Acta Cardiologia Indonesiana

Web page: jurnal.ugm.ac.id/v3/jaci

pISSN:2460-5700

eISSN:2579-4345

The Evolution of Physiologic Cardiac Pacing

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ARTICLE INFO

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Manuscript submitted: Desember 28, 2022

Keywords:
Right ventricular pacing; His-bundle pacing; Left bundle branch pacing; pacemaker

ABSTRACT

Conventional right ventricular pacing (RVP) methods are associated with an increased risk of atrial fibrillation, hospitalization for heart failure, pacing-induced cardiomyopathy (PICM) and associated death. Other methods such as biventricular pacing (BiVP) have indeed shown improvement in morbidity and mortality in patients with advanced heart failure with left bundle branch block, but the method used remains non-physiological in that the activation spreads between the right ventricular (RV) endocardium and left ventricular (LV) epicardium. Physiologic pacing stimulates the heart's natural conduction pathways, resulting in synchronous ventricular contractions. This can prevent complications such as in the RVP method. The possibility of stimulating His bundle and left bundle branch in patients with bradycardia and conduction system disorders in order to obtain the most physiological method and approach the intrinsic pathway makes the development of conduction system pacing more interesting. In this review, we summarize the evolution of physiologic cardiac pacing and the challenges it faces in order to achieve better outcomes for patients.

INTISARI

Metode pacu jantung ventrikel kanan yang konvensional dikaitkan dengan peningkatan risiko fibrilasi atrium, rawat inap karena gagal jantung, kardiomiopati yang diinduksi pacing dan kematian terkait. Metode lain seperti *biventricular pacing* (BiVP) memang telah menunjukkan peningkatan morbiditas dan mortalitas pada pasien dengan gagal jantung lanjut dengan blok cabang berkas kiri, tetapi metode yang digunakan tetap non-fisiologis karena aktivasi menyebar antara endokardium ventrikel kanan dan epikardium ventrikel kiri. Pacing fisiologis merangsang jalur konduksi alami jantung, menghasilkan kontraksi ventrikel yang sinkron. Hal ini dapat mencegah komplikasi seperti pada metode RVP. Kemungkinan stimulasi berkas His dan cabang berkas kiri pada pasien dengan bradikardia dan gangguan sistem konduksi untuk mendapatkan metode yang paling fisiologis dan mendekati jalur intrinsik membuat perkembangan sistem pacu jantung menjadi lebih menarik. Dalam ulasan ini, kami merangkum evolusi pacu jantung fisiologis dan tantangan yang dihadapinya untuk mencapai hasil yang lebih baik bagi pasien.

Introduction

When RV pacing (RVP) was first performed on a patient with Adam-Stokes syndrome on October 8, 1958 by Ake Senning, a Swedish surgeon, RV pacing (RVP) was a breakthrough in the pacemaker method[1]. The advantage of this method is that the procedure is relatively short and simple. However, RVP is not a physiological method of pacing. The placement of leads in the apical RV causes abnormal electrical and mechanical activation of the ventricles. This is because electrical waves are transmitted through the myocardium instead of the His bundle conduction system causing ventricular and atrioventricular asynchrony. Conventional RVP methods are associated with an increased risk of atrial fibrillation, hospitalization for heart failure, pacing-induced cardiomyopathy (PICM) and associated death[2].

The results of the MOST[3] study show that there is a 2.6-fold increased risk of hospitalization for heart failure in patients with ventricular pacing burden >40% (dual chamber/DDDR mode) compared to lower pacing burdens. This risk persists regardless of the pacemaker mode (DDDR vs ventricular/VVIR) and is associated with RVP-induced ventricular synchronization. Subsequent studies also showed that one-fifth of patients had pacemaker-associated cardiomyopathy in patients with a pacing burden of 20%[4]. In patients with a normal baseline ejection fraction (EF), PICM (where the LVEF less than 40%) occurred in 12.3% of patients. This tends to occur in patients with a pacing burden of 20% and with a lower baseline LVEF[5].

Other pacing options such as the septum and the RV Outflow Tract (RVOT) are also not superior to the apical RV[6,7]. Other methods such as biventricular pacing (BiVP) have indeed shown improvement in morbidity and mortality in patients with advanced heart failure with left bundle branch block, but the method used remains non-physiological in that the activation spreads between the RV endocardium and LV epicardium[8]. The use of CRT with BiVP is also not ideal in patients with permanent AF with a narrow QRS interval baseline undergoing AV node ablation procedures. In addition, the percentage of non-responders is also high[9]. Researchers search for a way to implement a pacing method that is close to the intrinsic pathway physiologic to solve this problem.

Discussion

The ideal physiological pacemaker requires continued proximity to the intrinsic cardiac conduction system that maintains a normal QRS complex or even narrows the QRS pattern in the presence of bundle branch block (BBB). Physiologic pacing stimulates the heart's natural conduction pathways, resulting in synchronous ventricular contractions. This can prevent complications such as in the RVP method. Some of the methods currently used are His-bundle pacing (HBP) and Left Bundle Branch-pacing (LBBP). As an illustration, the location of the permanent lead placement for ventricular pacing along with strategies for cardiac resynchronization therapy is shown in the following figure (Fig 1).

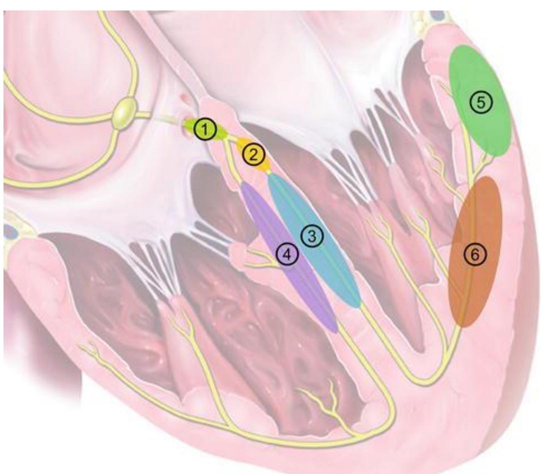

Figure 1. Locations of the permanent lead placement for ventricular pacing along with strategies for cardiac resynchronization therapy. 1 – His bundle pacing; 2 – Left bundle branch pacing; 3 – Left septal pacing; 4 – Right septal pacing; 5 – Epicardial left ventricular pacing; 6 – Endocardial left ventricular pacing. Cardiac resynchronization therapy strategies: 1 – SINGLE SPOT (1, 2, 3, 4); 2 – CRT (4 + 5); 3 – HOT-CRT (1 + 5); 4. LOT-CRT (2, 3 + 5); 5. CSP-RV (2, 3 + 4). SINGLE SPOT = pacing from a single site, CRT = cardiac resynchronization therapy, HOT-CRT = His-optimized cardiac resynchronization therapy, LOT-CRT = left bundle branch-optimized cardiac resynchronization therapy, CSP-RV = conduction system pacing + right ventricular pacing. (From Karpenko, I. , Skoryi, D. , Volkov, D. . The Evolving Concept of Cardiac Conduction System Pacing. In: Zima, E. , editor. Cardiac Arrhythmias - Translational Approach from Pathophysiology to Advanced Care [Internet]. London: IntechOpen; 2021 [cited 2022 Sep 12]. Available from: https://www.intechopen.com/chapters/78490 doi: 10.5772/intechopen.99987).

In 1969, Narula *et al*. proposed HBP using an electrophysiological catheter for HB stimulation and also suggested the possibility of the concept of longitudinal dissociation of HB (the concept that the bundles in His will continue distally according to the bundle branches) (Fig.2). Bundle Branch Block can occur due to a delay in the bundle in His which corresponds to the bundle branch below it. Deshmukh *et al.* first performed this method in patients with atrial fibrillation (AF) and AV nodal ablation as an alternative to the RVP method in 2000. Barba-Pichardo *et al.* did so in 2006 as an alternative to the CRT method[8].

Leads in HBP are implanted on His-bundle (HB) or adjacent structures, stimulating the bundle of His and causing downward activation of the distal conduction system including bundle branches and Purkinje fibers, thereby causing ventricular activation and contraction. Conduction delay in HB is a common cause of bundle branch block (BBB) and placing lead pacing distal to it can correct it[10].

There are 2 types of pacing on HB. Selective pacing stimulates the His bundle without involvement of the surrounding tissue where the stimulus for ventricular activation is the same as the intrinsic activation of the HV interval. The resulting QRS morphology is identical to the intrinsic QRS complex, concordant with the T wave, where the QRS width remains the same even at lower output pacing. In non-selective HB, stimulation includes the His-Purkinje system and surrounding ventricular tissue. This will create a fusion image where the HV interval will be shorter and the QRS width will vary depending on the output pacing. The electrical axis of the racing QRS complex remains concordant with spontaneous QRS. Although selective pacing appears to be more physiological than non-selective, non-selective pacing provides better protection in patients with infraHisian block because ventricular capture persists if His capture is lost. There were no significant differences in all-cause mortality and hospitalization for heart failure in the two methods. There was no increased risk with non-selective pacing even in high-risk patients (with high pacing burden or lower LVEF)[10].

HBP is indicated in sick sinus syndrome, permanent AF with AV node ablation, AV node block and high-grade AV infranodal block. HBP is recommended as class IIa in patients with an LVEF of 36-50% requiring ventricular pacing (>40%) and as class IIb in patients with AV block at the AV node level (2018 AHA/ACC/HRS)[11].

Several studies have reported that HBP is associated with significant improvements in LVEF and LV dimensions, NYHA functional class, and quality of life, reduced rates of hospitalization for heart failure, all-cause mortality and upgrades to BiVP[12]. The reduced left atrial dimension due to physiologic left ventricular activation and relaxation also allows the left atrium to function better and delays the onset of AF[10].

Some of the disadvantages of HBP are that it is a relatively more difficult procedure with a longer fluoroscopic time than RVP. This is because the target area for placing leads on the HBP is very small. In addition, the capture threshold required at implantation and at further follow-up is also higher so that the battery life will be shorter and require more frequent replacement. This is due to the structure of the His bundle which is covered by myocardial fibers.

Anatomically, HB has 3 variants (Fig.3)[13]. In type I (47%), the AV node is covered by a thin layer of myocardial fibers and runs along the lower border of the septal membrane. In this type, ns-HBP is captured at a higher current amplitude, while s-HBP is captured at a lower amplitude. In type II (32%), the AV node is covered by thick myocardial fibers and is clearly separated from the septal membrane. In these cases, adequate HB pacing is rare. In type III (21%), the AV node is not enveloped by the surrounding myocardial fibers and runs beneath the endocardium. This type is probably the best type for HB pacing[14,15].

Another reported complication of the HBP technique is the high lead revision rate (~3-6.7%) due to the unpredictable and increasing capture threshold over time. The low R wave amplitude in the HBP lead can lead to ventricular undersensing, far-field atrial oversensing and atrial capture [16,17]. In the follow-up period, a minority of patients may lose their capture of His resulting in an RV septal pacing. HBP is also ineffective in LBBB located below the His bundle. This challenge raises alternative methods that are considered to be able to overcome the weaknesses of HBP.

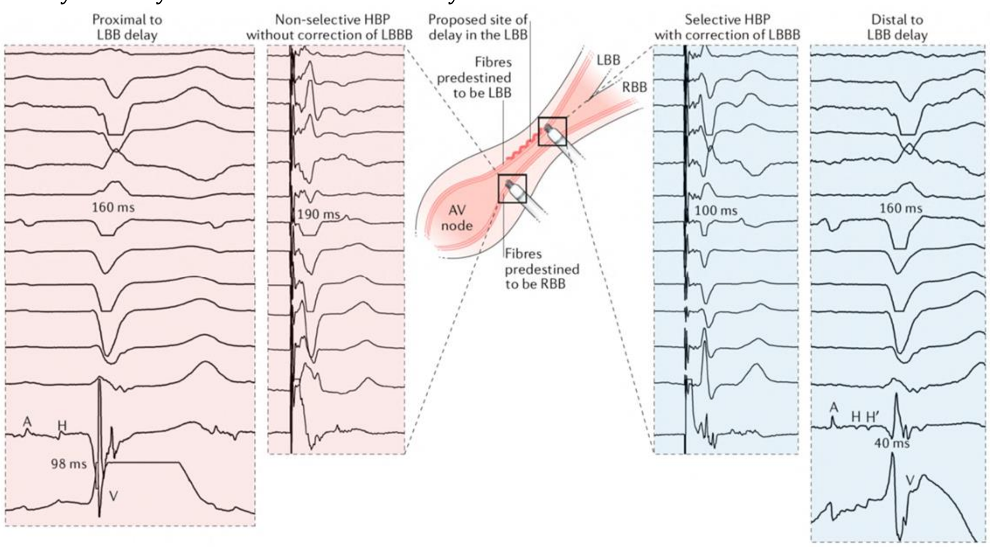

Figure 2. Longitudinal dissociation within the His bundle. Proposed model of longitudinal dissociation in the His bundle is depicted in the centre of the figure, demonstrating fibres predestined for either the right bundle branch (RBB) or the left bundle branch (LBB), with disease resulting in a delay in LBB conduction. The left panel shows mapping at a site proximal to the site of disease (with the His lead), revealing a long H–V interval (98 ms), and pacing at this site does not overcome LBB block (LBBB). The right panel shows mapping at a site distal to the site of disease, revealing a normal H′–V interval (40 ms), and pacing at this site results in complete normalization of conduction with selective His bundle capture.A , atrium; AV, atrioventricular ; H, His; H′, distal His; HBP, His bundle pacing; V, ventricle. (*From Sharma P, Vijayaraman P, Ellenbogen K. 2019. Permanent His bundle pacing: shaping the future of physiological ventricular pacing. Nature Reviews Cardiology. 17(1):22-36*).

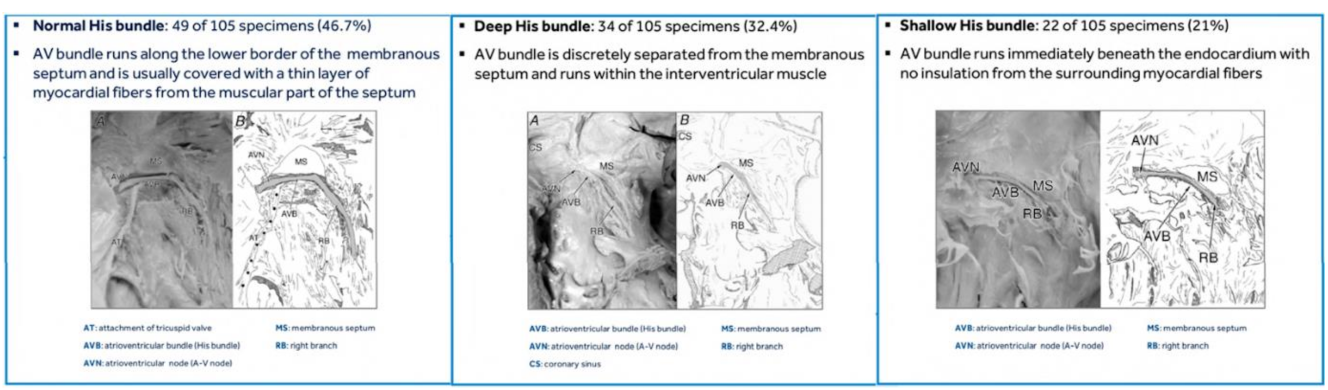

Figure 3. Anatomical variations of His-bundle (HB). The relationship of the HB to the membranous part of the IVS based on the autopsy material of 105 subjects. (From Kawashima T, Sasaki H. 2005. A macroscopic anatomical investigation of atrioventricular bundle locational variation relative to the membranous part of the ventricular septum in elderly human hearts. Surg Radiol Anat. 27(3):206-213)

Huang *et al.* introduced the Left Bundle Branch Pacing (LBBP) technique by inserting a pacing lead into the basal septum of the RV to stimulate the LBB area. A characteristic of LBBP is direct pacing of the left main bundle or individual fascicle branches along with LV septal myocardium at low output (<1V at 0.5 ms pulse width)[18]. The target area for LBBP in LBB fibers in the left subendocardium is wider when compared to HBP. In addition, because LBB is located in the myocardium, the pacing threshold is lower and stable compared to HB, which is located in fibrous tissue and relatively electrically non-conducting. Wang *et al.*[19] conducted a singular study with a subgroup of 8 patients who underwent LBBP along with 44 HBP patients who had undergone atrioventricular (AV) nodal ablation. The average follow-up is 30.5 months. The clinical outcome is improved LVEF and volumes. Patients receiving HBP/LBBP also have fewer inappropriate shocks compared to those who receive optimal medical therapy.

Unfortunately given the relatively novel this method has over HBP, there were only a limited number of studies that address it. LBBP has been used predominantly in China, in a nonischemic population having smaller body mass and septal thickness. Patients with ischemic cardiomyopathy need to be systematically studied. LBBP may also not be suited for patients with right bundle branch block patterns and indication for CRT as RV activation may be persistently delayed[12]. There are several potential complications of LBBP. The use of sheaths or pacing leads in the form of an open helix can cause temporary or permanent RBB injury[20,21] and has the potential to cause thromboembolism. Thus, patients with LBBB may require insertion of temporary pacemaker leads as backup pacing. Lead perforation and lead release into the LV[22], and RV[21] spaces, interventricular septal perforation[23], injury to the septal branch of the left anterior descending artery causing STEMI at implantation, and lead loss 2 years after implantation have been reported[24]. This finding requires close supervision both during treatment and at further follow-up.

Conclusions

The possibility of stimulating HB and LBB in patients with bradycardia and conduction system disorders in order to obtain the most physiological method and approach the intrinsic pathway makes the development of conduction system pacing more interesting. With the improvement of implantation techniques, delivery sheaths and lead designs and the increasing number of RCT studies on conduction system pacing, it is hoped that alternative pacing methods that are safe and ideal for patients will be improved.

Disclosures and Ethics

Author reported no conflicts relevant to the contents of this paper to disclose.

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