



Safety and Efficacy of His Bundle Area (Para-Hisian) Pacing Using a Mathematical Cross-Correlation Cardiac Synchrony Index

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Submitted: 2023, Dec 13; Accepted: 2024, Jan 05; Published: 2024, Jan 11

Citation: Zuloaga, C. D., Ferrari, A. D. L. (2024). Safety and Efficacy of His Bundle Area (Para-Hisian) Pacing Using a Mathematical Cross-Correlation Cardiac Synchrony Index. *Cardio Open*, 9(1), 01-11.

Abstract

Background: The deleterious effects of right ventricular (RV) apical pacing promoted the need for more physiological pacing techniques, such as conduction system, His bundle area, and mid-septal ventricular pacing. We aimed to compare permanent mid-septal and His bundle area pacing (HBAP) vs RV apical pacing to determine which is more physiological and to assess lead stability and pacing thresholds.

Methods: We retrospectively analyzed 137 consecutive patients undergoing permanent pacing (63% men, mean age 61 ± 24 years). Seventy-one (52%) had a baseline QRS of < 120 ms, with no evidence of intraventricular conduction abnormalities, 37 (27%) had right bundle branch block, and 29 (21%) had left bundle branch block. The ventricular lead was implanted at the RV apex in 54 patients, at the His bundle area in 66, and at the mid interventricular septum in 17. Twelve-lead electrocardiogram was recorded, and electrical synchrony was assessed using the Synchronax® cross-correlation cardiac synchrony index (CSI).

Results: QRS duration was prolonged in all pacing sites. There was no correlation between QRS duration and the CSI ($r = 0.028$, $p = 0.79$). The CSI was significantly improved only in patients undergoing HBAP, despite a slight widening of the QRS complex. There was no difference in pacing thresholds and sensed R wave voltage. Lead dislodgment occurred in only 1 lead implanted at the His bundle area.

Conclusions: HBAP successfully captures the conduction system, normalizing the CSI despite producing a wider QRS, meaning that coordination is more important than duration for achieving optimal cardiac synchrony.

Keywords: Artificial Cardiac Pacing, Heart Conduction System, Cardiomyopathy

1. Introduction

Permanent ventricular pacing has been the cornerstone treatment for patients with bradyarrhythmia. However, the quality of life and prognosis of these patients has been affected by the adverse effects of conventional pacing (apical), which are grouped in an entity called pacing-induced cardiomyopathy [1-5]. Right ventricular (RV) apical pacing causes loss of physiological activation, dyssynchronous contraction, and ventricular remodeling similar to complete left bundle branch block (LBBB) [6-8]. These anomalies prompted the search and use of more physiological pacing techniques.

LBBB is characterized by dyssynchronous activation between both ventricles resulting from late activation of the left ventricular (LV) lateral wall, causing a disagreement between the pre-ejection periods [9,10]. Ectopic RV pacing may exacerbate

this condition by increasing the contractile deficit and, consequently, decreasing the ventricular function indexes (ejection fraction).

Therefore, artificial pacing of the cardiac conduction system, in which the lead is placed precisely on or in close proximity to the His bundle, has been rapidly adopted. One such type of pacing, known as selective His bundle pacing (SHBP), can generate a paced QRS with the same duration and polarity of the native one, but several technical reasons including the difficulty to precisely locate the His bundle preclude the widespread use of this method [11-13]. In this study, we will demonstrate that SHBP might not be the only way to capture the conduction system [14].

For comparison, accessory and mid-septal pathways cause a pattern of electrical activation characterized by ectopic ventricle

activation near the His-Purkinje system and ventricular pre-excitation. This activation is observed on surface electrocardiogram (ECG) as a slurring of the initial segment of the QRS complex known as a delta wave.

However, the QRS normalizes and restores native direction and polarity immediately after the delta wave because, after activation from an accessory pathway, ventricular activation is generated by physiological transit through the His-Purkinje system. Based on these observations, any pacing site near the conduction system (His bundle area), as is the case with accessory pathways, could theoretically capture the conduction system and produce physiological pacing.

In order to have a marker of cardiac synchrony pre-during, and post-implantation of the ventricular pacemaker lead, we used the Synchronax® (Exo S.A., Buenos Aires, Argentina) cardiac synchrony index (CSI) as a determining parameter. The Synchronax® is a software that noninvasively records, during lead implantation and follow-up, the spatial coincidence, area under the spatial variation curves, and direction of the QRS in leads II (representing the interventricular septum [IVS] and RV) and V6 (LV) on the ECG.

The CSI is a result of graphic and mathematical processing of the signal averaged by the cross-variation of such leads. For this analysis, Synchronax® uses measurement of electric current flow (volume and direction) and analyzes the coincidence of intrinsic QRS deflections, as previously published [14-19].

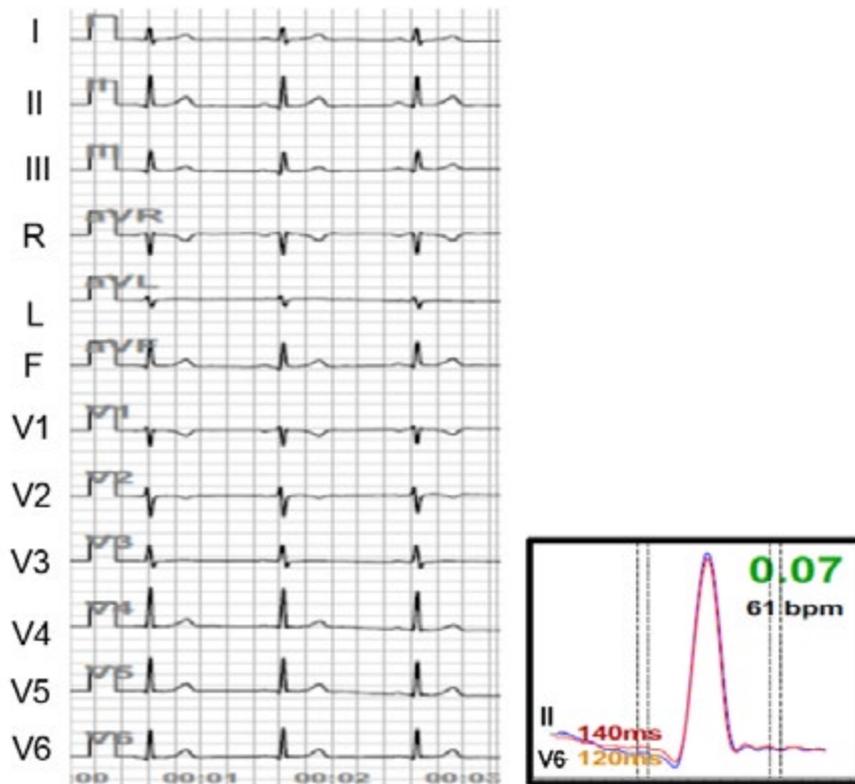
Therefore, using this analytic tool, the objective of this study was to compare cardiac synchrony during permanent mid-septal pacing and HBAP vs RV apical pacing to determine which is more physiological, as well as to assess lead stability and pacing thresholds in the 3 pacing sites.

2. Methods

A total of 137 patients undergoing permanent pacing due to bradyarrhythmia's were retrospectively analyzed. The ventricular lead of the pacemaker was implanted at the RV apex in 54 patients and at the His bundle area in 66, whereas the remaining 17 patients underwent empirical implantation at the mid IVS. Pacemaker implantation at the mid IVS was conducted in these 17 patients with the purpose of achieving more physiological pacing, as it is empirically closer to the conduction system (HBAP) than the apex. For IVS pacing, the mid-septal region, between the middle and upper third of the IVS region, was chosen. In these cases, we did not seek to stimulate any branch in particular (neither the left [LBB] nor right bundle branch [RBB]).

All ventricular leads consisted of conventional active-fixation leads, of which 58 were defibrillator leads. Of these, 22 were located at the RV apex, 3 at the mid IVS, and 33 at the His bundle area. Patients received an implantable cardioverter-defibrillator (ICD) for ventricular arrhythmias, 20 of them for primary prevention according to the New York Heart Association guidelines. The tip of the ICD lead was implanted in a way that captured the His bundle area, close to the conduction system, and all catheters were single coil. No patient had an indication for nor received biventricular cardiac resynchronization therapy.

Twelve-lead ECG was recorded in all patients at a paper speed of 25mm/s. Cardiac electrical synchrony was assessed by cross-correlation of spatial variance of the QRS in leads II and V6 (which correspond to right IVS and LV lateral wall activity, respectively) using the Synchronax® software (Exo S.A., Buenos Aires, Argentina) [16]. The software records spatial coincidence, area, and direction of both leads, generating a mathematical index called cross-correlation cardiac synchrony index (CSI). A CSI value of 0.0 corresponds to maximum coincidence between both leads (perfect synchrony), 0.0-0.39 corresponds to adequate synchrony, 0.4-0.7 corresponds to poor synchrony, and values > 0.71 correspond to dyssynchrony (Figure 1) [20].



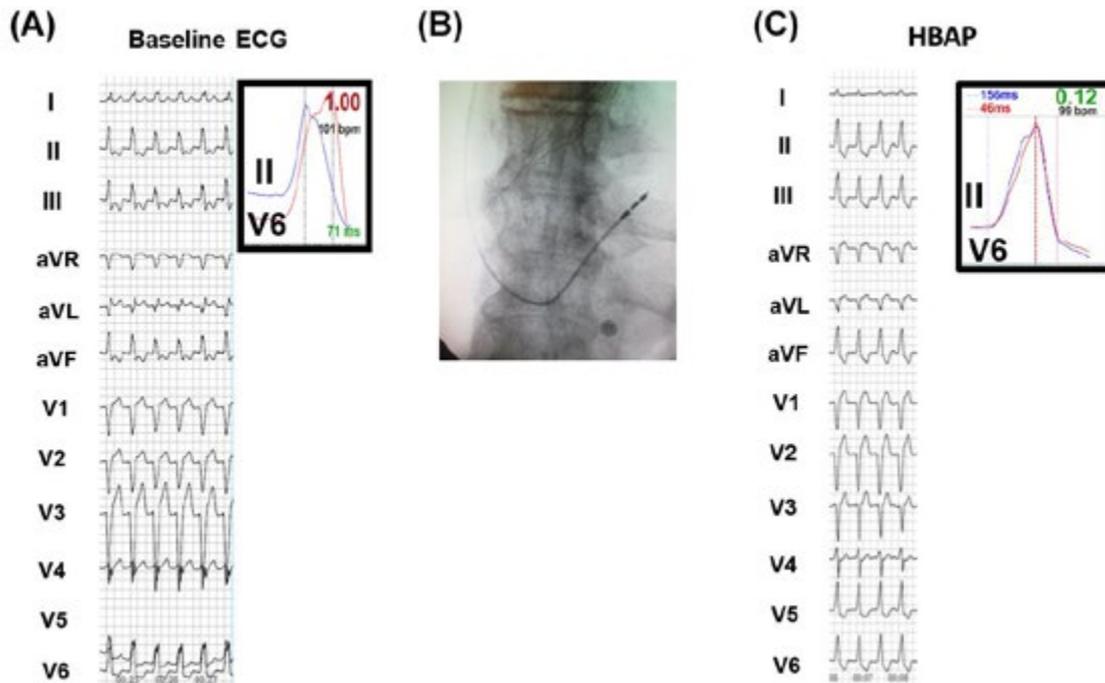
Twelve-lead electrocardiogram (ECG) showing coincidence between activation direction, QRS duration, and coincident intrinsicoid deflections (peak R wave). Both leads start and end at the same time, demonstrating that septal activation (II) is performed under identical conditions to left ventricular lateral wall (V6) activation, which is indicative of cardiac synchrony (cardiac synchrony index = 0.07); 120 ms and 140 ms correspond to average cross-correlation Synchronax® curves

Figure 1: Baseline 12-lead ECG Analyzed with Synchronax®

In this study, the effect of HBAP on LV synchrony was indirectly assessed using the CSI, as previously described by Ferrari et al and De Zuloaga & Ferrari. Physiological pacing was characterized by ventricular activation from right to left (QRS [+] in leads I and aVL) and from top to bottom (QRS [+] in II, III, and aVF), as well as a transition (R wave > S wave) to V3-V4 in the precordial leads [14,15]. The presence of all three criteria was considered a “physiological” axis, the presence of two criteria was considered “probably physiological”, and the presence of only one or none was considered “nonphysiological”.

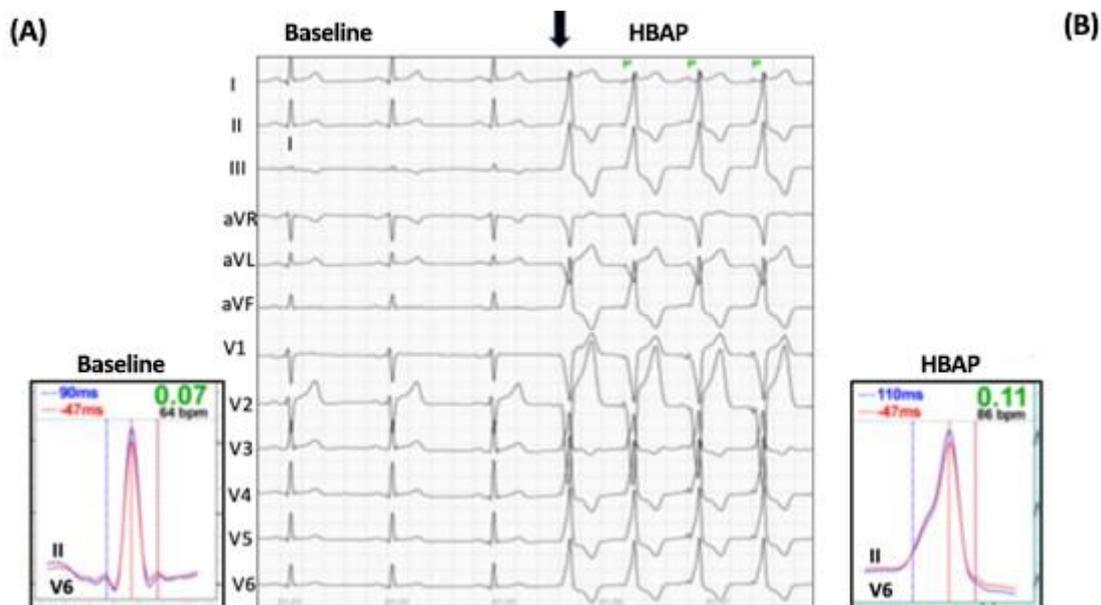
Specifically, ventricular lead implantation at the His bundle area was performed with conventional screw-in, active-fixation leads and guided by the CSI. The lead was advanced into the pulmonary artery and gently withdrawn until it reached the RV

outflow tract (RVOT). After the helix was fixated, pacing was initiated with simultaneous assessment of cross-correlation between ECG signals from II and V6. If spatial coincidence and polarity were coincident in II and V6, with a CSI < 0.40, the lead was permanently fixed; otherwise, the lead was repositioned to the adjacent area until a CSI < 0.40 was achieved (Figure 2). HBAP was characterized by an adequate CSI value (< 0.40) on Synchronax®, and His-Purkinje system capture was considered successful if, on surface ECG, leads II, III, and aVF were positive, lead aVL was negative, and leads V1-V6 were similar to the baseline ECG despite a wider QRS complex (Figure 3). Categorical variables are expressed as frequency (percentage) and were compared using the chi-square test. Continuous variables are expressed as mean ± SD and were compared using Student’s *t* test. A p-value of <0.05 was considered statistically significant.



(A) Baseline electrocardiogram (ECG) prior to implantation showing uncoupling of left ventricular (LV) activation, with a delay in LV lateral wall (V6) activation of 71 ms in relation to the interventricular septum (IVS) (II) and a highly abnormal cross-correlation cardiac synchrony index (CSI) value (CSI = 1.00) (normal value ≤ 0.4 , indicating cardiac synchrony). (B) Posteroanterior radiograph of the site of ventricular lead implantation. (C) ECG of a patient undergoing His bundle area pacing (HBAP) showing correction of LV lateral wall activation (V6). LV lateral wall activation is now synchronous with IVS activation (in the same direction and at the same time), with a normal CSI value (CSI = 0.12) despite a wide paced QRS compared with the native one. The red line shows the time between peak R wave and the end of the QRS complex; the blue line shows the duration of the QRS complex estimated by the synchrony curves

Figure 2: Correction of LV Lateral Wall Activation and Uncoupling in Patient with Cardiac Dyssynchrony



(A) Native QRS. (B) After HBAP, (arrow) the QRS complex is slightly wider, and the polarity of the QRS is similar to the native one. Leads II, III, aVF, V5 and V6 are positive, demonstrating that activation was achieved through the conduction system. The initial delay of the QRS, represented on the electrocardiogram as a pseudo delta wave, results from capture of adjacent cardiac muscle; after capture of the His-Purkinje system, the second half of the paced QRS (Rpeak-QRSend interval) has the same width as that of the baseline one (47 ms), producing an excellent cardiac synchrony index (from 0.09 to 0.11)

Figure 3: His Bundle Area Pacing (HBAP) in a Patient with Normal QRS

3. Results

The study sample consisted mostly of men (63%), with a mean age of 61 ± 24 years. Of 137 patients who received a pacemaker, 71 (52%) had a narrow baseline QRS complex (< 120 ms), with no indications of intraventricular conduction disorders, 37 (27%) had RBB block, and 29 (21%) had LBBB.

3.1. Paced QRS Duration

Paced QRS duration was significantly wider than the native one in all pacing sites. In patients undergoing apical pacing, QRS duration increased from 114 ± 28 ms to 160 ± 28 ms ($p = 0.0001$). The greatest QRS widening was observed in patients undergoing mid-septal pacing (from 122 ± 24 ms to 154 ± 30 ms; $p = 0.0005$). In patients with a wide QRS due to pre-existing conduction dis-

orders, only HBAP was able to reduce QRS duration, although without statistical significance (from 139 ± 12 ms to 132 ± 10 ms; $p = 0.06$). However, in patients with a wide QRS specifically due to baseline LBBB, HBAP significantly narrowed the QRS complex (from 145 ± 10 ms to 129 ± 7 ms; $p = 0.0044$).

3.2. Electronic Parameters

Pacing thresholds and sensed QRS voltage did not significantly differ between the defibrillation and pacemaker leads. Ventricular thresholds did not significantly differ between the 3 pacing sites: 0.9 ± 0.4 V at the RV apex, 1.0 ± 0.5 V at the mid septum, and 0.9 ± 0.3 V at the HBAP ($p = 0.42$). Detection (sensed R wave), thresholds, and other parameters were similar between the 3 pacing sites (Table).

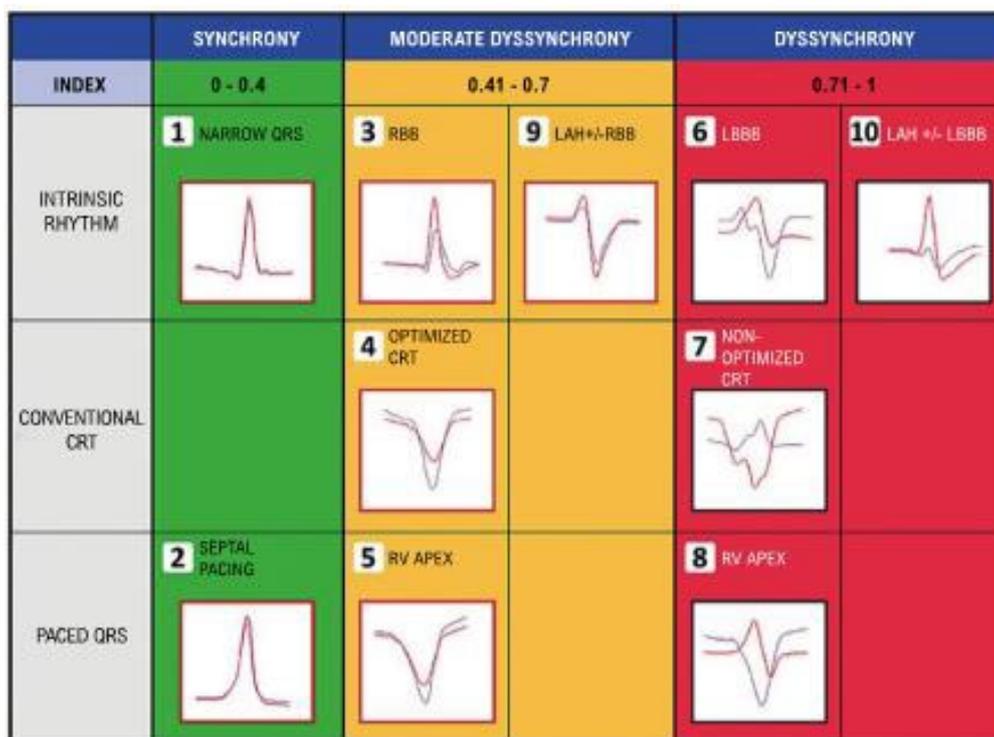
	Apex (n = 54)	Mid septum (n = 17)	HBAP (n = 66)	p-value
Pacing voltage	0.9 ± 0.4 V	1.0 ± 0.5 V	0.9 ± 0.3 V	0.42
R wave voltage	12.3 ± 5 mV	11.1 ± 4 mV	9.2 ± 4 mV	0.37
HBAP = His bundle area pacing				

Table: Pacing Threshold Variations and R Wave Detection in Each Pacing Site

3.3. CSI

The CSI score provided by SynchroMax® can potentially serve as a useful indicator of ventricular synchrony. However, it should be noted that the results can vary according to the underlying

heart disease, and such alterations might produce characteristic curves on the SynchroMax® polygraph. Example of these curves are extensively discussed by Ferrari et al, De Zuloaga & Ferrari and Ortega et al, and shown in Figure 4 [14-16].



CRT = cardiac resynchronization therapy; LAH: left anterior hemiblock; LBBB: left bundle branch block; RBB: right bundle branch; RV = right ventricular

Figure 4: SynchroMax Curves According to Different Underlying Heart Diseases

CSI values were significantly lower (denoting better cardiac electromechanics) in patients undergoing HBAP and always stayed within the range of cardiac synchrony ($CSI = 0.22 \pm 0.11$). Conversely, most patients undergoing RV apical pacing had intermediate synchrony ($CSI = 0.53 \pm 0.10$), whereas those undergoing mid-septal pacing presented the greatest dyssynchrony ($CSI = 0.66 \pm 0.28$) ($p < 0.0001$) (Figure 3). Lead dislodgement was observed only in 1 (1.5%) patient who underwent implantation at the His bundle area with a conventional lead, 48 hours after the procedure. Because there was no capture or detection failure, the lead was not repositioned. As for patients who received an ICD, although defibrillation thresholds were not tested, no defibrillator leads were dislodged in the immediate postoperative period nor during clinical follow-up, even in patients who received multiple shocks. In addition, there was no defibrillation failure due to increased thresholds in those who were implanted in the His bundle area.

4. Discussion

RV apical pacing has been shown to be detrimental to LV function by producing nonphysiological ventricle activation in an anisotropic pattern that alters segmental ventricular contraction [21,22]. Intrinsic conduction system properties are not the same in the retrograde as in the anterograde direction. This has prompted the search for more physiological pacing sites that can preserve ventricular function [23,24]. His bundle pacing (HBP) produces a paced QRS that is identical to the native one, which makes us believe that the electrophysiological properties and consequences are also identical, without the need for validation studies to assess ventricular function and pattern of electrical activation [25-27]. Conversely, any type of artificial cardiac pacing that produces a different QRS duration needs to be assessed with regard to electromechanical ventricular function in patients with heart failure secondary to branch blocks.

It should be noted that the use of SHBP is limited by several technical difficulties. A common limitation of SHBP is increased pacing thresholds when compared with other RV sites, which tend to further increase over time [28,29]. Changes in QRS detection and sensing parameters may also vary according to the type of lead [30,31]. The need to precisely locate the His potential for implanting the pacing lead in patients with junctional rhythm or no atrioventricular conduction may also constitute a limitation [31]. Another important aspect that should be considered is that direct His bundle or LBB area pacing, with anchoring of the lead's helix, may cause rapidly progressive degenerative injury to the His bundle fibrous sheath, leading to loss of capture over time [32-34].

The His-Purkinje system begins at the crest of the IVS, immediately under the membranous septum, and is subsequently divided into the LBB and RBB, which run along the mid-septal region until they take a subendocardial course. The muscle activation produced by upper septal or HBAP with conventional screw-in leads is represented on the ECG by a pseudo delta wave. This wave is most apparent in II and V6 because of the proximity to the native electrophysiological system. In HBAP, the electrical impulses enter the His-Purkinje system and capture it after

running through nonspecific tissue, promoting ventricular activation through the specific conduction system. Despite differences in QRS duration, the hemodynamic benefits of SHBP and high-output NSHBP were shown to be similar [35].

Because of its simplicity, HBAP has potential advantages over other pacing techniques, such as SHBP. For example, in cases of intra or infra His bundle blocks, HBAP can produce physiological pacing without the need for a backup lead. Compared with other physiological pacing techniques, HBAP is also simpler: it has a smaller learning curve, relies only on the radiological anatomy, and exposes the patient to a shorter fluoroscopy time. These advantages have been extensively discussed by our group of researchers and other authors [13-20].

Pacing of the His bundle area is followed by His Purkinje system capture, and this capture is evidenced by the morphology of the second half of the QRS, which is identical to that of a normal QRS [15]. Pacing this region and, as a result, producing a characteristic QRS morphology is of great importance when implanting a pacing device, as it will always be more physiological than pacing at any other RV site. However, the morphology of the native QRS should not be considered when choosing the pacing site; instead, physiological stimulation should always be sought, as even patients with sinus dysfunction or paroxysmal AV blocks with normal QRS will present, at some point in the evolution of the electrical disorder that required the implant, ventricular stimulation most of the time.

Another advantage of lead implantation at the His bundle area is the ease with which these leads can be removed in case of endovascular infection. Implantation at the apex region implies extensive fixation and fibrosis in the RV floor, which never occurs in high septal sites (such as the His bundle area). This issue is especially important in patients with an ICD, in whom endothelialization of the coil in the RV floor is frequently the greatest risk of cardiac rupture during lead extraction. The use of conventional pacing leads, as shown in this study, without the need for special materials is a clear advantage of HBAP over other systems, such as LBB pacing or biventricular pacing, allowing its widespread use without extensive training. Although LBB pacing and SHBP have been shown to be able to maintain electrical synchrony and physiological pacing, they cannot be widely used and, so far, represent only a small portion of total implants, which does not improve the global problem of artificially induced dyssynchrony associated with permanent cardiac pacing. The method proposed in this study is useful because it is simple and does not involve extensive operating time, specific materials, or specific training. The concept of physiological pacing should always be considered when implanting a pacing device, even in patients with a normal heart and narrow QRS, as we should avoid any damage that could be caused in patients without dyssynchrony - in fact, this might be more important in these patients than in those with dyssynchrony or heart failure.

RV pacing with a permanent pacemaker always increases QRS duration. If we consider that HBP generates a QRS that is identical to the native one, we can assume that it also maintains native

synchrony without the need for any demonstration. On the other hand, the further the pacing site is from the specific conduction system, the greater the difference between paced and native QRS durations. In this case, the pattern of activation will be different, hence the need for assessing synchrony. We could also speculate that, in patients with a wide QRS due to branch blocks or pre-existing conduction disorders, His-Purkinje activation distal to the block site could decrease QRS duration and thus produce more physiological pacing.

This study corroborates these speculations, although there is a lack of statistical significance, which could have been influenced by the small number of patients included. In addition, as demonstrated by Ferrari et al., HBAP is not inferior to NSHBP. We identified an interesting trend toward reduction of QRS duration in patients with baseline conduction disorders undergoing HBAP (from 139 ± 12 ms to 132 ± 10 ms; $p = 0.06$) [14]. However, when we consider only patients with LBBB, HBAP was able to significantly narrow the QRS interval (from 145 ± 10 ms to 129 ± 7 ms; $p = 0.0044$).

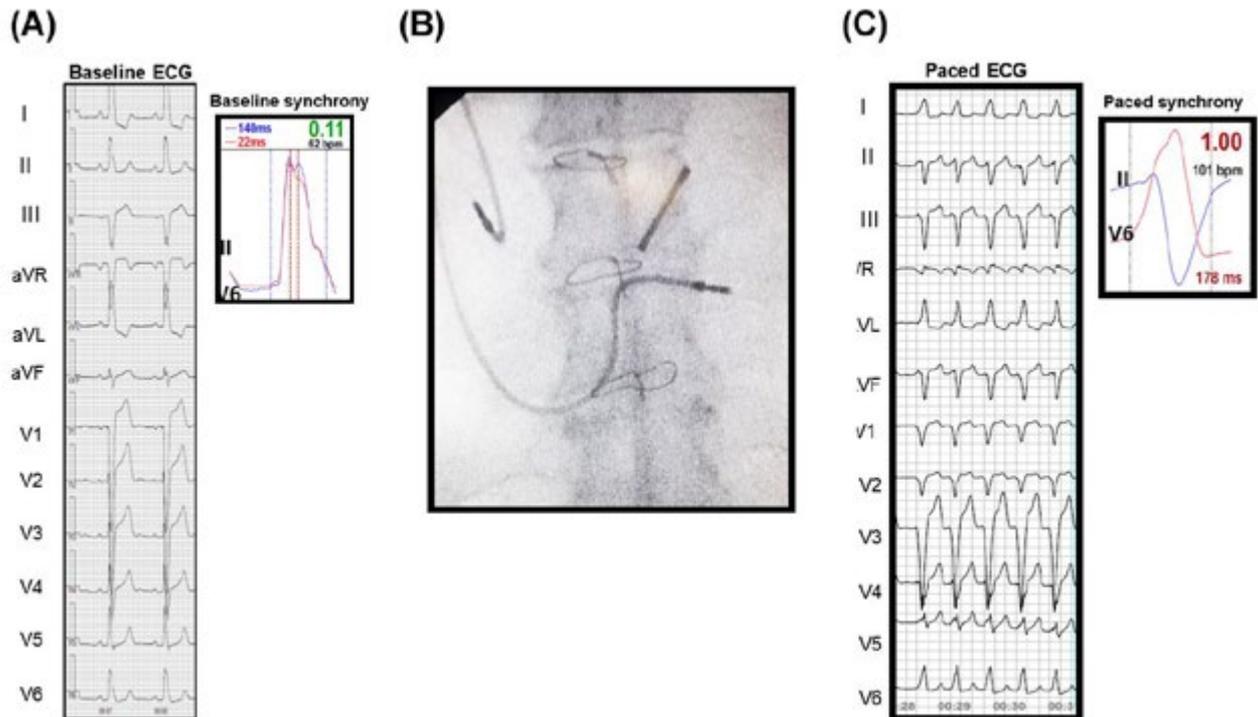
Although there is marked QRS shortening, the QRS does not normalize probably because nonspecific muscle stimulation of the conduction system causes the initial slurring of the QRS complex, similarly to accessory pathways in Wolff-Parkinson-White (WPW) syndrome. However, if we are able to stimulate the specific conduction system, the duration of the second part of the QRS should be similar or identical to the native one [15]. Pacing sites that are distant from the beginning of the His-Purkinje system, including any RV site, generate impulses that travel outside the specific conduction system. In these cases, a wide QRS with a polarity that is different from that of orthodromic beats is produced (Figure 3).

HBAP produces a paced QRS complex that is wider than the intrinsic one but with perfect inter and intraventricular synchrony, as measured by the CSI [14,15]. Upper septal pacing is not equal

to HBAP because, in pacing sites far away from the conduction system, the conduction system cannot be captured in the anterograde direction and, therefore, cannot achieve synchronous contraction and activation. For this, the LV lateral wall and the IVS must be simultaneously activated from base to apex [20]. This study showed mid-septal pacing to have deleterious effects, as patients undergoing mid-septal pacing had a systematic widening of the QRS interval with worse CSI values, similarly to results obtained with RV apical pacing (Figure 3).

The CSI mathematically assesses the cross-correlation of QRS width, peak, amplitude, and area under the curve in leads II and V6, generating a dyssynchrony index that correlates with the septal wall and LV lateral wall. Simultaneous activation of the septal wall (II) and LV lateral wall (V6) from base to apex by HBAP is represented on the ECG by a positive QRS in leads II, III, and aVF, with a coincidence in morphology and ventricular activation time between II and V6. When this happens, CSI values are normal (< 0.40), like in patients with normal ventricular activation, and superimposition of QRS complexes shows the same polarity, morphology, and duration in leads II and V6, with coincident intrinsicoid deflections (Figure 3).

As mentioned above, pacing the upper septum is not synonymous with conduction system capture nor a guarantee of electrical synchrony. Several explanations for the dyssynchrony caused by septal pacing have been shown in this study. Pacing far away from the His-Purkinje system causes nonphysiological septal activation (negative or isodiphasic) due to partial or total IVS activation from apex to base that is asynchronous from LV free wall activation. This activation is expressed by a different QRS morphology or polarity in V6 (Figure 5). Another aspect that should be considered is that patients with bundle branch blocks have distal intraventricular conduction disorders that could not be corrected by HBAP.

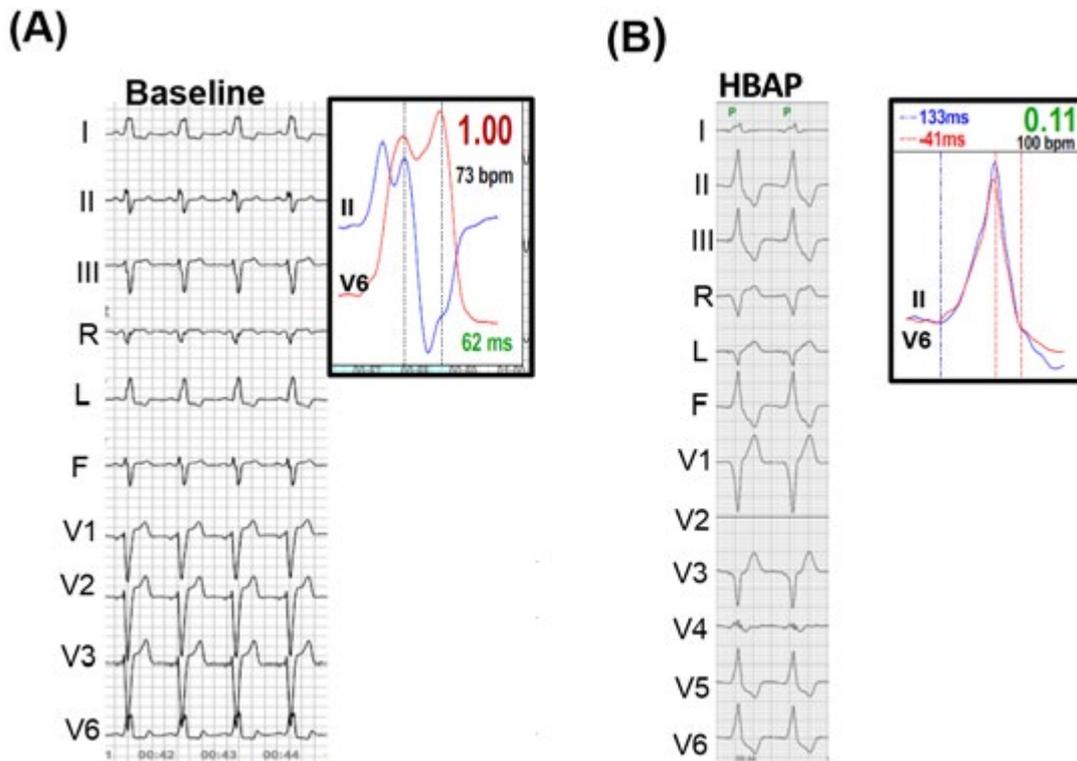


(A) Baseline electrocardiogram (ECG) with left bundle branch block (LBBB) and a normal synchrony curve (simultaneous activation in the same direction in II e V6) despite LBBB, with a cross-correlation cardiac synchrony index (CSI) of 0.11. (B) Postero-anterior radiograph showing a pacemaker lead implanted at the mid septum. (C) ECG of a patient undergoing mid-septal pacing, with consequent worsening of synchrony (CSI = 1.00). Left axial deviation expresses apex-to-base septal depolarization (negative II, III, and aVF), while the left ventricular free wall is more physiologically activated from base to apex (V6). The red line shows the time between peak R wave and the end of the QRS complex; the blue line shows the duration of the QRS complex estimated by the synchrony curves

Figure 5: Mid-Septal Pacing

In the case presented in Figure 6, although QRS activation time, magnitude, and morphology vary greatly between leads II and V6, HBAP produces a QRS complex that is almost identical in both leads [15]. Although it is difficult to speculate on the functional advantages that may arise with QRS normalization, it is likely to improve the muscle activation sequence in some ventricular regions. The clinical consequences should be investigat-

ed in future studies. Some authors have precisely demonstrated that high-output conduction system pacing is more likely to capture the His-Purkinje system and produce a paced HV interval identical to the baseline one, despite a widening of the QRS interval and the production of a pseudo delta wave due to capture of adjacent cardiac muscle [34].



(A) Baseline recording of a patient with left bundle branch block with a QRS duration of 137 ms and large uncoupling (maximum peak II to maximum peak V6 = 62 ms). (B) His bundle area pacing (HBAP) in the same patient showing great variation in QRS activation time, magnitude, and morphology compared with baseline. HBAP produces a paced QRS that is almost identical and symmetrical in both leads despite increasing QRS duration.

The red line shows the time between peak R wave and the end of the QRS complex; the blue line shows the duration of the QRS complex estimated by the synchrony curves

Figure 6: Baseline QRS Activation in II and V6 vs His Bundle Area Pacing

Therefore, His-Purkinje capture is possible despite the presence of a wider QRS, similar to the activation pattern seen in some WPW cases. In patients with bundle branch blocks, HBAP is able to narrow the QRS interval and resolve conduction abnormalities such as left anterior and posterior fascicular blocks, meaning that it could also resolve blocks in the main branch of the left bundle, proximal to the fascicles [15]. A particularly important aspect in the physiology of LV contraction that directly influences ventricular function is the mode of LV contraction, which occurs through helical muscle bands that originate in the lung, outline the ventricle, and end at the LV. This movement, called “twisting”, is similar to “wringing a towel” and ensures greater blood ejection. This phenomenon has long been studied and confirmed in the literature [35,36]. The “point of attachment” where the origin and end of the helicoidal band meet is called the fulcrum, a rigid structure within the cardiac skeleton that is coincidentally located at the base of the heart, at the level of the RV and LF outflow tracts (aorta and pulmonary artery, respectively). Therefore, it could be assumed that any pacing at the fulcrum region (at the level of the RVOT) at the site where the His-Purkinje branches divide should generate helical torsion and contribute to “twisting” the LV, which initiates at the beginning of this muscle band [35,36]. The role of HBAP in preserving this physiological helical torsion is being investigated with imaging

tests such as magnetic resonance imaging and echocardiography.

Therefore, HBAP has potential advantages over the other pacing techniques. Because it is a simple method that does not require special materials, tools, or training, in addition to causing less cardiac dyssynchrony and adverse effects such as lead dislodgement and increased pacing thresholds, HBAP could be widely used in the treatment of patients with bradyarrhythmia’s. The ease of extraction in case of endocarditis is another positive aspect of this method.

4.1. Limitations

This research has several limitations. Besides being from a single center research, the benefits of HBAP on left ventricular contraction, although are being rapidly learned and reported, lack of consistent data to support its efficacy. Also, since this research focuses on morpho-metric characteristics of the QRS and its relationship with cardiac - ventricular synchrony, the clinical background of the individuals is not presented. We do understand that conduction abnormalities might be linked not only to the His-Purkinje system but also to the ventricular myocardium. However, it is our objective to represent that cardiac synchrony is linked to lead position and the resulting QRS abnormalities that cause alterations in activation - contraction patterns. From

that point of view, this investigation shows in 137 consecutive patients divided into 3 groups (RV apex: 54, His bundle area:66 and mid interventricular septum: 17), purely QRS mathematical cross-correlation characteristics from the anatomical position of the ventricular lead and its impact upon QRS morphology and metrics during pacing, with the idea of proposing that these could eventually be corrected by placing the ventricular lead in a position where technology guided best electromechanical activation and physiology is restored.

This study has some limitations. In addition to the classic limitations of a single-center retrospective analysis, this study focuses mainly on synchrony and electrocardiographic parameters, and no clinical characteristics were addressed nor analyzed in depth. Moreover, the advantages of HBAP in ventricular function over other types of physiological pacing, such as LBB pacing and SHBP, have not yet been evaluated, and further studies are needed to address this gap in knowledge.

5. Conclusions

HBAP successfully captures the conduction system, normalizing cardiac electrical synchrony as measured by the CSI. In patients with a normal baseline QRS, it produces excellent CSI values despite prolonging QRS duration. However, in patients with a wide QRS and conduction abnormalities due to bundle branch or fascicular blocks, HBAP corrects these abnormalities by reducing QRS duration and normalizing cardiac synchrony, consequently producing more physiological pacing.

Data Availability

All data relevant to the study are included in the article.

References

1. Akerström, F., Arias, M. A., Pachón, M., Jiménez-López, J., Puchol, A., & Juliá-Calvo, J. (2013). The importance of avoiding unnecessary right ventricular pacing in clinical practice. *World Journal of Cardiology*, 5(11), 410-419.
2. Pachón Mateos, J. C., Pachón Mateos, E. I., & Pachón Mateos, J. C. (2009). Right ventricular apical pacing: the unwanted model of cardiac stimulation? *Expert Review of Cardiovascular Therapy*, 7(7), 789-799.
3. Tops, L. F., Schali, M. J., & Bax, J. J. (2009). The effects of right ventricular apical pacing on ventricular function and dyssynchrony: implications for therapy. *Journal of the American College of Cardiology*, 54(9), 764-776.
4. Sarvari, S. I., Sitges, M., Sanz, M., Tolosana Viu, J. M., Edwardsen, T., Stokke, T. M., ... & Bijnens, B. (2017). Left ventricular dysfunction is related to the presence and extent of a septal flash in patients with right ventricular pacing. *EP Europace*, 19(2), 289-296.
5. Ferrari, A. D. L., Oliveira, E. B., Tagliari, A. P., Kochi, A. N., Beuren, T. M. A., Cabral, G. C., ... & Danzmann, L. C. (2022). Cardiomyopathy Induced by Artificial Cardiac Pacing: To Whom, When, Why, and How? Insights on Heart Failure Development. *Brazilian Journal of Cardiovascular Surgery*, 38, 278-288.
6. Ploux, S., Lumens, J., Whinnett, Z., Montaudon, M., Strom, M., Ramanathan, C., ... & Bordachar, P. (2013). Noninvasive electrocardiographic mapping to improve patient selection for cardiac resynchronization therapy: beyond QRS duration and left bundle branch block morphology. *Journal of the American College of Cardiology*, 61(24), 2435-2443.
7. Tanaka, H., Hara, H., Adelstein, E. C., Schwartzman, D., Saba, S., & Gorcsan, J. (2010). Comparative mechanical activation mapping of RV pacing to LBBB by 2D and 3D speckle tracking and association with response to resynchronization therapy. *JACC: Cardiovascular Imaging*, 3(5), 461-471.
8. Del Greco, M., Zorzi, A., Di Matteo, I., Cima, A., Maines, M., Angheben, C., & Catanzariti, D. (2017). Coronary sinus activation patterns in patients with and without left bundle branch block undergoing electroanatomic mapping system-guided cardiac resynchronization therapy device implantation. *Heart Rhythm*, 14(2), 225-233.
9. Zanon, F., Baracca, E., Pastore, G., Fraccaro, C., Roncon, L., Aggio, S., ... & Prinzen, F. (2014). Determination of the longest intrapatient left ventricular electrical delay may predict acute hemodynamic improvement in patients after cardiac resynchronization therapy. *Circulation: arrhythmia and electrophysiology*, 7(3), 377-383.
10. Kawashima, T., & Sasaki, H. (2005). A macroscopic anatomical investigation of atrioventricular bundle locational variation relative to the membranous part of the ventricular septum in elderly human hearts. *Surgical and Radiologic Anatomy*, 27, 206-213.
11. Massing, G. K., & James, T. N. (1976). Anatomical configuration of the His bundle and bundle branches in the human heart. *Circulation*, 53(4), 609-621.
12. ELENCAWJG, B., ZAMAN, L., ROZANSKI, J. J., MYERBURG, R. J., & CASTELLANOS, A. (1982). Transverse dissociation of the human His bundle. *Pacing and Clinical Electrophysiology*, 5(3), 323-328.
13. Bonomini, M. P., Ortega, D. F., Barja, L. D., Logarzo, E., Mangani, N., & Paolucci, A. (2018). ECG parameters to predict left ventricular electrical delay. *Journal of electrocardiology*, 51(5), 844-850.
14. Ferrari, A. D. L., Gazzoni, G. F., Domingues, L. M. L., Willes, J. C. F., Cabral, G. C., Ferreira, F. V. C., ... & Reis, G. (2022). Ventricular Synchrony in Para-Hisian Cardiac Pacing as an Alternative for Physiological Cardiac Activation (Indirect Recruitment of the His Bundle?). *Arquivos Brasileiros de Cardiologia*, 118, 488-502.
15. de Zuloaga, C., & Ferrari, A. (2023). Electrophysiological demonstration of nonselective His-Purkinje system capture with para-Hisian pacing. *Journal of Electrocardiology*, 79, 38-45.
16. Daniel, O., Emilio, L., Luis, B., Analía, P., Nicolás, M., Mazzetti, E., & Bonomini, M. P. (2020). Novel implant technique for septal pacing. A noninvasive approach to nonselective his bundle pacing. *Journal of Electrocardiology*, 63, 35-40.
17. Logarzo, E., Ortega, D., Barja, L., Paolucci, A., Revollo, G., Aboy, J. M., & Mangani, N. (2019). Técnica de implante para-hisiano guiado por sincronía eléctrica. *Rev Electro Arritmias*, 11, 51-58.
18. Bonomini, M. P., Ortega, D. F., Logarzo, E., Mangani, N.,

- & Paolucci, A. (2022). Usefulness of ventricular sense response in last-generation cardiac resynchronization therapy devices. *Journal of Electrocardiology*, 71, 47-52.
19. Chango-Azanza, D. X., Munín, M. A., Sánchez, G. A., Arévalo-Pérez, L. M., Chango-Azanza, J. J., Pelayo, M. E., ... & Ortega, D. (2020). Left ventricular dyssynchrony as result of right ventricular permanent apical pacing. *Archivos de cardiología de México*, 90(3), 328-335.
 20. De Cock, C. C., Giudici, M. C., & Twisk, J. W. (2003). Comparison of the haemodynamic effects of right ventricular outflow-tract pacing with right ventricular apex pacing: a quantitative review. *EP Europace*, 5(3), 275-278.
 21. Slotwiner, D. J., Raitt, M. H., Del-Carpio Munoz, F., Mulpuru, S. K., Nasser, N., & Peterson, P. N. (2019). Impact of physiologic pacing versus right ventricular pacing among patients with left ventricular ejection fraction greater than 35%: a systematic review for the 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*, 140(8), e483-e503.
 22. Da Costa, A., Gabriel, L., Romeyer-Bouchard, C., Géraldine, B., Gate-Martinet, A., Laurence, B., ... & Isaaq, K. (2013). Focus on right ventricular outflow tract septal pacing. *Archives of cardiovascular diseases*, 106(6-7), 394-403.
 23. Alhous, M. H. A., Small, G. R., Hannah, A., Hillis, G. S., Frenneaux, M., & Broadhurst, P. A. (2015). Right ventricular septal pacing as alternative for failed left ventricular lead implantation in cardiac resynchronization therapy candidates. *EP Europace*, 17(1), 94-100.
 24. Fehske, W., Israel, C. W., Winter, S., Ghorbany, P., Nguyen, D. Q., & Voigt, J. U. (2020). Echocardiographic assessment of myocardial function during His bundle and right ventricular pacing. *Herzschrittmachertherapie+ Elektrophysiologie*, 31, 151-159.
 25. Deshmukh, A., Sattur, S., Bechtol, T., Heckman, L. I., Prinzen, F. W., & Deshmukh, P. (2020). Sequential His bundle and left ventricular pacing for cardiac resynchronization. *Journal of Cardiovascular Electrophysiology*, 31(9), 2448-2454.
 26. Ladia, V., Srivathsan, K., Mulpuru, S., & Shen, W. K. (2020). His bundle pacing: conduction system capture and clinical impact. *Current opinion in cardiology*, 35(1), 20-29.
 27. Arnold, A. D., Shun-Shin, M. J., Keene, D., Howard, J. P., Sohaib, S. A., Wright, I. J., ... & Whinnett, Z. I. (2018). His resynchronization versus biventricular pacing in patients with heart failure and left bundle branch block. *Journal of the American College of Cardiology*, 72(24), 3112-3122.
 28. Vijayaraman, P., Naperkowski, A., Subzposh, F. A., Abdelrahman, M., Sharma, P. S., Oren, J. W., ... & Ellenbogen, K. A. (2018). Permanent His-bundle pacing: long-term lead performance and clinical outcomes. *Heart rhythm*, 15(5), 696-702.
 29. Bhatt, A. G., Musat, D. L., Milstein, N., Pimienta, J., Flynn, L., Sichrovsky, T., ... & Mittal, S. (2018). The efficacy of His bundle pacing: lessons learned from implementation for the first time at an experienced electrophysiology center. *JACC: Clinical Electrophysiology*, 4(11), 1397-1406.
 30. Subzposh, F. A., & Vijayaraman, P. (2018). Long-term results of His bundle pacing. *Cardiac electrophysiology clinics*, 10(3), 537-542.
 31. Zanon, F., Marcantoni, L., Pastore, G., Baracca, E., Giau, G., Picariello, C., ... & Lanza, D. (2017). P1351 Long-term follow-up of His pacing in a single center experience. *European Heart Journal*, 38(suppl_1), ehx502-P1351.
 32. Zhang, J., Guo, J., Hou, X., Wang, Y., Qian, Z., Li, K., ... & Zou, J. (2018). Comparison of the effects of selective and non-selective His bundle pacing on cardiac electrical and mechanical synchrony. *EP Europace*, 20(6), 1010-1017.
 33. Haghjoo, M., Bonakdar, H. R., Jorat, M. V., Fazelifar, A. F., Alizadeh, A., Ojaghi-Haghjghi, Z., ... & Sadr-Ameli, M. A. (2009). Effect of right ventricular lead location on response to cardiac resynchronization therapy in patients with end-stage heart failure. *Europace*, 11(3), 356-363.
 34. Mahmud, R., Jamal, S., & Musheinessh, M. (2020). Voltage dependent conduction abnormalities in his bundle pacing in patients without His Purkinje system disease. *Journal of Electrocardiology*, 59, 1-6.
 35. Torrent-Guasp, F., Ballester, M., Buckberg, G. D., Carreras, F., Flotats, A., Carrió, I., ... & Narula, J. (2001). Spatial orientation of the ventricular muscle band: physiologic contribution and surgical implications. *The Journal of Thoracic and Cardiovascular Surgery*, 122(2), 389-392.
 36. Greenbaum, R. A., Ho, S. Y., Gibson, D. G., Becker, A. E., & Anderson, R. H. (1981). Left ventricular fibre architecture in man. *British heart journal*, 45(3), 248-263.

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