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Unipolar electrogram-guided radiofrequency catheter ablation in paroxysmal atrial fibrillation: electrogram patterns and outcomes

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Abstract

Background Transmural lesions (TLs) are the crucial point for radiofrequency catheter ablation (RFCA) in atrial fibrillation (AF) patients. Previous studies have reported that complete positive unipolar electrogram (UP-EGM) after ablation is associated with transmural lesions. However, UP-EGM patterns may differ in different regions of continuous circular lesions (CCLs) around the pulmonary vein ostia after ablation. We aimed to analyze the different UP-EGM patterns in different CCL regions after ablation and the effectiveness of UP-EGM guided RFCA in paroxysmal atrial fibrillation (PAF).

Methods A total of 43 patients with PAF (aged 59 ± 11 years; 65% male) were consecutively included. Pulmonary vein isolation was achieved by contiguous point-by-point RFCA. UP-EGM was recorded by the ablation catheter. Both CCLs were divided into six regions. Two points were randomly chosen from each region to analyze UP-EGM type after ablation. All the patients were followed for atrial arrhythmias recurrence.

Results All pulmonary veins were isolated with complete bidirectional block. A total of 1032 RFCA points with complete positive UP-EGM were collected. UP-EGM morphology after ablation was divided into four different types defined as R, rR′, Rr′, and M. M patterns mostly appeared in anterosuperior (65%) and roof (49%) regions of left CCLs. In the remaining regions, the percentage of non-M patterns (R, rR′, and Rr′) ranged from 63% in posteroinferior regions of right CCLs to 88% in anteroinferior regions of right CCLs. After a mean follow-up time of 19 months, 37 (86%) patients remained in sinus rhythm.

Conclusion Most (72%) UP-EGM types after ablation are non-M patterns. Pulmonary vein isolation guided by UP-EGM with a complete positive pattern in PAF patients is reliable.

Keywords Unipolar electrogram · Atrial fibrillation · Paroxysmal · Pulmonary vein isolation

1 Introduction

Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation procedures in patients with paroxysmal atrial fibrillation (PAF) [1]. However, the incidence of atrial fibrillation (AF) recurrence remains high [2], mostly due to pulmonary vein (PV) reconnection [3], emphasizing the formation of contiguous and transmural atrial lesions to achieve complete conduction block along the ablation lines [4].

Previous studies have shown that elimination of the negative component of the unipolar electrogram (UP-EGM) during radiofrequency applications reflects transmural lesions. The persistence of such a negative component consistently corresponds to non-transmural lesions [5]. In clinical practice, unipolar signal modification could also be a suitable electrophysiological criterion that indicates when to halt each RF energy application while performing point-by-point PVI (because a possible transmural lesion has been created) and when to continue its application (because the lesion deployed is presumed as non-transmural) [6].

However, UP-EGM patterns may differ in different regions of continuous circular lesions (CCLs) after ablation. In previous studies [5–8], some UP-EGMs do not have a notch while some have a notch on the downstroke or upstroke. The bottom of the notch is either above or at the isoelectric line. We assume that UP-EGM with notch at the isoelectric line may present in some certain regions. But no investigations have

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studied the UP-EGM patterns. The present study aimed to analyze the patterns of complete positive UP-EGM in different CCL regions after ablation and sought to determine the SR maintenance rate after PVI guided by UP-EGM with a complete positive pattern, as the endpoint in patients with PAF.

2 Methods

2.1 Study population

Patients with drug-refractory PAF admitted to Ningbo First Hospital for radiofrequency catheter ablation (RFCA) from January 2016 to November 2016 were consecutively enrolled in the study. The exclusion criteria were as follows: [1] age < 18 or > 80 years old, [2] left atrium (LA) diameter > 45 mm, [3] the presence of a mechanical mitral valve prosthesis, [4] impaired thyroid function, [5] left ventricular ejection fraction < 40%, [6] contraindication to anticoagulant therapy, [7] current malignancy, and [8] prior catheter or surgical AF ablation. This investigation was approved by the ethics committee of Ningbo First Hospital.

2.2 Mapping and RF catheter ablation

Antiarrhythmic drugs (AADs) were stopped five half-lives before the procedure. The patients were in the supine position under deep sedation for ablation. NavX™ Velocity System (St. Jude Medical, St. Paul, MN, USA) was used for creating a three-dimensional electroanatomic map and intracardiac electrogram recordings. A 4.0-mm 7F irrigated-tip ablation catheter (Therapy™, Cool Flex™, St. Jude Medical, St. Paul, MN, USA) was used to perform ablation and record UP-EGM. Radiofrequency ablation settings used were 35 W/43 °C/13 mL per minute. The complete positive UP-EGM was the endpoint for every radiofrequency point and was extended 5 s after elimination of the negative component of UP-EGM [8]. However, the ablation time for each point was limited to 30 s if the UP-EGM could not turn to complete positive [1]. PVI (entrance and exit block) by using contiguous point-by-point radiofrequency remains the ultimate endpoint of the ablation procedures in the current guidelines [1], and complete bidirectional block was systematically confirmed by pacing (output of 20 mA at a pulse width of 2 ms) each bipole of the Lasso catheter (St. Jude Medical, St. Paul, MN, USA).

Thirty minutes after PVI, the complete bidirectional blocks were rechecked for each PV. In the case of PV reconnection, supplemental RF applications were performed for the gaps in order to re-isolate PVs. No AF induction attempt was carried out at the end of the procedures.

2.3 Post-ablation electrogram characteristics

The filter settings were 30–500 Hz for the bipolar (BP) electrograms and 0.5–180 Hz for the UP electrograms. All procedures in this study were performed in sinus rhythm (SR) because accurate analysis of the unipolar electrogram modification is suboptimal during AF. Therefore, patients underwent cardioversion if presenting with AF at the beginning or during the procedure.

Both CCLs were divided into six regions [9], including roof, anterosuperior, anteroinferior, inferior, posteroinferior, and posterosuperior (Fig. 1). All the UP-EGMs were recorded in real time with the NavX™ Velocity System at a sweep speed of 200 mm/s during ablation. Two points were randomly chosen from each region in order to acquire complete positive UP-EGMs with high quality for analysis. The operators will stop ablation and take X-ray exposure to assure the stability and location of the ablation catheter. The rest of the lesion points were recorded consistently after the UP-EGMs turning complete positive and before switching to the next point to identify whether the chosen points were representative.

2.4 Post-ablation management and follow-up

All patients were discharged home within 4 days (limits, 2–4 days). AADs and anticoagulants (novel oral anticoagulant or vitamin K antagonists) were prescribed for 3 months. Subsequently, AADs were discontinued and usage of anticoagulants depended on the CHA_2DS_2-VASc score. Patients were followed in the outpatient department at 3, 6, and

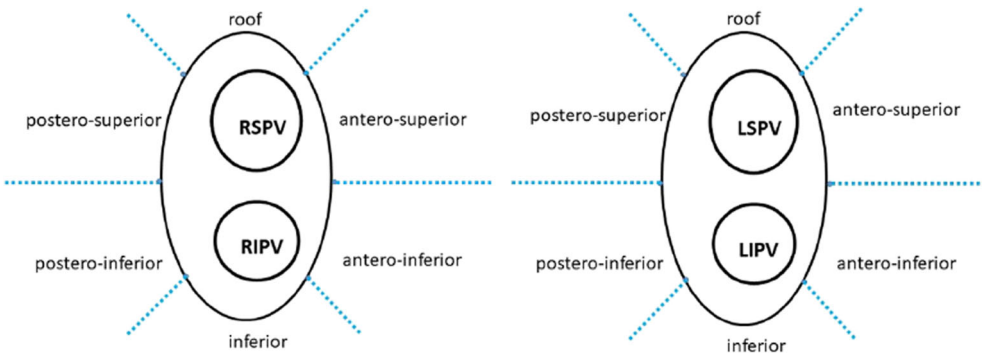

Fig. 1 Region definitions of right and left CCLs

12 months post-ablation and every 6 months thereafter. A 12-lead ECG and continuous 24-h Holter monitoring were performed routinely in all patients at each follow-up visit. Atrial tachycardia/AF recurrence was defined as any episode lasting > 30 s (either symptomatic or asymptomatic) subsequent to a 3-month blanking period [1].

2.5 Statistical analysis

Categorical variables are expressed as percentages. Continuous variables are expressed as the mean ± standard deviation for normally distributed variables or median (interquartile range) for variables with skewed distributions. Arrhythmia-free survival was analyzed by Kaplan–Meier survival curve. Statistical analyses were performed by SPSS 19.0 (IBM, Armonk, NY, USA).

3 Results

A total of 43 consecutive patients (aged 59 ± 11 years; 65% male) were enrolled in the study. Population characteristics are shown in Table 1. The mean left ventricular ejection fraction was 65%; mean LA size was 37 mm, and mean CHA_2DS_2-VASc score was 1.7.

All PVs were isolated with complete bidirectional block in all patients. Ten patients required targeting of the PV carina despite circular lesion creation around ipsilateral PV ostia exhibiting complete positive UP-EGMs. Thirty minutes after PVI, four patients presented PV reconnection. Three patients had one gap and the other had two gaps (Table 2). The UP-EGM morphology of the gaps demonstrated a negative component, and PVs were reisolated in the four patients by targeting those reversed UP-EGMs of gaps. One groin hematoma was reported. No other complications occurred.

Table 1 Baseline characteristics

Patient characteristics	
Age (year)	59 ± 11
Male, *n* (%)	28(65)
BMI (kg/m^2)	24.2 ± 3.6
LVEF (%)	65 ± 5
LA diameter (mm)	37 ± 6
Hypertension, *n* (%)	23(54)
Diabetes mellitus, *n* (%)	5(12)
History of stroke, *n* (%)	5(12)
History of thrombosis, *n* (%)	1(2)
Vascular disease, *n* (%)	22(51)
ALT (U/L)	23.1 ± 12.3
AST (U/L)	22.3 ± 11.1
Creatinine (μmol/L)	68.1 ± 13.5
Duration of AF (month)	28.7 ± 43.4
CHA2DS2-VASc score	1.74 ± 1.33
Combined with other arrhythmias, *n* (%)	4 (9)
Thyroid disorder, *n* (%)	3 (7)

The number of lesion points in each region ranges from 5 to 9. All the recorded UP-EGMs turned to complete positive. Most UP-EGMs in the same region were similar after ablation. Therefore, UP-EGMs of the two points chosen from each region were representative. Finally, a total of 1032 RFCA points with complete positive UP-EGM morphology were collected. The UP-EGM morphology of all points had a negative component before ablation (Fig. 2a). There were four different types of complete positive UP-EGM morphology patterns, as follows, which were named R, rR′, Rr′, and M (Fig. 2)b:

1. R pattern: there is no notch in the downstroke or upstroke.
2. rR′ pattern: there is a notch on the upstroke, and the bottom of the notch is upon the isoelectric line.
3. Rr′ pattern: there is a notch on the downstroke, and the bottom of the notch is upon the isoelectric line.
4. M pattern: there is a notch on the downstroke or upstroke, and the bottom of the notch is at the isoelectric line.

Among the points, there were 413 points with R pattern, 199 with rR′ pattern, 129 with Rr′ pattern, and 291 with M pattern (Table 3). M pattern in left CCLs was more frequent than that in the right CCLs (185 vs 106), which mostly appeared in anterosuperior (65%) and roof (49%) regions in the left CCLs and posteroinferior regions (37%) in the right CCLs. In the remaining nine regions, the percentage of M pattern ranges from 12% in anteroinferior regions of right CCLs to 33% in anteroinferior regions of left CCLs. Non-M patterns (R, rR′, and Rr′ patterns) in right CCLs were greater than those in left CCLs (410 vs 331). The unipolar EGM patterns mostly demonstrated non-M in right, left posterior, and left inferior CCLs.

After a mean follow-up of 19 ± 5 months, 37 patients (86%) remained in sinus rhythm without AADs. The Kaplan–Meier survival curve is shown in Fig. 3. Four patients (9%) presented paroxysmal AF recurrence, and 2 patients (5%) presented AT recurrence.

4 Discussion

The main findings of the present investigation are [1] the majority of complete positive UP-EGM patterns were non-M morphology. M patterns mostly appeared in anterosuperior and roof regions in the left CCLs and posteroinferior regions in the right CCLs, and [2] after a mean follow-up period of

Table 2 Distribution of gaps in the patients with pulmonary vein reconnection

Patient	No. of gap	Location of gap	Pattern(s) of UP-EGM[a]
1	1	Anterosuperior, left CCLs	M
2	1	Anteroinferior, right CCLs	rR′
3	2	1 in anterosuperior and 1 in roof, left CCLs	Rr′ and M
4	1	Inferior, left CCLs	R

[a] UP-EGM morphologies of the gaps before they were found to be reconnected

19 months, 86% of patients were free from atrial arrhythmia recurrence, indicating that UP-EGM-guided RFCA in PAF patients is reliable.

The UP-EGM can reflect the direction of electric wavefront propagation. When the electrical wavefront propagates toward the catheter electrode, the UP-EGM recorded by the catheter electrode exhibits positive morphology. When the electric wavefront propagates away from the catheter electrode, the UP-EGM exhibits negative morphology [10]. If the lesion of the ablation site is not transmural, the UP-EGM of the site recorded by the catheter electrode, which the electric wavefront can propagate away from, demonstrates a negative component. If the lesion of the ablation site is transmural, the UP-EGM recorded by the catheter electrode, which the electric wavefront cannot propagate away from, becomes a completely positive morphology [11]. Therefore, the elimination of the negative component of UP-EGM during radiofrequency applications reflects transmural lesions.

As described by Otomo et al. [5], TLs were always associated with complete elimination of the negative deflection in UP-EGM, irrespective of catheter orientation. Total elimination of the negative deflection in UP-EGM was an essential electrographic change indicating TL formation. Bortone et al. [12] reported that termination of ablation at the time of complete positive morphology partly resulted in reversible transmurality, and an extension of ablation was necessary. However, these two investigations were performed in animals. Bortone et al. [6] put theory into practice by carrying out the prospective study in humans in the setting of PAF catheter ablation. They compared PAF patients guided by UP-EGM with those following the standard approach. After a mean follow-up period of 21 months, the sinus rhythm maintenance rate was significantly higher in the UP-EGM group when compared to the control group (88 vs. 70%, $P = 0.027$). In our study, all PVs were isolated with complete bidirectional block in all patients, and after a mean follow-up of 19 ± 5 months, the success rate was 86%, which is consistent with the previous studies [6, 8]. Therefore, UP-EGM was a useful endpoint for radiofrequency energy delivery in patients with PAF.

However, all of the previous investigations had not analyzed the different UP-EGM patterns. UP-EGM patterns differ in different regions of continuous circular lesions (CCLs) after ablation. All the non-M patterns (R, rR′, and Rr′ patterns) may have the same meaning. The notch on the upstroke or the downstroke may represent the changing in the speed of propagation of the electric wavefront of depolarization [13].

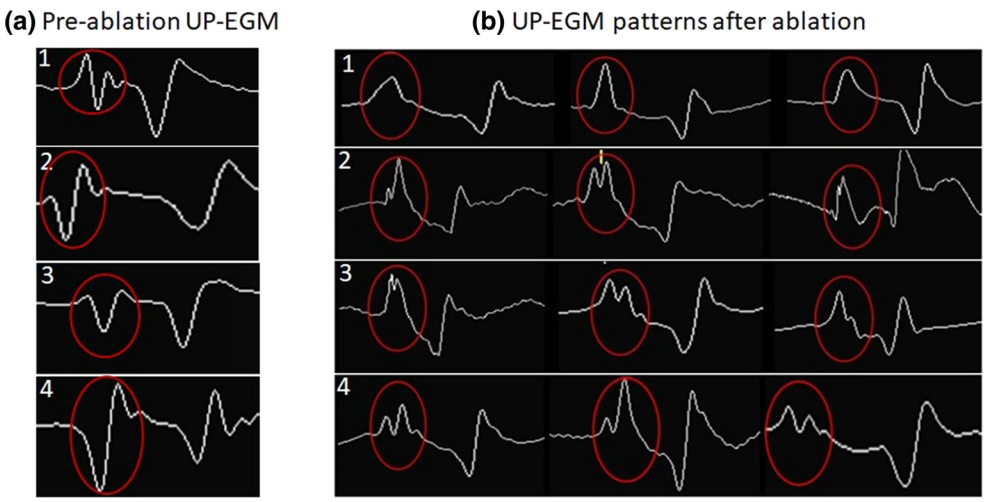

Fig. 2 Pre- (**a**) and post-ablation (**b**) UP-EGM patterns. **a** The UP-EGM morphology of the points has a negative component before ablation [1–4]. **b** UP-EGM patterns after ablation: [1] R pattern: there is no notch in the downstroke or upstroke. [2] rR′ pattern: there is a notch on the upstroke, and the bottom of the notch is upon the isoelectric line. [3] Rr′ pattern: there is a notch on the downstroke, and the bottom of the notch is upon the isoelectric line. [4] M pattern: there is a notch on the downstroke or upstroke and the bottom of the notch is at the isoelectric line

Table 3 UP-EGM patterns in different regions of right and left CCLs

	Right CCLs				Left CCLs			
	R	rR′	Rr′	M	R	rR′	Rr′	M
Roof	48 (56)	18 (21)	8 (9)	12 (14)	28 (32)	10 (12)	6 (7)	42 (49)
Anterosuperior	34 (40)	27 (31)	12 (14)	13 (15)	23 (28)	4 (4)	3 (3)	56 (65)
Anteroinferior	40 (46)	25 (29)	11 (13)	10 (12)	36 (42)	13 (15)	9 (10)	28 (32)
Posterosuperior	41 (47)	16 (19)	11 (13)	18 (21)	29 (34)	21 (24)	13 (15)	23 (28)
Posteroinferior	21 (24)	22 (26)	11 (13)	32 (37)	34 (40)	20 (23)	17 (20)	15 (17)
Inferior	36 (42)	12 (14)	17 (20)	21 (24)	42 (49)	12 (14)	11 (13)	21 (24)
Total	220 (43)	120 (23)	70 (14)	106 (20)	193 (37)	79 (15)	59 (11)	185 (36)

However, the direction of the propagation had not changed, which was toward the catheter electrode.

M patterns mostly appeared in anterosuperior (65%) and roof (49%) regions of left CCLs. In right CCLs, M patterns appeared mostly in posteroinferior regions (37%). In some regions with complicated structure, M patterns may develop as the integrated electrical signal from different directions. For example, the anterosuperior regions of left CCLs are next to the left atrial appendage (LAA) [14], and the catheter electrode (the diameter of which is 4.0 mm) may also record the signal from the LAA. The mechanism of M patterns developed in some regions without complicated structure is unknown and awaits further investigation.

5 Limitations

The limitations of the present study are as follows. First, this is a single-center investigation with a limited study sample, and our study has not been directly compared with the standard ablation approach. Second, no challenge with adenosine administration for PV-LA dormant conduction unmasking was performed, and no pacing along the lesions created was performed during the index PVI procedures. Third, we chose two lesion points with high-quality UP-EGMs in each region in order to reduce the procedure time and X-ray exposure, which might develop some selected bias. However, the UP-EGMs of the chosen points were representative. Thus, we believed that the findings of the present study were reliable. Finally, all the patients with atrial tachycardia/AF recurrence had not accepted a second PVI procedure. The mechanism of the recurrence is unclear.

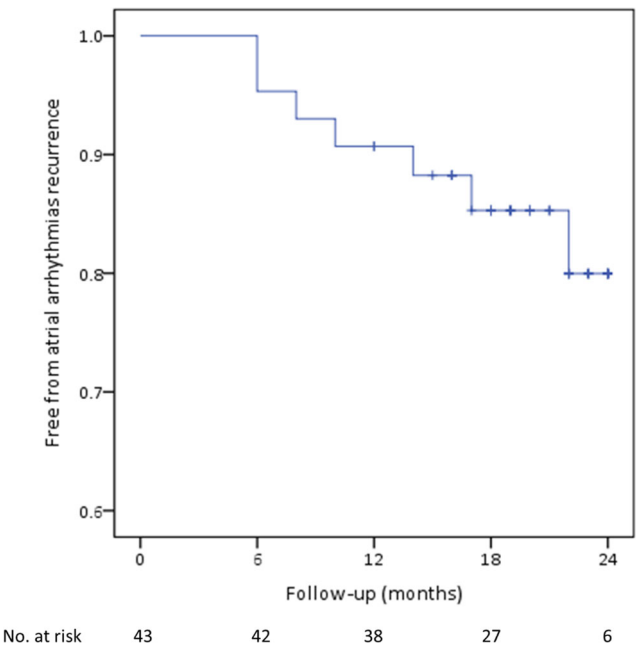

Fig. 3 The Kaplan–Meier survival curve for atrial arrhythmias recurrence

6 Conclusion

Pulmonary vein isolation guided by UP-EGM with a complete positive pattern in PAF patients is reliable. The majority of complete positive UP-EGM patterns were non-M morphology. M patterns mostly appeared in anterosuperior and roof regions in left CCLs and posteroinferior regions in right CCLs.

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Compliance with ethical standards

This investigation was approved by the ethics committee of Ningbo First Hospital.

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

Informed consent Informed consent was obtained from all individual participants included in the study.

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