were satisfactory and remained stable in all groups (Figure 2). Ventricular R-wave sensing amplitudes were increased during follow-up in the LBBP group (10.0 ± 6.1 mV vs 16.0 ± 9.3 mV, $P < .001$) (Figure 2). Impedances were decreased during follow-up in the LBBP (695.1 ± 201.7 Ω vs 515.6± 113.2 Ω, $P < .001$) and LVSP (712.6 ± 145.6 Ω vs 451.1 ± 137.9 Ω, $P < .001$) groups.

Table 2 Implant, electrocardiographic, and electrophysiologic characteristics

	LBBP (n = 52)	LVSP (n = 25)	DSP (n = 14)	*P* value
Implanted device type				.054
Single/dual-chamber PM	26 (50.0)	4 (16.0)	5 (35.7)	
CRT-P device	10 (19.2)	6 (24.0)	4 (28.6)	
CRT-D device	16 (30.8)	15 (60.0)	5 (35.7)	
Paced QRS duration, ms	133.6 ± 19.4	141.2 ± 20.2	151.1 ± 19.5	.011*
LVAT, ms	72.5 ± 15.3	103.1± 17.4	88.3 ± 13.3	<.001
Lead depth, mm	12.8 ± 3.8	10.3 ± 3.7	6.7 ± 1.5	.018†
Distance from the annulus, mm	23.0 ± 11.8	23.5 ± 9.6	31.2 ± 7.1	.294
Procedure time, min	146.1± 73.2	167.0 ± 105.2	158.6 ± 79.7	.578
Fluoroscopy time, min	28.8 ± 22.7	31.0 ± 30.3	34.6 ± 23.2	.738

Values are n (%) or mean ± SD. *In post hoc analysis, differences were present for pairs: LBBP vs LVSP ($P = .348$) and LBBP vs DSP ($P = .012$). †In post hoc analysis, differences were present for pairs: LBBP vs LVSP ($P = .251$) and LBBP vs DSP ($P = .034$).

CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; LVAT = left ventricular activation time; other abbreviations as in Table 1.

Echocardiographic outcomes

The LVEF increased from 35.9 ± 8.5% at baseline to 46.9 ± 10.0% ($P < .001$) at follow-up in the LBBP group and from 33.1 ± 7.5% to 41.8 ± 10.8% ($P < .001$) in the LVSP group; there was no significant increase in LVEF in the DSP group (Figure 3A). The LBBP and LVSP groups had a comparable LVEF incremental improvement (11.2 ± 7.9% vs 8.7 ± 8.6%, $P = .581$) and CRT response rate (69.8% vs 68.0%, $P = .913$), while the response rate in the DSP group was only 14.3% without significant LVEF improvement (Figure 3B and 3C). As shown in Figure 3D, the LBBP and LVSP groups had a significant decrease in LVESD ($P < .001$) at follow-up. Similarly, LVEDD significantly decreased in the LBBP (from 56.5 ± 8.0 mm to 51.6 ± 9.1 mm, $P < .001$) and LVSP groups (60.1 ± 7.9 mm to 56.9 ± 7.1 mm, $P = .017$). LVESD and LVEDD did not change significantly in the DSP group.

Multivariate analysis for CRT response

Univariate analysis revealed that intrinsic LBBB and a unipolar tip paced RBBB morphology in lead V1 during the procedure were associated with higher odds of CRT response (Table 3), while a higher LVEF at baseline and a broader paced QRS duration were associated with lower odds of CRT response. On multivariate analysis, a unipolar tip paced RBBB morphology in lead V1 during the procedure predicted better CRT response (adjusted odds ratio 13.75, 95% confidence interval [CI] 2.52–74.98, $P = .002$).

Clinical outcomes

The incidence rate of HF hospitalization was comparable between the LBBP and LVSP groups (9.1% vs 16.3%; hazard ratio [HR] 0.95, 95% CI 0.17–5.19, $P = .953$). There was a significant increase in HF hospitalization in patients with DSP (31.2%) compared with those with LBBP (HR 5.10, 95% CI 1.14–22.78, $P = .033$) (log-rank $P = .034$, Figure 4). Deaths from any cause occurred in 2.1% of patients in the LBBP group and 4.2% of patients in the LVSP group (HR 1.07, 95% CI 0.10–11.85, $P = .956$) compared with 38.6% of patients in the DSP group (HR 7.83, 95% CI 1.38–44.32, $P = .020$) (log-rank $P = .010$, Figure 5).

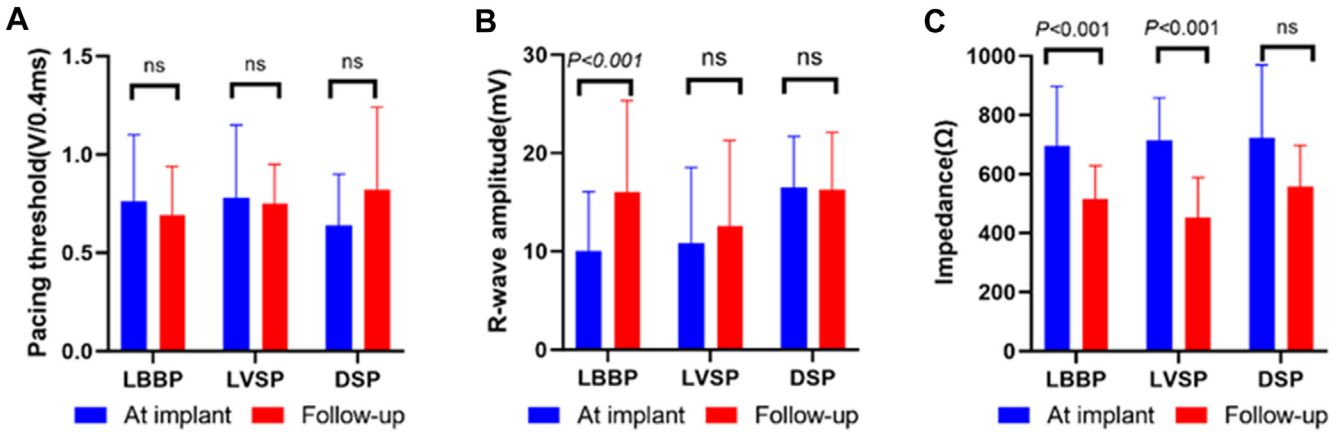


Figure 2 Pacing characteristics at implantation and follow-up in LBBP, LVSP, and DSP patients. A: Pacing threshold; B: R-wave amplitude; C: impedance. ns = not significant; other abbreviations as in Figure 1.

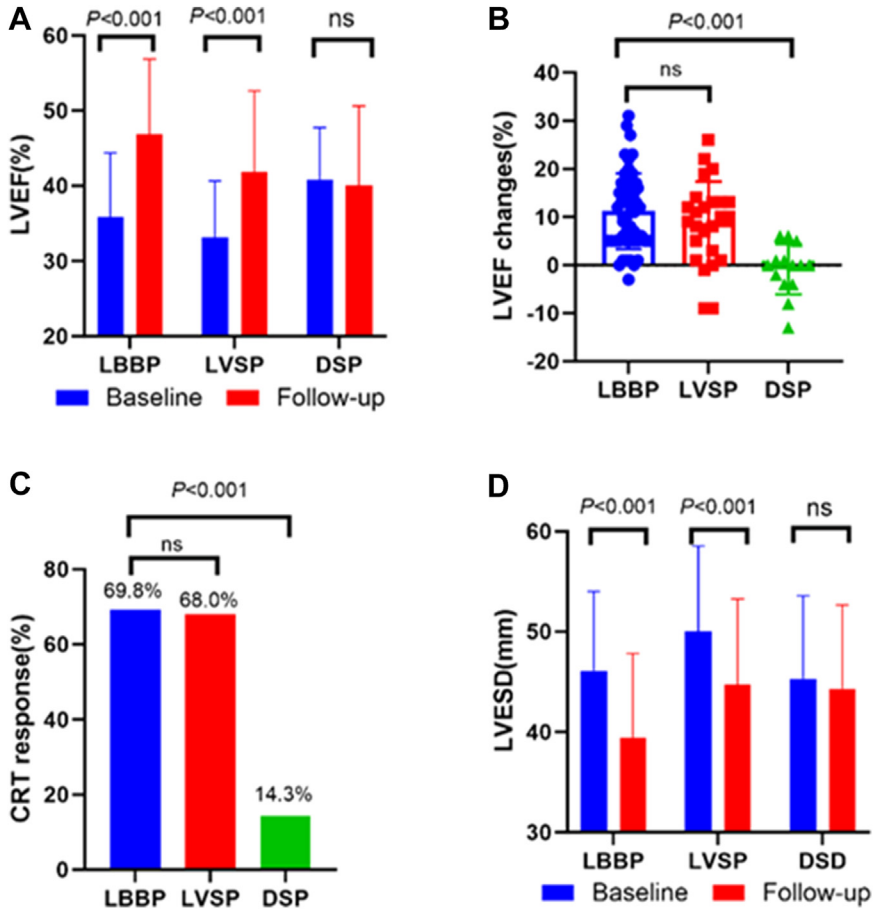


Figure 3 Comparisons of echocardiographic parameters at baseline and follow-up in patients with LBBP, LVSP, and DSP. A: Left ventricular ejection fraction (LVEF); B: LVEF change; C: cardiac resynchronization therapy (CRT) response rate; D: left ventricular end-systolic diameter (LVESD). ns = not significant; other abbreviations as in Figure 1.

Discussion

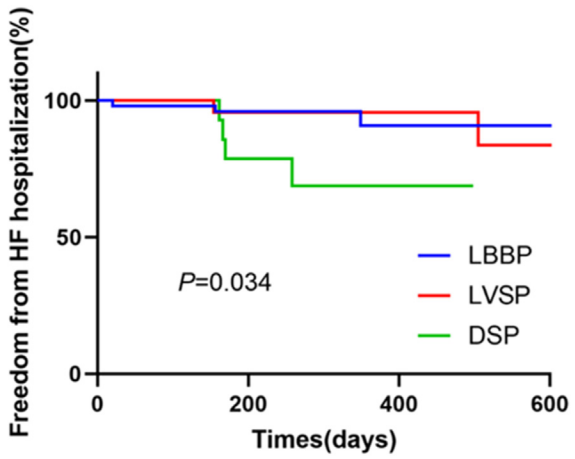
In this retrospective study of patients with HFrEF who underwent attempted LBBP, we found that (1) LVSP had a comparable cardiac resynchronization effect as LBBP with similar improvement in LVEF, rates of HF hospitalization, and overall survival; (2) DSP had no significant effect on improving LVEF and LV reverse remodeling; and (3) a unipolar paced RBBB morphology indicating LBBP or LVSP was predictive of a greater CRT response.

LV activation starts from the left bundle, and 3 areas on the left side of the interventricular septum are subsequently activated: an area high on the anterior paraseptal wall just below the attachment of the mitral valve, a central area on the left surface of the interventricular septum, and the posterior paraseptal area at about one-third of the distance from apex to base.[18] Capturing the left bundle or its branches by pacing facilitates a more physiologic and fast activation in the LV compared with ventricular septal

Table 3 Univariate and multivariate analysis to assess the predictors of CRT response

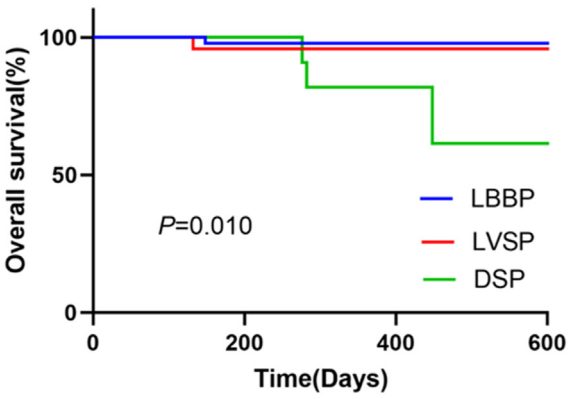
	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.01	0.97–1.05	.791	1.04	0.99–1.09	.101
Female	1.20	0.49–2.95	.692	0.59	0.17–2.01	.396
Diabetes	1.31	0.56–2.08	.536	1.03	0.34–3.06	.964
ICM	0.49	0.21–1.16	.105	0.38	0.14–1.04	.059
Intrinsic LBBB	2.71	1.05–7.00	.040*	2.07	0.63–6.83	.232
Baseline LVEF	0.94	0.89–0.99	.021*	0.94	0.89–1.00	.065
Paced RBBB	13.25	2.75–63.86	.001*	13.75	2.52–74.98	.002*
LVAT	0.99	0.97–1.01	.161	0.99	0.96–1.01	.371
Paced QRS duration	0.98	0.96–0.99	.038*	0.98	0.95–1.01	.113

CI = confidence interval; OR = odds ratio; other abbreviations as in Tables 1 and 2.
*$P < .05$.



Number at risks				
LBBP	52	38	16	12
LVSP	25	21	10	6
DSP	14	11	4	0

Figure 4 Kaplan-Meier curves demonstrating a comparison of time to first heart failure (HF) hospitalization among the 3 groups. A hazard ratio >1 represents an increase in HF hospitalization compared with the LBBP group. The hazard ratio for LVSP was 0.95 (95% confidence interval 0.17–5.19, $P = .953$) and for DSP was 5.10 (95% confidence interval 1.14–22.78, $P = .033$). Abbreviations are in Table 1.



Number at risks				
LBBP	52	39	17	13
LVSP	25	20	9	6
DSP	14	14	6	2

Figure 5 Survival curves and analysis for all-cause mortality. A hazard ratio >1 represents an increase in deaths compared with the LBBP group. The hazard ratio for LVSP is 1.07 (95% confidence interval 0.10–11.85, $P = .956$) and for DSP is 7.83 (95% confidence interval 1.38–44.32, $P = .020$). Abbreviations are in Table 1.

myocardial conduction in the presence of LBBB. LBBP resulted in a significant improvement in ventricular electrical synchrony assessed by the QRS area.[19]A recent study demonstrated impressive outcomes of LBBP in nonischemic cardiomyopathy with LBBB in which mean LVEF improved from 33 ± 8% to 52 ± 10% at 6-month follow-up and LVEF normalized in 75% of patients at 1 year.[20]

Our study, which included patients with severely reduced LVEF requiring CRT, demonstrated that both LBBP and LVSP groups had a significant improvement in LVEF and reduction of LVESD and LVEDD, suggesting LV structural reverse remodeling, even though the LVSP group had a lower baseline LVEF. The incidence of HF hospitalization and overall survival was comparable between the LBBP and LVSP groups. Despite the increasing experience with LBBP, it remains challenging to achieve LBB capture because of a blind lead advancement. When the lead penetrates the LV septum, the first appearance of an r-wave in lead V1 is considered a sign of LV synchrony through QRS area measurement.[19,21] A terminal r/R-wave in lead V1 appearing during postprocedure programming also indicates that the lead penetrated the LV endocardium. We found that a paced RBBB morphology in lead V1 in both the LBBP and LVSP groups was associated with a better CRT response and clinical outcomes. Although LVSP has a longer LVAT in the absence of left bundle capture, the LV activation is more likely to be completed before the RV, mitigating the electrical dyssynchrony of the LV lateral wall.[12,22] Based on these findings, LVSP seems to have acceptable and comparable outcomes to LBBP. Although, currently, LBBP is a desirable procedure endpoint, we could consider LVSP as a sufficient procedure endpoint if larger or more studies support this finding.

DSP, recognized as failure of penetrating the shared ventricular septum to reach the LV endocardium, has not been widely studied. Even though the DSP group had a higher LVEF at baseline, it exhibited a higher rate of HF hospitalization and mortality than the LBBP and LVSP groups. In patients with uncorrected or paced LBBB pattern without LV septal or LBB/Purkinje network capture, ventricular dyssynchrony may persist. This finding underscores the potential importance of LBBP or LVSP. Considering the poor CRT response rate in patients who underwent DSP in our study, a lead tip reaching the LV endocardium seems to be critical for better CRT response to mitigate ventricular dyssynchrony.[23] The lead in DSP had much shallower penetration into the LV septal endocardium, which is consistent with previous reports using computed tomography imaging to compare lead depth.[24] As the left bundle runs very close to the LV endocardium,[25,26] an effort should be made to place the lead in the left-sided ventricular septum using electrical and imaging guidance (>10 mm).

Limitations

First, this was a retrospective study with a small sample size and limitations inherent to the study design. Large prospective studies are needed to further assess the clinical outcomes of LBBP vs LVSP. Second, this is our initial real-world experience with LBB area pacing, and the procedure endpoint was at the operator's discretion. Third, patients may have been admitted to their local hospital for HF; therefore, the rate of HF hospitalization may be underestimated.

Conclusion

In patients undergoing conduction system pacing for CRT, LBBP should be aimed. LVSP had comparable cardiac resynchronization outcomes compared with LBBP. Therefore, LVSP may be considered as an acceptable procedure endpoint if larger and prospective studies support our observation.

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Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: Only patients who had previously consented to use their records for research purposes were included.

Ethics Statement: The study was approved by the Institutional Review Board of Mayo Clinic. The research reported in this article adhered to the Helsinki Declaration guidelines.

Data Availability: The data that support the findings of this paper are available from the corresponding author (Yong-Mei Cha) upon reasonable request.

References

1. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346:1845–1853.
2. Su L, Wang S, Wu S, et al. Long-term safety and feasibility of left bundle branch pacing in a large single-center study. Circ Arrhythm Electrophysiol 2021;14:e009261.
3. Chen X, Ye Y, Wang Z, et al. Cardiac resynchronization therapy via left bundle branch pacing vs. optimized biventricular pacing with adaptive algorithm in heart failure with left bundle branch block: a prospective, multi-centre, observational study. Europace 2022;24:807–816.
4. Jastrzębski M, Kiełbasa G, Cano O, et al. Left bundle branch area pacing outcomes: the multicentre European MELOS study. Eur Heart J 2022;43:4161–4173.
5. Zhang W, Chen L, Zhou X, et al. Resynchronization effects and clinical outcomes during left bundle branch area pacing with and without conduction system capture. Clin Cardiol 2023;46:287–295.
6. Cheng C, Sun L, Peng X, et al. Difference of ventricular synchrony between LBBP, LBFP and LVSP: a speckle tracking echocardiographic study. J Interv Card Electrophysiol 2023 [E-pub ahead of print Aug 14].
7. Padala SK, Master VM, Terricabras M, et al. Initial experience, safety, and feasibility of left bundle branch area pacing: a multicenter prospective study. J Am Coll Cardiol EP 2020;6:1773–1782.
8. Burri H, Jastrzebski M, Cano O, et al. EHRA clinical consensus statement on conduction system pacing implantation: endorsed by the Asia Pacific Heart Rhythm Society (APHRS), Canadian Heart Rhythm Society (CHRS), and Latin American Heart Rhythm Society (LAHRS). Europace 2023;25:1208–1236.
9. Jastrzębski M, Moskal P, Huybrechts W, et al. Left bundle branch-optimized cardiac resynchronization therapy (LOT-CRT): results from an international LBBAP collaborative study group. Heart Rhythm 2022;19:13–21.
10. Vijayaraman P, Ponnusamy S, Cano O, et al. Left bundle branch area pacing for cardiac resynchronization therapy: results from the International LBBAP Collaborative Study Group. J Am Coll Cardiol EP 2021;7:135–147.
11. Ponnusamy SS, Murugan M, Ganesan V, Vijayaraman P. Predictors of procedural failure of left bundle branch pacing in scarred left ventricle. J Cardiovasc Electrophysiol 2023;34:760–764.
12. Salden F, Luermans J, Westra SW, et al. Short-term hemodynamic and electrophysiological effects of cardiac resynchronization by left ventricular septal pacing. J Am Coll Cardiol 2020;75:347–359.
13. Epstein AE, DiMarco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2013;61:e6–e75.
14. Ezzeddine FM, Pistiolis SM, Pujol-Lopez M, et al. Outcomes of conduction system pacing for cardiac resynchronization therapy in patients with heart failure: A multicenter experience. Heart Rhythm 2023;20:863–871.
15. Huang W, Chen X, Su L, Wu S, Xia X, Vijayaraman P. A beginner's guide to permanent left bundle branch pacing. Heart Rhythm 2019;16:1791–1796.
16. Jastrzebski M. ECG and pacing criteria for differentiating conduction system pacing from myocardial pacing. Arrhythm Electrophysiol Rev 2021;10:172–180.
17. Xiao PL, Cai C, Zhang P, et al. Cardiac resynchronization therapy modulates peripheral sympathetic activity. Heart Rhythm 2020;17:1139–1146.
18. Durrer D, van Dam RT, Freud GE, Janse MJ, Meijler FL, Arzbaecher RC. Total excitation of the isolated human heart. Circulation 1970;41:899–912.
19. Heckman LIB, Luermans J, Curila K, et al. Comparing ventricular synchrony in left bundle branch and left ventricular septal pacing in pacemaker patients. J Clin Med 2021;10:822.
20. Huang W, Wu S, Vijayaraman P, et al. Cardiac resynchronization therapy in patients with nonischemic cardiomyopathy using left bundle branch pacing. J Am Coll Cardiol EP 2020;6:849–858.
21. Rijks J, Luermans J, Heckman L, et al. Physiology of left ventricular septal pacing and left bundle branch pacing. Card Electrophysiol Clin 2022;14:181–189.
22. Heckman L, Luermans J, Salden F, et al. Physiology and practicality of left ventricular septal pacing. Arrhythm Electrophysiol Rev 2021;10:165–171.
23. Peng XY, Wang YJ, Sun LL, et al. Is the pacing site closer to the left ventricular septal endocardium in left bundle branch pacing or in left ventricular septal pacing? J Interv Card Electrophysiol 2023;66:539–549.
24. Abhilash SP, Raja DC, Stolcman S, et al. Computerized tomography image correlation of His bundle/deep septal pacing location and outcomes: an analysis from the Canberra HIs bundle/deep septal Pacing Study (CHIPS). J Interv Card Electrophysiol 2022;64:137–148.
25. Cabrera JA, Porta-Sanchez A, Tung R, Sanchez-Quintana D. Tracking down the anatomy of the left bundle branch to optimize left bundle branch pacing. J Am Coll Cardiol Case Rep 2020;2:750–755.
26. Cabrera JA, Anderson RH, Macias Y, et al. Variable arrangement of the atrioventricular conduction axis within the triangle of Koch: implications for permanent His bundle pacing. J Am Coll Cardiol EP 2020;6:362–377.