



ORIGINAL ARTICLE

Clinical and electrophysiological significance of residual unipolar voltage after performing pulmonary vein isolation in patients with paroxysmal atrial fibrillation

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Abstract

Background: Pulmonary vein isolation (PVI) is the cornerstone strategy for paroxysmal atrial fibrillation (AF). Creating a transmural block line between pulmonary vein (PV) and left atrium (LA) is important for the risk of AF recurrence. Recently, emerging evidence indicates that endocardial unipolar voltage delineates lesions of intramural or epicardial substrate in patients with ventricular tachycardia (VT). However, there are few studies on unipolar voltage evaluation in the atrium. This study describes the clinical and electrophysiological significance of unipolar voltage mapping at the site of PV-LA conjunction after PVI in patients with paroxysmal AF.

Methods: Data from patients presenting for AF ablation from April 2023 to January 2024 at Tottori University Hospital were prospectively included. To assess the electrical isolation, high-resolution voltage mapping was performed comparing groups with and without residual unipolar voltage at the site of cryo-balloon application.

Results: Fifty-seven consecutive patients who underwent cryo-balloon ablation for paroxysmal AF were included in this study. Of these, residual unipolar voltage at the site of PV-LA conjunction after PVI was identified in 22 patients. Patients with residual unipolar voltage after PVI showed significantly thicker left atrial wall thickness and larger epicardial adipose tissue volume compared with patients without residual unipolar voltage after PVI. During follow-up periods, patients with residual unipolar voltage after PVI showed a higher AF recurrence rate than those without unipolar voltage.

Conclusions: Residual unipolar voltage at the site of PV-LA conjunction after PVI may be related to AF recurrence early after the ablation, suggesting the non-transmural block line between PV and LA.

KEYWORDS

atrial fibrillation, cryo-balloon ablation, unipolar voltage mapping

1 | INTRODUCTION

Pulmonary vein isolation (PVI) for the treatment of atrial fibrillation (AF) has emerged as a cornerstone strategy with its high therapeutic efficiency. However, a certain percentage of patients still experience AF recurrence, predominantly due to pulmonary vein (PV) reconnection. Hence, creating a transmural block line of the PV from the left atrium (LA) is critically important. With regard to the lesion transmural, emerging evidence indicates that endocardial unipolar voltage mapping delineates lesions of intramural or epicardial substrate in patients with ventricular tachycardia (VT).^{1,2} This is because unipolar electrograms reflect a wider field of view and the potential to identify deeper scar from the superficial endocardium in comparison with bipolar electrograms. However, these findings were verified only in the field of ventricular mapping. Whether these mapping techniques are directly applicable to atrial mapping has not been fully investigated. Limited studies reported the potential utility of atrial unipolar voltage mapping to identify the lesion transmural.³ The purpose of this study is to describe the clinical and electrophysiological significance of residual unipolar voltage at the site of PV-LA junction after cryo-balloon PVI in patients with paroxysmal AF.

2 | METHODS

2.1 | Study participants

Patients presenting for AF ablation from April 2023 to January 2024 at a single tertiary referral center (Tottori University Hospital) were reviewed for this prospective analysis. Patients were included if they underwent cryo-balloon ablation for paroxysmal AF. Exclusion criteria were as follows: (1) patients aged <18 years; (2) AF lasting continuously beyond 7 days (i.e., persistent AF); (3) patients who had experienced previous LA ablation or LA surgery; (4) patients with structural heart disease (e.g., clinically significant mitral valve regurgitation or stenosis); (5) AF due to reversible causes (e.g., hyperthyroidism). All patients underwent echocardiography and cardiac computed tomography (CT) to screen for the presence of structural heart disease as a part of routine care. Written informed consent was obtained in all cases. This study was approved by the Human Research Ethics Committee of Tottori University Hospital and complies with the Declaration of Helsinki.

2.2 | Catheter ablation strategy and electroanatomical mapping

Our ablation strategy has been previously described.⁴ In brief, patients were sedated with conscious sedation. Catheters were introduced to the LA transseptally. Systemic anticoagulation was administered after sheath insertion using intravenous unfractionated

heparin to maintain an activated clotting time >300s prior to LA access. Anti-arrhythmic drug therapy was withheld for five half-life pre-ablation. An over-the-wire 15F steerable sheath (FlexCath or FlexCath Advance Steerable Sheath; Medtronic, Inc.) delivered the 28-mm cryo-balloon ablation catheter (Arctic Front Advance; Medtronic, Inc.) into the LA. A spiral mapping catheter (Achieve®; Medtronic) was used to advance the cryo-balloon and to map the target PV potentials. The cryo-balloon catheter was inflated and placed at the antral surface of the PV. The cryo-application was administered after confirmation of antral occlusion of the PV. To avoid phrenic nerve injury or esophageal damage, we used the "double stop" procedures during each cryo-balloon application. The criteria for the double stop of cryoablation are (1) when balloon temperature drops below -55° , (2) when esophageal temperature drops below 18° , and (3) when diaphragmatic movement is weakened or lost. The procedural endpoints were defined as the establishment of bidirectional PV-LA block. If electrical isolation was not achieved after cryo-balloon applications (180s for each application) on each vein, additional touch-up ablation was performed using conventional radiofrequency.

A three-dimensional electroanatomical mapping of the LA was depicted with a multipolar mapping catheter (OCTARAY™, Biosense Webster Inc. Diamond Bar, CA, USA, 2-2-2-2-2mm electrode spacing) using the CARTO electroanatomic mapping system (version 7). Points were acquired evenly across the entire LA. The bipolar voltage map was depicted between two adjacent electrodes of the OCTARAY™ mapping catheter, and the unipolar voltage map was depicted using the OCTARAY™ mapping catheter with TRUEref™ technology. The filter settings for bipolar voltage mapping were set to 30–500Hz, and for unipolar voltage mapping, 0–250Hz. Strict criteria were employed to account for the lack of tissue contact data on the multipolar mapping catheter. Point collection was performed only by experienced operators after careful assessment of tactile catheter pressure, fluoroscopic motion, and application of an internal point filter to within 10mm of the chamber surface geometry and ensuring tissue contact using intracardiac echocardiography. The mapping fill threshold was set at 5mm. The mitral annulus was excluded from the analysis. Bipolar and unipolar voltage was defined as the peak-to-peak electrogram voltage. The high cutoff value was set as bipolar voltage $>0.5\text{mV}$ ⁵ and unipolar voltage $>1.08\text{mV}$ ³ based on the previous studies.

2.3 | Patients were classified into the following two patterns based on the appearance of unipolar voltage mapping after the PVI procedure

- (i) Bipolar/unipolar voltage discordant group (Bi-/Uni+ group): defined as remaining unipolar voltage at the site of PV-LA junction, where cryo-balloon ablation was applied. The residual potential clearly continues from PV to LA (Figure 1A). Patients were classified as Bi-/Uni+ group if they had residual unipolar voltage in at least one PV-LA junction.

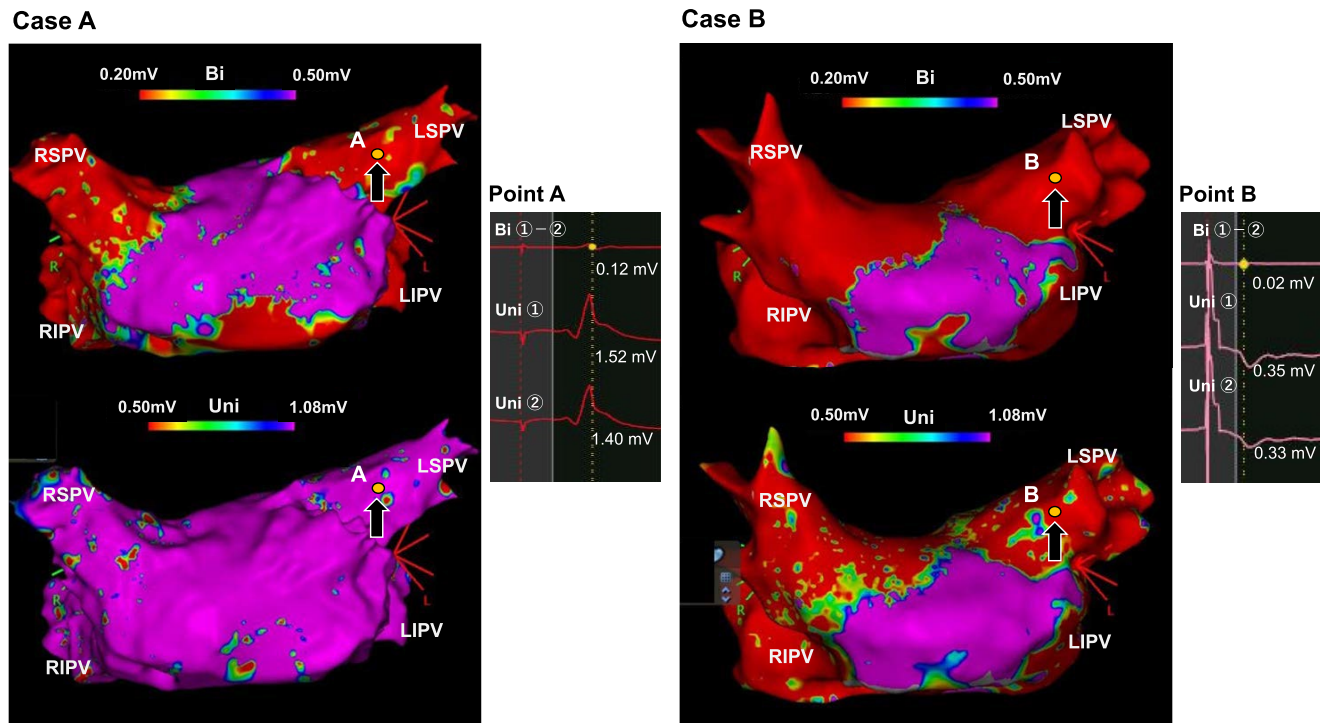


FIGURE 1 Comparison of presence or absence of pulmonary vein potential on unipolar voltage map after confirming pulmonary vein isolation on bipolar voltage map. The bipolar/unipolar voltage discordant group (Bi-/Uni+ group) was defined as the residual unipolar voltage at the PV-LA junction site where cryo-balloon ablation was applied. After cryo-balloon ablation, the residual potential continued from the PV to the LA (case A). The bipolar/unipolar voltage concordant group (Bi-/Uni- group) was defined as no residual unipolar voltage at the PV-LA junction site where cryo-balloon ablation was applied. The PV-LA junction was completely isolated by both bipolar and unipolar voltage mapping (case B). Actual bipolar/unipolar voltage amplitudes and waveforms at certain points in the pulmonary veins have been shown to the right-hand side of each figure. The top row shows the bipolar voltage and below, two rows show the unipolar voltages. Unipolar voltage map was depicted using the OCTARAY™ mapping catheter with TRUEref™ technology, and bipolar voltage map was depicted between two adjacent electrodes of the OCTARAY™ mapping catheter. Bi, bipolar; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; Uni, unipolar.

- (ii) Bipolar/unipolar voltage concordant group (Bi-/Uni- group): defined as having no residual unipolar voltage at the site of PV-LA conjunction, where cryo-balloon ablation was applied. In this group, the PV-LA conjunction was completely isolated in both bipolar and unipolar voltage mapping (Figure 1B).

measured at the thickest point in the transverse direction, and the average value of the anterior and posterior left atrial wall was defined as the LAWT as previously described.^{6,7} All measurements were performed by two independent investigators (T.T, Y.K) blinded to the study groups.

2.4 | Evaluation of computed tomography findings

2.4.1 | Left atrial wall thickness

A cardiac CT was performed using a Discovery RT (GE healthcare, Japan). The left atrial wall thickness (LAWT) was measured using the software (SYNAPSE Enterprise-PACS (Fujifilm, Japan)). LAWT was measured by CT using the commercially available software package zioM900 (Zio Software Inc., Tokyo). Cross-sectional images were reconstructed with a 0.6-mm slice at 5 mm intervals, triggering the electrocardiogram for the optimal image at the end-diastolic phase of the atrium. The left atrial wall was measured for the surface thickness outside the contrasted area of the cardiac cavity. The wall was

2.4.2 | Epicardial adipose tissue volume

Epicardial adipose tissue (EAT) volume was measured before catheter ablation as previously described.^{8,9} In short, EAT volume was calculated by a commercially available software package zioM900 (Zio Software Inc., Tokyo) using an algorithm of attenuation on cardiac CT. Using contrast-enhanced CT, an axial view of the heart was created with a 0.6 mm slice thickness. Volumetric measurement of EAT was obtained from the identification of the heart only within the pericardium. Tissue with hounsfield units between -200 and -50 within this lesion of interest was defined as fat tissue and measured semi-automatically. Lesions of interest containing EAT are created from the inferior of the pulmonary artery to the left ventricular apex. The LA volume was also quantified from the axial

view by manually tracing the endocardial border while excluding the PV ostia and LA appendage by using non-contrast CT.

2.4.3 | Follow-up

The hospital medical records and outpatient clinic assessments were used to complete the clinical follow-up. Recurrence of AF was defined based on existing clinical guidelines as AF lasting greater than 30s. Follow-up was defined from the date of the ablation procedure to the last clinical follow-up.

In this study, the hospital medical records and outpatient clinic assessments were used to complete the clinical follow-up. Patients were followed by symptoms, electrocardiography at 1, 3, and 6 months after discharge. Furthermore, AF recurrences were also assessed by implantable loop recorders or pacemakers/defibrillators when available.

2.5 | Statistical analysis

All statistical analyses were performed with JMP version 14 software (SAS Institute Inc.). The normality distribution of continuous data was tested using the Shapiro–Wilk test. Continuous variables were expressed as the mean \pm standard deviation (SD) if normally distributed: median and 25%–75% interquartile range (IQR) or full ranges were used if the data were clearly skewed. Continuous variables were compared using a Student *t*-test when normally distributed, or a Mann–Whitney *U*-test when they were not normally

distributed. A Chi-squared test was used when comparing categorical variables, or a Fisher's exact test when required. A two-tailed *p*-value $< .05$ was considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

Of the 169 consecutive AF patients who underwent PVI during the study period, 57 patients fulfilled the inclusion criteria (Figure 2). Baseline characteristics are shown in Table 1. The mean age of the population was 64.0 ± 12.7 years, 45 males (79%) with a mean LVEF of $56.9 \pm 9.5\%$.

3.2 | Patterns of post-ablation voltage map

Since the procedural endpoints were defined as the establishment of bidirectional PV–LA block, no residual bipolar voltage was identified in the area where cryo-balloon ablation was applied in all patients. On the other hand, when evaluated by unipolar voltage map, there were differences in the data regarding the prevalence of residual unipolar voltage lesions in each case. Based on our definition, 22 patients showed residual unipolar voltage at the site of PV–LA conduction after cryo-balloon ablation and were classified as Bi-/Uni+ group.

With regards to the distribution of residual unipolar voltage, among 22 cases, all 4 PVs were positive in 4 cases, 3 PVs remained

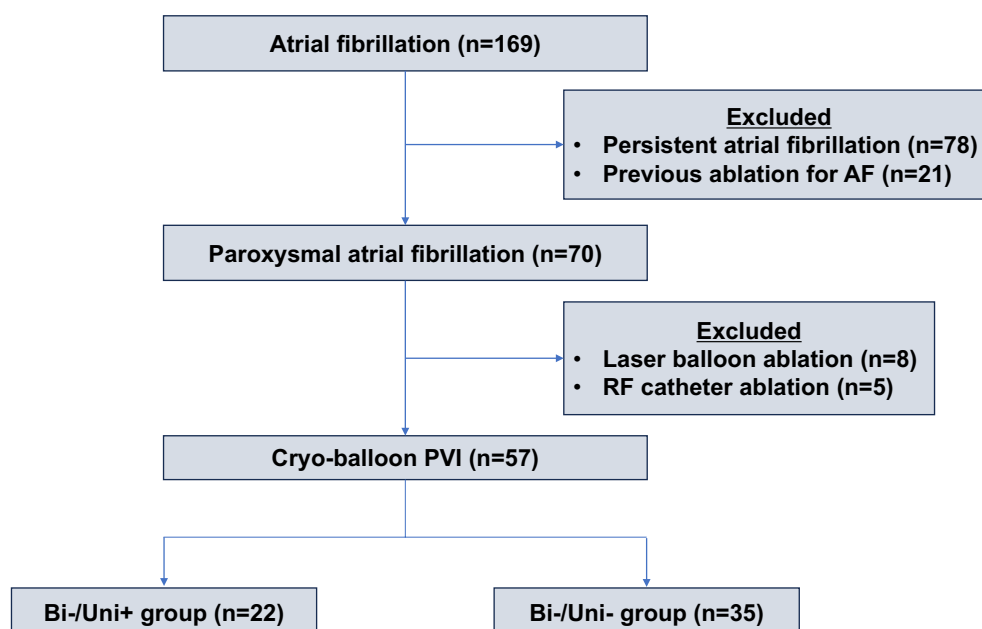


FIGURE 2 Study enrollment. During study periods, 169 patients who underwent AF ablation at Tottori University Hospital were reviewed. One hundred twelve patients were excluded due to the exclusion criteria as shown above. As a result, 57 patients were included in this study. Twenty-two patients were in the “Bi-/Uni+ group,” and 35 patients were in the “Bi-/Uni- group.” AF, atrial fibrillation; PVI, pulmonary vein isolation; RF, radio frequency.

TABLE 1 Baseline characteristics.

Variables	All patients (n = 57)
Male gender, n (%)	45 (79)
Age (years)	64.0 ± 12.7
Body mass index (kg/m ²)	24.0 (22.1–25.9)
Past medical history, n (%)	
Hypertension, n (%)	35 (61)
Diabetes, n (%)	11 (19)
Dyslipidemia, n (%)	20 (35)
Medications, n (%)	
β-blocker	26 (45)
Na channel blocker	11 (19)
Amiodarone	1 (1)
Bepidil	3 (5)
EHRA score, n (%)	
1	8 (14)
2	47 (82)
3	2 (4)
LV ejection fraction (%)	56.9 ± 9.5

Abbreviation: LV, left ventricular.

positive in 2 cases, 2 PVs remained positive in 3 cases, and 1 PV remained positive in 13 cases. From the anatomical point of view, in terms of the number of cases of residual unipolar voltage per each pulmonary vein, there were 14 residual unipolar voltage cases of LSPV, 11 cases of LIPV, 8 cases of RSPV, and 8 cases of RIPV.

Baseline characteristics comparing patients with Bi-/Uni+ group and Bi-/Uni- group were described in Table 2. Baseline characteristics were comparable between the two groups.

3.3 | Computed tomography characteristics

Preprocedural cardiac computed tomography was performed to screen for the presence of structural heart disease in all patients. Computed tomography characteristics comparing patients with Bi-/Uni+ group and Bi-/Uni- group are shown in Table 3. Patients with Bi-/Uni+ group show significantly thicker LAWT ($p = .001$) and larger EAT volume ($p = .007$) than those with Bi-/Uni- group. Figure 3 shows the representative case of patients with Bi-/Uni+ group and Bi-/Uni- group after PVI procedure. Patients with Bi-/Uni+ group show significantly thicker LAWT and larger volume of LAT compared with those with Bi-/Uni- group.

3.4 | Procedural findings and clinical outcomes

Table 4 shows the procedural findings and clinical outcomes. Entire LA voltage mapping was depicted in all patients after PVI procedure and comprised similarly distributed point densities between groups (Bi-/Uni+ vs. Bi-/Uni-; 10,802 [7172–13,853] vs. 11,741

TABLE 2 Patient characteristics.

Variables	Bi-/Uni+ (n = 22)	Bi-/Uni- (n = 35)	p value
Male gender, n (%)	16 (72)	29 (82)	.51
Age (years)	64.5 ± 12.1	63.6 ± 13.1	.79
Body mass index (kg/m ²)	24.6 (22.3–25.9)	23.7 (21.9–26.0)	.43
Past medical history, n (%)			
Hypertension, n (%)	15 (68)	20 (57)	.58
Diabetes, n (%)	5 (22)	6 (17)	.73
Dyslipidemia, n (%)	6 (27)	14 (40)	.40
Medications, n (%)			
β-blocker	12 (54)	14 (40)	.41
Na channel blocker	5 (22)	6 (17)	.73
Amiodarone	0 (0)	1 (2)	1.00
Bepidil	2 (9)	1 (2)	.55
EHRA score, n (%)			
1	1 (4)	7 (20)	.13
2	20 (90)	27 (76)	.21
3	1 (4)	1 (2)	1.00
LV ejection fraction (%)	57.3 ± 8.7	56.6 ± 10.1	.81

Abbreviations: EHRA, European Heart Rhythm Association; LV, left ventricular.

TABLE 3 Computed tomography findings.

Variables	Bi-/Uni+ (n = 22)	Bi-/Uni- (n = 35)	p value
LAWT (mm)	2.04 ± 0.23	1.83 ± 0.21	.001
Common PV, n (%)	3 (13)	2 (5)	.36
LAV (mL)	94.2 ± 19.7	89.8 ± 24.6	.48
EAT volume (mL)	14.1 ± 7.87	9.3 ± 5.6	.007

Note: A bold p value indicates the presence of statistical significance.

Abbreviations: EAT, epicardial adipose tissue volume; LAV, left atrial volume; LAWT, left atrial wall thickness; PV, pulmonary vein.

[8267–14,378], $p = .25$). Minimal balloon temperature was compared in all PVs; however, there was no significant difference between groups. The follow-up period was 6 months after the ablation procedure. During the follow-up period, patients with the Bi-/Uni+ group showed significantly higher early cumulative recurrence rates compared with those with the Bi-/Uni- group (1 week; 6% vs. 1%, $p = .01$ and 6 months; 7% vs. 1%, $p = .04$, respectively).

4 | DISCUSSION

Bipolar voltage mapping is commonly used during ablation procedures for evaluation of ablation-induced tissue effects. However,

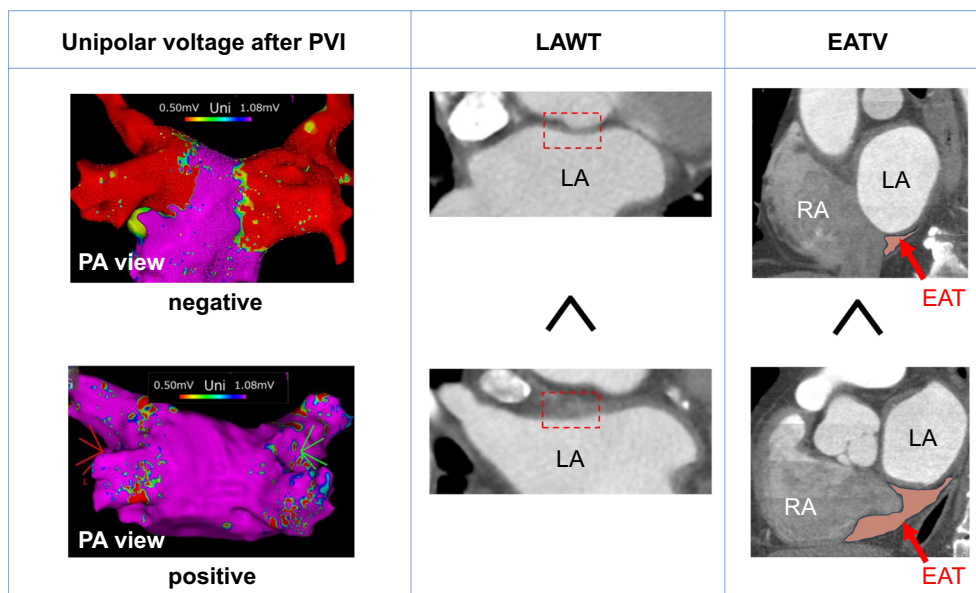


FIGURE 3 Comparison of CT findings with or without residual unipolar voltage. LAW T and EAT volume were significantly greater in patients with Bi-/Uni+ group than those with Bi-/Uni- group (2.04 ± 0.23 mm vs. 1.83 ± 0.21 , $p = .001$ and 14.1 ± 7.9 vs. 9.3 ± 5.6 , 26 $p = .007$). EAT, epicardial adipose tissue; EATV, epicardial adipose tissue volume; LA, left atrium; LAW T, left atrial wall thickness; PA, pulmonary artery; PVI, pulmonary vein isolation; RA, right atrium.

Variables	Bi-/Uni+ (n = 22)	Bi-/Uni- (n = 35)	p value
Minimum temperature (degree)			
LSPV	-52.1 ± 4.4	-52.8 ± 5.6	.65
LIPV	-45.9 ± 5.3	-46.4 ± 5.7	.80
RSPV	-54.6 ± 6.0	-55.6 ± 6.0	.63
RIPV	-50.4 ± 8.5	-49.7 ± 19.3	.87
Double stop, n (%)	8 (38)	9 (29)	.56
Multiple times, n (%)	9 (42)	19 (46)	.26
Mapping points (IQR)	10,802 (7172–13,853)	11,741 (8267–14,378)	.25
Short-term recurrence (6 months), n (%)	7 (32)	1 (3)	.003

Note: A bold p value indicates the presence of statistical significance.

Abbreviations: LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

TABLE 4 Procedural findings and clinical outcomes.

bipolar voltage amplitude is largely derived from tissue in the immediate vicinity of the mapping catheter (i.e., endocardium) so that its sensitivity to detect viable intramural-epicardial myocardium may be suboptimal. Previous studies reported the usefulness of unipolar voltage mapping for recognition of deeper intramural substrate for the VT ablation.^{10,11} Bipolar/Unipolar voltage discordance is thought to reflect the presence of imbalanced substrate, especially localized in intramural/epicardial compartments in the field of ventricular mapping. However, these are not evident in the atrium. The present study validates the utility of atrial unipolar voltage mapping in patients with paroxysmal AF. The main findings of this study are as follows:

1. Patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI showed significantly thicker LAW T.
2. Patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI showed a significantly greater amount of EAT volume.
3. During the follow-up period, patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI show a significantly higher early cumulative recurrence rate.

In our study, patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI showed thicker LAW T compared with patients without residual unipolar voltage. One of the possible explanations

why patients with residual unipolar voltage after PVI had thicker LAWT is the difficulty in creating the transmural lesion for thicker myocardium from endocardial ablation. From the anatomical viewpoint, in the field of ventricular mapping, a previous study reported that patients with VT originating from the basal septum were characterized by a larger unipolar voltage scar compared with a smaller bipolar voltage scar (i.e., bipolar/unipolar discordance).¹² This is due to the presence of imbalanced substrate especially localized in deep and intramural compartments in this thicker area. This may partly explain the relationship between bipolar/unipolar voltage discordance and thicker LAWT in patients with AF. Even in the atria, patients with thicker myocardium undergoing PVI may result in creating incomplete lesions at the site of PV-LA conjunction. The remaining intramural or epicardial myocardium may be represented as residual unipolar voltage. These data are consistent with previous studies in ventricles with subendocardial scar, and further extend this data to the atrial field.

Second, patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI showed a significantly greater amount of EAT volume in our study. EAT is considered an electrically active organ, in direct contact with the myocardium, ganglionated plexuses, and adipocytes.¹³ EAT not only has a direct effect on ablation, such as higher impedance than normal muscle,¹⁴ but also has an effect on the myocardium itself, such as electrical conduction disturbances or inflammation.¹⁵ Mahajan et al. reported that epicardial fat accumulation and subsequent fatty infiltration are associated with an inhomogeneous reduction in voltage and conduction abnormalities. These data support that patients with a greater EAT may have an inhomogeneous substrate directly or indirectly after ablation.

Lastly, patients with residual unipolar voltage at the site of PV-LA conjunction after cryo-balloon PVI show a significantly higher early cumulative recurrence rate in our study. As described above, patients with residual unipolar voltage tended to have thicker LAWT and a greater amount of EAT volume. Thicker LAWT or greater EAT volume may cause an anatomical barrier or thermal conductive obstacle during cryo-balloon ablation and incomplete lesion formation. With regard to EAT, several recent studies have demonstrated that EAT is closely associated with an increased risk of AF recurrence after catheter ablation.¹⁶ Our data strengthen our knowledge regarding the role of EAT in post-ablation AF recurrence, suggesting a potential electrophysiological role of EAT associated with AF recurrence. To the best of our knowledge, there have been no systematic data on unipolar voltage mapping after AF ablation in humans. The only reported data on unipolar voltage maps after atrial ablation have been demonstrated in animal studies.³ Our data are consistent with this atrial unipolar mapping study demonstrated in swine, extending to clinical practice in humans with AF.

4.1 | Limitations

This study had several limitations. First, the small sample size resulted in a lack of randomization, and there might have been hidden bias. Second, there were no patients who underwent simultaneous endocardial and epicardial high-density voltage mapping. Therefore, we could not assess

the relationship between endo- and epicardial voltage mapping. Third, LAWT measurements assessed the anterior and posterior LA wall and not directly the PV-LA junction site. This is due to simplifying the measurement method and minimizing measurement bias in individual cases. Similarly, EAT was not measured directly at the PV-LA junction site, but rather at the area around the heart within the pericardial sac. Fourth, the clear definition of the unipolar voltage threshold has not fully been validated to differentiate the abnormal scar in humans. There have been no systematic reports of atrial unipolar voltage threshold for the evaluation of ablation-induced tissue effects except for a single report of an animal experiment, and the present study used these criteria.³ Further studies will be needed to identify the ideal cutoff of unipolar voltage in patients with AF. Fifth, we do not have sufficient data to validate the electrical conduction from the pulmonary vein to the left atrium using a pacing study. Further study, including basic research, will be required to demonstrate the relationship between residual unipolar voltage and epicardial connection in the atria. Sixth, this is a retrospective study, and unipolar voltage mapping was analyzed offline after the ablation procedure. Therefore, we do not have data on whether residual unipolar voltage disappears with an additional ablation application. Again, further studies will be required to assess the clinical significance of additional ablation to the lesion of residual unipolar voltage. Furthermore, implantable electrocardiograms and/or long-term electrocardiogram monitoring were not available in all cases. This may have led to an underestimation of AF recurrence. Lastly, follow-up data are only 6 months in this study. It is controversial to define AF recurrence after PVI ablation within 6 months. However, recent studies have reported that recurrence during this period is associated with PV re-conduction.¹⁷⁻²⁰ To further validate the clinical significance of atrial unipolar voltage mapping, longer follow-up data will be needed.

5 | CONCLUSIONS

Patients with the residual unipolar voltage following PVI showed a higher recurrence rate of AF early after the ablation. Residual unipolar voltage might be related to thick LAWT and large EAT volume and be the predictor of early AF recurrence, reflecting the non-transmural lesion for PVI. This study highlights the limitation of bipolar electrograms for transmural evaluation of ablation-induced tissue effects. Unipolar voltage mapping may be beneficial for assessing post-ablation endpoints in patients with AF.

CONFLICT OF INTEREST STATEMENT

Dr. Yamamoto has received lecturer fees from Otsuka Pharmaceutical Co., Ltd., Daiichi-Sankyo Co., Ltd., and Novartis and research grants from Abbott, Otsuka Pharmaceutical Co., Ltd., Medtronic Japan Co., Ltd., Daiichi-Sankyo Co., Ltd., Boston Scientific Co., Ltd., Biotronik Japan Inc., Japan Lifeline Co., Ltd., Mitsubishi Tanabe Pharma Co., Ltd., Fukuda Denshi, Takeda Pharmaceutical Co., Ltd., Ono Pharmaceutical Co., Ltd., and Novartis. Dr. Kato has received research grants from Medtronic Japan Co., Ltd. [grant number: ERP-2022-13342].

DATA AVAILABILITY STATEMENT

The data presented in this study are not officially available due to upcoming publications but are available at the request of the corresponding author.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of Tottori University Hospital (Reference no. 18A034).

PATIENT CONSENT STATEMENT

Written informed consent was obtained from each patient.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

This study does not need permission to reproduce material from other sources.

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