



# Reduced atrial conduction velocity is associated with the recurrence of atrial fibrillation after catheter ablation

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## Abstract

The recurrence of atrial fibrillation (AF) after catheter ablation (CA) is still an unsolved issue. Although structural remodeling is relatively well defined, the method to assess electrical remodeling of the atrium is not well established. In this study, we evaluated the relationship between atrial conduction properties and recurrence after CA for AF. One hundred six consecutive patients ( $66 \pm 11$  years old, male: 68%) who underwent CA for AF with a CARTO system from July 2016 to July 2019 were enrolled in this study. An activation map of both atria was constructed to precisely evaluate the total conduction time, distance, and conduction velocity between the earliest and latest activation sites during sinus rhythm. All parameters were compared between the patients with or without AF recurrence. Of the patients, 27 had an AF recurrence (Rec group). The left atrial (LA) conduction velocity was significantly slower in the Rec group than in the non-Rec group ( $101.2 \pm 17.9$  vs.  $116.9 \pm 18.0$  cm/s,  $P < 0.01$ ). Likewise, the right atrial (RA) conduction velocity was significantly slower in the Rec group than in the non-Rec group ( $81.1 \pm 17.5$  vs.  $103.6 \pm 25.4$  cm/s,  $P < 0.01$ ). A multivariate logistic analysis demonstrated that the LA and RA conduction velocities were independent predictors of AF recurrence, with adjusted odds ratios of 0.95 (95% confidential interval: 0.91–0.98,  $P < 0.01$ ) and 0.94 (0.89–0.98,  $P < 0.01$ ), respectively. In conclusion, slower conduction velocity of the atrium was associated with AF recurrence after pulmonary vein isolation.

**Keywords** Atrial fibrillation · Catheter ablation · Recurrence · Conduction property

## Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in clinical practice. The prevalence of AF is increasing as the population ages, and the existence of AF yields a poorer prognosis by increasing heart failure, stroke, and sudden cardiac death [1].

Pulmonary vein isolation (PVI) is a cornerstone for the maintenance of sinus rhythm. Currently, catheter ablation (CA) is widely indicated for drug-refractory AF [2]; however, recurrence after AF ablation is still an unsolved issue. Atrial structural and electrical remodeling is thought to be associated with AF recurrence after PVI. Evaluating the structural remodeling of the atria has been established by

imaging modalities such as echocardiography and cardiac magnetic resonance [3]; however, electrical remodeling is still a challenging issue. The relationship between atrial conduction properties and AF recurrence after PVI is not yet well known. In this study, we evaluated the relationship between the atrial conduction properties of both atria and recurrence after PVI for AF.

## Materials and methods

### Study population

Consecutive patients who underwent an initial CA for AF with CARTO3® (Biosense Webster, Inc., Diamond Bar, CA, USA) at Kitasato University Hospital from July 2016 to July 2019 were retrospectively evaluated in this study. Patients who continued to take class I, III, or IV antiarrhythmic drugs (AADs) at the time of the CA and underwent additional procedures without a PVI, such as posterior wall isolation

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and linear ablation, were excluded because they could affect the atrial conduction velocity. This study was approved by the Ethics Committee of Kitasato University Hospital (No. B20-251).

### Ablation procedure

Class I, III, or IV AADs were discontinued for at least five half-lives of each drug before CA. Because of the long half-life of amiodarone, we excluded all patients taking amiodarone irrespectively of preoperative withdrawal. Electrophysiological studies and CA were performed by experienced operators (HF, JO, NI, and JK). The procedure was performed under intravenous sedation with propofol, fentanyl citrate, and dexmedetomidine. Respiratory management was performed with mechanical ventilation using an adaptive servo-ventilation system or airway securement device (i-gel™, Intersurgical, Berkshire, UK). Two long sheaths were inserted into the left atrium (LA) after a single transseptal puncture was performed. Heparin was administered as needed to maintain the intraoperative activated clotting time at 300–400 s.

The anatomical geometry of the atrium was created using a high-density mapping catheter (PENTARAY®, Biosense Webster, Inc., Diamond Bar, CA, USA). A circular 20-electrode catheter (LASSO®, Biosense Webster, Inc., Diamond Bar, CA, USA) was inserted into the left or right superior PV, and an ipsilateral extensive encircling PVI (EEPVI) was performed with an open-tip irrigated contact-force sensor radiofrequency (RF) ablation catheter (THERMOCOOL SMARTTOUCH®, Biosense Webster, Inc., Diamond Bar, CA, USA). The RF applications were delivered in a power-controlled mode (without ramping) with 25 W and 40 W (irrigation flow up to 18 ml/min). All procedures were performed under ablation index (AI)-guided ablation. The target AI was set at 500 on the anterior wall and 400 on the posterior wall. After EEPVI, bidirectional block of each PV was confirmed using a circular catheter. Subsequently, activation and voltage maps of the LA and right atrium (RA) were created during sinus rhythm. We used Pentaray® for the mapping after PVI, similar to the pre-mapping. We used post-PVI mapping data for the analysis of conduction properties. The endpoint of mapping was to adequately record both atrial entire surface areas needed for measurements. The signal acquisition setting of CARTO system was as follows; color thresholds: from 390.0 to 490.0, position stability: 2 mm, LAT stability: 3 ms, and cycle length:  $\pm 50$  ms of sinus rhythm. If the patients had an AF rhythm at the time of the mapping, cardioversion was performed to return the patient to sinus rhythm. Patients who could not maintain sinus rhythm after PVI were excluded from the study. In addition, cavo-tricuspid isthmus (CTI) linear ablation was also performed at the discretion of the

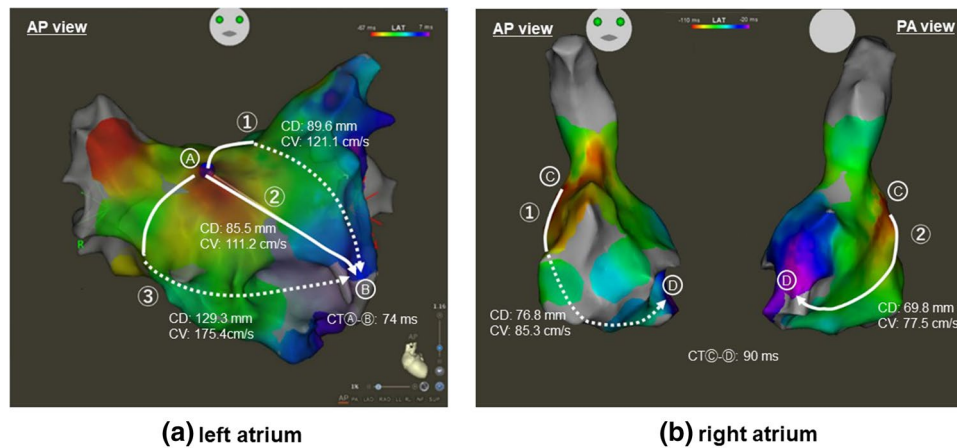
operators. After 15 min of observation, 2  $\mu$ g of isoproterenol (ISP) and 20 mg of adenosine triphosphate were administered intravenously to confirm the presence of any dormant conduction. Additional ablation was applied when dormant conduction was detected. Furthermore, 4–12  $\mu$ g of ISP was also administered to confirm the presence of non-PV foci, and additional ablation was performed if they reproducibly appeared; however, patients undergoing additional ablation other than PVI were excluded from this study.

### Measurement of the electrophysiological properties of the atria

Using the CARTO system, the LA and RA conduction times were evaluated. The earliest and latest activation sites during sinus rhythm were identified for the evaluation of the conduction distances. We evaluated the conduction time and distance on the endocardial mapping surface instead of the direct distance between the earliest and latest activation sites.

In terms of the LA conduction distance, we divided the pathways into three routes, i.e., roof, anterior, and septal routes (Fig. 1a). In general, the earliest LA activation site was at the Bachmann bundle area, and the activation propagated to the mitral isthmus area. The roof route started from the earliest activated Bachmann bundle site, passed through the roof and posterior wall, and the latest activated site was in the mitral isthmus area. Likewise, the anterior route started from the Bachmann bundle site and traveled through the anterior wall, left appendage area, and then to the latest activated area. The septal route also started from the Bachmann bundle area and traveled through the lower part of the right inferior pulmonary vein and posterior wall and then to the latest activated area. For the evaluation of the RA conduction distance, the pathways were classified into two routes, i.e., the lateral and posterior routes (Fig. 1b). The lateral route started at the sinus node and traveled to the right lateral wall, inferior wall, and then to the latest activated area, which was usually the coronary sinus (CS) ostium. The posterior route started from the sinus node and traveled to the posterior wall, septum, and then the CS ostium. The conduction velocity was calculated as each conduction distance divided by the conduction time.

We evaluated interobserver variability in measurements of LA and RA conduction velocities. We calculated in 20 randomly selected patients as the difference in two measurements in the same patient by two different observers. There was no difference in the value of those data between the two examiners for LA roof route (116.2 [90.8, 127.0] vs. 115.9 [92.2, 126.6]  $P=0.49$ ), LA anterior route (100.7 [85.2, 119.3] vs. 100.4 [84.4, 116.3]  $P=0.27$ ), LA septal route (119.5 [91.8, 135.5] vs. 118.2 [92.1, 136.1]  $P=0.85$ ), RA lateral route (93.8 [81.9, 113.6] vs. 91.0 [80.8, 114.5]



**Fig. 1** Methods of measuring the atrial conduction time, distance, and velocity. Representative LA (a) and RA (b) geometries created by CARTO® and the routes evaluated are shown. The conduction time was calculated between the earliest (A) and latest activation sites

(B), which was 74 ms in this case. The conduction distances and conduction times of each route are shown on the figure, respectively. *AP* anteroposterior, *PA* posteroanterior, *CD* conduction distance, *CT* conduction time, *CV* conduction velocity

$P=0.65$ ), and RA posterior route (93.9 [81.1, 112.2] vs. 95.2 [82.3, 113.9]  $P=0.76$ ), respectively.

We evaluated the relationship between LA low voltage areas and conduction velocities. Low voltage area was defined as the area of bipolar peak-to-peak less than 0.5 mV covering more than 5 cm<sup>2</sup> of LA. The size of each low voltage region was measured manually. LA was divided into six regions: septal, anterior, roof, posterior, inferior, lateral, as previously reported [4].

### Post procedure follow-up

Recurrence was defined as the detection of AF or atrial tachyarrhythmias lasting more than 30 s after the 3-month blanking period based on the symptoms or ECGs performed at every visit to the outpatient clinic. Holter ECGs were also performed at least 6 and 12 months after the index CA. All patients were divided into two groups based on recurrence at 1 year after the index procedure: recurrence (Rec) and nonrecurrence (non-Rec) groups.

### Statistical analysis

JMP Ver. 13.2 software (SAS Institute, Cary, NC, USA) was used to analyze the data. Continuous variables were compared using an unpaired *t* test and are described as the mean value  $\pm$  standard deviation. Categorical data were analyzed using the Chi-squared test. To assess the impact of conduction velocity on recurrence, the odds ratio was evaluated by adjusting for significant factors in the univariate analysis and previously reported relative confounders by multivariate logistic regression analysis. Receiver-operator characteristic (ROC) curve analyses were performed to determine the

diagnostic cutoff values of LA and RA conduction velocities. Statistical significance was considered to be demonstrated by two-tailed *P* values of less than 0.05.

## Results

### Baseline patient characteristics

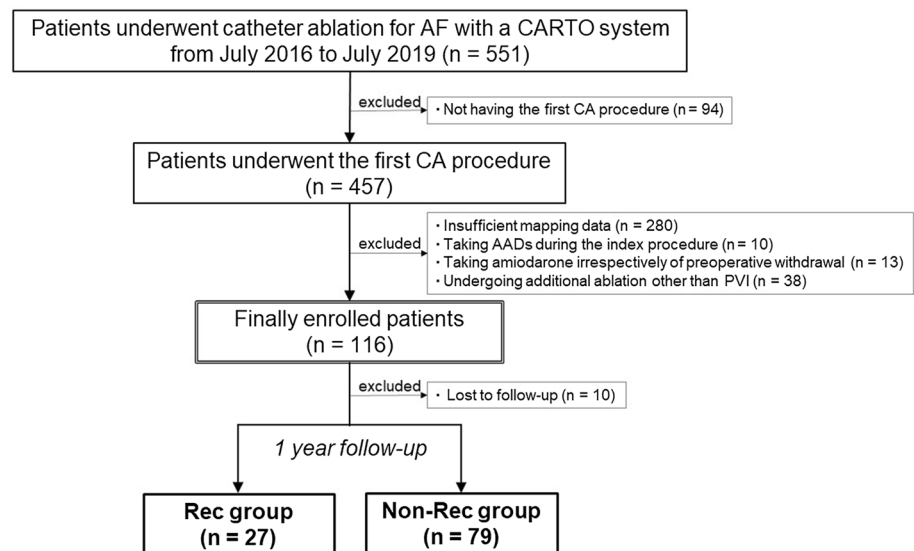
A total of 551 patients were evaluated in this study. Among those patients, 445 patients were excluded because of (1) not having the first CA procedure ( $n=94$ ), (2) insufficient mapping data ( $n=300$ ), (3) taking AADs during the index procedure ( $n=3$ ), (4) undergoing additional ablation other than PVI ( $n=38$ ), and (5) loss to follow-up ( $n=10$ ). After that, a total of 106 patients were finally enrolled in this study (Fig. 2). In terms of the RA assessment, 55 patients did not have RA mapping data; therefore, the data from the remaining 51 patients were evaluated.

The patient characteristics are shown in Table 1. There were no significant differences between the Rec and non-Rec groups except for age ( $61 \pm 12$  vs.  $68 \pm 10$  years old,  $P=0.02$ ) and incidence of heart failure (33% vs. 14%,  $P=0.03$ , respectively).

### Conduction properties and recurrence

The upper part of Table 2 shows the comparisons of the LA conduction characteristics in the Rec and non-Rec groups. The conduction time in the Rec group was significantly longer than that in the non-Rec group, whereas there was no difference in the conduction distance between them. The conduction velocity was significantly slower in the Rec

**Fig. 2** Flow chart of the patients in this study. *AAD* anti-arrhythmia drag, *AF* atrial fibrillation, *CA* catheter ablation, *PVI* pulmonary vein isolation



**Table 1** Patient characteristics

|                                 | Total (n = 106)    | Rec group (n = 27) | Non-Rec group (n = 79) | P value |
|---------------------------------|--------------------|--------------------|------------------------|---------|
| Age (years)                     | 66 ± 11            | 61 ± 12            | 68 ± 10                | 0.02    |
| Female, n (%)                   | 32 (30)            | 7 (26)             | 25 (32)                | 0.58    |
| BMI (kg/m <sup>2</sup> )        | 23.8 ± 4.4         | 24.3 ± 4.0         | 23.6 ± 4.6             | 0.53    |
| AF type                         |                    |                    |                        |         |
| Paroxysmal, n (%)               | 57 (54)            | 13 (48)            | 44 (56)                |         |
| Persistent, n (%)               | 41 (38)            | 11 (41)            | 30 (38)                |         |
| Long-standing persistent, n (%) | 8 (7)              | 3 (11)             | 5 (6)                  | 0.65    |
| CHF, n (%)                      | 20 (19)            | 9 (33)             | 11 (14)                | 0.03    |
| Hypertension, n (%)             | 58 (55)            | 13 (48)            | 45 (57)                | 0.43    |
| DM, n (%)                       | 9 (8)              | 2 (7)              | 7 (9)                  | 0.81    |
| Stroke, n (%)                   | 11 (10)            | 5 (19)             | 6 (8)                  | 0.11    |
| Duration of AF (months)         | 68 [4–66]          | 61 [9–84]          | 70 [9–84]              | 0.07    |
| LAD (mm)                        | 40.6 [37.6–44.7]   | 42.0 [38.6–46.3]   | 40.0 [37.0–44.3]       | 0.23    |
| LVEF (%)                        | 65.6 [61.2–70.0]   | 64.1 [56.7–69.9]   | 65.7 [61.5–70.4]       | 0.34    |
| HANP (pg/mL)                    | 118.7 [44.8–160.5] | 132.8 [85.9–200.3] | 114.8 [43.0–153.0]     | 0.11    |
| BNP (pg/mL)                     | 163.0 [50.6–227.1] | 184.3 [72.1–253.6] | 155.8 [39.5–217.3]     | 0.23    |
| CCr (mL/min)                    | 60.7 [49.4–76.6]   | 57.3 [45.7–86.5]   | 60.9 [49.8–86.5]       | 0.94    |
| Medication                      |                    |                    |                        |         |
| Bisoprolol, n (%)               | 36 (34)            | 10 (37)            | 26 (33)                | 0.70    |
| Carvedilol, n (%)               | 9 (8)              | 3 (11)             | 6 (8)                  | 0.57    |
| RASI, n (%)                     | 48 (45)            | 11 (41)            | 37 (47)                | 0.58    |
| MRA, n (%)                      | 6 (6)              | 1 (4)              | 5 (6)                  | 0.61    |
| Statin, n (%)                   | 25 (24)            | 9 (33)             | 16 (20)                | 0.17    |
| Concomitance with AFL, n (%)    | 10 (9)             | 2 (7)              | 8 (10)                 | 0.68    |

Values are presented as the mean ± SD and n (%) or median (first quartile–third quartile). *AF* atrial fibrillation, *AFL* atrial flutter, *BMI* body mass index, *BNP* brain natriuretic peptide, *CCr* creatinine clearance, *CHF* chronic heart failure; *DM* diabetes mellitus, *HANP* human atrial natriuretic peptide, *LAD* left atrial diameter, *LVEF* left ventricular ejection fraction, *MRA* mineral corticoid antagonists, *RASI* renin-angiotensin system inhibitors

group than in the non-Rec group. The results were consistent with the three evaluated routes. The lower part of Table 2

shows the comparisons of the RA conduction characteristics. Similar to the findings in the LA, the conduction time was

**Table 2** Comparisons of the atrial conduction characteristics with and without recurrence

| LA                                 | Rec group ( <i>n</i> = 27) | Non-Rec group ( <i>n</i> = 79) | <i>P</i> value |
|------------------------------------|----------------------------|--------------------------------|----------------|
| Conduction time (msec)             | 107.3 ± 32.9               | 86.2 ± 14.0                    | < 0.01         |
| Conduction distance (mm)           |                            |                                |                |
| Roof route                         | 101.0 ± 20.9               | 96.1 ± 17.1                    | 0.27           |
| Anterior route                     | 97.2 ± 18.7                | 92.0 ± 15.4                    | 0.28           |
| Septal route                       | 112.3 ± 19.1               | 108.9 ± 17.0                   | 0.54           |
| Conduction velocity (cm/s)         |                            |                                |                |
| Roof route                         | 98.4 ± 24.3                | 113.2 ± 21.6                   | 0.01           |
| Anterior route                     | 94.9 ± 20.9                | 109.0 ± 23.6                   | 0.02           |
| Septal route                       | 109.4 ± 24.3               | 128.5 ± 23.9                   | < 0.01         |
| Conduction velocity average (cm/s) | 101.2 ± 17.9               | 116.9 ± 18.0                   | < 0.01         |
| RA                                 | Rec group ( <i>n</i> = 14) | Non-Rec group ( <i>n</i> = 37) | <i>P</i> value |
| Conduction time (msec)             | 117.5 ± 33.0               | 94.1 ± 19.5                    | 0.02           |
| Conduction distance (mm)           |                            |                                |                |
| Lateral route                      | 90.2 ± 16.1                | 95.3 ± 17.1                    | 0.36           |
| Posterior route                    | 91.8 ± 14.5                | 92.6 ± 14.3                    | 0.70           |
| Conduction velocity (cm/s)         |                            |                                |                |
| Lateral route                      | 80.3 ± 18.1                | 105.2 ± 29.1                   | < 0.01         |
| Posterior route                    | 81.9 ± 18.0                | 102.0 ± 24.5                   | < 0.01         |
| Conduction velocity average (cm/s) | 81.1 ± 17.5                | 103.6 ± 25.4                   | < 0.01         |

significantly longer in the Rec group than in the non-Rec group, without any significant difference in each distance. The conduction velocity was also significantly slower in the Rec group than in the non-Rec group for each route.

We also investigated the differences in the conduction properties between the AF types. The patients were classified into two subgroups: paroxysmal AF (PAF) and persistent AF or long-standing persistent AF (non-PAF). Tables 3, 4 show the comparisons of the atrial conduction characteristics in the PAF and non-PAF groups. In both atria, the conduction time was longer in the Rec group and more markedly longer in the non-PAF subgroup than in the PAF subgroup. The conduction velocity and conduction distance were relatively preserved in the non-Rec group regardless of the AF type.

Table 5 shows the multivariate logistic analysis, including age, history of chronic heart failure (CHF), LA diameter (LAD), and LA conduction velocity. The analysis demonstrated that the LA conduction velocity was an independent predictor of AF recurrence after PVI, with an adjusted odds ratio of 0.95 (95% confidential interval [CI]: 0.91–0.98,  $P < 0.01$ ). Likewise, multivariate analysis, including age, history of CHF, LAD, and RA conduction velocity, demonstrated that RA conduction velocity was an independent predictor of AF recurrence after PVI, with an adjusted odds ratio of 0.94 (95% CI: 0.89–0.98,  $P < 0.01$ ).

Table 6 shows the comparisons of the LA low voltage area in the PAF and non-PAF group. In both groups, the

low voltage area was more prevalent in the Rec group. However, the position of a low voltage area was partially but not entirely consistent with the decrease in the conduction velocity.

### Cutoff values for the prediction of AF recurrence

We evaluated the best cutoff values of LA and RA conduction velocities to detect AF recurrence using ROC curve analysis (Fig. 3). In the LA conduction velocity, the values were determined as 92.9 cm/s (AUC, 0.67; sensitivity, 0.52; specificity, 0.78,  $P < 0.01$ ) in the roof route, 108.1 cm/s (AUC, 0.66; sensitivity, 0.81; specificity, 0.47,  $P < 0.01$ ) in the anterior route, and 98.5 cm/s (AUC, 0.70; sensitivity, 0.44; specificity, 0.90,  $P < 0.01$ ) in the posterior route, respectively. Likewise, in the RA conduction velocity, the values were determined as 96.5 cm/s (AUC, 0.75; sensitivity, 0.93; specificity, 0.54,  $P < 0.01$ ) in the lateral route, and 97.1 cm/s (AUC, 0.75; sensitivity, 0.93; specificity, 0.57,  $P < 0.01$ ) in the posterior route, respectively.

### Discussion

In the present study, we evaluated the relationship between atrial conduction characteristics and AF recurrence after PVI. The main findings of this study were as follows: (1) the conduction time and conduction velocity in the LA were

**Table 3** Comparisons of the left atrial conduction characteristics in the PAF group and non-PAF group

| LA (PAF group)                     | Rec group ( <i>n</i> = 13) | Non-Rec group ( <i>n</i> = 44) | <i>P</i> value |
|------------------------------------|----------------------------|--------------------------------|----------------|
| Conduction time (msec)             | 97.1 ± 19.5                | 83.1 ± 13.7                    | 0.03           |
| Conduction distance (mm)           |                            |                                |                |
| Roof route                         | 108.6 ± 17.5               | 95.4 ± 17.6                    | 0.01           |
| Anterior route                     | 93.8 ± 20.9                | 92.0 ± 13.1                    | 0.76           |
| Septal route                       | 105.5 ± 17.7               | 106.0 ± 14.4                   | 0.79           |
| Conduction velocity (cm/s)         |                            |                                |                |
| Roof route                         | 113.9 ± 18.4               | 116.7 ± 22.9                   | 0.80           |
| Anterior route                     | 97.7 ± 16.7                | 113.4 ± 25.0                   | 0.03           |
| Septal route                       | 111.4 ± 22.0               | 130.1 ± 23.7                   | 0.02           |
| Conduction velocity average (cm/s) | 107.7 ± 13.2               | 120.1 ± 19.6                   | 0.06           |
| LA (non-PAF group)                 | Rec group ( <i>n</i> = 14) | Non-Rec group ( <i>n</i> = 35) | <i>P</i> value |
| Conduction time (msec)             | 116.8 ± 40.1               | 90.1 ± 13.5                    | <0.01          |
| Conduction distance (mm)           |                            |                                |                |
| Roof route                         | 93.9 ± 21.8                | 97.0 ± 16.7                    | 0.43           |
| Anterior route                     | 100.4 ± 16.6               | 93.6 ± 17.6                    | 0.16           |
| Septal route                       | 118.5 ± 18.7               | 112.4 ± 19.3                   | 0.39           |
| Conduction velocity (cm/s)         |                            |                                |                |
| Roof route                         | 83.9 ± 20.0                | 108.9 ± 19.4                   | <0.01          |
| Anterior route                     | 92.2 ± 24.5                | 104.9 ± 19.8                   | 0.19           |
| Septal route                       | 107.5 ± 26.8               | 126.5 ± 24.2                   | 0.03           |
| Conduction velocity average (cm/s) | 95.2 ± 20.0                | 113.5 ± 15.2                   | <0.01          |

**Table 4** Comparisons of the right atrial conduction characteristics in the PAF group and non-PAF group

| RA (PAF group)                     | Rec group ( <i>n</i> = 7) | Non-Rec group ( <i>n</i> = 22) | <i>P</i> value |
|------------------------------------|---------------------------|--------------------------------|----------------|
| Conduction time (msec)             | 101.0 ± 17.8              | 93.6 ± 16.9                    | 0.36           |
| Conduction distance (mm)           |                           |                                |                |
| Lateral route                      | 85.1 ± 10.9               | 93.6 ± 16.3                    | 0.21           |
| Posterior route                    | 88.5 ± 10.5               | 93.2 ± 14.6                    | 0.32           |
| Conduction velocity (cm/s)         |                           |                                |                |
| Lateral route                      | 82.7 ± 20.4               | 101.7 ± 18.1                   | 0.04           |
| Posterior route                    | 85.3 ± 17.8               | 101.3 ± 15.7                   | 0.04           |
| Conduction velocity average (cm/s) | 84.0 ± 18.8               | 101.5 ± 15.6                   | 0.03           |
| RA (non-PAF group)                 | Rec group ( <i>n</i> = 7) | Non-Rec group ( <i>n</i> = 15) | <i>P</i> value |
| Conduction time (msec)             | 134.0 ± 37.5              | 94.9 ± 23.5                    | 0.02           |
| Conduction distance (mm)           |                           |                                |                |
| Lateral route                      | 94.7 ± 19.5               | 97.9 ± 18.5                    | 0.65           |
| Posterior route                    | 96.3 ± 17.1               | 91.7 ± 14.2                    | 0.65           |
| Conduction velocity (cm/s)         |                           |                                |                |
| Lateral route                      | 73.7 ± 17.2               | 110.2 ± 40.5                   | 0.03           |
| Posterior route                    | 75.4 ± 17.9               | 103.1 ± 34.2                   | 0.04           |
| Conduction velocity average (cm/s) | 74.6 ± 16.8               | 106.7 ± 35.8                   | 0.04           |

significantly prolonged and decreased in the Rec group compared to the non-Rec group, (2) similar findings were also observed in the RA, (3) in the non-PAF subgroup, the

conduction velocity was significantly slower in the Rec group than in the non-Rec group in both atria, (4) after adjusting for age, LAD, type of AF, and history of HF, a



**Table 5** Multivariate logistic regression analysis of the factors affecting atrial fibrillation recurrence after catheter ablation

| Variable                       | Univariate analysis |           |                | Multivariate analysis |           |                |
|--------------------------------|---------------------|-----------|----------------|-----------------------|-----------|----------------|
|                                | OR                  | 95% CI    | <i>P</i> value | Adjusted OR           | 95% CI    | <i>P</i> value |
| LA conduction velocity average | 0.95                | 0.92–0.98 | <0.01          | 0.95                  | 0.91–0.98 | <0.01          |
| Age                            | 0.95                | 0.91–0.99 | 0.01           | 0.94                  | 0.89–0.98 | 0.01           |
| CHF                            | 3.09                | 1.11–8.60 | 0.03           | 2.07                  | 0.59–7.14 | 0.25           |
| LAD                            | 1.04                | 0.97–1.12 | 0.96           | 1.02                  | 0.93–1.11 | 0.72           |
| Variable                       | Univariate analysis |           |                | Multivariate analysis |           |                |
|                                | OR                  | 95% CI    | <i>P</i> value | Adjusted OR           | 95% CI    | <i>P</i> value |
| RA conduction velocity average | 0.94                | 0.90–0.98 | <0.01          | 0.94                  | 0.89–0.98 | <0.01          |
| Age                            | 0.31                | 0.02–4.14 | 0.38           | 0.98                  | 0.91–1.05 | 0.56           |
| CHF                            | 1.38                | 0.22–8.50 | 0.74           | 1.02                  | 0.09–9.26 | 0.99           |
| LAD                            | 1.08                | 0.96–1.22 | 0.19           | 1.03                  | 0.88–1.22 | 0.72           |

AF atrial fibrillation, CHF chronic heart failure, CI confidence interval, LA left atrium, LAD left atrial diameter, OR odds ratio, RA right atrium

**Table 6** Comparisons of the left atrial low voltage area in the PAF group and non-PAF group

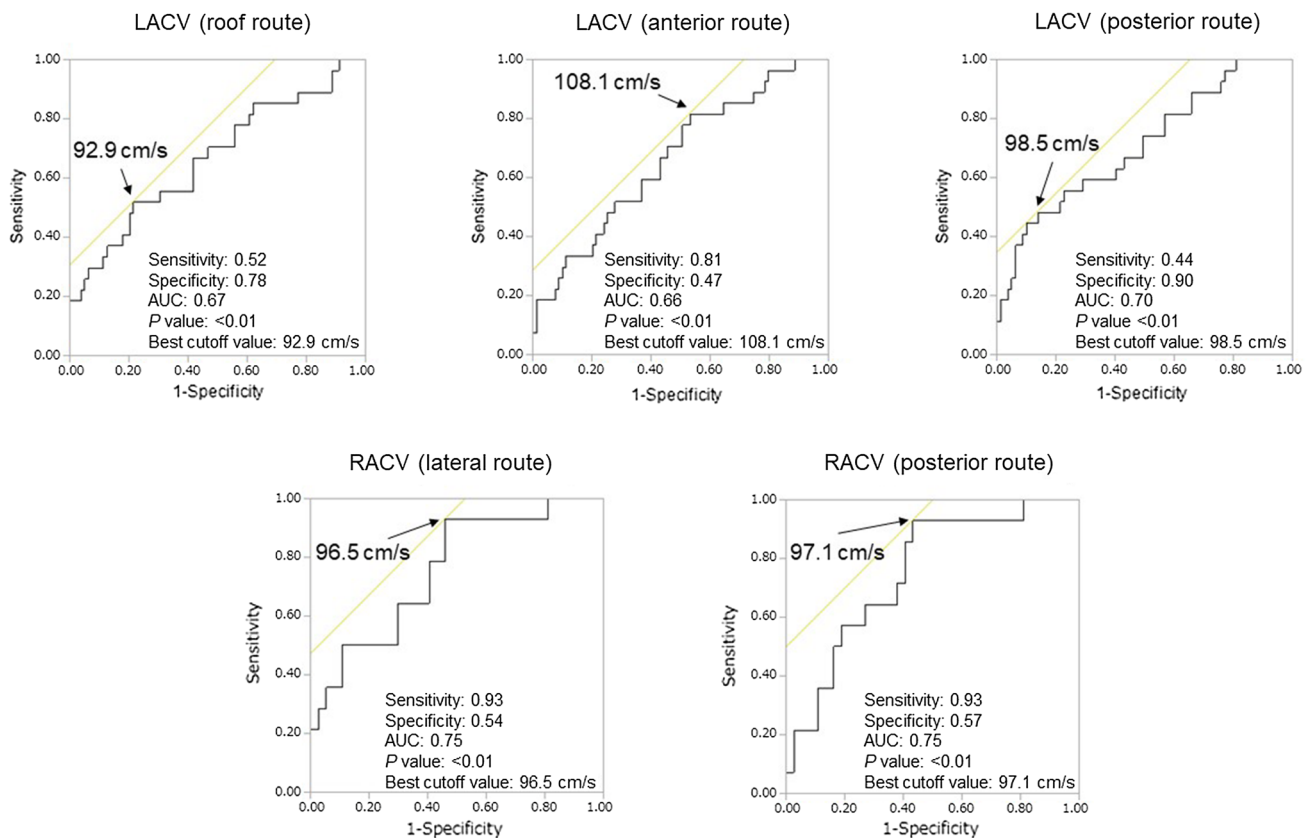
| LA (PAF group)                              | Rec group ( <i>n</i> = 13) | Non-Rec group ( <i>n</i> = 44) | <i>P</i> value |
|---|----------------------------|--------------------------------|----------------|
| Existence of low voltage area, <i>n</i> (%) | 5 (38)                     | 3 (7)                          | <0.01          |
| Septal, <i>n</i> (%)                        | 1 (8)                      | 1 (2)                          | 0.35           |
| Anterior, <i>n</i> (%)                      | 2 (15)                     | 1 (2)                          | 0.06           |
| Roof, <i>n</i> (%)                          | 0 (0)                      | 1 (2)                          | 0.58           |
| Posterior, <i>n</i> (%)                     | 2 (15)                     | 0 (0)                          | <0.01          |
| Inferior, <i>n</i> (%)                      | 1 (8)                      | 1 (2)                          | 0.35           |
| Lateral, <i>n</i> (%)                       | 0 (0)                      | 1 (2)                          | 0.58           |
| LA (non-PAF group)                          | Rec group ( <i>n</i> = 14) | Non-Rec group ( <i>n</i> = 35) | <i>P</i> value |
| Existence of low voltage area, <i>n</i> (%) | 9 (64)                     | 6 (17)                         | <0.01          |
| Septal, <i>n</i> (%)                        | 5 (36)                     | 1 (3)                          | <0.01          |
| Anterior, <i>n</i> (%)                      | 4 (29)                     | 3 (9)                          | 0.07           |
| Roof, <i>n</i> (%)                          | 3 (21)                     | 0 (0)                          | <0.01          |
| Posterior, <i>n</i> (%)                     | 2 (14)                     | 2 (6)                          | 0.32           |
| Inferior, <i>n</i> (%)                      | 3 (21)                     | 1 (3)                          | 0.03           |
| Lateral, <i>n</i> (%)                       | 0 (0)                      | 3 (9)                          | 0.26           |

slowed conduction velocity of each atrium was a significant predictor of AF recurrence after PVI, and (5) in the non-PAF subgroup, the slow conduction velocity in the septal and roof regions was associated with the existence of low voltage areas.

### Reduced conduction velocity and remodeling in the atria

Structural and electrical remodelings have been reported as the cause of arrhythmias [5]. Structural remodeling of the atria could be assessed as dilatation of the atrium by

noninvasive modalities such as echocardiography or computed tomography. A larger diameter of the LA and larger LA volume has been reported as predictors of AF recurrence after CA [6, 7]. On the other hand, electrical remodeling is hard to evaluate by noninvasive methods. *P* wave prolongation on the surface electrocardiogram has also been reported as one of the noninvasive markers of structural remodeling as well as electrical remodeling [8], and was associated with the dilatation of atria, new-onset AF [9], and AF recurrence after the CA [5]. However, electrical and structural remodelings are not always coincident. In clinical practice, there are some patients who do not show dilatation



**Fig. 3** ROC curve analysis for the prediction of AF recurrence. The best cutoff values of LACV were 92.9 cm/s, 108.1 cm/s and 98.5 cm/s for the roof route, the anterior route and the posterior route, respectively (upper panels). The best cutoff values of RACV were

96.5 cm/s and 97.1 cm/s for the lateral route and the posterior route, respectively (lower panels). *AF* atrial fibrillation, *AUC* area under the curve, *LACV* left atrial conduction velocity, *RACV* right atrial conduction velocity

of the atria but have high inducibility of AF. Those patients probably have advanced electrical remodeling other than structural remodeling. Those patients potentially have a higher risk of AF recurrence even after PVI. For this issue, we additionally evaluated the relationship between the LA diameters and LA conduction velocity in this study. As a result, LA diameters obtained by echocardiography were not related with the LA conduction velocities in the present study ( $R^2 = -0.001$ ,  $P = 0.38$ , detailed data not shown). Therefore, conduction slowing as the electrical remodeling could not be speculated by the LA diameter at least in the patients who enrolled in this study. During an invasive CA, the electrical properties can be directly evaluated. A recent paper has shown that a reduced conduction velocity in the LA is a predictor of AF recurrence after PVI [10]. In the present study, we evaluated the electrical properties in both atria in this study and revealed that the conduction velocity in the RA was also more reduced in the Rec group than in the non-Rec group. Atrial remodeling causes AF origin and maintenance [11, 12]. These changes occur both in LA and RA [13–16]; therefore, it is reasonable that the RA conduction velocity was also slower in the Rec group in this study.

Reduced conduction velocity of each atrium could cause AT/AFL; however, since almost all patients underwent CTI linear ablation regardless of the history of CTI-dependent AFL, it might affect the inducibility of AT/AFL during the procedure. It is worth noting that conduction properties were significantly different between the two groups in both atria despite LAD or duration of AF not being significantly different. Therefore, conduction properties would be another strong predictor for recurrence after PVI.

### Relationship between the AF type and conduction characteristics

Compared to PAF, the conduction distance in non-PAF would be longer due to the enlargement of the atrium. It has been reported that more fibrosis is found in the LA in patients with non-PAF than in those with PAF, suggesting that it causes the maintenance of AF and the incidence of non-PV triggers [3, 17]. This trend was also observed in the present study. In the non-PAF group, the areas of slow conduction velocity were partially associated with the low voltage areas (Table 6). On the other hand, it is also meaningful



that the conduction velocity and conduction distance were relatively preserved in the non-Rec group, even in the non-PAF subgroup (Tables 3, 4). PVI has been effective for patients with PAF but has not been adequate for those with non-PAF because non-PV foci are more prevalent in non-PAF due to the progression of remodeling. In the STAR-AF2 trial study, the efficacy of a PVI alone versus PVI plus LA linear ablation or CFAE ablation of persistent AF was evaluated, and there was no significant difference among the three procedures in terms of the maintenance of sinus rhythm for a mean of 18 months [18]. However, there have been several reports that linear ablation [19], posterior wall isolation [20], and substrate modification [21] added to the PVI are effective for patients with non-PAF. The contemporary definition of PAF and non-PAF is originally the duration of AF [1]. Therefore, non-PAF potentially also includes patients without advanced remodeling, as well as further advanced remodeling. Our data suggested that the PVI would be sufficient in patients without electrical remodeling, i.e., a preserved conduction velocity, even in the non-PAF group. By assessing the electrical remodeling of the atria, we could obtain more information on whether an additional procedure to the PVI would be needed for each patient independent of the time-defined AF type.

### Limitations

There were several limitations to this study. First, this was a single-center retrospective study with a relatively small number of patients. Second, since the entire atrial activation mapping was created after the PVI, the ablation procedure might affect the conduction properties. Third, the measurements of the atrial conduction properties were evaluated during sinus rhythm. Patients in an AF rhythm during CA underwent cardioversion. Therefore, cardioversion up to the last minute could have affected the measurement of the conduction velocity. Furthermore, patients who could not maintain sinus rhythm were excluded from this study. Fourth, the cause of recurrence, i.e., PV reconnections or other non-PV foci, could not be determined because only a few patients underwent a second procedure. Further prospective studies are needed to evaluate the relationship between electrical remodeling and AF recurrence after CA.

### Conclusion

While the main cause of AF recurrence would be PV reconnection, a longer conduction time and slower conduction velocity of each atrium were in part associated with AF recurrence after the PVI.

### Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

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