Identification of epicardial connections can improve the success rate of first-pass right pulmonary vein isolation

Tadashi Wada, MD, Keita Matsuo, MD, Shin Takayama, MD, Masahiko Ochi, MD, Yurie Arisuda, MD, Hiroaki Akai, MD, Yuji Koide, MD, Hiroaki Otsuka, MD, Kenji Kawamoto, MD, Machiko Tanakaya, MD, Yusuke Katayama, MD

From the Department of Cardiovascular Medicine, National Hospital Organization, Iwakuni Clinical Center, Yamaguchi, Japan.

BACKGROUND Epicardial connections between the right pulmonary vein (PV) and the right atrium have been reported.

OBJECTIVE The purpose of this study was to evaluate the usefulness of our new pulmonary vein isolation (PVI) strategy with identification of these epicardial connections.

METHODS Overall, 235 patients with atrial fibrillation were included. High-density mapping of the left atrium was performed to identify the earliest activation sites (EASs) before PVI in all patients. With our new strategy, if EASs around the right PV carina were identified, we ablated these sites and performed usual first-pass circumferential PVI. The patients were divided into 2 groups according to the ablation strategy. One hundred fifteen patients underwent first-pass PVI without information on EASs (nonanalyzed group), and 78 patients underwent ablation at EASs around the right PV carina in addition to PVI (analyzed group). After first-pass ablation around the PV antrum, remapping was performed.

RESULTS High-density mapping before PVI showed that the prevalence of EASs around the right PV carina was 10.9% in all patients (9.6% in the nonanalyzed group, 12.8% in the analyzed group; $P = .74$. The first-pass right PVI success rate was higher in the analyzed group than in the nonanalyzed group (93.6% vs 82.6%; $P = .04$). The radiofrequency application time for PVI was significantly shorter in the analyzed group than in the nonanalyzed group (45.6 ± 1.0 minutes vs 51.2 ± 0.9 minutes; $P < .05$).

CONCLUSION Identification of epicardial connections before ablation could improve the success rate of first-pass right PVI.

KEYWORDS Atrial fibrillation; Pulmonary vein isolation; First-pass isolation; Epicardial connection; High-density mapping; Application time; Ablation strategy

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Introduction

Pulmonary vein (PV) isolation (PVI) is a widely accepted cardiac ablation procedure used to treat atrial fibrillation (AF).[1] Complete electrical isolation of all 4 PVs is essential. However, acute or chronic electrical reconnection can occur.[2] Reconnection can be caused by residual conduction gaps along the ablation line or other connections between the PVs and the left atrium (LA). Previous studies have reported that the presence of epicardial connections via intercaval fibers that connect the right PVs with the right atrium (RA) can preclude successful PVI.[3–5] These epicardial connections can be identified using high-density mapping before PVI.[6] Epicardial connections between the right PVs and the RA can be found more frequently than other epicardial connections around the LA.[7,8] Therefore, when the earliest activation sites (EASs) around the right PV carina are identified beforehand, ablating these sites in addition to usual first-pass circumferential PVI might be reasonable. In this study, we hypothesized that this ablation strategy might improve the success rate of first-pass right PVI.

Methods

Study population

Two hundred thirty-five consecutive patients with AF (mean age 69.8 ± 8.4 years; 69.6% male) who had undergone ablation for AF between October 2019 and April 2023 at the National Hospital Organization Iwakuni Clinical Center were retrospectively included in this study. Patients with longstanding persistent AF for more than 3 years and patients who had structural heart disease were excluded from the study. All antiarrhythmic drug therapy was discontinued 4–5 half-lives before the procedure, except for amiodarone, which was discontinued 8 weeks beforehand. Written

Address reprint requests and correspondence: Dr Tadashi Wada, Department of Cardiovascular Medicine, National Hospital Organization, Iwakuni Clinical Center, 1-1-1 Atago-machi, Iwakuni City, Yamaguchi 740-8510, Japan. E-mail address: wd.tadashi@gmail.com.

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KEY FINDINGS

- The prevalence of earliest activation sites around the right pulmonary vein carina was 10.9% with high-density mapping before pulmonary vein isolation.
- The success rate of right pulmonary vein isolation was 93.6% in the new strategy group with pulmonary vein isolation.
- The success rate of right pulmonary vein isolation was 82.6% in the conventional strategy group with pulmonary vein isolation.
- The radiofrequency application time for pulmonary vein isolation was significantly shorter in the new strategy group than in the conventional group.

informed consent for data acquisition was obtained from all patients. The study conformed to the 1975 Declaration of Helsinki and was approved by the institutional review board of our institution.

LA mapping before ablation

Electrophysiological evaluation and catheter ablation were performed with patients under conscious sedation using dexmedetomidine, propofol, and fentanyl. Surface electrocardiograms and intracardiac electrograms were continuously monitored and stored on an EP-WorkMate recording system (Abbott, St. Paul, MN). A 6F, 20-pole, dual-site mapping catheter (BeeAT, Japan Lifeline Co. Ltd., Tokyo, Japan) was inserted through the subclavian vein and positioned in the coronary sinus and RA throughout the procedure. An intracardiac echocardiography catheter (Soundstar, Biosense Webster, Diamond Bar, CA) was advanced to the RA via the femoral approach to guide transseptal puncture. A long sheath (SL0, AF Division, Abbott) and a steerable sheath (Sure-Flex, Scentific Corporation, MA) were then advanced into the LA. During high right atrial (HRA) pacing, each PV and the LA were mapped with a duodecapolar mapping catheter (PentaRay, Biosense Webster). Points were acquired using the CARTO CONFIDENSE module (Biosense Webster) in auto-freeze mode. The filters of the CONFIDENSE continuous mapping module were as follows. (1) LA mapping before ablation was performed during HRA pacing with a cycle length of 600 ms under sinus rhythm (SR). When AF persisted, cardioversion was performed before mapping. Patients in whom SR could not be maintained during LA mapping were excluded. (2) Local activation time stability filter, which compares the local activation time of each new beat to the previous beat and rejects those with a local activation time of 3 ms. (3) Position stability filter, which rejects points, was collected 2 mm away from a previous beat. (4) Tissue proximity filter, which uses impedance measurements to determine an electrode's proximity to the cardiac surface. The PV and LA maps were displayed as a voltage map or anatomic map throughout mapping and ablation.

High-density mapping in the LA revealed the EASs, suggesting the presence of epicardial connections between the LA and the RA. To identify EASs around the right PV carina, as many points as possible were mapped around these sites in the right PVs. The EASs were judged using multiple pieces of information, including the local potential, local activation time, and coherent map (Figure 1A).

Catheter ablation

For the 141 patients who underwent ablation for AF between October 2019 and October 2022, an operator (TW) performed PVI without information about the EASs in the LA. The EASs were judged offline after the procedure by the operator, who was blinded to the study aim and concept. For the 94 patients who underwent ablation for AF between November 2022 and April 2023, the same operator received information about the EASs in the LA and ablated depending on the presence of the EASs. If EASs were identified around the right PV carina, the point ablation at these sites in the right PV was created in addition to usual first-pass circumferential PVI (Figure 1B). If the EASs were identified around the right PV antrum, the anterior part of the PVI line in the right PV was created inside or above the EASs.

The ipsilateral PV antrum was circumferentially ablated with a ThermoCool SmartTouch or STSF catheter under CARTO guidance (Biosense Webster). Radiofrequency energy was delivered at a power of 30–35 W at the posterior aspect and at 35–40 W at the anterior aspect of the PV antrum. Radiofrequency energy was delivered until an ablation index $\geq$380 was reached at the posterior wall/roof and $\geq$420 at the anterior wall. PVI was considered complete when entrance and exit block were confirmed with the multipolar high-density mapping catheter, defined by both loss of PV potentials and failure to conduct to the LA by pacing at 10 mA from bipolar pairs of electrodes on the multipolar high-density mapping catheter positioned at the PV entrance.

LA mapping after first-pass PVI

After first-pass PVI, LA mapping during HRA pacing was performed, regardless of whether bidirectional PVI was attained. Residual conduction gaps were mapped. All conduction gaps were classified as 1 of 2 types: endocardial or nonendocardial.[8] Endocardial conduction gaps were defined as gaps that satisfied the following conditions: (1) the EASs inside the initial PVI lines on remapping were located on the PVI lines; and (2) the PV antrum connection was eliminated by ablation along the PVI lines. Nonendocardial gaps were defined as gaps that satisfied the following conditions: (1) both the EASs inside the initial PVI lines on remapping and outside the PVI lines during PV pacing were located >5 mm away from the PVI lines; and (2) the connections between the right PVs and the RA were eliminated by ablation at the EASs.

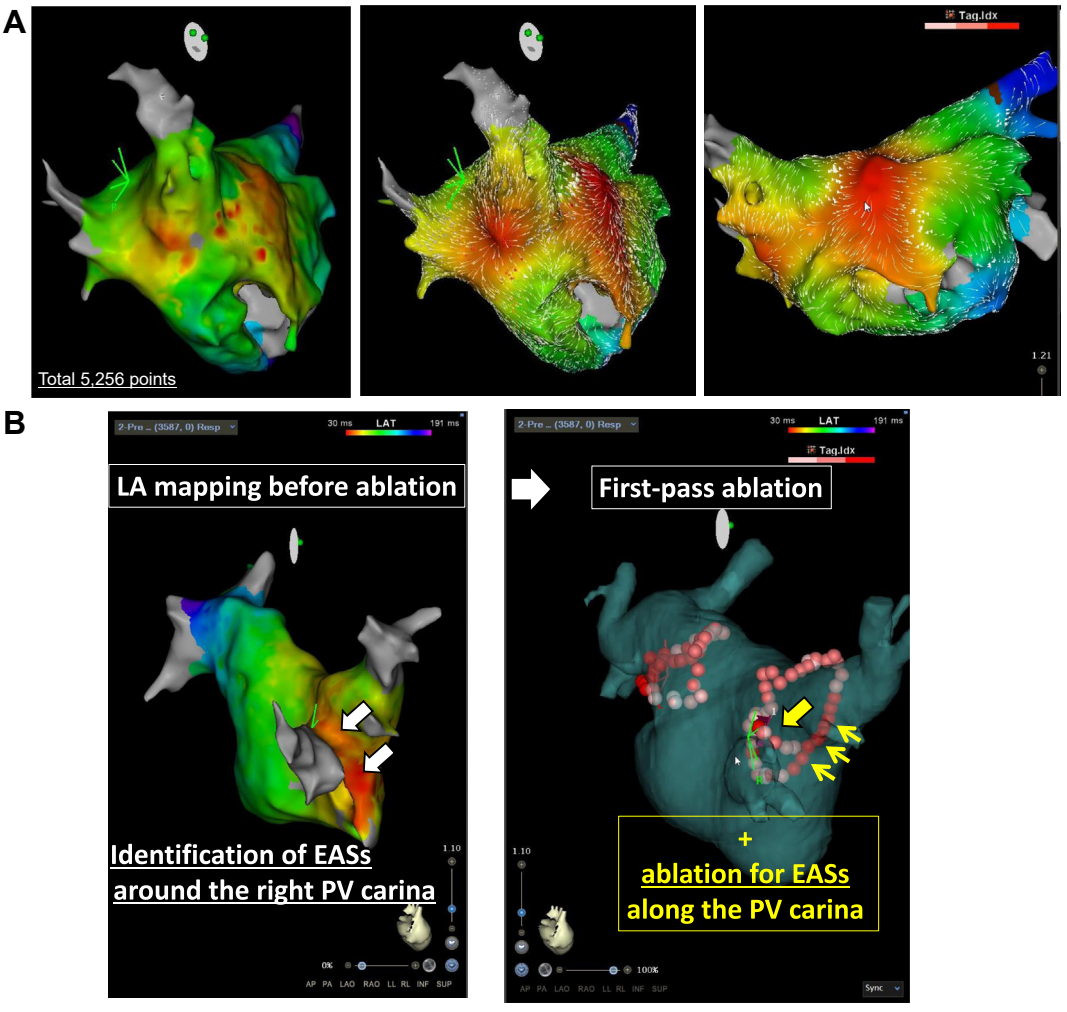

Figure 1 Mapping of the left atrium (LA) before ablation. **A:** Case of mapping of the LA to identify the earliest activation sites (EASs) along the right pulmonary vein (PV) before ablation. High-density mapping of the LA under pacing from the high right atrium (RA) identified conduction from the RA to the LA. The EASs from the RA to the LA were identified. The EASs in the LA were evaluated according to the local activation time, vector display, and local potentials. **Left:** Activation map. **Middle, right:** Activation using the coherent map. In the representative case, 2 EASs at the right PV carina and the Bachmann bundle can be seen. **B:** Our new pulmonary vein isolation (PVI) strategy involving ablation at the EASs along the right PV carina in addition to circumferential PVI. **Left:** Preablation mapping of the LA identifies the earliest site of excitation in the right PV carina. In the representative case, 2 EASs around the right PV carina were identified. One was at the middle portion of the right PV carina *(top white arrow),* while the other was along the anterior side of the right PV antrum *(bottom white arrow).* **Right:** In this case, we created an anterior line inside or along the lower EAS *(3 thin yellow arrows)* and applied point ablation at the upper EAS *(thick yellow arrow).*

Procedural time

To evaluate the usefulness of the 2 strategies, procedural time was measured during ablation. Total PVI time was the time required to complete bilateral PVI. We also measured the procedural time to create the first-pass ipsilateral circumferential radiofrequency lesion, regardless of completion of bidirectional block along the PV antrum. The time to achieve complete PVI was defined as the duration from the start of ablation for PVI to achievement of bidirectional block along the PV antrum, including the time required for remapping to identify the residual gaps.

Statistical analysis

Continuous variables are given as mean ± SD. The mean was compared between the 2 groups using the Student *t* test or the Mann-Whitney *U* test. Discrete variables and nominal variables are given as frequency (percentage). Differences between the 2 groups were tested by the χ^2 test or Fisher exact test. $P < .05$ was considered significant. The time to arrhythmia recurrence was estimated using the Kaplan-Meier method and compared between the groups using the log-rank test. All analyses were performed using JMP Version 7 statistical software (SAS Institute, Cary, NC).

Results

Patient baseline characteristics

The study flow is shown in Figure 2. Among the 235 patients, 42 were excluded because SR could not be maintained during LA mapping before ablation. A total of 193 patients were divided into 2 groups according to the ablation strategy: 115 patients who underwent first-pass PVI without information about EASs (nonanalyzed group) and 78 patients who

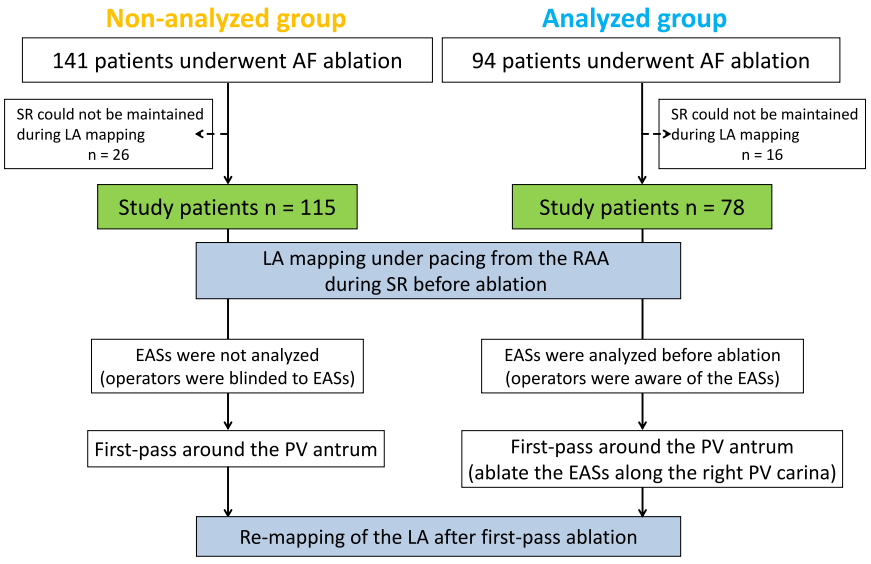

Figure 2 Study flowchart. A total of 193 patients were divided into 2 groups according to the ablation strategy used for atrial fibrillation (AF), including 115 patients who underwent first-pass pulmonary vein (PV) isolation without information about the earliest activation sites (EASs) (nonanalyzed group) and 78 patients who underwent ablation at the EASs along the right PV carina in addition to PV isolation based on the information about the EASs (analyzed group). RAA = right atrial appendage; SR = sinus rhythm.

underwent ablation at the EASs along the right PV carina in addition to PVI (analyzed group).

Baseline characteristics of the 193 patients are listed in Table 1. In the nonanalyzed group and the analyzed group, mean age was 68.1 ± 9.3 years and 70.8 ± 7.5 years, respectively, and the proportion of male patients was 68.7% and 69.2%, respectively. All patients were undergoing AF ablation for the first time. The prevalence of paroxysmal AF was 60.9% and 57.7% in the nonanalyzed and analyzed groups, respectively. No significant differences in baseline characteristics were observed between the 2 groups. Additionally, no differences were identified in the usage of antiarrhythmia drugs between the 2 groups.

Presence of EASs along the right PV carina before ablation

As a result of LA mapping before ablation among the 193 patients, a total of 4085 ± 1485 points were obtained on the LA. The EASs were classified into 4 sites: Bachmann bundle,

Table 1 Comparison of baseline characteristics between the nonanalyzed and analyzed group

	Nonanalyzed group (n = 115)	Analyzed group (n = 78)	*P* value
Age (y)	68.1 ± 9.3	70.8 ± 7.5	.06
Male sex, male, n (%)	79 (68.7)	54 (69.2)	.93
Paroxysmal AF	70 (60.9)	45 (57.7)	.33
Persistent AF	45 (39.1)	33 (32.3)	.33
First session	115 (100.0)	78 (100.0)	
Hypertension	73 (63.5)	59 (75.6)	.07
Diabetes mellitus	12 (10.4)	11 (14.1)	.44
History of heart failure	13 (11.3)	13 (16.6)	.13
History of stroke	6 (5.2)	6 (7.7)	.48
$CHADS_2$ score	1.2 ± 0.9	1.3 ± 0.9	.21
CHA_2DS_2-VASc score	2.89 ± 1.31	2.43 ± 1.12	.25
Body mass index (kg/m^2)	23.6 ± 3.2	23.7 ± 3.1	.99
eGFR ($mL/min/1.73\ m^2$)	62.1 ± 15.8	58.3 ± 15.3	.12
LA diameter (mm)	39.5 ± 6.5	40.2 ± 0.7	.32
LA volume index (mL/m^2)	36.7 ± 10.5	40.7 ± 11.9	.18
Antihypertensive medication			
Beta-blocker	72 (62.6)	51 (65.3)	.45
Potassium channel blocker	0 (0)	0 (0)	.48
Bepridil	9 (7.8)	7 (8.9)	.35
Amiodarone	5 (4.3)	3 (3.8)	.48

Values are given as mean ± SD or n (%) unless otherwise indicated.
AF = atrial fibrillation; eGFR = estimated glomerular filtration rate; LA = left atrium.

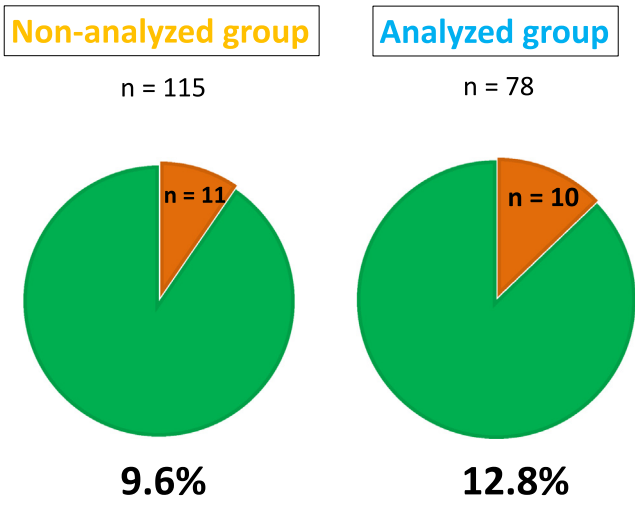

Figure 3 Presence of earliest activation sites (EASs) along the right pulmonary vein (PV) carina before ablation. The prevalence of EASs along the right PV carina was 9.6% (11 patients) in the nonanalyzed group and 12.8% (10 patients) in the analyzed group.

right PV carina, septum, and right superior PV. The prevalence of EASs along the right PV carina was 9.6% (11 patients) in the nonanalyzed group and 12.8% (10 patients) in the analyzed group (Figure 3). No significant differences were observed between the 2 groups.

Relationship between identification of EASs and success of first-pass PVI

In the left PVs, the number of patients with successful first-pass PVI was 101 (87.8%) in the nonanalyzed group and 70 (89.7%) in the analyzed group (Figure 4A). The incidence of residual conduction gap was 12.7% and 10.2% in the nonanalyzed and analyzed groups, respectively. There were no significant differences in the incidences of endocardial and nonendocardial gaps between the 2 groups.

In the right PVs, the number of patients with successful first-pass PVI was 95 (82.6%) in the nonanalyzed group and 73 (93.6%) in the analyzed group (Figure 4B). In the right PVs, the rate of first-pass PVI success in the analyzed group was significantly higher than in the nonanalyzed group ($P = .04$). The rate of residual conduction gap was 17.4% in the nonanalyzed group and 6.4% in the analyzed group. Figure 5 shows a representative case with nonendocardial gaps after unsuccessful first-pass PVI in the analyzed group. Although no early excitation was detected in the right PV carina during mapping before ablation, first-pass PVI was not successful. The EASs appeared in the middle portion of the right PV carina during subsequent mapping, and PVI was achieved by ablation at this site.

Procedural duration

Table 2 shows comparisons of the procedural and fluoroscopy durations between the 2 groups. There were no significant differences in the total procedural and fluoroscopy times between the 2 groups. However, the total radiofrequency application time for PVI was significantly shorter in the analyzed group (45.6 ± 1.0 minutes vs 51.2 ± 0.9 minutes; $P = .03$). There was no difference in the time taken to create the first-pass lesion between the 2 groups, but the time taken to achieve complete right PVI was significantly shorter in the analyzed group (24.6 ± 4.6 minutes vs 29.0 ± 4.1 minutes; $P = .01$).

Complications

No PV stenosis or phrenic nerve palsy involving ablation around the right PV carina occurred in either group.

Discussion

Main findings

The major findings of this study are as follows. First, we proposed a new AF ablation strategy, which involves

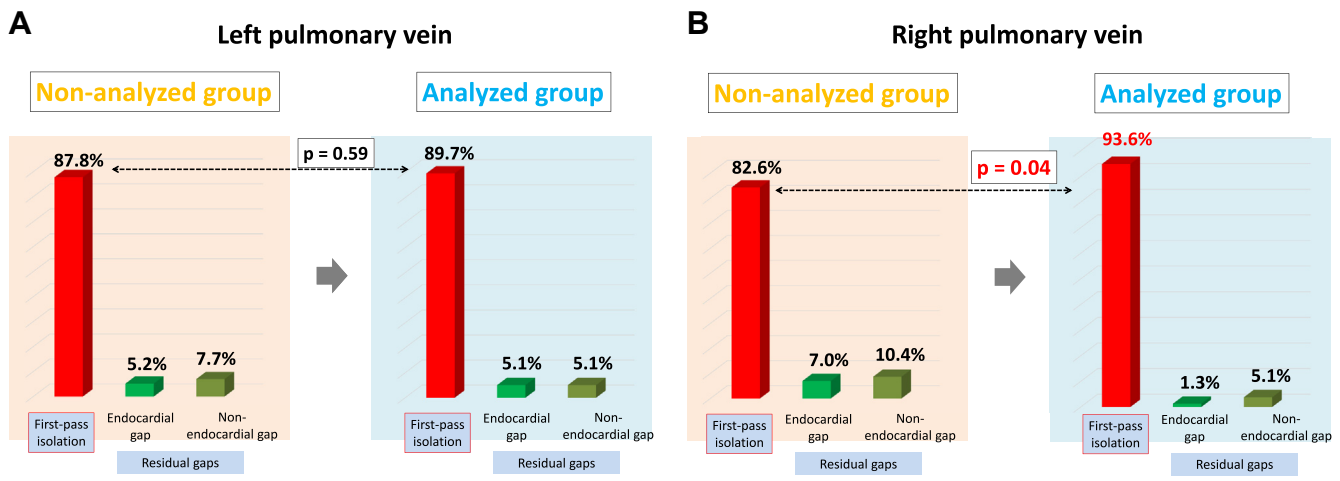

Figure 4 Proportion of patients with successful first-pass pulmonary vein isolation (PVI) and residual gaps after first-pass PVI. **A:** Proportion of patients with successful first-pass left PVI *(red bars)* in the nonanalyzed group **(left)** and analyzed group **(right).** *Green bars* show the proportion of patients with residual gaps. **B:** Proportion of patients with successful first-pass right PVI *(red bars)* in the nonanalyzed group **(left)** and analyzed group **(right).** *Green bars* show the proportion of patients with residual gaps.

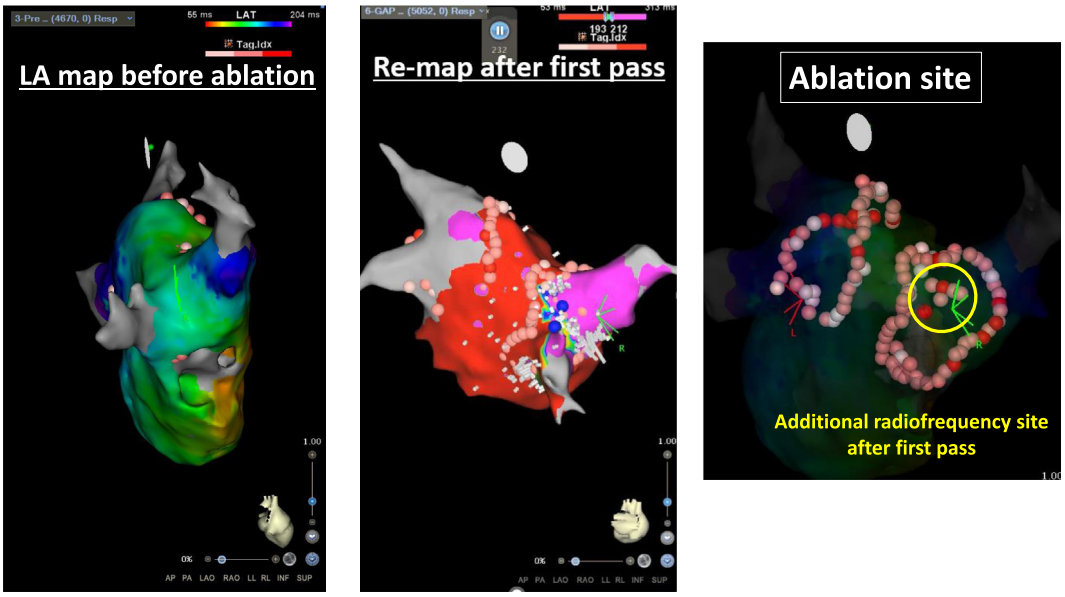

Figure 5 Representative case of a patient with nonendocardial gaps after unsuccessful first-pass pulmonary vein isolation (PVI) in the analyzed group. **Left:** In a 72-year-old woman with paroxysmal atrial fibrillation, the map of the left atrium (LA) before ablation showed no EASs around the right pulmonary vein (PV) carina. **Middle:** PVI could not be achieved after the first-pass, and subsequent mapping revealed the residual new earliest activation sites along the right PV carina. **Right:** Successful PVI was completed by ablation at the EAS.

ablating the EASs around the right PV carina before performing usual first-pass circumferential PVI. This ablation strategy significantly increased the success rate of first-pass right PVI. Second, this strategy meant that the total procedural time and radiofrequency application time for PVI were significantly shorter in the analyzed group. These results illustrate the usefulness of identifying epicardial connections before ablation.

Table 2 Comparison of procedural characteristics between the nonanalyzed and analyzed group

	Nonanalyzed group (n = 115)	Analyzed group (n = 78)	*P* value
Procedural time (min)	138.3 ± 11.9	130.6 ± 8.2	.08
Fluoroscopy time (min)	11.3 ± 0.9	12.6 ± 1.2	.88
Radiofrequency application time			
PVI total (min)	51.2 ± 0.9	45.6 ± 1.0	.03
Time to create first-pass lesion			
Left PV (min)	24.3 ± 0.9	24.6 ± 1.2	.82
Right PV (min)	21.0 ± 1.1	22.6 ± 1.6	.35
Time to achieve complete PVI			
Left PVI (min)	30.3 ± 3.9	29.6 ± 4.2	.60
Right PVI (min)	29.0 ± 4.1	24.6 ± 4.6	.01

Values are given as mean ± SD unless otherwise indicated.
PV = pulmonary vein; PVI = pulmonary vein isolation.

Difficulty in complete first-pass PVI

PVI is the cornerstone of treatment of AF ablation. Improvements in 3-dimensional mapping systems,[9,10] steerable sheaths,[11] and radiofrequency systems[12] have improved the rate of successful PVI compared with previous methods. Even when the latest radiofrequency systems are used, achieving first-pass PVI can be difficult. In some cases, endocardial and nonendocardial conduction gaps exist. The efficacy of radiofrequency ablation using the index guide has been reported, and some recent reports have shown a first-pass success rate of 80%–90%, even with index guide ablation.[13–15] However, even with these procedures, acute or chronic electrical reconnection can occur.[2] Reconnection can be caused by residual conduction gaps along the ablation line or epicardial connections between the RA and the LA.[3–5]

Epicardial conduction in the right PV

The presence of epicardial connections in the LA identified by high-frequency mapping is reported to be approximately 10%.[7,8,16,17] Previous studies have reported that the presence of epicardial connections via intercaval fibers that connect the right PVs with the RA can preclude successful PVI.[3–5] Many reports have evaluated epicardial connections after achieving first-pass circumferential PVI, and the prevalence of epicardial connections between the RA and the right PVs varies from 11%[16] to 17.9%.[17] In case the connections are identified after PVI, this might be widely influenced by the ablation line, especially close to the ablation site, which is one reason for the variation in

the prevalence of epicardial connections between the RA and the right PVs. Therefore, it is reasonable to identify epicardial connections before ablation, as in the present study. To the best of our knowledge, with the exception of the present study, only 1 study has shown the presence of epicardial connections, with a prevalence of 13.5%.[7]

In the analyzed group, first-pass PVI was not successful in all patients. Specifically, first-pass PVI could not be achieved in 5 cases. One of these cases showed a gap along the line, which was thought to be due to inadequate creation of the ablation layer or the thickness of the atrial muscle at the site of the gap. In the other 4 cases, nonendocardial gaps were detected. In all 4 cases, the epicardial connections of the right PV carina could not be identified during initial mapping. However, remapping after unsuccessful first-pass PVI revealed the presence of new epicardial connections along the right PV carina (Figure 5). The reasons for this finding may be as follows. First, the epicardial connections might have had slow conduction properties. If the conduction velocity of these connections was slower than that of the Bachmann bundle, the activation map would not have been able to unmask the presence of epicardial connections during initial mapping. In the 4 patients with nonendocardial gaps, definite fragmented potentials were identified in 2 patients; however, these potentials were not identified in the other 2 patients. These findings suggest that there might have been slow conduction in the epicardial connections into the right PV carina in the former 2 cases. Second, the epicardial connections between the right PVs and the RA do not occur along a single pathway; rather, multiple connections and pathways may exist.[5,6] In a report of mapping during open heart surgery, it was reported that the mode of electrical propagation between the RA and the LA differs when the pacing site is changed, and it has been verified that the preferred pathway changes depending on the direction of conduction.[18] The preference among epicardial interatrial connections was determined by the site of stimulation and propagation. It was difficult to identify all epicardial connections in only one mapping attempt. One reason for this may be the presence of multiple connections. Recently, changing the pacing site or conduction direction has been considered as a useful method to unmask such connections.[19–21]

Clinical implications

We compared the 2 treatment strategies in this study. Ablating the EASs around the right PV carina before usual first-pass circumferential PVI increased the first-pass right PVI success rate. With the use of balloon ablation devices, the clinical implication of the analysis of epicardial connections might become less important. These balloon devices ablate around the PV carina regardless of the presence of epicardial connections. As the present study showed that the presence of epicardial connections around the right PV carina was approximately 11%, it should not be necessary to ablate the right PV carina in all cases from the point of concern of PV stenosis and phrenic nerve palsy.

In addition, a significant reduction in the radiofrequency application time for right PVI and the overall procedural time occurred with this strategy, which may allow more time to be allocated to search for AF substrates of non-PV origin.

Study limitations

First, this study was conducted at a single medical institution in a nonrandomized fashion, and the study population was small. Therefore, the findings should be further evaluated in a multicenter randomized controlled study. Second, the definition of epicardial connections, especially in remapping after first-pass PVI, might be inadequate. In remapping after radiofrequency application, in case of epicardial connections close to the ablation line, it is possible that the epicardial connection is simply endocardial edema. We could not avoid the effect of radiofrequency application when evaluating local potentials around thermal lesions. Third, some reports have revealed that some types of epicardial connection demonstrate unidirectional or bidirectional conduction between the RA and the right PVs.[22,23] In the present study, only epicardial connections with unidirectional conduction from the RA to the right PVs were evaluated.

Conclusion

Identification of epicardial connections before ablation could improve the success rate of first-pass right PVI. Our strategy might contribute to more efficient AF ablation than could previously be achieved.

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Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: Written informed consent for data acquisition was obtained from all patients.

Ethics Statement: The study conformed to the 1975 Declaration of Helsinki and was approved by the institutional review board of our institution.

Data Availability: The data that support the fundings of this study are available from the corresponding author upon reasonable request.

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