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The impact of the procedural parameters on the lesion characteristics associated with AF recurrence: late-gadolinium enhancement magnetic resonance imaging (LGE-MRI) analysis

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Abstract

Background: Lesion gaps assessed by late-gadolinium enhancement magnetic resonance imaging (LGE-MRI) are associated with the atrial fibrillation (AF) recurrence after pulmonary vein isolation (PVI). Animal studies have demonstrated that the catheter-contact force (CF), stability, and orientation are strongly associated with lesion formation. However, the impact of those procedural factors on the lesion characteristics associated with AF recurrence has not been well discussed.

Methods: A total of 30 patients with paroxysmal AF who underwent catheter ablation were retrospectively enrolled. Radiofrequency (RF) applications were performed with 35W for 30s in a point-by-point fashion under esophageal temperature monitoring. The inter-lesion distance was 4mm. The lesions were visualized by LGE-MRI three months post-procedure and assessed by the LGE volume (ml), gap number (GN), and average gap length (AGL [mm]). The gaps were defined as non-enhancement sites of >4 mm. The procedural factors including the catheter-CF, stability, and orientation were calculated on the NavX system.

Results: Six (20%) of 30 patients had AF recurrences 12 months post-ablation. A univariate analysis demonstrated that the AGL was associated with AF recurrence (hazard ratio [HR]: 1.20, confidence interval [CI]:1.03 - 1.42, $p = 0.02$). All AF recurrence were found in patients with an AGL of >7 mm. The catheter-CF and stability were associated with an AGL of >7mm, but not the orientation (CF: HR: 0.62, CI: 0.39-0.97, p=0.038; stability: HR: 0.8, CI: 0.66-0.98, p=0.027).

Conclusions: RF ablation with a low CF and poor catheter stability has a potential risk of creating large lesion gaps associated with AF recurrence.

Keywords

Atrial fibrillation, catheter ablation, ablation lesion, late-gadolinium enhancement magnetic imaging

Abbreviations

AF, atrial fibrillation; AGL, average gap length; CE-MRA, contrast enhancement magnetic resonance angiography; CC Time, constant contact time; CF, contact force; CI, confidence interval; ECG, electrocardiography; eGFR, estimated glomerular filtration rate; FFE, fast field echo; GN, gap number; HR, hazard ratio; LA, left atrium; LAD, left atrial dimension; LGE-MRI, late-gadolinium enhancement magnetic resonance imaging; LSI, Lesion Size Index; LPV, left pulmonary vein; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; RF, radiofrequency; RPV, right pulmonary vein; TGL, total gap length.

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Introduction

The lesions after atrial fibrillation (AF) ablation with radiofrequency (RF) energy can be visualized by late-gadolinium enhancement magnetic resonance imaging (LGE-MRI) and the visual lesion gaps and gap lengths are reported to be associated with AF recurrence after pulmonary vein isolation (PVI). [1-3] A previous study found that the total relative gap length (absolute gap length divided by the total length of the PVI line) assessed by LGE-MRI was associated with the AF recurrence rate. [4]

The contact force (CF) between the catheter tip and the myocardium is reported to be associated with the RF lesion size. [5] Furthermore, it is reported that it is necessary to maintain a minimum CF during the RF application for durable lesions and a reduction in AF recurrence. [6,7] The ablation catheter (Tacti Cath; Abbott, St. Paul, MN) can measure the CF using optical fibers. Further, the Lesion Size Index (LSI) is a lesion quality marker calculated by the contact force (CF), RF time, and RF current. Several studies have reported that the optimal LSI is almost 5.0, however, long and frequent RF applications are necessary to achieve the target LSI in cases it is difficult to stabilize the ablation catheter with an adequate CF due to the cardiac anatomy or respiratory motion. [8,9] Of note, long and frequent RF applications have a risk of steam pops, cardiac tamponade, and esophageal injury.

We considered that the appropriate procedural factors including the ablation settings and catheter manipulation could create more continuous and durable lesions, which could reduce AF recurrence without compromising serious complications. The aim of this study was to identify the lesion characteristics including the volume, gap number, and length that could be associated with AF recurrence and investigate the procedural factors required to achieve the better ablation lesions.

Method

1. Patients

A total of 30 patients with paroxysmal AF who underwent catheter ablation with RF energy between May 2018 and April 2020 were retrospectively enrolled. Patients who underwent non-contrast enhanced MRI due to the renal dysfunction (estimated glomerular filtration rate [eGFR] was less than 60 mL/min/1.73 m2) were excluded. The protocol for this research project has been approved by the suitably constituted Ethics Committee of the institution, and it conforms to the provisions of the Declaration of Helsinki (Committee of 2020.2.16., Approval No. 200366).

2. Mapping and ablation procedure

Transesophageal echocardiography was performed prior to the procedure to rule out any thrombus formation. The patients were examined under sedation with dexmedetomidine with spontaneous breathing. Unfractionated heparin was administered in a bolus before the transseptal puncture to maintain an activated clotting time of more than 350 seconds. When AF occurred, internal electrical cardioversion was performed to restore sinus rhythm.

A three-dimensional (3D) model of the anatomy of the left atrium (LA) and PVs obtained from a pre-interventional MRI was integrated, and mapping and ablation were performed using a NavX system (Abbott, Chicago, IL) as a guide. Before the ablation, the LA anatomy was reconstructed with a mapping catheter (Optima or Advisor HD Grid; Abbott), and the ablation catheter was aligned with the 3D image.

The RF alternating current was delivered in the unipolar mode between the irrigated tip electrode of the ablation catheter (Tacti Cath, Abbott, St. Paul, MN) and the external backplate electrode. The initial settings of the RF generator were as follows: upper catheter tip temperature limit of 43 °C, RF power of 35 W, and irrigation flow rate of 30 mL/min using the NavX system. RF ablation was applied in a “point-by-point” manner. The maximum RF time was 30 seconds. An extensive encircling PVI was performed in all patients. The PVI line was created approximately 0.5 to 1 cm from the PV ostia. Animal studies reported that LSI of 5 with a stable CF of 10 g could create the lesion width of 6 mm but the lesion width could be attenuated to 4 mm in case of intermittent CF.[10,11] Therefore, to create the continuous lesion, the interlesion distance was 4mm. The esophageal temperature was measured with a probe (Sensi Therm, Abbott, St Paul, MN), and the RF time was reduced to 10 seconds for ablation on the posterior wall near the esophagus. If the esophageal temperature rose to > 39 °C, the ablation was stopped immediately. After the esophageal temperature decreased to a normal range (37 °C), the RF application was resumed. RF power of 25 W and CF adjusted to less than 10 g were used during RF applications on the posterior wall near the esophagus. For the safety, RF application was stopped at the LSI of 5. At the posterior wall near the esophagus, RF application was stopped at the LSI of 4. Catheter navigation was performed using a steerable sheath (Agilis, Abbott, St. Paul, MN).

3. MRI acquisition

We performed contrast-enhanced MRI in all patients three months after the AF ablation using a 1.5-T MR system (Achieva; Philips Medical, Best, The Netherlands) equipped with a 5-channel cardiac coil. This scan technique is well established, and we used the acquired images for the AF ablation procedure. [12] First, we acquired contrast-enhancement magnetic resonance angiography (CE-MRA) of the PV-LA anatomy with a breath-hold 3D fast field echo (FFE) sequence in the coronal plane during the first pass of a contrast agent (gadobutrol, Gadovist; Bayer Yakuhin, Osaka, Japan) injection at a dose of 0.1 mmol/kg.[13] Scanning in the coronal plane could reduce the number of acquisition slices and breath-holding time. Next, we acquired the LGE-MRI of the LA with the PVs using a 3D inversion recovery, respiration navigated, electrocardiogram-gated, T1-FFE sequence in the transverse plane 15 minutes after the contrast injection as previously reported. [14] The typical parameters were: repetition time/ echo time = 4.7/1.5

ms, voxel size = 1.43 × 1.43 × 2.40 mm (reconstructed to 0.63 × 0.63 × 1.20 mm), flip angle = 15, sense = 1.8, and 80 reference lines. The inversion time was 280- 320 ms, and Look-Locker scans were used. The data were acquired during the mid-diastolic phase of the left ventricle. The typical scan time for the LGE-MRI study ranged from 7 to 12 minutes, which depended on the patient's heart rate and respiration pattern. The CE-MRA and LGE- MRI images were transferred to a workstation (Ziostation ver. 2.4.2.3; Ziosoft Inc, Tokyo, Japan; MRI LADE Analysis; PixSpace Inc, Fukuoka, Japan) for image processing and image analysis.

4. 3D visualization of the ablation lesions

We performed the following image post-processing with a consensus of a board-certified diagnostic radiologist and radiological technologist. The 3D visualization method for the LGE was as follows. First, the LA of the LGE-MRI was segmented semi-manually using the endocardial and epicardial boundaries of the atrium, including the PVs, as a contour while referring to the CE-MRA. Second, the mean value and SD of the voxel intensity were measured on the "healthy" LA wall without any hyperenhanced areas in the LGE-MRI. Third, a voxel intensity histogram analysis of the LA wall was used to identify intensities > 2SD on the "healthy" LA wall as LGEs. Furthermore, we categorized the degree of the intensity with color-coded scaling (green: > 2SD: yellow: 3 – 4SD; red: > 4SD). Finally, we semi-automatically fused the 3D reconstruction, color-coded LGE, and volume-rendered LA and PV images created by CE-MRA. The definition of the ablation lesion in the previous study was an artificial LGE site with a signal intensity of > 2SD around the PV. [12,13]

5. Assessment of the ablation lesion

The region around the PVs was divided into the following four segments: anterior, roof, posterior, and bottom segments (Figure 1A). The details of the segmentation process were as follows: First, we manually adjusted the inner view to maximize the PV ostium on the NavX system. Second, the shape of the cross-section was evaluated, and curved areas were defined as "roof segment" or "bottom segment". Third, the others were defined as anterior segment or posterior segment. The volume of the lesions, gap number (GN), and average gap length (AGL) in each segment were measured. An animal study reported that the maximum gap length with conduction block was 4 mm. [15] According to their result, the lesion gaps were defined as non-enhancement sites of > 4mm. A representative case is shown in Figure 1B. MRI data and Ablation data were independently assessed by two experienced electrophysiologists. Both electrophysiologists were blinded to the MRI data and ablation results with each other.

6. Procedural parameters

The NavX system records the following parameters such as the CF, impedance, LSI, etc., during ablation at intervals of 0.01 seconds. Furthermore, the lateral and axial CF were also simultaneously recorded according to the CF direction. If the catheter orientation was perpendicular to the myocardium, the axial CF increased and the lateral one decreased. If the catheter orientation was parallel to the myocardium, the lateral CF increased and the axial one decreased. An ex vivo study demonstrated that RF applications with a lateral CF could create large ablation lesions as compared to that with the same axial CF [11]. The % Lateral CF (ratio of the Lateral CF and CF) was calculated as a surrogate marker of the catheter orientation. Furthermore, the % constant contact time (percentage of time of CF > 2 g) was calculated as a surrogate marker of the catheter stability.

7. Procedural complications

The occurrence of serious complications, including cardiac tamponade and esophageal mucosal injury, was investigated to assess the safety. It was reported that LGE-MRI could assess the extent and follow the progression of esophageal wall injury after catheter ablation of atrial fibrillation, so all patients were assessed for esophageal injury on their MRI. [16]

8. AF recurrence

To evaluate AF recurrence after ablation, the patients underwent follow-up with electrocardiography (ECG) at 1, 3, 6, and 12 months after the ablation. If they had palpitations, they were asked to come to our hospital and we assessed the AF recurrence by ECGs or Holter ECGs.

9 : Statistical analysis

Continuous data are presented as the mean ± SD if normally distributed. If not normally distributed, medians and quartiles are presented. For normally distributed variables, they were tested with an unpaired t test or Welch test. For non-normally distributed variables, they were tested with a Mann-Whitney test. Categorical variables were tested with the Fisher's exact test. The LGE volume, GN, and AGL were selected for the univariate Cox proportional hazards regression model to clarify the impact of the lesion characteristics on AF recurrence. In addition, the age, gender, BMI, eGFR, left ventricular ejection fraction (LVEF) and left atrial diameter (LAD) were also selected as cofounders. To clarify the association between the procedural parameters including the catheter-CF, stability, orientation, and lesion characteristics associated with AF recurrence, univariate and multivariate regression analyses were performed. A value of $P < .05$ was considered statistically significant. All statistical analyses were performed using EZR [17], a software package that adds statistical functions to R and R Commander.

Results

1. Patient characteristics

The patient characteristics are shown in Table 1. The mean age was 63 ± 10 years, and 18(60 %) were male. All 30 patients had paroxysmal AF. They had no structural heart disease and only slight dilatation of the left atrium (LA).

2. Lesion volume, gap number, and gap length assessed by LGE-MRI

The total lesion volume was 6.3 ± 2.6 ml. The lesion volume in each segment was as follows. The lesion volume of the left pulmonary veins (LPVs) was 2.8 ± 1.4 ml (anterior: 0.9 ± 0.6 ml; roof: 0.6 ± 0.4 ml; posterior: 0.6 ± 0.4 ml; and bottom: 0.7 ± 0.4 ml), and that of the right pulmonary veins (RPVs) was 3.5 ± 1.4 ml (anterior: 0.9 ± 0.4 ml; roof: 1.2 ± 0.6 ml; posterior: 0.7 ± 0.4 ml; and bottom: 0.8 ± 0.4 ml). The lesion volume of the LPVs was significantly smaller than that of RPVs ($p = 0.005$).

The GN and AGL were 2.5 ± 1.8 and 7.7 ± 5.3 mm. As for the RPVs, the GN and AGL were 1.3 ± 1.3 and 5.8 ± 5.7 mm. As for LPVs, the GN and AGL were 1.2 ± 1.1 and 7.4 ± 6.6 mm, respectively. There was no significant difference in the GN between the LPVs and RPVs ($p = 0.466$), and there was also no significant difference in the AGL between the LPVs and RPVs ($p = 0.724$). The distribution of the visual lesion gaps is shown in Figure 2A.

3. Lesion characteristics and AF recurrence

Six (20 %) of 30 patients had AF recurrences at 12 months. According to the univariate Cox proportional hazard regression analysis, the most predictive model of AF recurrence consisted of the AGL (hazard ratio [HR]: 1.20, confidence interval [CI]: 1.03 - 1.42, p = 0.019) (Table 2). According to the ROC curve, an AGL of 7.6 mm was considered the most optimal cutoff value for predicting AF recurrence. The sensitivity, specificity, and positive and negative predictive values for the cut off values were 100 % (CI: 54 - 100 %), 54 % (CI: 33 - 74 %), 35 % (CI: 26 - 46 %) and 100 %, respectively.

4. Procedural parameters associated with AGL > 7 mm

In the univariate analysis, the CF and stability were the predictive factors of an AGL of > 7 mm (CF HR: 0.576, CI: 0.37 - 0.89, p = 0.013, % CC Time HR: 0.802, CI: 0.66 - 0.98, p = 0.027) (Table 3). However, in the multivariate analysis with the CF and stability, neither parameter was significantly associated with an AGL > 7 mm. Of note, the CF was significantly correlated with the stability (correlation coefficient: 0.773, CI: 0.572 - 0.886, p < 0.001) (Figure 2B). As compare to the 18 patients with an AGL > 7mm, the CF was significantly higher and the stability was better in the patients with an AGL < 7mm (CF:

13.9 ± 2.1 vs. 10.9 ± 2.5 g, p = 0.002; stability: 92 ± 3 vs. 87 ± 6 %, p = 0.009). The CF, stability and orientation for each segment are shown in Figure 3. There was a significant difference in CF in each segment except for LPV bottom and RPV roof, and there was a significant difference in Catheter stability in each segment except for the anterior and posterior LPVs. As for the catheter orientation, there were no significant differences (80 ± 7 vs. 83 ± 8 %, p = 0.312).

5. Visual gap and electrical reconnection in the 2nd session

All of 6 patients with AF recurrence underwent second procedures. Two of the 6 patients had no electrical reconnections of the PVI. Figure 2A shows the distribution of the visual lesion gaps by LGE-MRI and the electrical reconnection sites in the 2nd procedure. A total of 6 (27 %) of 22 visual lesion gaps had electrical reconnections. No electrical reconnection was found in 25 (89 %) of 28 segments without a visual lesion gap. The sensitivity, specificity, and positive and negative predictive values for detecting the electrical reconnection sites were 67% (CI: 30 - 93 %), 61% (CI: 45 - 76 %), 27% (CI: 17 - 41 %), and 89 % (CI: 76 - 96 %), respectively. The average of gap length with an electrical reconnection was 8.6 ± 2.8 mm.

6. Procedural complication

There was no cardiac tamponade or symptomatic cerebral infarctions in any patients. No patients exhibited any esophageal symptoms such as epigastric pain or irritation on swallowing after the ablation, and the LGE-MRI demonstrated no esophageal enhancement in any patients.

Discussion

1. Main findings

The study presented here demonstrated the following: (a) the AGL was associated with AF recurrence after the PVI in patients with paroxysmal AF, (b) the optimal cutoff value of the AGL for predicting AF recurrence was 7.6 mm, (c) both low CF and poor catheter stability were associated with an AGL > 7mm, and (d) the CF and catheter stability were strongly correlated with each other.

2. Lesion volume, gap number and gap length assessed by LGE-MRI

The previous studies reported that the lesions after RF ablation could be visualized by LGE-MRI. In most of those reports, the ablation lesions were two-dimensionally assessed by the lesion width or lesion gap, but not three-dimensionally. [4] In our study, the ablation lesions could be three-dimensionally visualized and this made it possible to calculate the lesion volume. The lesion volume of the LPVs was significantly smaller than that of the RPVs (2.8 ± 1.4 ml vs. 3.5 ± 1.4 ml, p = 0.005). A previous study demonstrated that the lesion width of the RPVs was wider than that of the LPVs. [18] Considering the consistency of those two-dimensional analyses, the ablation lesion of the RPVs might be created more deeply as well as widely than that of the LPVs.

As for the relationship between the AGL and lesion volume, the AGL in each patient was

7.7 ± 5.3 mm and we found no significant difference between the LPVs and RPVs (5.8 ± 5.7 vs. 7.4 ± 6.6 mm, $p = 0.724$). Whereas, as we mentioned above, the lesion volume of the LPVs was significantly smaller than that of the RPVs (2.8 ± 1.4 ml vs. 3.5 ± 1.4 ml, $p = 0.005$). These results suggested that the lesion volume was not associated with the less GN or shorter AGL. Of importance, this discrepancy could also have been caused by the several unknown reasons such as a different myocardial thickness or the anatomical complexity rather than the RF ablation settings.

Bisbal et al. reported that the GN of the RSPV was the highest and that of the LIPV was the fewest. [2] Our study also demonstrated that the GN of the RPV roof was the highest, which was consistent with their results. However, the GN of the LPV bottom was similar to that of the RPV roof. In our study, the esophagus was mostly found to be close to the LPV bottom. Therefore, the CF or % Lateral CF at the LIPV bottom was likely to be less than that at the RIPV bottom to prevent esophageal complications. This might be the reason why the GN of the LPV bottom was not the fewest.

3. Lesion characteristics and AF recurrence

According to the univariate analysis, the lesion volume and gap number was not predictive factors of AF recurrence, and only the AGL was the most predictive factor. A previous study found that the total relative gap length (absolute gap length divided by the total length of the PVI line) assessed by LGE-MRI was associated with AF recurrence, but the GN was not.[4] Our study results were consistent with their results. Akita et al. reported that the lesion gap length with electrical reconnections after a PVI by using the Cryoballoon or Hot balloon was 6.8 mm, which was longer than that without electrical reconnections in the 2nd session.[19] According to the ROC curve, an AGL of 7.6mm was considered the most optimal cutoff value for predicting AF recurrence in our study. Of note, no patients with an AGL of < 7mm had an AF recurrence, so it was inferred that < 7mm visual gaps might include gaps without electrical reconnections. That indicated that the PVI lesions with long visual lesion gaps could have electrical reconnections after the PVI and lead to AF recurrence, regardless of the ablation device.

4. Procedural parameters associated with an AGL > 7mm

An ex-vivo study reported the width and depth of RF lesions made with the different CF settings (0-20g) and different catheter orientations (perpendicular or parallel) [11]. There was no significant difference in the width and depth between the different CF settings with the same target of the LSI, but the RF lesions were significantly wider when the catheter orientation was parallel than when it was perpendicular. In our study, the segments with a shorter Gap had a higher CF but the same RF application time of 30s, which indicated that lesions with a higher CF also had a higher LSI. Further, the catheter orientation was not a predictive factor of an AGL > 7mm. In the clinical setting, differing from the ex-vivo studies, no RF applications with a 100% perpendicular or 100% parallel angulation to the myocardial tissue could be performed. In our study, the % Lateral CF of the RPV roof was lower than of the other segments at 64%, but it was generally 60 - 90% in all segments, and the catheter contact was not completely perpendicular or parallel as in the ex-vivo studies. Furthermore, the % Lateral CF was significantly higher in the segments with an AGL of > 7mm in the LPV posterior, but the GN and AGL were similar to the other segments. This might suggest that the impact of the catheter orientation on the lesion continuity was less in the clinical setting and it was not associated with the clinical outcome.

5. Visual gap and electrical reconnection in the 2nd session

In this study, the sensitivity, specificity, and positive and negative predictive values for detecting electrical reconnection sites by visual lesion gaps detected on LGE-MRI were similar to the previous studies. [19] Recently, the utility of the high-power short-duration (HPSD) RF ablation was reported. HPSD ablation could reduce the procedure time.

However, an experimental study demonstrated that lesion size were the smallest for RF applications at 90 W/4 s, followed by 50 W/10 s, and the greatest for 30 W/30 s. [20] This indicated that HPSD ablation has a potential risk of lesion gap especially in the thick myocardium. An ex-vivo study reported that the surface lesion diameter, maximum lesion diameter, and lesion depth were significantly larger with a low-power ablation than with a high-power ablation when the same LSI was targeted. [21] Therefore, it may be necessary to consider a conventional power and duration ablation for shorter lesion gaps, especially in cases where the myocardium is assumed to be thick. It was reported that electrical reconnections are more frequently detected in thicker segments of the PVs, the antero-inferior, anterior carina and antero-superior segments of the LPVs are thicker, and the antero-superior, anterior-carina, and roof of the RPVs are thicker. [22] In our study, 4 (67%) of 6 reconnection sites were found in thicker myocardium (LSPV roof in one, RPV anterior in one, and RPV roof in two). To reduce the lesion gap in the thicker segment, a conventional power and duration ablation may be a reasonable option.

The lesion gaps were defined as non-enhancement sites of > 4 mm in this study, but if the definition of the lesion gaps was extended from 4 mm to 6 mm and 8 mm, the sensitivity for electrical reconnection dramatically decreased and the specificity slightly increased (4mm [sensitivity: 66.7%, specificity: 61%], 6mm [sensitivity: 44.4%, specificity:

63.4%], 8mm [sensitivity: 44.4%, specificity: 65.9%]). Thus, both the PPV and NPV decreased if the definition of the lesion gaps was extended from 4mm to 6mm and 8mm (4mm [PPV: 27.3%, NPV: 89.3%], 6mm [PPV: 21%, NPV: 83.9%], 8mm [PPV: 22.2%, NPV: 84.4%]). Therefore, the 4mm threshold was considered to be the best to identify the reconnection sites and exclude the durable ablation lesions. The previous study also reported that the lesion without visual gap could rule out the PV reconnection with high negative predictive value. [23] Meanwhile, the visual gap detected by LGE-MRI could not identify the PV reconnection with high positive predictive value. Although this low positive predictive value for detecting electrical reconnection site might be improved by adjusting the visualization method, we speculated that the main cause might be associated with the dormant conductive tissue or pre-existing fibrotic and non-conductive tissue. [24] Other study demonstrated that the muscular discontinuities in PV-LA segments were found in 36% patients [25].

6. Procedural complications and an LA posterior wall ablation

In our study, no patients had any procedural complications, but there will be a higher risk of complications if the CF, power, and duration of the RF ablation will be excessive. Therefore, we should keep an adequate CF without sacrificing the safety. As for the RF applications on the LA posterior wall, it has been reported that the AF recurrence rate increases when the LSI of the LA posterior wall is less than 4 [26]. In our study, there was no difference in the lesion volume or AGL (Lesion volume: 0.6 ± 0.3 vs. 0.8 ± 0.5 ml, $p = 0.233$, AGL: 2.4 ± 5.8 vs 6.7 ±5.5 mm, $p = 0.11$). However, of interest, the LSI of the LA posterior wall was also significantly lower in the patients with AF recurrence than in those without AF recurrence similar to the previous study (3.6 ± 0.8 vs. 4.4 ± 0.9, $p < 0.001$). Although there will be a higher possibility of longer gap and more AF recurrence if the current and CF are inadequate, the safety should be prioritized more than the efficacy to avoid esophageal injury in cases when RF ablation is performed on the posterior wall close to the esophagus.

7. Study limitations

There were several limitations to this study. First, the sample size was really small and follow-up period was relatively short. However, AGL varied between the patients with and without AF recurrence. This statistical significance should be assessed in the longer follow-up period in the further large-scale study. Second, some patients did not undergo LGE-MRI before the ablation procedure. Therefore, it was not possible to distinguish between the ablation lesions and pre-existing atrial fibrosis around the PV and LA.

However, no persistent AF patients were included in this study and all patients actually had no low-voltage areas before the ablation procedure. Third, AF recurrence might be underestimated, because follow-up was performed routinely with symptom and ECG, but not 24h Holter ECG were performed in all patients. Forth, imaging quality of MRI depends on the cardiac rhythm. Fortunately, MRI could be performed during sinus rhythm in all patients.

Conclusion

Long visual lesion gaps assessed by LGE-MRI were the only predictor of AF recurrence after PVI. Both a low CF and poor catheter stability have the potential risk of creating large lesion gaps associated with AF recurrence.

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Figure legends

Figure 1

A: Segmentation of the ablation lesion after PVI B: Representative case of LGE-MRI after PVI The lesion gaps were defined as no-enhancement sites of >4 mm.

LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; PVI, pulmonary vein isolation

Figure 2

The visual lesion gaps detected by LGE-MRI

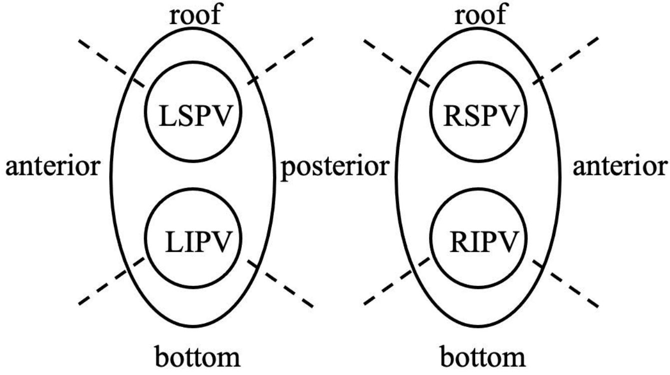
Gaps marked in red had electrical reconnection. Gaps marked in black had no reconnection.

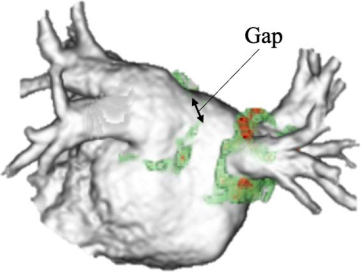
Figure 3

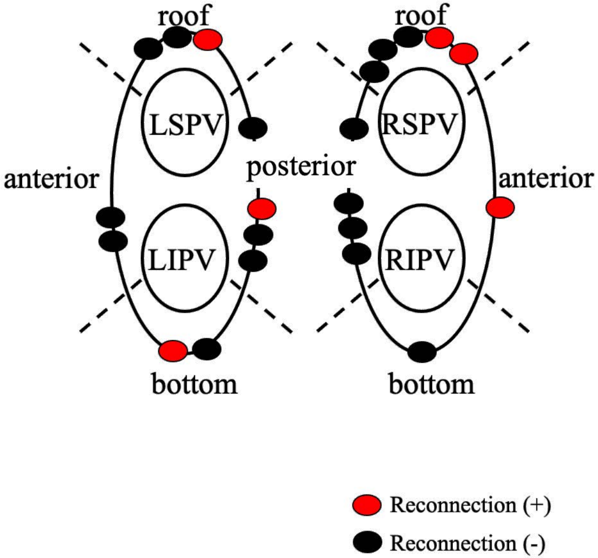
The comparison of the CF, catheter - stability (% CC Time), catheter - orientation (% Lateral CF) at each segment between 12 patients with AGL < 7mm and 18 patients with AGL > 7mm

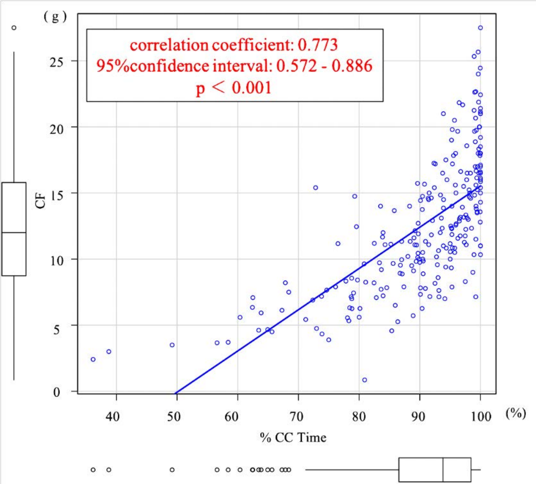
CF, contact force; % CC Time, % constant contact time (= percentage of time of CF >2g);

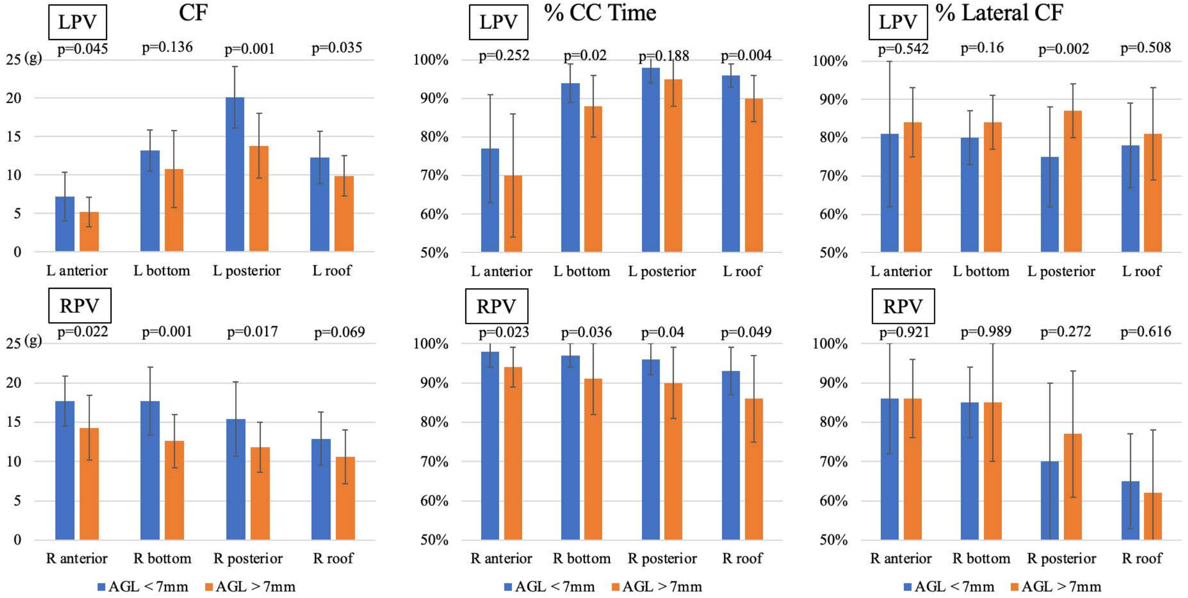
AGL, average gap length


roof
roof
LSPV
RSPV
anterior
posterior
anterior
LIPV
RIPV
bottom
bottom


Gap


roof
roof
LSPV
RSPV
anterior
posterior
anterior
LIPV
RIPV
bottom
bottom
Reconnection (+)
Reconnection (-)


correlation coefficient: 0.773
95%confidence interval: 0.572 - 0.886
p < 0.001
(g)
CF
25
20
15
10
5
0
40
50
60
70
80
90
100
(%)
% CC Time



LPV
CF
p=0.045
p=0.136
p=0.001
p=0.035
25 (g)
20
15
10
5
0
L anterior
L bottom
L posterior
L roof
LPV
% CC Time
p=0.252
p=0.02
p=0.188
p=0.004
100%
90%
80%
70%
60%
50%
L anterior
L bottom
L posterior
L roof
LPV
% Lateral CF
p=0.542
p=0.16
p=0.002
p=0.508
100%
90%
80%
70%
60%
50%
L anterior
L bottom
L posterior
L roof
RPV
p=0.022
p=0.001
p=0.017
p=0.069
25 (g)
20
15
10
5
0
R anterior
R bottom
R posterior
R roof
AGL < 7mm
AGL > 7mm
RPV
p=0.023
p=0.036
p=0.04
p=0.049
100%
90%
80%
70%
60%
50%
R anterior
R bottom
R posterior
R roof
AGL < 7mm
AGL > 7mm
RPV
p=0.921
p=0.989
p=0.272
p=0.616
100%
90%
80%
70%
60%
50%
R anterior
R bottom
R posterior
R roof
AGL < 7mm
AGL > 7mm

Table 1 Patient characteristics

Age, year	63 ± 10
Male, n (%)	18 (60 %)
BMI, kg/m^2	23.5 ± 3.6
eGFR, ml/min/1.73m^2	68.9 ± 10.7
BNP, pg/ml	60.7 ± 87.4
LAD, mm	37.6 ± 5.0
LVEF, %	63.3 ± 5.2
$CHADS_2$ score, point	0.8 ± 1.0
Lesion volume, ml	6.3 ± 2.6
GN, n	2.5 ± 1.8
AGL, mm	7.7 ± 5.3

Abbreviations

BMI, Body Mass Index; eGFR, estimated glomerular filtration rate; BNP, Brain Natriuretic Peptide; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; GN, gap number; AGL, average gap length.

Table 2 Univariate analysis of factors associated with AF recurrence

Variables	**Univariate HR**	**95% CI**	P value
Age, year	1.01	0.92 - 1.1	0.862
Sex, male	0.72	0.13 - 3.94	0.707
BMI, kg/m^2	1.17	0.92 - 1.49	0.193
LAD, mm	0.94	0.81 - 1.08	0.378
LVEF, %	1.01	0.87 - 1.18	0.889
LGE volume, ml	1.02	0.76 - 1.38	0.883
GN, n	1.6	0.93 - 2.76	0.088
AGL, mm	1.2	1.03 - 1.42	0.019

Abbreviations

BMI, Body Mass Index; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; GN, gap number; AGL, average gap length.

Table 3 Univariate and multivariate analysis of factors associated with AGL > 7mm

Variables	**Univariate Unadjusted HR**	**95% CI**	P value	**Multivariate Adjusted HR**	**95% CI**	P value
Age, year	0.98	0.9 - 1.06	0.628			
Sex, male	1.6	0.35 - 7.3	0.544			
BMI, kg/m^2	1.090	0.88 - 1.36	0.429			
LAD, mm	0.948	0.81 - 1.11	0.507			
LVEF, %	0.969	0.84 - 1.12	0.67			
CF, g	0.576	0.37 - 0.89	0.013	0.656	0.37 - 1.16	0.146
% CC Time, %	0.802	0.66 - 0.98	0.027	0.92	0.71 – 1.19	0.522
% Lateral CF, %	1.05	0.95 - 1.16	0.302			

Abbreviations

BMI, Body Mass Index; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; CF, contact force; CC Time, constant contact time.