Available online at www.sciencedirect.com

ScienceDirect

Journal of Electrocardiology xx (2016) xxx – xxx

JOURNAL OF Electrocardiology

www.jecgonline.com

Review

History of His bundle pacing ☆

Gopi Dandamudi, MD, [a,*] Pugazhendhi Vijayaraman, MD [b]

[a] Indiana University School of Medicine, Indianapolis, IN
[b] Geisinger Heart Institute, Wilkes-Barre, PA

Abstract Chronic right ventricular (RV) pacing has been shown over the years to exert detrimental physiological changes including increased risk for heart failure and atrial fibrillation. His bundle pacing offers the promise of physiological activation of the ventricular tissue, with the potential for reducing the detrimental effects of RV pacing. We describe His bundle pacing in a historical context and briefly highlight several clinical trials that have helped shape the landscape of permanent His bundle pacing.

Keywords: His bundle pacing; Chronic RV pacing; Heart failure; QRS complex

Introduction

Permanent His bundle pacing (PHBP) offers a very attractive option to pace the ventricles. It is by far the most physiological form of pacing and its theoretical benefits are unquestioned. Limited studies have shown the potential clinical benefits that can be derived from this form of pacing [1–5]. Other forms of pacing currently employed in clinical practice have their limitations. Chronic RV pacing has been shown to increase heart failure (HF) and atrial fibrillation (AF) [6,7]. Biventricular pacing (BiV) has limited benefits in patients with a non-LBBB ECG and significantly reduced ejection fraction (EF) [8]. In mildly reduced EF patients, BiV pacing benefits are equivocal at best [9,10]. We discuss the anatomy and physiology of the His bundle (HB) in a historical context and briefly discuss some clinical trials that have demonstrated safety and efficacy of PHBP.

First anatomical descriptions

As a practicing anatomist and physiologist, Johann Evangelist Purkinje first described the existence of Purkinje fibers in 1839. The first descriptions of the HB were made in 1893 by Wilhelm His Jr., a Swiss cardiologist and anatomist. He was the first to coin the term "heart block" and described the significance of the HB as a conduit to conduction from the auricles to the ventricular septal walls. In 1903, Sunao Tawara, a Japanese pathologist, published his monograph on the cardiac conduction system and made several seminal observations including the existence of the AV node, detailed descriptions of the bundle branches and the Purkinje system, and histology of the cardiac conduction system [11].

Physiological recordings

It was not until 1958 when Alanis and colleagues demonstrated the first HB recordings in Mexico City [12]. Using isolated perfused hearts of dog and cats, steel needles were used to record physiological signals that were identified as HB recordings for the first time. They described the HB as a "zone" with changing HV intervals, as the HB was mapped from a proximal to distal location. They also demonstrated that decremental conduction occurred in the AV node and HB conduction was non-decremental in nature.

The first known human recordings of the HB were carried out by Giraud et al. in 1959 in a patient with tetralogy of Fallot [13]. Ten years later, Benjamin Scherlag and colleagues used intravascular catheters to record HB recordings in humans [14].

Over the next several years, numerous observations were made about the HB that would increase our understanding of the anatomy and physiology of this complex cardiac structure.

Earlier observations

As mentioned before, Scherlag and colleagues published their technique for recording HB activity in humans in 1969 [14]. This led to the rapid growth of cardiac electrophysiology and is considered one of the pivotal events in this field. They were able to place bipolar catheters percutaneously and demonstrate HB physiology in humans that was first reported by Alanis et al. in animals. Over the next decade, this group

☆ COI: Dr. Dandamudi and Dr. Vijayaraman serve as consultants to Medtronic, Inc.

* Corresponding author at: Indiana University Health Cardiac Electrophysiology, Indiana University School of Medicine, 1801 N. Senate Boulevard, Indianapolis, IN 46202.

E-mail addresses: gdandamu@iu.edu, gdandamudi1@gmail.com

http://dx.doi.org/10.1016/j.jelectrocard.2016.09.011
0022-0736/

published several studies assessing the physiology of the HB. Specifically, they reported their findings on complete heart block patients and bundle branch block patients as detailed below.

Narula and colleagues published an elegant series on patients with Wenckebach and Mobitz II heart block [15]. They were able to demonstrate that Mobitz II heart block could occur either with bilateral bundle branch blocks or due to intra-Hisian heart blocks (i.e. more proximal in the common bundle). They also suggested that intra-Hisian block was not uncommon and that heart block could be intra-Hisian in location even in patients with abnormal QRS durations. James and Sherf published a detailed anatomical description of the HB in humans using light and electron microscopy in 1971 [16]. They demonstrated the architecture of the HB, including their longitudinal orientation with collagen interspersed between the cells. They also described sparse transverse connections between these bundles. In 1973, Lazzara et al. demonstrated that in partially transected (80–90%) right and left bundle branches in canine hearts, conduction could resume with no significant delay [17]. They also demonstrated that the transverse conduction velocity was significantly less than the longitudinal conduction velocity in the common bundle.

The concept of functional longitudinal dissociation of the HB was first proposed by Kaufman and Rothberger in 1919 [18]. Predestined fibers within the His bundle conducted selectively to each fascicle and these fibers originated within the proximal portions of the common bundle. This concept was very elegantly demonstrated by Narula in 1977 [19]. Patients with LBBB and baseline prolonged HV intervals were studied and pacing slightly distal to the proximal His bundle resulted in narrowing of the QRS. El-Sherif et al. published both clinical and experimental evidence for longitudinal dissociation in the diseased His bundle in humans in 1978 [20]. They evaluated patients with both RBBB and LBBB, and prolonged HV intervals. With distal HB pacing, they were able to normalize the QRS duration. They demonstrated this in canine models with ligated septal arteries that resulted in intra-His conduction delay and bundle branch blocks. Once again, with slightly distal pacing within the common bundle, they were able to normalize QRS complexes and conduction times.

Even though there was mounting evidence that heart blocks and bundle branch blocks could be manifestations of proximal HB disease and that pacing from the common bundle can result in resumption of conduction with recruitment of the bundle branches as described earlier, further clinical studies were not undertaken at that time. With the advent of biventricular pacing a few years later, there was a stalemate in further development of PHBP.

Clinical evidence for PHBP

In the year 2000, Deshmukh et al. published the seminal paper demonstrating the safety and feasibility of PHBP in humans [1]. They attempted PHBP in 18 patients with chronic AF, EF <40%, QRS <120 ms, and NYHA class III–IV HF symptoms who underwent AV nodal ablation. They were successful in achieving PHBP in two thirds of their patients. They were able to demonstrate positive LV remodeling in this cohort, with an improvement in LV EF from 20 ± 9% to 31 ± 11% ($P < 0.01$). This set the stage for clinicians around the world to pursue PHBP as an alternative to RV pacing. Selected PHBP clinical trials and related observations are outlined below.

Dyssynchronous RV pacing vs. physiological PHBP

It has been demonstrated that PHBP does not induce ventricular dyssynchrony unlike RV apical pacing [2]. In this study, intra-patient acute comparisons were made between both forms of pacing and it showed that indices of ventricular dyssynchrony were significantly reduced, including the degree of mitral regurgitation and improvement in LV systolic function Tei index with PHBP. There was no difference in these indices whether pure His bundle pacing (termed selective His bundle pacing) or His bundle pacing plus local septal myocardial capture (termed non-selective His bundle pacing) occurred. LV ejection fraction significantly decreased in the RV paced group compared to that in the PHBP group (50.1 ± 8.8% vs. 57.3 ± 8.5%, $P < 0.001$). In another study, patients underwent implantation of an HB lead as well as an RV apical pacing lead [3]. During long-term follow-up, pacing was temporarily switched in patients with HB pacing to RV apical pacing. Acutely, LV EF decreased significantly along with worsening mitral regurgitation and inter-ventricular delay.

Clinical benefits of His bundle pacing

In a small study of 12 consecutive patients who underwent PHBP along with RV apical pacing, coronary perfusion was significantly better with PHBP compared to that with RV apical pacing [21]. Also, there was a significant reduction in mitral regurgitation and ventricular dyssynchrony in PHBP. In another study, PHBP outcomes were compared to RV pacing outcomes in an unselected patient population who had indications for permanent pacemaker placement [4]. PHBP could be achieved in 80% of patients without the use of a separate mapping catheter in this cohort. More importantly, in patients with >40% ventricular pacing, heart failure hospitalizations were significantly reduced (2% vs. 15%) in the PHBP pacing group compared to those in the RV pacing group. In six of the nine patients in the RV pacing group, there was a significant reduction in LV EF (from a mean of 58% to 33%). Recently, it was also shown that direct HB pacing can improve acute hemodynamic function in patients with heart failure and PR interval prolongation without LBBB [22]. AV optimization was performed acutely with both HB pacing and BiV pacing. There was improvement in systolic BP in both groups but the QRS duration was lengthened in the BiV pacing group (change = +22 ms [95% CI: +18 to +25 ms]) but not in the His pacing group (change = +0.5 ms [95% CI: −2.6 to +3.6 ms).

His bundle pacing in patients with heart block

In one small study, PHBP was able to be achieved in 5 patients with infra-Hisian heart block [23]. Ventricular dyssynchrony (as measured by 2D echo) that was present in patients