Predictive factors for increase in pacing threshold after transcatheter pacing system implantation owing to micro-dislodgement

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Abstract

Introduction: Achievement of a favorable pacing threshold with a Micra transcatheter pacing system (Micra-TPS) is important for reducing battery depletion; in some cases, the threshold increases shortly after the device is implanted, and a higher pacing threshold may be required. This study aimed to define the causes and predictors of the increase in pacing threshold observed shortly after Micra-TPS implantation. Methods and Results: The study included 64 consecutive patients who underwent Micra-TPS implantation between 2017 and 2020. Patients were divided into two groups depending on their pacing threshold, namely, the increased pacing threshold (IPT) group (threshold increased by [?]0.5 V/0.24 msec within 1 month of implantation) and the stable pacing threshold (SPT) group. Excluding 4 patients we were unable to conduct follow-up on, 9 of the 60 remaining patients (15%) were in the IPT group and 51 (85%) were in the SPT group. The IPT group had significantly lower implant impedance values and higher implant thresholds than the SPT group: 582 ± 59 vs 755 ± 167 Ω (P <0.001) and 1.29 ± 0.87 vs 0.71 ± 0.40 V/0.24 msec (P =0.014), respectively. Implant impedance and threshold may serve as predictors of a threshold increase after implantation (area under the curve: 0.737–0.943 and 0.586–0.926, respectively). Conclusion: An increased pacing threshold was noted shortly after Micra-TPS implantation owing to micro-dislodgement because of insufficient anchoring of the device on the myocardium. Impedance >660 Ω and threshold <1.0 V/0.24 msec may be predictive factors for an increased pacing threshold.

INTRODUCTION

Permanent pacemaker implantation is the only established treatment for bradyarrhythmia that contributes to improved life prognosis as well as quality of life. In the last 10 years, 50,000 implantable pacemakers have been introduced in Japan every year, and more than 60,000 cases have been recorded annually in recent years. In the United States, more than 350,000 pacemakers are implanted annually, and this number has doubled in the last 30 years.[1] Elderly people are more prone to bradyarrhythmias, and it is estimated that more patients will need more pacemaker implants as the aging society advances. On the other hand, it has been reported that lead trouble and subcutaneous pocket complications, which are complications of conventional transvenous pacemakers, are present in 7% and 11% of cases at 5 years after implantation, respectively.[2] The introduction of transcatheter pacing systems (TPSs) was expected to reduce lead and pocket complications. In previous studies, the TPS was shown to be an effective and safer option, reducing the common complications from conventional pacemakers and providing a more stable pacing threshold.[3-6] However, some cases require a

higher pacing threshold, because the latter increases post-implantation, which subsequently decreases battery longevity and increases the risk of an adverse heart event due to pacing issues. Predictors that require long-term high pacing thresholds have been reported,[6]but the cause of increased thresholds after implantation has not been clarified. Most of the rapid increases in pacing threshold occurred within one month of implantation, but there were few cases where the threshold was increased in the medium-to-long term.[7-9]Therefore, we hypothesized that it would be possible to obtain a stable pacing threshold in the long term if the increase could be avoided in the short term.

In this study, we investigated the clinical significance of early increased pacing threshold by comparing patient background characteristics, procedure-related indications, and threshold transition.

METHODS

Subjects

The study included 64 consecutive patients who underwent Micra-TPS (Medtronic, Dublin, Ireland) implantation using the transfemoral vein approach at our hospital between October 2017 and April 2020. The inclusion criteria were successful placement of the TPS, no clear dislodgement of the device, and patient consent to use their data. The exclusion criterion was missing data owing to patient loss to follow-up. Micra-TPS implantation was performed by two cardiologists; one conducted 35 implantation procedures and the other 29 procedures. The pull-and-hold method was used for all subjects during implantation to confirm that the device was hooked onto the myocardium, followed by extension of at least two of the four tines on the TPS. Pacemaker impedance, threshold, and sensitivity were measured at the time of discharge from the hospital and postoperative follow-up examinations at 1, 3, 6, 12, and 24 months. Additionally, chest radiography (CXR) was also performed during each follow-up examination to assess whether the position of the Micra-TPS device had changed from that at implantation. The Micra-TPS output pacing threshold setting was initially set to +1.5 V during implantation and for 1 month postoperatively. Thereafter, the output setting was set by the Micra-TPS Capture Management system (Medtronic). This study was approved by the Mito Saiseikai General Hospital ethics committee.

Endpoints

After subsequent pacemaker examinations and CXR procedures showing no clear dislodgement of the Micra-TPS, we divided the patients into the following two groups based on their pacing threshold: (1) the increased pacing threshold (IPT) group where the pacing threshold increased by [?]0.5 V/0.24 msec within 1 month after implantation and (2) the stable pacing threshold (SPT) group where the pacing threshold increased by <0.5 V/0.24 msec within 1 month of implantation.

The IPT and SPT groups were compared with respect to the following variables:

(a) Patient demographics and clinical characteristics: age, sex, body mass index (BMI), monitoring period, indication for TPS implantation, underlying diseases, B-type natriuretic peptide (BNP) level at hospitalization, left ventricular ejection fraction (LVEF), hypertension, diabetes, and blood dialysis.

(b) Procedure-related indicators: Implantation position, implantation time, number of deployments, number of tines hooked, electrical impedance immediately after implantation, and threshold at a pulse width of 0.24 msec.

(c) Transition of pacing threshold: Changes in the individual thresholds were measured in both groups, while the mean threshold values were measured in the SPT group.

(d) Event: (1) Adverse events: all deaths and cases of rehospitalization; (2) device dysfunction: pacing issues, device reimplantation, and device infection; and (3) complications during device implantation: major complications (cardiac injury requiring therapeutic intervention, access trouble, and dislodgment associated with embolization) and minor complications (pericardial effusion not requiring therapeutic intervention, and complications associated with puncture sites).

Statistical analysis

For continuous variables, the Shapiro-Wilk test was used to determine the normality of the data of the IPT and SPT groups. If the distribution was normal, Levene's test was used to confirm equal variance between the two groups. When the distribution did not follow a normal distribution, the Mann-Whitney U test was used. If the variance was uniform, the Student's t-test was used, and if not, the Welch t-test was used. In addition, Fisher's exact probability test was used to compare categorical variables between the two groups. Furthermore, when statistically significant differences were found, a receiver operating characteristic (ROC) curve was generated to determine the cut-off value for assessing the pacing threshold increase. All analyses were performed using EZR version 1.42 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria). In all tests, the significance level was set at P [?] 0.05.

RESULTS

Patient demographics and clinical characteristics

Excluding 4 patients that could not be followed up, of the 60 remaining patients, 9 (15%) were in the IPT group and 51 (85%) were in the SPT group. We found no significant differences between the two groups with respect to the patient demographics and clinical characteristics (Table 1).

Procedure-related indicators

We also observed no differences in the number of deployments, number of tines, or the indwelling site; however, a significantly longer implantation time, lower impedance, and higher pacing threshold were observed in the IPT group than in the SPT group (P<0.05; Table 2).

Transition of the pacing threshold

We found that 44% (4/9) of the patients in the IPT group did not have improved pacing thresholds after 3 months and required a higher pacing threshold of [?]2.0 V/0.24 msec (Figure 1). In the SPT group, the pacing thresholds for most patients improved after implantation. The pacing threshold was [?]1.0 V/0.24 msec in all cases after 3 months (Figure 2).

The ROC curves for impedance and the pacing threshold at implantation are shown in Figures 3A and 3B. The area under the curve (AUC) for impedance and pacing threshold was 0.756 (95% confidence interval [CI]: 0.586–0.926) and 0.840 (95% CI: 0.737–0.943), respectively. Comparison of the AUC for the two ROC curves showed no significant difference (P = 0.364; Figure 3C). The cut-off values based on the ROC curve were 660 Ω for impedance and 1.0 V/0.24 msec for the pacing threshold. The sensitivity and specificity cut-off values for impedance were 100% and 66.7%, respectively, and those for the pacing threshold were 66.7% and 78.4%, respectively.

Events

There were no cases of cardiovascular mortality or rehospitalization due to cardiac events. We observed two cases of pacing failure in the IPT group; however, the devices were not re-implanted. There were only two cases of complications: one case of lymph leakage at the puncture site in the IPT group and one case of pericardial effusion not requiring intervention in the SPT group. No other major complications were noted in either group.

DISCUSSION

This study compared patients with an increased pacing threshold shortly after TPS implantation with those who maintained a stable pacing threshold. Our results suggest that impedance and threshold at the time of implantation may serve as predictive factors for an increased pacing threshold (AUC: 0.737–0.943 and 0.586–0.926, respectively). All patients requiring a higher pacing threshold were in the IPT group, suggesting that if a threshold increase can be avoided within the first month after TPS implantation, a stable threshold may be obtained in the medium-to-long term.

Impedance is the sum of resistance in the electrode lead and the myocardium owing to contact between the two. Therefore, the difference in impedance is a measure of whether the TPS is sufficiently anchored to the myocardium. To anchor the device, four nitinol tines at the tip of the TPS are hooked to the myocardium. It has been shown that at least two tines must be applied to minimize dislodgement of the device, which may occur due to the cardiac rhythm.[10] However, there are conflicting reports where, despite two tines being anchored to the myocardium, the TPS tail was reported to shift, leading to an increase in the threshold with a changing bodily position.[11,12]To achieve sufficient fixation to the myocardium with two tines, the tines must be attached perpendicular to the myocardial wall.[10] If the tines are leaning against the myocardial wall, they do not provide enough force to secure the device; thus, the device may shift with an increase in the cardiac rhythm during exercise conditions. Therefore, a slight movement between the heart muscle and the device could result in micro-dislodgement. In this study, at least two or more tines were anchored by the pull-and-hold method in all patients. However, the low impedance at the time of implantation in the IPT group meant that the tines were not sufficiently anchored to the myocardial wall, resulting in micro-dislodgement. We observed that the pacing threshold increases shortly after implantation in this group, suggesting that additional investigations are required for the evaluation of adequate anchoring of the TPS to the myocardium other than the number of tine connections. While it was expected that impedance at the time of implantation would function as a predictive factor for the altered threshold status, it was also observed that the pacing threshold at the time of implantation served as a predictor in that it tended to be low if the device was well-anchored. This finding is similar to a report by Tolosana et al., who showed that impedance and threshold at the time of implantation play important roles in achieving a pacing threshold of [?]2.0 V/0.24 msec.[7]

We observed that the pacing threshold improved in the majority of cases in the IPT group, while a higher threshold was maintained in a few cases. This may be due to fixation and adhesion of the dislodged device. However, we do not have sufficient evidence to support this claim, and further studies are needed.

We experienced two cases of pacing failure in the IPT group. This may be because the pacing threshold was higher than the initial pacing threshold (+ 1.5 V) set at implantation. Our results suggest that if the electrode impedance is low and the pacing threshold level is high immediately after TPS implantation, maintenance of a sufficient margin to the established output with periodic monitoring will help lower the risk of pacing failure. The results of this study indicate that if the electrode impedance is low or the pacing threshold is high at the time of TPS implantation, it is better to maintain a sufficient margin of the set output.

In addition, pericardial effusion was observed in one case in the SPT group. In this case, the Micra-TPS was attached to the inferior wall. When positioning the Micra-TPS, the thickness of the myocardium should be considered to ensure safety of the right ventricular septum.[13] To achieve sufficient compression fitting of the Micra-TPS and myocardium, it is necessary to press the Micra-TPS with adequate force onto the myocardium. It is, therefore, recommended that the Micra-TPS be positioned on the right ventricular septum, if possible.

Limitations

There are several limitations to this study. First, the Micra-TPS was implanted by two different cardiologists, which may have led to technical differences in implantation. As the procedure was performed on consecutive patients, the degree of proficiency of the cardiologists in performing the procedure may have slightly varied. Second, there is a limit in accurately determining the number of tines stably anchored to the myocardium by the pull-and-hold method. Currently, some facilities[13] are making efforts to investigate tine anchoring to the myocardium using intracardiac echo. If it is possible to accurately evaluate the number of anchored tines, the number of tines may potentially function as another predictor. Third, the follow-up period for the SPT group was short, approximately 7 months on average, and there is a possibility that a threshold increase may occur beyond the follow-up period. Long-term continuous follow-up is, therefore, necessary. We aim to clarify the involvement of threshold rise and impedance by conducting a prospective study on the transition of the pacing threshold according to implant impedance.

CONCLUSIONS

The pacing threshold increased shortly after Micra-TPS implantation due to micro-dislodgement of the device because of insufficient anchoring of the device to the myocardium. Our results suggest that if an early threshold increase can be avoided after implantation, a stable threshold can be potentially reached in the medium-to-long term. When implanting the Micra-TPS, we showed that impedance >660 Ω and threshold <1.0 V/0.24 msec may be good indicators that the device is sufficiently anchored to the myocardium. We intend to evaluate the increase in the threshold by assessing implant impedance in a further study.

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Figure Legends

Figure 1. Graph showing time-course of threshold changes in the increased pacing threshold (IPT) group. The change in the pacing threshold for nine patients in the IPT group is shown. Patients who required a threshold [?]2.0 V at 3 months after implantation are shown in red lines, and patients who had a threshold of [?]2.0 V at 3 months after implantation are shown in gray lines.

Figure 2 : **Graph showing time-course of the pacing threshold in the stable pacing threshold (SPT) group** . Each boxplot represents the total number of patients assessed at each time point. The upper and lower whiskers show the maximum and minimum values (excluding outliers), respectively, and the line that divides the box represents the median threshold value.

Figure 3 : **The receiver operating characteristic (ROC) curves for impedance and the pacing threshold at implantation.** A) ROC curve of implant pacing threshold to determine the probability of increased pacing threshold shortly after Micra-TPS implantation. B) ROC curve of implant impedance to determine the probability of increased pacing threshold shortly after Micra-TPS implantation. C) Comparison of the area under the curve (AUC) for the two ROC curves. The numbers in the graphs in 3A and 3B represent the cutoff values with the best sensitivity and specificity. The numbers in parentheses indicate the rates of sensitivity and specificity. The p-value in 3C was obtained using the chi-square test.

Tables

Table 1. Patient baseline demographics and clinical characteristics grouped according to pacing threshold

			SPT group (n=9)	IP
Monitoring period (months)	Monitoring period (months)	Monitoring period (months)	13.8 ± 6.9	7.
Age (years)	Age (years)	Age (years)	89.1 ± 4.4	85
Sex: Female, n (%)	Sex: Female, n (%)	Sex: Female, n (%)	5 (56%)	27
BMI (kg/m^2)	BMI (kg/m^2)	BMI (kg/m^2)	20.0 ± 3.8	21
Indication for implantation	Indication for implantation	Indication for implantation	Indication for implantation	In
	SSS, n (%)	SSS, n (%)	2 (22%)	12
	CAVB, n (%)	CAVB, n (%)	5 (56%)	32
	Type II AVB, n (%)	Type II AVB, n (%)	0	3
	AF bradycardia, n (%)	AF bradycardia, n (%)	2 (22%)	4
Underlying disease	Underlying disease	Underlying disease	Underlying disease	U
		IHD	1 (11%)	2
		Valvular disease	3 (33%)	11
		Cardiomyopathy	1 (11%)	0
		Others	4 (44%)	38
BNP	BNP	BNP	707 ± 729	43
LVEF	LVEF	LVEF	57.2 ± 11.2	57
HT, n (%)	HT, n (%)	HT, n (%)	5 (56%)	5
DM, n (%)	DM, n (%)	DM, n (%)	4 (44%)	4
HD, n (%)	HD, n (%)	HD, n (%)	0 (0%)	0

In the increased pacing threshold (IPT) group, the pacing threshold increased by [?]0.5 V/0.24 msec within 1 month after implantation, and in the stable pacing threshold (SPT) group, the pacing threshold increased by <0.5 V/0.24 msec within 1 month after implantation. Abbreviations: AF: atrial fibrillation; BNP: B-type natriuretic peptide; CAVB: complete atrial ventricular block; DM: diabetes mellitus; HD: hemodialysis; HT: hypertension; IHD: ischemic heart disease; LVEF: left ventricular ejection fraction; SSS: sick sinus syndrome; Type II AVB: type second-degree atrioventricular block. *P-values<0.05 were considered statistically significant.

Table 2. Procedure-related indicators grouped according to pacing threshold

		SPT group (n=9)	IPT group (n=51)	*P*-value
Implantation time (minutes)	Implantation time (minutes)	52±25	35±18	0.029*
Number of deployments	Number of deployments	2.2±1.7	1.6	0.259
Implantation site	Implantation site	Implantation site	Implantation site	Implantation site
	Mid-septal, n (%)	6 (67%)	45 (88%)	0.127
	Apical septal, n (%)	2 (22%)	5 (10%)	
	Inferior, n (%)	1 (11%)	1 (2%)	
Tines	Tines	2.3 ± 0.5	2.4 ± 0.5	0.585
Sensitivity	Sensitivity	5.1 ± 1.9	8.3 ± 4.1	0.220
Impedance	Impedance	582 ± 59	756 ± 167	<0.001*
Threshold	Threshold	1.29 ± 0.87	0.71 ± 0.40	0.014*

In the increased pacing threshold (IPT) group, the pacing threshold increased by [?]0.5 V/0.24 msec within 1 month after implantation, and in the stable pacing threshold (SPT) group, the pacing threshold increased by <0.5 V/0.24 msec within 1 month after implantation. *P-values<0.05 were considered statistically significant.

Table 3. Patient outcomes grouped according to pacing threshold

		IPT group (n = 9)	SPT group (n = 51)	*P*-value
Adverse events, n (%)	Adverse events, n (%)	6 (66%)	10 (20%)	0.005*
All deaths, n (%)	All deaths, n (%)	1 (11%)	5 (10%)	1.000
	Cardiovascular deaths	0	0	
	Others	1	2	
	Unknown	0	3	
Rehospitalization n (%)	Rehospitalization n (%)	5 (55%)	7 (14%)	0.011*
	Due to heart failure	0	2	
	Others	5	5	
Device dysfunction, n (%)	Device dysfunction, n (%)	2 (22%)	0 (0%)	0.020*
	Pacing issue	2	0	
	Device reimplantation	0	0	
	Infection	0	0	
Complications, n (%)	Complications, n (%)	1 (11%)	1 (2%)	0.275
	Major complications	0 (0%)	0 (0%)	
	Minor complications	1^{+} (11%)	1^{++} (2%)	

In the increased pacing threshold (IPT) group, the pacing threshold increased by [?]0.5 V/0.24 msec within 1 month after implantation, and in the stable pacing threshold (SPT) group, the pacing threshold increased by <0.5 V/0.24 msec within 1 month after implantation. *P-values<0.05 were considered statistically significant.$^{+}$Puncture site lymphatic leakage.$^{++}$Pericardial effusion.

Figure 1

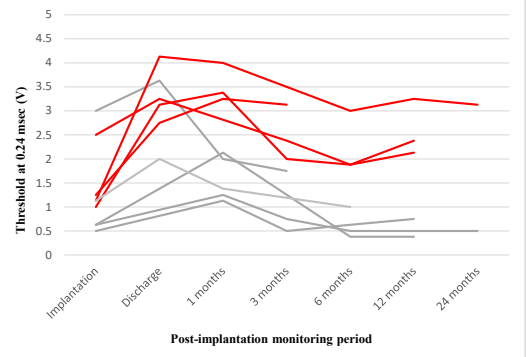

Figure 2

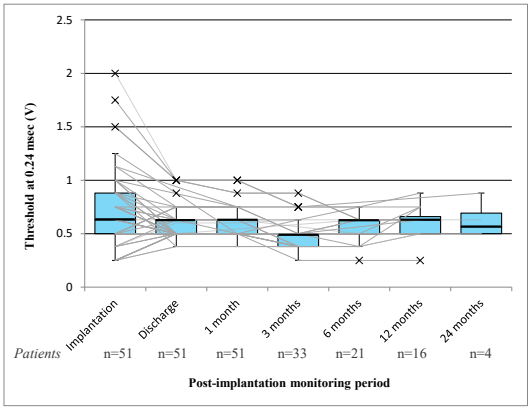

Figure 3