Acute His-Bundle Injury Current during Permanent His-Bundle Pacing Predicts Excellent Pacing Outcomes

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Introduction: His-bundle (HB) pacing (P) is a physiological alternative to right ventricular pacing (RVP), but is technically challenging and limited by higher pacing thresholds. Myocardial injury current (IC) recorded during right ventricular lead placement implies good tissue contact and is associated with low-pacing thresholds. IC at the HB has not been previously described. We hypothesized that HBIC during permanent HBP may be associated with lower pacing thresholds.

Methods: Permanent HBP was performed using Medtronic Select Secure™ (Medtronic Inc., Minneapolis, MN, USA) delivered via a fixed-curve (C315 His) sheath. HB electrogram (EGM) was recorded in a unipolar fashion from the lead tip. Presence or absence of HBIC was documented. HBP threshold, sensing, and impedances were recorded at implant, 2 weeks, 2 months, and 1 year.

Results: Sixty patients (age 72 ± 15 years; male 55%, sick sinus syndrome 40%, atrioventricular block 60%, fluoroscopy duration 9.2 ± 3.7 minutes) underwent successful permanent HBP. HBIC was recorded in 22 (37%) patients (group I). HBEGM without IC was recorded in the remaining 38 (63%) patients (group II). Pacing threshold at implant, 2 weeks, 2 months, and 1 year were significantly lower in group I (1.16 ± 0.4 V; 1.18 ± 0.5 V; 1.23 ± 0.6 V; 1.3 ± 0.6 V @ 0.5 ms) compared to group II (1.75 ± 0.7 V; 1.82 ± 0.8 V; 1.93 ± 0.8 V; 1.98 ± 0.9 V @ 0.5 ms, P < 0.05), respectively.

Conclusions: IC can be recorded at the HB during permanent HBP in 37% of patients. HBIC is associated with significantly lower pacing thresholds compared to patients in whom HBIC was not recorded. HBIC may be a marker for superior short-term HBP thresholds. (PACE 2015; 38:540–546)

His-bundle pacing, pacing, heart failure

Background

Conventional right ventricular (RV) apical pacing has been the standard practice for patients requiring permanent ventricular pacing. However, long-term RV apical pacing is associated with asymmetric ventricular hypertrophy and dilatation,1 myofibrillar disarray,2 ventricular dyssynchrony,3 negative inotropy,4 and structural left ventricular changes.5,6 Long-term RV pacing is also associated with an increased risk of death, heart failure (HF) hospitalizations, and persistent atrial fibrillation (AF).7–10 Deshmukh et al.,11 first described successful permanent direct His-bundle (HB) pacing (HBP) in a small series of patients with AF and dilated cardiomyopathy. Subsequently, there have been multiple reports on permanent HBP, which have demonstrated that it is feasible and is associated with an improvement in exercise capacity and left ventricular ejection fraction.12–17 Permanent HBP is technically challenging and often associated with high-pacing thresholds. Many patients require placement of an additional RV backup pacing lead.

The anchoring of the active-fixation leads into the myocardium causes injury to the tissue known as injury current (IC). The IC manifests as an increase in the duration of the intracardiac electrogram (EGM) and elevation of the ST-segment compared to the baseline. It has been shown that the magnitude of ST-segment elevation can predict adequate acute performance of active-fixation leads.18,19 Myocardial IC can be recorded in both right atrial and RV myocardium. During successful permanent HBP, HBEGMs are recorded in the majority of patients. However, IC during permanent HBP has previously not been described. The objective of this study is to determine if recording of HBIC can predict improved thresholds and outcomes compared to patients in whom IC was not recorded.
Methods

Consecutive patients who underwent successful permanent HBP were included in the study. Patients were excluded from the study if (1) permanent HBP was unsuccessful, (2) there was a prior history of device implant, (3) patients were subsequently not followed in our practice. The study protocol was approved by the institutional review board.

Implantation Technique

In all patients, HBP was performed using the Select Secure™ (Model number 3830, 69 cm, Medtronic Inc., Minneapolis, MN, USA) pacing lead using a fixed-curve delivery catheter (C315 HIS, Medtronic Inc.). The C315 His catheter was inserted into the right ventricle distal to the tricuspid annulus over a guidewire through a left cephalic or axillary vein. Subsequently the pacing lead was advanced through the catheter such that only the distal electrode/screw is beyond the tip of the catheter. Unipolar EGMs were recorded from the tip at maximum gain setting (0.05 mV/mm) and displayed on a Medtronic Pacing System analyzer (model number 2290) at a sweep speed of 50 mm/s. Medtronic PSA has one fixed filter setting available and this was routinely used. The preinstrumentation amplifier high-pass filter is a passive resistive-capacitive filter that will normally be set to 0.064 Hz. The high-pass filter allows signals between 1 kHz and 10 kHz. The low-pass filter allows signals between 20 Hz and 70 Hz. The HBEGM was identified by mapping the atrioventricular septum. The lead was then screwed into this position with four to five clockwise rotations. The rhythm strips of all recorded HBEGMs at implant were stored. HB current of injury was considered present if there was (1) greater than 0.2-mV elevation of the ST segment from the baseline (the isoelectric portion before the EGM in the segment of the atrial-His interval) following the intrinsic deflection of the HBEGM, and/or (2) ST segment elevation of >25%
Figure 2. Direct His-bundle pacing. The top panel shows the 12-lead electrocardiogram in a patient with sinus node dysfunction and advanced AV block. The middle panel shows the final intracardiac electrogram recorded from the permanent His-bundle pacing lead at the time of implantation. Note the His-bundle electrogram (H) with injury current (arrow). Bottom panel shows AV sequential His-bundle pacing. The pacing spike is followed by an isoelectric interval of 40 ms and then QRS complexes narrow and identical to the baseline QRS morphology. His-bundle pacing threshold was 0.7 V @ 0.5 ms. R waves were 2.4 mV and pacing impedance was 540 Ohms. A = atrial; V = ventricular.

of recorded HBEGM (Fig. 1). Duration of HBIC could not be consistently assessed as it is often masked by the ventricular EGM. His- and para-Hisian capture thresholds were measured and accepted if found to be less than 2.5 V at 1.0 ms. If acceptable HB capture could not be achieved after five attempts at lead positioning, the lead was then placed in the mid-RV septum. When HBEGMs were not recordable during mapping, pacing was performed in unipolar fashion to identify the successful site. During implantation, attempts were made to obtain direct HBP (DHBP), but if para-Hisian pacing (PHP) with RV fusion was obtained, this position was accepted. In addition, if the patient had any evidence of significant His-Purkinje disease (left bundle branch block, infra-Hisian atrioventricular [AV] block), the lead was preferentially placed in the para-Hisian region to ensure RV myocardial capture in addition to HBP. Permanent HBP was considered successful, if the paced QRS morphology was identical to the baseline QRS morphology with or without RV fusion; in cases of preexisting bundle branch block or infra-Hisian conduction block, paced QRS may be narrower than the baseline QRS. Of note, a mapping catheter was not used to locate the HB and a back-up RV pacing lead was not used.

Definitions

DHBP was defined based on the original criteria published by Deshmukh et al.11 These include: (1) His-Purkinje-mediated cardiac activation and repolarization as evidenced by electrocardiographic (ECG) concordance of QRS and T-wave complexes, (2) the paced-ventricular interval was almost identical to the His-ventricular interval (Fig. 2), and (3) absence of QRS widening at a lower pacing output (high output pacing may cause widening of QRS due to myocardial capture).

PHP was defined as: (1) interval between pacing stimulus and QRS (stimulus-QRS interval) less than baseline His-ventricular interval or no isoelectric interval, (2) the electrical axis of the paced QRS must be concordant with the electrical
axis of the spontaneous QRS (Fig. 3), and (3) narrowing of QRS with higher output.

In addition to recording the presence or absence of current of injury in the HB, capture threshold of HB, sensing, and pacing impedance were recorded at implant, at 2 weeks, 2 months, and 1 year of follow-up. In patients with PHP, RV myocardial thresholds were also recorded. Fluoroscopy and procedure duration were recorded. Procedural complications including subsequent lead revisions were documented.

**Statistical Analysis**

Data are reported as mean ± standard deviation. All statistical tests were two-tailed; \( P < 0.05 \) was considered to indicate statistical significance.

**Results**

Permanent HBP was attempted in 67 consecutive patients during February 2013 to September 2013. RV lead implantation at the HB region was successful in 60 patients (90%) and was included in this study. HBP was unsuccessful in seven patients: inability to record HB (large right atrium) in two patients, infra-Hisian block with no HB capture in two patients, and high thresholds in three patients. Average age of the patients was 72 ± 15 years (41–92 years) and 55% of patients were men. The indication for the implantation of the pacemaker included sinus node dysfunction in 40% of patients and AV conduction disease in 60% of patients. Baseline patient characteristics are listed in Table I.

**Implant Outcomes**

Of the 60 patients, 22 (37%, group I) demonstrated evidence for HBIC at the final pacing site. In the remaining 38 patients (63%, group II), HBEGMs were recorded without any evidence for IC (Fig. 4). DHBP was achieved in 27 (45%) patients, while PHP was obtained in 33 (55%) patients. In group I, DHBP was achieved in 59% (n = 13) of patients compared to 37% (n = 14) of patients in group II. Mean procedural
Table I.
Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>HB Injury</th>
<th>HB Injury</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>22 (37%)</td>
<td>38 (63%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70 ± 14</td>
<td>73 ± 12</td>
</tr>
<tr>
<td>Male</td>
<td>11 (50%)</td>
<td>22 (57%)</td>
</tr>
<tr>
<td>HTN</td>
<td>17 (77%)</td>
<td>30 (78%)</td>
</tr>
<tr>
<td>DM</td>
<td>7 (31%)</td>
<td>13 (34%)</td>
</tr>
<tr>
<td>CAD</td>
<td>1 (5%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Sinus node dysfunction</td>
<td>10 (45%)</td>
<td>14 (37%)</td>
</tr>
<tr>
<td>Atroventricular block</td>
<td>12 (55%)</td>
<td>24 (63%)</td>
</tr>
<tr>
<td>Fluoroscopy duration (minutes)</td>
<td>8.9 ± 4</td>
<td>9.5 ± 3.5</td>
</tr>
<tr>
<td>Procedure duration (minutes)</td>
<td>64 ± 10</td>
<td>67 ± 13</td>
</tr>
<tr>
<td>DHBP</td>
<td>13 (59%)</td>
<td>14 (37%)</td>
</tr>
<tr>
<td>PHP</td>
<td>9 (41%)</td>
<td>24 (63%)</td>
</tr>
<tr>
<td>R wave (mV)</td>
<td>4.1 ± 2.8</td>
<td>5.4 ± 3.2</td>
</tr>
<tr>
<td>Pacing impedance (Ohms)</td>
<td>557 ± 97</td>
<td>639 ± 159</td>
</tr>
<tr>
<td>HB pacing thresholds (V @ 0.5 ms)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant</td>
<td>1.16 ± 0.4</td>
<td>1.75 ± 0.7</td>
</tr>
<tr>
<td>2 weeks</td>
<td>1.18 ± 0.5</td>
<td>1.82 ± 0.8</td>
</tr>
<tr>
<td>2 months</td>
<td>1.23 ± 0.6</td>
<td>1.93 ± 0.8</td>
</tr>
<tr>
<td>1 year (N = 41)</td>
<td>1.31 ± 0.6</td>
<td>1.98 ± 0.9</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; DHBP = direct His-bundle pacing; DM = diabetes mellitus; HB = His-bundle; HTN = hypertension; PHP = para-Hisian pacing.

Our study demonstrated that IC can be recorded in a high number (37%) of patients undergoing permanent HBP pacing. HBIC has not been reported in previous published reports of permanent HBP.11,14–17 The fixation of the lead into the myocardium causes injury to the tissue known as IC. IC is recorded during placement of the leads, presumably because of focally damaged cell membranes consequent to the trauma of electrode pressure against the endocardium. Previous studies have shown that the presence of

Discussion

Our study demonstrated that IC can be recorded in a high number (37%) of patients undergoing permanent HBP pacing. HBIC has not been reported in previous published reports of permanent HBP.11,14–17 The fixation of the lead into the myocardium causes injury to the tissue known as IC. IC is recorded during placement of the leads, presumably because of focally damaged cell membranes consequent to the trauma of electrode pressure against the endocardium. Previous studies have shown that the presence of
an adequate IC at the time of an active-fixation pacing or defibrillation lead placement correlates with adequate lead fixation and excellent pacing thresholds.\textsuperscript{18,19}

Permanent HBP has traditionally been associated with high-pacing thresholds leading to placement of a back-up RV pacing lead.\textsuperscript{12,14,16,20} Recent reports suggest pacing in a para-Hisian location may be associated with improved pacing threshold compared to direct HBP.\textsuperscript{17} In this study, IC at the HB was associated with significantly lower pacing thresholds compared to patients in whom IC was not recorded at the HB. In fact, we recorded HBP thresholds less than 1 V @ 0.5 ms in a significant number of patients (eight of 22, 36\%) in group I compared to only four patients (11\%) in group II. It is important to note that more patients in group I (59\%) had DHBP suggestive of lead placement in the tricuspid valve annulus compared to predominant para-Hisian location (63\%) in group II. The HBP thresholds were lower in group I, irrespective of the location of the lead and type of HB capture (DHBP or PHP). In a large series of permanent HBP using the Medtronic 3830 pacing lead, reported by Zanon et al.,\textsuperscript{17} the implantation pacing threshold was 2.5 ± 2.3 V (0.5 ms) in the DHBP group compared to 1.3 ± 1.1 V (0.5 ms) in the PHP group. Kronborg et al.\textsuperscript{20} also reported pacing thresholds at implantation of 2.3 ± 1 V in patients with DHBP compared to 1.7 ± 1.5 V in patients with PHP. They did not report recording of IC at the HB in their series. Most of the recent HBP series\textsuperscript{15,17,20} utilized the deflectable delivery sheath (SelectSite\textsuperscript{\textregistered}, model C304, Medtronic Inc.) for implantation of the HBP lead. This sheath has unidirectional deflection and allows it to easily identify the HB location. However, the fixation of the lead may be inadequate due to the sheath being aligned parallel to the septum. In our series, we utilized the C315 HIS fixed-curve sheath that has an orthogonal distal curve that orients the lead perpendicular to the cardiac tissue. This sheath provides a greater degree of stability and allows the lead to be fixed adequately to the cardiac tissue. This could explain why a significant number of patients in our series had excellent pacing thresholds compared to prior reports.

\textbf{Figure 4.} The top panel shows the baseline 12-lead electrocardiogram of a patient with a complete heart block and wide complex escape rhythm of LBBB morphology. The middle panel shows the intracardiac electrogram from the permanent His-bundle pacing lead at the time of implantation. Note the far-field atrial electrogram (A) and the sharp His (H) potential without injury current. S represents pacing stimulus from temporary ventricular pacing. The bottom panel shows atrial-sensed ventricular pacing. In this panel, the pacing spike is immediately followed by QRS complexes with evidence of fusion from ventricular and His-bundle capture with recruitment.
While HBIC was recorded in a significant number of patients (37%) in our series, IC was not recorded in 63% of patients. It is possible that when IC is recorded, the lead placement is directly on the HB causing local IC. When IC is not recorded, it is likely the lead placement is close to the HB without penetrating it or possibly the HB is located deeper to the lead location. Improvements in lead designs can potentially improve HBP outcomes. While IC recording at the HB can cause theoretical concern of damage to HB and worsening AV conduction, we did not see any acute worsening or progression of HB conduction disease in this series with medium-term follow-up of 1 year. In our experience, during implantation of more than 350 permanent HBP leads, two patients developed transient infra-Hisian AV block that resolved within 10 minutes. Two patients in this series developed transient RBBB that resolved within 24 hours. Rare development of persistent RBBB has also been reported and in our experience HBP generally improves and customizing the implantation tools (lead and delivery system) may help achieve superior HBP outcomes.

Limitations

While Zanon et al. have reported long-term characteristics of HBP to be stable at 24 months, it is unclear if IC at the HB can lead to increase in fibrous reaction causing unacceptable increase in pacing thresholds. While our medium-term follow-up does not support such concerns, long-term follow-up is necessary to confirm stable chronic pacing thresholds. While statistically significant, the differences in pacing thresholds may not be clinically significant.

Conclusions

This study records IC at the HB during permanent HBP. IC at the HB was recorded in 37% of patients undergoing successful permanent HBP. HBIC is associated with significantly lower pacing thresholds compared to patients in whom IC is not recorded. IC at the HB may be a marker for superior HBP outcomes.

References
