Conduction System vs Biventricular Pacing for Heart Failure

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Introduction

Take Home Messages

- Biventricular pacing (BiVP) remains the standard of care for heart failure with reduced ejection fraction and left bundle branch block, but conduction system pacing (CSP) is an alternative if BiVP is not feasible.
- CSP is non-inferior to BiVP in reducing QRS duration and improving left ventricular ejection fraction.
- It is uncertain whether there is a difference in mortality and morbidity between the two groups.

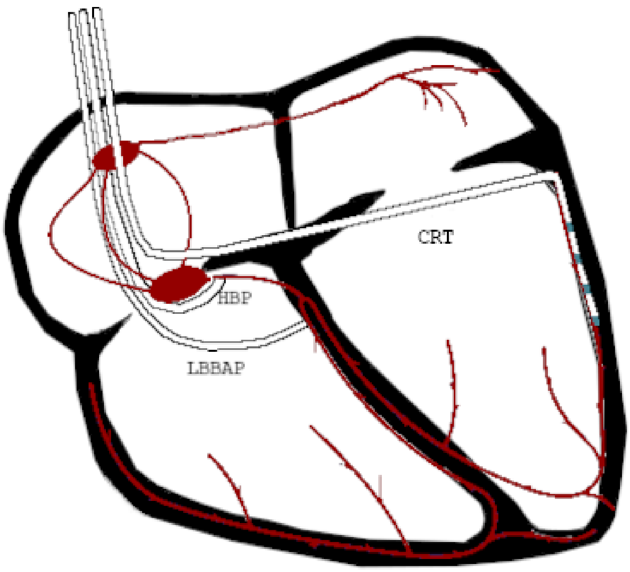
Biventricular pacing (BiVP) is an established treatment for reducing morbidity and mortality in heart failure with reduced ejection fraction (HFrEF) and left bundle branch block (LBBB). (1) It works by reducing ventricular dyssynchrony. However, approximately one third of patients are non-responders to BiVP, particularly those with non-LBBB morphology or QRS complex duration <150ms. Procedural factors also impact the success rate of BiVP (Figure 1). Thus, alternative pacing modalities are being explored. Conduction system pacing (CSP) is being increasingly utilised as an option for those with a bradycardia pacing indication to prevent ventricular dyssynchrony and the resulting decline in cardiac function. It is also being investigated as a first-line alternative to BiVP in HFrEF and LBBB.

Conduction system pacing: Techniques and challenges

CSP encompasses several techniques, including left bundle branch area pacing (LBBAP) and His-bundle pacing (HBP). Theoretically, capture of the His-Purkinje system should produce a more physiological ventricular activation than other modalities. However, pacing the His-bundle, which is small, centrally-located and insulated by inert fibrous tissue, results in a low R-wave amplitude which can lead to ventricular oversensing and atrial undersensing. (2) Many operators find HBP procedurally challenging and this is reflected in the lower procedural success rates seen in trials. (3) LBBAP has been developed as an alternative technique and is increasingly being used in place of HBP.

LBBAP includes pacing of left bundle branch, left fascicle and left ventricular septum. Observational data suggest non-selective capture (septal or fascicular pacing) may be less effective than left bundle branch pacing in achieving synchrony and left ventricular function improvement. (4) Additionally, two hybrid modalities, His-optimised cardiac resynchronisation therapy (HOT-CRT) and left-bundle branch-optimised cardiac resynchronisation therapy (LOT-CRT), have been developed. Combining CSP and coronary sinus pacing allows for resynchronisation of those with LBBB and intraventricular conduction delay. (2)

Figure 1: Different cardiac resynchronisation pacing modalities and their limitations.



BiVP
- Challenges with coronary sinus cannulation including risk of coronary sinus perforation
- Anatomical variation in veins may lead to suboptimal lead position leading to higher thresholds or loss of capture
- Unintentional phrenic nerve stimulation
- The presence of myocardial scar or fibrosis impact success.
- More expensive

HBP
- Higher baseline pacing thresholds and increasing thresholds over time
- Risk of ventricular undersensing and P wave far-field oversensing
- Inability to correct infra-Hisian conduction disease
- Challenges in performing AV nodal ablation, TAVI or AVR after HBP

LBBAP
- Harder to prove capture; a combination of EGM and ECG parameters
- Risk of septal perforation, septal haematoma or coronary vessel injury

Current evidence

Observational data suggest a potential benefit of CSP in HFrEF, but only eight randomised controlled trials (RCTs) have directly compared CSP with BiVP (Table 1). (5,6) Initial data confirmed that CSP achieves comparable reduction in QRS duration to BiVP, suggesting successful ventricular resynchrony. Subsequent studies demonstrated that resynchrony led to equivalent improvements in left ventricular function, NT-ProBNP and left ventricular end diastolic volume between groups at 6 months. These studies are limited by small sample sizes, short follow-up periods and high crossover rates between groups.

Only two RCTs have primarily evaluated clinical outcomes such as mortality and heart failure hospitalisations. The CONSYST-CRT trial demonstrated that CSP was non-inferior to BiVP for a composite outcome of death, heart failure hospitalisations, and LVEF improvement. (7) Secondary outcome measures, such as improvement in NYHA class, were also non-inferior. In contrast, the PhysioSync-HF trial found worse outcomes with CSP compared to BiVP. (8) A possible explanation is that they had high proportions of female patients and those with dilated cardiomyopathy, who are known to be super-responders to BiVP. These two trials were both non-inferiority studies and were not powered for superiority. They left the decision to use LBBAP or HBP to individual operator preference. It remains uncertain whether clinical outcomes differ between the two techniques at this stage. In addition, they predominantly included non-ischaemic cardiomyopathy patients and used strict LBBB criteria, making universal applicability uncertain. Furthermore, it remains unclear whether LBBAP pacing requires selective capture of the left bundle branch to achieve comparable prognostic benefit to BiVP.

Table 1: Summary of randomised controlled trials comparing CSP to BiVP

Author (year)	**Patients**	**Comparison**	**Follow-up**	**Primary end-point**	**Results**
Upadhyay et al. (2019) (9)	41	HBP vs BiVP	12 months	QRS duration	HBP led to a significant reduction in QRS duration (-28ms P=0.002). No significant between group differences.
Vinther et al. (2021) (10)	50	HBP vs BiVP	6 months	Implantation success rate	HBP successful in 72% , BiVP successful in 96%.
Wang et al. (2022) (11)	40	LBBAP vs BiVP	6 months	LVEF	Significantly higher LVEF improvement in LBBAP compared to BiVP (5.6% P=0.039)
Pujol-Lopez et al. (2022) (12)	70	CSP vs BiVP	6 months	LVAT decrease	Similar LVAT decrease by CSP and BiVP (-28ms vs -21ms, p<0.001)
Vijayaraman et al. (2023) (13)	100	HOT-CRT vs BiVP	6 months	LVEF	HOT-CRT non-inferior to BiVP for LVEF improvement (12.4% vs 8.0% ; *P* = 0.02)
Pujol-Lopez et al. (2025) (7)	134	CSP vs BiVP	12 months	Mortality, cardiac transplant HFH, LVEF	CSP was non-inferior to BiVP for composite endpoint (23.9% vs 29.8%, p=0.02)

Zimerman et al. (2025) (8)	173	CSP vs BiVP	12 months	Mortality, HFH, LVEF	Hierarchical endpoint favoured BiVP across all individual endpoints (OR 2.36, p=0.002)
Žižek et al. (2025) (14)	62	LBBAP vs BiVP	6 months	LVEF	LBBAP was non inferior to BiVP for LVEF improvement (14% vs 8.5%, P <0.001)

Abbreviations: BiVP, Biventricular pacing. CSP, Conduction system pacing. HBP, His-bundle pacing. HFH, Heart failure hospitalisations. HOT-CRT, His-optimised cardiac resynchronisation therapy. LBBAP, Left bundle branch area pacing. LVAT, Left ventricular activation time. LVEF, Left ventricular ejection fraction.

BiVP is well established in patients with an LVEF ≤35% , but its role in heart failure with mildly reduced ejection fraction (HFmrEF) (EF35−50%) is less clear. Observational data from the I-CLAS study evaluating cardiac resynchronisation therapy in HFmrEF demonstrated a significant reduction in death or heart failure hospitalisations in the CSP group compared with BiVP (22% vs 34%, $P = 0.025$). (15) Further RCTs are needed in this area. There also remains uncertainty regarding the role of CSP in those with a HFrEF and non-LBBB morphology. Observational data suggest electrical optimisation, but no clinical outcome data are yet available. (16)

Conclusions

Initial data for CSP in HFrEF is promising. Several ongoing RCTs aim to strengthen the evidence base, the largest of which is the Left vs Left study, which aims to randomise more than 2000 patients to LBBAP vs BiVP, with completion expected in 2029. (17) The most recent ESC consensus statement (May 2025) advises CSP may be appropriate as a first-line alternative to BiVP in HFrEF and LBBB, particularly for those who are non-responders to BiVP. It should be considered as a rescue therapy in patients for whom BiVP is unsuccessful. (2) The RCTs published since the consensus statement do not fundamentally alter this position, as their results are conflicting.

Disclosures

The author declares no conflicts of interest related to this work.

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