Circulation Reports
Circ Rep 2024; **6:** 294–302
doi:10.1253/circrep.CR-24-0035

ORIGINAL ARTICLE
Arrhythmia/Electrophysiology

Long-Term Outcomes in Patients With Relatively High His-Bundle Capture Threshold After Permanent His-Bundle Pacing

— A Multicenter Clinical Study —

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Background: Outcomes in patients with relatively high His-bundle (HB) capture thresholds at implantation are unknown. This study aimed to compare changes in the HB capture threshold and prognosis between patients with a relatively high threshold and those with a low threshold.

Methods and Results: Forty-nine patients who underwent permanent HB pacing (HBP) were divided into two groups: low (<1.25 V at 1.0 ms; n=35) and high (1.25–2.49 V; n=14) baseline HB capture threshold groups. The HB capture threshold was evaluated at implantation, and after 1 week, 1, 3, and 6 months, and every 6 months thereafter. HB capture threshold rise was defined as threshold rise ≥1.0 V at 1.0 ms compared with implantation measures. We compared outcomes between the groups. During a mean follow-up period of 34.6 months, the high-threshold group showed a trend toward a higher incidence of HB capture threshold of ≥2.5 V (50% vs. 14%; P=0.023), HBP abandonment (29% vs. 8.6%; P=0.091), lead revision (21% vs. 2.9%; P=0.065), and clinical events (all-cause death, heart failure hospitalization, and new-onset or progression of atrial fibrillation; 50% vs. 23%; P=0.089) than the low-threshold group. A baseline HB capture threshold of ≥1.25V was an independent predictor of clinical events.

Conclusions: A relatively high HB capture threshold is associated with increased risk of HBP abandonment, lead revision, and poor clinical outcomes.

Key Words: Conduction system pacing; His-bundle capture threshold; His-bundle pacing; Lead abandon; Lead revision

His-bundle pacing (HBP) delivers physiological ventricular activation via an intrinsic conduction system. It prevents mechanical and electrical dyssynchrony relevant to conventional right ventricular (RV) pacing. In a prior observational study, permanent HBP potentially reduced the risk of death and heart failure (HF) hospitalization in patients with atrioventricular block compared with RV pacing.[1] Previous studies have also reported that HBP is superior to biventricular pacing in the recovery of cardiac function in patients with reduced left ventricular ejection fraction (LVEF) and dyssynchrony.[2–5]

However, permanent HBP is associated with several concerns during the chronic phase. Significantly, a His-bundle (HB) capture threshold rise during the follow-up period carries risks of early battery consumption and lead revision.[6] To prevent the risk of a HB capture threshold rise, it is essential to implant the HBP lead in a position where the threshold at the time of implantation is as low as possible.[6] A HB capture threshold of <2.0–2.5 V at implantation is generally used as the criterion for a successful HBP,[7–9] although sometimes patients with a relatively high HB capture threshold of 1.0–2.0 V during HBP implanta-

Received April 5, 2024; revised manuscript received June 3, 2024; accepted June 18, 2024; J-STAGE Advance Publication released online July 12, 2024 Time for primary review: 24 days

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ISSN-2434-0790

tion are encountered despite several attempts to achieve a lower HB capture threshold. This population may be at further risk of a HB capture threshold rise during follow up. However, the prognosis and clinical outcomes in patients with relatively high HB capture thresholds remain unclear.

Thus, the present study aimed to compare the changes in HB capture thresholds and long-term outcomes between patients with relatively high HB capture thresholds and those with low HB capture thresholds in a multicenter study.

Methods

Study Population

The study population was retrospectively recruited from a database of pacemaker devices at two institutions, Chukyo Hospital and Nagoya University Hospital, Japan. Patients who underwent permanent HBP between July 2017 and April 2020 at Chukyo Hospital and between March 2018 and September 2021 at Nagoya University Hospital were included in this study. Of the whole population, patients with a baseline HB capture threshold of <2.5 V at 1.0 ms were included in the study. The exclusion criteria were as follows: (1) patients with a HB capture threshold of ≥2.5 V at implantation; and (2) patients who met the indication for cardiac resynchronization therapy due to left bundle branch block. The indications for pacemaker implantation were in accordance with recent guidelines.[10,11] Informed consent was obtained from all patients prior to the procedure. The study protocol was approved by the institutional review board of each hospital. This study complied with the principles of the Declaration of Helsinki.

HBP Lead Implantation

Details of the HBP lead implantation have been described previously.[12,13] Briefly, a specific lead (SelectSecure™ 3830; Medtronic Inc., Minneapolis, MN, USA) and a fixed curve-delivery sheath (C315HIS delivery catheter; Medtronic Inc., Minneapolis, MN, USA) were used for the implantation. The delivery sheath was inserted toward the RV and advanced into the anterior mid-septum. Unipolar electrograms from the distal tip of the lead were recorded using an electrophysiological recording system at a sweep speed of 100 mm/s and a pacing system analyzer (model 2290; Medtronic Inc., Minneapolis, MN, USA) identified the HB electrogram. The high- and low-pass filters were set to 30 and 500 Hz, respectively. When a HB electrogram was identified, pacing stimuli from the lead were applied to ensure HB capture. Pacing output was gradually reduced from starting at 5.0 V at 1.0 ms to the lowest output that could capture the HB or RV myocardium while continuously monitoring the intracardiac electrograms and pacing morphology on a surface 12-lead electrocardiogram to determine whether the HB capture was successful or not. HBP was further classified into selective and nonselective HBP. The pacing pattern of selective HBP, nonselective HBP, or RV pacing was assessed based on the recent criteria proposed by a multicenter HBP collaborative working group.[14] If the HB electrogram was not confirmed, pace-mapping was performed on the HB region, and we judged whether HB was captured based on the pacing morphology and intracardiac electrograms.[13] The site of the atrioventricular block was carefully evaluated by assessing the presence of the HB electrogram on the unipolar electrogram, which was obtained intraoperatively from the distal tip of the lead. When a His-ventricular or intra-Hisian block was identified, the block site was classified as an infra-nodal block. In the absence of an infra-nodal block finding, the site of block was determined as an atrioventricular nodal block.[13]

According to previous reports, we tried to achieve a HB capture threshold of <2.5 V at 1.0 ms.[7,8] The injury current of the HB was evaluated after fixation of the lead using a pacing analyzer system.[15] The absence of a rate-dependent conduction block from HB to ventricle was confirmed by a high-rate HBP of 120 beats/min.[7] When the pacing parameters were acceptable, the delivery sheath was gently retracted, leaving sufficient lead slack. The atrial lead was fixed to the right atrial appendage or atrial septum. At least 1 pacemaker device and electrophysiology expert in both facilities undertook or supervised all procedures.

Follow up and Outcomes

Patients were followed up at 1 week, 1, 3, and 6 months after implantation, and every 6 months thereafter in the outpatient device clinics at each institution. The HB and RV capture thresholds, R-wave amplitude, and lead impedance were evaluated at every visit using a pacing system analyzer and a surface electrocardiogram. We generally set the pacing output according to the RV threshold plus a safety margin (i.e., ≥1.5 times the RV threshold). However, in some patients with selective HBP and a high RV threshold at ≥2.5–3.0 V, the pacing output was set at 1.5–2.0 times HB capture threshold for longer pacemaker battery life. The HB capture threshold rise was defined as a threshold rise of 1.0 V or more (at a pulse width of 1.0 ms) from baseline during follow up. Adverse events including lead revision and abandoned permanent HBP were assessed during follow up. Although there were no strict criteria for HBP abandonment, we typically decided to abandon permanent HBP in patients with a continuous HB capture threshold of >3.0 V with no recovery. Composite clinical events included all-cause death, hospitalization for HF, and new-onset or progressive atrial fibrillation (AF). New-onset AF was defined as the first episode of AF persisting for more than 1 h after implantation in patients without a history of AF. AF progression was defined as a relative increase in AF burden of >25% from baseline in patients with a history of AF.[16] The position of the HBP lead was visually assessed using postoperative echocardiography or computed tomography with respect to the distal tip of the lead fixed to the interventricular septum beyond the tricuspid valve (atrial side or RV side), if applicable.[13]

The study population was divided into two groups according to the HB capture threshold at implantation: the low-threshold group included patients with a baseline HB capture threshold of <1.25 V, and the high-threshold group included those with a HB capture threshold of 1.25–2.49 V. Outcomes and prognosis after HBP were compared between the two groups.

Statistical Analysis

Continuous data were presented as mean±standard deviation or median (first and third quartiles), and categorical values were presented as numbers and percentages. Differences in the numeric values of the two groups were analyzed using the Student's t-test for normally distributed data and the Mann-Whitney U test for data not normally distributed. Categorical variables were analyzed using

Fisher's exact test or the chi-square test. Survival curves were generated using Kaplan-Meier estimates, and time-to-event analyses were performed using the log-rank test. Univariate and multivariate Cox regression analyses were performed to examine the predictors of outcomes. Significant factors in the univariate Cox regression analysis were included in the multivariate model using the forward stepwise method. For logistic regression analysis, factors with P values <0.10 in the univariate analysis were entered into a multivariate logistic regression model. Statistical significance was set at P<0.05. All statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA).

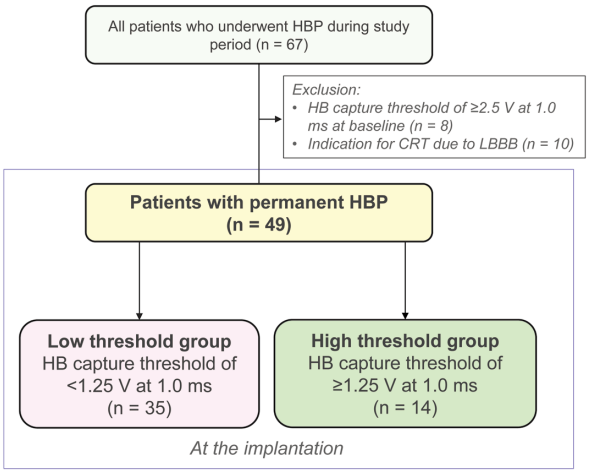

Figure 1. Flow diagram of the study population. CRT, cardiac resynchronization therapy; HB, His bundle; HBP, His-bundle pacing; LBBB, left bundle branch block.

Results

Baseline Characteristics and Procedural Results in the Study Population

Among 67 patients who underwent permanent HBP, 18 patients were excluded due to a high HB capture threshold of ≥2.5 V (n=8) or an indication for cardiac resynchronization therapy (n=10). A total of 49 patients was included in this study. Of them, 35 patients were included in the low-threshold group and the remaining 14 were included in the high-threshold group (**Figure 1**). The baseline characteristics of the two groups are presented in **Table 1**. The mean age in the total population was 77.2±8.2 years, and 29 (59%) patients were female. The indications for pacemaker placement were atrioventricular block and sick sinus syndrome in 38 (78%) and 11 (22%) patients, respectively. Eleven (22%) patients had a history of HF. The baseline LVEF was 62.0±11.0%. There were no significant differences in baseline characteristics between the two groups, except for chronic kidney disease (estimated glomerular filtration rate of <60 mL/min/1.73 m^2) with a significantly higher prevalence in the high-threshold group than the low-threshold group (57% vs. 17%; P=0.012).

Thirty-six and 13 patients were enrolled from Chukyo Hospital and Nagoya University Hospital, respectively. The success rate of a baseline HB capture threshold of <1.25 V did not significantly differ between the two facili-

Table 1. Baseline Characteristics of the Low and High HB Capture Threshold Groups

Parameter	Total (n=49)	HB capture threshold <1.25 V (n=35)	HB capture threshold ≥1.25 V (n=14)	P value
Age (years)	77.2±8.2	76.7±7.8	78.4±9.4	0.539
Female sex	29 (59)	21 (60)	8 (57)	0.854
Indication for pacemaker				
SSS	11 (22)	9 (26)	2 (14)	0.475
AVB	38 (78)	26 (74)	12 (85)	0.475
2:1 or advanced AVB	16 (33)	11 (31)	5 (36)	0.999
Complete AVB	18 (18)	13 (37)	5 (36)	0.925
Escape rhythm	19 (39)	15 (43)	4 (29)	0.354
QRS duration (ms)	116.9±31.9	115.2±31.7	121.1±33.1	0.582
History of AF	14 (29)	10 (29)	4 (29)	0.999
Paroxysmal AF	8 (16)	7 (20)	3 (8.6)	0.999
Persistent AF	6 (12)	1 (7.1)	3 (21)	0.999
Hypertension	32 (65)	25 (71)	7 (50)	0.193
Diabetes	13 (27)	9 (26)	4 (29)	0.999
CKD	14 (29)	6 (17)	8 (57)	0.012
CAD	6 (12)	5 (14)	1 (7.1)	0.659
HF	11 (22)	8 (23)	3 (21)	0.999
BNP levels (pg/mL)	168 (64–400)	129 (62–326)	373 (119–379)	0.299
LVEF (%)	62.0±11.0	62.4±10.9	61.0±11.7	0.690
<40%	4 (8.3)	2 (5.9)	2 (14)	0.569

Unless indicated otherwise, data are presented as n (%), mean±SD, or median (first and third quartiles). AF, atrial fibrillation; AT, atrial tachycardia; AV, atrioventricular; AVB, atrioventricular block; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CKD, chronic kidney disease; HB, His bundle; HBP, His-bundle pacing; HF, heart failure; LVEF, left ventricular ejection fraction; SSS, sick sinus syndrome.

Table 2. Comparison of Procedural Characteristics and Pacing Parameters Between the Low and High HB Capture Threshold Groups

Parameter	Total (n=49)	HB capture threshold <1.25 V (n=35)	HB capture threshold ≥1.25 V (n=14)	P value
Site of block				
AV nodal	11 (22)	9 (26)	2 (14)	0.475
Infra-nodal	21 (43)	14 (40)	7 (50)	0.523
Unknown site	6 (16)	3 (25)	3 (12)	0.357
Type of HBP (at baseline)				
Selective HBP	30 (61)	23 (66)	7 (50)	0.308
Non-selective HBP	19 (39)	12 (34)	7 (50)	0.308
Paced QRS duration (from onset to offset; ms)	124.0±22.2	125.5±22.7	119.6±20.9	0.459
HB injury current	18 (37)	11 (31)	7 (50)	0.223
R wave amplitude (mV)	4.3±3.6	4.6±3.9	3.6±2.7	0.363
HB capture threshold, V at 1.0 ms	0.99±0.49	0.74±0.21	1.63±0.39	<0.001
RV capture threshold, V at 1.0 ms	1.50±1.02	1.41±0.97	1.71±1.14	0.353
Procedure time (min)	148.4±36.0	147.0±35.9	152.3±37.8	0.682
HBP lead location*				
Atrial side	12 (26)	9 (27)	3 (25)	0.621
RV side	34 (69)	25 (74)	9 (75)	0.621

Unless indicated otherwise, data are presented as n (%), or mean±SD. *HBP lead location was identified using echocardiography or computed tomography in 46 patients. RV, right ventricular. Other abbreviations as in Table 1.

Table 3. Clinical Outcomes After Implantation in the Low and High HB Capture Threshold Groups

Parameter	Total (n=49)	HB capture threshold <1.25 V (n=35)	HB capture threshold ≥1.25 V (n=14)	P value
Ventricular pacing burden (%)	99 (36–100)	99 (46–100)	89 (1.8–99)	0.391
HB capture threshold rise ≥1.0 V at 1.0 ms	13 (27)	9 (26)	4 (29)	0.999
Time to HB capture threshold rise ≥1.0 V (months)	8.1±9.0	11.1±9.3	1.3±1.3	0.065
Occurrence of HB capture threshold of ≥2.5 V at 1.0 ms during follow up	12 (25)	5 (14)	7 (50)	0.023
Time to occurrence of HB capture threshold of ≥2.5 V (months)	9.0±11.5	19.2±8.9	7.6±13.2	0.121
Abandoned permanent HBP	7 (14)	3 (8.6)	4 (29)	0.091
Time to abandon HBP (months)	25.7±18.7	34.0±18.3	19.5±18.9	0.356
Lead revision	4 (8.2)	1 (2.9)	3 (21)	0.065
Time to lead revision (months)	44.5±9.9	55.0	41.0±8.5	0.292
Clinical endpoints*	15 (31)	8 (23)	7 (50)	0.089
HF hospitalization	2 (4.1)	1 (2.9)	1 (7.1)	0.494
All-cause death	9 (18)	5 (14)	4 (29)	0.254
Cardiovascular death	3 (6.1)	1 (2.9)	2 (14)	0.193
New-onset or progression of AF	7 (14)	3 (8.6)	3 (21)	0.334

Unless indicated otherwise, data are presented as n (%), or mean±SD. *Clinical endpoints were defined as hospitalization for HF, death, and new onset or progression of AF. Abbreviations as in Table 1.

ties (24 [67%] vs. 11 [85%] patients; P=0.297, respectively).

Table 2 compares the procedural characteristics and pacing parameters between the low and high HB capture threshold groups. Selective HBP was confirmed in 30 (61%) patients. The mean HB capture threshold was 0.74±0.21 V in the low-threshold group, and 1.63±0.39 V in the high-threshold group. The site of atrioventricular block, paced QRS duration (from onset to offset of QRS complex), prevalence of current His injury, R-wave amplitude, RV capture threshold at implantation, and procedure time did not significantly differ between the two groups (**Table 2**).

Clinical Outcomes After HBP

During the mean follow-up period of 34.6 months, a HB capture threshold rise (≥1.0 V) occurred in 13 (27%) patients. **Table 3** shows the clinical outcomes after implantation. The incidence of HB capture threshold rise did not differ between the low- and high-threshold groups (9 [26%] vs. 4 [29%] patients; P=0.99; **Table 3**). The mean time to HB capture threshold rise was 1.3±1.3 months in the high-threshold group, which was shorter than that in the low-threshold group (9.0±11.5 months; P=0.065). The HB capture threshold of ≥2.5 V at 1.0 ms was seen in 12 (25%) patients during follow up. The high-threshold group showed

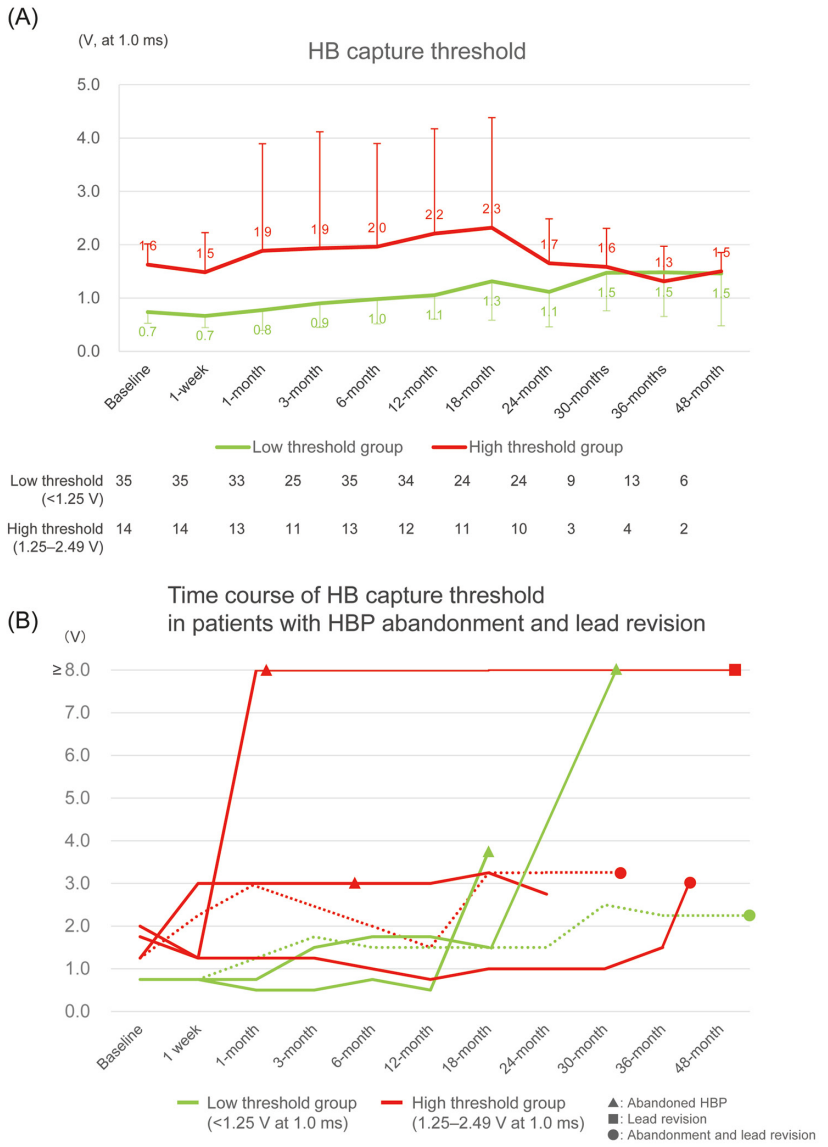

Figure 2. Changes in the His bundle (HB) capture threshold in the low-threshold and high-threshold groups. Time course of HB capture thresholds after HB pacing (HBP) lead implantation (**A**). Changes in HB capture thresholds in patients resulting in HBP abandonment and lead revision (**B**). Seven and 4 patients had HBP abandonment and lead revision, respectively.

a higher incidence of HB capture threshold of ≥2.5 V compared with the low-threshold group (7 [50%] vs. 5 [14%]; P=0.023). The time course of the HB capture threshold after permanent HBP is shown in **Figure 2A**. Both the high- and low-threshold groups demonstrated a gradual rise in the HB capture threshold after implantation. However, after 18 months, the mean threshold decreased in the high-threshold group, probably due to the exclusion of patients with high thresholds requiring HBP abandonment and lead revision.

Permanent HBP was abandoned in 7 (14%) patients. Among them, four (8.2%) required lead revision (switching to left bundle branch area pacing). The remaining 3 patients had low and stable RV capture thresholds; hence, they did not require lead revisions. Among the 4 patients who required lead revisions, 1 patient with sick sinus syndrome abandoned permanent HBP and switched to the AAI pacing mode due to the loss of HB capture 2 months after implantation. After 49 months, the patient underwent lead revision during battery replacement. The remaining 3 patients had a high HB capture threshold, and battery depletion occurred at 32, 42, and 55 months after implantation. Most cases of HBP abandonment and lead revision were observed in the high-threshold group (29% vs. 8.6% for abandoned HBP; P=0.091; 21% vs. 2.9% for lead revision; P=0.065; **Table 3**). The mean time from implantation to HBP abandonment and lead revision were 25.7±18.7 months and 44.5±9.9 months, respectively. There were no significant differences in the time to HBP abandonment or lead revision between the two groups. The time course of the HB capture threshold in patients who required HBP abandonment and lead revision is shown in **Figure 2B**.

Kaplan-Meier survival curve analyses for HBP abandonment and lead revision demonstrated a trend toward worse prognosis in the high-threshold group compared with the low-threshold group (log-rank P=0.085 and log-rank P=0.042, respectively; **Figure 3**).

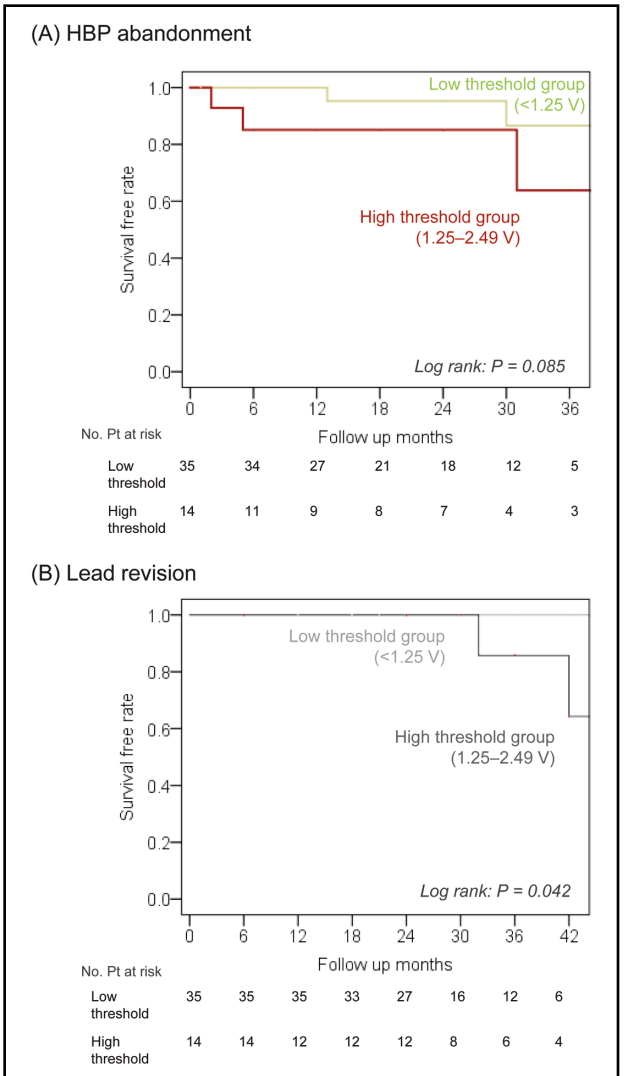

Figure 3. His-bundle pacing (HBP) abandonment and lead revision during the follow-up period. Comparison of the Kaplan-Meier survival curves of HBP abandonment (**A**) and lead revision (**B**) between the low- and high-threshold groups.

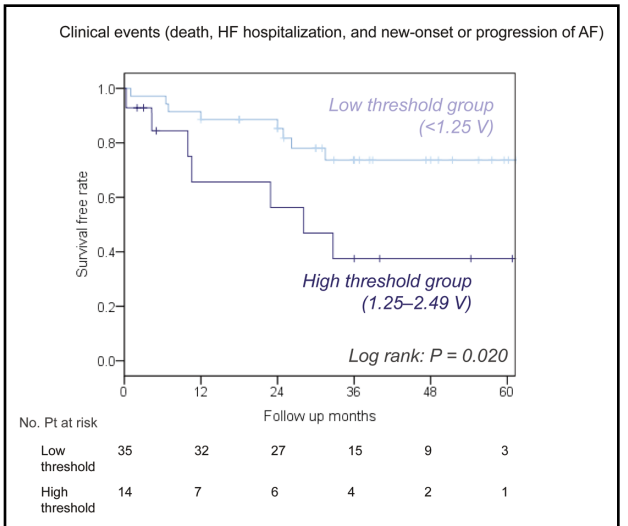

Figure 4. Comparison of Kaplan-Meier survival curves of clinical events after His-bundle pacing (HBP) lead implantation between the low- and high-threshold groups. Clinical events included all-cause death, hospitalization for heart failure (HF), and new-onset or progression of atrial fibrillation (AF).

Prognosis After HBP Lead Implantation

Hospitalization for HF, all-cause death, and new-onset or progression of AF occurred during follow up in 2, 9, and 7 patients, respectively. The composite clinical endpoint occurred more frequently in the high-threshold group than in the low-threshold group (7 [50%] vs. 8 [23%] patients; P=0.089; **Table 3**). The Kaplan-Meier survival curves show a significantly worse prognosis for clinical outcomes after HBP in the high-threshold group compared with the low-threshold group (log-rank P=0.020; **Figure 4**). Patients who reached clinical endpoints continued HBP, except for 1 patient in the low-threshold group because of the need for HBP abandonment and revision.

Univariate Cox regression analysis demonstrated that age, history of HF, and a baseline HB capture threshold of ≥1.25 V were significantly associated with increased risks of composite clinical endpoints. Subsequent multivariate analysis showed that a history of HF (hazard ratio 4.898; 95% confidence interval 1.764–13.602; P=0.002) and baseline HB capture threshold of ≥1.25 V (hazard ratio 3.020; 95% confidence interval 1.087–8.385; P=0.034) were independent predictors for the composite endpoints (**Table 4**).

Predictors of a High HB Capture Threshold of ≥1.25 V at Baseline

A univariate logistic regression model was conducted to investigate which patient characteristics were attributed to a baseline HB capture threshold of ≥1.25 V (**Supplementary Table**). Subsequent multivariate analysis incorporating possible baseline characteristics of a history of chronic kidney disease and B-type natriuretic peptide levels >100 pg/mL demonstrated that a history of chronic kidney disease was independently associated with a baseline HB capture threshold of ≥1.25 V (**Supplementary Table**).

Discussion

This 2-institution observational study evaluated the outcomes and prognosis of patients with a relatively high baseline HB capture threshold. A HB capture threshold of 1.25–2.49 V at implantation was noted in 14 (29%) of 49 enrolled patients who underwent permanent HBP. Although the HB capture threshold rise of ≥1.0 V occurred equivalently between the two groups, the incidence of the HB capture threshold of ≥2.5 V during follow up was significantly higher in the high-threshold group. There was a trend toward a higher incidence of HBP abandonment, lead revision, and clinical events after HBP in the high-threshold group compared with the low-threshold group. The baseline HB capture threshold of ≥1.25 V was independently associated with increased risks of clinical events using a multivariate analysis. In addition, a history of chronic kidney disease was correlated with a relatively high HB capture threshold of 1.25–2.49 V at implantation.

The HB capture threshold rise during follow up is a major concern in permanent HBP. The HB capture thresh-

Table 4. Univariate and Multivariate Cox Proportional Hazard Models of Clinical Endpoints

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)	1.098 (1.017–1.186)	0.017		
Female sex	1.290 (0.440–3.778)	0.643		
SSS	0.213 (0.028–1.625)	0.136		
Hypertension	0.748 (0.266–2.103)	0.581		
CAD	1.758 (0.495–6.243)	0.383		
History of HF	5.061 (1.816–14.109)	0.002	4.898 (1.764–13.602)	0.002
Baseline LVEF <40%	1.831 (0.412–8.125)	0.427		
Infra-nodal block	1.631 (0.591–4.505)	0.345		
Non-selective HBP	0.692 (0.220–2.174)	0.528		
Paced QRS duration (ms)	1.007 (0.982–1.034)	0.584		
Baseline HB capture threshold of ≥1.25 V	3.132 (1.132–8.664)	0.028	3.020 (1.087–8.385)	0.034
Ventricular pacing burden (%)	1.006 (0.992–1.022)	0.397		

CI, confidence interval; HR, hazard ratio. Other abbreviations as in Table 1.

old rise has been reported to occur in 5.7–30.0% after permanent HBP.[1,6,8,13,17–22] Subsequently, HBP abandonment and lead revision were required in 4.3–6.0% and 1.8–11.0% of the patients, respectively.[1,6,8,13,17–22] These events occurred more frequently in previous reports with a long-term follow-up of >1 year.[6,17,20,23] Our outcomes are in line with that of previous studies. Notably, several patients experienced HBP abandonment and lead revision over 1 year after implantation with a mean duration of 25.7 and 44.5 months, respectively. As most studies primarily focused on the benefits of HBP in a short-term follow up via the clinical improvement of cardiac function and mechanical synchronization, there may be another concern regarding early battery consumption and HB capture threshold rise in the decades following the introduction of HBP in clinical events.[24] The pacemaker system remains with patients for a long period of 10–30 years. Thus, long-term safety and the feasibility of the pacing system are crucial in patients undergoing pacemaker implantation.[25]

The present study was unique because it focused on a specific population with relatively high baseline HB capture thresholds. Ideally, the HB capture threshold should be lower as often as possible. However, because of the narrow targeting region of the HB and injured site of the atrioventricular block, we reluctantly decided to observe and continue HBP with a relatively high HB capture threshold of 1.0–2.0 V in clinical cases. This situation was more common in the present study, with one-third of patients assigned to the high HB capture threshold group. Another previous study demonstrated that only 25% of patients had a HB capture threshold of <1.0 V at implantation, indicating that permanent HBP is challenging because of the narrow target HB region and its anatomical complexity. No studies have focused on the patients with a relatively high HB capture threshold so far; however, a recent study showed that a higher HB capture threshold at baseline (2.0±1.1 vs. 1.1±0.9 V) was an independent predictor for further threshold rise.[13] Generally, a high HB capture threshold at implantation is likely due to procedural factors such as inappropriate lead placement proximal to the block site or micro-dislodgement after lead fixation. These factors may be associated with an early threshold rise.[17] Conversely, at the chronic phase, development of local fibrosis, progression of conduction system disturbance, and decrease in a virtual electrode polarization might be relevant for the mechanism of the HB capture threshold rise, regardless of the extent of baseline thresholds.[12,24] The threshold rise can be critical, especially in patients with a high baseline threshold, even if the same extent of the threshold rise occurs, easily linking to the risk of lead abandonment and revision as demonstrated in the present study. Thus, careful observation of pacing parameters should be performed in patients with relatively high baseline HB capture thresholds, even though the HB capture threshold is stable in the early phase.

In the present study, the high-threshold group showed a higher incidence of composite clinical endpoints than the low-threshold group, possibly because of differences in baseline characteristics between the two groups. The high baseline HB capture threshold might indicate the involvement of various diseases, such as chronic kidney disease, with damaged tissue and fibrosis. Such pathologies behind the high-threshold group might be linked to a poor clinical prognosis. In other words, the poor prognosis might be caused by the complicated diseases indirectly represented by the high HB capture threshold. For instance, chronic kidney disease facilitated the onset of myocardial fibrosis; this association was well demonstrated in a cardiac magnetic resonance imaging study.[26] However, a direct relationship between local fibrosis in the HB area and the high-pacing capture threshold should be validated in a further study. Selection of permanent HBP for these subsets of patients should be carefully considered, as this procedure is likely to result in a high HB capture threshold at implantation. Otherwise, an additional backup RV lead might be required in these populations to mitigate the risk of high pacing capture thresholds;[27] alternately, left bundle branch area pacing, developed with a higher success rate and a lower pacing threshold than HBP, may be considered.[28–30] Nonetheless, in patients requiring conduction system pacing, HBP might be the better option with the benefit of synchronized RV activation when left bundle branch area pacing cannot be achieved for some reason (e.g., failure of septal advancement).[30,31] Forthcoming evidence and large-scale studies with long-term follow up are required to determine a first-choice or an appropriate population to undergo HBP or left bundle branch area pacing.

Study Limitations

This was a retrospective, observational, non-randomized study with a small sample size. Although HBP lead implantation was performed in line with previous reports,[12] the procedure was not strictly standardized between the two institutes and different operators. The learning curve of HBP due to the different numbers of cases experienced by multiple operators might have affected the outcomes. The present study sorted the population based on the HB capture threshold at baseline, and the threshold might have temporarily increased due to the local inflammatory response immediately after lead fixation, and then fallen to a plateau level when stable.[32] This inflammatory response or temporal tissue edema from injury might decrease and stabilize the HB capture threshold at the chronic phase on some occasions, which might have led to a bias of overestimating the threshold at the acute phase in the present study. In addition, the cutoff point of the threshold of 1.25 V was determined based on half of the maximum threshold of 2.49 V. Ideally, the optimal cutoff value of the capture threshold should have been evaluated by an original analysis of this study cohort with an adequate sample. The present study also included patients with sick sinus syndrome who did not generally require ventricular pacing; therefore, the prevalence of lead revision might have been underestimated. The follow-up period was inconsistent and varied in each case, although all patients were tracked using a remote monitoring system and medical records.

Conclusions

Patients with a relatively high HB capture threshold at implantation had a greater incidence of a HB capture threshold >2.5 V, HBP abandonment, lead revision, and clinical events during follow up than those in the low-threshold group, despite a similar incidence of HB capture threshold rise of ≥1.0 V. Preoperative patient stratification and careful follow up after HBP implantation are required in these patients.

Acknowledgments

None.

Sources of Funding

This study was funded by Medtronic Japan and a Grant-in-Aid for Young Scientists (19K17558).

Disclosures

S.Y. and R.S. are affiliated with a department sponsored by Medtronic Japan. T.M. is a member of *Circulation Reports*' Editorial Team. The other authors have no conflicts of interest to disclose.

IRB Information

The present study was approved by the Human Research Ethics Committee of Nagoya University Hospital (No. 2018-0402).

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
https://doi.org/10.1253/circrep.CR-24-0035