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The immediate trends in atrial electrical remodeling for paroxysmal atrial fibrillation across different modes of catheter ablation

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Abstract

Background: Catheter ablation has emerged as a major strategy for paroxysmal atrial fibrillation (PAF). Atrial electrical remodeling (AER) plays a critical role in the recurrence of PAF after ablation.

Hypothesis: To characterize the immediate trends of AER during ablations in patients with PAF, and assess the relationship between immediate trends and recurrence.

Methods: We performed this prospective observational study of 135 patients to investigate AER following three ablation modes: radiofrequency ablation (RFA), cryoablation (CA) and 3D mapping-guided cryoablation (3D-CA). The atrial effective refractory period (AERP) and atrial conduction time (ACT) were measured via electrophysiology before and immediately after ablation, and P-wave indices were measured via electrocardiography before and within 24 h after ablation. Follow-up visits were conducted for at least 1 year or until relapse.

Results: Different approaches of ablation caused a fairly significant increase in the shortest P-wave duration and AERP in both the proximal coronary sinus (PCS) and distal coronary sinus (DCS) but caused a shortened P-wave dispersion. No different effect was found at the AERP among the three modes. Compared to patients who received CA, among patients who received RFA, a significant reduction in total ACT and right ACT was seen. Statistically, there was a weakly positive association between changes in total ACT and early recurrence.

Conclusions: Injury during ablation for PAF was associated with an increase in the AERP but not in the ACT. Total ACT and right ACT were shorter after RFA than after CA. The increase in total ACT were slightly predictive of early recurrence.

KEYWORDS
atrial electrical remodeling, catheter ablation, immediate trends, paroxysmal atrial fibrillation

1 | INTRODUCTION

Atrial fibrillation (AF) is a frequent type of atrial arrhythmia that significantly increases cardiovascular and cerebrovascular morbidity and mortality.[1] However, its electrophysiological mechanisms are still poorly understood, and the selection of optimum treatment strategies remains a major challenge.[2-4] Atrial electrical remodeling (AER) plays a central role in the initiation and perpetuation of AF. Time has been considered an important factor for AER in AF.[5]

For patients with drug-refractory symptomatic paroxysmal atrial fibrillation (PAF), recent studies have demonstrated that pulmonary vein isolation (PVI) by catheter ablation is an effective therapy,[6] especially the FIRE AND ICE trial which have demonstrated the non-inferiority of cryoablation (CA) versus radiofrequency ablatio (RFA). Under both methods, the reversal of AER contributes to the success rate after ablations, although the mechanisms of them are dissimilar. To date, the time course and pattern of AER are still not entirely clear.[7] There has been limited information on AER after ablation for PAF regarding short-term trends, mostly in animal or in vitro experiments, and immediate trends, only from surface electrocardiogram studies in vivo.[8-11] Electrophysiological studies and mappings always placed emphasis on long-term trends after months or a year.[7] There are few comparative data on immediate trends of AER in patients after different ablations.

Therefore, this study was set up to characterize the immediate trends of AER under three common ablation modes, RFA, CA, and 3D-CA, in patients suffering from PAF. To evaluate the trends more comprehensively, the atrial effective refractory period (AERP) from high lateral/low lateral, the proximal coronary sinus (PCS) and distal coronary sinus (DCS), and the total conduction time the atrial/right atrial/coronary sinus (CS) were measured and validated against P-wave indices from an electrocardiogram. Finally, the relationship between immediate trends and recurrence after ablation was assessed for further analysis.

2 | METHODS

2.1 | Patient samples

The protocol for this clinical observation was approved by the Ethics Committee of the Second Hospital of Hebei Medical University, and all patients gave written informed consent before entering. Patients willing to undergo catheter ablation for PAF referred to our institution were screened between December 1, 2017, and July 1, 2019. Patients who fulfilled the following criteria were included: (1) PAF confirmed by electrocardiography or 24 h Holter monitors, appearing more than twice in the last year; and (2) poorly controlled AFP after the use of class I or III antiarrhythmic drugs. Patients who fit the following criteria were excluded: (1) persistent AF; (2) >75 years old; (3) hyperthyroidism congenital heart disease or valvular heart disease; (4) underwent catheter ablation for AF or prosthetic heart valve replacement before; (5) atrial thrombosis; (6) LA dimension >50 mm; and (7) diagnosed with malignant tumors, severe liver or kidney diseases, or serious infections.

2.2 | Groups and randomization

A total of 135 subjects were recruited into three different groups (45 for each group): (1) the RFA group: ablation was achieved by a standardized RFA procedure; (2) the CA group: ablation was achieved by a standardized protocol with a second generation cryoballoon; repeated CA was performed for each pulmonary vein until complete PVI; (3) the 3D-CA group: for each pulmonary vein, CA was performed less than twice under guidance with a 3D-mapping system with a second generation cryoballoon; if PVI was not achieved, RFA was applied for the additional points. All operators were blinded to the electrophysiological data during the surgeries.

2.3 | Ablation procedures

For all the patients, the routine biochemical indexes, clinical characteristics, and reconstructive computed tomography images of the pulmonary vein were obtained before ablation. For the RFA group, the standardized RFA procedure which defined as to create a circle surrounding the two ipsilateral pulmonary veins (PV) was performed with a 3D electro-anatomical mapping system (Carto 3; Biosense Webster) and a mapping catheter (Lasso NAV Eco; Biosense Webster). The radiofrequency energy was at a power of 30 Watts. For the CA group, single-balloon ablation with a cryoballoon of 28 mm in diameter (Arctic Front Advance Cardiac CryoAblation Catheter, Medtronic, Minneapolis, MN) was performed according to the results of angiographic images of the PV. The mapping catheter (Achieve, Medtronic, MN) was used to record PV potentials. The cryoballoon was placed at each PV ostium, and cryothermal energy was released and the single-time cryoablation was performed for up to 180 s for the procedures. The cryoablation could be repeatedly performed until complete isolation was achieved. For the 3D-CA group, a circular mapping catheter (Achieve, Medtronic) was used to construct the configuration and build the structures of the LA and PV guided by the EnSite NavX 3D mapping system. For each PV, cryoablation as described in the CA group was performed less than three times to achieve complete PVI. If not, RFA was applied for additional points. More details of the standard ablation technique can be obtained from our previously published clinical trials.[12,13] All steps of ablation were performed by a single group of four experienced ablationists led by a Chief physician (Dr. Ruiqin Xie).

2.4 | Electrophysiological study

2.4.1 | Atrial effective refractory period

The AERP and its dispersion (AERPd) were assessed by a 6F decapolar catheter (2-mm interelectrode and 5-mm interbipole distance: "2–5–2 mm spacing") from the high-right atrium (HRA, the junction of the right atrium and superior vena cava, near the sinus node), the low-right atrium (LRA, the junction of the right atrium and inferior vena

cava, on the free wall side of the right atrium) and two positions of the CS (CS7.8 and CS1.2: catheter was positioned in the CS, and the proximal bipole was at the level of the CS ostium.) at three basic drive cycle lengths (CLs) of 600, 500, and 400 ms before and after the procedure. The AERP was measured by a current output of twice the local diastolic threshold with a pulse width of 2 ms using a single extrastimulus with an 8-beat drive train, which increased by 10 ms from a start site of 170 ms. The measurements were conducted in triplicate and were recorded as an average of three times. The AERPd for each CL was recorded as the difference between the maximum and the minimum of the four sites.

2.4.2 | Atrial conduction time

(1) Measurement of the surface electrocardiogram: A 12 lead electrocardiogram in sinus rhythm was taken before and 24 h after the procedure. The P-wave duration (Pmax, maximum P-wave duration, the longest P wave duration of all measurable leads; Pmin, minimum P-wave duration, the shortest P wave duration of all measurable leads) and Pd (Pd = Pmax − Pmin) were measured by two cardiologists, and the mean values were recorded. (2) Measurement of atrial electrophysiology: Preoperative and postoperative atrial conduction time (ACTs) from HRA and CS were tested after 30 seconds of constant pacing from the distal bipole of the decapolar catheter at CLs of 400, 500, and 600 ms. The data were calculated from the pacing artifact to the onset of the first initial sharp deflection recorded from the first A wave at CS9.10 and CS1.2. The total ACT was measured from the wave of HRA to Acs1.2, right ACT from HRA to Acs9.10, and left ACT from Acs9.10 to Acs1.2.

2.5 | Follow-up

The patients needed to complete a 12-month postoperative follow-up. In addition, 24 h Holter monitoring was performed at the 1st, 2nd, 3rd, 6th, 9th, and 12th months, and both immediate electrocardiogram and Holter monitoring were performed immediately if the patient suffered from palpitations. Recurrent arrhythmia was defined as AF, atrial flutter or atrial tachycardia lasting more than 30 s, and it was documented by Holter or electrocardiogram monitoring. Early recurrence was defined as the presence of arrhythmia recurrence within the first 3 months.

2.6 | Statistics

Continuous variables are expressed as the mean ± *SD*, whereas categorical variables are expressed as counts and percentages. ANOVA was used to compare continuous variables among the three groups, as were chi-square analyses for categorical variables. The least significant difference (LSD) multiple comparison post hoc test was used for multiple hypothesis correction. Logistic regression analysis was used to test the effect of the explanatory factors on paroxysmal AF recurrence. All tests were two sided, and a p value less than .05 was considered significant. Analyses were performed by SPSS software (version 20.0, Chicago, IL), and images were generated by SPSS software (version 20.0, Chicago, IL) or GraphPad Prism (version 6.0).

3 | RESULTS

3.1 | Baseline characteristics

One patient in the 3D-CA group, two patients in the CA group, and two patients in the RFA group were excluded as the electrophysiological examinations were terminated due to new-onset arrhythmia or hypotension. Two patients in the RFA group were lost to follow-up. All their data was excluded. Finally, a total of 128 patients were selected for this study (41 in the RFA group, 44 in the 3D-CA group, and 43 in the CA group). The baseline characteristics according to the modes of catheter ablation are compared in Table 1. Only one case of procedure-related phrenic nerve injury occurred in the freeze group. There were no other complications. The surgical X-ray results were significantly lower in the RFA group (57.22 ± 36.29 mGycm2) than in the 3D-CA group (103.05 ± 53.87 groupmGycm2) and CA group (121.90 ± 90.66 mGycm2, both $p < .05$), as was the procedure time (47.36 ± 8.60 vs. 56.34 ± 17.43 vs. 64.81 ± 20.14 mGycm2, all $p < .05$). There was no difference in early recurrence or late recurrence among the three groups (26.7% vs. 15.9% vs. 20.9% and 17.1% vs. 11.4% vs. 18.6%, all $p > .05$).

3.2 | Electrophysiological study

3.2.1 | Atrial effective refractory period

Table 2 lists the baseline AERP data in each group. There was no significant difference among the three groups in the preoperative AERP in all CLs (all $p > .05$). However, the AERP was variable in different regions of the atrium. The AERP was measured as the longest in the HRA (all $p < .01$) and the shortest in the PCS (vs. HRA, $p < .01$, rest $p < .05$, Table 2 and Supplementary Figure Supplementary Figure 1). Most of the length of the postoperative AERP seemed to be greater than the preoperative AERP, but this difference only reached statistical significance in the PCS and DCS at all three CLs ($p < .05$, Table 2 and Supplementary Figure Supplementary Figure 2). However, there was no significant difference across the three groups at any of the four positions or three CLs, and the same was true for the AERP dispersion.

3.2.2 | Atrial conduction time

Significant differences among the three groups could be seen in the total ACT at all CLs (600 ms, $p < .05$; 500 ms, $p < .05$; 400 ms, $p < .01$;

TABLE 1 Comparison of characteristics among the three groups according to different modes of catheter ablations. Results are n (%) or mean ± *SD*. HF, heart failure; LAEF, left atrium ejection fraction; LVEF, left ventricle ejection fraction; CHA_2DS_2VASc, congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74, female; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; FBG, fasting blood glucose; SCr, serum creatinine; BUN, blood urea nitrogen

	RFA N = 41	3D-CA N = 44	CA N = 43	*p* value
Male, n (%)	22 (53.7)	27 (61.4)	21 (48.8)	.496
Age (years)	60.56 ± 9.12	61.57 ± 11.50	58.33 ± 10.72	.344
Hypertension, n (%)	21 (51.2)	23 (52.3)	17 (39.5)	.423
Diabetes, n (%)	4 (10.5)	5 (12.2)	9 (20.9)	.276
Stroke, n (%)	4 (10.5)	3 (6.8)	6 (14.0)	.542
HF, n (%)	5 (12.2)	9 (20.4)	3 (7.0)	.174
LAEF (%)	55.0 ± 11.2	55.1 ± 11.6	55.5 ± 9.7	.975
LVEF (%)	65.7 ± 4.3	64.2 ± 4.0	64.6 ± 3.9	.229
LA-diameter (mm)	35.2 ± 3.9	34.4 ± 3.6	34.8 ± 3.3	.587
CHA2DS2VASc score	1.73 ± 1.30	1.98 ± 1.69	1.79 ± 1.19	.703
Course of AF	6.22 ± 6.97	9.07 ± 9.88	11.21 ± 12.07	.075
Current smoker, n (%)	5 (12.2)	6 (13.6)	7 (16.3)	.799
Alcohol,n (%)	2 (10.3)	3 (6.8)	5 (11.6)	.729
SBP (mmHg)	130.02 ± 17.39	135.59 ± 17.83	136.51 ± 15.16	.167
DBP (mmHg)	78.80 ± 9.23	80.41 ± 12.33	80.79 ± 10.51	.673
HR(bpm)	74.89 ± 16.74	75.05 ± 18.90	78.23 ± 12.76	.566
FBG (mmol/L)	5.50 ± 1.42	4.97 ± 1.13	5.18 ± 1.26	.833
SCr (umol/L)	70.30 ± 16.07	69.74 ± 13.38	66.22 ± 12.26	.345
BUN (mmol/L)	5.52 ± 1.46	4.95 ± 1.17	5.21 ± 1.20	.153
Surgical X-ray (mGycm2)	57.22 ± 36.29	103.05 ± 53.87	121.90 ± 90.66	.000
Fluoroscopy time (min)	2.92 ± 2.01	11.04 ± 5.97	11.01 ± 7.44	.000
Procedure time (min)	47.36 ± 8.60	56.34 ± 17.43	64.81 ± 20.14	.000
Phrenic nerve injury, n (%)	0	0	1 (2.3)	.369
Vascular injuries, n (%)	0	0	0	–
Early recurrence, n (%)	11 (26.7)	7 (15.9)	9 (20.9)	.467
Late recurrence, n (%)	7 (17.1)	5 (11.4)	8 (18.6)	.619

Table 3; Supplementary Figure Supplementary Figure 3 left); however, the interaction between time and ablation group was only seen at CLs of 500 ms ($p < .05$) and 400 ms ($p < .01$, Table 3). Similar numerical trends were also found for the right ACT, but differences among the three groups were only observed at CLs of 600 ms and 400 ms (both $p < .05$, Table 3; Supplementary Figure Supplementary Figure 3 right). Differences in the left ACT among groups were not statistically significant. The LSD multiple comparison post hoc test showed that there were two separate trends across the RFA group and CA group in the total ACT at all CLs (both $p < .05$, Supplementary Figure Supplementary Figure 4), and the same change in trends could also be seen in the right ACT at CLs of 600 ms and 400 ms (both $p < .05$, Supplementary Figure Supplementary Figure 5).

A significant difference between before and after procedure could be observed in both Pmin and Pd (both $p < .001$, Table 4), but the interaction between time and ablation group was only seen in Pmin ($p < .01$, Table 4 and Supplementary Figure Supplementary Figure 6). For Pmax, there was no difference in time or interaction (both $p > .01$, Table 4). The effects of group were all nonsignificant for both kinds of P-wave durations (both $p > .01$, Table 4).

3.3 | Effects of atrial electrophysiology on AF recurrence

Early recurrence was documented in 11, 7, and 9 patients in each group ($p < .05$, Table 1), and late recurrence was documented in 7, 5, and 8 patients in each group ($p < .05$, Table 1). Alterations in the total ACT, left ACT, PCS, DCS, Pmin, and Pd were taken into account for logistic regression analysis separately. Regarding the results, only the increase in the total ACT were a risk factor for early recurrence (B = 0.026, SE = 0.010, Wals = 6.68, $p = .010$, OR = 1.026, 95% CI = 1.006–1.047). None was judged to be related to late recurrence.

TABLE 2 Preoperative and postoperative atrial effective refractory period in different pacing sites and drive CLs. *, $p < .05$

AERP (ms) site and CL Variables	600 ms				500 ms			400 ms		
	Groups	Preoperative	Postoperative	*p* value	Preoperative	Postoperative	*p* value	Preoperative	Postoperative	*p* value
HRA	RF	280.53 ± 39.32	283.42 ± 43.91	.829	273.42 ± 39.48	275.37 ± 40.44	.979	257.18 ± 41.04	254.39 ± 35.78	.177
	Freeze 3D	280.86 ± 37.13	277.67 ± 33.65		272.73 ± 29.60	274.65 ± 28.98		249.55 ± 26.93	247.67 ± 24.09	
	Freeze	282.62 ± 38.51	285.58 ± 40.02		275.48 ± 36.64	276.05 ± 33.32		258.14 ± 29.22	259.07 ± 33.01	
	p value	.812			.647			.787		
LRA	RF	260.26 ± 32.59	256.34 ± 34.26	.709	254.47 ± 28.92	250.24 ± 30.62	.610	247.44 ± 25.62	235.37 ± 27.40	.926
	Freeze 3D	257.05 ± 34.21	259.54 ± 32.44		251.14 ± 29.67	258.84 ± 28.13		251.14 ± 29.67	258.84 ± 28.13	
	Freeze	253.57 ± 23.36	256.98 ± 27.56		250.71 ± 22.02	251.16 ± 27.27		250.71 ± 22.02	251.16 ± 27.27	
	p value	.862			.696			.388		
PCS	RF	249.47 ± 25.78	254.00 ± 30.95	.886	245.41 ± 19.66	250.51 ± 25.75	.901	236.05 ± 21.12	237.37 ± 28.63	.870
	Freeze 3D	249.32 ± 28.48	256.98 ± 21.33		245.68 ± 28.89	254.88 ± 19.44		233.41 ± 24.58	243.26 ± 25.61	
	Freeze	249.52 ± 22.63	253.26 ± 26.88		247.38 ± 20.09	251.67 ± 22.30		233.72 ± 19.52	240.71 ± 19.68	
	p value	.025*			.029*			.019*		
DCS	RF	258.11 ± 27.27	264.25 ± 37.41	.947	254.60 ± 26.20	263.00 ± 33.53	.772	239.19 ± 23.97	242.44 ± 33.53	.731
	Freeze 3D	254.55 ± 30.99	270.47 ± 35.32		250.91 ± 28.52	266.28 ± 33.60		233.41 ± 27.53	243.72 ± 27.78	
	Freeze	257.62 ± 22.93	265.35 ± 30.97		252.86 ± 22.77	259.77 ± 23.45		232.56 ± 18.14	243.02 ± 22.10	
	p value	.002*			<.001*			.001*		
Dispersion	RF	53.68 ± 27.35	53.90 ± 32.47	.877	48.42 ± 26.87	51.71 ± 31.46	.792	46.05 ± 26.05	45.61 ± 28.90	.377
	Freeze 3D	53.41 ± 23.62	52.79 ± 26.03		47.50 ± 20.81	48.37 ± 21.37		41.59 ± 21.13	41.40 ± 25.78	
	Freeze	51.43 ± 23.95	52.79 ± 32.68		49.27 ± 23.31	49.77 ± 21.55		47.44 ± 20.01	44.19 ± 25.19	
	p value	.748			.463			.832		

Abbreviations: AERP, atrial effective refractory period; CL, cycle length; DCS, distal coronary sinus; HRA, high-right atrium; LRA, low-right atrium; PCS, proximal coronary sinus.

TABLE 3 Preoperative and postoperative atrial conduction time in three drive CLs. *, $p < .05$

ACT (ms) site and CL	Groups	600 ms			500 ms			400 ms		
		Preoperative	Postoperative	*p* value	Preoperative	Postoperative	*p* value	Preoperative	Postoperative	*p* value
HRA-PCS	RF	45.94 ± 18.64	39.78 ± 22.73	.049*	45.45 ± 19.06	37.41 ± 21.82	.189	48.60 ± 21.45	35.24 ± 22.51	.031*
	Freeze 3D	47.60 ± 17.99	46.85 ± 20.71		46.04 ± 19.04	47.08 ± 19.24		46.44 ± 20.00	48.28 ± 18.34	
	Freeze	50.90 ± 16.69	54.58 ± 21.87		50.18 ± 16.29	48.93 ± 19.62		52.53 ± 17.04	52.68 ± 23.68	
	p value	.388			.085			.081		
HRA-DCS	RF	72.30 ± 20.67	64.57 ± 24.93	.023*	70.86 ± 18.00	59.26 ± 23.94	.045*	75.45 ± 21.97	59.71 ± 26.42	.007*
	Freeze 3D	72.22 ± 18.69	70.87 ± 24.13		69.54 ± 19.88	73.12 ± 22.10		70.53 ± 21.22	72.51 ± 21.70	
	Freeze	76.72 ± 18.90	81.31 ± 22.37		75.54 ± 18.82	73.85 ± 17.35		78.56 ± 18.80	80.85 ± 23.87	
	p value	.475			.125			.135		
PCS-DCS	RF	26.37 ± 10.38	25.34 ± 10.13	.446	26.86 ± 8.85	23.11 ± 11.99	.453	26.80 ± 9.16	24.07 ± 9.89	.313
	Freeze 3D	26.04 ± 9.45	24.03 ± 11.52		25.77 ± 7.83	26.04 ± 12.63		25.71 ± 11.79	24.22 ± 12.91	
	Freeze	26.73 ± 8.16	26.98 ± 9.78		26.20 ± 7.22	27.15 ± 7.93		26.03 ± 7.51	28.00 ± 8.51	
	p value	.468			.491			.702		

Abbreviations: ACT, atrial conduction time; CL, cycle length; DCS, distal coronary sinus; HRA, high-right atrium; PCS, proximal coronary sinus.

4 | DISCUSSION

Growing evidence suggests that AF is a kind of progressive disease that is not only a result of structural, electrophysiological and haemodynamic remodeling but also a cause of these processes described above.[10,14,15] Restoration of sinus rhythm by successful ablative treatment in patients suffering from AF causes reverse left atrial remodeling.[16,17] AER, which was outlined by Wijffels et al in 1995 as an important component of reversal, can affect the prognosis of AF. Reverse electrical remodeling starts within hours to days, and structural remodeling ensues over a period of months; however, relevant studies mostly focus on a period of a few months or even a year.[10,18] Electrophysiological findings have not been described in detail during ablation for PAF. One of the important advantages of our study was that it first evaluated immediate trends in AER for PAF across different modes of catheter ablation and assessed the predictive value of changes for AF recurrence.

Different approaches of catheter ablation can lead to a series of changes in atrial electrophysiological conditions, although the mechanisms of injury are different. However, the electrophysiological differences among different types of ablation remain unclear, which may significantly influence the understanding of the underlying mechanisms of recurrence. Several previous studies have confirmed that CA with a second-generation cryoballoon was noninferior to RFA for patients with drug-refractory PAF. Herrera[19] found that both CA and RFA energy would result in a comparable increase in cell damage, but CA did not show an improved safety profile or success rate. Inamura[20] found that patients who first underwent CA for PAF had fewer LA-PV reconnections but more frequent LA AF foci than those who underwent RFA after 2 years of follow-up. It was even observed that myocardial injury markers were significantly higher in patients with CA than with RFA, and a longer delivery energy duration and a larger lesion size might be the reason.[21] In contrast, linear myocardial necrosis, which consists of spot-like but transmural necrosis, might have a tremendous impact on electrophysiological conditions. RFA may cause greater immediate damage to myocardial tissues. PVI by RFA could result in damage to the epicardial fat pads, which can progressively lead to less ERP shortening in vagal stimulation.[22] In recent years, the use of low-energy RF currents delivered with a suction electrode catheter has resulted in a lower risk of perforation.[23] In our study, we found that RFA reduced the total ACT and right ACT, which might because RFA caused dramatic damage to cardiomyocyte membrane integrity.[24] Damage caused by CA, which always extended beyond the targeting sites, presented as a larger annular lesion, but cardiomyocytes remained intact. This might explain the lesser immediate effect after CA.

Our data suggested that all three kinds of ablation could alter atrial conductive properties, which were characterized by an increase in Pmin and a decrease in Pd according to the electrocardiography. There was no significant difference before or after procedure in either the Pmax or ACT, which could prove that our results were not artifacts. The changes in Pd after catheter ablation have exhibited controversial results in different studies. Several researchers believe that

TABLE 4 The difference of preoperative and postoperative *p* wave value. Pmax, maximum P-wave duration; Pmin, minimum P-wave duration; Pd, P-wave dispersion. *, $p < .05$

Variables(ms)	Groups	Preoperative	Postoperative	*p* value
Pmin	RF	79.24 ± 14.85	77.95 ± 18.36	.601
	Freeze 3D	76.82 ± 13.14	85.00 ± 17.72	
	Freeze	73.52 ± 13.72	82.61 ± 112.86	
	p value	<.001*		
Pmax	RF	122.80 ± 15.56	117.73 ± 16.42	.471
	Freeze 3D	123.79 ± 15.18	124.02 ± 19.45	
	Freeze	121.00 ± 16.04	119.62 ± 18.22	
	p value	.116		
Pd	RF	43.56 ± 16.49	39.77 ± 15.61	.888
	Freeze 3D	46.97 ± 11.19	39.02 ± 13.86	
	Freeze	47.47 ± 13.43	37.01 ± 16.31	
	p value	<.001*		

atrial remodeling is reflected early on surface electrocardiography by several P-wave indices, including the P-wave duration and Pd.[25,26] Evidence suggests that the Pd index is an independent predictor of AF.[27] A large Pd was associated with an increased risk of AF recurrence after CA.[28] Another study showed that Pd did not change 1 day or 1 month after CA in patients with AF but was significantly decreased at the 3rd and 6th months.[29] In our study, there did not appear to be differences in Pd from ablation, and different types of ablation could provide similar prognoses to PAF.

Our data showed that the AERP was clearly different among regions: longest in the HRA and shortest in the PCS. AER after AF leads to a decreased AERP and enhances its dispersion.[30] Due to electrical remodeling, the mean AERP was shorter in patients with persistent AF than in those with PAF.[31] This might suggest that the risk of AF and electrical remodeling might be evaluated by changes in the AERP. Unfortunately, the AERP in people without PAF was not measured and needs to be investigated in our future studies. In this study, the table indicated that all of the injuries during different kinds of ablation for PAF could cause an increase in the AERP. The AERP in two positions, the CS ostium and distal CS, were significantly affected, probably owing to their anatomical location closer to the pulmonary veins. Accumulating evidence indicates that AERPd can be used to evaluate AF recurrence in paroxysmal supraventricular tachycardia patients after RFA.[32] Increased AERPd is associated with recurrence after catheter ablation. PVI significantly reduced AF recurrence in paroxysmal supraventricular tachycardia patients with high AERPd values.[30] In contrast to the conclusions above, no difference was observed in AERPd during our study, which might be because it did not arrive by the time course.

We found that alterations in the total ACT by catheter ablation might predict early recurrence in patients. However, the predictive value was not as strong. This probably resulted from unstable conditions due to acute myocardial tissue injury and inflammatory responses induced following all three kinds of procedure. The inflammatory process is generally believed to be the cause of AF recurrence, and acute inflammatory changes after ablation may be related to immediate AF recurrence.[33] However, Maille[34] found that individual variables of remodeling at 2 months were not associated with AF recurrence. The electrical remodeling process after ablation might be much more complex than the structural remodeling process. It will be important to ensure clearer predictive value by adding the amount or designing a more detailed and complete electrophysiological assessment in future studies.

For this study, available data were mainly limited by the low patient numbers. Thus, patient enrolment may not represent the whole PAF population. Second, it was reported that after AF was maintained for 15 min, ERP alterations were pronounced in the pulmonary veins compared with the atria.[15] We did not measure the AERP in pulmonary veins around ablation or in the normal population as blank, so further studies with larger groups and more complete electrophysiological data are needed to confirm our findings. Third, the definition of AF recurrence was only based on electrocardiogram or Holter monitoring; therefore, symptom-free recurrence might have been missed. Fourth, five patients were excluded for terminated electrophysiological examinations due to new-onset arrhythmia or hypotension, four of whom had recurrence during follow-ups. This might have led to a low-predictive value of our last conclusion. Finally, this study was a single-centre study; thus, large-scale multicentre studies are needed to further confirm our conclusion.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

Ruiqin Xie conceived of the study, Qian Hou collected literature, performed the statistical analysis and was a major contributor in writing the manuscript, Yuliang Zhao prepared Figures 1–3. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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