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Use of preprocedural multidetector computed tomography to decrease atrial fibrillation recurrence following extensive encircling circumferential pulmonary vein isolation

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ABSTRACT

Background: Myocardial thickness is particularly thick at the ridge between the left pulmonary vein (PV) and the left atrial appendage (LAA) by dissection. We investigated whether atrial fibrillation (AF) ablation outcome was influenced by altering ablation strategies according to the thickness of the PV–LAA ridge using preprocedural multidetector computed tomography (MDCT).
Methods and results: Patients with AF scheduled for extensive encircling circumferential pulmonary vein isolation (EEPVI) (110 patients) were divided into 2 groups. In the nonmodulation group (32 patients), EEPVI lines were created using a 3.5-mm tip irrigated catheter at a maximum power of 30 W for 20–30 s at each site. In the modulation group (78 patients), ablation was extended (40–60 s) at the PV–LAA ridge if its thickness was >4.0 mm on MDCT examination. Extended ablation at the PV–LAA ridge was noted in 37 patients in the modulation group. During 25 ± 9 months of follow-up, recurrence was significantly less in the modulation group than in the nonmodulation group (10% vs. 28%; $p = 0.018$). Logistic regression analysis showed that modifications in the ablation time and left atrium volume index were independent predictors of arrhythmia-free recovery after ablation.
Conclusions: Recurrence following EEPVI could be reduced by modifications in the ablation time at the PV–LAA ridge.

1. Introduction

Radiofrequency (RF) catheter ablation has emerged as an important treatment option for patients with atrial fibrillation (AF). However, a wide variation in success rates after catheter ablation has been reported, and AF recurrence remains an important problem.

Arrhythmia recurrence after AF ablation is often associated with pulmonary vein (PV) reconnection [1,2]. In particular, the ridge between the left PV orifices and the os of the left atrial appendage (LAA) is a location where conduction recurs easily [3]. Electrophysiologists have recognized the presence of several endocardial ridges that may make catheter positioning for ablation difficult in this region, resulting in incomplete ablation lines [4–6]. The most prominent ridge in the left atrium (LA) is the PV–LAA ridge [5]. In addition, myocardial thickness varies among different regions in the heart, and the myocardial thickness at the PV–LAA ridge is particularly thick when examined by dissection [7,8], indicating that the creation of transmural lesions in this section may be difficult in some patients.

We examined LA thickness preprocedurally by multidetector computed tomography (MDCT) and investigated whether modifying the ablation strategies according to the thickness of the PV–LAA ridge could decrease AF recurrence.

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2. Methods

2.1. Study population

This study included 110 consecutive patients who underwent their first AF ablation for drug-refractory symptomatic AF (89 men and 21 women; mean age 60 ± 11 years; range 25–77 years). Patients were randomly assigned in a 1:2 sequential fashion into 2 groups receiving different PV–LAA ridge ablation therapies. In the nonmodulation group (NM group, 32 patients), RF energy was delivered for 20–30 s at each point, whereas in the modulation group (M group, 78 patients), it was prolonged to 40–60 s at the PV–LAA ridge if its thickness was >4.0 mm on preprocedural MDCT examination. Written informed consent for the ablation and randomization was obtained from each patient.

2.2. Electrophysiological study and radiofrequency ablation

Transesophageal echocardiography was performed within 24 h of the ablation procedure to exclude LA thrombus. Antiarrhythmic drugs were discontinued ≥5 half-lives before the electrophysiological study, except for amiodarone, which was discontinued ≥4 weeks prior to the study. All patients received anticoagulants for >1 month. We performed extensive encircling pulmonary vein isolation (EEPVI) guided by 2 circular mapping catheters (Lasso; Biosense Webster, Diamond Bar, CA, USA) and electroanatomical mapping (CARTO; Biosense Webster) with CT integration (CARTOMERGE™; Biosense Webster).

2.3. MDCT angiography

CT examinations were performed using a 64-slice CT scanner (LightSpeed VCT; GE Healthcare, Waukesha, WI, USA). The precise scan protocol of the retrospective electrocardiogram-gated scan has been previously described [9]. Raw scan data were transferred to a computer workstation, where the images were reconstructed (Virtual Place Advance; AZE Inc., Tokyo, Japan) and analyzed in a blinded fashion. During image acquisition in patients with a sinus rhythm, the phase corresponding with end-diastole of the atria, just before mitral valve opening, was selected for evaluation [10]. During image acquisition in patients with AF, the phase that appeared to have the largest LA volume was selected for assessment.

First, the LA volume was calculated as described in previous CT imaging studies [11]. For the biplane area-length method, maximal area was measured with a planimeter for 4- and 2-chambered views by tracing the endocardial border, excluding the confluence of the pulmonary veins and LA appendage, and the length was measured from the midline of the mitral annulus plane to the opposite superior aspect of the left atrium. LA volume was calculated using the following formula: 0.85 × 4-chamber area × 2-chamber area/average of the 2 lengths.

Next, LA wall thickness was measured in preselected locations on the EEPVI line at their thickest points, using cross-sectional sources and orthogonal to the source images. Wall thickness was measured from the density of the intracavitary contrast medium that filled the PV and LA, and epicardial organization was identified by an abrupt change in signal density. The measured points were as follows: the superior sites of the LA at 5–10 mm apart from each superior PV ostium, and the inferior sites of the LA at 5–10 mm apart from each inferior PV ostium, the PV–LAA ridge, and the roof, floor, and posterior walls of the LA (Fig. 1).

2.4. Catheter ablation

A 6F decapolar catheter (St. Jude Medical, St. Paul, MN, USA) was positioned in the coronary sinus for pacing and recording. A transeptal puncture was performed, and intravenous heparin was administered to maintain an activated clotting time of 300–350 s. EEPVI was performed to electrically isolate the left and right PVs in pairs at 5–20 mm from their ostia [12,13]. Ablation was attempted along the PV–LAA ridge at the anterior part of the left PV and was performed with an irrigated 3.5-mm tip electrode catheter (THERMOCOOL; Biosense Webster). The flow rate was 17–30 mL/min, energy settings were 25–35 W, and temperatures were 40–45 °C. In the NM group, RF energy was delivered for 20–30 s at each point around the EEPVI line. In the M group, ablation time was extended to 40–60 s at the PV–LAA ridge if its thickness was >4.0 mm on preprocedural MDCT examination. Ablation was performed during baseline rhythm with no attempt to perform pharmacological or direct current cardioversion. The EEPVI endpoint was the creation of a bidirectional conduction block from the atrium to the PVs. If AF was still detected after completion of the EEPVI line, transthoracic cardioversion was performed to restore sinus rhythm. After completing the EEPVI, each vein was rechecked for isolation after ≥30-min waiting period. Following EEPVI, the cavotricuspid isthmus line was ablated, with the endpoint being a bidirectional conduction block [14].

2.5. Post-ablation management

All patients were followed up for at least 12 months. Follow-up consisted of outpatient visits, and 12-lead and 24-h Holter monitoring at 1, 3, and 6 months, and every 6 months thereafter if the patient remained asymptomatic. Patients were also asked to report any arrhythmia symptoms that occurred between scheduled visits. Recurrent AF was diagnosed when (1) patients reported

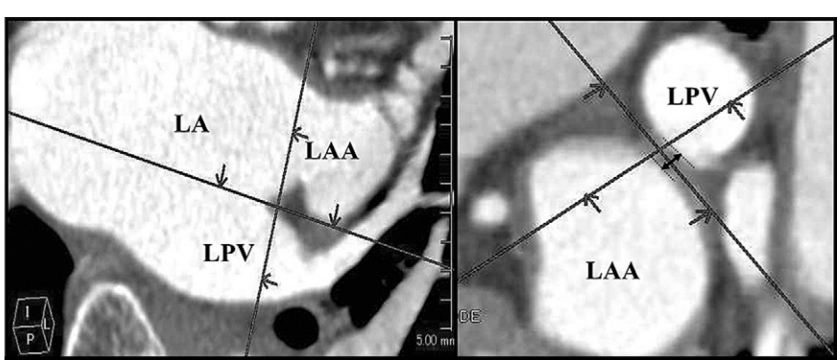

Fig. 1. Thickness of the ridge (two-headed arrow) between the left pulmonary vein (LPV) orifices and the os of the left atrial appendage (LAA) from a multiplanar reconstruction image generated from an axial source image (left panel) by multidetector computed tomography. We selected the view that did not include the low intensity area considered to be epicardial organization. LA, left atrium.

symptoms suggestive of tachycardia, and (2) a >30-s episode of AF was recorded on 12-lead or 24-h Holter monitoring. Early AF recurrences (within 3 months after ablation) were not considered for data analysis because these episodes are often transient phenomena reflecting a reverse remodeling process [15]. All patients continued oral anticoagulation medication to maintain an international normalized ratio of 2.0–3.0 for a minimum of 3 months. Antiarrhythmic drugs were discontinued 2 months after the ablation procedure. The primary endpoint of the study was freedom from recurrence of AF after the initial ablation procedures.

2.6. Statistical analysis

Categorical variables are expressed as numbers and percentages. Continuous data are presented as means ± standard deviations. Continuous and categorical variables were compared by Student's *t*-test and chi-square test, respectively. A Kaplan–Meier analysis was used to determine the percentage of patients free of AF after the initial procedure, and any differences in the AF-free survival were evaluated using the log-rank test. Univariate and multivariate logistic regression analyses were performed to identify the predictors of AF recurrence after the ablation procedure. p-values < 0.05 were considered statistically significant.

3. Results

3.1. Clinical characteristics

No significant differences were observed between patients of the NM and M groups in baseline clinical characteristics, including AF duration, the presence of hypertension or structural heart disease, LA diameter, or left ventricular ejection fraction (Table 1).

Table 1
Clinical characteristics and MDCT parameters in the NM and M groups.

	NM group (n = 32)	M group (n = 78)	p-Value
Clinical characteristics			
Age, years	61 ± 11	60 ± 11	0.56
Male sex	27 (84%)	62 (79%)	0.55
Body mass index, kg/m^2	23.9 ± 2.5	23.1 ± 2.6	0.12
Duration of AF, years	6.0 ± 4.4	4.7 ± 4.6	0.17
Antiarrhythmic drugs	25 (78%)	50 (64%)	0.14
Amiodarone	1 (3%)	8 (10%)	0.22
ACEI/ARB	11 (34%)	19 (24%)	0.29
Hypertension	16 (50%)	38 (49%)	0.90
Diabetes	2 (6%)	9 (12%)	0.40
Structural heart disease	5 (16%)	15 (19%)	0.65
LA diameter, mm	39.8 ± 7.5	39.0 ± 6.9	0.60
Left ventricular ejection fraction, %	62.5 ± 10.4	63.7 ± 8.6	0.56
MDCT parameters			
PV–LAA ridge, mm	4.3 ± 1.4	4.1 ± 1.0	0.34
Left superior site, mm	2.1 ± 0.3	2.1 ± 0.3	0.85
Left inferior site, mm	1.7 ± 0.3	1.7 ± 0.3	0.78
Right superior site, mm	2.0 ± 0.3	2.0 ± 0.3	0.90
Right inferior site, mm	2.0 ± 0.4	1.9 ± 0.4	0.41
Roof, mm	3.0 ± 0.6	2.8 ± 0.7	0.29
Floor, mm	2.5 ± 0.5	2.4 ± 0.5	0.72
Posterior, mm	2.0 ± 0.3	2.0 ± 0.4	0.47
LA volume index, ml/kg/m^2	35.6 ± 10.4	37.9 ± 14.8	0.44

Results are presented as mean ± SD. AF: atrial fibrillation; LA: left atrial; LAA: left atrial appendage; MDCT: multidetector computed tomography; M: modulation; NM: nonmodulation; PV: pulmonary vein.

Table 2
Results of EEPVI in the NM and M groups.

	NM group (n = 32)	M group (n = 78)	p-Value
Completion of PV–LA block on the first EEPVI line	10 (31%)	31 (40%)	0.40
Additional RF duration on the PV–LAA ridge, s	33.5 ± 39.5	11.3 ± 20.6	0.0002
Total RF duration on the PV–LAA ridge, s	197.8 ± 46.8	190.7 ± 52.3	0.65
Total RF energy on the PV–LAA ridge, J	5934 ± 1403	5720 ± 1568	0.65

Results are presented as mean ± SD. EEPVI: extensive encircling circumferential pulmonary vein isolation; NM: nonmodulation; M: modulation; PV: pulmonary vein; LA: left atrial; RF: radiofrequency; LAA: left atrial appendage.

3.2. MDCT parameters

In this study, the PV–LAA ridge was the thickest of all measured regions, with a median thickness of 4.0 mm. No significant differences were found between the NM and M groups for the MDCT parameters, including mean wall thickness or LA volume index (Table 1).

3.3. Catheter ablation outcome

The EEPVI endpoint was achieved in all patients. The PV–LAA ridge was thicker than 4.0 mm in 37 cases (47%) of the M group and we extended ablation time in these cases. The ratio of patients in whom a complete bidirectional conduction block from the PVs to the atrium by the first line was achieved was similar in both groups (31% in the NM group vs. 40% in the M group; p = 0.40). The application duration and delivered RF energy at the PV–LAA ridge were not significantly different between both groups. The duration of additional RF on the PV–LAA ridge to achieve complete bidirectional conduction block was longer in the NM group than in the M group (33.5 ± 39.5 s vs. 11.3 ± 20.6 s, respectively; p = 0.0002) (Table 2).

At the last follow-up (25 ± 9 months), 93 of the 110 patients (85%) were free of AF. Beyond a blanking period of 3 months, the AF-free rate at 12 months after a single ablation was significantly higher in the M group compared to the NM group (70 patients [90%] vs. 23 patients [72%], respectively; p = 0.018).

3.4. Second ablation procedure

In a total of 17 AF recurrence patients, 7 patients (NM group, 4; M group, 3) underwent a second ablation procedure. The remaining 10 patients did not wish to undergo a second procedure because of the significant reduction in arrhythmia burden after the first ablation. All but 1 patient in the recurrence patients exhibited reconnection of the PVs (86%). During the second ablation, a mean of 2.4 ± 1.3 PVs were reconnected. Left PV (LPV) reconnection was seen in the PV–LAA ridge (6 patients), posterior wall (1 patient), superior site (1 patient), inferior site (3 patients), and the carina region (1 patient). Right PV (RPV) reconnection was seen in the posterior wall (4 patients), superior site (2 patients), inferior site (2 patients), and the carina region (2 patients). In NM group, in all patients PV–LAA ridge was reconnected.

3.5. Predictors of atrial fibrillation recurrence

Univariate and multivariate analyses were performed to identify whether the modification of the procedure based on LA thickness quantified by preprocedural MDCT examination predicted AF recurrence (Table 3). Patients were divided into groups based on outcome: those with clinical success and those with AF recurrences

Table 3
Univariate and multivariate logistic regression analyses for predictors of recurrence of atrial fibrillation.

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*p*-Value	OR (95%CI)	*p*-Value
Age	1.00 (0.95–1.05)	0.99		
Male sex	1.06 (0.57–2.29)	0.87		
Body mass index	1.08 (0.88–1.32)	0.48		
Duration of AF	1.06 (0.95–1.17)	0.26		
Hypertension	3.04 (1.04–10.2)	0.052		
Diabetes	1.24 (0.18–5.45)	0.79		
Structural heart disease	2.17 (0.62–6.83)	0.20		
LA diameter	1.10 (1.02–1.19)	0.020		
Left ventricular ejection fraction	1.00 (0.95–1.06)	0.87		
Thickness of the PV–LAA ridge	1.57 (1.02–2.45)	0.041	1.76 (0.97–3.43)	0.072
Thickness of the left superior site	0.46 (0.06–2.76)	0.42		
Thickness of the left inferior site	1.11 (0.16–7.23)	0.91		
Thickness of the right superior site	0.89 (0.19–4.40)	0.89		
Thickness of the right inferior site	1.02 (0.27–3.75)	0.97		
Thickness of the roof	0.84 (0.35–1.89)	0.67		
Thickness of the floor	0.82 (0.28–2.19)	0.71		
Thickness of the posterior	1.32 (0.32–5.42)	0.70		
LA volume index	1.09 (1.04–1.14)	0.0005	1.13 (1.07–1.23)	0.0003
Modification	0.29 (0.099–0.85)	0.023	0.083 (0.013–0.39)	0.0032

Results are presented as mean ± SD. CI: confidence interval; OR: odds ratio; AF: atrial fibrillation; LA: left atrium; PV: pulmonary vein; LAA: left atrial appendage.

following catheter ablation. Predictors of AF recurrence following catheter ablation by the univariate analysis were LA diameter ($p = 0.020$), thickness of the PV–LAA ridge ($p = 0.041$), LA volume index ($p = 0.0005$), and modification ($p = 0.023$). Multivariate analysis using the thickness of the PV–LAA ridge, LA volume index, and modification revealed that the LA volume index [odds ratio (OR), 1.13; 95% confidence interval (CI), 1.07–1.23; $p = 0.0003$) and modification (OR, 0.083; 95% CI, 0.013–0.39; $p = 0.0032$) remained significantly and independently associated with AF recurrence.

3.6. Comparison of results in patients with thick ridges

Of the 110 patients, there were 52 (47%) with PV–LAA ridge thickness >4.0 mm. The application duration was prolonged at the PV–LAA ridge in 37 of these patients and RF energy was delivered for the same duration at each point in the remaining 15 patients.

AF recurrence occurred in 11 of the 52 patients. In these patients with AF recurrence, the percentage of patients with modified RF application was significantly lower and the LA volume index was significantly greater (Table 4) than those in the non-recurrence patients. A Kaplan–Meier survival analysis showed that the AF-free rate during 12-month follow-up periods after a single ablation was significantly higher in the M group compared to the NM group among the patients with thick ridges [33 patients (89%) vs. 8 patients (53%), respectively; $p = 0.003$ by the log-rank test; Fig. 2].

Table 4
Comparison of characteristics in patients with thick ridges.

	AF recurrence ($n = 11$)	Free from AF ($n = 41$)	*p*-Value
Univariate analysis			
Clinical characteristics			
Age, years	59 ± 11	63 ± 9	0.25
Male sex	9 (82%)	33 (80%)	0.92
Body mass index, kg/m^2	23.1 ± 3.1	23.6 ± 2.6	0.46
Duration of AF, years	6.6 ± 5.3	4.1 ± 3.7	0.094
Hypertension	8 (73%)	29 (71%)	0.90
Diabetes	1 (9%)	4 (10%)	0.95
Structural heart disease	3 (27%)	4 (10%)	0.15
LA diameter, mm	42.8 ± 6.7	39.4 ± 5.0	0.077
Left ventricular ejection fraction, %	63.3 ± 11.3	64.2 ± 8.6	0.77
MDCT parameters			
PV–LAA ridge, mm	5.3 ± 1.3	5.0 ± 0.8	0.28
Left superior site, mm	2.0 ± 0.2	2.1 ± 0.3	0.39
Left inferior site, mm	1.8 ± 0.3	1.7 ± 0.3	0.49
Right superior site, mm	2.1 ± 0.2	2.1 ± 0.3	0.64
Right inferior site, mm	2.0 ± 0.3	1.9 ± 0.4	0.57
Roof, mm	2.9 ± 0.5	2.9 ± 0.7	0.88
Floor, mm	2.4 ± 0.4	2.5 ± 0.5	0.67
Posterior, mm	1.9 ± 0.2	2.0 ± 0.4	0.15
volume index, ml/kg/m2	49.4 ± 16.8	36.8 ± 11.0	0.015
Modification	4 (36%)	33 (80%)	0.0076
Multivariate analysis			
	OR	95%CI	*p*-Value
LA volume index	1.14	1.05–1.28	0.0069
Modification	0.027	0.0013–0.23	0.0048

Results are presented as mean ± SD. AF: atrial fibrillation; LA: left atrium; MDCT: multidetector computed tomography; PV: pulmonary vein; LAA: left atrial appendage.

4. Discussion

This study produced several findings. Firstly, there is regional variability in LA wall thickness and that the PV–LAA ridge is the thickest region of all regions quantified in this study. Secondly, the AF recurrence rate is lower in patients whose RF duration was modified based on the PV–LAA ridge thickness. Thirdly, few patients underwent a second ablation procedure, and the reconnection was seen most commonly around the PV–LAA ridge and posterior wall of the RPV. Fourthly, modification of the procedure and the LA volume index remained significantly and independently associated with AF recurrence. Our findings have potential clinical implications in the determination of appropriate ablation strategy. Longer lesions may be required in thicker areas, particularly at the PV–LAA ridge, in order to achieve transmural lesions.

Arrhythmia recurrence following AF ablation is often associated with pulmonary vein reconnection [1,2]. A repeat procedure consisting of reisolation of the recovered veins further eliminates AF and improves clinical outcomes [16,17]. The PV–LAA ridge, a fold of the lateral LA wall protruding into the endocardial LA surface, is recognized as a section where conduction commonly recurs [3]. Its shape and size is relevant during AF catheter ablation when it encircles the LPV orifices. Anatomical information can be obtained with current MDCT and magnetic resonance imaging reconstructions of the endocardial aspect of LA [4–6]. The width of the PV–LAA ridge measures 5–6 mm on average. A narrow ridge in some patients can make it technically difficult to stabilize a catheter directly on these folds during ablation; hence, it may be challenging to obtain a complete circumferential ablation line at this site [18].

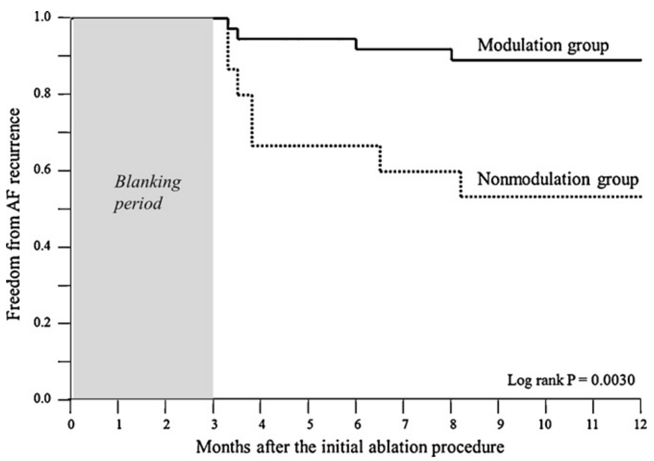

Fig. 2. Kaplan–Meier curves for maintaining sinus rhythm in patients with thick pulmonary vein-left atrial appendage ridge after a single ablation procedure. Significant differences were observed in the recurrence of atrial fibrillation (AF) between the modulation and the nonmodulation groups. A blanking period of 3 months was applied.

In addition, it has been reported that myocardial thickness at the PV–LAA ridge is particularly thick when examined by dissection [7,8]. The myocardial thickness of PVs is thickest at the venoatrial junction with a mean thickness of 1.1 ± 0.4 mm; the thickness tapers toward the lung hila. In contrast, the myocardial thickness of the PV–LAA ridge is 1.7 ± 0.8 mm at the inferior level and 2.8 ± 1.1 mm at the superior level. The width of the PV–LAA ridge, including the non-myocardial components, is 5.6 ± 0.4 mm at the superior level and 10.2 ± 0.5 mm at the inferior level.

In this study, we measured wall thickness by MDCT examination and found that the thickness varied at different parts of the EEPVI line. In particular, the PV–LAA ridge was thick, suggesting that transmural lesions at the PV–LAA ridge are difficult to achieve in some patients. The ratio of patients in whom a complete bidirectional conduction block from the PVs to the atrium was achieved was similar whether the RF time on the PV–LAA ridge was (M group) or was not (NM group) prolonged during the first linear EEPVI. However, after we ended the first linear ablation, more in the NM group required additional RF on the PV–LAA ridge than in the M group to achieve a complete block between PV and LA. This resulted in efficient and effective elongation of RF time on the PV–LAA ridge when we ablated the first EEPVI line. We were able to improve the prognosis of patients with a prolonged ablation time at the PV–LAA ridge. These factors, in combination with the technical difficulties in catheter stability, highlight the importance of these sites in AF ablation and PV isolation.

Moreover, LA volume index was also a predictor of AF recurrence after catheter ablation in this study. Studies have examined the relationship between LA volume and the outcome of AF ablation, and demonstrated that LA volume is an independent predictor of outcome following AF ablation [19–24]. Helms et al. attempted to explain this observation, stating that (1) electrical reconnection of PVs is more likely in patients with larger LA and/or (2) structural remodeling within a very enlarged LA is so extensive that the ablation lesions do not sufficiently modify the atrial substrate. Better techniques for creating continuous ablation lines with no gaps between lesions may help, but the number and location of these lines remain to be determined [25]. Alternatively, additional ablation techniques to modify the substrate, such as ablation guided by complex fractionated electrograms [26], identifying and ablating ganglionated plexuses, or epicardial foci, may be beneficial in these patients.

5. Conclusions

Preprocedural MDCT examinations revealed varying thickness on parts of the EEPVI line, and that the PV–LAA ridge was particularly thick. Catheter ablation along this aspect may be associated with difficulty in achieving transmural lesions, suggesting that controlled ablation in terms of duration along this area may decrease AF recurrence after EEPVI.

6. Limitations

Our study had several limitations. Firstly, this study was performed with a relatively small number of patients and had a short follow-up period. Secondly, we conducted MDCT examinations before the procedure, meaning that the RF location may not necessarily agree with the location measured by MDCT examination. Thirdly, we did not seek to identify triggers at the initial procedure. In addition, some patients did not undergo a second procedure, and we therefore could not evaluate the cause of AF recurrence, the reconnection of PV–LA conduction or the contribution of non-PV foci in these patients. Fourthly, the PV–LAA ridge contains not only myocardium but also non-muscular tissues such as nerves and vessels. We cannot completely eliminate these factors through the performance of MDCT. Fifthly, the resolution of 64-slice MDCT used in this study can recognize minimum 0.625 mm resolution ability and the measured thickness value using the MDCT has an accuracy within a range of 0.625 mm. Finally, the mechanism for the variability in the thickness of the PV–LAA ridge remains unclear because we did not conduct a histopathological examination.

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