A novel alternating second-generation cryoballoon or radiofrequency catheter ablation technique strategy for repeat ablation in patients with recurrent atrial fibrillation: A two-year follow-up outcome

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Research Article

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Abstract

Background

Pulmonary vein (PV) reconnection after radiofrequency ablation (RFC) or 2nd generation cryoballoon (CB) pulmonary vein isolation (PVI) is common.

Method

We report a single-center experience of 156 patients who underwent an alternating redo procedure-ablation strategy for recurrent atrial fibrillation (AF) after a failed index RFC or CB procedure. During the redo procedure, alternating ablation technique was applied in a reverse sequence: RFC was applied for redo ablation in 60 patients with failed index CB ablation(CB-RFC-redo); 2nd generation CB was used for redo ablation in 96 patients after failed index RFC ablation (RFC-CB redo);

Results

During the redo procedure, the proportion of patients with PV reconnection was lower after index CB PVI procedure compared with the proportion of patients after index RFC PVI (88.3% versus 98.9%, $p = 0.01$). Additionally, 82.8% of all PVs and left common trunks PV (CTs) isolated by index RFC were reconnected, compared with 42% PVs reconnected after index CB PVI ($p = 0.005$). A mean number of 1.50 ± 0.8 PVs /patient were reconnected after index CB PVI, compared with 3.36 ± 0.9 PVs /patient after index RFC PVI ($p = 0.001$). Patients after index RFC PVI frequently presented with ≥ 3 reconnected PVs, compared with index CB PVI(70.8% vs 10%, $p < 0.001$). A total of 60 patients after index CB PVI underwent RFC-redo ablation, and 96 patients after index RFC PVI underwent CB-redo ablation. At a two year follow-up, 43 patients (27.6%) developed recurrence after redo ablation, with a similar AF- free outcome (CB-RFC redo:73.3% vs RFC-CB redo: 71.9%, $p = 0.873$). In the multivariate analysis, persistent AF (HR = 2.107, 95% CI: 1.085–4.091, $p = 0.028$) and early AF recurrence after the initial ablation (HR = 2.431, 95% CI: 1.279–4.618, $p = 0.007$) were independent predictors of AF recurrence after repeat ablation.

Conclusions

The extent and distribution of PV reconnections were different after index RFC and CB PVI procedures. Alternating CB or RFC ablation technique strategy is effective with a similar long-term outcome, and it may be an appropriate option for repeated AF ablation regardless of index ablation technique used.

Background

Atrial fibrillation (AF) is the most common clinical arrhythmia throughout the world, which often impairs the quality of life and leads to serious complications [1]. Radiofrequency catheter (RFC) or cryoballoon

(CB) ablation therapy based on pulmonary vein isolation (PVI) is a well-established treatment strategy for drug–refractory AF [2–3]. Long -lasting PVI is fundamental to avoid late AF recurrence and is the primary goal of AF ablation regardless of the RFC or CB ablation [3–4]. However, 30–45% of patients may suffer from PVs-left atrium(LA) reconnection and AF recurrence [5–6]. Due to high PVs reconnection rate after an index RFC or CB ablation procedure, repeated ablation is very common in the clinical practice [6–7]. However, the optimal approach and choice of the technique for repeated procedures still remain controversial [4, 6]. Patients after index RFC ablation usually showed a higher incidence of PV reconnection and presented multiple PVs reconnection [4, 8]. CB redo procedure-ablation in these patients could reduce the total procedure time and improved durability of PVI compared to PV isolation by RFC [8, 9]. CB ablation usually showed less frequently reconnected PVs but more non-PV triggers [9, 10]. Additionally, the PVI area using the CB technique was significantly smaller than the area encircled by circumferential PVI using the point-by-point RFC technique [10, 11]. In these patients after index CB ablation, RFC redo ablation could treat part of the left atrium substrate with extensive PV antrum isolation and eliminate non-PV AF triggers [11, 12]. Recently, repeat AF ablation using the alternating technique (CB or RFC) in a reverse sequence based on the index ablation technique was suggested [9]. However, there are few studies investigating the long-term efficacy or safety of this alternating ablation technique strategy in patients with recurrent AF [9]. Therefore, in order to take advantage of the potential benefits of each technique, the present study aimed to investigate the long-term efficacy of alternating reverse sequence strategy of the two ablation techniques for repeated AF ablation following index ablation procedure.

Methods

Patients

We retrospectively recruited 156 patients from September 2016 to December 2019, who underwent first redo ablation after a failed index RFC or 2nd generation CB PVI procedure in this study. The study protocol was approved by the Human Research Ethics Committee of Fuwai hospital according to the Helsinki Declaration. Repeat ablation strategy was performed by the alternating ablation technique in a reverse sequence from the index PVI procedure. For instance, 60 patients initially treated with CB ablation (index CB) underwent redo procedure-ablation with RFC (the CB- RFC redo group); 96 patients initially treated with RFC ablation (index RFC) underwent redo procedure-ablation with CB (the RFC-CB redo group) .The study flowchart is shown in **Fig 1**. All patients provided written informed consent.

Index ablation procedure

The ablation procedure was performed using an uninterrupted oral anticoagulant drug on the ablation procedural day. All the anti-arrhythmic drugs except amiodarone were stopped at five half-live times before the procedure. In this study population, 60 patients underwent the index PVI procedure completed with CB, and 96 patients were initially treated with RFC. In the index RFC PVI procedure, LA map construction was performed using the CARTO 3 system (Biosense Webster Inc, Diamond Bar, CA, USA)

and a 3.5-mm tip irrigated contact-force ablation catheter (SmartTouch catheter (Biosense Webster)) was used in a point-by-point method. Each PV ostium was identified by selective venography and then it was tagged on the LA electroanatomic map. RFC applications were performed in a power controlled mode with a power limit of 35 W (25 W at the posterior wall) and at a maximum temperature of 43 ℃ during the procedure. The infusion rate of perfusion during RFC ablation was 17 ml / min, the contact force was set at 10 – 20 g, and each ablation point took at least 30 s to achieve more than 70% local voltage reduction. In all patients, a wide antral circumferential ablation was performed with isolation of both ipsilateral veins together. In the index CB PVI procedure, PVI was performed using a 28 mm second-generation CB catheter (Art Front Advance, Medtronic, Minneapolis, Mn, USA), the CB catheter was inserted through a 15F steerable sheath (FlexCath, Medtronic, Minneapolis, Mn, USA) and a 20-mm-diameter inner lumen Achieve catheter (Achieve™, Medtronic, MN, USA) was directed to each targeted PV ostium to record PV signals during ablation procedure. CB occlusion was evaluated using the selective angiography injection of the contrast agent via the inner lumen of the CB catheter, and the ideal occlusion was indicated by the absence of contrast reflux into the LA with contrast agent retention. Single ablation cycle time for the CB procedure was ≤ 180 s. If PVI was completed within 60 s, only one ablation cycle was used. If the time-to-isolation (TTI) was ≥ 60 s, a second CB cycle application within 180 s was performed. The nadir temperature was not lower than -55℃. Phrenic nerve stimulation (cycle length 1000 ms, 15 mA/3.0 ms pulse width) was applied through a quadripolar catheter in the superior vena cava (SVC) during isolation of the right-sided PVs to reduce the risk of phrenic nerve palsy. Using an irrigated contact force ablation catheter, RFC touch-up ablation was performed for CB ablation failure guided by the Achieve Mapping Catheter. In both index RFC and CB ablation procedures, PVI was the only target, with no additional ablation lines being performed. A bidirectional isolation was confirmed in all PVs with a circular mapping catheter after a waiting period of 30 minutes with the adenosine challenge. If patients with typical atrial flutter(AFL) were documented, additional isolation of the cavo-tricuspid isthmus (CTI) by an irrigated contact force ablation catheter was required. If non-PV AF triggers were documented in either the index RFC or CB PVI procedure, then they were ablated using an irrigated contact force RF catheter.

Redo procedure-ablation

All repeat ablations were performed using alternating CB or RFC ablation in a reverse sequence based on the index ablation technique. **CB-RFC redo procedure:** In patients with a failed index CB ablation, redo procedure-ablation of augmented PV ostium area isolation was performed using RFC with the 3D mapping system (CARTO3, Biosense Webster). PV reconnection was evaluated at the onset of the redo procedure using Lasso® catheter (Biosense Webster, USA). The Lasso catheter was placed in each PV ostium for evaluation of the reconnected PVs as well as the type of the reconnection gaps. RFC energy was delivered at 25 W on the posterior wall and at 35 W on the anterior wall for a duration of at least 30 s. Electric isolation of each PVs was confirmed by entrance and exit block, assessed by Lasso catheter. If patients without PV reconnection were documented at the redo procedure, augmented PV ostium area isolation by RFC were also performed. No other additional linear lesions in the LA were performed. Any repetitive premature atrial complex, atrial tachycardia, and beats triggering AF were identified as non-

PVs triggers and were targeted for re-ablation by RFC ablation. **RFC-CB redo procedure:** In patients with a failed index RFC ablation, redo procedure-ablation was performed with second-generation CB catheter (Advance 28mm, Medtronic, Minneapolis, MN, USA). The freezing protocol for the CB procedure has been described above. RFC touch-up ablation using an irrigated ablation catheter, was performed to reach the PVI for CB failure guided by the Achieve Mapping Catheter. If non-PV triggers were documented, they were targeted for re-ablation by RFC ablation. In both groups, if patients presented recorded typical AFL, linear ablation of the CTI by an irrigated contact force ablation catheter was required. Pulmonary veins ostia were the only target, and no additional ablation lines were performed in the LA during the redo PVI procedure.

Clinical Follow-up

Continuous telemetric monitoring was performed for 24-48 h in all patients post-ablation. After hospital discharge, patients were seen in outpatient clinic every month for the 1st year post-ablation, and every 3 months thereafter. All patients underwent 48-h Holter monitoring and transthoracic echocardiography during follow-up. If patient with recurrent arrhythmias or with serious symptoms, more frequent follow-up should be arranged as patients needed. Any episode of atrial tachyarrhythmia of longer than 30 s as detected by 48-h Holter beyond the 3-month blacking period was considered as AF recurrence.

Statistical analysis

Continuous variables are expressed as mean ± SD, while classified variables are expressed as percentage. The survival curve was analyzed by the Kaplan Meier method. Univariate and multivariate regression analyses using the backward likelihood ratio method were employed to determine the risk predictors of AF recurrence. The Student t test or Mann Whitney U test were used to examine continuous outcomes and Pearson's chi-squared test was used to compare categorical outcomes among groups. A P-value of < 0.05 was considered statistically significant. All statistics were performed using the SPSS version 25.0 (SPSS Inc, Chicago, IL, USA).

Results

Baseline characteristics of patients

A total of 156 patients (mean age: 58.19 ± 9.26 years, 78.2% paroxysmal AF, 73.1% male dominance) with a repeat PVI procedure after a failed index RFC or CB PVI were enrolled in this study, and they had a mean LA diameter of 38.85 ± 4.60 mm. During the index procedure, 96 patients treated with RFC PVI tended to require longer total procedure times (83.5 ± 28.2 min), compared to 60 patients treated with the CB PVI (57.6 ± 12.2 min, $p = 0.01$). However, mean fluoroscopy times (17.5 ± 6.2 min) was longer for the index CB PVI procedure compared to the index RFC PVI procedure (9.5 ± 2.5min,$p = 0.02$). Other baseline clinical characteristics are shown in Table 1. Early recurrence during the three-month blanking period after the index PVI procedure was not significant in both groups (the post index CB PVI group:31.7% versus the post index RFC PVI group 27.1%, $p = 0.515$). The mean time delay between re-detection of AF and redo-

PVI was not different between both groups (11.8 ± 1.9 months in the post index CB PVI group and 10.3 ± 0.9 months in the post index RFC PVI group, p = 0.475).

Table 1
Clinical baseline characteristics of patients

Variables	post index CB PVI (n = 60)	post index RFC PVI(n = 96)	P value
Male n(%)	45(75%)	69(71.9%)	0.854
Age(y)	56.63 ± 9.66	59.12 ± 8.93	0.102
Current smoking n(%)	15(25%)	21(21.9%)	0.125
Alcohol intake n(%)	14(23%)	24(25%)	0.325
BMI(Kg/m^2)	25.9 ± 2.8	26.2 ± 2.5	0.215
AF duration, months(SD)	52.78 ± 51.48	69.31 ± 64.69	0.039
Paroxysmal AF n(%)	44(73.3%)	78(81.3%)	0.323
Complication			
Hypertension n(%)	34(56.7%)	52(54.2%)	0.745
Diabetes n(%)	8(13.3%)	10(10.4%)	0.606
CHF n(%)	2(3.3%)	1(1%)	0.556
CAD history n(%)	6(10%)	12(12.45%)	0.472
Previous stroke/TIA n(%)	2(3.3%)	5(5.2%)	0.486
CHA2DS2-VASc	1.02 ± 1.01	1.29 ± 1.09	0.249
Echocardiography	39.03 ± 4.97	38.74 ± 4.38	0.170
LA diameter, mm			
LVEF (%)	63.6 ± 3.73	62.9 ± 4.54	0.694
Antiarrhythmic drugs	0.85 ± 0.60	0.80 ± 0.55	0.325
Procedure duration (min)	57.6 ± 12.2	83.5 ± 28.2	0.010
Fluoroscopy duration (min)	17.5 ± 6.2	9.5 ± 2.5	0.020
Delay time to redo PVI	11.8 ± 1.9	10.3 ± 0.9	0.475
ER recurrence, n (%)	19(31.7%)	26(27.1%)	0.515

Data were expressed as mean ± SD, median with 25th and 75th percentile or n (%).

AF: atrial fibrillation; BMI: body mass index; CAD: coronary artery disease; CHF: chronic heart failure; TIA: transient ischemic attack; ER recurrence: atrial arrhythmia recurrence within three-month blanking period; LVEF: left ventricular ejection fraction; LAD: Left atrial diameter.

Reconnection Pvs Patterns After The Index Cb Vs Rfc Pvi Procedure

The incidences of pulmonary vein reconnection in both groups at the time of the redo PVI procedure are presented in Table 2. Altogether, 148 patients (94.8%) exhibited PV reconnection and the proportion of patients with PV reconnection was lower after index CB PVI compared with the proportion of patients after index RFC PVI procedure (88.3% versus 98.9%, p = 0.01). In the post index CB group, 96 out of the 229 initially isolated PVs/CTs (42.0%) were reconnected to the LA, while 299 out of the 361 PVs/CTs (82.8%) were reconnected after index RFC PVI procedure (p = 0.005).Of note, a mean number of 1.50 ± 0.8 PVs per patients were reconnected after the index CB PVI procedure, as compared with a mean number of 3.36 ± 0.9 PVs per patients after the index RFC PVI procedure (p = 0.001). A total of 90.5% of the left common trunk(s)(CTs) -counted as one PV in the post index RFC PVI group were reconnected, in contrast to 55.6% in the post index CB PVI group (p = 0.035). After the index CB PVI procedure, the left superior PV (64%) was mostly likely to exhibit late reconnection, while the lowest rate of PV reconnection was detected in the left inferior PV (29.4%)(Fig. 2). As was shown in Fig. 2, the frequency of left superior PV reconnection (89.3%) was greater than that of other PVs after index RFC PVI procedure. Additionally, we found that left-sided – (86.6% vs 47.3%, p = 0.001), right sided (79.4% vs 36.9%, p = 0.001), superior- (84.8% vs 47.1%, p = 0.001) and inferior – (80.6% vs 36.3%, p = 0.001) PVs were more frequently reconnected after index RFC PVI procedure, compared with the post index CB PVI group. The distribution of patients with 0, 1, 2, 3, and 4 reconnected PVs is presented in Fig. 3. One patient (1.7%) after index CB PVI exhibited 4 reconnected PVs, while 43 patients (44.8%) after index RFC PVI exhibited 4 reconnected PVs. The percentage of patients after index RFC PVI with ≥ 3 reconnected PVs was significantly higher compared to the percentage of patients in the post index CB PVI group (68 patients, 70.8% vs 6 patients, 10%, p < 0.001), while the percentage of patients with no PV reconnection was lower after index RFC PVI compared to the percentage of patients after index CB PVI procedure (1% vs 11.7%,p = 0.020).

Table 2
Pulmonary vein reconnection following index PVI procedure

Variables	post CB PVI group(n = 60)	post RFC PVI group(n = 96)	p value
Angiographically delineated PVs / CTs	222/9	342/21	1.000
Isolated PVs / CTs at index procedure	220/9	340/21	1.000
Pts. with PV reconnections	53(88.3%)	95(98.9%)	0.010
Reconnected PVs and CTs at redo procedure			
Number of pulmonary veins reconnection			
PV reconnections per patient #:	1.50 ± 0.8	3.36 ± 0.9	0.001
Reconnected PVs and CTs at redo procedure	96/229(42.0%)	299/361(82.8%)	0.005
Reconnected left-sided PVs/CTs	52/110(47.3%)	149/172(86.6%)	0.001
Reconnected CTs	5/9(55.6%)	19/21(90.5%)	0.035
Reconnected LSPV	32/50(64%)	67/75(89.3%)	0.039
Reconnected LIPV	15/51(29.4%)	63/76(82.9%)	0.001
Reconnected right-sided PVs	44/119(36.9%)	150/189(79.4%)	0.001
Reconnected RSPV	19/60(31.7%)	76/95(80%)	0.001
Reconnected RIPV	25/59(42.3%)	74/94(78.7%)	0.008
Reconnected superior PVs	56/119(47.1%)	162/191(84.8%)	0.001
Reconnected inferior PVs	40/110(36.3%)	137/170(80.6%)	0.001
Pts. with reconnected PVs			
0	7(11.7%)	1(1%)	0.020
1	17(28.3%)	2(2%)	0.001
2	30(50%)	25(26%)	0.015
3	5(8.3%)	25(26%)	0.001
4	1(1.7%)	43(44.8%)	0.001

Pts: Patients; CB: 2nd generation cryoballoon; PVs: Pulmonary veins; CTs: Left common trunks; LSPV: Left superior pulmonary vein; LIPV: Left inferior pulmonary vein; RSPV Right superior pulmonary vein and RIPV Right inferior pulmonary vein.

Redo Pvi Procedural Data

During the redo ablation procedure, in the CB-RFC redo group, 60 patients after index CB procedure were performed with extensive PV antrum isolation using RFC technique, including 7 patients without PVs reconnection. While, in the RFC-CB redo group, 95 patients with PV reconnection underwent CB redo-PVI and one patients without PV reconnection who exhibited SVC triggers underwent SVC isolation by the CB technique (Table 3). Of note, complete PVI was achieved in all these patients during the redo PVI procedure. The total redo procedure time (CB-RFC redo:49.6 ± 20.7 min versus RFC-CB redo: 48.5 ± 12.7 min, p = 0.265) and LA dwell time(CB-RFC redo:45.6 ± 20.7 min versus RFC-CB redo:46.3 ± 12.7 min, p = 0.268) were similar between the two groups. However, patients in the RFC -CB redo group required a longer fluoroscopy time (15.9 ± 0.8 min vs 4.2 ± 0.9 min, p = 0.001) and higher fluoroscopy dose (202.5 ± 13.6 mGy vs 156.3 ± 15.3 mGy, p = 0.02) compared to patients in the CB -RFC redo group. Ablation of non-PV triggers was more frequently performed in the CB-RFC redo group (26.7%), compared to the RFC-CB redo group (2%; P = 0.001). CTI ablation was performed more frequently in the CB-RFC redo group (18 patients, 30%), compared to the RFC-CB redo group (20 patients, 19.8%, p = 0.035). Minor complications were transient phrenic nerve palsy in two patients and mild hemoptysis in two patients in the RFC- CB redo group. Fifteen patients (6 patients, 10% in the CB-RFC redo group, 9 patients, 9% in the RFC-CB redo group) demonstrated a short-time vagal reflex. No severe adverse events, including acute cerebrovascular event, major bleeding event, embolic complication, vascular complication, PV stenosis, or death, were reported.

Table 3
Repeat Ablation Procedure Features and Complication

	CB-RFC Redo (n = 60)	RFC- CB Redo (n = 96)	p value
Rhythm at repeat ablation			
Sinus rhythm, n (%)	43(71.7%)	78(81.3%)	0.215
Atrial fibrillation, n (%)	9(15%)	15(15.6%)	0.375
Atrial tachycardia, n (%)	8(13.3%)	3(3.1%)	0.032
Procedural features			
Procedural time, min	49.6 ± 20.7	48.5 ± 12.7	0.265
Fluoroscopy time, min	4.2 ± 0.9	15.9 ± 0.8	0.001
LA dwell time, min	45.6 ± 20.7	46.3 ± 12.7	0.268
Fluoroscopy dose, mGy	156.3 ± 15.3	202.5 ± 13.6	0.020
Acute success	100%	100%	-
RFC touch-up, n(%)	2(3.3%)	5(5.2%)	0.358
Cavotricuspid isthmus ablation	18(30%)	20(19.8%)	0.035
Cardioversion	9 (15%)	15(15.6%)	0.352
Non-Pulmonary Vein triggers	16(26.7%)	2(2%)	0.001
SVC, n(%)	6(10%)	2(2%)	0.025
Intra-atrium septum, n(%)	2(3.3%)	-	-
Left atrium ,n(%)	3 (5%)	-	-
Right atrium, n(%)	5(8.3%)	-	-
Complication			
Phrenic paralysis	0	2(2%)	-
Vagus reflex,n(%)	6(10%)	9(9%)	0.257
Hemoptysis, n(%)	0	2(2%)	-
Hydropericardium, n(%)	0	0	-
Acute cerebrovascular event	0	0	-
Atrial esophageal fistula	0	0	-
Pulmonary vein stenosis	0	0	-

Recurrence Of Af And Predictors

After a two-year follow-up, 43 patients (27.6% of the total population) had AF recurrence after redo ablation, and 72.4% of patients were free from recurrence of AF (Fig. 4), with no significant differences between the two groups (CB-RFC redo:44 patients,73.3% vs RFC-CB redo: 69 patients, 71.9%, p = 0.873).In the multivariate Cox regression analysis, persistent AF(HR = 2.107, 95% CI: 1.085–4.091, P = 0.028) and early AF recurrence after index ablation (HR = 2.431, 95% CI: 1.279–4.618, P = 0.007) were the independent predictors of AF recurrence after redo-ablation in the long term follow-up (Table 4). Patients without early AF recurrence (ERAF) after the index ablation procedure achieved a better redo ablation outcome compared with those with ERAF regardless of the ablation technology used (78.4% vs 57.8%, Log-rank P = 0.010). The AF-free rate of persistent AF (58.8%) was lower, compared to that of paroxysmal AF (76.2%, Log-rank P = 0.035) (Fig. 5). No severe complications or embolism events occurred during the follow-up period.

Table 4
Univariate and multivariate Cox regression analysis results.

Variable	Univariate model			Multivariate model		
	HR	95% CI	p	HR	95% CI	p
Gender (Female)	1.167	0.522–2.609	0.707			
Age ≥ 65 yrs	1.429	0.672–3.036	0.353			
Persistent AF	1.942	1.051–3.588	0.035	2.107	1.085–4.091	0.028
AF Duration time	1.037	0.426–1.645	0.606			
ER after index ablation	2.527	1.296–4.927	0.001	2.431	1.279–4.618	0.007
Hypertension	1.113	0.404–2.064	0.828			
Body weight index	1.720	0.615–4.810	0.301			
Coronary heart disease	1.180	0.426–3.267	0.751			
Left atrial diameter > 40 mm	1.566	0.799–3.149	0.208			
CHA2DS2-VASc score	1.065	0.586–1.539	0.834			
Index ablation technique	1.528	0.775–1.439	0.658			
Number of veins reconnected	1.035	0.543–1.509	0.452			
Delay time to redo PVI	1.112	0.652–1.336	0.667			

AF: atrial fibrillation; ER recurrence: atrial arrhythmia recurrence within three-month blanking period; PVI: pulmonary vein isolation.

Discussion

Major findings

We analyzed the LA-PV reconnection patterns in 156 patients withrecurrent AF who underwent redo procedure-ablation after index RFC or CB PVI. The main findings of our study were as follows: (I) PV

reconnection rate was significant lower after index CB PVI versus index RFC PVI (1.50 ± 0.8 PVs/ per patients vs 3.36 ± 0.9 PVs/per patient , p=0.001); Moreover, patients after index RFC PVI frequently presented multiple-veins reconnection(≥3 reconnected PVs)(70.8%, p<0.001), while patients after index CB PVI more often had reconnection of one or two PVs (78.3%, p=0.001); (II) Non-PV triggers were more frequent after the index CB PVI (26.7%vs 2%; P=0.001) than after index RFC PVI; different PV reconnection patterns could be identified after index RFC and CB PVI procedures; (III)After a two year follow up, 43 patients (27.6 % of the total population) developed recurrence after redo ablation, with no differences between the two groups (p= 0.873). (IV) In the multivariate Cox-regression analysis, the persistent AF (p=0.028) and early AF recurrence after the initial ablation procedure (p=0.007) were independent predictors of AF recurrence after repeat ablation regardless of the index ablation technique used. Consequence, earlier active surveillance for those patients may be justified.

Factors associated with PV reconnection after RFC ablation

Although several approaches have aimed at the identification of factors associated with PVs reconnection after RFC PVI (i.e. related force–time integral score/ablation index and adenosine challenge), PV reconnection is still the typical finding in recurrent AF patients after index RFC ablation [2,3]. For example, Balt et al reported that 98% of all patients had PV reconnection(s) on repeat ablation after RFC PVI, with 34% exhibiting reconnections of three PVs [13]. Aryana et al reported that 60.9% of patients exhibited PV reconnection and most of the patients had multiple PVs reconnections after RFC PVI [14]. Low contact force RF applications resulted in a non-transmural lesion and were related to late PV reconnection [13,14]. Different PVs reconnection rates were observed

in patients with recurrent AF after index RFC procedure, the left superior pulmonary vein (LSPV) (89.3%) and CTs (90.5%) were most frequently affected by electrical reconnection in the present study. This was similar to that reported by Wieczorek et al [8] with a 94% reconnection rate for CTs and a 85% reconnection rate for LSPV after RFC ablation. The ridge between the left atrial appendage (LAA) and LSPV is a common reconnection site, which may possibly be explained by the left atrial anatomy itself [14,15]. It is often a challenge to achieve and maintain a stable catheter position with an adequate contact force by RFC ablation in this area [15,16].

Factors associated with PV reconnection after CB ablation

PV reconnection is also common in patients with recurrent AF after index CB PVI [3,4] . In the present study, PVs reconnection after index CB PVI was also frequently observed in LSPV and left common trunks, and it has also been reported by other authors [8,10]. The difficulty of CB PVI for LSPV is influenced by the thickness between LSPV and LAA, the angle between LSPV and the top of LA, and the ovality of the pulmonary vein opening [15,17]. During the CB PVI procedure, an adequate coverage of the ridge area between LSPV and LAA with a satisfactory temperature might be difficult [17]. The difficulty in common trunks(CTs) isolation by the CB technique may depend on the size, length, and angle of the branches of the CTs [8,18]. In the clinical practice, sequential CB isolation of the superior and inferior branches of CTs, may increase the risk of PV stenosis and may result in smaller PV antral lesions [18,19].

Furthermore, PVI using the CB technique can sometimes achieve only PV isolation, excluding the carina and LA antral regions, where AF triggers often originate in the clinical practice [20]. Remarkably, in the previous studies, the right inferior PV showed the highest rates of PV reconnection [20], which is different from our finding of index CB PVI. This might be explained by the regular use of the “pull-down” and “hockey stick” techniques during the CB PVI procedure, which are particularly helpful in improving the inferior pulmonary veins isolation [20,21].

Alternating ablation technique strategy and recurrence of AF

So far, few reports have evaluated the advantages of the usage of the alternating reverse technique for repeat ablation in patients with recurrent AF. AF recurrence after index RFC PVI usually presented multiple PVs reconnections, the alternating reverse sequence for redo PVI used by the CB technique could reduce total redo procedure time and obtain durable PV isolation in patients with previously failed index RFC PVI [9,10]. However, non-PV triggers were significantly more frequently observed in the patients after index CB PVI [10,21]. It is usually necessary to target and eliminate the non-PV focal triggers during the redo ablation after failed CB PVI procedure [12,22]. However, CB ablation cannot perform substrate modification or non-PV focal triggers elimination due to its intrinsic balloon design [22,23]. Consequently, the RFC technique is an ideal option for redo ablation after failed CB PVI procedure. In previous studies, several reports have investigated the redo procedure regarding CB or RFC techniques for recurrent AF with PV reconnection [24,25]. In the recent study by Miao et al [24], who analyzed a cohort of patients after failed index RFC ablation, about 32.8% of patients had AF recurrence during the one-year follow-up after the RFC redo ablation procedure. Additionally, Glowniak Andrzej et al reported a group of 61 patients undergoing CB redo PVI for either the index RFC or CB procedure, with 70.3% of them being free of arrhythmia after a 15-month observation [25]. However, there are still scarce data regarding the alternating reverse sequence strategy for redo PVI based on the index ablation technique. In our study, the advantage of the alternating reverse sequence strategy for repeat ablation in patients with recurrent AF was evident, 72.4% patients were free from recurrence of any atrial arrhythmia after redo procedure ablation at the two-year follow-up. Additionally, the alternating ablation technique strategy could reduce the total procedure time with few complications.

Predictors of AF recurrence after redo procedure-ablation

Several factors, such as the persistent AF, greater LA diameter, obesity, and ERAF, have been established as the potential predictors for AF recurrence in previous studies [23,24,25]. In a detailed multivariate Cox regression analysis, ERAF during the blanking period after the initial PVI procedure and persistent AF were associated with a poor repeat ablation outcome regardless of the ablation technique used. The Kaplan-Meier analysis showed that those patients with ERAF during the blanking period after index PVI had more AF recurrence compared with those without ERAF (42.2 % vs 21.6%, Log-rank P=0.01) after redo ablation. In the present study, the index or redo ablation technique used was not an independent predictor of AF recurrence after repeat ablation. However, the recent study by Verlato et al [9] reported that different ablation techniques used was an independent predictor of AF recurrence after the redo procedure. In their

study, patients who had undergone repeat ablation with RFC after the index CB procedure tended to exhibit less AF recurrence compared to patients who underwent re-ablation with CB after index RFC ablation [9], which is different from the result of the present study. In our study, both ablation sequence groups (CB-RFC redo or RFC-CB redo) were effective, with a similar long-term outcome regardless of the ablation technique used. This discrepancy might be explained by multiple confounding factors, such as different ablation tools used across different studies and non-standardization of ablation parameters used by different electrophysiologists in different eras. Compared with the study by Verlato [9], this study was started later and the CB or RFC ablation technique was improved. In additional, partly first generation CB used , more persistent AF, and longer AF duration were observed in the patients with index RFC ablation reported by Verlato et al[9], which may hamper the ablation outcomes.

Study Limitations

The present study had several limitations. First, this study is a non-randomized and single-center analysis. Larger multi-center studies must be warranted to provide conclusive evidence; Second, not all the patients in the present study underwent provocation of non PV triggers with isoproterenol. Thus, the non PV triggers documented in this study may have been underestimated. Third, some patients with asymptomatic AF recurrence during the follow-up may have been undetected and thus not recruited for the analysis.

Conclusions

Alternating ablation technique strategy for re-ablation of patients with recurrent atrial fibrillation in a reverse sequence was safe and effective, regardless of index ablation technique used, with 72.4% success rate at the two-year follow-up.

Abbreviations

AF
atrial fibrillation
LA
Left atrial
LVEF
left ventricular ejection fraction
LAD
Left atrial diameter
RFC
radiofrequency current
CB
cryoballoon
HR

Hazard ratio
PV
Pulmonary vein. CTs:left common trunk(s)
LAA
Left atrial appendage
LSPV(s)
Left superior pulmonary vein(s)
LIPV(s)
Left inferior pulmonary vein(s)
RSPV(s)
Right superior pulmonary vein(s)
RIPV(s)
Right inferior pulmonary vein(s)

Declarations

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Authors' contributions

QHT and XGG: Conceptualization, Investigation, Data curation,

Methodology, Formal analysis, Validation, Writing original draft; JM: Conceptualization, Methodology, Validation, Formal analysis. All the authors were involved in the draft, revision and approval of the final version.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The retrospective study was approved by the Ethics Committee of the Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College ((No.2016-829) according to the Helsinki Declaration.

Consent to participate

Written informed consent was provided by all participants or their legal guardians. All methods were performed in accordance with the relevant guidelines and regulations of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing Interests

All authors had no conflicts of interest.

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Figures

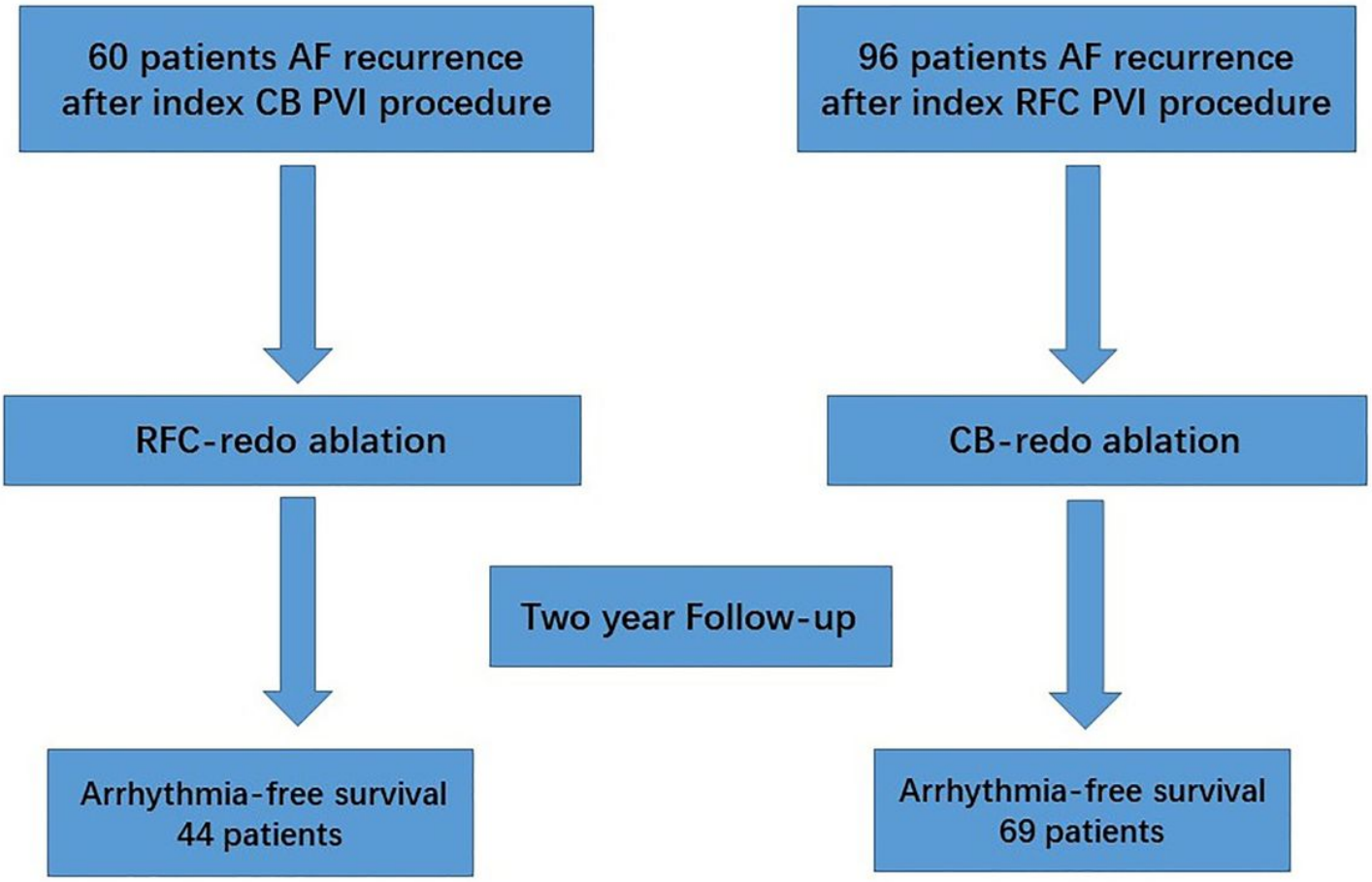

Figure 1

The study flowchart.

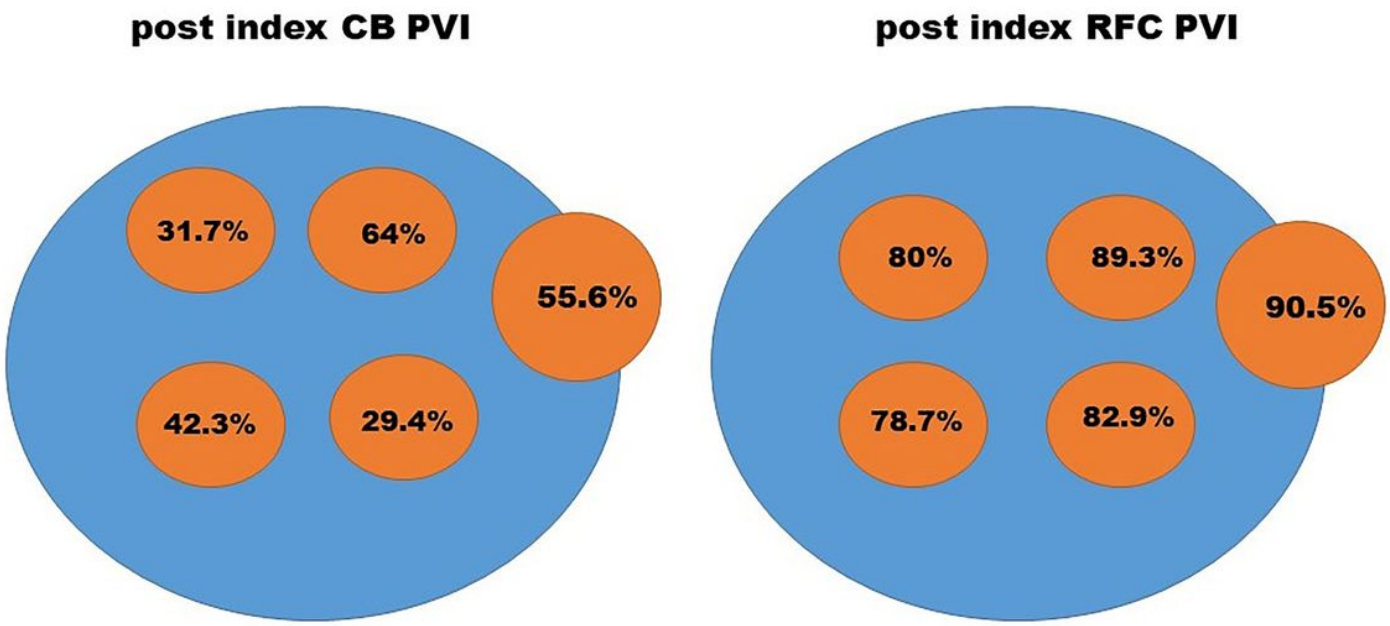

Figure 2

Schematic left anterior oblique view to LA with percentage of reconnection observed for each pulmonary vein / left common trunk after index CB (left) and RFC PVI (right) procedure

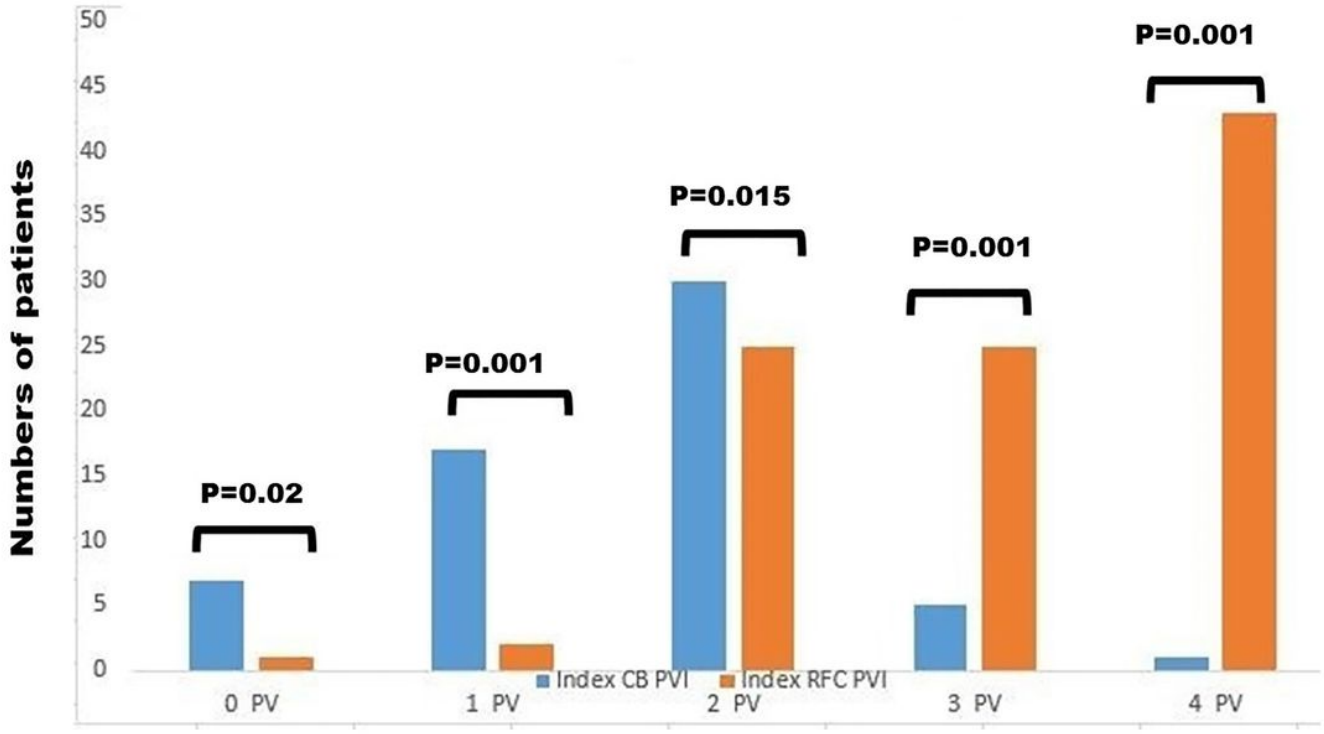

Figure 3

Percentage of patients with 0 to 4 reconnected PVs per patient according to index CB PVI group and index RFC PVI group.

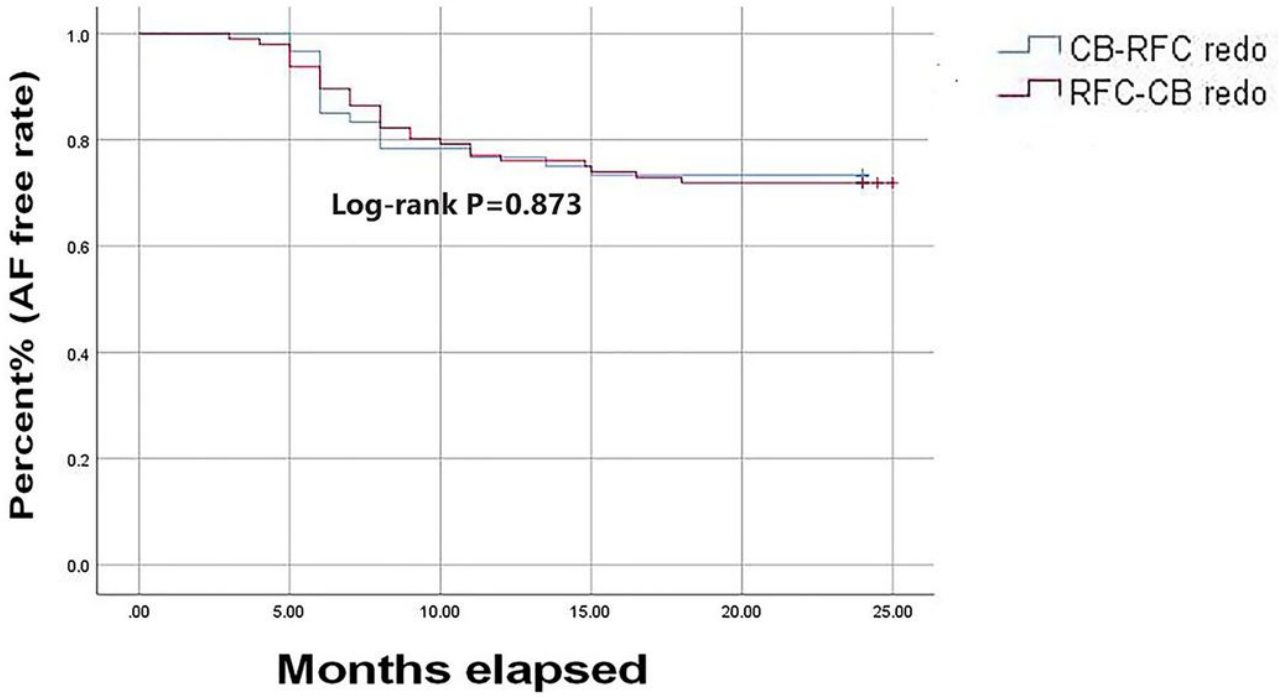

Figure 4

Freedom from recurrent atrial fibrillation (AF) following the repeat catheter ablation. CB- RFC-redo group: patients initially treated with CB underwent redo PV isolation with RFC; RFC-CB-redo group: patients initially treated with RFC ablation underwent redo PV isolation with CB.

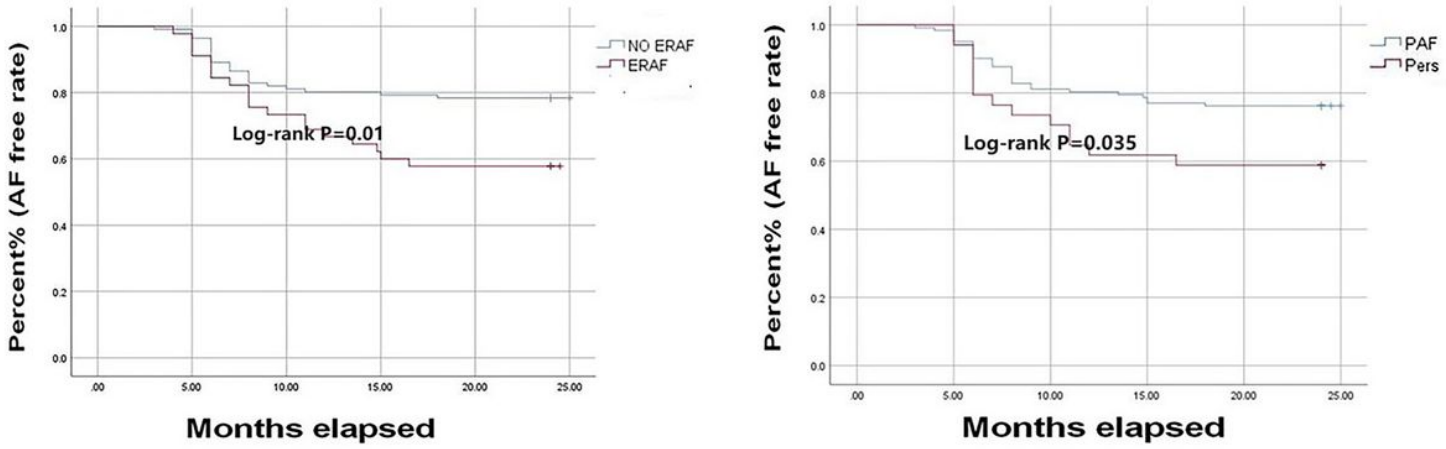

Figure 5

Subgroup analysis of freedom from recurrent atrial fibrillation (AF) following the repeat catheter ablation. With early recurrence (ERAF) after the initial ablation vs without early recurrence (ERAF) after the initial ablation; PAF, paroxysmal atrial fibrillation vs PersAF, persistent atrial fibrillation.