ESC European Society of Cardiology

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EHRA DOCUMENT

EHRA European Heart Rhythm Association

European Society of Cardiology (ESC) clinical consensus statement on indications for conduction system pacing, with special contribution of the European Heart Rhythm Association of the ESC and endorsed by the Asia Pacific Heart Rhythm Society, the Canadian Heart Rhythm Society, the Heart Rhythm Society, and the Latin American Heart Rhythm Society

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Abstract Conduction system pacing (CSP) is being increasingly adopted as a more physiological alternative to right ventricular and biventricular pacing. Since the 2021 European Society of Cardiology pacing guidelines, there has been growing evidence that this therapy is safe and effective. Furthermore, left bundle branch area pacing was not covered in these guidelines due to limited evidence at that time. This Clinical Consensus Statement provides advice on indications for CSP, taking into account the significant evolution in this domain.

Keywords Conduction system pacing • His bundle pacing • Left bundle branch area pacing • Cardiac resynchronization therapy • Biventricular pacing • Indications

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Abbreviations

AF	atrial fibrillation
APHRS	Asian Pacific Heart Rhythm Association
AV	atrioventricular
AVN	atrioventricular node
AVNA	atrioventricular node ablation
BiV-CRT	biventricular cardiac resynchronization therapy
BiVP	biventricular pacing
BNP	brain natriuretic peptide
CHRS	Canadian Heart Rhythm Society
CI	confidence interval
CSP	conduction system pacing
CSP-CRT	conduction system pacing cardiac resynchronization therapy
CRT-D	cardiac resynchronization therapy defibrillator
EHRA	European Heart Rhythm Association

ESC	European Society of Cardiology
HBP	His bundle pacing
HF	heart failure
HFH	heart failure hospitalization
HFmrEF	heart failure and mildly reduced ejection fraction
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HOT-CRT	His-optimized cardiac resynchronization therapy
HR	hazard ratio
HRS	Heart Rhythm Society
ICD	implantable cardioverter–defibrillator
LAHRS	Latin America Heart Rhythm Society
LBBAP	left bundle branch area pacing
LBBB	left bundle branch block
LBBP	left bundle branch pacing
LFP	left fascicular pacing
LOT-CRT	left bundle branch optimized CRT
LV	left ventricular
LVEF	left ventricular ejection fraction
LVSP	left ventricular septal pacing
ms	millisecond
NIVCD	non-specific intra-ventricular conduction delay
nsHBP	non-selective His bundle pacing
NYHA	New York Heart Association
PICM	pacing-induced cardiomyopathy
QoL	quality of life
QRSd	QRS duration
RCT	randomized clinical trials
RBBB	right bundle branch block
RBBP	right bundle branch pacing
RV	right ventricular
RVP	right ventricular pacing
RWPT	R-wave peak time
sHBP	selective His bundle pacing
SND	sinus node dysfunction
TAVI	transcatheter aortic valve implantation
TR	tricuspid valve regurgitation
V	volt

Preamble

Conduction system pacing (CSP) is an overarching term including His bundle pacing (HBP) as well as left bundle branch area pacing (LBBAP). This is a relatively new area of pacing that is continuing to gain popularity among pacing specialists as being more physiological than the traditional form of right ventricular pacing (RVP), as well as emerging as an alternative to biventricular cardiac resynchronization therapy (BiV-CRT) in cases of heart failure (HF) with conduction system disease.

When the 2021 European Society of Cardiology (ESC) guidelines on pacing[1] were being formulated, CSP had already been investigated for several years, mainly in the form of HBP in cases of atrioventricular (AV) block, for pacing in the setting of AV nodal ablation and as a substitute for BiV-CRT in selected patients. At that point, most of the information on HBP was observational with short-term follow-up, and there were only two small randomized controlled pilot trials that included more than one centre.[2–5] A conservative approach towards HBP was therefore taken, and no recommendations regarding LBBAP were formulated due to limited available data at that time.

Ever since the publication of the 2021 guidelines, the use of CSP has greatly evolved, mainly with LBBAP,[6] due to perceived greater ease of implantation and superior electrical parameters compared with HBP. Recent European surveys[7,8] and the recent MELOS registry[9] are examples of the extensive use of CSP. The European Heart Rhythm Association (EHRA) published a consensus document on CSP implantation to standardize the technique.[10] The 2024 updated EHRA core curriculum now includes CSP in its syllabus.[11] This emphasizes the importance of proper training and patient selection for CSP.

Recently, the Heart Rhythm Society (HRS) guidelines on physiological pacing have expanded the indications for CSP.[12] Given the increasing published evidence and consensus among European experts on the likely benefits of CSP and to reconcile the European recommendations on pacing and cardiac resynchronization with current practice, we decided to update advice on indications for CSP.

This document represents a collaborative effort of the ESC and EHRA, as well as EHRA's sister societies: the Asia Pacific Heart Rhythm Society (APHRS), Canadian Heart Rhythm Society (CHRS), HRS, and Latin American Heart Rhythm Society (LAHRS). It follows the principles of the ESC and EHRA scientific document committees in terms of evaluating evidence and providing advice. All advice was submitted to anonymous voting and had to be approved by >70% of the writing group to be implemented (the patient representative did not vote, due to the technical nature of the advices). The authors include early CSP adopters (all of whom have extensive experience with BiV-CRT), experts in CRT who primarily perform biventricular pacing (BiVP), non-implanting HF specialists, and a patient representative (I.D.). We thus aim to provide a balanced and consensual view, from multiple perspectives.

Definition of categories of advice and areas of uncertainty

Definition	Categories of advice	Icons
Evidence or general agreement that a given measure is clinically useful and appropriate	Advice TO DO	
Evidence or general agreement that a given measure may be clinically useful and appropriate	May be appropriate TO DO	
Evidence or general agreement that a given measure is not appropriate or harmful	Advice NOT TO DO	
No advice can be given because of lack of data or inconsistency of data. The topic is important to be addressed	Areas of uncertainty	

Type of supporting evidence	Strength of evidence	Icons
Published data[$]	>1 high quality RCT Meta-analysis of high quality RCT	
	High quality RCT >1 moderate quality RCT Meta-analysis of moderate quality RCT	
	High quality, large observational studies	
Expert opinion*#	Strong consensus >90% of writing group supports advice	>90% agree
	Consensus >70% of writing group supports advice	>70% agree

$ The reference for the published data that fulfil the criteria is indicated in the table of advice, if applicable

*Expert opinion also takes into account randomized, nonrandomized, observational or registry studies with limitations of design or execution, case series, meta -analyses of such studies, physiological or mechanistic studies in human subjects

For areas of uncertainty:strong consensus that the topic is relevant and important to be addressed by future trials

Advice: CSP implantation and training	Strength of evidence
Advice TO DO	
Conduction system pacing implantation should be performed by physicians who have undergone adequate training and who have acquired the necessary skills to perform the procedure safely and effectively, with systematic evaluation of type of pacing that is achieved [e.g. selective vs. non-selective HBP (nsHBP), LBBP, left fascicular pacing (LFP), left ventricular septal pacing (LVSP), etc.]	 >90% agree

Scientific background—an update

In 1925, Wiggers first highlighted the potential detrimental effects of RVP due to the asynchronous activation of the ventricles.[13] Following the advent of cardiac pacing in the late 1950s, numerous observations have since underscored the progressive sequence of harm. This process begins at the molecular level and extends to macroscopic changes, such as asynchronous hypertrophy, leading to a progressive decline in left ventricular (LV) function (*Figure 1*). This decline is associated with increased episodes of HF and, consequently, higher mortality.[15]

Evidence suggests that pacing at any myocardial site within the right ventricle (RV), not just the apex, is associated with detrimental haemodynamic effects.[16] The slow electrical propagation through the myocardium can lead to ventricular mechanical dyssynchrony,[17] LV dysfunction, and HF, particularly in patients who require a high percentage of pacing.[18]

Among the first studies to report detrimental outcome associated with RVP, in both patients with and without pre-existing HF, were the DAVID and MOST trials.[18–20] The clinical entity of pacing-induced cardiomyopathy (PICM) was introduced over the following years, which affects 10–20% of patients who receive RVP.[21,22] It is difficult to ascertain which patients will develop PICM, despite some predictors having been described [e.g. paced QRS duration (QRSd)[23]]. In addition, there is no evidence of clinical benefit of alternative pacing sites such as RV septal pacing over RV apical pacing.[24] For these reasons, pacing strategies such as BiVP or CSP have been developed to avoid or to attenuate PICM.

Differences between conduction system pacing methods

Capture of the conduction system is present with HBP, proximal right bundle branch pacing (RBBP), left bundle branch pacing (LBBP), and LFP. For the purposes of this document and in the interest of simplification, proximal RBBP is not distinguished from HBP, and LFP is not distinguished from LBBP. Although CSP implies capture of the conduction system,[10] for the purposes of this document we also included LVSP as being part of CSP.

Left bundle branch area pacing includes LBBP, LFP, and LVSP.[10] Capture of the conduction system may be either selective (with exclusive capture of conduction tissue) or non-selective (with concurrent capture of conductive tissue and local myocardium). With HBP, approximately two-thirds of patients have nsHBP at programmed output,[25,26] while LBBP, LFP, and RBBP are almost always non-selective due to more surrounding myocardial tissue.[27–29] Previous studies showed that despite the differences in QRSd, ventricular synchrony during nsHBP is similar to selective HBP (sHBP) and much more physiological than RV septal pacing.[30–33] Also, no difference in clinical outcomes between nsHBP and sHBP has been observed.[25]

During LVSP, the conduction tissue is not captured; however, capturing myocytes close to the left septal endocardium leads to more synchronous ventricular activation than during RVP.[16,34,35] Both LBBP and LVSP have

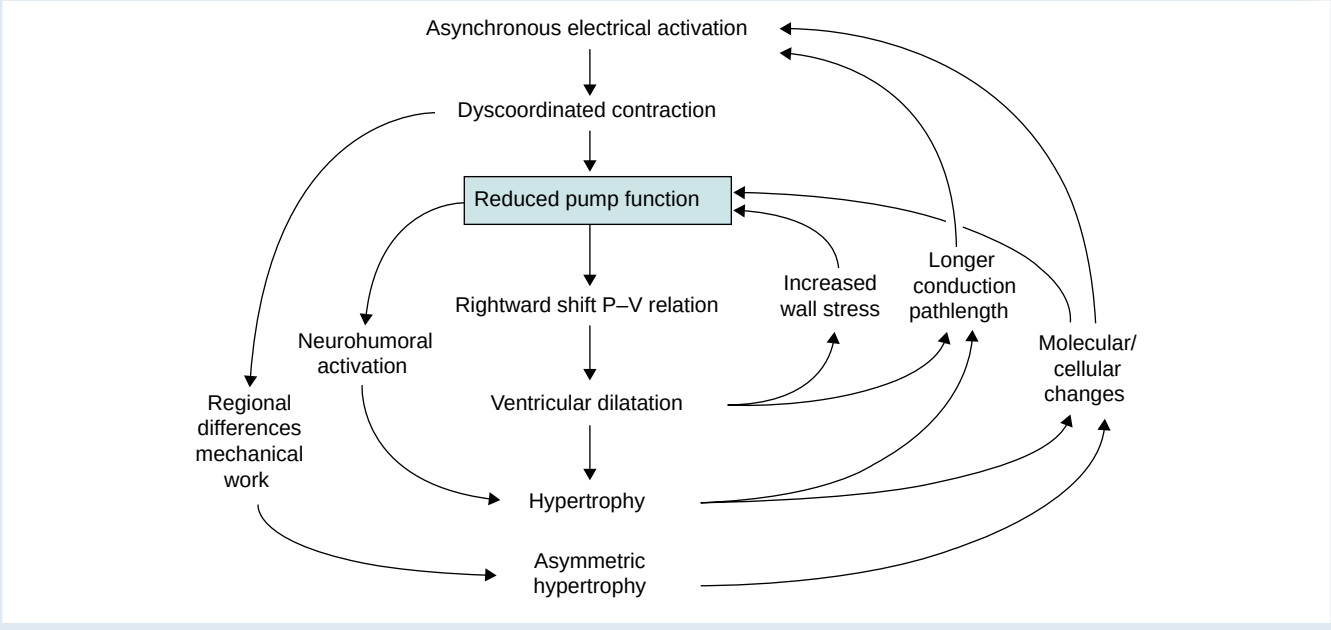

Figure 1 Relationship between asynchronous ventricular activation leading to reduced pump function. P–V, pressure volume. Reproduced, with permission, from Vernooy *et al.*[14]

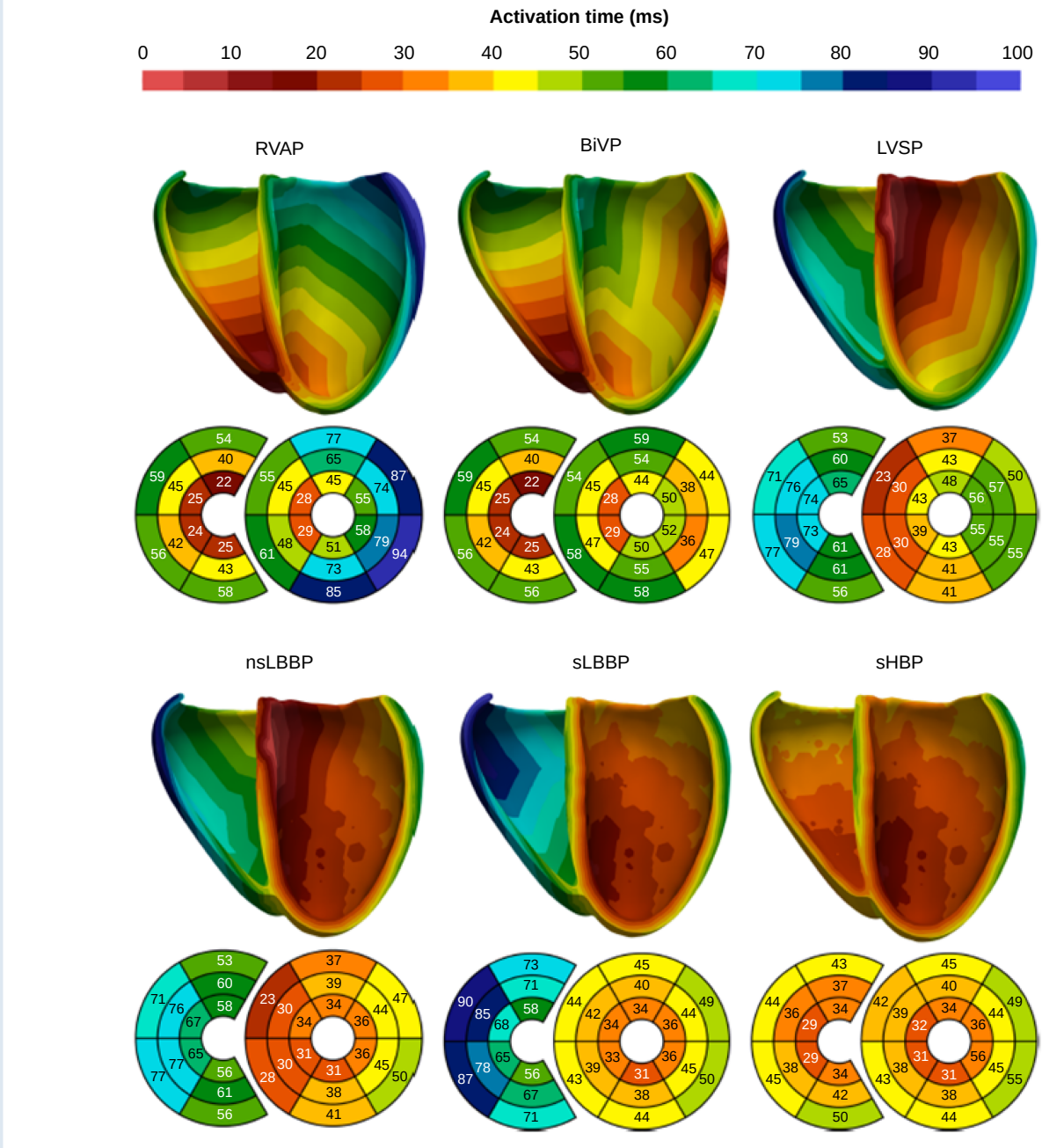

Figure 2 Computer-simulated three-dimensional activation maps following different pacing strategy and their corresponding segmental activation time in bullseye form. Reproduced with permission from Meiburg *et al.*[38]

similar ECG characteristics and paced QRSd,[36] but they differ in their ventricular activation patterns.[37] Whereas LVSP produces less interventricular dyssynchrony than LBBP (due to delayed LV activation, which nevertheless occurs before RV activation), the latter is associated with better LV synchrony (due to more rapid and homogenous LV activation) (see *Figures 2* and *3*).[36] It is still a matter of debate whether capture of the left-sided conduction system impacts clinical outcomes. Most probably, this makes little difference in patients without documented structural heart disease,[36] but some observational studies have reported worse outcomes for patients with HF with LVSP compared with LBBP.[39,40] Another open question is whether LBBP is superior to LFP, as suggested by a small observational study in patients with HF.[41]

His bundle pacing vs. left bundle branch area pacing

Conduction system pacing utilizing HBP and LBBAP has been utilized for the management of both bradycardia and HF indications. While HBP provides excellent synchronous biventricular activation, LBBAP preserves or restores intra-ventricular LV synchrony, with both modalities providing comparable mechanical performance of the heart.[30,31,34,36,38,42–46] The clinical impact of RV dyssynchrony or delayed activation induced by LBBAP is currently unclear.

While there are no high-quality long-term randomized comparisons between HBP and LBBAP,[42,47–55] observational data comparing HBP

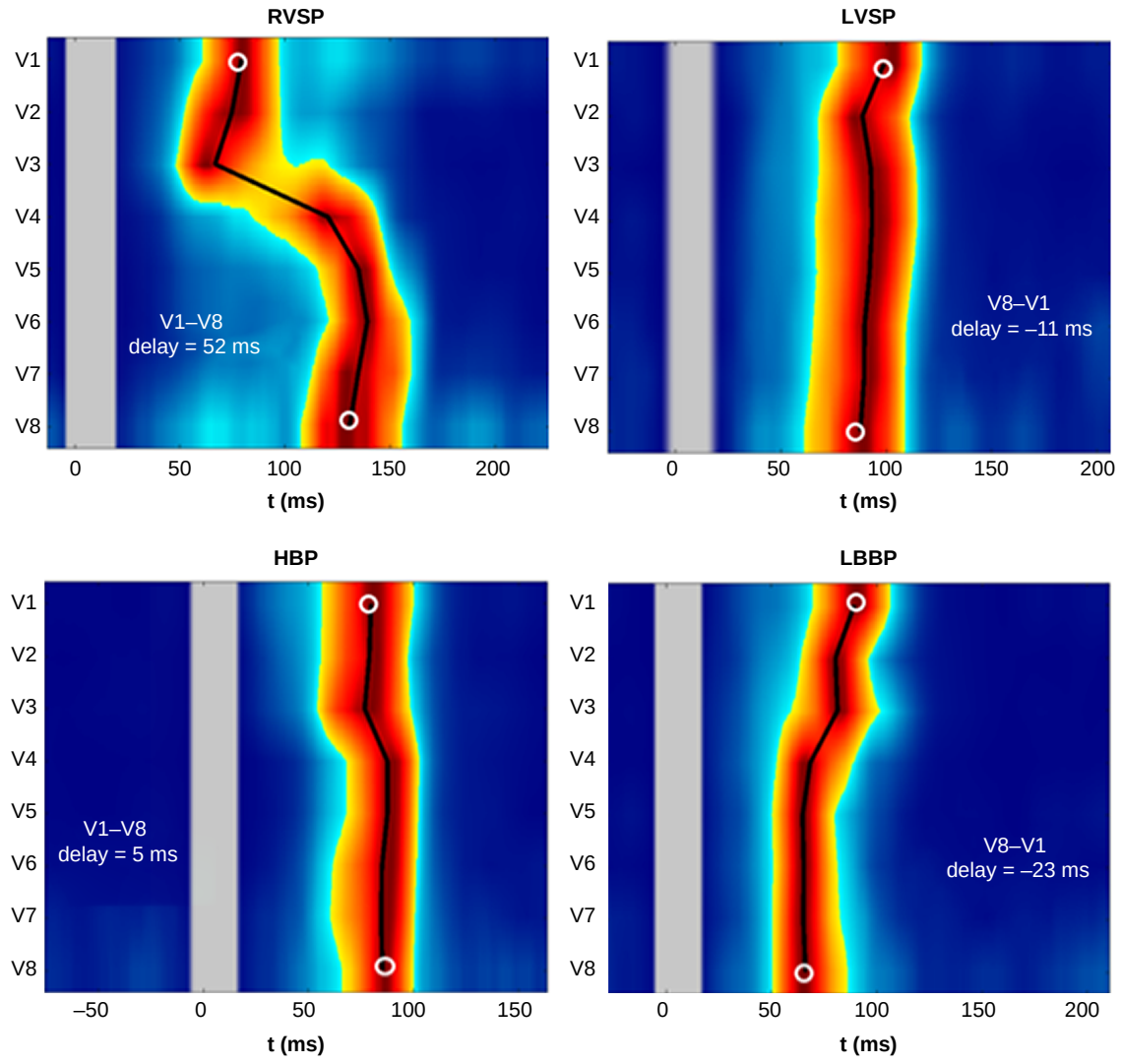

Figure 3 Examples of ventricular dyssynchrony assessed by ultra-high-frequency ECG (sampled at 5 KHz and evaluating the 150–1000 hz spectrum of the QRS complex, with V1–V8 electrodes placed in standard positions). In each of the UHF-ECG maps, time is visualized on the *x*-axis, and chest leads are visualized on the *y*-axis. Local activations under the specific leads are connected by a black line. The difference between V1 and V8 activations (white circles) indicates interventricular electrical dyssynchrony, whereas the width of the coloured band informs of local activation duration. Note that all CSP methods, as well as LVSP, are associated with less interventricular dyssynchrony than RVSP. CSP, conduction system pacing; ECG, electrocardiogram; HBP, His bundle pacing; LBBP, left bundle branch pacing; LVSP, left ventricular septal pacing; RVSP, right ventricular septal pacing.

and LBBAP indicate that the success rates, capture thresholds, sensing amplitude, and lead complication rates are more favourable with LBBAP, while acute haemodynamic improvement and clinical outcomes including LVEF, HF, and mortality outcomes appear overall comparable.[46,47,51,56–58] The only randomized trial comparing HBP and LBBAP was a small crossover study in 23 patients who underwent AVN ablation followed by 6 months of pacing in each modality, without any significant differences in LVEF.[59]

The more favourable electrical parameters and perceived ease of implantation have led to preferential adoption of LBBAP over HBP in clinical practice over the past years.[6–8,51,56] There are nevertheless inherent advantages and disadvantages with both CSP techniques (see *Table 1*), which makes it worthwhile to encourage acquiring proficiency with HBP as well as LBBAP.

Despite certain challenges associated with HBP (achieving favourable electrical parameters, difficulty in correcting distal conduction disease),[25,56,58,70–74] employment of the implant technique outlined in the EHRA CSP consensus document (e.g. ensuring torque buildup, current of injury of the His potential, stability testing, etc.) and application of strict implant criteria (e.g. capture threshold of ≤1.5 V/0.5 ms and sensing >2 mV) may allow stable and effective HBP delivery. Implantation at the distal His bundle offers several advantages compared with the proximal His bundle: lower thresholds, larger R-wave sensing, less *P*-wave oversensing, nsHBP with septal myocardial capture as backup in case of loss of HB capture, and less interference with subsequent AV node ablation (AVNA).[75,76]

The learning curve for HBP implantation is sometimes perceived to be unduly prolonged. However, in a multicentre report, a success rate

Table 1 Comparison of HBP vs. LBBAP

	HBP	LBBAP
Pacing threshold and energy consumption	May be high (ideally accept only if pacing threshold ≤1.5V/0.5ms)	Low (usually ≤1.5V/0.5 ms)
Sensing	Usually smaller R waves, P wave far-field oversensing (accept only if R waves >2 mV with far-field P waves <0.5 mV)	R waves comparable to RV leads (usually >4 mV), no *P* wave far-field oversensing
Guidance at implantation	Clear physiological landmarks (His EGM and paced QRS similar to intrinsic QRS or with bundle branch correction, QRS transition with decrementing output if nsHBP)	Predominantly anatomical and surrogate ECG markers (e.g. RWPT, QRS transition with decrementing output often absent)
Proof of conduction system capture	Very clear definition, easy documentation in close to 100% of implants	More difficult, combination of different EGM and ECG parameters with often uncertain confirmation of conduction system capture
QRS duration	Identical to native narrow QRS in sHBP; nsHBP is wider	Wider than native narrow QRS
Use of ST segment for ischaemia diagnosis[60–62]	Equal to intrinsic ischaemia diagnosis in sHBP (STE, STD)	ST segment deviation and ischaemia diagnosis feasible in proximal LBBP
AV node ablation after device implantation	May be challenging, with risk of threshold increase in proximal HBP implantation, and higher risk of recurrence of AV conduction	Easy, no risk of threshold increase
Requirement for backup lead	Advised in specific subgroups of patients (AV node ablation, pacemaker dependency, high capture threshold, poor sensing)	Usually not required
Loss of conduction system capture[48]	Easy to assess (paced QRS morphology resembles intrinsic or with bundle branch correction, QRS transition with decrementing output in case of nsHBP). Reported to be up to 23.5%	More difficult to assess (QRS transitions with decrementing output infrequently encountered, requirement for digital callipers for RWPT measurements) Reported to be up to 13.5%
Late Threshold Increase	Not uncommon ~10–14%	Unusual
Long-term data	Available	Accumulating
Complications	(1) Long-term threshold increase/loss of capture (2) Ventricular undersensing (3) *P* wave oversensing (4) Lead micro/macrodislodgment	(1) Septal perforation (2) Permanent RBBB up to 6.3% (3) Permanent CHB in patients with LBBB (4) Loss of conduction system capture (mainly due to microdislodgment) (5) Lead macrodislodgment (6) Tricuspid regurgitation (7) Septal haematoma (8) Coronary vessel trauma/fistula (9) Myocardial infarction (10) Lead fracture
Pacemaker-lead induced tricuspid regurgitation	Rare; none in atrial/proximal HBP[63]	Up to 33%[64]
Synchronization in narrow QRS	Biventricular synchrony[30,42]	Similar LV synchrony but less favourable RV synchrony[36]
Resynchronization in RBBB	More favourable (also with nsHBP without correction of RBBB)[65,66]	Less favourable[67]
Resynchronization in LBBB	LV resynchronization but at higher thresholds and lower success[2,68]	LV resynchronization with very low thresholds and greater success[69]
Extractability	Relatively easy, with minimal complications, similar to RV lead extraction	May potentially be complex and challenging (long-term data are lacking for the time being)

ECG, electrocardiogram; EGM, electrogram; HBP, His bundle pacing; LBBAP, left bundle branch area pacing; nsHBP, non-selective His bundle pacing; RWPT, R-wave peak time; sHBP, selective His bundle pacing; STD, ST segment depression; STE, ST segment elevation.

Table 2 Preferred pacing modality of HBP or LBBAP according to indication (assuming expertise of the operator with both techniques, and acceptable electrical parameters)

HBP may be preferred	LBBAP may be preferred	Either HBP or LBBAP suitable
Tricuspid valve dysfunction/prosthesis/transcatheter repair.[63,64,79]	Scheduled AVN ablation[53]	Heart failure indication
	Infra-nodal AV block[80]	Nodal AV block
Bailout in case of unsuccessful/unsatisfactory LBBAP (e.g. in patients with septal scar[81])	Previous or scheduled TAVI or aortic valve surgery	
	Bailout in case of unsuccessful/unsatisfactory HBP	

Table based upon expert opinion of the writing group. Nodal AV block = supra-Hisian block; infra-nodal block = intra- or infra-Hisian block. Definite diagnosis of level of block may be obtained by mapping the His with the pacing lead, which is routinely performed for HBP.
AV, atrioventricular; AVN, atrioventricular node; HBP, His bundle pacing; LBBAP, left bundle branch area pacing; TAVI, transcatheter aortic valve implantation.

of 87% was achieved after 40 cases.[70] In another report from three centres, the success rate flattened after ~30–40 cases.[77] However, HBP success was defined as a threshold of ≤ 3.5V/1ms, and required numbers are likely to be higher to achieve lower capture thresholds. Conversely, LBBAP may seem to be relatively easy and with a high success rate, even for beginners. However, many implantations in inexperienced hands represent only deep septal pacing rather than true LBBAP. Even in experienced centres, success may be met in only 92% of patients with bradycardia and is even lower in patients with HF (82%), although these figures included the learning curves of the operators.[9] The learning curve for successful LBBAP implantation has been reported to flatten after 50–100 patients in a single-centre report with one main operator.[78] In another single-centre study with three operators, LBBAP implantation success was evaluated for the first 126 cases and was 79% for the first 42 patients and increased to 90% for the following 42 cases and to 95% for the last tertile. In the multicentre MELOS registry,[9] success rate continued to increase over the first 270 cases, with fluoroscopy time and V_6RWPT reaching a plateau after approximately 110 cases. Therefore, the learning curve for LBBAP may not be shorter than for HBP, and each technique presents its own set of challenges.

There may be instances where one pacing modality is preferred (*Table 2*).

The capture thresholds are higher and success rates of HBP are lower among patients with bundle branch block, infra-nodal AV block, and those with aortic valve replacement.[25,71,80,82–84] It is preferable to opt for LBBAP in patients with significant aortic valve disease, as transcatheter aortic valve implantation (TAVI) or aortic valve surgery may compromise HBP lead function. As discussed in the following sections, patients with infra-nodal AV block or those requiring AV nodal ablation are better served with LBBAP than with HBP.

A final consideration is the potential worsening of tricuspid valve regurgitation (TR), observed in up to one-third of patients undergoing LBBAP, particularly in a basal position.[64,79,85] However, this finding requires validation in large studies. Notably, this issue does not appear to be as prevalent with HBP, although sheath and lead manipulation at the level of the valve may risk entanglement in the subvalvular apparatus.[63] The His bundle may be paced from the atrial aspect of the tricuspid valve (thereby avoiding the valve altogether) or from the ventricular aspect as it courses in proximity to the commissure between the septal and anterosuperior leaflets.[86] In instances where the tricuspid valve needs to be spared, such as patients with a history of tricuspid valve surgery or transcatheter repair, HBP is preferrable.[87] Long-term evolution of TR with CSP needs to be further studied.

In general, implanters may use the CSP modality that best suits them. However, CSP implanting centres should ideally be able to perform both HBP and LBBAP and should also be able to perform BiVP implantation (as CSP is not always successful). Being proficient with all techniques offers the operator an alternative for a bailout solution in case the initial technique is unsuccessful or suboptimal.

Criteria for His bundle capture

Confirming HB capture during the implantation procedure is clinically important since myocardial pacing in the para-Hisian area actually corresponds to right ventricular septal pacing (RVSP) and leads to dyssynchronous ventricular activation (unlike nsHBP, where conduction system capture is achieved in addition to myocardial capture).[30,32] Confirmation of HBP in patients with narrow QRS is straightforward because QRS complex morphology and duration are the same as spontaneous complexes during sHBP with an isoelectric interval corresponding to the HV interval, or only slightly different with a pseudo-delta wave during nsHBP.[65,73] It is more complex in case of nsHBP with uncorrected bundle branch block, where the QRS complexes may be even wider than with intrinsic rhythm.[65]

The gold standard for confirming HB capture is to demonstrate transitions in QRS morphology with decrementing output (from nsHBP to either sHBP or to myocardial capture, or loss of correction of bundle branch block) .[65,73] Transitions are absent in 5–10% of patients (e.g. due to near-identical thresholds between the HB and myocytes), and in those cases, other methods of confirmation have to be used (such as programmed stimulation, which leverages differences in refractory periods between tissues).[65,88–90] QRS morphology criteria have also been described and are detailed in the recent EHRA consensus document on CSP implantation.[10]

Criteria for left bundle branch area pacing

Left bundle branch area pacing consists of LBBP and LVSP with both being associated with better ventricular synchrony and LV haemodynamics than RVP.[16,33–35,37,91] For evaluation of LBBAP, correct positioning of the V1 chest electrode is essential as the terminal *r′/R′* deflection may be missed if the electrode is placed too high. In some cases, LBBAP without a terminal *r′/R′*-wave in V1 can be observed,[10] presumably due to rapid transseptal activation, or right ventricular activation occurring via rapid retrograde conduction to the HB and down the RBB, or slow propagation via diseased LBB, resulting in simultaneous biventricular activation, which is probably the dominant mechanism in patients with HF. Other causes for absence of a terminal *r′/R′* in V1 are anodal capture with bipolar pacing,[92] or fusion with intrinsic conduction.

A number of criteria have been described in the EHRA consensus document on CSP implantation to confirm conduction system capture in LBBP, the gold standard of which is transitions in QRS morphology during decremental output with unipolar pacing (i.e. with transitions from non-selective LBBP to LVSP or to selective LBBP).[10] The accuracy of R-wave peak time (RWPT) criteria is uncertain, especially in patients with low septal and/or apical lead placements,[93,94] as these pacing locations can produce V_6RWPT shortening and V_6–V_1 interpeak interval prolongation without conduction system capture and can cause misclassification of LVSP as LBBP. In addition to pacing site, the

V_6RWPT depends upon heart size and conduction velocity (e.g. with misclassification of LBBP as LVSP due to long V_6RWPT in patients with slow conduction or dilated hearts). It is therefore important to realize that none of the V_6RWPT cut-offs (or for the V_6–V_1 interpeak interval) are 100% accurate for diagnosing conduction system capture and there is little information on the optimal cut-offs in patients with HF. Also, a terminal *r*/*R* wave in V1 may occasionally be visible when pace mapping from the RV septum and is therefore *per se* not diagnostic of LBBAP.[95]

The criteria for LVSP are as follows: (i) deep septal deployment of the pacing lead together with (ii) terminal *r*′/*R*′-wave in lead V1, without criteria for conduction system capture.[10]

Success rates, procedural outcomes, and complications of His bundle pacing and left bundle branch area pacing

A meta-analysis of 15 observational studies involving 2491 patients found that LBBAP had significantly higher success rates compared with HBP (91.1 vs. 80.9%; $P < 0.001$), along with significantly lower lead-related complications over follow-up, which included lead failure, inactivation for elevated thresholds and dislodgment (1.1 vs. 4.3%; $P = 0.003$).[96] The meta-analysis also found no significant difference in lead dislodgement rates between CSP and traditional RVP.[96]

In a multicentre study involving 870 subjects, of whom 849 were followed for 6 months, CSP lead implantation was successful in 768 patients (90%), with a success rate of 95% for LBBAP and 88% for HBP ($P = 0.002$).[58] The two pacing modalities had no significant differences in procedural or fluoroscopy duration. However, the threshold at implantation was higher for HBP (1.44 ± 1.03 V at 0.71 ± 0.33 ms) than for LBBAP (0.69 ± 0.39 V at 0.46 ± 0.15 ms, $P < 0.001$). At 6-month follow-up, HBP continued to have a higher threshold than LBBAP (1.59 ± 0.97 V at 0.67 ± 0.31 ms vs. 0.79 ± 0.33 V at 0.44 ± 0.13 ms; $P < 0.001$). An increase in the pacing threshold of more than 1 V at 6 months was observed in 3 of 208 patients (1.4%) with LBBAP and 55 of 418 patients (13.2%) with HBP ($P < 0.001$). Serious adverse events related to the implantation procedure or the CSP lead occurred in 5 of 251 patients (2.0%) with LBBAP and 25 of 598 patients (4.2%) with HBP ($P = 0.11$).

Advice: HBP vs. LBBAP	Strength of evidence
Advice TO DO	
It is advised that CSP implantation centres should ideally be capable of performing both HBP and LBBAP, and should be able to perform BiVP implantation	 >90% agree
In patients with significant aortic valve disease (which may require future intervention), infra-nodal AV block or AVNA, it is advised that LBBAP is preferred over HBP[25,71,80,82–84]	
In patients requiring sparing of the tricuspid valve (e.g. after tricuspid valve surgery or transcatheter repair), it is advised that HBP is preferred over LBBAP[63]	

Conduction system pacing for atrioventricular block with left ventricular ejection fraction > 40%

In patients with high-grade AV block and normal systolic function, BiVP has been shown to preserve LVEF during follow-up compared with a significant decline in patients who had been randomized to RVP (without, however, any differences in clinical outcome).[97,98] Biventricular pacing nevertheless bypasses the His–Purkinje system, inevitably resulting in ventricular dyssynchrony[38,43,99] (see *Figures 2* and *4*). As BiVP requires a more complex implantation procedure which coincides with a higher risk of complications,[100] it has not been recommended as an alternative to RVP in patients with AV block and LVEF >40% in the 2021 ESC pacing guidelines.[1] According to these guidelines, HBP may be considered for treating these patients, who were anticipated to have >20% ventricular pacing, without giving any recommendation for LBBAP due to the limited amount of data available at that time. More recently, the 2023 HRS/APHRS/LAHRS guidelines on physiological pacing stated that LBBAP may be useful (along with CRT) in AV block patients with LVEF 36–50% and that it may be considered in those with LVEF >50%.[12]

In patients with AV block in whom ventricular pacing is anticipated to be infrequent (<20%), strategies that minimize ventricular pacing are appropriate, similar to what is outlined in the 2021 ESC pacing guidelines.[1,101] However, as the course of evolution of the conduction disorders in these patients may be unforeseeable, CSP may be an option in proficient centres to provide a physiological means of delivering pacing therapy in case ventricular pacing burden increases.

Over the past years, various studies have compared either HBP and/or LBBAP with RVP in patients with AV block (most of whom had mildly reduced to normal LVEF) and showed that this emerging pacing strategy seems very promising. Unfortunately, so far only a few small randomized clinical trials (RCTs) have compared CSP with RVP in patients with bradycardia and near-normal LVEF, none of which have long-term follow-up. One early trial showed in 38 patients that HBP preserved LVEF and mechanical synchrony as compared to RVP after 12 months.[4] A recent RCT in 92 patients also showed superiority of HBP over RVP, with a higher LVEF and lower levels of TGFβ1 during follow-up.[102] Two small RCTs focusing on ECG parameters compared LBBP with RVP and showed that LBBP resulted in significant narrower QRS duration than RVP.[103,104] In another study, however, in 50 randomized patients, the LVEF was not significantly different between LBBP and RVP after 12 months.[105] Nevertheless, global longitudinal strain, QRS duration, as well as echocardiographic measurements of dyssynchrony were significantly better during LBBP as compared to RVP. In the single-centre STAY study, 70 patients with AV block, LVEF > 40% (mean ~60%), and an expected high ventricular pacing burden (mean ~91%) were randomized to either RVP or CSP (9 HBP, 17 LBBP, and 10 LVSP).[106] Over a 6-month follow-up, RVP was associated with a significant decrease in LVEF {mean difference, −5.8% [95% confidence interval (CI), −9.6 to −2%]; $P < 0.01$} and increase in LV end-diastolic diameter [mean difference 3.2 mm (95% CI, 0.1–6.2); $P = 0.04$]. In addition, HF-related admissions were higher in the RVP group (22.6 vs. 5.1%; $P = 0.03$).

Besides the few small short-term RCTs that show superiority of CSP over RVP in patients with AV block, larger observational studies have been performed (for which data should be interpreted with caution due to the inherent caveats of non-randomized studies). In a comparison of 304 patients with HBP at one hospital with 433 patients receiving RVP at a sister hospital,[26] a significant reduction in the primary endpoint with HBP (all-cause mortality, HF hospitalizations (HFH), or need for upgrade to BiVP) was found after a mean follow-up of ~2 years (with a requirement for lead revision in 4.2% of patients with HBP

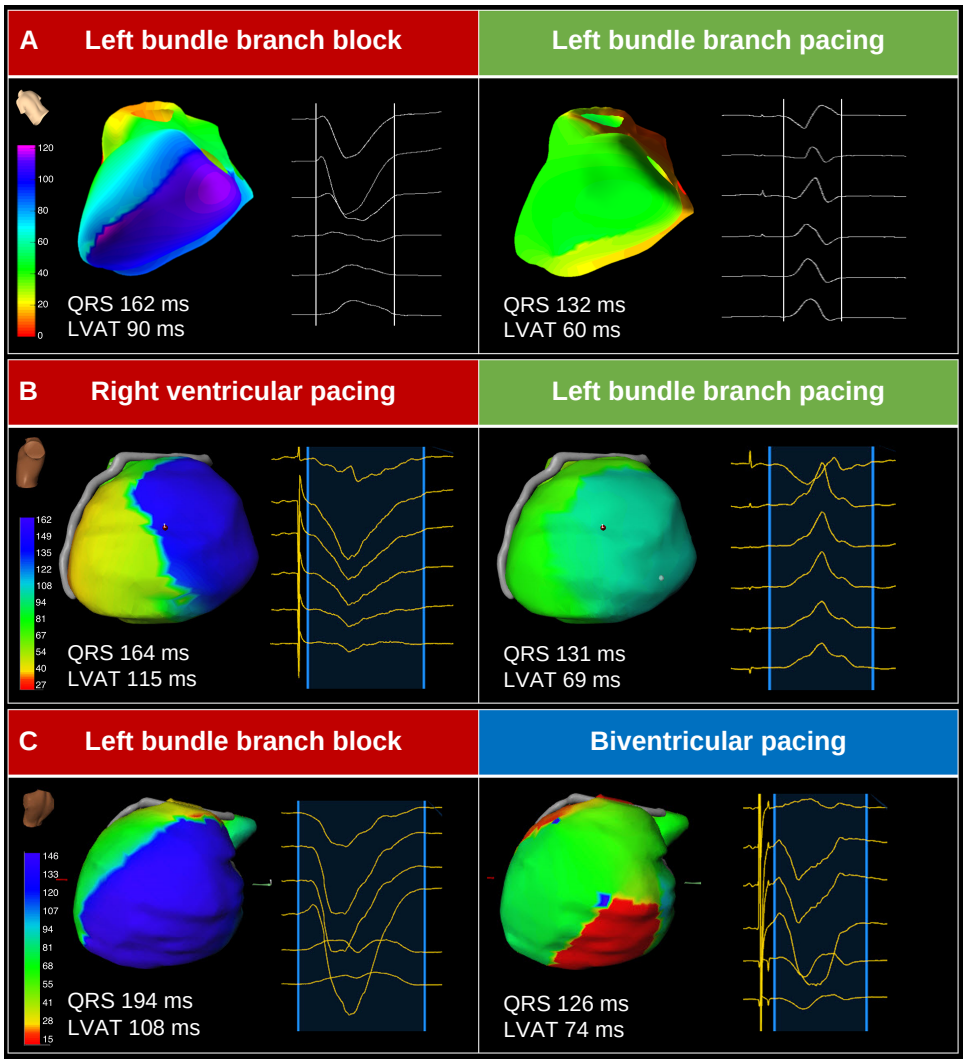

Figure 4 Electrocardiographic imaging (ECGi) with examples of LVAT shortening and change of activation pattern with CSP and BiVP. All 3 cases show long LVAT with delayed activation of the left ventricle (blue or purple during intrinsic rhythm with left bundle branch block or with right ventricular pacing. With CSP and BiVP, all showed decrease in LVAT and faster activation of the left ventricle (green or red). (*A*) Maps with an imageless ECGi technology and (*B*) and (*C*) maps with ECGi that requires computed tomography. BiVP, biventricular pacing; CSP, conduction system pacing; LVAT, left ventricular activation time.

due to high thresholds). The same group also reported improved outcome of the same primary endpoint in 321 patients with LBBAP compared with 382 patients with RVP after a mean follow-up of 1.6 years.[107] Among patients with ventricular pacing >20%, LBBAP was associated with a significant reduction in mortality [7.8 vs. 15%; hazard ratio (HR) 0.59; $P = 0.03$] and HFH (3.7 vs. 10.5%; HR 0.38; $P = 0.004$) as compared to RVP. Another series reported similar results in 628 patients who received RVP compared with 231 patients received CSP (95 HBP and 136 LBBAP), with a reduction in HFH in patients with >20% ventricular pacing in a multivariable-adjusted model, with a HR of 0.40 (95% CI, 0.17–0.95).[108] These studies did not specifically target a population with AV block and LVEF >40%, but ~50–65% of patients had AV block and the mean LVEF was >50%. Reduced mortality was also reported in a large population-based study in patients with dual-chamber pacemakers using data from Medicare claims in 6197 patients with CSP (4738 LBBAP and 1459 HBP) compared with 16 989 patients with RVP, roughly half of whom had an AV block indication for pacing (LVEF was not reported but was presumably preserved overall).[51] All-cause mortality at 6 months was lower in the CSP group (HR 0.66; $P < 0.0001$) as was HFH (HR 0.70; $P = 0.02$). Other observational studies showed that the incidence of HFH and need for an upgrade to BiVP was significantly lower in patients undergoing LBBP as compared to those receiving RVP.[109,110] Also, for other populations such as AV block after TAVI[111,112] and for patients with AV block and HF with preserved ejection fraction,[113] LBBP seems to be a better alternative compared with RVP.

Meta-analyses of the few randomized trials and larger observational cohorts comparing CSP with RVP in patients with AV block showed that CSP was significantly superior in preserving LVEF, shortening paced QRS duration, and reducing rates of HFH.[114–116] On the contrary, RVP was associated with higher implantation success rate and shorter procedure/fluoroscopy duration and had fewer lead complications.

While awaiting the results of the ongoing larger RCTs in patients with AV block and mildly reduced to normal LVEF (>40%) requiring

frequent (>20%) ventricular pacing, both HBP and LBBP might be considered as alternatives to RVP in these patients. It has nevertheless been shown that HBP implantation is less successful in infra-nodal block compared with nodal block (76 vs. 93%, $P < 0.05$).[80] A backup lead may be useful to avoid asystole in HBP patients with AV block, particularly if the block is infra-nodal or in case of sensing issues.[1,10,117] Left bundle branch area pacing may be a more effective and reliable form of pacing in these instances and has been shown to require fewer lead revisions, yield lower pacing thresholds, greater R-wave amplitudes, and similar paced QRS duration compared with HBP in patients with AV block.[47,118]

Conduction system pacing for atrioventricular block in reduced left ventricular ejection fraction (≤40%)

Current ESC pacing guidelines state, based on several RCTs,[119–121] that BiV-CRT rather than RVP is recommended for patients with HF with reduced EF (HFrEF, LVEF ≤40%) who have AV block and an indication for ventricular pacing, regardless of New York Heart Association (NYHA) class and QRS duration, in order to reduce morbidity; this includes patients with AF.[1] The largest relevant trial is BLOCK HF,[119] which included 208 patients who had LVEF < 35% (30% of the total cohort of the trial). HOBIPACE[120] and COMBAT[121] (which both only included patients with LVEF < 40%) totalled 90 patients together. Therefore, the evidence for the efficacy of BiVP in the context of AV block is relatively scarce compared with that of BiV-CRT for treating HF.

The 2023 HRS/APHRS/LAHRS guidelines on physiological pacing do not give any specific recommendations for pacing in patients with AV block and LVEF < 35%, and refer the reader to the recommendations for treating HF.[12]

There is a paucity of evidence regarding CSP in AV block patients with LVEF < 40%. Randomized trials comparing conduction system pacing cardiac resynchronization therapy (CSP-CRT) to BiV-CRT typically do not indicate the percentages of patients with AV block, but these presumably are low[3,68,122–124] (see Supplementary material online, *Table S1*). Randomized trials involving CSP as a treatment modality focusing on patients with AV block and LVEF < 40% have not been performed to date. Patients with AV nodal ablation or upgrades are separate entities and are discussed in following sections. Likewise, most observational studies on CSP do not separately report outcomes of patients with AV block and LVEF < 40%. They mostly included patients with LVEF < 50% and a mix of indications for CRT, AVNA, or device upgrade and a minority of patients with AV block, without separate reporting of results in these subgroups[9,40,49,69,125–135] (see Supplementary material online, *Table S1*). Patients included in observational studies dedicated to CSP in AV block had an average LVEF of >50%.[80,118]

A small ($n = 50$) observational case–control matched study evaluated the benefits of CSP in patients with LVEF ≤45% who were candidates for CRT due to either AV block or an upgrade from RVP.[130] Conduction system pacing (with either HBP or LBBP) and BiVP resulted in similar echocardiographic response and LVEF improvement at 6-month follow-up; decreased mitral regurgitation and improved functional class were observed with CSP.

In patients with HF, CSP implant success rate is lower compared with bradycardia indication.[9] In the specific population with complete AV block and LVEF ≤40% ($n = 77$), an 88.3% implant success rate has been reported.[136] Owing to the pros and cons of CSP and of BiVP for treating AV block in patients with LVEF < 40%, it is a matter of debate whether one or the other pacing modality should be preferred. This is particularly the case in patients with a narrow QRS,[137] where

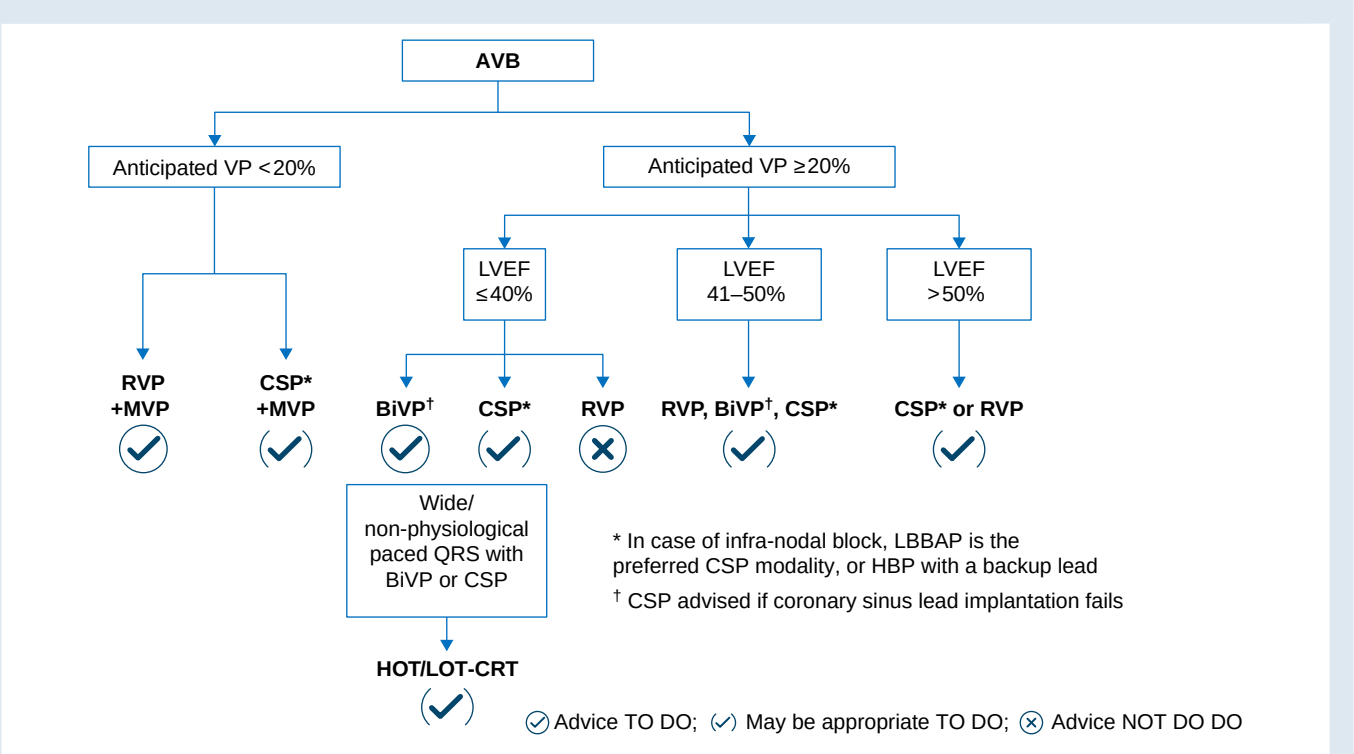

Figure 5 Summary of CSP indications in AVB. AVB, atrioventricular block; BiVP, biventricular pacing; CSP, conduction system pacing; HBP, His bundle pacing; HOT/LOT-CRT, His-optimized or left bundle-optimized cardiac resynchronization therapy; LBBAP, left bundle branch area pacing; LVEF, left ventricular ejection fraction; MVP, minimized ventricular pacing; RVP, right ventricular pacing.

BiVP circumvents the His–Purkinje system and delivers myocardial pacing. Conduction system pacing may provide a more physiological form of pacing with similar dyssynchrony and strain correction over time.[138] Even patients with AV block with a wide QRS rhythm may benefit from CSP, as it has been shown that 96% of AV block lies at the nodal or intra-Hisian level, and is therefore amenable to correction with CSP (which was successful in 97% of patients).[118]

Trials studying CSP in AV block and LVEF <40% are ongoing and vary in the patient population recruited, and usually also include a CRT indication (e.g. Left vs. Left, CONSYST-CRT 2, etc.). The LVEF cut-off differs but generally includes patients with LVEF <40% as a subset. The interventions broadly compare CSP with RVP or BiVP depending on the patient cohort (c.f. *Figure 11* and supplementary material online, *Table S9*).

A summary for CSP indications in AV block, as opposed to BiVP and to RVP, is shown in *Figure 5* (for HOT/LOT-CRT, see relevant section).

Advice: CSP for AV block	Strength of evidence
Advice TO DO	
In patients with AV block in whom BiVP is desired, it is advised to implant CSP[a] as a rescue strategy if coronary sinus lead implantation fails[139]	 >90% agree
May be appropriate TO DO	
It may be appropriate to implant CSP[a] in patients with LVEF >40% with an anticipated ventricular pacing burden >20%.[4,26,51,102–106,108,114–116]	
It may be appropriate to implant CSP[a] in lieu of BiVP in patients with AV block and LVEF <40% with an anticipated ventricular pacing burden >20%[130,132]	
In patients with AV block and infrequent (<20%) anticipated ventricular pacing, it may be appropriate to implant CSP[a] in combination with minimized ventricular pacing strategies, in order to provide physiological ventricular pacing in case the conduction disorder progresses	 >90% agree
It may be appropriate to choose CSP[a] as opposed to BiVP as a primary strategy, taking into account operator experience, in the presence of specific patient populations where a simpler device is desired (e.g. frail patients, patients with limited life expectancy, or those requiring a smaller device)	 >90% agree
Advice NOT TO DO	
It is advised to avoid RV pacing inpatients with AV block, LVEF <40%, and frequent (>20%) anticipated ventricular pacing[119–121]	

[a]The decision for implanting HBP vs. LBBAP can be based on the relevant advice Table and *Table 2*. In patients undergoing HBP, a backup lead may be useful, particularly if the block is infra-nodal or in case of sensing issues.

Conduction system pacing in atrioventricular node ablation

In patients with rapidly conducted and symptomatic atrial tachyarrhythmias refractory to medical or ablative therapy, AVNA is an established therapeutic strategy. In patients with atrial fibrillation (AF), the combined effects of loss of AV synchrony, beat-to-beat irregularity, and rapid ventricular rates can lead to a reduction in cardiac output with adverse cardiac remodelling, and HF symptoms. These patients may benefit from a 'pace-and-ablate' strategy (*Figure 6*).[140–143] In a recent network meta-analysis comparing AF therapies including pharmacological treatment and different AF ablation modalities (radiofrequency, cryoballoon, and surgical ablation), the 'pace-and-ablate' strategy showed a consistent trend compared with other treatments in reducing cardiovascular and all-cause mortality, re-hospitalization, and stroke.[144]

The combination of AVNA and conventional RVP has shown to be effective in controlling heart rate and regularizing ventricular response. Overall, quality of life (QoL), cardiac symptoms, exercise tolerance, and LVEF were significantly improved with AVNA + RVP in observational and randomized studies in comparison with pharmacological rate control (see Supplementary material online, *Table S2*).[145–160] However, concerns about the potential deleterious effects of RVP have led to the emergence of BiVP as an alternative modality for patients undergoing AVNA. Multiple studies including RCTs comparing BiVP with RVP have shown variable benefits of BiVP in terms of QoL, 6-min walking distance, and/or LVEF in patients undergoing AVNA (see Supplementary material online, *Table S3*).[161–169] In the APAF-CRT mortality trial,[169] 133 elderly patients with severely symptomatic permanent AF, narrow QRS (≤110 ms), and at least one HFH during the previous year were randomly assigned to AVNA + BiVP vs. pharmacological rate control. A significant absolute mortality reduction of 18% was obtained with AVNA + BiVP at 4-year follow-up [11% mortality in the AVNA + BiVP group vs. 29% in the pharmacological rate control group (HR 0.26, 95% CI 0.10–0.65)].

The different available pacing modalities for combination with AVNA are outlined in *Table 3*. Conduction system pacing appears to be an effective method for pace-and-ablate therapy due to its ability to maintain normal ventricular activation in this pacing-dependent group who are at risk of developing PICM, particularly if the baseline QRS is narrow. This approach is further supported by previously reported positive outcomes of BiVP in this setting.

The 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy (CRT) stated that the 'pace-and-ablate' strategy using HBP with an additional RV backup lead may be considered.[1] Since its publication, new data exploring the 'pace-and-ablate' strategy using both HBP and LBBAP have become available. Most of the currently published studies have an observational and retrospective design, with limited prospective and randomized data, and have included mostly patients with baseline impaired LVEF and HF.[5,76,170–184] Overall, CSP was associated with a similar improvement in LVEF, NYHA, and QoL parameters when compared with BiVP but was superior to RVP (see Supplementary material online, *Table S4*). A single-centre retrospective study included 223 patients who underwent AVNA and who received either CSP ($n = 110$, HBP 84, LBBAP 46) or RVP ($n = 113$).[179] After a mean follow-up of 27 ± 19 months, LVEF significantly increased in both groups but the combined primary outcome of time to death or HFH was significantly reduced with CSP (48% for CSP vs. 62% for RV myocardial pacing, HR 0.61, 95% CI 0.42–0.89, $P < 0.01$), although patients in the RVP group were sicker with significantly lower baseline LVEF and wider baseline QRS duration. In the ALTERNATIVE-AF trial,[177] 50 patients with persistent AF and LVEF ≤40% with QRS < 120ms or RBBB underwent AVNA and sequentially received 9 months of treatment with both HBP and BiVP in a randomized, crossover trial. Improvement in LVEF was significantly greater with HBP compared

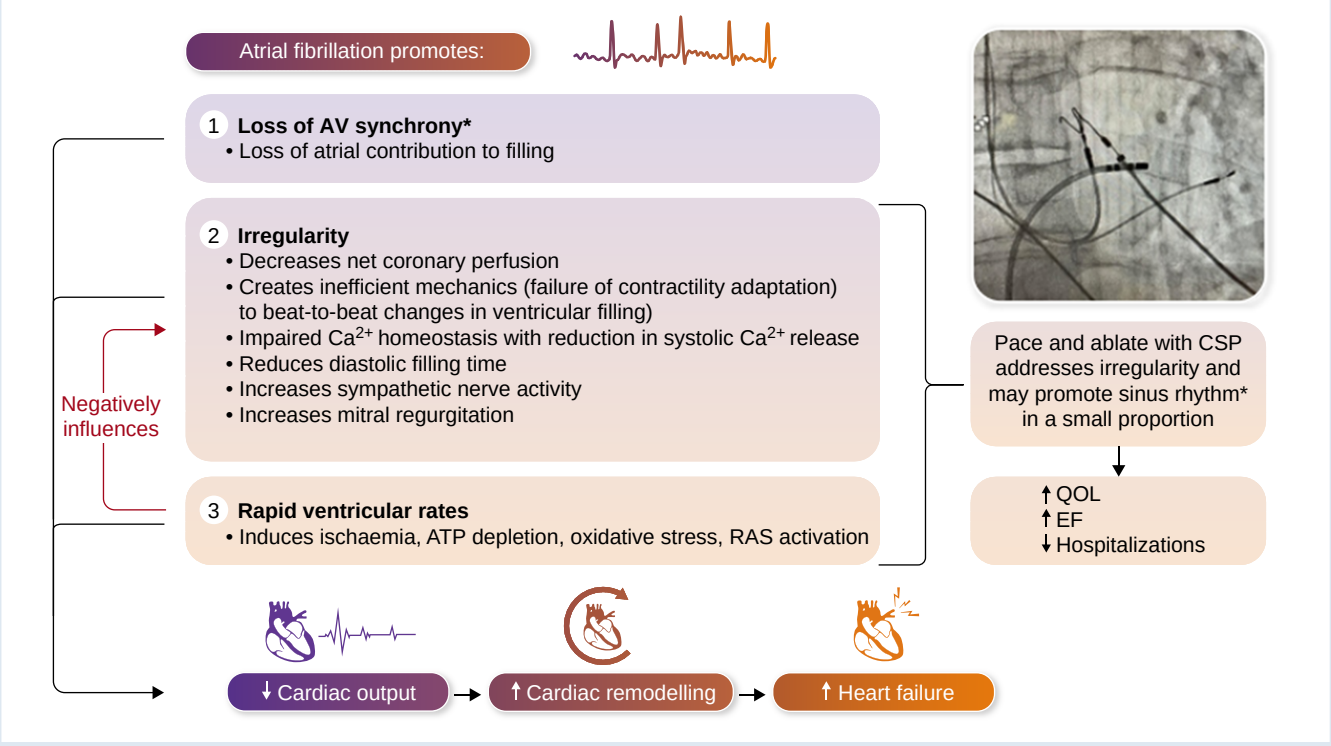

Figure 6 Haemodynamic consequences of AF and potential benefits of the 'pace-and-ablate' therapy. AF, atrial fibrillation; ATP, adenosine triphosphate; AV, atrioventricular; CSP, conduction system pacing; EF, ejection fraction; QOL, quality of life; RAS, renin-angiotensin system. Reproduced, with permission, from Joza *et al.*[140].

Table 3 Comparison of the different pacing modalities for the 'pace-and-ablate' strategy

	RV pacing	BiV-CRT	HBP	LBBAP
Implant technique	Easy	May be complex	May be complex	May be complex
LV synchrony	Impaired	Preserved/restored	Preserved/restored	Preserved/restored
LVEF	Impaired	Preserved/restored	Preserved/restored	Preserved/restored
Pacing threshold	Low	High	High	Low
Lead-related complications	Low	Intermediate	High	Low
Battery longevity	Long	Shorter	Shorter	Long
AVN ablation	Easy	Easy	Challenging	Easy
Risk of rise in capture threshold due to AVN ablation	No	No	Yes	No
Risk of recurrence of AV conduction at follow-up	Low	Low	Intermediate	Low
Backup lead advised	No	No	Yes	No

with BiVP, with similar improvement in NYHA class, LV end-diastolic diameter, and B-type natriuretic peptide levels. In a retrospective study, the outcomes of 68 patients with permanent AF and uncontrolled heart rate undergoing AVNA and LBBAP were compared with a control group including both RVP ($n = 44$) and BiVP ($n = 24$) using propensity matching.[183] Patients with LBBAP had a higher LVEF improvement and a lower 1-year rate of the composite score of HFH or mortality, whereas AVNA procedure data and complications were comparable.

Notably, CSP allows the use of a more straightforward device with less hardware in the venous system and usually a relatively simple procedure in experienced hands. As a result, in the presence of specific patient populations where a simpler device or procedure is desirable (e.g. older and frail patients or those requiring a smaller device), CSP could be chosen over BiV-CRT.

Direct comparisons between HBP and LBBAP in patients undergoing AVNA are scarce. Improvement in LVEF was similar between the two

pacing modalities in a series of 162 patients with propensity-matched groups[52] and in a small randomized crossover study with 23 patients.[59] A prospective, multicentre study reported the incidence of device-related complications in patients undergoing AVNA and implantation of either BiVP ($n = 263$) or CSP (HBP $n = 68$, LBBAP $n = 42$).[181] At 12-month follow-up, the risk of device-related complications was comparable (5.7% for BiVP, 4.4% for HBP, and 2.4% for LBBAP, $P = 0.65$) as was the risk of HFH (2.7, 1.5, and 2.4%, respectively, $P = 0.85$). However, compared with BiVP and HBP, LBBAP was associated with shorter procedural and fluoroscopy times, lower pacing thresholds, and longer estimated residual battery longevity. Similar findings were reported in 164 patients who underwent either HBP ($n = 68$) or LBBAP ($n = 96$) and AVNA, with shorter mean pacemaker implantation and AVNA times for LBBAP.[182] Higher acute and 12-month follow-up complete AV block rates were also obtained with LBBAP in comparison with HBP with a comparable improvement in NYHA class and LVEF. A significant rise in the pacing threshold > 1V occurred in 11% of HBP patients (with one patient undergoing lead revision) with no such cases among LBBAP patients. The relatively short follow-up in these two studies should be noted when commenting on long-term safety. In a multicentre series of 98 AVNA patients with CSP (48 HBP, 50 LBBAP), a > 1V rise in capture threshold was noted in 14.5% patients with HBP, without any lead issues in the LBBAP patients.[53]

The risk of threshold rise due to AVNA rises exponentially when the ablation site is <6mm from the HBP lead tip and is not mitigated by cryoablation.[184] Due to the risk of threshold rise and loss of capture, the 2021 ESC pacing guidelines stated that a backup lead should be considered in HBP patients who are planned for AVNA[1] (a backup LBBAP lead is an option[185]). Notably, a backup lead may be considered according to the HRS document on physiological pacing.[12] Experienced operators who perform HBP implantation and AVNA in the same session may opt to not implant a backup lead. However, a backup lead may otherwise be useful in the interest of patient safety.

Due to the potential issues with HBP in the setting of AVNA (difficult ablation with risk of rise in capture thresholds and recurrence of AV conduction, requirement for a backup lead, etc.), LBBAP is the preferred CSP option.

Ongoing large, multicentre, RCTs are currently evaluating the role of CSP in patients undergoing AVNA in comparison with RVP (included in the patient population of PROTECT-HF, NCT05815745), pharmacological treatment (PACE-FIB,[186] NCT05029570 and RAFT *P*&A study, NCT06299514) or AF ablation (ABACUS, NCT06207383). They will provide the definite answers as to superiority of one treatment modality over another.

A summary of indications for CSP in the setting of AVNA, as opposed to BiVP and RVP, is shown in *Figure 7* (for HOT/LOT-CRT, see relevant section).

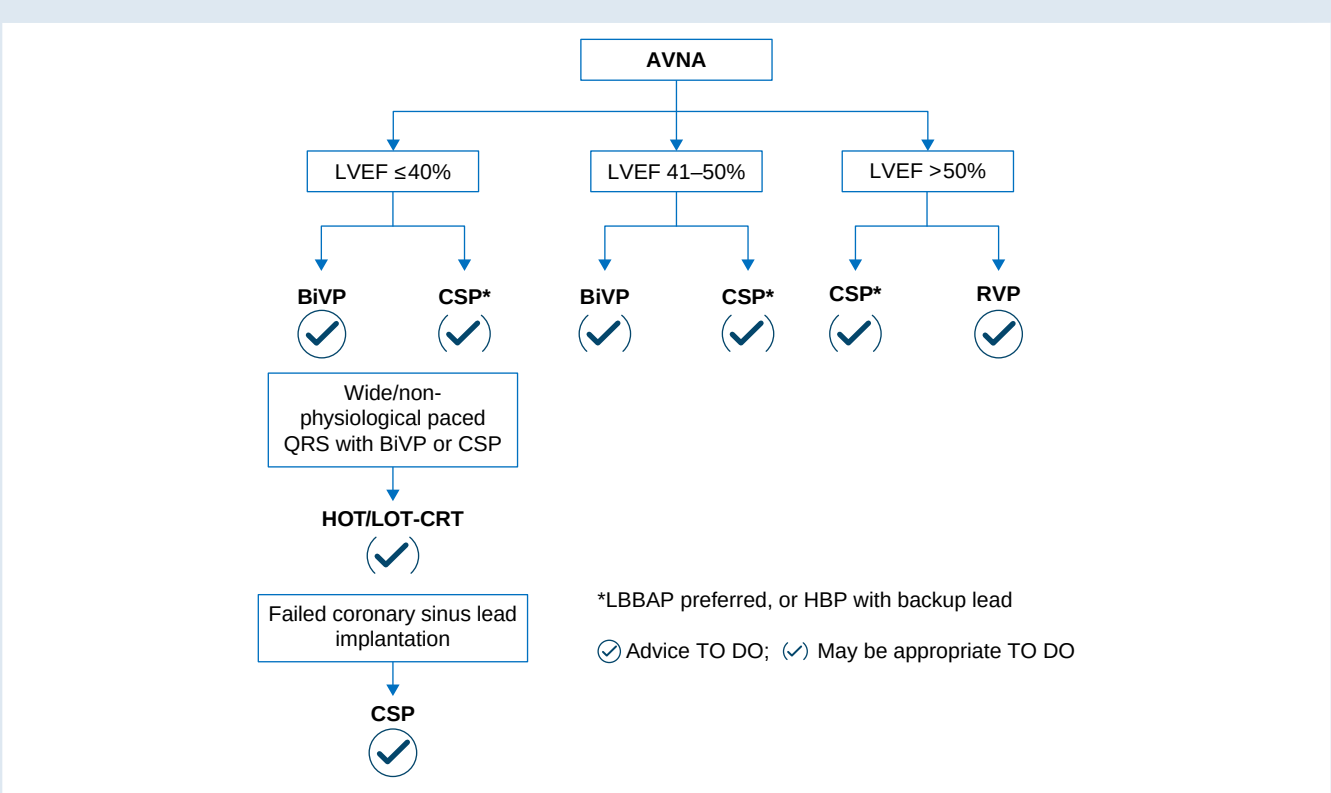

Figure 7 Indications for CSP in patients scheduled for AVNA. AVNA, atrioventricular nodal ablation; BiVP, biventricular pacing; CSP, conduction system pacing; HBP, His bundle pacing; HOT/LOT-CRT, His-optimized or left bundle-optimized cardiac resynchronization therapy; LBBAP, left bundle branch area pacing; LVEF, left ventricular ejection fraction; RVP, right ventricular pacing.

Advice: CSP for AVNA	Strength of evidence
Advice TO DO	
It is advised that CSP is implanted as a rescue strategy if coronary sinus lead implantation fails	 >90% agree
May be appropriate TO DO	
It may be appropriate that patients undergoing HBP as a primary strategy for 'ablate-and-pace' therapy receive a 'backup' ventricular lead in the interest of safety, taking into account operator experience and whether the procedures are performed concomitantly or in a staged manner[1,117]	 >90% agree
In patients scheduled for AVNA, it may be appropriate that LBBAP is preferred over HBP to simplify the ablation, avoid increase in capture thresholds and recurrence of AV conduction, and avoid requirement for a backup lead	 >90% agree
In patients with an LVEF >40% undergoing AVNA, it may be appropriate to implant CSP in lieu of RVP or BiVP in order to preserve LV function and improve HF symptoms.[5,76,172,173,175,179–181,183]	
In patients with an LVEF ≤ 40% undergoing AVNA, it may be appropriate to implant CSP in lieu of BiVP in order to improve LV function and HF symptoms[170,171,174,176,178]	
In the presence of specific patient populations where a simpler device is desired (e.g. frail patients, patients with limited life expectancy, or those requiring a smaller device), it may be appropriate to choose CSP instead of BiVP as a primary strategy, taking into account operator experience	 >90% agree

Conduction system pacing in sinus node dysfunction

There is good evidence that in patients with sinus node dysfunction (SND), unnecessary RVP should be minimized to avoid AF and HF, particularly if systolic function is impaired or borderline.[20,187] This may be achieved by programming long AV intervals or specific algorithms, which may, however, lead to long PR intervals with AV dyssynchrony.[101,188,189] Atrial pacing significantly lengthens PR intervals[190] and may even result in AV block due to decremental conduction during rate-adaptive pacing. Implanting the atrial lead first in these patients allows for evaluation of AV conduction to help decide whether CSP may be useful. The physio-VP AF study (NCT05367037) is randomizing patients with SND or second-degree AV block to either CSP or RVP with minimized ventricular pacing.

Sinus node dysfunction and AF often coexist with 40–70% of patients with SND having a history of atrial arrhythmias at the time of diagnosis.[191] Some of these patients may later require AVNA, and in this instance, having a CSP lead from the onset may be desirable. In a recent analysis using Medicare data in patients with dual-chamber pacemakers, as many as 37% of patients implanted with CSP had SND as the indication for pacing.[51]

Due to the paucity of data, it was decided not to formulate advice on this topic for the time being.

Conduction system pacing for heart failure without bradycardia pacing indication

Left bundle branch block causes interventricular dyssynchrony and delayed activation of the LV, which negatively impacts cardiac function, especially in patients with HFrEF.[192] Landmark clinical trials have clearly demonstrated that BiV-CRT enhances QoL, reduces LV remodelling, and decreases cardiovascular events such as hospitalizations and mortality in patients with impaired LV function and LBBB, and this effect is less pronounced in patients with a less wide QRS and non-LBBB.[193,194] The efficacy of BiV-CRT stems from correcting the delayed LV electrical activation through pacing, which involves leads placed in the RV and an appropriate branch of the coronary sinus to deliver epicardial LV stimulation. However, despite significant advancements in delivery tools and leads, BiVP is not always feasible.[195] Challenges in coronary sinus cannulation, a lack of suitable coronary sinus tributaries, high pacing threshold, or phrenic nerve capture hinder successful implantation in ~5–10% of cases.[73,195] Additionally, one-third of patients do not respond to BiV-CRT, with the rate of non-responders remaining consistent over time, particularly among patients with non-LBBB or QRS complexes < 150 ms.[66,196,197] Given these challenges, alternative pacing modalities to deliver CRT have been explored. In recent years, CSP has gained attention as a potential alternative to BiVP by restoring resynchronized ventricular activation.[3,123,198–200] Cardiac resynchronization therapy with CSP has been employed either as the initial therapy for CRT,[12] in cases when BiVP is not possible and as a rescue approach.[1,12,201]

His bundle pacing

His bundle pacing and LBBAP restore LV synchrony to a greater extent, with superior acute haemodynamic response, compared with BiVP.[42] Permanent HBP was first reported as an alternative to BiVP for CRT in 2013.[201] In a randomized crossover study of 29 patients referred for CRT, all implanted with an HBP lead and a coronary sinus lead, significant QRS narrowing was observed in 21 of the 29 patients (72%), and HBP delivered an equivalent clinical response to BiVP over 6 months.[3]

The His Bundle Pacing vs. Coronary Sinus Pacing for Cardiac Resynchronization Therapy (His-SYNC) pilot trial was the first prospective, randomized controlled trial aiming to assess the feasibility and efficacy of HBP as a first-line strategy compared with BiV-CRT.[2] Among the 41 patients enrolled, HBP demonstrated superior QRS narrowing with a trend to greater improvement in LVEF compared with BiV-CRT. However, the study was limited by high crossover rates towards the BiV-CRT group, mainly due to the inability to correct the QRS complex because of non-specific intra-ventricular conduction delays.

The Direct His pacing as an Alternative to BiVP in Symptomatic HFrEF Patients with True LBBB (His-Alternative) trial randomized 50 patients to HBP vs. BiV-CRT.[68] In the HBP group, 72% achieved successful LBBB correction, and HBP provided comparable clinical and echocardiographic improvements, though with higher pacing

thresholds. When LBBB correction can be achieved with HBP, it is a reasonable alternative to BiV-CRT, especially when effective CRT cannot be achieved with an LV/coronary sinus lead (see Supplementary material online, *Table S5*).

Despite these encouraging preliminary results, technical difficulties in achieving the target pacing site, unsatisfactory electrical lead parameters, especially regarding increases in pacing thresholds over time, and the inability to correct infra-Hisian or more distal conduction disease limit the adoption of HBP as a standard alternative to conventional BiV-CRT.[71,202,203]

In patients with HFrEF, impaired LV filling due to AV dyssynchrony resulting from prolonged PR intervals may contribute to pump failure.[188] The HOPE-HF study[204] was a randomized double-blind crossover study in 167 patients with HFrEF, PR > 200 ms (average 249 ms) and either QRS <140 ms or RBBB and found no meaningful benefit of HBP over backup ventricular pacing. Therefore, there is currently insufficient evidence that CSP-CRT is indicated solely for the purpose of correcting slight PR prolongation in patients with HF.

Left bundle branch area pacing

With the above-mentioned limitations of HBP, LBBAP might address these issues by capturing the conduction system more distally, with more stable pacing parameters. Following the encouraging results in bradycardia indications,[115,205] LBBP was investigated in patients with HF and CRT indications.[206] Observational data suggest than conduction system capture with LBBP (rather than LVSP) impacts clinical outcome in patients with CRT indications,[39,40] but this deserves further study as results are heterogenous.[207]

In a cohort of 325 patients with LVEF < 50% and an indication for CRT, LBBP was successfully achieved in 85% of patients.[69] This was associated with a significant reduction in QRS duration (from 152 ± 32 to 137 ± 22 ms, $P < 0.01$) and an improvement in LVEF at 6-month follow-up (from 33 ± 10 to 44 ± 11%, $P < 0.01$). Additionally, data suggest that patients with RBBB may benefit from LBBP, with QRS narrowing, a reduction in interventricular mechanical delay,[208] and an increase in LVEF.[67]

In a large retrospective study of 1778 CRT patients, LBBP was compared to BiVP.[134] After a mean follow-up of 33 ± 16 months, time to death or HFH was superior in the LBBP group (HR 1.5, 95% CI 1.2–1.8, $P < 0.001$) with significantly reduced HFH and a trend in improved survival. At follow-up, NYHA and LVEF were also significantly superior with LBBAP. The results were consistent in patients with LBBB (a subgroup which is most likely to respond to BiVP).

The MELOS study, a large observational registry on LBBP outcomes, reported a lead implantation success rate of 82.2% for HF indications and an overall complication rate of 11.7%, including both acute and late complications.[9] This rate is comparable to previously reported data for BiVP implantations. Specifically, 8.3% of the complications were related to the LBBP lead, including 3.7% of acute LV perforations, which were managed by lead repositioning and were not associated with adverse clinical consequences.

There are currently three published modest size randomized controlled trials with limited follow-up duration comparing LBBAP and BiV-CRT. The LEVEL-AT study included 70 patients with HF with LVEF < 35%, LBBB >130 ms, or non-LBBB >150 ms.[123] Patients were randomized 1:1 to CSP (4 HBP, 31 LBBAP) or to BiVP. Conduction system pacing was non-inferior in terms of reduction of LV activation time (LVAT) measured by ECG imaging (the primary endpoint), HFH or mortality (combined endpoint), LV remodelling (LV end-systolic volume), improvement in NYHA, and QRS shortening. The LBBP-RESYNC trial included 40 patients in sinus rhythm with non-ischaemic cardiomyopathy and LBBB (i.e. at high likelihood of responding to BiV-CRT), randomized to either LBBP or BiVP.[209] At 6-month follow-up, LBBP was associated with a significantly greater improvement in LVEF compared with BiVP (mean difference: 5.6%; 95% CI: 0.3–10.9; $P = 0.039$). The HOT-CRT trial[124] included 100 patients with LVEF < 50% and an indication for CRT and randomized patients to either CSP-CRT (39 LBBAP, 5 LBBAP + coronary sinus pacing, 4 HBP, and 2 crossover) or BiV-CRT (41 BiVP and 9 crossover). The primary endpoint was improvement in LVEF at 6 months, which was greater with CSP-CRT compared with BiV-CRT (12.4 ± 7.3 vs. 8.0 ± 10.1%, $P = 0.02$). Complications were more frequent in the BiV-CRT group, mainly driven by rises in coronary sinus lead pacing threshold and phrenic nerve capture (see Supplementary material online, *Table S5*).

In a meta-analysis of seven randomized controlled trials comparing 200 CSP-CRT patients with 208 BiV-CRT patients, CSP-CRT was superior in terms of improvement in NYHA class and LVEF, with no significant differences in HF hospitalization and mortality over limited follow-up time.[210]

Conduction system pacing in non-left bundle branch pacing patients

Patients with HF and non-LBBB present a significant challenge in clinical practice, as data from large BiV-CRT clinical trials do not indicate favourable outcomes for these patients.[211] According to the 2021 ESC guidelines, BiVP should be considered for patients with non-LBBB and a QRS duration >150 ms, and a Class IIb recommendation for those with a QRS duration of 130–150 ms, without any indication for CSP.[1] The 2023 HRS/APHRS/LAHRS guidelines attribute a Class 2b indication for CSP in patients with non-LBBB with NYHA III–IV + QRS 120–149 ms, as well as NYHA II + QRS ≥150 ms.[12]

His bundle pacing has been shown to achieve electrical resynchronization and improve clinical outcomes in a small multicentre observational study with 37 patients with right bundle branch block (RBBB) and reduced LVEF.[66] Similarly, data from some observational studies indicate that LBBAP is a feasible alternative for delivering CRT or physiological ventricular pacing in patients with RBBB, HF, and LV dysfunction.[67,208] The number of patients with non-specific intra-ventricular conduction delay (NIVCD) who have been studied with LBBAP is very small, and treatment efficacy in this patient subgroup has not been reported separately.[69] No randomized trial has yet assessed the benefit of CSP-CRT compared with BiV-CRT in this population, and further studies are needed to establish its advantages. Observational data on LBBAP combined with coronary sinus pacing, known as left bundle branch-optimized CRT (LOT-CRT), have shown encouraging results in patients with NIVCD and are discussed later.[212,213]

Conduction system pacing in patients with left ventricular ejection fraction 36–50%

Indications for BiV-CRT in patients with an LVEF ≤35% are well established. However, the criteria for patients with HF with an LVEF of 36–50% are less clear. In a substudy of the multicentre PROSPECT study, patients with NYHA functional Class III–IV status and a QRS duration >130 ms who had an LVEF >35% and underwent BiV-CRT, experienced significant clinical benefits, as well as structural improvements compared with baseline.[214] A recent randomized crossover trial in 76 patients with LVEF 35–50% and LBBB showed significant improvement in LVEF and ventricular remodelling after 6 months of CRT.[215]

There is also scant evidence of CSP efficacy in HF patients with LVEF > 35%, who do not have an indication for pacing. Most studies on CSP in patients with HF and mildly reduced ejection fraction (HFmrEF) also included a mix of patients with AV block or PICM. A meta-analysis[216] and some additional series[217–219] reported together <300 HFmrEF patients without a pacing indication, the largest of these being I-CLAS[219] which included 168 such patients. Although the results were not reported separately for this specific subgroup of patients with HFmrEF and LBBB, 260 patients with CSP had significantly lower composite

outcome of death or HFH compared with 75 patients who had received BiVP (HR 0.49, $P = 0.006$). However, randomized, large prospective studies are needed to evaluate the effects of CSP-CRT on patients with HF and an LVEF >35%.

Conduction system pacing cardiac resynchronization therapy in non-responders to biventricular cardiac resynchronization therapy

A substantial number of patients do not respond to CRT (in terms of symptoms and/or ventricular remodelling). Among the different causes, a suboptimal resynchronization with BiVP can be responsible for non-response, especially in patients with remaining QRS prolongation despite BiVP. To optimize the quality of cardiac resynchronization, CSP has emerged as a potential solution. A multicentre international observational study tested the hypothesis of whether LBBAP could be a viable alternative in 44 BiV-CRT non-responders with a mean QRS duration of 150 ± 22 ms with BiVP, at a median of 5.1 years after the original implant. This strategy was associated with a significant shortening of QRS duration, improvements in NYHA functional class, and improved echocardiographic parameters (LVEF and LV end-systolic and end-diastolic volumes). However, death or hospitalization due to HF occurred in 30% of patients at 1-year follow-up.[139]

Another non-randomized, prospective, multicentre, case–control study evaluated the feasibility, clinical efficacy, and outcomes of upgrading to LBBAP in 48 BiV-CRT non-responders. The results indicated that upgrading to LBBAP is both feasible and effective, with significant clinical improvements being observed.[220] This makes LBBAP a potential pacing strategy, albeit with limited evidence at this point, for patients who do not respond to traditional BiV-CRT and remain with wide QRS despite it. Randomized studies are needed to assess the efficacy and safety of this strategy in CRT non-responder patients.

Clinical implications

Conduction system pacing cardiac resynchronization therapy , particularly with LBBP, has increasingly gained support as an alternative to conventional BiV-CRT due to encouraging initial results (even compared with patients with the highest likelihood of responding favourably to BiV-CRT), simpler (and more economical) pacing systems, and enthusiasm generated by new pacing techniques. However, the lack of data from large randomized studies refrains routine adoption of this approach over BiV-CRT in daily clinical practice. While awaiting results from ongoing large randomized controlled trials assessing the role of CSP in patients with HF (see section below), CSP-CRT may be used as an alternative to BiV-CRT in selected patients. This is particularly applicable as rescue therapy when effective CRT cannot be achieved due to the inability to place a coronary sinus lead in a suitable, stable location, or in non-responders to BiV-CRT.[139] Another option is combining CSP and coronary sinus-based CRT, which is covered below.

A summary of indication for CSP-CRT, as opposed to BiV-CRT, is shown in *Figure 8* (for PICM and HOT/LOT-CRT, see later corresponding sections).

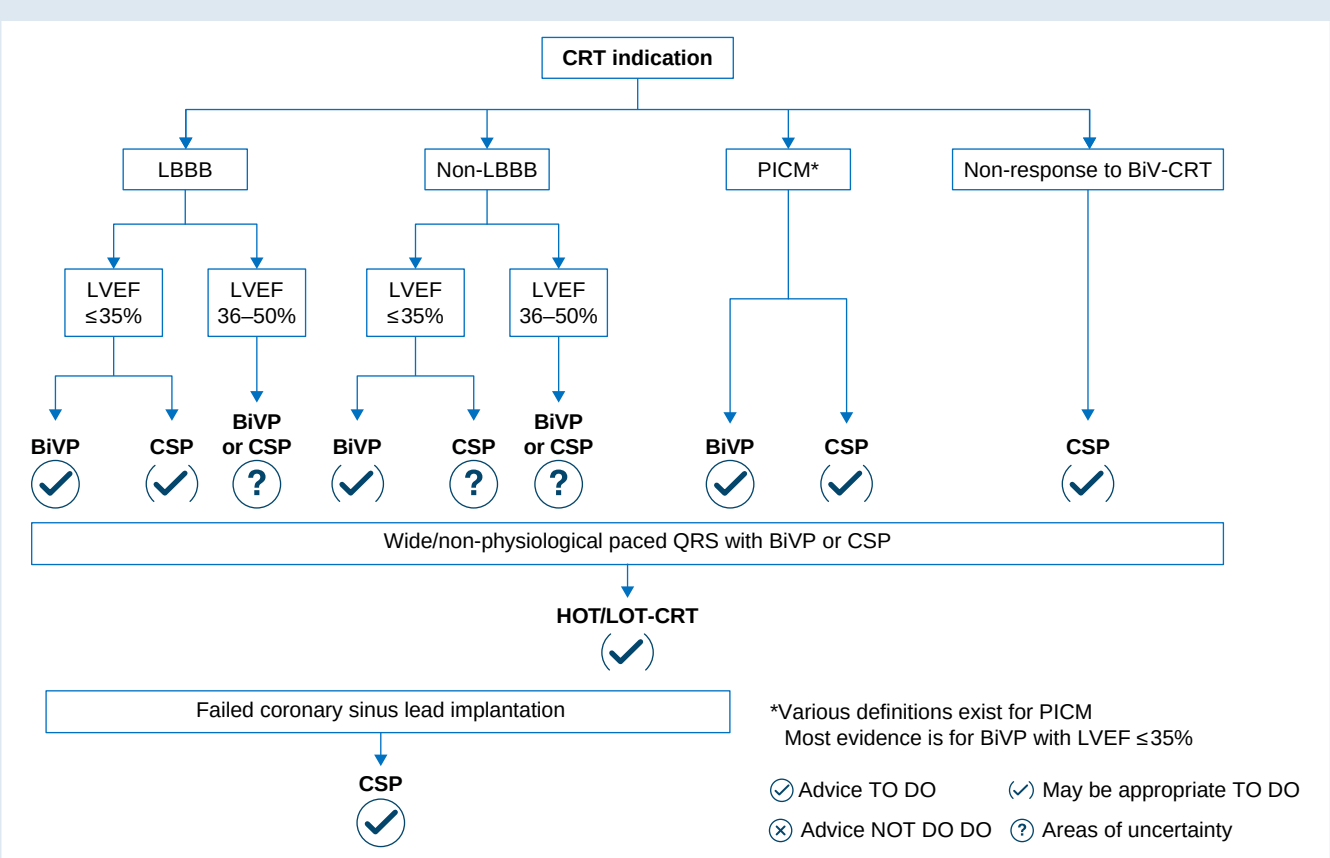

Figure 8 Indication for CSP-CRT. BiV-CRT, biventricular pacing cardiac resynchronization therapy; BiVP, biventricular pacing; CSP, conduction system pacing; HOT/LOT-CRT, His-optimized or left bundle-optimized cardiac resynchronization therapy; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; PICM, pacing-induced cardiomyopathy.

Advice: CSP-CRT	Strength of evidence
Advice TO DO	
In candidates for BiVP in whom coronary sinus lead implantation is unsuccessful, CSP is advised as rescue therapy.[139,201]	
May be appropriate TO DO	
For patients with LVEF ≤ 35%, LBBB with QRS ≥130 ms, and Class II–IV HF symptoms despite GDMT, CSP may be appropriate as an alternative to BiVP to improve LVEF, exercise capacity, and symptoms and to reduce HFH[9,68,123,134,209,210]	
In non-responders to BiV-CRT, it may be appropriate to implant CSP to improve HF symptoms and LVEF[139,220]	 >90% agree
In the presence of specific patient populations where a simpler device is desired (e.g. frail patients, patients with limited life expectancy, or those requiring a smaller device), it may be appropriate to choose CSP instead of BiVP as a primary strategy, taking into account operator experience	 >90% agree
Areas of uncertainty	
For patients with a CRT indication and non-LBBB, the clinical impact of CSP is uncertain[66,67,208]	 >90% agree
For patients with HF and LVEF >35% without an indication for ventricular pacing, the clinical impact of CSP is uncertain	 >90% agree

His-optimized and left bundle branch pacing-optimized cardiac resynchronization therapy

Delineation and rationale

Two hybrid pacing modalities combining CSP and coronary sinus pacing were recently introduced: His bundle-optimized CRT (HOT-CRT)[221] and left bundle branch-optimized CRT (LOT-CRT).[222] In the setting of sHBP without correction of RBBB, RVP may be used to correct RV electrical dyssynchrony and potentially also qualify as HOT-CRT.[99] The rationale for adding a coronary sinus lead to a CSP lead (or vice versa, depending on the initial CRT strategy) stems from the limitations of CSP-CRT, and BiV-CRT and the not infrequently observed suboptimal electrical, echocardiographic, and clinical outcomes with each of these CRT modalities. Delayed activation of the LV lateral wall in patients with HF may result not only from a discrete lesion in the left bundle branch that can be bypassed/corrected by CSP, but also from widespread delay, distal focal lesion(s) in the conduction system, electrical uncoupling, myocardial scar, and functional conduction block. In patients with wider QRS, non-typical LBBB and more advanced HF, both mechanisms (focal proximal lesion and distal delay) often coexist. Analysis of V_6RWPT—an electrocardiographic marker of LV lateral wall activation time, indicates that such conduction delay cannot be corrected by CSP alone.[223] In patients with narrow QRS complexes or isolated RBBB, the V_6RWPT during LBBP closely follows the intrinsic native activation times and remains within the norm for the V6 intrinsic deflection time (i.e. 50–60 ms). This value plus the left bundle branch latency of 20–30 ms yields physiologically paced V_6RWPT values of 70–90 ms. However, in patients with wide baseline QRS complexes due to LBBB or NIVCD, V_6RWPT values during confirmed left bundle branch capture are often non-physiological (>90 ms), suggesting that despite proximal LBB capture, additional LV conduction delay remained and coronary sinus pacing may be required to correct this.[223] Furthermore, in a significant percentage of patients in whom LBBP is attempted, only LVSP is achieved,[9] resulting in a potentially important additional delay in LV lateral wall activation.

On the contrary, conventional BiV-CRT is also limited in its ability to fully restore physiological LV activation. This is due to several factors: potentially desynchronizing effects of myocardial pacing with the RV lead, localized non-physiological epicardial LV pacing, latency, and suboptimal LV lead position (paraseptal/apical) due to unfavourable cardiac venous anatomy and/or LV scar. Failure of BiV-CRT to restore physiologic activation may manifest as QRS prolongation rather than narrowing. This is observed in one-third of BiV-CRT patients and is associated with a poor prognosis compared with patients with narrowing of QRS after BiV-CRT.[224]

The combination of CSP and coronary sinus pacing/RVP (*Figure 9*) may address some of the limitations of both techniques, providing more physiological LV activation and thus a narrower QRS and a more efficient form of CRT. Although more data from long-term RCTs are needed, this approach may be pursued in difficult cases with suboptimal electrocardiographic results of CSP or coronary sinus pacing-based CRT at implantation. Furthermore, His-optimized and left bundle branch pacing-optimized cardiac resynchronization therapy (HOT/LOT-CRT) is an option in patients who do not respond clinically to BiV-CRT or to CSP-CRT and in whom the paced QRS is considered suboptimal.

Published data and practical considerations

His-optimized and left bundle branch pacing-optimized cardiac resynchronization therapy has been evaluated in a number of observational studies.[99,212,213,221,222,226,227] These studies were primarily multicentre and prospective, with sample sizes ranging from 19 to 112, included patients with a mean LVEF <30% and compared HOT/LOT-CRT with BiVP, LBBAP, or HBP. The principal outcomes and conclusions of these studies are presented in more detail in Supplementary material online, *Table S6*. All studies showed superior electrical resynchronization (QRS narrowing or LVAT reduction) and some also superior echocardiographic or haemodynamic outcomes when LOT-CRT was compared to BiVP and/or CSP alone. The absence of studies examining mortality with long-term follow-up and randomized trials represents a significant limitation to the current understanding of the benefits and risks of hybrid pacing approach for CRT. A further significant practical limitation is the lack of uniform criteria for the addition of a coronary sinus lead to a CSP-based CRT system and the increased complexity of the procedure. The prevailing expert opinion is that there is no necessity to add a coronary sinus lead to a CSP-based CRT system if the obtained paced QRS already indicates a physiological, i.e. fast and synchronous LV activation. If the paced QRS is not deemed satisfactory (based on criteria

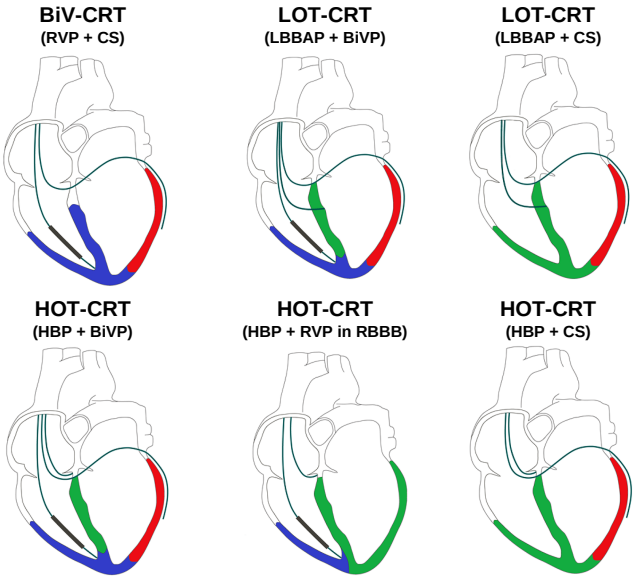

Figure 9 Schematic illustration of ventricular activation wavefronts BiV-CRT, HOT-CRT, and LOT-CRT. Approximate activation by the right ventricular lead is indicated in blue, by the conduction system pacing lead in green, and by the coronary sinus lead in red. Adapted with permission from Zweerink *et al.*[225] BiV-CRT, biventricular pacing cardiac resynchronization therapy; BiVP, biventricular pacing; CS, coronary sinus pacing; HBP, His bundle pacing; HOT-CRT, His bundle pacing-optimized cardiac resynchronization therapy; LOT-CRT, left bundle branch-optimized cardiac resynchronization therapy; RBBB, right bundle branch block; RVP, right ventricular pacing.

Table 4 Criteria used to determine whether HOT/LOT-CRT may be required after having implanted a CSP lead

Paced QRS width
Presence of conduction system capture
V_6 or aVL RWPT
V_6V_1 interpeak interval
Paced QRS notching
QRS axis (normal vs. axis deviation)
Anatomical position of LBBAP lead (basal, mid, or apical)
Absence or minimal acute haemodynamic response to pacing

LBBAP, left bundle branch area pacing; RWPT, R-wave peak time.

outlined in *Table 4*), there may be benefit from the HOT/LOT-CRT approach (*Figure 10*).

A recent randomized study investigating CSP-based vs. BiVP-based CRT strategies used that criterion and determined that LOT-CRT was necessary for 10% of CRT candidates in the CSP-CRT arm.[124] The multicentre CSPOT study, which specifically addresses this question, found that the haemodynamic benefit of LOT-CRT over LBBAP was present when there was distal conduction disease, as indicated by a longer QRS duration (>171 ms, which was the mean value for the group) or when the obtained QRS was suboptimal (lacking a terminal *r* wave in lead V1). When both these conditions were met, the benefit of LOT-CRT was most pronounced, with a 14.5% greater improvement in LV dP/dtmax and a 20.8 ms shorter QRS duration than during LBBAP.[213]

The selection of LOT-CRT over HOT-CRT or vice versa is currently based on the operator's preference, experience, and ability to implement HBP and LBBP, as well as on case-dependent anatomical and physiological factors that influence the feasibility of HBP and LBBAP. It is important to note, however, that LOT-CRT usually offers superior pacing parameters and normal sensing without compromising arrhythmia detection in cardiac resynchronization therapy defibrillator (CRT-D) systems, while HOT-CRT may provide superior QRS narrowing due to the direct recruitment of the right bundle branch in the setting of LBBB.

Patients with permanent AF cannot benefit from algorithms which adjust AV delays to promote fusion between intrinsic conduction and ventricular pacing, used in BiV-CRT.[228] In these patients, HOT-CRT with HBP (usually using the off-label configuration of connecting the lead to the unused atrial channel of the generator) combined with coronary sinus and/or RV pacing may be used to deliver controlled and constant fusion pacing by adjusting AV delay, even in patients in whom bundle branch block remains uncorrected by HBP.[99,225]

Although there are no dedicated randomized studies on HOT/LOT-CRT, it is pertinent to note that, unlike CSP-CRT, these pacing modalities do not deviate too much from conventional BiV-CRT as they also include a coronary sinus lead (which is considered the dominant factor in conventional resynchronization) and a septal pacing lead (due to non-selective septal capture during HBP or LBBAP). In contrast to CSP-CRT, the HOT/LOT-CRT approach does not replace key BiV-CRT components, but builds on them. Therefore, it is anticipated that favourable major endpoint results from CRT trials will be maintained with HOT/LOT-CRT. Nevertheless, operator experience and patient risk need to be carefully taken into account, particularly when evaluating upgrade procedures. Randomized clinical trials are still needed to determine the safety of a more complex procedure and whether the superior electrical resynchronization translates into hard outcomes such as mortality and hospitalization for HF.

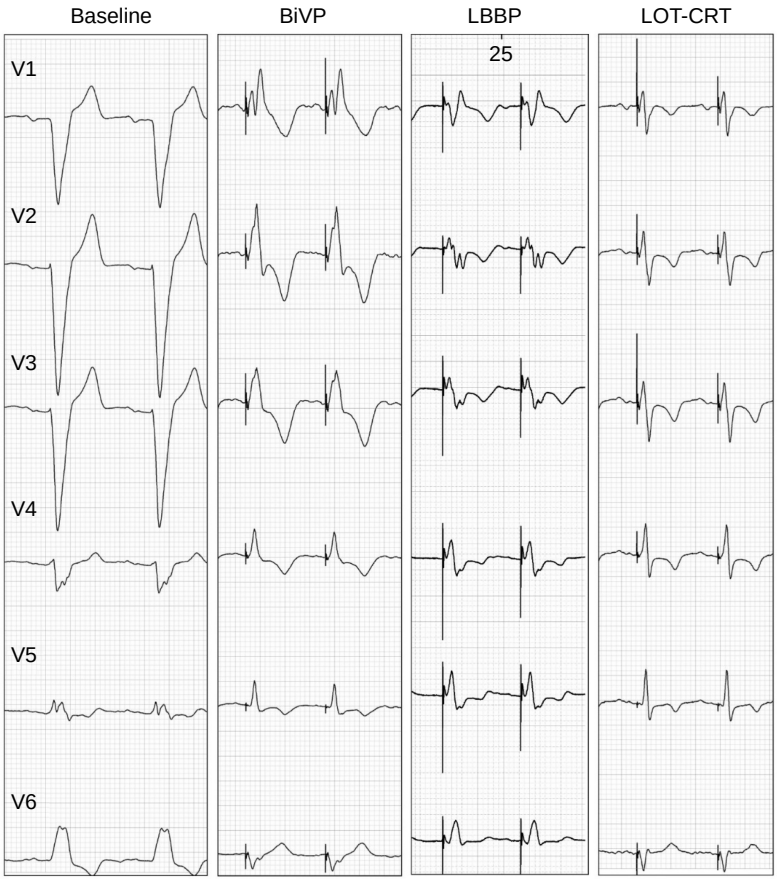

Figure 10 Superior electrical resynchronization with LOT-CRT compared with BiVP. Note the presence of QRS notching with BiVP and LBBP, which disappears with LOT-CRT. BiVP, biventricular pacing; LBBP, left bundle branch pacing; LOT-CRT, left bundle branch-optimized cardiac resynchronization therapy.

Advice: HOT/LOT-CRT	Strength of evidence
May be appropriate TO DO	
It may be appropriate to propose HOT/LOT-CRT at implantation in case of suboptimal electrocardiographic results of CSP or BiVP, taking into account operator experience and patient risk.	
It may be appropriate to propose HOT/LOT-CRT as an upgrade procedure in selected CRT candidates in case of suboptimal clinical and electrocardiographic result with CSP-CRT or BiV-CRT, especially in the setting of non-specific intra-ventricular conduction delay or mixed conduction disease,[a,99,212,213,221,222,226,227] taking into account operator experience and patient risk.	

[a]Mixed conduction disease refers to association of bundle branch/fascicular conduction delay with peripheral conduction disease and/or intra-myocardial propagation delay, which cannot be corrected by CSP alone.

Upgrade to conduction system pacing

Device upgrade can be considered in patients with a cardiac implantable electronic device (CIED) in whom worsening of ventricular function occurs, either due to disease progression or secondary to PICM, defined as a decline in LVEF (with variable cut-offs in different studies, usually to <40–50% or decline by ≥10% from baseline[229]) secondary to chronic ventricular pacing. Upgrade to BiVP in these patients has been shown to improve LVEF in randomized controlled trials.[230–232] A meta-analysis of six RCTs (including 161 patients, baseline LVEF 35 ± 10%) and 47 observational studies (including 2644 patients, baseline LVEF 26 ± 8%) showed improvement in LVEF, NYHA class, QoL, and brain natriuretic peptide (BNP) levels.[230] The more recent BUDAPEST CRT trial randomized 360 pacemaker patients with LVEF ≤35% (mean 25%) who had >20% RVP with paced QRS >150 ms to an upgrade with either an implantable cardioverter–defibrillator (ICD) or CRT-D. The primary outcome was the composite of all-cause mortality, HFH, or <15% reduction of LV end-systolic volume assessed at 12 months, with a odds ratio of 0.11 (95% CI 0.06–0.19) in the CRT-D arm.[232]

Conduction system pacing has been shown to achieve greater improvement in LVEF and reduction in QRS duration in small short-term RCTs[68,122,177,209] and has been associated with improved clinical outcomes in observational studies, compared with BiVP.[132,134]

Conduction system pacing therefore might be expected to be a suitable alternative to BiVP in patients requiring device upgrade for PICM. Several small observational studies have already shown this with a significant LVEF increase in patients undergoing CSP, as well as reductions in LV end-systolic volume, improvement in functional capacity, and QRS duration, with similar improvements observed with both HBP and LBBAP.[129,230,233–239] These observational studies show scope for improvement in those patients with mild–moderate LV impairment as well as those with severe LV dysfunction (see Supplementary material online, *Table S7*). In a meta-analysis of eight observational studies including 217 patients (mean baseline LVEF 38.4%± 8.8), LVEF, NYHA, and QoL were significantly improved by upgrade to CSP.[230]

Predictors of PICM or HF development after RVP include a lower baseline LVEF, a larger LV end-diastolic diameter, a longer paced QRS duration, and a higher RVP percentage.[233] Importantly, although upgrading to CSP may improve echocardiographic parameters in patients with PICM, the mechanism of improvement is unclear and the mechanistic contribution of factors including change in activation pattern (broad QRS to narrower QRS) and reverse remodelling is unknown. That said, in observational studies with up to 12-month follow-up, the improvements in LVEF and LV end-diastolic dimension do not appear to return to the levels seen in individual patients prior to RVP.[128,129,234] Thus, identifying patients at a higher risk of developing PICM prior to initial device implant may be important when selecting between RVP and CSP, as CSP has been seen to be associated with a lower risk of adverse outcomes associated with PICM and subsequent HF-related hospitalization.[26,107]

Device upgrade to BiV-CRT may be considered in patients with PICM and LVEF ≤35% according to the 2021 ESC guidelines on cardiac pacing and resynchronization therapy, acknowledging the possibility of increased risk of procedure-related complications,[1] including infection, pneumo/hemothorax, and lead-related complications. Although the benefits of upgrading may exceed the risks, interventions aimed at reducing these risks must be undertaken.[240]

Clinicians need to have an appropriate care pathway in place to enable the screening of CIED patients to identify patients who might benefit from a device upgrade. Pacing burden and patient symptom assessment are likely to form the cornerstone of this evaluation and be complemented by measurement of BNP levels and echocardiographic assessment where indicated. Assessment should be performed in advance of all planned generator replacements and considered at any point in a patient's follow-up if symptoms change or pacing percentage increases. Suitability criteria and threshold for an upgrade might be different contingent on the patient frailty, as well as whether a patient is at the elective replacement indicator vs. other earlier time points. A multidisciplinary team opinion should be sought for borderline cases.

Current ESC guidelines for upgrade to BiV-CRT suggest waiting until LV dysfunction has become severe (≤ 35%) as evidence is strongest in this patient population. However, for de novo device implantation, the ESC guidelines recommend CRT for patients with AV block and EF < 40% or even milder LV dysfunction after AVNA.[1] The 2023 HRS/APHRS/LAHRS guidelines on physiological pacing recommend the use of CSP approaches for patients with even mild LV dysfunction (LVEF < 50%).[12] Therefore, the indication of device upgrade requires further attention. The PROTECT UP clinical trial (NCT06052475) is currently recruiting and aims to assess the benefit of device upgrade on QoL in 155 patients with mild-to-moderate LV impairment only.

Depending on the existing device, several strategies can be used during device upgrade, including use of the same device (abandoning the existing ventricular lead), implanting a new generator with an additional port to connect the CSP lead and avoid abandoning the existing ventricular lead or performing HOT/LOT-CRT (see Supplementary material online, *Figures S1–S3*).

Currently, most transvenous defibrillators use the DF-4 standard, in which both the high- and low-voltage (i.e. pacing) connections are in a single pin, thus reducing the need for bulky device headers and facilitating connection during implant. Although this advantage has led to widespread adoption of this type of connection, patients in whom device *downgrade* is required (i.e. from a defibrillator to a pacemaker) will require either the utilization of a DF-4 ICD with deactivation of the high energy capabilities or insertion of an additional IS-1 lead to facilitate the use of a standard pacemaker.[241] Moreover, patients who have a defibrillator implanted may, during their lifetime, require upgrading to a device capable of CRT. In this scenario, the use of a DF-1 device may facilitate LBBAP and even avoid having to change the generator if the residual longevity is considered to be adequate (see Supplementary material online, *Figure S2 and Table S8*). When using a DF-1 device, the CSP lead (usually LBBAP, as HBP provides suboptimal sensing parameters) is connected to the IS-1 port in the defibrillator block, and the IS-1 connector pin from the DF-1 lead is capped and abandoned. Thus, CRT can be achieved with a less expensive device and without the need for a new generator.[242] As sensing parameters are favourable in the left bundle branch area, it is anticipated that arrhythmia detection using a LBBAP lead will be similar to that of a lead located in the RV apex. A small study showed no significant differences in the detection duration of an induced ventricular fibrillation episode between left bundle branch area and RV lead locations.[243] Alternative approaches here include utilization of a new generator with a DF-4 connector and IS-1 connector for the upgraded lead. This has the advantage of no abandoned lead component.

A concept that is emerging is the use of ICD leads for delivering CSP.[244,245] However, the long-term safety and efficacy of this approach needs to be evaluated.

Advice: upgrade to CSP	Strength of evidence
Advice TO DO	
It is advised that patients should be assessed regularly and particularly prior to elective generator replacement for need for device upgrade. Considerations include: pacing percentage, symptoms, LVEF, BNP, risk of infection, and patient frailty[230,231]	 >90% agree
May be appropriate TO DO	
In patients with PICM, it may be appropriate to upgrade to CSP to improve HF symptoms and LVEF[129,230,233–239] particularly in patients with an intact His–Purkinje system[a] (where CSP is likely to deliver synchronous activation).[129,230,233–239]	
When upgrading to CSP, it may be appropriate to incorporate all pacing leads into the pacing system rather than abandoning the existing ventricular lead, as it enables backup pacing and facilitates MRI-conditionality	 >90% agree

[a]Patients with narrow QRS or nodal AV block.

Patient education and shared decision-making

Patients face a broad range of treatment options when in need of pacing. Not only are they confronted with single, dual- or biventricular devices, but there is also transvenous vs. leadless pacing. The emergence of CSP in the form of HBP and LBBAP adds even more choices to the decision-making process, making it more complex.

This document therefore reinforces the importance of patient-centred care and shared decision-making between patients and clinicians.[1,246] When implanting a pacemaker or CRT, the patient's preferences, values, and goals of care must be considered and carefully balanced with the best available evidence and the individual risks and benefits.

It is the healthcare provider's responsibility to encourage shared decision-making. As part of such a process, all treatment options, their risks, and benefits must be explained in a way the patient and their caregivers can understand. The physician should explore together with the patient which of the alternatives best fits their medical needs and personal preferences and goals. It is important to recognize that while shared decision-making should be encouraged, it cannot be imposed; some patients may decide to not engage in the process for various reasons which must be respected. If CSP is considered in the setting of device revision or replacement, it is important to keep in mind that a patient's personal preferences and expectations may have changed as compared to when the device was first implanted. Therefore, they must be assessed again as part of the shared decision-making process.

Whenever new technologies or approaches for treatment are available, shared decision-making including the communication of evidence becomes even more important because there are not only potential benefits associated with them but there typically is less evidence and there is uncertainty regarding mid- and long-term outcomes and risks. Hence, as CSP is still lacking evidence from large, randomized trials, it is of outmost importance to be transparent about what is known and not yet known about this recent pacing modality. Patients should be able to not only understand the potential benefits it may offer compared with more well-established pacing techniques, but also be aware of the lack of evidence that exists regarding aspects such as lead longevity, impact on the device's battery, experiences with lead removal and the possibility of yet unknown long-term risks of CSP. Furthermore, they must be aware of risks associated with the implanter's experience in CSP; many patients are being treated by physicians who are new to this pacing modality and so the operator's learning curve is another aspect that should not be neglected.

An important aspect of patient's education should take place following CSP implantation. This is especially relevant in an emergency setting, in particular, when the patient is in a medical centre that is not familiar with new CSP technologies. Such efforts can include supplying the patient with a card and / or digital records of the new pacing hardware and programming, as well as establishing a central medical entity that can be approached by patients, as well medical staff in need for specific instructions. Finally, establishing in-person and online medical education approaches to transfer the knowledge on the new pacing technologies to a broad spectrum of medical personnel could improve patients' care and long-term safety.

Advice: shared decision-making	Strength of evidence
Advice TO DO It is advised that CSP is part of shared decision-making, emphasizing the novelty of the procedure, lack of large RCTs and of long-term follow-up, as well as the existing alternatives	 >90% agree

Future perspectives

As CSP continues to gain traction, several ongoing RCTs are underway (see *Figure 11* and Supplementary material online, *Table S9*). Several small-/mid-sized studies are expected to be completed soon, while larger studies with hard primary endpoints are anticipated to conclude by the end of the decade. The outcomes of these RCTs have the potential to significantly influence the future pacing guidelines directing the broader implementation of CSP in clinical practice across various patient groups. Cost-effectiveness analyses of these RCTs will clarify possible long-term economic benefits of CSP, potentially influencing reimbursement models. Additionally, there are trials studying treatment strategies involving CSP such as a pace-and-ablate strategy compared with AF ablation as well as studies evaluating different types of leads used for CSP.

Although CSP is gaining increasing adoption, many aspects of CSP implantation are likely to be improved in the near future. The pacing leads currently used for CSP were initially designed for conventional endocardial pacing sites, and concerns remain regarding their long-term performance.[10] In particular with LBBAP, the lead is screwed deeply into the septum, creating novel forms of mechanical stress on these leads. Despite several pacing leads being approved for CSP by regulatory boards, data on the impact of these new use conditions on long-term lead performance are scarce. Early conductor fractures, especially with LBBAP, have been reported in case studies or as single-centre experiences.[247–251] The recent LIFE-LBBAP study,[252] a large international multicentre registry, showed a lead survival probability of 99.7% at mid-term follow-up, with lead fracture rates varying between 0.04 and 0.4%, depending on the lead design. Some of these early conductor fractures with LBBAP have been attributed to implant-related conditions, such as kinking of the lead during septal deployment or excessive angulation within the septum, while others might result from fatigue due to repeated bending over time.[248,251] Identifying these mechanisms can guide future developments in CSP-specific lead designs. Prototypes of new dedicated CSP lead designs are in the pipeline, and the feasibility of using ICD leads for LBBP (HV-LBBAP)[244,245,253] and leadless CSP systems are being explored.[254,255] Until dedicated CSP leads become available, proper lead handling and awareness of the potential higher risk of lead failure are advised. Further data on long-term lead performance are needed to implement CSP in future guidelines.

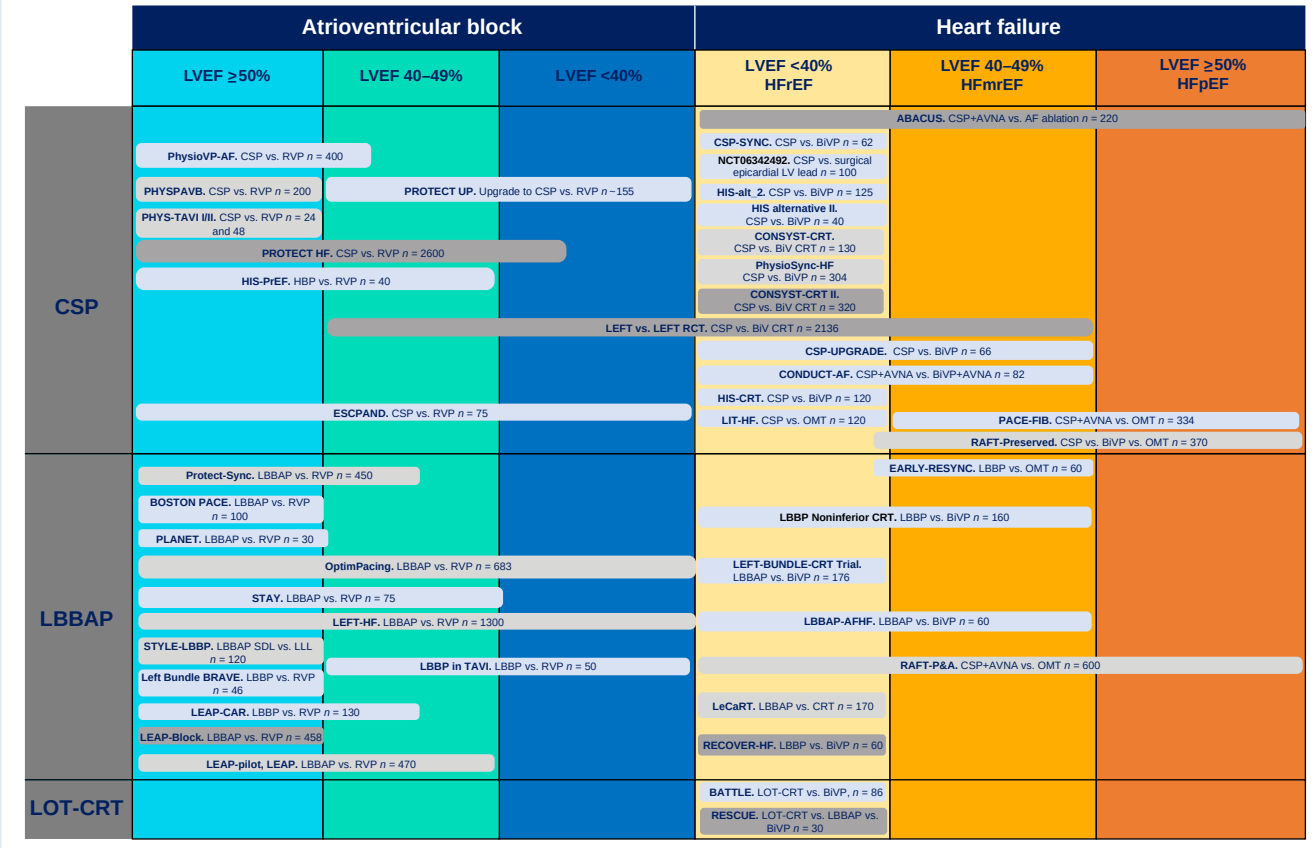

Figure 11 Summary of ongoing RCTs on conduction system pacing. The background colours of the study names represent different types of study endpoints: light grey indicates soft endpoints, dark grey indicates hard endpoints, and medium grey indicates a combination of soft and hard endpoints. AF, atrial fibrillation; AVNA, atrioventricular node ablation; BiVP, biventricular pacing; CRT, cardiac resynchronization therapy; CSP, conduction system pacing; HBP, His bundle pacing; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; LBBAP, left bundle branch area pacing; LBBP, left bundle branch pacing; LOT-CRT, left bundle branch-optimized cardiac resynchronization therapy; LV, left ventricle; LVEF, left ventricular ejection fraction; OMT, optimal medical therapy; RVP, right ventricular pacing.

Implantation will also be facilitated by accessories such as pin connectors which allow continuous pacing during lumenless lead deployment, and delivery catheters with a range of shapes to better suit variable anatomies.

For implanting centres lacking a dedicated electrophysiology recording system, affordable laptop/programmer/tablet-based solutions capable of continuously recording multilead ECGs and electrograms (both filtered and unfiltered), delivering pacing and equipped with digital callipers for precise measuring of time intervals (V_6RWPT, V_6–V_1 interpeak intervals, QRS duration, etc.) and current of injury amplitude, would greatly facilitate implantation. Ideally, these systems may automatically perform these measurements on a beat-to-beat basis during lead deployment, which would standardize them, streamline the procedure, and reduce the need for specialized personnel. Eventually, artificial intelligence might help to identify conduction system capture or physiological pacing at implantation and follow-up.

Dedicated pulse generators designed for CSP are being developed and might further facilitate CSP programming and follow-up. These generators might include algorithms that offer automated capture management to ensure conduction system capture, automated fusion of CSP, and intrinsic right ventricular activation during LBBAP or HOT/LOT-CRT. Remote monitoring of CIEDs offers several advantages over traditional in-office visits, including the early detection of lead failures, device malfunctions, and significant arrhythmias through automated alerts. For patients with CIEDs, remote monitoring is part of standard of care.[1,256] More data are needed on the usability of remote monitoring specifically in CSP.

Data on the safety of extracting CSP leads are limited, and data on extraction of CSP leads with long lead dwell times are needed. In the recent international TECSPAM study, the success and safety of extracting HBP and LBBAP leads were high, although the average lead dwell time was only 2 years. Retained distal fragments might pose a risk during the extraction of fractured lead segments, indicating the need for expertise with femoral extraction tools in CSP lead extraction.[257] Additionally, specific extraction tools may be needed in the future to extract CSP leads with longer dwell times.

There are scant data regarding CSP in populations such as children, patients with complex congenital heart disease, or specific conditions such as genetic conditions or sarcoidosis. There is a need for more data collection in these populations in the future.

Conclusions

The field of CSP is rapidly moving forward. We are continuing to gain a better understanding of its physiological principles and basic

mechanisms (for which there is yet much to learn). Following the currently available data from observational studies and small short-term RCTs which report encouraging results for this pacing modality, the foundations to provide solid evidence have been laid for large ongoing RCTs which will serve to strengthen recommendations in future guidelines. In the meantime, our Clinical Consensus Statement aims to provide guidance for patient indications in daily clinical practice, bearing in mind that knowledge in this field is rapidly evolving.

Supplementary material

Supplementary material is available at *Europace* online.

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Data availability

Data availability does not apply since no patient data are involved.

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