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Review article

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The evolution and future of conduction system pacing

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Abstract

Cardiac pacing has undergone a fundamental paradigm shift from conventional right ventricular apical pacing towards physiological activation of the native conduction system of the heart. Decades of evidence have established that chronic right ventricular pacing induces ventricular dyssynchrony, contributing to pacing-induced cardiomyopathy and adverse clinical outcomes. Conduction system pacing, which engages the intrinsic His–Purkinje network of the heart, has emerged as a transformative approach that preserves or restores the natural ventricular activation sequence. His bundle pacing, the earliest form of conduction system pacing, provided proof of concept but is limited by technical challenges and high capture thresholds. Left bundle branch area pacing has since become the dominant modality, offering greater procedural success, lead stability and broader applicability: from management of bradycardia and prevention of pacing-induced cardiomyopathy to cardiac resynchronization therapy in heart failure. Bachmann bundle area pacing is an emerging atrial counterpart: by capturing a preferential interatrial conduction pathway, this approach reduces interatrial conduction delay and produces a more physiological atrial activation sequence than conventional right atrial appendage pacing. Bachmann bundle area pacing might, therefore, help to prevent atrial fibrillation. In this Review, we bring these ventricular and atrial strategies together under the unifying principle of physiological pacing, describe their mechanistic basis and technical evolution, appraise the latest evidence from randomized trials and address the practical questions that arise in clinical application, indicating where more evidence is required.

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Key points

- Conduction system pacing (CSP), such as His bundle pacing and left bundle branch area pacing, preserves the native ventricular activation sequence, representing a paradigm shift from conventional right ventricular apical pacing.
- Left bundle branch area pacing has emerged as the dominant CSP modality, offering higher procedural success rates and more stable long-term pacing thresholds than His bundle pacing.
- CSP effectively prevents pacing-induced cardiomyopathy in patients with high anticipated pacing burdens, and emerging data from randomized trials support its use as a primary pacing strategy over conventional right ventricular pacing.
- In heart failure with reduced ejection fraction, CSP-based cardiac resynchronization therapy can provide physiological resynchronization in appropriately selected patients with effective conduction system capture, particularly those with left bundle branch block.
- CSP followed by atrioventricular node ablation is an effective rate-control strategy in atrial fibrillation, offering ventricular synchrony and haemodynamic benefit similar to that from conventional biventricular pacing.
- Bachmann bundle area pacing reduces interatrial conduction delay and might improve left-sided atrioventricular synchrony, holding promise for the prevention of atrial fibrillation, although evidence from randomized trials is awaited.

Introduction

Cardiac pacing uses an implanted device to deliver low-energy electrical impulses that initiate cardiac contraction when the intrinsic conduction of the heart is too slow or is interrupted. Cardiac pacing is indicated principally for symptomatic bradycardia due to sinus node dysfunction or atrioventricular block, as well as for the delivery of cardiac resynchronization therapy (CRT) in heart failure (HF). Historically, cardiac pacing has been performed at the right ventricular apex because of the reliability and technical simplicity of this strategy. However, the convenience of this approach is offset by the substantial long-term cost of mechanical dyssynchrony. By initiating ventricular contraction from a non-physiological site, apex pacing strains the myocardium and causes pacing-induced cardiomyopathy (PICM) in approximately 20% of patients with a high pacing burden[1]. Although CRT involving biventricular pacing (BiVP) improves outcomes in patients with HF[2], its epicardial-to-endocardial activation pattern is a poor substitute for intrinsic conduction in the heart. These limitations drove a shift towards conduction system pacing (CSP). The development of His bundle pacing (HBP) demonstrated that physiological ventricular activation via a permanent lead was possible. However, unreliable capture thresholds (the minimum pacing output required to depolarize the tissue and initiate a heartbeat, which with HBP are often high at implantation and can rise over time) and lead instability prevented HBP from gaining widespread traction. Left bundle branch area pacing (LBBAP) addressed most of these problems. By positioning the lead deep in the interventricular septum to engage the left bundle branch directly, operators achieved stable, low thresholds and superior electrical synchrony, resulting in rapid global adoption of the technique.

As these techniques have matured, numerous consensus statements and guidelines have addressed the individual components of CSP, but the field is evolving faster than any single document can capture. Unlike documents that each focus on a single domain, in this Review, we bring the ventricular and atrial applications of physiological pacing together in a single framework, spanning the spectrum of contemporary indications. We trace the journey of CSP from the early lessons of HBP to the expanding evidence for LBBAP across bradycardia and HF, through special populations, device programming and complications. We discuss CSP in its established sense — capture of the ventricular His–Purkinje system by HBP or LBBAP — and consider Bachmann bundle area pacing as an emerging atrial counterpart. By targeting a preferential interatrial conduction pathway, Bachmann bundle area pacing reduces interatrial conduction delay and yields a more physiological atrial activation sequence than conventional right atrial appendage pacing. Throughout this Review, we pay particular attention to contested areas and to data anticipated in the near future, making clear when the evidence is not yet conclusive.

His bundle pacing

Lead implantation

In 1906, Tawara described the atrioventricular node (AVN) and its anatomical link to the penetrating bundle of His[3]. In 2000, a technique was described for the implantation of stylet-driven leads for HBP[4]. The subsequent adoption of lumenless leads delivered via dedicated sheaths resulted in higher success rates and lower capture thresholds than with stylet-driven leads[5,6]. The current technique uses an electrophysiology recording system to allow continuous recording of the bundle of His potential (the sharp, local electrogram generated by depolarization of the bundle of His, recorded from the lead tip and used to confirm proximity to the conduction system) in a unipolar manner, with a high-pass filter setting of 0.5 Hz to assess the bundle of His current of injury (a reversible injury pattern manifesting as an elevation in the recorded electrogram that appears when the lead engages the tissue and indicates direct contact with the bundle of His)[7,8]. The success of HBP implantation has been improved by the use of contrast to delineate the tricuspid annulus summit, the dual-lead technique, and strict criteria to confirm capture of the bundle of His and correction of the bundle branch block (BBB)[9–11].

Use in atrioventricular block and BBB

HBP is an attractive therapy in patients with AVN disease and those requiring AVN ablation (AVNA). Low capture thresholds of <1.5 V at 0.5 ms can be achieved in 80–90% of patients at experienced centres[11]. HBP can also correct BBB and infranodal atrioventricular block in a substantial number of patients because the block is discrete in the bundle of His[12–14]. HBP can be effective in patients with left BBB (LBBB) and HF who require CRT[12,15,16]. However, higher capture thresholds to correct BBB and an unpredictable late rise in thresholds have limited the widespread adoption of this technique[17].

Clinical evidence

In an observational, case–control study involving 765 patients, a significant reduction in the composite end point of HF hospitalization, mortality or the need for an upgrade to BiVP–CRT was observed with HBP compared with right ventricular pacing (RVP; 25% versus 32%; HR 0.71, $P = 0.02$)[18]. In a large, population-based cohort, CSP

(1,459 patients receiving HBP and 4,738 receiving LBBAP) was associated with significantly lower rates of hospitalization for incident HF (HR 0.70, $P = 0.02$) and all-cause mortality (HR 0.66, $P < 0.0001$) at 6 months than dual-chamber pacemakers providing RVP ($n = 16,989$)[19].

Several observational studies have demonstrated the feasibility of using HBP as an alternative to BiVP for CRT in patients with HF, reduced left ventricular (LV) ejection fraction (LVEF) and either LBBB or needing AVNA, with improvements in functional status and LVEF[13,15,16]. Subsequent small, randomized studies have confirmed the utility of HBP as an effective alternative to BiVP–CRT[20–22], but were limited by crossover because of high thresholds or an inability to correct BBB.

Future directions

LBBAP has overcome some of the challenges associated with HBP and, therefore, has been adopted more rapidly. Nevertheless, HBP retains a defined place in the pacing armamentarium. Because the lead is fixed at the bundle of His region without deep penetration into the interventricular septum, HBP avoids potential septal perforation and interaction with the tricuspid apparatus that can accompany intraseptal lead deployment. Furthermore, HBP has not been associated with deterioration in tricuspid valve function[23]. HBP delivers the most proximal, and therefore the most physiological, engagement of the conduction system and can be used as an alternative to LBBAP in difficult cases.

Whether HBP regains a broader role will depend largely on advances in technology. The obstacles to its adoption have been predominantly those of lead delivery and long-term electrical performance rather than of physiological principle, and the earlier transition from stylet-driven leads to lumenless leads delivered through dedicated sheaths has already produced higher success rates and lower capture thresholds[5,6]. Continued refinement of delivery systems and renewed development of stylet-driven leads designed for CSP might further reduce the technical barrier. However, the limitations most responsible for the decline in use of HBP — the higher outputs required to correct BBB, the unpredictable late rise in thresholds, sensing difficulties and the inability to correct block occurring distal to the pacing site — will not be addressed by improvements to the delivery tools alone. Until these limitations are resolved, HBP is likely to remain the preferred approach only in selected settings, such as AVN disease and AVNA, rather than becoming a general alternative to LBBAP[11].

Left bundle branch area pacing

Anatomy and procedure

After traversing the central fibrous body, the bundle of His enters the branching segment beneath the membranous interventricular septum, adjacent to the septal leaflet of the tricuspid valve. The bundle of His then extends anteriorly and rightwards as the right bundle branch (RBB) and runs along the LV subendocardium anteriorly and inferiorly as the left bundle branch (LBB). The LBB trunk and its branches form a complex, interwoven network surrounded by abundant ventricular myocardium. This structure facilitates LBB capture but induces variable pacing morphologies and complicates interpretation for inexperienced operators.

The concept of LBBAP, encompassing LBB pacing (LBBP) and LV septal pacing (LVSP), was originally introduced to facilitate widespread clinical adoption. Nevertheless, LBBAP has been associated with substantial heterogeneity in outcomes across studies and a relatively low reported rate of LBB capture[24,25]. Therefore, throughout this Review, we use 'LBBAP' only as the umbrella procedural term, reserving the use of 'LBBP' for confirmed capture of the left conduction system and 'LVSP' for capture of the septal myocardium alone (Fig. 1). Capture of the LBB trunk and capture of its fascicles both constitute LBBP, because the conduction system is engaged in each case; left fascicular capture satisfies the criteria for conduction system capture but arises from a fascicle rather than from the common LBB trunk and, therefore, differs in the paced axis rather than in whether the conduction system is captured[10]. As such, the distinction from LVSP depends on whether

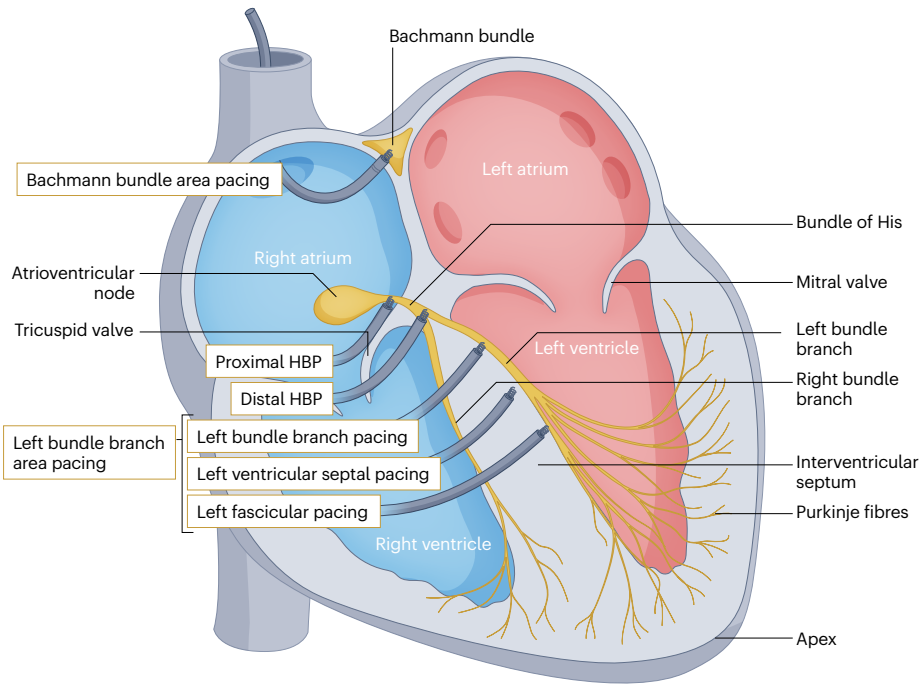


Fig. 1 | Overview of physiological pacing modalities. The illustration shows the sites and capture types of physiological pacing in the atrium and throughout the cardiac conduction system, which is depicted as a continuous network. Ventricular conduction system pacing comprises proximal or distal His bundle pacing (HBP) or left bundle branch area pacing, which is subclassified by capture type into left bundle branch pacing (trunk or fascicular capture) or left ventricular septal pacing. Bachmann bundle area pacing is an emerging atrial pacing counterpart.

the conduction system is captured, not on how proximally within the conduction system that capture occurs. In practice, however, capture status cannot always be verified, and a definite–intermediate–absent gradation retains real-world value: a 2023 multi-society consensus statement has accordingly defined a 'likely LBBP' category between definite LBBP and LVSP[10]. A similar intermediate designation, 'unclassified LBBAP' (UC-LBBAP), defined by a terminal R/r-wave in lead V1, has been proposed when LBB capture cannot be confirmed[26]. In the ChiCSP study[27], LBBP, UC-LBBAP and LVSP accounted for 84.2%, 12.5% and 3.3% of LBBAP implants, respectively, and in patients with LBBB and HF, the composite end point of death or HF hospitalization was lowest with LBBP (8.6%), intermediate with UC-LBBAP (15.4%) and highest with LVSP (33.3%). Consistent with these observations, the term LBBAP should not be used to imply confirmed capture of the conduction system; cases of unconfirmed capture are best described as such rather than treated as a separate physiological entity.

Efficient LBBP implantation requires accurate initial targeting, proper lead depth and reliable identification of capture. The relatively fixed anatomical relationships between the bundle of His, RBB, tricuspid septal leaflet and LBB can guide initial lead positioning; however, fluoroscopy alone is often insufficient due to individual anatomical variability. The lead should be advanced perpendicular to the interventricular septum. Real-time, dual-channel recordings with different filter settings can monitor myocardial injury and LBB potential. Fixation-induced premature ventricular complexes and the amplitude of LBB potentials help to assess lead position. Selective RBB block (RBBB) premature beats or injury current of LBB potentials (particularly the latter) suggests contact with the LBB. Confirmation of LBB capture depends on selective pacing features and an abrupt transition to a paced QRS morphology. Absolute R-wave peak time (RWPT) has limited diagnostic value, whereas modified criteria, such as individualized or global RWPT, improve accuracy[28,29]. Variable antegrade and retrograde conduction thresholds, together with concurrent capture of adjacent conduction tissue, can produce multiple capture thresholds and variable peak times.

In atrioventricular block, pacing must bypass the conduction lesion. Multisite pacing can provide additional benefit when the lesion is incompletely bypassed or no electrical connection exists between the bundle branches[30]. Proximal and distal CSP differ in electrical synchrony, which requires further clinical investigation.

Electrophysiological criteria and ventricular synchrony

Confirming LBB capture is an important procedural end point because registry data — most notably, from the large, multicentre MELOS RELOADED study[31] — indicate that direct LBBP, rather than LVSP alone, confers meaningful clinical benefit, including improved long-term survival. Rapid multipoint depolarization of the LV working myocardium, typically obtained with LBBP, leads to shorter LV activation time, reflected by a shorter time to RWPT in the lateral leads and often other features suggestive of physiological LV activation, such as a steeper initial rise in the QRS complex and no repolarization abnormalities in the lateral leads. These phenomena allow electrocardiogram-based differentiation between LBBP and LVSP. The most useful and popular electrocardiographic markers are V6-RWPT and lead I-RWPT[28,29]. RWPT values are shorter during LBBP than during LVSP, and a fixed V6-RWPT cut-off of <75 ms offers excellent specificity for confirmation of LBBP. However, RWPT values also overlap considerably, especially in patients with HF, due to slow conduction via diseased LBB[28] (Fig. 2a). This overlap limits the sensitivity of any fixed RWPT cut-off criterion in this population. The accuracy of RWPT criteria can be much improved by individualizing cut-off values, justifying the use of this approach. Individualization can be achieved by comparing the paced V6-RWPT in question with the V6-RWPT during ascertained LBB activation in the same patient[28]. However, an unquestionable confirmation of LBB capture can be made only using dynamic manoeuvres, such as the threshold test or programmed stimulation[32] (Fig. 2b). The electrophysiological hallmark of LBBP at the usual output of approximately 2 V is non-selective capture (the simultaneous depolarization of two tissues: the conduction system and the adjacent working myocardium). Given that these two tissues usually differ in excitability and refractory periods, it is possible to obtain a QRS transition caused by the loss of capture of one of them. During the threshold test, decremental output pacing results in a QRS transition when capture of the conduction system or the working myocardium is lost at a low output. Similarly, a QRS transition occurs during programmed stimulation when the extra stimulus finds one of the two tissues refractory[32]. An important caveat in considering LBBAP capture type is that LBBP versus LVSP is not a binary situation. LBB capture can often be incomplete (single-fascicle capture), leading to residual dyssynchrony, or the LBB can contribute little to depolarization of the left ventricle due to a severely diseased left conduction system (the functional deep septal pacing phenomenon observed mainly in patients with HF and/or nonspecific intraventricular conduction delay)[30,33].

CSP for bradycardia

Clinical imperative: preventing PICM

Chronic RVP produces a LBBB-like activation pattern, leading to electrical and mechanical dyssynchrony, adverse LV remodelling and ultimately PICM, defined as an absolute decline in LVEF of ≥10% to a final value of <50% after pacemaker implantation[34,35]. The reported incidence of PICM ranges from 6% to 25%, with the risk rising sharply at RVP burdens exceeding 20–40%, and further increased by male sex, older age, wider native and paced QRS complex, and lower baseline LVEF[1]. Given that PICM can be largely irreversible even with an upgrade to CRT, the contemporary paradigm has shifted from reactive management towards upfront prevention through physiological pacing[36]. Accumulating evidence from observational and randomized studies has shown that LBBAP attenuates the decline in LVEF and reduces the composite end point of PICM, HF hospitalization and the need for an upgrade to CRT compared with RVP in patients with a high anticipated pacing burden[31,37–42]. Reflecting this evidence, the 2023 Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin America Heart Rhythm Society (HRS/APHRS/LAHRS) guideline on cardiac physiological pacing and a 2025 European Society of Cardiology (ESC) clinical consensus statement endorse CSP as a reasonable alternative to BiVP in patients with a high anticipated pacing burden (class IIb in the HRS/APHRS/LAHRS guideline, irrespective of LVEF)[43,44]. With several large-scale trials underway, both the strength and the class of these recommendations are expected to be updated, positioning CSP as a preferred strategy to prevent PICM.

Comparative outcomes: CSP versus conventional pacing

RVP imposes a non-physiological activation sequence that, with a high pacing burden, drives adverse remodelling and PICM. Therefore, clinical outcomes with either physiological CSP or conventional RVP in patients with bradycardia have been compared in observational registries and randomized clinical trials.

Early observational data provided strong signals of clinical benefit with CSP. In a two-centre, prospective cohort study, successful HBP

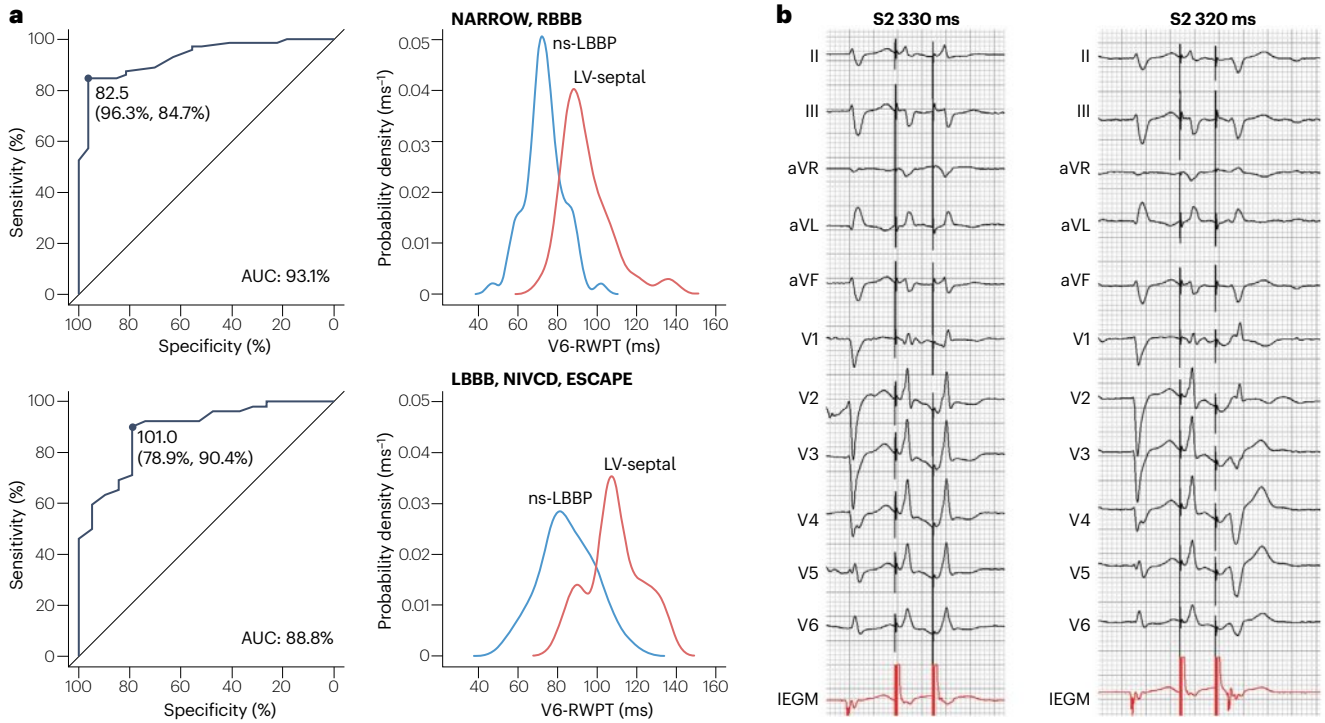


Fig. 2 | Electrophysiological criteria for confirming left bundle branch capture. a, Receiver operating characteristic curves for lead V6 R-wave peak time (RWPT) and the distribution of V6-RWPT values during non-selective left bundle branch pacing (ns-LBBP) and left ventricular septal myocardial pacing (LV-septal). The upper panels show data for patients with a narrow QRS complex (NARROW) or right bundle branch block (RBBB). The lower panels show data for patients with left bundle branch block (LBBB), nonspecific intraventricular conduction delay (NIVCD), or escape rhythm or asystole (ESCAPE). **b**, Programmed stimulation produces a transition of the QRS complex during left bundle branch pacing. An S2 coupling interval of 330 ms produces little change in QRS morphology (left panel), whereas an S2 coupling interval 10 ms shorter produces an abrupt change (a terminal broad R wave in V1 and a polarity change in aVR and V2–V6), indicating loss of local myocardial capture and selective left bundle branch capture (right panel). AUC, area under the curve; aVF, augmented vector foot; aVL, augmented vector left; aVR, augmented vector right; IEGM, intracardiac electrogram. Panel **a** adapted with permission from ref. 28, Elsevier.

reduced the composite end point of death, HF hospitalization or the need for an upgrade to BiVP compared with RVP (25% versus 32%; HR 0.71)[18]. An analysis using the Geisinger–Rush CSP registry compared data from 321 patients receiving LBBAP and 382 patients receiving RVP undergoing de novo implantation of a pacemaker for bradycardia[37]. LBBAP was associated with a significantly lower occurrence of the primary composite end point of all-cause mortality, HF hospitalization or need for an upgrade to BiVP (10.0% versus 23.3%), with the difference being driven by patients who needed >20% ventricular pacing[37]. The large, propensity-matched MELOS RELOADED analysis of data from expert European centres demonstrated improved long-term survival with LBBAP compared with RVP in patients with atrioventricular block and an LVEF of >40%, with an absolute improvement in 4-year survival of 11.8%[31]. Of note, the absence of confirmed LBB capture was independently associated with worse outcomes (HR 1.85), reinforcing that not all LBBAP phenotypes are equivalent and that true conduction system capture is likely to confer the greatest clinical benefit[31]. The prospective, multicentre ChiCSP study[27] involving >3,000 patients undergoing HBP or LBBAP for any pacing indication reported that, among those with LBBB and HF with reduced ejection fraction (HFrEF), confirmed conduction system capture was associated with better LV remodelling and fewer HF events and deaths than LVSP. Intermediate outcomes were achieved with unclassified LBBAP, whereas no such difference in outcomes was apparent in patients with atrioventricular block.

Small, randomized clinical trials have generally shown that CSP is associated with less adverse remodelling than RVP in patients with atrioventricular block and an LVEF of >40%[39–42]. Lower rates of PICM have also been reported with CSP than with RVP[39–42], although PICM was typically defined as a ≥10% decline in LVEF to a final value of <50%, raising questions about the clinical relevance of modest echocardiographic changes. The LBBP-FAVOUR trial[39], involving 160 patients with a high pacing burden and a high risk of cardiac dysfunction, found a lower rate of the composite end point of death, HF hospitalization or PICM with LBBP than with RVP after 36 months of follow-up, primarily driven by fewer PICM events. Similarly, the Prague CSP[40] (n = 249) and CSPACE[41] (n = 202) trials reported a smaller decline in LVEF and fewer PICM-related or HF-related events with CSP than with RVP, whereas the PACE-HF trial[42] reported better preservation of LVEF with CSP than with RVP, but clinical end points were underpowered. Ongoing, adequately powered trials will clarify whether CSP should replace RVP as the default strategy in patients with bradycardia who require ventricular pacing.

Translating guidelines into clinical practice

The 2023 HRS/APHRS/LAHRS guideline on cardiac physiological pacing outlines indications for CSP, BiVP and RVP in patients with

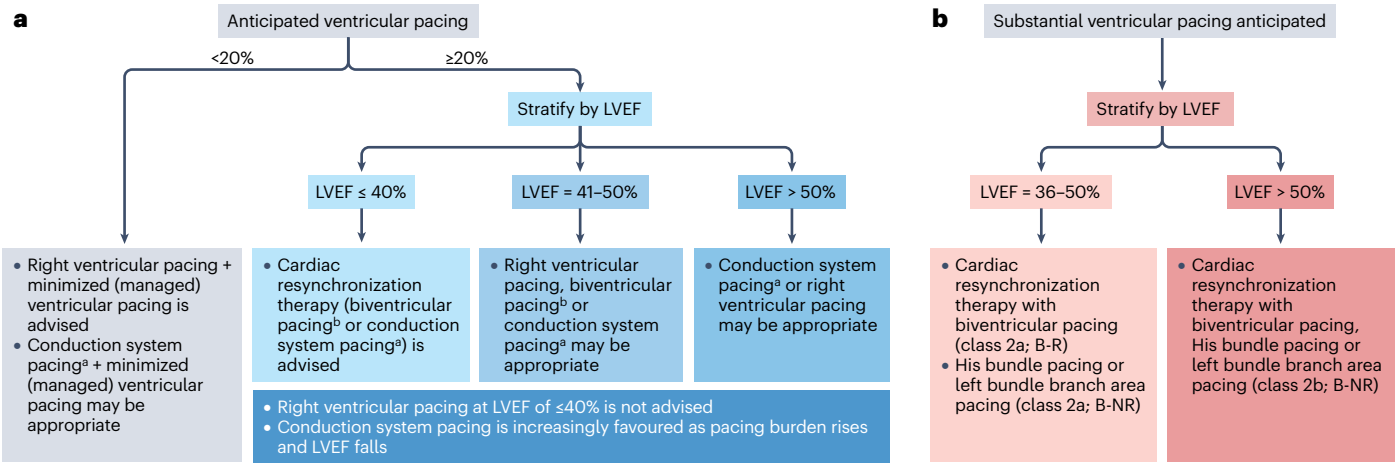


Fig. 3 | Indications for pacing modalities in atrioventricular block according to current clinical guidelines. Recommended ventricular pacing strategies in atrioventricular block as a function of anticipated ventricular pacing burden and baseline left ventricular ejection fraction (LVEF). **a**, Recommendations from the 2025 European Society of Cardiology/European Heart Rhythm Association consensus document on conduction system pacing[44]. With infrequent ventricular pacing (<20%), right ventricular pacing with managed ventricular pacing is advised, whereas conduction system pacing becomes increasingly favoured as the anticipated pacing burden rises and LVEF falls. At LVEF of ≤40%, chronic right ventricular pacing is not advised, whereas cardiac resynchronization therapy (biventricular or conduction system pacing) is advised. **b**, Recommendations from the 2023 Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin America Heart Rhythm Society guideline for patients in whom substantial ventricular pacing is anticipated, with the class of recommendation and level of evidence shown for each option[43]. In a randomized trial, conduction system pacing was superior to right ventricular pacing in patients with a high pacing burden and additional markers of vulnerable myocardium[39]. The results of ongoing trials might generate some broader guidance for patients with an LVEF of 41–50%. B-NR, level of evidence B (non-randomized); B-R, level of evidence B (randomized). [a]In infranodal block, left bundle branch area pacing is the preferred modality of conduction system pacing (or His bundle pacing with a back-up lead). [b]Conduction system pacing is advised if coronary sinus lead implantation for biventricular pacing fails.

atrioventricular block[43]. In the 2025 ESC clinical consensus statement, endorsed by the HRS and other societies, recommendations are based on the anticipated percentage of ventricular pacing and the baseline LVEF[44] (Fig. 3). Patients with infrequent (<20%) ventricular pacing (such as those with paroxysmal atrioventricular block) can receive either RVP or CSP with managed ventricular pacing algorithms that avoid unnecessary pacing. PICM has been reported in patients with >20% RVP[1]. In these patients, CSP can be appropriate, irrespective of LVEF. Until 2026, randomized data comparing CSP with RVP were limited to patients with a LVEF of >40%, with no comparisons with BiVP[31,41,45]. BiVP is superior to RVP in patients with a LVEF of <50%[46], but not in those with preserved LVEF[47]. In patients with a LVEF of <40%, RVP is detrimental and is not advised[48]. This evidence gap is now beginning to be addressed. Rather than enrolment based on LVEF alone, the LBBP-FAVOUR trial[39] enrolled patients with a high anticipated pacing burden as well as additional markers of vulnerable myocardium and found that, compared with RVP, LBBP was associated with a lower rate of the composite end point of death, HF hospitalization and PICM, mainly driven by a reduction in PICM. These findings reinforce the trajectory shown in Fig. 3a, in which CSP is increasingly favoured as the pacing burden rises and the LVEF falls. Because eligibility for the LBBP-FAVOUR trial was defined by a high-risk profile rather than by LVEF alone, the trial findings do not by themselves reclassify the entire group of patients with an LVEF of 41–50%, and definitive guidance will follow the completion of ongoing, adequately powered trials enrolling participants over a broader range of LVEF, such as the LEAP, LEFT-HF, OptimPacing and PROTECT-HF trials (Table 1).

Other than atrioventricular block, sinus node dysfunction is another indication for pacing in bradycardia. In a Medicare report, 37% of patients who received CSP had sinus node dysfunction as the indication for pacing[19]. Unnecessary RVP should be minimized in these patients[48,49]. Atrial pacing significantly lengthens PR intervals[50] and can also result in atrioventricular block due to decremental conduction during rate-adaptive pacing, meaning that CSP can be useful in these patients. Furthermore, sinus node dysfunction and atrial fibrillation (AF) often coexist, with 40–70% of patients with sinus node dysfunction having a history of atrial arrhythmias at the time of diagnosis[51]. Some of these patients might later require AVNA and, in this situation, a CSP lead can be desirable. However, because of the absence of comprehensive data on CSP in patients with sinus node dysfunction, no formal advice has been given in guidelines or consensus documents[43,44].

CSP for CRT

Clinical evidence in LBBB HF

Since 2005, the feasibility of correcting LBBB by pacing distal to the site of block had been understood[52], and its clinical application through LBBP was reported in 2017 (ref. 53). Several multicentre studies have subsequently confirmed LBBP as an alternative to BiVP–CRT. An observational, non-randomized study involving 325 CRT-eligible patients reported an 85% rate of successful LBBP, with a significant increase in LVEF and QRS complex narrowing compared with baseline[54]. In a multicentre study of 1,778 patients, LBBP produced a greater increase in LVEF than BiVP (13 ± 12% versus 10 ± 12%; $P < 0.001$) and a lower rate of the composite end point of death or HF hospitalization[55]. When correction of LBBB is incomplete owing to distal conduction or myocardial disease, LBBP-optimized CRT (LOT-CRT) — combining LBBP with a coronary sinus lead — provides greater resynchronization and better outcomes than BiVP[56]. Within LBBAP, the type of capture also influences resynchronization. Two observational studies comparing

Table 1 | Ongoing clinical trials and studies of CSP

Trial	Trial design	Number of participants	Duration of follow-up	Research question	Primary end points	Estimated completion
CSP versus RVP in bradycardia						
LEFT-HF (NCT05015660)	Multicentre RCT. LBBP versus standard RVP in patients with high-degree atrioventricular block, anticipated ventricular pacing > 90% and LVEF > 35%	1,300	36 months	Does LBBP reduce the risk of cardiovascular death, HF events and adverse remodelling versus RVP in patients with bradycardia requiring ventricular pacing?	Composite of cardiovascular death, HF events and worsening LVESVi (≥15%)	January 2030
PROTECT-HF (NCT05815745)	Multicentre RCT. Physiological pacing (HBP or LBBAP) versus conventional RVP in patients with a pacing indication for bradycardia and LVEF > 35%	2,600	Approximately 78 months	Does CSP lower the risk of death and HF morbidity versus RVP in patients with an anticipated high pacing burden?	All-cause death and HF morbidity (unplanned acute care for HF)	December 2029
OptimPacing (NCT04624763)	Prospective, multicentre RCT. LBBP versus conventional RVP in patients with atrioventricular block (LVEF > 35%, NYHA class I–III)	683	≥3 years	Is LBBP superior to conventional RVP for preventing death, HF hospitalization and PICM in atrioventricular block with LVEF > 35%?	Composite of all-cause mortality, HF hospitalization and/or PICM	January 2028
LEAP-BLOCK (NCT04730921)	Multicentre RCT. LBBAP versus conventional RVP in patients with atrioventricular block and normal LV function (LVEF ≥ 50%) requiring ventricular pacing > 40%	486	2 years	Does LBBAP reduce the risk of death, HF hospitalization and upgrade to CRT versus RVP in patients with atrioventricular block and normal LV function?	Composite of all-cause death, HF hospitalization and upgrade to CRT	Completed; awaiting results
LEAP (NCT04595487)	Multicentre RCT. LVSP versus conventional RVP in patients with atrioventricular conduction disorders, anticipated ventricular pacing > 20% and LVEF ≥ 40%	470	1 year	Does LBBAP reduce the risk of death, HF hospitalization and decline in LVEF versus RVP in patients requiring ventricular pacing?	Combined end point of all-cause death, HF hospitalization and 10% reduction in LVEF to <50%	Completed; awaiting results
PROTECT-Sync (NCT05585411)	Multicentre RCT. LBBAP versus RVP in patients with bradyarrhythmia and anticipated ventricular pacing > 40%	450	2 years	Does LBBAP reduce the risk of death, HF hospitalization, PICM and upgrade to CRT versus RVP in patients with bradyarrhythmia and an anticipated pacing burden > 40%?	Composite of all-cause death, HF hospitalization, PICM and upgrade to CRT	November 2026
CLOSE-AV (NCT07314008)	Multicentre RCT. LBBAP (with physiological atrioventricular interval) versus MVP (with prolonged atrioventricular interval) in patients with SSS and atrioventricular conduction delay (PR interval > 200 ms)	440	2 years	Does physiological-interval LBBAP reduce the risk of death, HF hospitalization and persistent AF versus prolonged-interval, managed ventricular pacing in patients with sinus node disease with atrioventricular conduction delay?	Composite of all-cause death, HF hospitalization and persistent AF	January 2029
CSP versus BiVP in HF						
Left vs Left (NCT05650658)	Prospective, multicentre RCT. HBP or LBBP versus BiVP in patients with HF (LVEF ≤ 50%) and wide QRS complex (≥130 ms) or anticipated ventricular pacing > 40%	2,136	5.5 years	Is CSP–CRT superior to BiVP–CRT for reducing the risk of death and HF hospitalization in patients with an indication for CRT?	Composite of all-cause death and HF hospitalization	June 2029
Nordic-CSP (NCT07492979)	Multicentre RCT. HBP or LBBP (CSP) versus conventional BiVP–CRT in patients with HF (LVEF ≤ 35%) and an indication for CRT	1,100	≥2 years	Does CSP–CRT reduce the risk of death or unplanned HF hospitalization versus conventional BiVP–CRT?	Composite of death or non-planned HF hospitalization	July 2031
HIS-CRT (NCT05265520)	Prospective, multicentre RCT. HBP-enhanced CRT (His–CRT) versus conventional BiVP–CRT in patients with HF and RBBB	120	24 months	Does HBP-enhanced CRT improve LVEF versus conventional BiVP–CRT in patients with HF and RBBB?	Change in LVEF at 6 months	July 2028

Table 1 (continued) | Ongoing clinical trials and studies of CSP

Trial	Trial design	Number of participants	Duration of follow-up	Research question	Primary end points	Estimated completion
CSP in AF with AVNA						
RAFT-P&A (NCT06299514)	RCT. CSP followed by AVNA (pace-and-ablate) versus pharmacological rate control or optimal medical therapy in patients with permanent or persistent AF and HF	600	12 months	Does CSP improve a hierarchical composite of clinical outcomes, biomarkers and quality of life in patients with AF managed by AVNA?	Win ratio of hierarchical composite of all-cause death and HF events, plasma NT-proBNP level and quality of life	December 2029
PACE-FIB (NCT05029570)	Multicentre, RCT. CSP followed by AVNA versus pharmacological rate control in patients with permanent AF and HF with LVEF > 40% (HFpEF or HFmrEF)	334	36 months	Is CSP followed by AVNA superior to pharmacological rate control for preventing the risk of death and HF events in patients with permanent AF and HFpEF or HFmrEF?	Composite of all-cause death, HF hospitalization and worsening HF	September 2030
HF-RELIEF (NCT06833138)	Multicentre, RCT. CSP plus AVNA versus optimal pharmacological therapy in patients with permanent AF and HFpEF (LVEF ≥ 50%)	266	24 months	Does CSP plus AVNA improve outcomes versus optimal medical therapy in patients with permanent AF with HFpEF?	Composite of all-cause death, HF hospitalization or need for intravenous diuretics	December 2029
ABACUS (NCT06207383)	Multicentre, RCT. CSP plus AVNA versus AF ablation (pulmonary vein isolation) in patients with persistent AF and HF who are eligible for AF ablation	220	1–4 years	Does CSP plus AVNA reduce mortality and the risk of cardiovascular hospitalization versus AF ablation in patients with persistent AF with HF?	Mortality and cardiovascular hospitalization (superiority); mortality and HF hospitalization (non-inferiority)	December 2028
PALLIATE-AF (NCT06699342)	Multicentre RCT. LBBAP plus AVNA versus optimized pharmacological therapy in patients with symptomatic, permanent AF refractory or intolerant to drugs or ablation and LVEF > 40%	50	6–24 months	Does LBBAP plus AVNA reduce plasma NT-proBNP level versus optimized drug therapy in patients with symptomatic, permanent AF refractory to drugs or ablation?	Change in plasma NT-proBNP level at 6 months	December 2027
BBAP						
BRAVE (NCT07360067)	Single-centre cohort study (100 prospective plus 100 retrospective). BBAP versus RAAP in patients with SSS	200	12 months	Does BBAP improve LA function and remodelling versus right atrial appendage pacing in patients with sinus node disease?	LA volume index and LA strain (functional echocardiographic parameters) at 6 and 12 months	December 2028
AHRE-BLAST (NCT07305194)	Prospective, observational study. BBAP plus LBBP versus RAAP plus LBBP versus conventional RAAP plus RVP in patients with a pacing indication and no previous AF	460	24 months	Does adding BBAP reduce the atrial high-rate episode burden versus conventional atrial and ventricular pacing?	Atrial high-rate episode burden at 24 months	April 2028
Atrial Synchrony Evaluation of BB Pacing in SSS (NCT07055035)	Prospective RCT. BBAP versus conventional RAAP in patients with SSS, assessed by 2D speckle tracking imaging	72	3 months	Does BBAP shorten inter-atrial electromechanical delay versus RAAP in patients with sinus node disease?	Change in inter-atrial electromechanical delay at 1 and 3 months	Completed; awaiting results
BRIDGE-HF (NCT07547306)	Prospective, crossover RCT. Accelerated BBAP (LRL 70 bpm, DDDR plus APP) versus BBAP off (LRL 30 bpm, VVI) and a separate RAAP cohort in patients with HFrEF (LVEF ≤ 40%), interatrial block and an indication for a dual-chamber ICD	120	6 weeks for primary outcome	Does accelerated BBAP lower the plasma NT-proBNP level versus minimal atrial pacing in patients with HFrEF and interatrial block?	Relative change in plasma NT-proBNP level at 6 weeks (BBAP on versus baseline or BBAP off)	December 2030

AF, atrial fibrillation; APP, atrial preference pacing; AVNA, atrioventricular node ablation; BB, Bachmann bundle; BBAP, Bachmann bundle area pacing; BiVP, biventricular pacing; CRT, cardiac resynchronization therapy; CSP, conduction system pacing; DDDR, dual-chamber rate-responsive pacing mode; HBP, His bundle pacing; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter–defibrillator; LA, left atrial; LBBAP, left bundle branch area pacing; LBBP, left bundle branch pacing; LRL, lower rate limit; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; LVSP, left ventricular septal pacing; MVP, minimized (managed) ventricular pacing; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PICM, pacing-induced cardiomyopathy; RAAP, right atrial appendage pacing; RBBB, right bundle branch block; RCT, randomized controlled trial; RVP, right ventricular pacing; SSS, sick sinus syndrome; VVI, ventricular demand pacing mode.

LBBP, LVSP and BiVP found that LVSP was associated with worse clinical outcomes than LBBP and similar clinical outcomes to those with BiVP, whereas LBBP was superior to both, with the difference mainly driven by reductions in HF hospitalization rather than all-cause mortality[57,58]. These findings indicate that the resynchronization benefit of LBBAP depends on engaging the conduction system rather than on the septal lead position alone.

Randomized trials comparing CSP with BiVP have yielded conflicting results. In the LEVEL-AT trial[59] involving 70 patients with an indication for CRT, either CSP or BiVP produced similar LV remodelling and rates of death or HF hospitalization. In the HeartSync-LBBP trial[25] involving 200 patients with LBBB and an LVEF of ≤35%, the rates of death or HF hospitalization were significantly lower with LBBP than with BiVP (8% versus 28%; HR 0.26, $P < 0.001$). By contrast, in the PhysioSync-HF trial[24] involving 173 patients with HFrEF and LBBB, CSP was inferior to BiVP for a hierarchical composite end point of death, HF events and change in LVEF at 12 months (OR 2.36, $P = 0.99$ for non-inferiority, $P = 0.002$ for between-group difference). Likewise, the LEFT-BUNDLE-CRT trial involving 176 patients with LBBB and eligible for CRT did not establish the non-inferiority of LBBAP compared with BiVP, although both groups achieved high rates of a positive response to CRT[60]. Preliminary results from the LeCaRT trial[61] were presented at the European Heart Rhythm Association Congress in 2026 and suggested a possible advantage for LBBAP over BiVP, but peer-reviewed publication is awaited before they can be interpreted. In summary, these divergent results mean that the relative roles of CSP and BiVP remain unresolved. Differences in patient populations and in the success of achieving true conduction system capture are likely to have influenced the trial outcomes, and data from upcoming larger trials are awaited.

The presence of septal scarring at the implantation site is a major limiting factor for successful LBBP. Cardiac magnetic resonance imaging with late gadolinium enhancement helps to quantify scarring, tailor treatment and assess prognosis. In a prospective study, cardiac magnetic resonance imaging with late gadolinium enhancement was used to risk stratify 225 patients with LBBB and an LVEF of ≤35%; those with a low scar burden (<10%) received LBBP alone and those with a high scar burden (≥10%) received LBBP plus a defibrillator[62]. At 2 years, the composite end point of death, HF hospitalization or ventricular arrhythmia was more frequent in the high-scar group than in the low-scar group (26.1% versus 6.9%; HR 16.52, $P = 0.005$), and normalization of LVEF (that is, an LVEF of >50%) occurred in 25% of the high-scar group compared with 82.2% of the low-scar group[62]. Therefore, cardiac magnetic resonance imaging before CRT might help to optimize device selection and predict response, and further large-scale, randomized trials are needed to establish LBBP as an effective CRT modality.

Emerging evidence in RBBB and non-LBBB HF

Patients with a reduced LVEF and RBBB have historically been grouped as wide QRS phenotypes in landmark trials of CRT, with the aim of restoring interventricular synchrony with BiVP[63]. However, a substantial subset of these patients are likely to have concomitant intraventricular conduction delay in the left ventricle, masked by the RBBB pattern, that is itself central to the pathophysiology of reduced LVEF[64]. Clinical guidelines give BiVP–CRT in patients with RBBB a class IIa indication (QRS complex of >150 ms, NYHA class III/IV) or a class IIb indication (QRS complex of 120–150 ms, NYHA class II)[65].

Trials of CRT have not shown a consistent reduction in mortality in patients with non-LBBB, with most evidence limited to post hoc subgroup analyses in which patients with non-LBBB accounted for a small minority of participants. In the long-term follow-up of the MADIT-CRT trial[66] over a median of 5.6 years, CRT with a defibrillator increased survival in patients with LBBB but was associated with increased mortality in the 536 patients with non-LBBB (RBBB or intraventricular conduction delay) compared with a defibrillator alone (adjusted HR 1.57, 95% CI 1.03–2.39, $P = 0.04$; $P < 0.001$ for interaction with QRS morphology). Similarly, in an analysis of a large Medicare database of 14,946 recipients of CRT with a defibrillator, those with RBBB had an increased risk of death compared with those with LBBB (HR 1.37, 95% CI 1.26–1.49)[67]. A meta-analysis of randomized trials found no significant reduction in HF or death with BiVP–CRT in patients with non-LBBB (including RBBB)[68], and a patient-level meta-analysis showed a modest benefit from BiVP–CRT in patients with intraventricular conduction delay but none in patients with RBBB[69].

Evidence from dedicated trials involving patients with RBBB and HFrEF is scarce. The ongoing HIS-CRT trial (NCT05265520) is, to our knowledge, the first multicentre, randomized comparison of BiVP and CSP in 120 patients with RBBB and an indication for CRT. The primary end point is improvement in LVEF, and secondary end points are mortality and HF hospitalization.

The substrate underlying an RBBB pattern is heterogeneous. Invasive septal mapping in LBBB has demonstrated that a typical BBB pattern might reflect either complete conduction block or intact Purkinje activation, in which the surface pattern arises from delayed conduction through working myocardium rather than from block in the specialized conduction system[14]. The same distinction is expected to apply to RBBB, in which block might be located proximally in the right bundle, more distally or be absent altogether, although direct mapping data in RBBB are lacking, and this extrapolation remains hypothetical. However, the distinction is of practical importance, because CSP can only bypass a lesion that exists. When Purkinje activation is intact, neither HBP nor LBBAP would be expected to correct the QRS complex, and this situation might contribute to the inconsistent response to resynchronization reported in populations of patients with RBBB. By contrast, when block is proximal and unifocal, its location can be defined by intracardiac mapping (Fig. 4a), and HBP distal to this site can correct the RBBB pattern and narrow the QRS complex (Fig. 4b). In patients with HF and RBBB, either HBP[70] or LBBAP[71] has been shown to improve LVEF. Because LBBAP pre-excites the LV septum and leaves an incomplete RBBB pattern without alleviating right ventricular delay, its benefit is likely to derive from early LV septal activation in those with left-sided intraventricular conduction delay. Novel strategies such as His-optimized CRT (HOT-CRT) and LOT-CRT might add benefit in patients with concomitant intraventricular conduction delay by combining conduction system capture with pacing of the lateral LV wall from a coronary sinus lead, with the timing between the conduction system lead and the coronary sinus lead programmed so that the two wavefronts fuse consistently on every beat.

Translating evidence into clinical practice

The use of CSP to provide CRT is strongly supported by direct evidence of electrical and mechanical resynchronization and by large, multicentre, observational studies showing the clinical benefits of CSP–CRT[55,71–73]. However, whether CSP–CRT should be preferred over conventional BiVP–CRT is unknown. Clinical reasoning and expert consensus indicate that CSP–CRT is appropriate if the conventional BiVP–CRT procedure fails[44]. Whether CSP–CRT should be used as the initial approach remains a matter of ongoing debate. The lack of large, randomized studies showing the superiority of CSP–CRT over

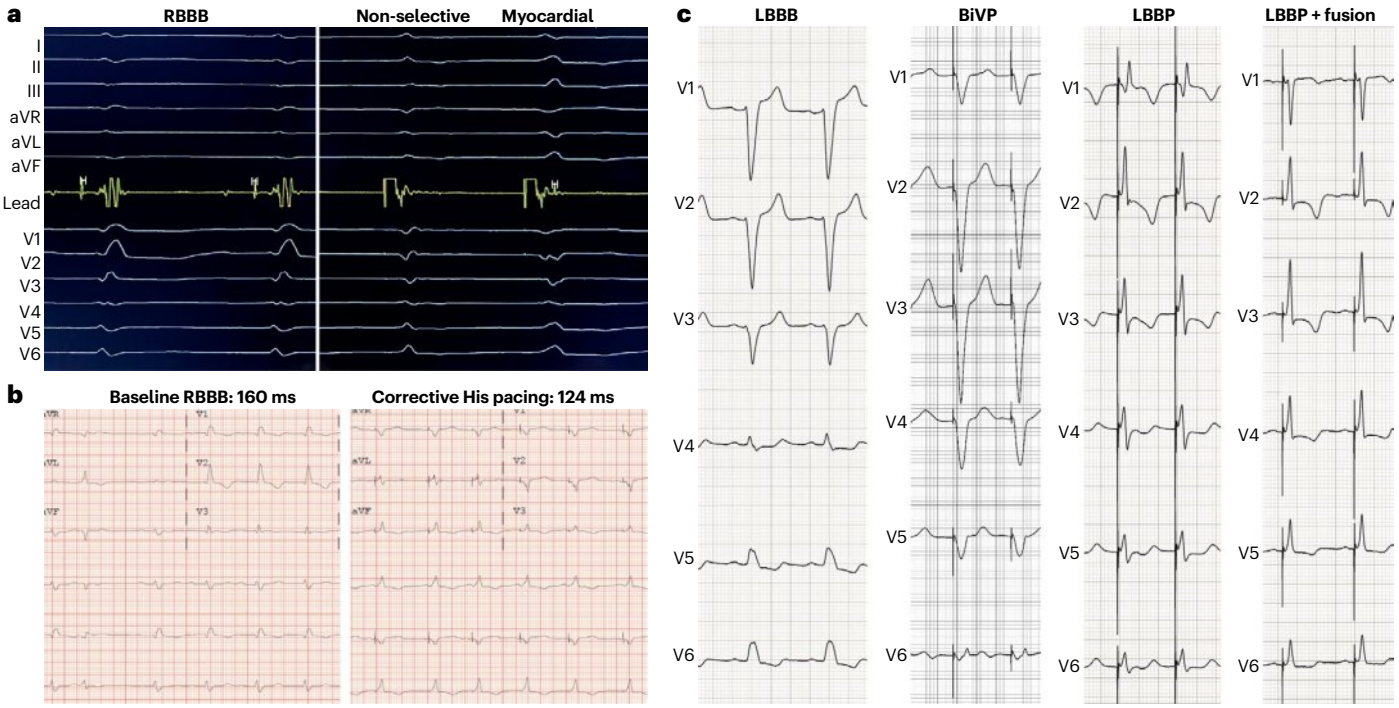


Fig. 4 | Conduction system pacing for resynchronization in bundle branch block. a, Mapping of the level of right bundle branch block (RBBB). Intracardiac electrograms demonstrate the proximal site of conduction delay (left) and confirmation of correction with non-selective conduction system capture versus pure myocardial capture (right). The level of block guides whether His bundle or left bundle branch area pacing will achieve resynchronization. **b**, Correction of RBBB with His bundle pacing. Baseline RBBB with a QRS duration of 160 ms (left) is corrected by His bundle pacing, with the QRS duration narrowing to 124 ms (right), consistent with recruitment of the conduction system beyond the site of block or compensation of myocardial delay by direct activation of the right side of the interventricular septum. **c**, Superior electrical resynchronization during left bundle branch pacing (LBBP) in left bundle branch block (LBBB). Biventricular pacing (BiVP) did not narrow the QRS complex relative to the native LBBB QRS, whereas fusion of LBBP with native conduction through the healthy right bundle branch nearly normalized the QRS complex. aVF, augmented vector foot; aVL, augmented vector left; aVR, augmented vector right.

BiVP–CRT prevents strong recommendations in clinical guidelines. Nevertheless, several high-volume centres in various parts of the world have already adopted CSP–CRT as one of their options for delivering CRT on the basis of local experience and small studies.

The evidence from randomized trials performed to date is contradictory, and none of these trials has been definitive. Some reported benefits with CSP–CRT over BiVP–CRT or found CSP–CRT to be non-inferior[25,59,74], whereas others did not[24,60]. These trials also differed substantially in what they measured and over what period, from the echocardiographic response at 6 months to death or HF hospitalization at a median of 3 years, so their results are not directly comparable. We would emphasize that the following considerations apply to all these trials and limit the conclusions that can be drawn: the quality of CSP delivery (for example, LBB capture at implantation and follow-up and degree of physiological QRS complex restoration), patient selection (myocardial scar distribution, conduction system condition and baseline QRS morphology) and crossover between the randomized groups.

Quality of CSP delivery is difficult to compare across these trials because it is defined and documented differently in each trial. The LEFT-BUNDLE-CRT trial[60] applied the strictest definition, accepting only a QRS transition during decremental unipolar pacing and adjudicating the final capture pattern centrally. On this basis, left bundle capture was confirmed in 41% of patients randomly assigned to LBBAP, with LV septal capture in 54%, and those with confirmed capture showed more pronounced LV reverse remodelling than those with LV septal capture in an exploratory analysis. The HeartSync-LBBP trial[25] has reported direct evidence of left bundle capture in 75.5% of patients and applied indirect criteria in the remainder of the patients, without systematic reassessment during follow-up. The PhysioSync-HF trial[24] classified lead position by the operator, with deep septal pacing in 20% of the CSP group, which the investigators considered might have attenuated the response. Because the clinical effect of CSP depends on whether the conduction system is engaged, incomplete or inconsistently documented capture limits the interpretation of a favourable result as much as an unfavourable one.

The use of CSP–CRT not only when BiVP–CRT fails but also as an easy bailout when BiVP–CRT is suboptimal was probably responsible for the substantial crossover in the LEFT-BUNDLE-CRT trial[60] (20.7% from the BiVP group and 9.8% from the LBBAP group). This high rate of crossover means that the trial essentially compared the outcomes of different strategies (that is, which CRT delivery method should be used initially), rather than being a randomized comparison of the different CRT delivery methods per se. This interpretation is a strength in terms of pragmatic relevance and a limitation in terms of mechanistic inference, and it applies to any trial in which crossover is permitted.

Together, these considerations suggest that the divergent results might reflect differences in end-point definition, follow-up duration,

patient selection and quality of delivery as much as any real difference in the therapeutic potential of the two approaches. Hopefully, the uncertainty will be resolved by the adequately powered trials now in progress (Table 1).

The LOT-CRT method, which involves LBBP coupled with coronary venous pacing, was introduced fairly early in the development of the LBBP method and became the dominant hybrid approach to CRT delivery[56]. LOT-CRT was proposed to address the limitations of both the LBBP method and the BiVP method. The recommendations for LOT-CRT are primarily based on physiological reasoning and observational data from fairly small studies, as summarized in the ESC clinical consensus statement[44]. The recommendation is to add a coronary venous lead when LBBP results in a lack of full electrical resynchronization, as indicated by a long RWPT in lateral leads, a lack of LBB capture, and functional or anatomical deep septal pacing[73]. Similarly, adding an LBBP lead seems reasonable when BiVP does not narrow the baseline QRS complex[75] (Fig. 4c).

CSP in special populations

AF with AVN ablation

In patients with refractory AF and uncontrolled ventricular rates, AVNA combined with permanent pacing — the 'ablate-and-pace' strategy — provides reliable rate and rhythm regularization. The landmark APAF-CRT mortality trial[76] established that AVNA with BiVP reduces the rate of HF hospitalization and all-cause death compared with pharmacological rate control in patients with permanent AF, a narrow QRS complex and previous HF hospitalization, regardless of baseline LVEF. However, the international CAAN-AF trial[77], in which 143 patients with permanent AF, HFrEF and an existing CRT–defibrillator were randomly assigned to either AVNA or optimized medical rate control, was stopped early for futility, with no significant difference in mortality or the rate of HF events between the two groups. Together, these trials suggest that the incremental value of AVNA depends on the baseline pacing strategy, the adequacy of rate control and the HF phenotype.

Because BiVP after AVNA necessarily imposes epicardial-to-endocardial activation, CSP (particularly LBBAP) has emerged as a more physiological alternative. The randomized, crossover ALTERNATIVE-AF trial[22] in patients with AF and HFrEF undergoing AVNA showed a greater gain in LVEF with HBP than with BiVP. The CONDUCT-AF trial, in which CSP was compared with BiVP before AVNA in patients with AF and reduced or mid-range LVEF, was presented at the ESC HF Congress in 2026 but has not yet been published in a peer-reviewed journal. Observational data supporting the use of LBBAP rather than BiVP after AVNA in patients with AF and HF include a retrospective analysis of 223 patients from the Geisinger Health System showing a lower risk of death or HF hospitalization with CSP than with BiVP or RVP (HR 0.61)[78], a multicentre registry showing shorter procedure times and lower thresholds with LBBAP than with HBP or BiVP[79], and a 2025 meta-analysis including 2,021 patients showing a narrower paced QRS complex and greater symptomatic improvement and a similar gain in LVEF with CSP compared with BiVP[80]. Evidence is most robust in patients with AF and HFrEF, accumulating in those with HF with mildly reduced LVEF (HFmrEF), but is limited in those with HF with preserved LVEF (HFpEF).

Reflecting this landscape, the 2023 HRS/APHRS/LAHRS guideline[43] and the 2025 ESC clinical consensus statement[44] endorse BiVP as the standard for AVNA in patients with AF and HFrEF, with CSP as a reasonable alternative to BiVP. In those with AF and HFmrEF, both BiVP and CSP are considered to be appropriate. In those with AF and HFpEF, either CSP or RVP can be selected, depending on the patient characteristics. CSP (particularly LBBAP) offers advantages in patients with a narrow native QRS complex, in whom BiVP provides no resynchronization benefit, and in patients requiring a simpler device[81]. In patients with an implantable cardioverter–defibrillator (ICD), AVNA additionally abolishes rapidly conducted AF and thereby reduces inappropriate device detections and shocks arising from AF in tachycardia-detection zones; delivering the required pacing via CSP rather than RVP preserves ventricular function while retaining this benefit. Accordingly, HBP or LBBP combined with AVNA and ICD therapy has been reported to reduce the rate of HF hospitalization, inappropriate shocks and death compared with ICD therapy alone in patients with persistent AF and HF[82]. Procedurally, CSP lead implantation typically precedes AVNA, with an adequate lead-to-AVN distance to minimize acute threshold rise. Outcome data from dedicated trials involving patients with AF and HFpEF remain sparse, and ongoing randomized trials are expected to address this gap: the HF-RELIEF (NCT06833138), PACE-FIB (NCT05029570) and PALLIATE-AF (NCT06699342) trials are comparing CSP plus AVNA versus medical therapy in patients with AF and HFmrEF or HFpEF. In addition, the ABACUS trial (NCT06207383) is comparing CSP plus AVNA versus AF ablation in patients with persistent AF and HF.

Optimization and management

Device programming and longitudinal follow-up

Conduction system capture should be reassessed at the first follow-up visit after implantation (typically within 1–3 months) and at each subsequent visit, because capture can be lost over time. At each of these visits, a 12-lead electrocardiogram should be recorded to evaluate conduction system capture[83–86]; if a 12-lead recording is unavailable, modified V1 and V6 leads can be recorded using limb lead electrodes only[87]. With HBP, capture is confirmed by a QRS morphology identical to that of the native rhythm, or by transitions in QRS morphology during threshold testing, the latter being uncommon with LBBP. The absence of QRS transitions implies either myocardial capture alone or identical capture thresholds of the myocardium and the conduction system.

Programming depends on which generator port the CSP lead is connected to, which in turn reflects the indication, the underlying rhythm and the presence of additional leads. Connection to the RV port is the most common configuration, and programming is relatively standard, although sensing issues, atrial oversensing or ventricular undersensing can be encountered with HBP. The LV port is generally used when a backup lead is present (which can mitigate high capture thresholds or sensing problems[88]) or in the setting of an ICD. Connection to the atrial port is the most demanding, requiring attention to ventricular safety pacing and sensing behaviour, and to dual-chamber discriminator algorithms, which must be inactivated when an ICD is present. Importantly, currently available generators do not offer programming modes designed specifically for CSP, and comprehensive guidance is available in dedicated documents[10,84,85].

Complications and practical troubleshooting

Acute complications during implantation include septal perforation, septal haematoma, iatrogenic right bundle injury, acute coronary syndrome and venous channel perforation. The reported incidence of septal perforation is between 3.2% and 14.1%[89]. Septal perforation can be identified by the loss of current of injury in the unfiltered unipolar electrogram together with a QS (type 1 or complete perforation) or RS (type 2 or partial perforation) pattern, unipolar impedance <450 Ω, or current of injury amplitude in the ring electrode greater than in the tip electrode, although this finding is relative and is neither sensitive nor specific for

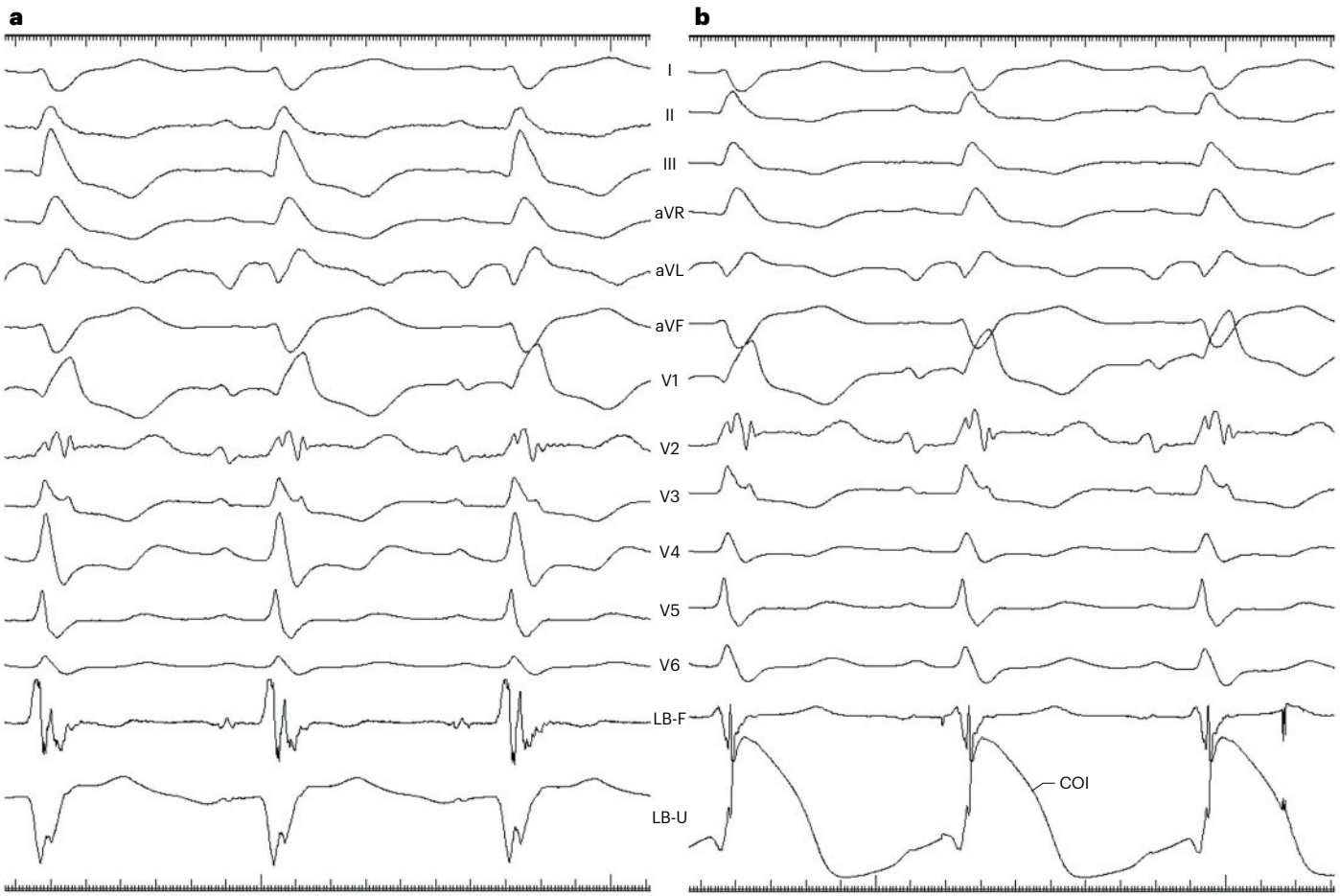


Fig. 5 | Septal perforation during left bundle branch pacing. a, Absent current of injury (COI) in the unfiltered unipolar left bundle electrogram (LB-U) with a QS pattern, suggestive of septal perforation. **b**, Unfiltered unipolar left bundle electrogram showing significant COI after repositioning the lead at a different site. Filtered unipolar electrograms (LB-F) are of lesser value than the unfiltered channel for identifying septal perforation; nevertheless, the sharp near-field high-frequency components in the ventriculogram most often disappear with complete perforation, and occasionally with microperforation, so they are not entirely uninformative. aVF, augmented vector foot; aVL, augmented vector left; aVR, augmented vector right.

perforation (Fig. 5). Furthermore, an RS pattern does not invariably indicate partial perforation, because it can also be seen with complete perforation in the setting of LBBB or RVP[90]. The lead must be repositioned at a different site, rather than just withdrawn, to prevent future dislodgements. Delayed perforations occurring within days or weeks after the procedure are rare, with an incidence of 0.08–0.33%[91,92]. Tricuspid valve regurgitation worsens after LBBP in 7–33% of patients[93]. In a multicentre registry involving 523 patients undergoing LBBAP, incident moderate-or-greater tricuspid valve regurgitation occurred in 6.7% of patients at 1 year and was more frequent after LVSP than after confirmed LBB capture[94]. Damage to the helix (the fixation screw at the lead tip) has been observed in 0.8–5.0% of patients[95–97]. A higher incidence of lead fracture was observed with stylet-driven leads (inter-electrode segment) than with lumenless leads (proximal to the ring electrode)[97].

Loss of conduction system capture during follow-up, defined as partial or complete loss of RBB delay together with prolongation of RWPT and QRS duration, is observed in 4–6% of patients[91,98], although higher rates (approximately 12%) have been reported with stylet-driven leads or in less experienced centres[99]. Predictors of loss of conduction system capture include multiple attempts for successful lead deployment, the lack of non-selective to selective capture transition during implantation and micro-dislodgement by >2 mm (ref. 100). Demonstration of LBBP as opposed to LVSP during implantation and minimizing deployment attempts ensure consistent LBB capture during follow-up. In patients with persistent or new-onset LV dysfunction, loss of conduction system capture during follow-up warrants repositioning of the LBBP lead or an upgrade to LOT-CRT.

Bachmann bundle area pacing

Whereas the preceding sections have focused on ventricular CSP, this section addresses an emerging atrial counterpart, Bachmann bundle area pacing, which aims to extend the principles of physiological pacing to the atria. The standard target for atrial lead placement (the right atrial appendage) accounts for a substantial proportion of lead perforations[101], and pacing in the appendage prolongs atrial activation time[102], which is likely to contribute to the independent association between atrial pacing and incident AF[103]. The Bachmann bundle offers an alternative site (Fig. 1). Anatomical and microstructural mapping has

localized the target to the region where the right atrial inputs to the Bachmann bundle converge, which is thick and resistant to perforation. Pacing at this site recapitulates sinus activation of both atria, so that the paced P wave shares or normalizes the sinus P wave morphology, while shortening the interatrial conduction time[104,105] (Fig. 6). Two consequences follow from restoring a more physiological sequence of atrial activation. First, correcting interatrial conduction delay by pre-exciting the Bachmann bundle advances left atrial timing, so that both atria are activated over the pathways used by the healthy sinus node, which would be expected to lessen the iatrogenic pro-fibrillatory effect of appendage pacing. Second, this pre-excitation lengthens the interval available for atrial contraction to complete before ventricular systole, which might lower the elevated left atrial pressures that contribute to AF through atrial stretch and dilatation[106]. Whether these effects translate into a reduction in clinical AF burden — that is, whether the approach is merely less pro-arrhythmic than appendage pacing or is actively antiarrhythmic — remains to be established.

As with ventricular CSP, the interpretation of clinical outcomes depends on confirming that the intended structure was captured. Capture of the Bachmann bundle is identified using paced P wave morphology together with electrogram-based criteria: a paced P wave that is positive and of greater amplitude in the inferior leads with shortening of the P wave duration relative to sinus rhythm, and a discrete, high-frequency Bachmann bundle potential on the intracardiac electrogram recorded at the lead tip[105,107]. These criteria are more recent and less extensively validated than their ventricular equivalents, and their application has not been uniform across published studies — a consideration that is relevant to interpretating the outcome data below.

The clinical evidence for Bachmann bundle area pacing remains limited. In a multicentre, randomized trial of 120 patients with paroxysmal AF and a pacing indication, pacing in the region of the Bachmann bundle reduced progression to chronic AF compared with conventional atrial pacing[108]. In a comparative study using electrocardiographic capture criteria, Bachmann bundle pacing was associated with a lower atrial arrhythmia burden than nonspecific right atrial septal or appendage pacing[109]. Electrogram-guided implantation has been shown to be feasible, with a high success rate, resulting in correction of interatrial block in most patients[107,110]. Biatrial resynchronization has also been demonstrated directly[110]. In a randomized, patient-blinded, crossover trial in 42 symptomatic patients with non-obstructive hypertrophic cardiomyopathy, HFpEF and interatrial block, accelerated Bachmann bundle area pacing reduced the plasma levels of N-terminal pro-B-type natriuretic peptide compared with either no pacing or right atrial appendage pacing, with accompanying improvements in diastolic filling, NYHA functional class and exercise capacity[111]. Together, these data establish feasibility and demonstrate the expected electrophysiological effects of Bachmann bundle area pacing, but the studies are small, heterogeneous in technique and short in follow-up, and none has yet been powered for clinical AF outcomes.

These questions are now being addressed prospectively in several ongoing observational and randomized studies (Table 1). The AHRE-BLAST (NCT07305194) and BRAVE (NCT07360067) trials are examining whether Bachmann bundle area pacing reduces atrial arrhythmia burden relative to conventional atrial pacing. A randomized trial (NCT07055035) is assessing Bachmann bundle area pacing in patients with sinus node disease, with atrial synchrony as a physiological end point. Finally, the BRIDGE-HF trial (NCT07547306) is evaluating Bachmann bundle area pacing in patients with HFrEF. Until the results of these trials are reported, Bachmann bundle area pacing is best regarded as a physiologically well-founded but clinically unproven approach.

Ongoing trials

A common thread runs through the preceding sections: the physiological rationale for CSP is well established, and the observational evidence is substantial, but data from adequately powered, randomized trials with hard clinical end points remain limited in most domains in which CSP is now used. Table 1 summarizes the ongoing, randomized trials across the four principal indications, together with the principal question each is designed to answer. In bradycardia, ongoing trials are examining whether CSP prevents the ventricular dysfunction associated with a high RVP burden and are extending enrolment to a broader range of LVEFs than in previous trials. In HF, ongoing trials are addressing whether CSP–CRT can be recommended as an initial strategy rather than as a bailout approach, with prespecified clinical rather than surrogate end points, and in a wider range of substrates, including RBBB and non-LBBB conduction delay, than in previous trials. In AF managed by AVNA, ongoing trials are comparing CSP with BiVP and with pharmacological rate control. In the atrium, ongoing trials

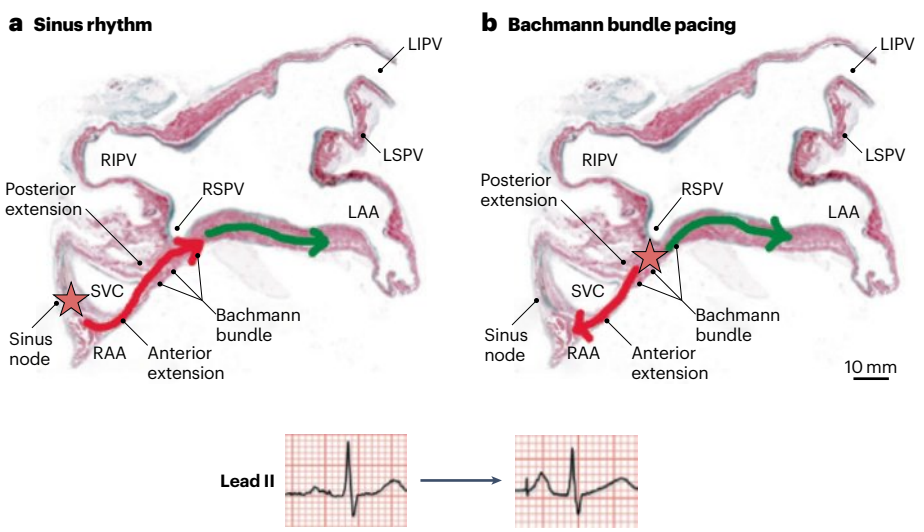


Fig. 6 | Electrical resynchronization with Bachmann bundle pacing. a, During sinus rhythm, the impulse originating at the sinus node reaches the left atrium after traversing the Bachmann bundle, and serial right-then-left atrial activation produces a broad or split P wave in lead II. **b**, Bachmann bundle pacing captures the bundle directly, advancing left atrial activation and shortening interatrial conduction, so that the paced P wave in lead II becomes narrower. LAA, left atrial appendage; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RAA, right atrial appendage; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; SVC, superior vena cava.

are testing whether Bachmann bundle area pacing improves atrial synchrony and function and reduces atrial arrhythmia burden relative to conventional atrial appendage pacing. Together, findings from these studies should help to transform a physiologically compelling but incompletely proven therapy into one with a defined evidence base.

Future directions

Available CSP tools remain suboptimal for clinical demands and require iterative upgrades to delivery systems, lead design and device platforms to improve deep septal accessibility, targeting accuracy and procedural safety, and to achieve better compatibility with clinical CSP applications. Advances in imaging might further improve procedural guidance, including zero-fluoroscopy approaches, real-time three-dimensional mapping and visualization of the conduction system. The rapid development of artificial intelligence technologies might support CSP across the care pathway, including procedural guidance, real-time capture recognition and optimization after implantation; however, these applications depend on the availability of standardized and representative training data to ensure reliability and generalizability.

Clinically, the overgeneralized use of the term 'LBBAP' remains problematic, and a standardized definition of conduction capture is essential. Long-term lead safety, extractability and effects on the tricuspid valve require further confirmation. Leadless and ICD-based deep septal pacing show promising clinical value; however, both approaches require further evaluation of their efficacy and long-term role. Emerging Bachmann bundle area pacing might facilitate physiological interatrial synchronization, but unresolved challenges persist regarding its anatomical targeting consistency, unified capture standards and long-term clinical outcomes. With continuous technological innovation, physiological pacing is expected to become a mainstream strategy, encompassing ventricular CSP and its emerging atrial counterpart.

Conclusions

Cardiac pacing has moved decisively towards preserving or restoring the natural activation sequence of the heart. Within this framework of physiological pacing, the advent of His bundle pacing established that conduction system capture is achievable but proved technically demanding, and LBBAP has become the dominant ventricular modality. The evidence supporting the use of LBBAP is now strongest for the prevention of PICM in patients with bradycardia and a high burden of pacing, whereas randomized comparisons between LBBAP and BiVP for CRT remain contradictory, and the relative roles of the two approaches are unresolved. Across both settings, outcomes are better if the conduction system is genuinely captured, which makes rigorous confirmation of conduction system capture both at implantation and during follow-up central rather than incidental. Bachmann bundle area pacing extends the same physiological logic to the atrium, but adequately powered trials in this setting are awaited. Realizing the promise of physiological pacing will depend less on new hardware than on consistent definitions, verified conduction system capture and evidence from appropriately powered, randomized trials.

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Author contributions

The authors contributed substantially to all aspects of the manuscript.

Competing interests

P.V. has served as a consultant for Abbott, Biotronik, Boston Scientific, Eaglepoint and Medtronic; has served as a speaker for and received fellowship support and research support from Medtronic; and has a patent for a His bundle pacing delivery tool. J.J. holds an investigator-initiated external research grant from Medtronic, grants from the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Canada; and has consultancy agreements with Abbott and Medtronic. H.B. has received institutional research and fellowship support and/or speaker fees from Abbott, Biotronik, Boston Scientific, Medtronic and Microport. E.-K.C. has received research grants or speaking fees from Abbott, Bayer, BMS/Pfizer, Biosense Webster, Chong Kun Dang, Daewoong Pharmaceutical, Daiichi-Sankyo, DeepQure, Dreamtech, Jeil Pharmaceutical, Medtronic, Samjinpharm, Samsung Electronics, Seers Technology, Skylabs and Yuhan Corporation. The other authors declare no competing interests.

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