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Mid-term outcomes of delivery catheter-based and stylet-based right ventricular septal pacing: Follow-up results from a multicenter, prospective, randomized study

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Abstract

Background: The Mt FUJI study was a multicenter, prospective, randomized, single-blind, controlled trial comparing delivery catheter-based and stylet-based right ventricular (RV) lead placement at the RV septum. This study extended the follow-up duration to 1 year after implantation.

Methods: Seventy patients with pacemaker indications for atrioventricular block were randomly assigned to the delivery catheter and stylet groups. We compared the mid-term efficacy and safety between the two groups at 1 year after implantation. The primary outcome was the change in the left ventricular ejection fraction (LVEF), and the secondary outcomes were changes in brain natriuretic peptide (BNP) levels, lead parameters, paced QRS duration, and the incidence of adverse events.

Results: At the 1-year follow-up, no significant differences were observed in the changes in the LVEF (+1.0% ± 8.6% vs. +3.1% ± 8.1%, $p = .332$), BNP levels (+8.0 [−11.1, 26.5] pg/mL vs. −8.7 [−15.3, 13.2] pg/mL, $p = .193$), or lead performance between the delivery catheter and stylet groups. The QRS duration was significantly shorter in the delivery catheter group than in the stylet group (128 ± 23 ms vs. 146 ± 17 ms, $p < .001$). All-cause death, hospitalization for heart failure, new development of atrial fibrillation, and pacing-induced cardiomyopathy occurred in seven patients in the delivery catheter group and five in the stylet group.

Conclusion: The delivery catheter system was similarly useful and safe compared to the stylet system in the mid-term follow-up from the Mt FUJI trial. Further long-term evaluations are warranted.

KEYWORDS
delivery catheter, pacemaker, pacing-induced cardiomyopathy, QRS duration, right ventricular lead

1 | INTRODUCTION

Pacemaker implantation is an established treatment for managing patients with atrioventricular block (AVB), and most patients undergo right ventricular (RV) pacing without complications. However, chronic RV pacing causes electrical and mechanical ventricular dyssynchrony, occasionally leading to a reduced left ventricular ejection fraction (LVEF) and the development of heart failure (HF), known as pacing-induced cardiomyopathy (PiCM). The incidence of PiCM varies widely, from 6% to 25% as previously reported.[1,2] In addition to several risk factors, including high RV pacing percentage, long-paced QRS duration, and the baseline left ventricular (LV) systolic function, RV apical pacing is associated with the incidence of PiCM.[3] Although RV septal pacing has been suggested as an alternative pacing site with less dyssynchrony than RV apical pacing, the prognostic benefits of RV septal pacing over RV apical pacing in clinical settings remain controversial.[4–6]

One of the concerns regarding RV pacing is the low success rate of lead placement on the true RV septum. In this context, a recently introduced delivery catheter system with a pre-shaped curve may be able to overcome the aforementioned issue. The Mt FUJI (coMparison of delivery caTheter- and stylet-based RV lead placement at the RV septum under FIUoroscopic guidance Judged by cardIac CT) trial[7] was a multicenter, prospective, randomized controlled study assessing the efficacy of a delivery catheter system versus a traditional stylet-based technique for accurate lead placement on the RV septum in patients with AVB. The primary result of the study revealed a significantly higher success rate of lead placement on the RV septum in the delivery catheter group than that in the stylet group. Currently, few reports have evaluated outcomes after lead implantation on the conventional RV septum using the delivery catheter system.[8]

The present study therefore compared the medium-term efficacy, safety, and incidence of PiCM between the two groups using the extended 1-year follow-up cohort of the Mt FUJI trial.

2 | METHODS

2.1 | Study design

The rationale and design of the Mt FUJI trial have been previously described.[9] The study compared the efficacy and safety of using the delivery catheter versus the stylet for RV lead deployment during pacemaker implantation in patients with AVB at seven tertiary hospitals in Japan who were >20 years old and provided their written informed consent. The exclusion criteria were an LVEF <35%, persistent atrial fibrillation (AF), congenital heart disease, prior open-heart surgery, and chronic renal failure on hemodialysis at baseline. Seventy patients were randomly assigned to either the delivery catheter group ($n = 36$) or stylet group ($n = 34$). The RV lead tip position was assessed using electrocardiogram (ECG)-gated cardiac computed tomography (CT) performed within 4 weeks after implantation. Unintended physiological pacing occurred in four patients (His-bundle pacing in one and left bundle branch area pacing in three) in the delivery catheter group.

This study was a prespecified analysis of the Mt FUJI trial. All patients were scheduled for follow-up for 12 months after implantation. We compared the medium-term efficacy and safety between the two groups. The primary outcome of the present study was the change in LVEF from postprocedure (1 week) to 1 year after pacemaker implantation. The secondary outcomes included changes in brain natriuretic peptide (BNP) levels from postprocedure (1 week) to 1 year after implantation, the incidence of RV lead dislodgement, R-wave amplitude, pacing threshold, impedance of RV lead, paced QRS duration, incidence of complications, all-cause death, heart failure hospitalization, new-onset atrial fibrillation, and PiCM 1 year after pacemaker implantation. The baseline echocardiography data in the present study were obtained 1 week after the implantation, which was slightly different from those in the prior-original paper (before implantation).[7] To minimize the impact

of pacing condition differences during echocardiographic parameter measurements, all patients were examined by echocardiography at 1 week after implantation with the pacing mode of VVI and fixed rate of 90 bpm, and at 1 year with atrial sense ventricular pace mode or VVI 90 mode.

The study was coordinated by the Center for Clinical Research at Hamamatsu University Hospital in Hamamatsu, Shizuoka, Japan, and complied with the Declaration of Helsinki and the Clinical Trials Act. The study protocol was approved by the Clinical Research Review Board of the Hamamatsu University School of Medicine (approval number: 20-038), and by the hospital administrator in each participating hospital, and written informed consent was obtained from all patients or their legal guardians before inclusion and randomization.

2.2 | Pacemaker implantation procedure

The details of the pacemaker implantation procedure of the Mt FUJI trial are described in the protocol article.[9] The Mt FUJI trial involved pacemaker implantation under local anesthesia by experienced operators. The RV lead was placed on the RV septum in all patients under fluoroscopic guidance, and no attempts were made to use left bundle branch area pacing or His bundle pacing. During the procedure, the left anterior oblique view of 40–60° was used to confirm the RV tip facing the spine, and the cardiac silhouette was divided perpendicularly into quadrants in the right anterior oblique (RAO) view of 30°. The RV lead was intended to anchor to the second or third quadrant.[10] In cases where the location of the RV lead tip was not in the target position, the lead was sometimes screwed in a stable position to avoid lead dislodgement. All patients in the delivery catheter group used a C315-HIS (Medtronic, Minneapolis, MN, USA) catheter and a specific lead (SelectSecure Model 3830; Medtronic). In the stylet group, a conventional, manually shaped stylet was mostly used in 28 patients. A soft stylet was used as a first choice. A steerable stylet (Locator™; Abbott) and a pre-shaped stylet (Ez stylet™; Japan Lifeline) were additionally selected in three patients each. In addition, the longitudinal lead-tip position was assessed using fluoroscopic RAO views of 30° at the end of the implantations. The silhouette of the ventricle was longitudinally divided into three equal parts and RV lead-tip positions were classified as basal, mid, or apical area (Figure S1).

2.3 | Follow-up assessments

All patients were followed in the outpatient clinics of each hospital where pacemaker implantation had been performed. The timing of the 1-year follow-up was set at 52 weeks, with a permissible range of 40–64 weeks after implantation. Echocardiography and a 12-lead surface ECG were performed within 1 week after implantation and at the 1-year follow-up. The LVEF was calculated using Simpson's method. A physician (K.I.) analyzed the echocardiography data without knowledge of the allocation or clinical outcomes. During the ECG recording, the pacemaker was programmed to the VVI mode at 90 beats per minute to avoid fusion with its own beats. The paced QRS duration was measured by a physician who was not involved in pacemaker implantation. We also assessed the BNP levels just before discharge from pacemaker implantation and at the 1-year follow-up. Device interrogation was performed in all patients at the 1-year follow-up. If applicable, managed ventricular pacing modes were used to reduce unnecessary ventricular pacing. RV lead dislodgment at the 1-year follow-up was diagnosed when chest radiography showed apparent lead perforation, lead dislocation, or abnormal RV lead parameters, including an R-wave amplitude of <1.0 mV or pacing threshold of >3.0 V with a nominal pulse width were observed.

The incidence of all-cause death, HF hospitalization, and AF development was assessed during the follow-up period. We defined the composite endpoints including all-cause death, HF hospitalization, new-onset AF, and PiCM. Complications related to device implantation, such as pacemaker infection, lead dislodgement, and lead fracture, were also recorded. In this study, PiCM was defined using the most commonly accepted definition based on a recent systematic review and meta-analysis,[11] which involves the deterioration of LVEF ≥10% from 1 week after implantation, resulting in an LVEF <50%, regardless of HF symptoms.

2.4 | Statistical analyses

Continuous variables were expressed as the mean ± standard deviation or median and interquartile range, whereas categorical variables were expressed as numbers (percentages). Baseline characteristics between the two groups were compared using Student's *t*-test for parametric data and the Mann–Whitney *U* test for nonparametric data or the chi-square test. Differences between the postprocedure and follow-up values of the outcome parameters were compared using a paired *t*-test or Wilcoxon's signed-rank test. The Kaplan–Meier method was used to analyze the events, and survival curves were compared using a log-rank test. Univariate and multivariate Cox regression analyses were performed to examine the predictors of composite endpoints. Factors with a p value <.05 in the univariate logistic regression analysis were included using a forward stepwise method in the multivariate model. Statistical significance was considered when the p value was <.05.

All statistical analyses were performed using the SPSS version 28.0 software program (SPSS Inc., Chicago, IL, USA).

3 | RESULTS

3.1 | Baseline characteristics in the study population

Among the 70 patients enrolled in the Mt FUJI trial, 1 patient withdrew consent, and 1 was lost to follow-up before the 1-year follow-up visit. A total of 68 patients (34 in the delivery catheter group and

34 in the stylet group) were thus included in the study analysis. In the prior-original paper, there was one case of RV lead dislodgement in the stylet group, and the lead position was assessed by the cardiac CT after re-implantation of the lead during hospitalization in the case, which was included in the analysis of this study. The mean age was 78 ± 11 years old, and 43% were male. The LVEF at 1 week after implantation was 61.4% ± 7.4%. The paced QRS duration at 1 week after implantation was significantly shorter in the delivery catheter group than in the stylet group (128 ± 20 ms vs. 142 ± 16 ms, $p = .002$) (Table 1). The paced QRS duration after 1 week remained to be significantly shorter in the delivery catheter group than in the stylet group, even after excluding four patients with unintended physiological pacing (132 ± 15 ms vs. 142 ± 16 ms, $p = .009$). The delivery catheter group achieved a significantly higher success rate in fixing the lead tip to the RV septum than the stylet group (79% vs. 52%, $p = .037$). The RV leads were implanted in the free-wall position in two patients in the stylet group after the assessment of ECG-gated CT findings. In contrast, none of the patients in the delivery group had a free wall position of the RV lead. The mean LVEF and BNP levels at 1 week after implantation were not significantly different between the two groups. There was no significant difference in the prevalence of septal lead position (57%, 33%, and 33%, $p = .716$) or paced QRS duration (144 ± 16 ms vs. 125 ± 9 ms vs. 138 ± 5 ms, $p = .111$) among the three different stylets (the conventional manually shaped stylet, steerable stylet, and preshaped stylet) in the stylet group, respectively.

3.2 | Outcomes after implantation

One year after implantation, the LVEF on echocardiography was 63.8% ± 8.0% versus 63.4% ± 7.8% in the delivery catheter and stylet groups, respectively ($p = .850$). Similarly, BNP levels were not significantly different between the delivery catheter and stylet groups (45.9 [27.7, 88.5] pg/mL vs. 44.1 [17.4, 75.9] pg/mL, respectively; $p = .586$). The paced QRS duration was shorter in the delivery catheter group than in the stylet group (128 ± 23 ms vs. 146 ± 17 ms, $p < .001$). The paced QRS duration was also significantly shorter in the delivery catheter group than in the stylet group after excluding four patients with unintended physiological pacing (131 ± 23 ms vs. 146 ± 17 ms, $p = .006$). The incidence of RV lead dislodgement, R-wave amplitude, pacing threshold, and impedance of the RV lead after 1 year was not significantly different between the two groups. No complications occurred in either group (Table 2).

Changes in the LVEF paced QRS duration, and BNP levels from 1 week after implantation to 1 year are shown in Table 2. No significant differences were observed in the primary endpoint or changes in the LVEF between the delivery catheter and stylet groups (+1.0% ± 8.6% vs. +3.1% ± 8.1%, $p = .332$). Similarly, there were no significant differences in changes in BNP levels between the delivery catheter and stylet groups (+8.0 [−11.1, 26.5] pg/mL vs. −8.7 [−15.3, 13.2] pg/mL, $p = .193$).

During the follow-up period, all-cause death and HF hospitalization occurred in one and no patients in the delivery catheter group

TABLE 1 Baseline characteristics of the study population after implantation.

Variables	Delivery catheter group ($N = 34$)	Stylet group ($N = 34$)	p-value
Age (years)	77 ± 13	79 ± 10	0.481
Male, *n* (%)	14 (41)	15 (44)	1.0
NYHA class I/II/III/IV, *n*	9/13/7/5	11/8/12/3	0.361
Diabetes mellitus, *n* (%)	8 (24)	7 (21)	1.0
Hypertension, *n* (%)	25 (73)	27 (79)	0.776
Atrial fibrillation, *n* (%)	4 (12)	3 (9)	1.0
Prior myocardial infarction, *n* (%)	0 (0)	2 (6)	0.493
Chronic kidney disease, *n* (%)	6 (18)	13 (38)	0.104
Tricuspid Regurgitation, *n* (%)	2 (6)	1 (3)	1.0
BNP levels (pg/mL)	48.8 (14.1, 104.1)	56.2 (36.0, 83.2)	0.811
Echocardiography data			
LVEF (%)	62.7 ± 5.5	60.1 ± 8.9	0.155
LVEF <50% (%)	1 (3)	4 (12)	0.356
LVEDD (mm)	40.9 ± 5.4	42.5 ± 6.3	0.244
LVESD (mm)	27.5 ± 3.4	28.7 ± 5.5	0.277
LAD (mm)	35.1 ± 5.7	37.2 ± 5.6	0.131
Paced QRS duration (ms)	128 ± 20	142 ± 16	0.002
RV lead position			
Septum, *n* (%)	27 (79)	18 (52)	
His-bundle pacing, *n* (%)	1 (3)	0 (0)	
Left bundle branch area pacing, *n* (%)	3 (9)	0 (0)	
Anterior edge of the septal wall, *n* (%)	7 (21)	14 (42)	
Free wall, *n* (%)	0 (0)	2 (6)	0.037
Pacing parameters			
R-wave sensing (mV)	14.0 ± 4.8	11.8 ± 4.7	0.111
Bipolar pacing threshold at 0.4 ms (V)	0.68 ± 0.23	0.76 ± 0.23	0.184
Lead impedance (Ω)	567 ± 71	574 ± 109	0.761
Medications			
Anticoagulant therapy, *n* (%)	2 (6)	0 (0)	0.493
Antiplatelet therapy, *n* (%)	10 (29)	7 (21)	0.576

Note: Values are expressed as numbers (percentages), mean ± standard deviation, or median and interquartile range. The baseline echocardiography data in the present study were obtained 1 week after the implantation, which was slightly different from those in the prior-original paper (before implantation).[7]

Abbreviations: ACE-Is, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BNP, brain natriuretic peptide; LAD, left atrial dimension; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; RV, right ventricular; NYHA, New York Heart Association.

TABLE 2 Follow-up outcomes after 1 year.

Variables	Delivery catheter group ($N=33$)[a]	Stylet group ($N=31$)[a]	p-value
BNP levels (pg/mL)	45.9 (27.7, 88.5)	44.1 (17.4, 75.9)	0.586
Changes in BNP levels (pg/mL)	+8.0 (−11.1, 26.5)	-8.7 (−15.3, 13.2)	0.193
Echocardiography data			
LVEF (%)	63.8 ± 8.0	63.4 ± 7.8	0.850
LVEF <50% (%)	2 (6)	2 (6)	1.0
Changes in LVEF (%)	+1.0 ± 8.6	+3.1 ± 8.1	0.332
LVEDD (mm)	41.5 ± 5.9	43.5 ± 7.1	0.106
LVESD (mm)	28.0 ± 4.9	28.9 ± 6.1	0.262
LAD (mm)	37.8 ± 12.8	35.9 ± 5.8	0.227
Paced QRS duration (ms)	128 ± 23	146 ± 17	<0.001
Changes in QRS duration (ms)	+1 ± 19	+4 ± 14	0.518
Pacing parameters at 1 year			
RV pacing rate (%)	83 ± 31	67 ± 41	0.081
R-wave sensing (mV)	14.6 ± 4.2	13.5 ± 6.1	0.516
Changes in R-wave sensing (mV)	+4.7 ± 4.9	+4.1 ± 4.9	0.687
Bipolar pacing threshold at 0.4 ms (V)	0.98 ± 0.28	0.95 ± 0.45	0.784
Changes in bipolar pacing threshold at 0.4 ms (V)	+0.33 ± 0.35	+0.31 ± 0.5	0.827
Lead impedance (Ω)	529 ± 81	526 ± 117	0.917
Changes in Lead impedance (Ω)	−156 ± 102	−104 ± 121	0.063
Incidence of RV lead dislodgement, n (%)	0 (0)	0 (0)	1.0
Complications, n (%)	0 (0)	0 (0)	1.0

Note: Values are expressed as numbers (percentages), means ± standard deviations, or medians and interquartile ranges. The amount of change was calculated as (1 year to 1 week after implantation).

Abbreviations: BNP, brain natriuretic peptide; LAD, left atrial dimension; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; RV, right ventricular.

[a]Follow-up outcomes at 1 year were analyzed in the population after excluding those who died within 1 year after implantation.

TABLE 3 Follow-up events after 1 year.

Variables	Delivery catheter group ($N=34$)	Stylet group ($N=34$)	p-value
All-cause death, n (%)	1 (3)	3 (9)	0.614
Death from HF, n (%)	1 (3)	1 (3)	1.0
HF hospitalization, n (%)	0 (0)	1 (3)	1.0
New development of AF, n (%)	4 (12)	3 (9)	1.0
Development of pacing-induced cardiomyopathy, n (%)	2 (6)	0 (0)	0.492

Note: Values are expressed as numbers (percentages).

Abbreviations: AF, atrial fibrillation; HF, heart failure.

and three and one patient in the stylet group, respectively. The cause of death in the delivery catheter group was heart failure because of severe aortic stenosis, while heart failure, cholecystitis, and senility were the causes of death in the stylet group. Four and three patients had newly developed AF in the delivery and stylet groups, respectively. PiCM occurred in two and no patients in the delivery and stylet groups, respectively (Table 3). The cumulative ventricular pacing rate was lower in the stylet group than in the delivery group (67% ± 41% vs. 83% ± 31%, $p=.081$). Kaplan–Meier analyses demonstrated no significant difference in the composite endpoint of death, HF hospitalization, AF development, or PiCM between the groups (log-rank test; $p=.563$) (Figure 1). The composite endpoint partially overlapped, with occurrences in seven patients in the delivery catheter group and five in the stylet group. A multivariate Cox regression analysis revealed that female gender (hazard ratio [HR], 0.153; 95% confidence interval [CI], 0.031–0.759; $p=.022$) and the change in LVEF per 1% (HR 0.920, 95% CI 0.851–0.994, $p=.035$) were independent predictors of the composite endpoints.

3.3 | Details of patients with PiCM

There were two cases of PiCM in the delivery catheter group. One patient showed a 10.4% decrease in LVEF from 57.5% at 1 week after implantation to 47.1% at 1-year follow-up and an increase in BNP levels from 110.4 to 350.5 pg/dL but no change in the paced QRS duration of 150 ms. The lead position was the anterior edge of the mid-RV septum, with an RV pacing rate of 94%. No apparent anatomical abnormality or lack of operator skill was noted. The other patient showed a 19.1% decrease in LVEF from 67.5% to 48.4%, with BNP levels remaining stable from 13.0 to 8.1 pg/dL. The paced QRS duration decreased from 130 to 123 ms, and the lead position was the RV septum, with a ventricular pacing rate of 65% after implantation. However, no apparent cause of the LVEF deterioration was observed in this case. Neither patient experienced hospitalization for HF, upgrade to cardiac resynchronization therapy (CRT), nor death during the follow-up period.

3.4 | Subgroup analyses in patients with a cumulative ventricular pacing rate ≥90%

We conducted a subgroup analysis of cases with a cumulative ventricular pacing rate of ≥90%. Among the 64 total patients, 42 (66%) had a ventricular pacing rate ≥90%, including 25 in the delivery catheter group and 17 in the stylet groups. As shown in Table S1, there were no significant differences in primary or secondary outcomes within this subgroup. The Kaplan–Meier survival curves for

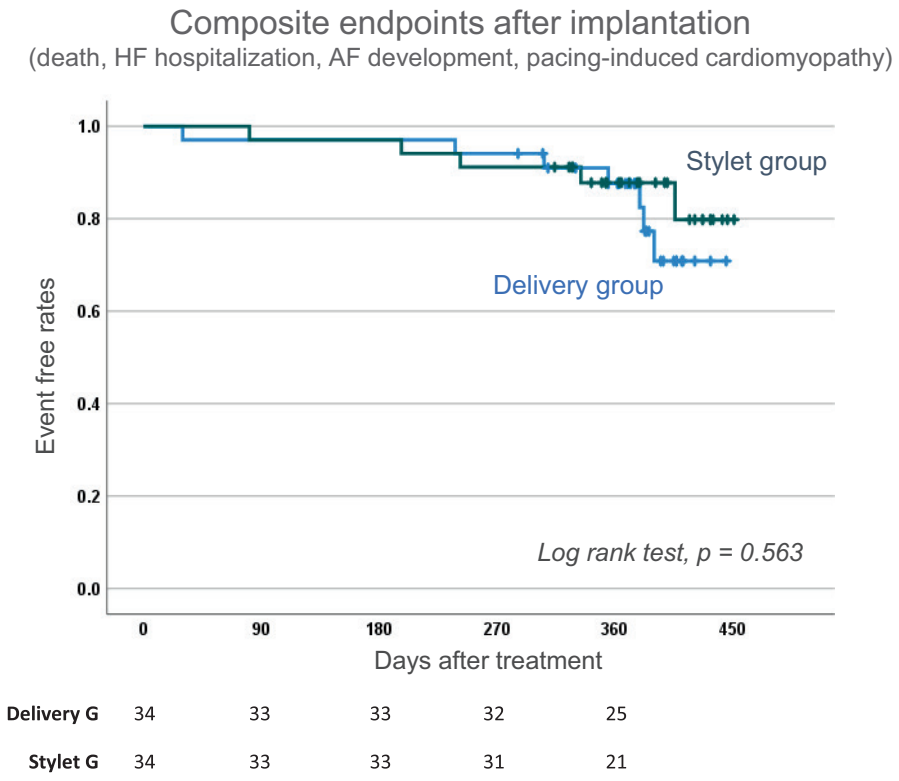

FIGURE 1 Comparisons of the Kaplan–Meier survival curves of the composite endpoint, including death, HF hospitalization, AF development, and pacing-induced cardiomyopathy, between the delivery catheter group and stylet group. AF, atrial fibrillation; HF, heart failure.

composite endpoints showed no significant differences between the groups (log-rank test: $p = .309$).

3.5 | Subgroup comparisons of patients with the lead-tip position at the RV septum and non-RV septum

A subgroup comparison was conducted between patients with a lead-tip position at the RV septum ($n = 43$) and at the non-RV septum ($n = 21$). The paced QRS duration was narrower in the delivery catheter group than in the stylet group both in patients with a lead-tip position at the RV septum as well as at the non-RV septum (128 ± 17 ms vs. 140 ± 14 ms; $p = .015$, and 131 ± 23 ms vs. 145 ± 16 ms; $p = 0.125$, respectively). Figure S1 shows the distribution of lead-tip positions in the basal, middle, and apical regions in patients with a lead-tip position at the RV septum in both groups. Most leads were fixed in the basal region in the delivery catheter group compared to those in the stylet group (44% vs. 25%) (Figure S1). Furthermore, in patients with a lead-tip position at the non-RV septum, the stylet catheter group exhibited a significantly longer paced QRS duration after 1 year than at 1 week after implantation (153 ± 14 ms vs. 145 ± 16 ms, $p = .023$) (Figure 2).

Patients were divided into four groups based on the paced QRS duration: <120, 120 to <150, 150 to <180, and ≥180 ms. Figure 3 shows the distribution and trends of paced QRS duration for the delivery catheter and stylet groups at 1 week after implantation and after 1 year. In patients with a lead-tip position at the RV septum, six patients (five in the delivery group and one in the stylet group) experienced shortening of the paced QRS duration. However, in all patients with a lead-tip position at the non-RV septum except for one, the paced QRS duration was not shortened. In patients with a lead-tip position at the RV septum, the prevalence of patients with paced QRS duration <120 ms was increased, and no patients had a narrow paced QRS <120 ms at 1-year follow-up in patients with a lead-tip position at the non-RV septum.

4 | DISCUSSION

The main finding of our study is that the delivery catheter system was similarly useful and safe compared to the conventional stylet system in the mid-term results of the Mt FUJI trial, which was the first multicenter, prospective, randomized controlled study of its kind. Although no significant changes in the LVEF or BNP levels were observed at the 1-year follow-up between the two systems, the paced QRS duration at 1 year was significantly shorter in the delivery catheter group than in the stylet group. Neither group differed significantly with regard to pacing parameters and the occurrence of all-cause death, HF hospitalization, new development of AF, and PiCM.

4.1 | The efficacy and safety of the delivery catheter system in the mid-term

Few studies have reported the mid- to long-term efficacy and safety of the delivery catheter system. Suzuki et al.[8] reported that no lead-related complications were observed in 21 patients using the delivery catheter system during a mean follow-up period of 49.5 ± 13.1 months,

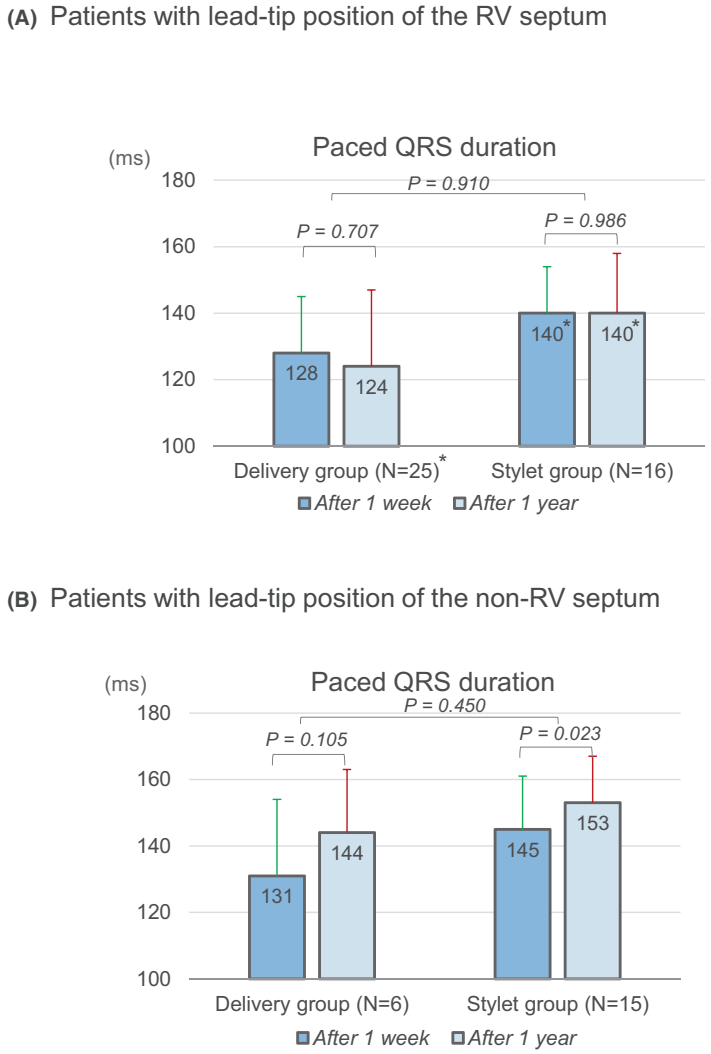

FIGURE 2 Changes in the paced QRS duration in patients with a lead-tip position at the RV septum (A) and at the non-RV septum (B) from after postprocedure (1 week) to after 1 year between the delivery catheter group and stylet group. *Two cases were excluded because of missing electrocardiogram data after 1 year. RV, right ventricular.

* P < 0.05. Delivery group vs. Stylet group

and it was effective for producing a narrow-paced QRS duration in RV septal pacing. They also reported that the RV pacing threshold in the chronic phase was higher in the delivery catheter group than in the conventional stylet lead group. In contrast, our study demonstrated that various lead parameters, including RV pacing thresholds, were similar to those in the stylet group. However, the follow-up period in our study was only 1 year after the procedure, requiring verification of the long-term efficacy and safety of the delivery catheter system.

4.2 | The association of the RV lead position with the risk of PiCM

One of the deleterious effects of pacemaker implantation is PiCM. Chronic RV pacing may lead to desynchronization of ventricular activation, resulting in LV dysfunction and HF development. PiCM is associated with a significantly increased risk of HF hospitalization.[3,12] Various definitions of PiCM, such as a reduced LVEF to <40%–50% or a decrease in the LVEF by 10%–15%, have been reported previously,[1,2] and the most common definition of PiCM has been the deterioration of the LVEF ≥10% from baseline, resulting in an LVEF <50%, regardless of HF symptoms. A recent systematic review and meta-analysis[11] reported that the pooled PiCM prevalence was 12% with a 95% CI of 11%–14%, and the baseline LVEF, native QRS duration, RV pacing percentage, and paced QRS duration were key risk factors for PiCM. In contrast to the above-mentioned predictors, nonseptum RV pacing may be a procedural and preventable factor that can increase the risk of PiCM development.[13] Although a distal portion of the delivery catheter is naturally oriented toward the RV septum, approximately 20% of cases had the unexpected lead position of the anterior edge of the RV septum in our study. While not performed in our study, it may be better to perform ventriculography in the RAO view from the distal tip of the delivery catheter to avoid an unintended lead position against the anterior edge of the RV septum. This additional procedure can help verify whether the lead would be directed toward the true septum, potentially preventing the placement of the anterior edge of the RV septum. Furthermore, in our study, the paced QRS duration remained significantly shorter

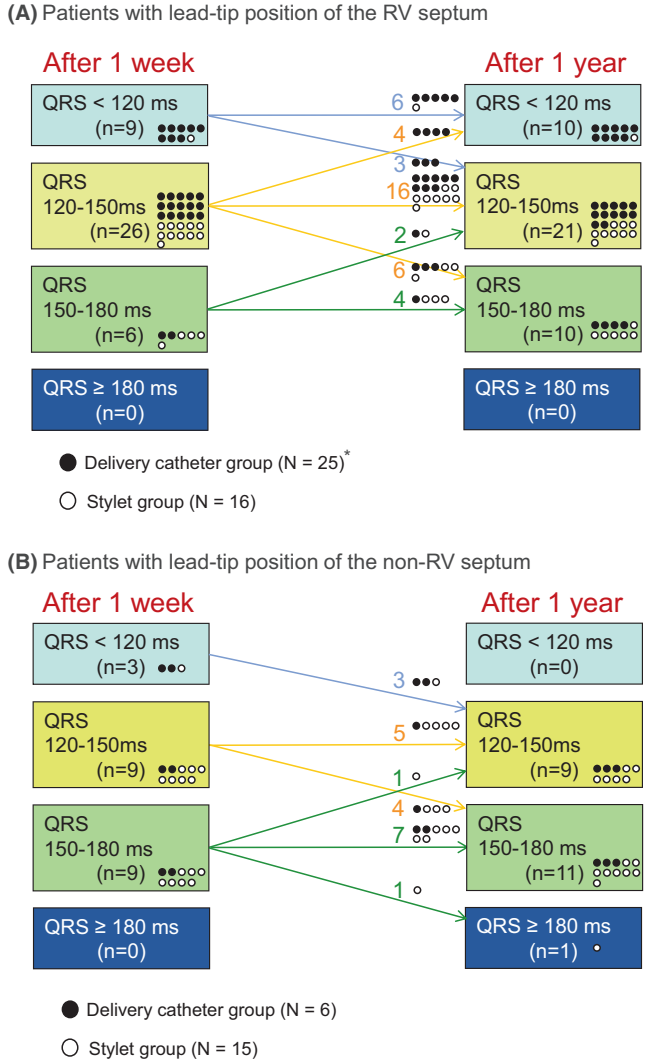

FIGURE 3 Distribution and trends in the paced QRS duration for the delivery catheter group and the stylet group after postprocedure (1 week) and after 1 year. (A) The paced QRS duration was shortened in 6 patients with lead-tip position at the RV septum. (B) The paced QRS duration was not shortened in all but one patient with lead-tip positions at the non-RV septum. *Two cases were excluded because of missing electrocardiogram data after 1 year. RV, right ventricular.

in the delivery catheter group than in the stylet group, even after 1 year. In patients with a lead-tip position at the RV septum, the lead was positioned at the basal portion of the RV more frequently in the delivery catheter group, which might contribute to the shorter-paced QRS duration. These findings have suggested that a lead-tip position at the RV septum achieved by the delivery catheter system may effectively prevent PiCM by achieving narrow-paced QRS duration. Treatment strategies of biventricular CRT and conduction system pacing are effective in improving the cardiac function after the occurrence of PiCM; however, it is also essential to prevent and decrease the risk of PiCM at the initial pacemaker implantation stage through an optimal implantation strategy. Although our study demonstrated that only two patients had developed PiCM (2.9%) among the total population, our observation period might not have been long enough, as the median time from the implantation to the onset of PiCM was reported to range from 13 months to 5.2 years after implantation.[13,14] Further extended follow-up of these populations is warranted. In the present study, no significant differences were found between the stylet and delivery catheter groups in terms of decreased LVEF, BNP levels, HF hospitalization, new development of atrial fibrillation, all-cause death, and increased prevalence of PiCM. However, the relatively short follow-up period may have made it difficult to detect any significant differences.

Khurshid et al.[15] identified a prolonged paced QRS duration at follow-up as strongly associated with the development of PiCM. Specifically, a paced QRS duration ≥150 ms was reported to be associated with 95% sensitivity for the presence of PiCM. In addition to LV desynchrony because of RV pacing at baseline, an increase in LV volume because of PiCM may occur in the late phase in such cases. Patients with an increased paced QRS duration ≥150 ms may need to undergo more careful echocardiographic screening or closed follow-up to detect the development of PiCM at an early stage.

4.3 | Study limitations

Several limitations associated with the present study warrant mention. This study had a small sample size and a short observation period. Because this study was a sub-analysis of the main study, the primary and secondary outcomes were not evaluated according to the sample size. Since most patients in both groups had a preserved LVEF with relatively few comorbidities and structural heart disease, changes in the LVEF and the incidence of adverse events may have been minimally estimated during the 1-year follow-up. Thus, it might have been difficult to assess the differences in the prognosis and safety outcomes between the two arms. The RV pacing rate in the stylet group was relatively low, which might have added a further unintended effect of reducing the development of PiCM and the incidence of the endpoints in those populations. This study did not evaluate mechanical dyssynchrony on echocardiography, which might lead to cardiac dysfunction and HF. Cumulative ventricular pacing rate was relatively low in the delivery catheter group (67% vs. 83%), however, the sensitivity analysis (analyzing only patients with cumulative ventricular pacing rate >90%) did not show any significant change in the results. Operator skills might also have influenced the outcomes. Further studies with long-term follow-up are necessary to assess whether or not RV septal pacing using the delivery catheter system reduces the incidence of PiCM compared to that using the stylet system and to determine its impact on outcomes such as HF hospitalization and all-cause death.

5 | CONCLUSIONS

The delivery catheter system was similarly useful and safe compared to the existing stylet system according to the mid-term follow-up

evaluation of the Mt FUJI trial. The paced QRS duration remained significantly shorter in the delivery catheter group than in the stylet group at 1 year. Further long-term follow-up is required to assess PiCM in these patients.

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CONFLICT OF INTEREST STATEMENT

Dr. Yuichiro Maekawa received research and fellowship grants from Biotronik, Medtronic, and Abbott. The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL STATEMENT

The study protocol was approved by the Clinical Research Review Board of the Hamamatsu University School of Medicine (approval number: 20-038) and by the hospital administrator in each participating hospital.

PATIENT CONSENT STATEMENT

Written informed consent was obtained from all patients or their legal guardians before inclusion and randomization.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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