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CASE REPORT

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Safety and efficacy of first-line cryoablation for para-hisian ventricular arrhythmias using a cryomapping protocol approach: A case series

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Abstract
A first-line cryoablation for para-Hisian VAs using a strict cryomapping protocol is useful and safe, even if the His bundle potential is recorded on the ablation catheter.

KEYWORDS
atrioventricular block, cryoablation, cryomapping, para-hisian region, ventricular arrhythmias

1 | INTRODUCTION

Four patients with para-Hisian ventricular arrhythmias (VAs) underwent successful first-line cryoablation without atrioventricular conduction disturbance using a strict cryomapping approach. Even if the His bundle potential was recorded on the ablation catheter, cautious first-line cryoablation for para-Hisian VAs using a cryomapping protocol can be performed with safety and efficacy.

Ventricular arrhythmias (VAs) arising from the para-Hisian region sometimes occur. Previous reports have demonstrated that para-Hisian VAs accounted for approximately 3% of all idiopathic ventricular tachycardias.[1,2] However, catheter ablation for VAs arising from the para-Hisian region was reported to be challenging due to the risk of atrioventricular (AV) conduction disturbance.[3,4] A cryoablation system has been recently developed as an alternative approach to treat arrhythmia, and the system is considered as a feasible approach to avoid the risk of injury to conduction systems, such as the His bundle.[5-9] Nevertheless, there is no guarantee that AV conduction disturbances will not occur even while using cryoenergy. Previous study reported a permanent AV block that occurred during cryoablation for para-Hisian VAs.[8] We herein reported the safety and efficacy of cryoablation for the treatment of VAs originating from the para-Hisian region using a strict cryomapping protocol.

2 | CASE SERIES REPORT

2.1 | Cryomapping and ablation protocol

The 4-polar electrode catheter was placed in the right ventricle or the His bundle region for recording an intracardiac electrogram and for pacing stimulation. First, the location of the His bundle and the earliest activation site of the VAs were searched using a multielectrode mapping catheter (PENTARAY, Biosense Webster, Inc) under fluoroscopy guidance and a three-dimensional (3-D) mapping system (CARTO 3 system, Biosense Webster, Inc). A 6-mm tip cryoablation catheter (Freezor Xtra, Medtronic, Inc, Minneapolis, MN) was used for ablation. At first, cryomapping at −30°C was performed to assess the disappearance of VAs and lack of occurrence of AV conduction disorder. After confirming the safety and efficacy of cryoablation by cryomapping, subsequent freezing with a target temperature of −70 to −80°C was applied while monitoring the AV conduction system. If an AV block developed, the cryoapplication was immediately stopped, and a cryoablation catheter was repositioned slightly toward to ventricular apex site which was below the previous ablation site. A procedural protocol for cryomapping and cryoablation was based both on safety (avoiding AV block) and efficacy (eliminating VAs) (Figure 1). If the His bundle potential was not visible in the distal electrode of the ablation catheter placed at the earliest ventricular activation site, cryoenergy was delivered at the myocardial site exhibiting the earliest ventricular activation after confirmation of the QS pattern on a local unipolar electrocardiogram and perfect pace mapping. When the His bundle potential was visible in the distal electrode of the ablation catheter placed at the earliest activation site, we first evaluated the effect of the elimination of VAs on cryomapping slightly toward to ventricular apex site (below the earliest activation site). The efficacy was defined as the disappearance of VAs within 20 seconds after starting cryomapping.[10] If the effect was poor but no AV block was found, cryomapping was performed by shifting the catheter to the earliest ventricular activation site where the His bundle potential was visible in the distal electrode of the catheter. When no AV block occurred during cryomapping, freezing was started with AV conduction monitoring. Before performing cryoablation at any site, tests to confirm the efficacy and safety of cryomapping were consistently performed. If the efficacy was poor, but no AV block was found during cryomapping at the earliest ventricular activation site, a cryoablation catheter was repositioned slightly above the previous ablation site. When an AV block occurred during cryomapping at any region, cryomapping was immediately stopped, and the ablation catheter was moved slightly toward to ventricular apex site, and then, cryomapping was attempted repeatedly to evaluate the safety and efficacy in the same manner. The primary target ablation site was the earliest activation site of VAs without visible His bundle potential at which the efficacy and safety were confirmed by cryomapping. However, the earliest activation site of VAs with visible His bundle potential, at which the efficacy and safety of cryomapping were confirmed, was also acceptable as the ablation site. When there were no progressive complications during subsequent cryoablations, cryoapplication was continued for up to 240 seconds with freeze-thaw-freeze cycles. One cycle of freeze-thaw-freeze was counted as twice of cryoablation. We confirmed no recurrence of VAs by isoproterenol infusion or burst pacing from the ventricle for 20 minutes after cryoablation. If the clinical VAs recurred during waiting time, recryomapping was attempted again to evaluate the safety and efficacy according to the protocol and cryoablation was applied in the same manner. A bonus freezing was not generally performed after successful freeze-thaw-freeze ablation. When the efficacy and safety of cryomapping were not obtained at any region, an alternative approach like retrograde approach or radiofrequency ablation was considered. The procedure was performed at Yokkaichi Municipal Hospital, Mie, Japan. All patients provided written informed

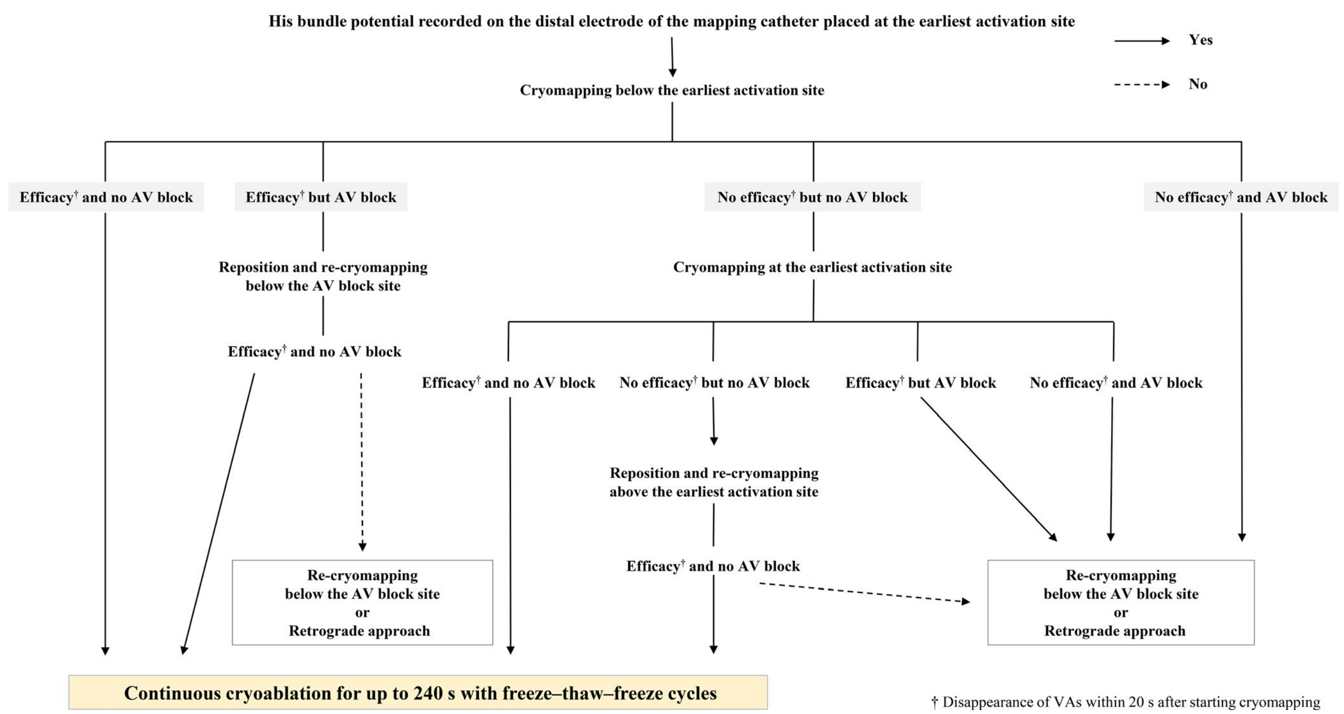

FIGURE 1 Protocol of the cryomapping and cryoablation procedures. AV, atrioventricular; VAs, Ventricular arrhythmias

consent before the ablation procedure. The procedure complied with the principles of the Declaration of Helsinki.

2.2 | Case 1

A 72-year-old female patient had frequent VAs originating from the His bundle region. She had a history of dual-chamber pacemaker implantation due to sick sinus syndrome. The 24-h Holter monitoring detected 40,618 of VAs per day. The VA morphology on ECG suggested the origin of VA to be near the His bundle region (Figure 2A). The earliest activation site of VAs was very close to the His bundle region. At the earliest activation site, the QRS morphology of pace mapping was similar to that of the clinical VA (Figure 2B). The His bundle potential was recorded on the distal electrode of the ablation catheter placed at the earliest activation site. Thus, cryomapping was attempted below the earliest activation site, but VAs did not disappear. Thereafter, cryomapping was attempted at the earliest activation site. The intracardiac electrogram showed a local potential which preceded the QRS on the surface ECG by 30 ms at VA and a His bundle potential in the distal electrode of the ablation catheter at sinus rhythm (Figure 2C). After starting cryomapping, the VA disappeared within 12 seconds, and no conduction disorder occurred at this point (Figure 2D). Freezing at a target temperature of −70°C to −80°C was performed subsequently. Cryoapplication was performed for 240 seconds with freeze-thaw-freeze cycles. However, the clinical VA recurred during waiting time after freezing. Therefore, cryomapping was attempted above the earliest activation site. After we confirmed the efficacy and safety of the cryomapping at the site, cryoablation was performed subsequently. However, a second-degree AV block occurred 26 seconds after cryoablation. Thus, cryoapplication was immediately stopped. After the recovery of the normal PQ interval, the cryoablation catheter was repositioned toward to ventricular apex site. A tiny His bundle potential was still recorded on

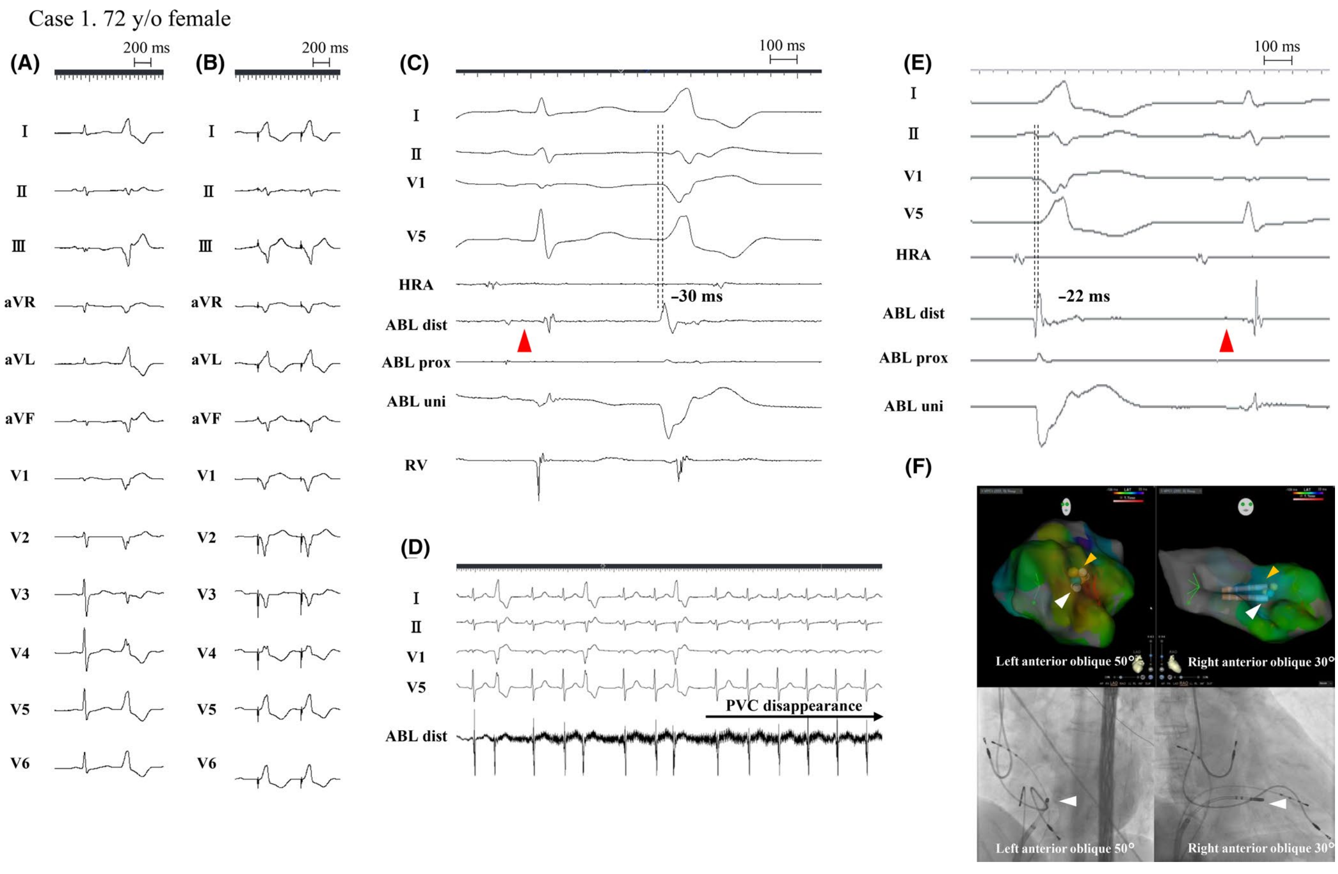

FIGURE 2 Case 1: A 72-year-old female patient who underwent cryoablation for the first time. A: PVC on body surface ECG. B: Perfect pace mapping at the earliest activation site. C: Earliest ventricular activation site. The red triangle denotes the His bundle potential. A local potential preceded QRS by 30 ms at the distal electrode of the ablation catheter. A local unipolar electrocardiogram shows the QS pattern. D: PVC disappeared 12 s after the start of cryomapping. E: The intracardiac electrocardiogram of final ablation point resulting in successful elimination of PVC. The red triangle denotes the His bundle potential. F: Three-dimensional (3-D) mapping and fluoroscopy images taken during cryoablation. The orange arrows denote the atrioventricular block site during cryoablation, and the white arrows denote the site of successful cryoablation. The yellow tag on 3-D mapping shows the site showing a visible His bundle potential, and the blue tag shows the earliest activation site. PVC, premature ventricular contraction; ECG, electrocardiogram

the distal electrode of the ablation catheter (Figure 2E). Once again, we confirmed the efficacy and safety of the cryomapping at this site, and then, cryoapplication was performed for 240 seconds with freeze-thaw-freeze cycles (Figure 2F). The target VAs were successfully eliminated, and no permanent AV block or recurrence of VA occurred during waiting time after ablation. The numbers of the cryomapping and cryoablation times were 7 and 5 times, respectively.

2.3 | Cases 2-4

Figure 3 shows the detailed ECGs and mapping images of 3 patients (Cases 2-4) with VAs originating from the para-Hisian region, which were successfully eliminated by the cryoapplication system without a transient AV block. Cryoablation was finally performed even at the site where the His bundle potential could be confirmed on the distal electrode of the ablation catheter in 2 patients and on the proximal electrode of the ablation catheter in 1 patient. However, the disappearance of VAs without the occurrence of AV block was confirmed during previous cryomapping at these sites. All 3 patients achieved the disappearance of VAs within 20 seconds after starting cryomapping (11, 18, and 6 seconds, in cases 2, 3, and 4, respectively). Cryoenergy was delivered up to the target freezing time with safety and efficacy in all 3 patients. Cryoapplication was reperformed in cases 2 and 4 because the VAs recurred during the waiting time after freezing. The numbers of times that cryomapping and cryoablation were applied were 4, 2, and 2 times and 6, 2, and 4 times in cases 2, 3, and 4, respectively.

2.4 | Procedural and clinical outcome

The procedure results and outcomes in the population are summarized in Table 1. The total number of cryomapping and cryoablation were 3.8 ± 2.4 times and 4.3 ± 1.7 times, respectively. All patients underwent 24-h Holter monitoring during a median follow-up period of 125 days (75-227 days) and had no significant recurrences without the use of antiarrhythmic therapy. Further, no patients had any AV block after the procedure.

2.5 | Discussion

This case series demonstrates the utility of the cryomapping approach and reports the outcomes of first-line cryoablation for VAs arising from the para-Hisian region. The radiofrequency (RF) catheter ablation near the electrical conduction system has the risk of AV block, whereas the cryothermal

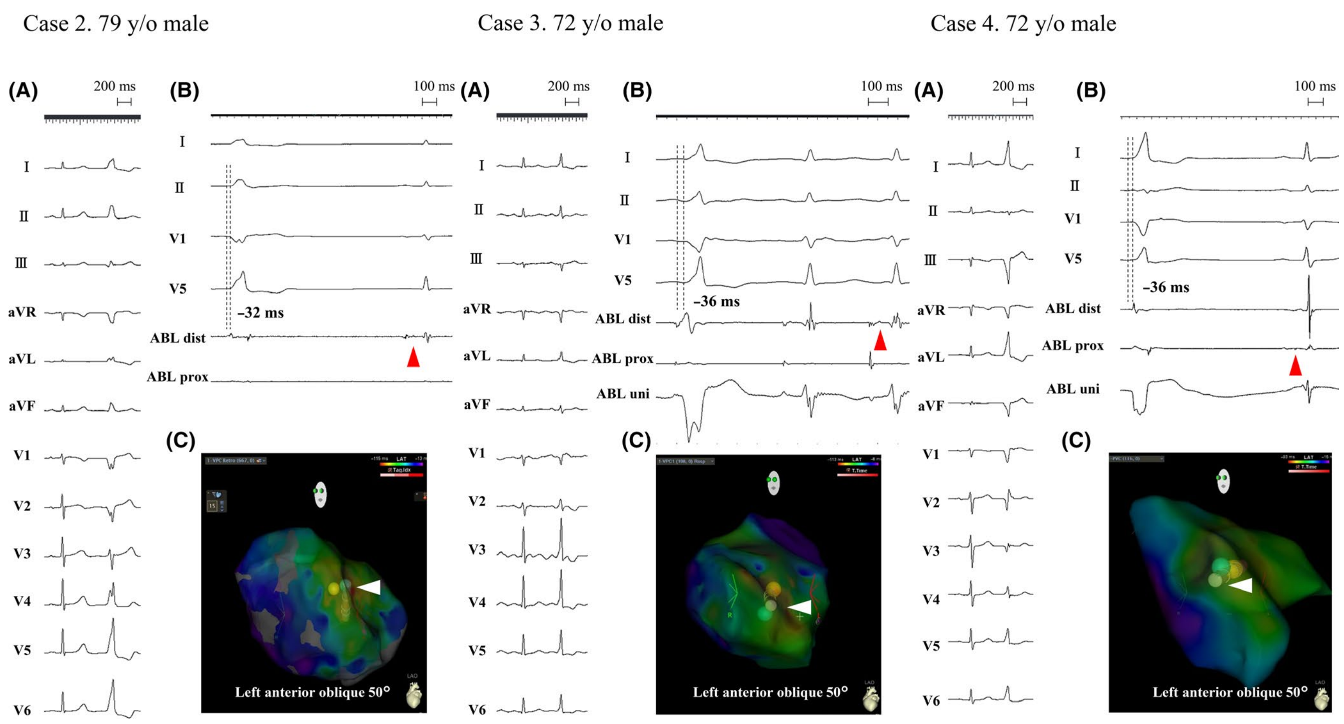

FIGURE 3 Cases 2-4: Successful elimination of ventricular arrhythmias originating from the para-Hisian region by first-line cryoablation. A: PVC on body surface ECG. B: Earliest ventricular activation site on intracardiac electrogram. The red triangles denote the His bundle potential. C: Successful cryoablation sites on 3-D mapping. The yellow tag shows the site showing a visible His bundle potential, and the blue tag shows the earliest activation site. The white arrow denotes the site of successful cryoablation. PVC, premature ventricular contraction; ECG, electrocardiogram

TABLE 1 Patient characteristics and procedure results

Case No.	Case 1	Case 2	Case 3	Case 4
Patient characteristics				
Sex	Female	Male	Male	Male
Age (y)	72	79	72	72
Body mass index (kg/m^2)	20	22	21	23
Left ventricular ejection fraction (%)	69	61	56	54
PQ interval before ablation (ms)	152	151	145	175
Ventricular arrhythmia				
Nonsustained ventricular tachycardia	Yes	–	–	Yes
Premature ventricular contraction	–	Yes	Yes	–
Total number of ventricular arrhythmias before ablation/day	40,618	18,006	15,330	15,473
Cryoapplication results				
Total number of cryomappings	7	4	2	2
Total number of cryoablations	5	6	2	4
His bundle potential at the cryoablation site	Distal	Distal	Distal	Proximal
PQ interval after ablation (ms)	156	165	148	174
HV interval before ablation (ms)	42	40	42	40
HV interval after ablation (ms)	50	46	46	44
Procedural and clinical success	Success	Success	Success	Success

system has an advantage of avoiding AV conduction disturbance.[6,11] However, to date, little has been reported on the safety and efficacy of cryoablation for para-Hisian VAs.[5,8,9] Miyamoto et al[8] reported that cryoablation was performed in 10 patients with VAs arising from the para-Hisian region and clinical success was obtained in 4 patients. In their study, only 2 patients (20%) underwent cryoablation as first-line treatment, while 8 patients underwent cryoablation secondary to the failure of previous RF ablation. Most patients underwent RF ablation as first-line treatment, and only a few patients underwent cryoablation as first-line treatment in their study. Therefore, the modification of the previous RF ablation could somewhat effect on the tissue of the VA origin and AV conduction before cryoablation. In contrast, we reported that the VAs originating near the His bundle region were successfully eliminated by first-line cryoablation in all 4 patients. Furthermore, the efficacy may be explained by a strict cryomapping protocol of the disappearance of VAs within 20 seconds after starting cryomapping.[10] Another study also reported a successful cryoablation for VAs from para-Hisian region. However, cryotest (cryomapping) was attempted before the cryoablation only in 40% of the patients, and detailed approach and mapping protocol of the cryotest were not reported in their study.[5] In the present case series, we reported detailed procedure-related results and clinical outcomes for all 4 patients who underwent first-line cryoablation using a strict cryomapping protocol. The VAs originating near the His bundle region were successfully eliminated by cryoablation. Furthermore, there were no permanent complications, including AV block or recurrence in those patients. First-line cryoablation using a cryomapping protocol may be considered as an alternative approach to RF ablation for para-Hisian VAs with appropriate feasibility and safety.

Of interest, in all patients, we had to finally freeze the site at which the His bundle potential was recorded on the ablation catheter, which was a high-risk area in terms of AV block. A unique therapeutic approach of cryomapping made it possible for us to apply ablation energy to the para-Hisian region or even to a site at which the His bundle potential was recorded. Cryoenergy has several desirable characteristics in terms of avoiding AV conduction disturbances. First, effectiveness and safety can be confirmed by cryomapping at less severe temperatures before using the cryoablation mode. Reversible and smaller lesions formed during cryomapping could reduce the risk of AV blocks.[12,13] Therefore, we could approach a more optimal ablation site that is in proximity to the His bundle using cryomapping based on the results of electrophysiological studies. The safety of this approach could be explained by the cryomapping and cryoablation protocol. Before cryoablation, we consistently used cryomapping at the target site to determine whether an AV block and a prolonged AV interval occurred even at the mild temperature. Cryoablation was never applied to the site at which a transient AV block occurred during cryomapping. Second, the cryoablation catheter tip adheres to the myocardium once cryoablation starts, with freezing of both the tip and myocardium, and the adherence is strong and not affected by the heartbeat.[5-7] In contrast, the RF ablation catheter moves according to the heartbeat during ablation, which may cause extensive unintentional tissue damage. Additionally, since the VAs in our cases might arise from not deep in the myocardium rather than the His bundle, the delivery of cryoenergy to the site of origin could be achieved. Nevertheless, there is no guarantee that AV conduction disturbances will not occur even while using cryoenergy. Transient AV blocks have been reported in 2%–23% of cryoablation procedures, and this proportion is relatively high, although most AV blocks were transient.[5,14] Furthermore, Miyamoto et al[8] reported a complete AV block that occurred during cryoablation for para-Hisian VAs in a patient with a first-degree AV block at baseline, which required the implantation of a permanent pacemaker. Thus, extreme caution is needed, especially in patients with AV conduction disturbances at baseline or when both RF ablation and cryoablation are performed for para-Hisian VAs.

3 | CONCLUSION

Cautious first-line cryoablation near the His bundle region using the strict cryomapping approach can be performed with safety and efficacy. Nonetheless, caution is needed because of the risk of AV conduction disturbance during ablation.

ETHICS STATEMENT

All patients provided written informed consent before the ablation procedure. The procedure complied with the principles of the Declaration of Helsinki.

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Published with written consent of the patient.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

YM: wrote the main manuscript, prepared Table and Figures, and reviewed the manuscript. S. Y.: interpreted the data and helped to draft the manuscript. MK, YI, and TM: critically reviewed and revised the manuscript. All authors: discussed and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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