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Original Article

His bundle pacing—is it the final frontier of physiological pacing ?—A single centre experience from the Indian sub—Continent

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ABSTRACT

Background: Long term right ventricular pacing can have deleterious effects on left ventricular (LV) function. His bundle pacing (HBP), a novel procedure can probably circumvent this setback. We investigated if (1) HBP is associated with pacing induced LV dysfunction by using LV global longitudinal strain (GLS) and (2) intermediate term performance of the Select Secure (3830) lead in the His bundle location. This report is probably the first on HBP in the Indian population.

Methods: 61 patients, with normal LV ejection fraction (EF) with a guideline based indication for permanent pacing underwent a HBP pacemaker implantation using the His Select Secure 3830 lead; with lead guided mapping for locating the His bundle. The patients underwent GLS assessment; evaluation of the His lead parameters - sensing, impedance and capture thresholds immediately after implantation and at 6 months in addition to the standard follow up.

Results: At 6 month follow up, the average GLS did not show significant variation from baseline in patients requiring ventricular pacing more than 40% and was similar, irrespective of selective or non selective His bundle pacing. All the patients had stable pacemaker parameters - with little change in capture threshold, lead impedance or sensing of the His bundle lead - implying electrical and mechanical stability on intermediate term follow-up.

Conclusion: HBP is a feasible procedure in the hands of an experienced operator, with stable lead performance. It does not appear to be associated with pacing mediated left ventricular dysfunction at intermediate term follow up. It should probably become the default method of permanent pacing.

1. Introduction

It is an established fact that long term right ventricular apical pacing can have detrimental effects on left ventricular systolic function that may result in long term adverse outcomes like atrial fibrillation, heart failure and even death.[1–5] To circumvent these issues, various other sites have been proposed as alternatives for pacing including the interventricular septum and the right ventricular outflow tract, though results have not been promising.[6,7] The first breakthrough came in 2000 when Deshmukh et al explored ventricular activation via the His bundle as a form of physiological pacing. This technique had the advantage of avoiding electrical and therefore mechanical dyssynchrony associated with right ventricular (RV) apical pacing by utilizing the intrinsic conduction system for the activation of the ventricles.[8]

Despite being near physiological pacing, the technique was not readily adopted due to various reasons ranging from difficulty in positioning the lead to being associated with high capture threshold that required a lead revision. The advent of the steerable sheath to deliver the 4 F lumen less lead has been a great leap that has facilitated the use of this form of pacing in a variety of indications. Electrophysiologists across the world are now exploring various aspects of this mode of ventricular activation like selective and non-selective His bundle pacing.[9] Selective His bundle pacing (SHBP) results in His bundle capture only at both high and low capture thresholds - an all or none phenomenon - with the paced QRS morphology being identical to the intrinsic rhythm. There is an isoelectric segment between the pacing spike and the QRS complex

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that is equal to the intrinsic HV delay. On the contrary, non-selective HBP (NS-HBP) results when there is capture of the surrounding myocardium that results in a pseudo delta wave and the absence of the isoelectric segment between the pacing spike and the QRS onset. Demonstration of His bundle capture is imperative either at higher or lower capture thresholds in NS-HBP. Following further developments and magnetic resonance imaging conditional labeling of the 3830 lead in early 2017, patients at our institute have undergone His Bundle Pacing (HBP) implantation.

RV pacing has been known to cause pacemaker induced cardiomyopathy. Studies have shown that these patient subsets show changes in the average GLS predating the change in LVEF as early as 1 month post pacemaker implantation. We tried to assess if HBP - selective or non selective was associated with pacemaker induced cardiomyopathy, while at the same time studying the performance of the Select Secure 3830 HBP lead. This article reports experience at our institute.

2. Materials and methods

2.1. Patient population

Consecutive patients with a standard indication for pacing according to the current guidelines, and normal LVEF in whom frequent ventricular pacing was anticipated and in whom HBP was performed by a single operator were included. Patients were recruited from the Cardiology Department at M S Ramaiah Medical College. The protocol was approved by the institutional ethics committee and patients gave an informed consent to participate in the study. The exclusion criteria were patients with underlying structural heart disease, or cardiomyopathies.

2.2. Implantation technique

HBP was performed according to implantation techniques previously described[10–12] using the Medtronic 3830 lead with the C315 His delivery catheter. The His lead was implanted with the help of mapping for the His potential using the open helix of the 3830 lead, in a unipolar sensing configuration (as the ring electrode was within the sheath during mapping). The lead was connected to the atrial channel of the pulse sense analyser at 50 mm/s sweep speed and 0.05 mV amplification and intracardiac electrogram recorded from the lead tip by a digital electrophysiological recording system (St. Jude EnSite Velocity Cardiac Mapping System) and was filtered at 30–500 Hz. Pace mapping ensured paced QRS near identical to the native QRS before fixing the lead by twisting the body 4 to 5 clockwise turns. Active recoil ensured the lead fixation to the fibrous body typical of the His bundle region. Intracardiac EGM and 12-lead ECG was recorded during lead testing in all instances to confirm His capture and evaluate the transition from NS-HBP to SHBP (Figs 1 and 2). Details on His lead positioning (visualization of the His potential, current of injury, thresholds etc) were recorded.

2.3. Assessment of global longitudinal strain

All patients underwent echocardiography immediately after to implantation and at 6 months post pacemaker implantation. Echocardiography was performed by one of the co-investigators, who were blinded to the indication for the pacemaker implant. It was performed using the Vivid E9 (GE Healthcare System, Horten, Norway) ultrasound system with M4S transducer (volume phased matrix array with a frequency range of 1.5–4.0 MHz). LV ejection fraction was calculated using the Simpson's biplane method and LV strain was calculated using Auto LVQ software (GE Healthcare system, GE Vingmed Ultrasound A/S, Horten, Norway) offline.

Assessment of global longitudinal strain by speckle tracking was performed in the apical 2- and 4-chamber and apical long axis views and images were recorded at frame rates of >40 frames per second. From an end systolic frame, a region of interest on the endocardial cavity interface was selected by a single point and click approach. The semi-automated tracking algorithm followed the endocardium from this single frame through the cardiac cycle. Adjustments of the regions of interest were made as required while ensuring that the pericardium was avoided. For strain assessment, an automated display of the LV based on at the AHA/ASE guidelines,[13] with the strain rate of individual segments being displayed in Bull's eye format. Quantification of fibre shortening was made assigning numbers such that greater the negative number greater was the fibre shortening. Only the average GLS was used for analysis. Criteria for pacemaker induced ventricular dysfunction was defined as a decrease in the LVEF by 10% or a decrease in the average LV GLS to < -14.5 from the baseline.

2.4. Statistical analysis

The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements have been presented on Mean ± SD (Min-Max) and results on categorical measurements have been presented in Number (%). Significance was assessed at 5% level of significance. The following assumptions on data were made: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random and Cases of the samples should be independent.

Student *t* test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven's test for homogeneity of variance was performed to assess the homogeneity of variance. Student *t* test (two tailed, dependent) was used to find the significance of study parameters on continuous scale within each group. The Chi-square/Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. The Fisher Exact test was used when cell samples are very small.

3. Results

Between 2017 and 2019, a total of 61 patients underwent HBP implant, majority were above 60 years of age with the average age being 62.98 ± 15.21 years ($n = 36$, 59%). There was an overall male preponderance ($n = 51$, 83.6%). More than half the total number of patients ($n = 40$, 65.6%) had a HBP implantation for degenerative and advanced atrio-ventricular block; others underwent the procedure for sick sinus syndrome and carotid sinus hypersensitivity as well. Only patients requiring >40% ventricular pacing were included in the study.

Among patients, 37.7% had coexisting coronary artery disease, a little more than half of the study population were diabetic (65.6%) and about 60.7% patients were found to be hypertensive.

When the electrocardiographic parameters at baseline were considered, most patients had a normal QRS morphology and duration. Those patients with advanced atrio ventricular block also

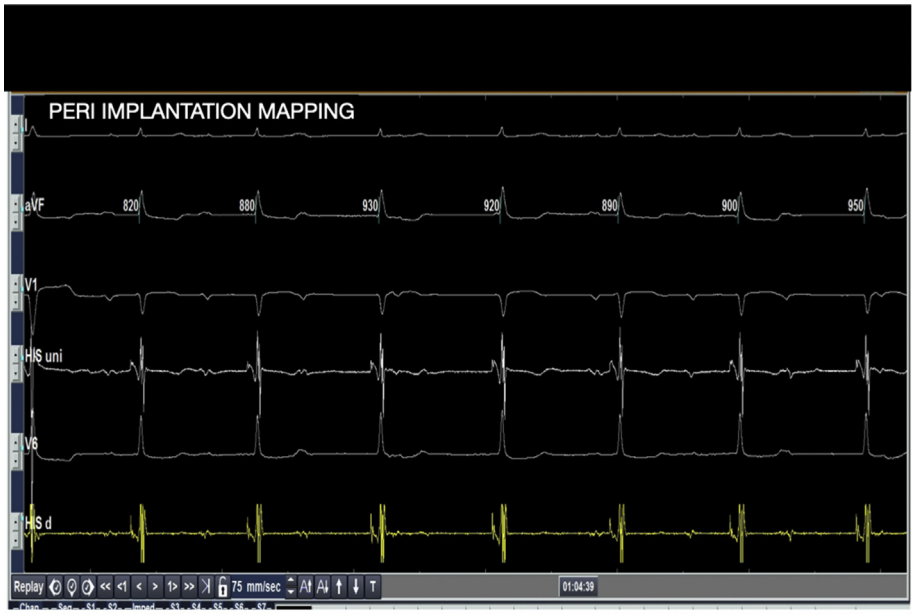

Fig. 1. Peri implantation mapping (His bundle EGM & surface ECG).

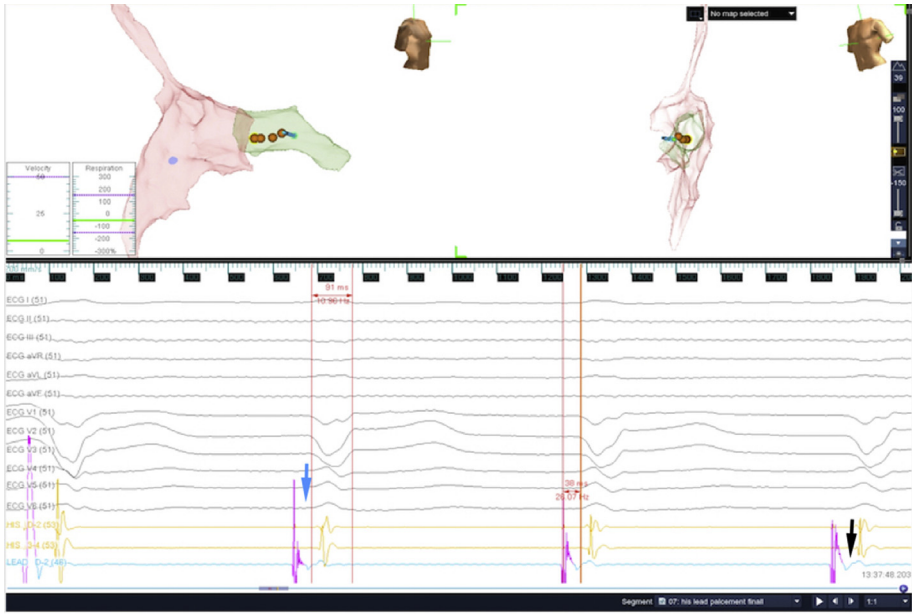

Fig. 2. Isoelectric line between stimulus to ventricular capture noted during selective His bundle capture on the intra cardiac EGM (blue arrow). Non selective His bundle capture with pseudo-delta wave (black arrow).

were found to have a narrow QRS during escape. 2 patients had underlying paroxysmal atrial flutter. Following implantation, the average paced QRS duration was found to be 110 ± 20 ms (Tables 1–4). We also found that the average fluoroscopy time (20 ± 8 min V 8 ± 6 min) and the time required for HBP lead implantation were longer when compared with a RV lead implantation at our centre (35 ± 6 min V 18 ± 5 min).

His bundle current of injury after lead fixation, associated with reduced capture thresholds was observed in 64% patients with a visible His potential. The capture threshold of the His bundle with unipolar pacing was 1.13 ± 0.55 V/0.5 ms (range 0.58–1.68 V/0.5 ms). Bipolar sensing was 7.51 ± 3.11 mV (range 4.4–10.6 mV). Unipolar impedance was 813.27 ± 194.48 Ohms. The average Global Longitudinal Strain in the immediate post implantation period was −16.96 ± 2.43.

At follow-up, the capture threshold of the His bundle with unipolar pacing was 1.32 ± 0.98 V/0.5 ms; Bipolar sensing was 7.51 ± 3.11 mV. Unipolar impedance was 686.27 ± 201.87 Ohms. The average Global Longitudinal Strain was noted to be −17.27 ± 2.07 (Table 5).

When we compared the average GLS at baseline and at 6 month follow up based on the probability of cumulative pacing, we did not find any significant change in the average GLS at follow up, implying that HBP does not result in pacing induced LV dysfunction or cardiomyopathy (Table 6).

Table 1
Overall demographics.

Patient characteristics	
Patient population (n = 61)	
Age (years)	62.98 ± 15.21
Males/females	51/10
Indication	
Sick Sinus syndrome	13
Degenerative atrioventricular block	17
Advanced atrioventricular block	23
Tachy brady syndrome	1
Carotid sinus hypersensitivity	7
Intrinsic QRS duration (ms)	110 ± 10
Paced QRS duration (ms)	110 ± 20
Baseline rhythm	
Sinus rhythm	59
Paroxysomal Atrial flutter	2
Comorbidities	
Ischemic heart disease	23
Diabetes	40
Hypertension	37
Others (Renal insufficiency, thyroid disorders, reactive airway disease)	7
Average Fluoroscopy time	20 ± 8 mins
Time for HBP lead implantation	35 ± 6 mins

Table 2
Age distribution of patients studied.

Age in years	No. of patients	%
<50	6	9.9
50–60	19	31.1
61–70	21	34.4
71–80	12	19.7
81–90	3	4.9
Total	61	100.0

Mean ± SD: 62.98 ± 15.21 years.

Table 3
Gender distribution of patients studied.

Gender	No. of patients	%
Male	51	83.6
Female	10	16.4
Total	61	100.0

4. Discussion

The main findings of this report are that (1) HBP is a procedure that can be performed for nearly all patients with indications for permanent pacemaker implantation (2) Electrical parameters are acceptable over intermediate term follow-up and (3) HBP is associated with stable average GLS parameters at 6 months follow-up which probably may translate into reduced incidence of pacemaker induced left ventricular dysfunction or cardiomyopathy long term.

Reported success with HBP with experienced operators has been >90%[14,15] which is nearly the same at our centre. It could be attributed to the fact that the learning curve in implanting the 3830 lead is steep. Factors contributing to this include the fact that the His bundle is a small area of focus, the high chances of lead displacement as the lead is fixed against the fibrous body and that the lead is a sheath driven and not stylet driven. Capture thresholds were acceptable and comparable to other studies[16,17] and remained stable at follow up. While 33 patients (54.1%) had SHBP, 28 patients (45.9%) had NS-HBP.

Table 4
Indications for pacemaker implantation.

Indication	No. of patients	%
Sick Sinus Syndrome	13	21.3
Degenerative Heart Block	17	27.9
Advanced AV Block	23	37.7
Carotid Sinus Hypersenitivity	7	11.5
Tachy Brady Syndrome	1	1.6
Total	61	100.0

Three patients (4.92%), however, had a displacement of the His bundle lead requiring repositioning. Among these, one patient had a right sided implant. In the three cases, the displacement occurred in the first 24 h post implantation and in the early phase of our study. Three to four additional clockwise turns while fixing the lead should circumvent this problem. No back up ventricular pacing lead was implanted; even in patients with advanced atrioventricular block. At the time of submission of this paper, we did not have any patient with any significant lead problems subsequently - electrical or mechanical; even in those who had had an earlier lead displacement.

Another aspect that we have looked into in this study was HBP associated change in LV ejection fraction and global longitudinal strain. LV systolic dysfunction is a frequent accompaniment to RV pacing when pacing fraction is >40%.[18,19] The challenge stems from the fact that predictors of this dysfunction is difficult. One such tool that was used to mitigate this challenge was GLS.[20–23] The Pacing and Ventricular Dysfunction (PAVD) study clearly demonstrated that a significant reduction in both average GLS and LVEF at one month following pacemaker implantation in patients portended a pacemaker induced cardiomyopathy at 12 months. More importantly, it was shown that the average GLS measured at one month following pacemaker implantation, but not LVEF, could identify a subgroup of patients who were prone for this effect. The study also showed that patients with an average GLS < -14.5 at the end of 1 month had a high sensitivity of predicting pacing induced LV dysfunction. Hence we used the 6 month criteria to assess the LVEF and GLS post implantation.[24]

Similar to the PAVD study, we used semi automated non contrast 2D methods to assess the LV ejection fraction, a practice that closely reflects real world practice scenario. Patients in our study did not show a decline in the LV ejection fraction or average GLS at the end of 6 months when compared to baseline. Rather the LVEF and average GLS tended to remain same at follow up as it was at baseline. Average GLS was found to be similar irrespective of SHBP or NS-HBP. Previous studies looked into either acute or chronic effects of RVA pacing in isolation. There have been limited reports on serial assessment of average GLS compared to LVEF systematically. Moreover, these studies were not without limitations in that, they tended to focus on individual measurements (e.g. GLS or LVEF, rather than assessment of both parameters in the same patients), a one time-point follow-up, or highly selected populations without considering factors like variations in pacing burden.[20–23]

Whether cumulative pacing would be associated with changes in GLS long term, could probably be an area of interest in future studies.

Most of the current published literature is predominantly from the Western world, including long term outcomes. A Swiss group led by Burri et al has also looked into the feasibility of HBP in clinical practice.[25] This may be one of the first reports of HBP in the Indian population.

Another important aspect in this publication is that, patients had only the atrial and His leads in place with no RV lead for back up pacing. None of the patients had any issues with either mechanical or electrical with the atrial or His bundle lead. In other

Table 5
Study variables at baseline and at 6 month follow up.

Variables	Immediately post implantation	6 months post implantation	% difference	95% CI	t value	*p* value
Average GLS	−16.96 ± 2.43	−17.27 ± 2.07	0.310	0.072–0.548	2.628	0.012*
Atrial Sensing (mV)	3.00 ± 1.15	3.00 ± 1.15	–	–	–	–
Atrial lead impedance (Ohms)	572.51 ± 172.49	478.39 ± 111.77	94.122	68.840–123.404	6.496	<0.001**
Atrial lead pacing threshold (V)	1.07 ± 0.49	1.01 ± 0.53	0.068	−0.071–0.206	0.985	0.331
His lead Sensing (mV)	7.51 ± 3.11	7.51 ± 3.11	–	–	–	–
His lead impedance (Ohms)	813.27 ± 194.48	686.27 ± 201.87	127.00	79.108–174.892	5.360	<0.001**
His lead pacing threshold (V)	1.13 ± 0.55	1.32 ± 0.98	−0.187	−0.466–0.093	−1.348	0.185

Table 6
Comparison of GLS immediately after implantation and at 6 month follow up in relation to indication for HBP implant.

Average GLS	Indication	
	Group I	Group II
Immediately after implantation	−17.08 ± 2.38	−16.45 ± 2.74
6 months Post implantation	−17.38 ± 2.02	−16.80 ± 2.34
Difference	0.300	0.350
p value	0.017*	0.382

Group I (Degenerative Heart Block, Advanced AV Block, Sick Sinus Syndrome), Group II(Tachy Brady Syndrome, Carotid Sinus Hypersensitivity).

words, at the hands of an experienced operator, when properly done, HBP is safe, even without back up RV pacing.

The current study shows that HBP may not be associated with the propensity of RV pacing to cause cardiomyopathy as evident from the preserved LVEF and average GLS at 6 months. We hypothesize that it may be considered in all patients requiring a dual pacemaker to offset RV pacing associated left ventricular dysfunction and cardiomyopathy, especially considering the potential long-term health economic burden that is associated with heart failure and other complications.

4.1. Limitations

The number of patients and followup duration are relatively limited. Long term follow up of these patients would need to be looked into. 3D analysis for assessment of left ventricular ejection fraction would have been ideal. In this study we had only looked in to the average GLS and not into the individual segmental strain rates. Additionally, estimation of radial and circumferential strain rates would have been ideal.

5. Conclusions

HBP has been performed at our centre for nearly two years and a half with good results without complications and stable patient profiles at follow up. HBP does not appear to be associated with pacing associated ventricular dysfunction. It may even be feasible to offer patients with chronic RV pacing, as an upgrade. We hypothesize that it should be considered as a feasible alternative to RV pacing in clinical practice in patients requiring frequent ventricular pacing. Further long term and RCT's may be required however.

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Conflict of Interest

All the authors hereby declare that:

The content of this article has not been previously published or submitted elsewhere for publication.

We also agree to transfer the copyright to the *Indian Heart Journal* upon the acceptance of the manuscript for publication.

We have reviewed the article and agree with its contents.

None of us have any conflicts of interest.

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