Efficacy and safety of the application of extensive ablation in patients with atrioventricular re-entrant tachycardia (a retrospective study).

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20   **Abstract**

Introduction: Radiofrequency catheter ablation (RFCA) has become the standard effective therapy for supraventricular tachycardias, but the reported success rates of ablation have differed across a large number of single-center studies. The main reason for tachycardia recurrence is accessory pathway (Ap)-mediated tachycardia, and the RFCA strategy may be related to recurrence. This study 25 aims to compare the efficacy and safety of two different RFCA strategies for Ap-mediated tachycardia.

Methods：We compared patients (group M) who underwent RFCA at extensive sites to patients (group S) with RFCA at a single site during the index procedure for Ap-mediated tachycardia. The efficacy and safety were assessed in the two groups.

Results: A total of 882 patients with 898 Aps were enrolled in group S, and 830 patients with 843 Aps 30 were enrolled in group M. The results showed that the cumulative numbers of recurrences (rates) at the 1st, 3rd, 6th, 12th, and 24th months after ablation were 4 (0.5%) and 17 (1.9%), $p<0.05$; 5 (0.6%) and 27 (3.0%), $p<0.05$; 6 (0.7%) and 34 (3.8%), $p<0.05$; 6 (0.7%) and 43 (4.8%), $p<0.05$; and 7 (0.8%) and 45 (5.0%), $p<0.05$ in group M and group S, respectively. Complications of chest pain, overactive vasovagal reaction, steam pop, and angina pectoris were rare in both groups. No valve damage, cardiac 35 tamponade, or other serious adverse events occurred in either group.

Conclusion: The strategy of performing extensive ablation reduced the recurrence rate and need for subsequent ablation of the Ap without increasing the risk of complications.

Keywords: Cardiology; Accessory pathway; Recurrence; Radiofrequency ablation

40 **Introduction**：

Radiofrequency catheter ablation (RFCA) has been widely performed in more than 600 hospitals in China since 1991. In 2018, the annual number of RFCA procedures performed in China was 133,900[1], of which approximately 50% were conducted to treat paroxysmal supraventricular

tachycardias (PSVT). Although the success rate of RFCA for PSVT was higher than that of RFCA for other arrhythmias, 2-5% of the patients experienced recurrence, as reported by various electrophysiology (EP) laboratories[2-6]. More than 3,000 cases/per year of PSVT were estimated to recur after ablation in China, and atrioventricular re-entrant tachycardia (AVRT) cases accounted for the greatest proportion. Accessory pathways (Aps) in the patients with failed initial procedures were successfully ablated during a second or third procedure, suggesting that modification of the ablation strategy could improve the success rate. After alteration of the ablation strategy, the overall success rate at the 2-year follow-up after initial ablation of AVRT in our center increased from 95% to 99.2%. We report the relevant methods and experience.

1. Materials and methods:

1.1. Study population:

A total of 1712 consecutive patients with 1741 Aps were enrolled in this study from 2002 to 2018. They were divided into the S group (882 patients with 898 Aps) and the M group (830 patients with 843 Aps), based on the ablation strategy. Ablation in our hospital was performed by the S method, with a single ablation, before 2011, while ablation has been performed with the M method, with multiple ablations, since 2012. Patients with Ebstein's anomaly and epicardial bypass tracts were excluded. We also excluded patients with para-Hisian Aps. Preoperatively, patients with the following severe diseases were excluded: acute myocardial infarction, hemodynamic instability, intracardiac thrombus, significant coagulation dysfunction, severe coronary heart disease without revascularization, symptomatic aortic valvular disease, active infective endocarditis, incompatible mental disorders, and extreme heart failure.

1.2. Electrophysiology study, mapping, and ablation strategy:

EP studies were performed after all cardioactive drugs had been discontinued for at least five elimination half-lives. The Seldinger method was used to puncture the femoral vein in all patients. Under X-ray guidance (DSA, UNIQ FD20, Koninklijke Philips, Netherlands), four 6F multi-electrode mapping catheters with spaces of 2-4-2 mm between the electrodes were introduced percutaneously through the right femoral or jugular veins. They were placed in a stable position to record the bundle, lateral right atrium, right ventricular apex, and coronary sinus (CS) activities as required. Anticoagulation was started before the left ventricle was accessed (heparin, 100 U/kg iv bolus, followed by 1000 U/h infusion) to maintain the activated clotting time (ACT) between 250 and 300 seconds. Intrathecal heparinization was given for right bypass during the EP study.

A 4-mm-tip conventional ablation catheter (∅7 Fr) was randomly selected from various manufacturers (Biosense Webster ™, Abbott ™, Triguy™, or Synaptic ™). A 0.5~500 Hz filter was set for the unipolar recording of the electrocardiogram of the endocardium, while a 30~150 Hz filter was set for the bipolar recording. Three surface electrocardiographic leads were displayed and recorded simultaneously with intracardiac electrograms at a paper speed of 100 mm/second. High amplification in the range of 0.1 mV/cm was used to record the potentials. A Cardio-clab EP recorder (GE, USA), Stockert Ep-shuttle RF ablation apparatus (Johnson & Johnson, USA), and cardiac electrophysiological stimulators (St. Jude Medical, USA) were used in the EP procedure. Swartz R0 long sheaths were routinely used to facilitate mapping along the tricuspid annulus. 3D mapping geometry: Carto (Johnson & Johnson, USA) were randomly used for few of the patients.

All selected patients underwent detailed EP evaluation at our institution, and the diagnostic criteria used for AVRT/Wolff-Parkinson-White syndrome (WPW) were those in the 3rd edition of **Clinical**
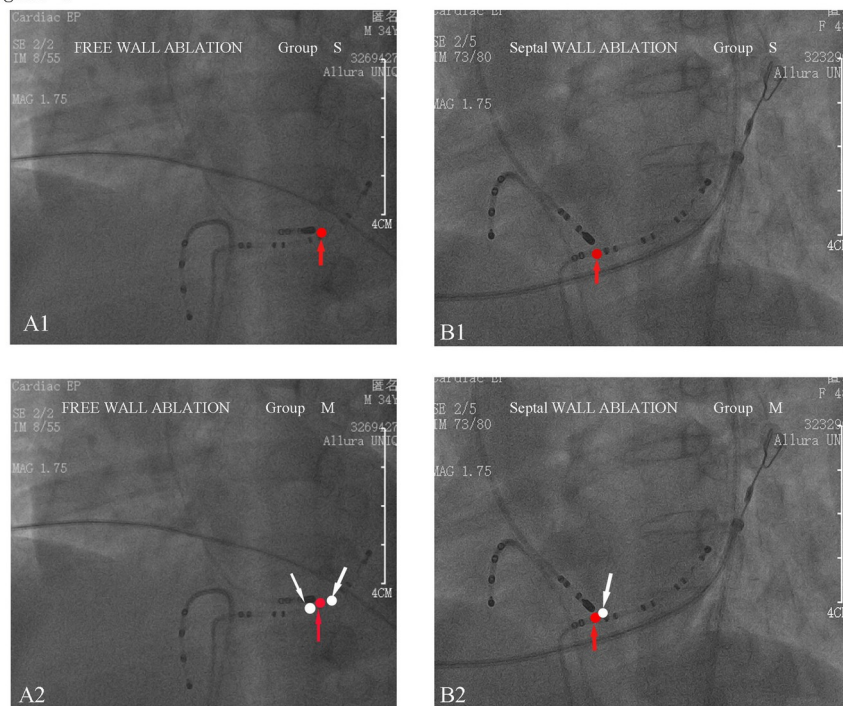
Cardiac Electrophysiology Techniques and Interpretation[7]. Multiple atrioventricular Aps were defined as the two earliest excitatory sites more than 2 cm apart or located bilaterally.

90 Most procedures were primarily performed by the transaortic (retrograde) approach, but the transseptal approach facilitated mapping of the atrial aspect of the mitral annulus in patients in whom mapping and/or ablation in the ventricular aspect failed. Some patients chose the transseptal approach due to the rapid post-procedure discharge. The presence and location of an Ap were confirmed by the standard criteria. The methods of stimulation, recording and mapping used in our

95 laboratory and the definitions used have been previously described in detail[8-10].

A power of 30~50 W targeting a temperature of 50~60°C was used for the procedure. If Ap conduction was not blocked within 5 seconds, energy delivery was discontinued, and the mapping criteria and catheter contact were re-examined. If the Aps were blocked within 5 seconds (loss of anterograde and retrograde conduction), energy delivery was continued for up to 90 seconds. The

100 impedance, atrial/ventricular (A/V) electrogram, and catheter position were continuously monitored during the ablation procedure. Complete bidirectional blockage of the Aps was set as the end point of the ablation procedure. To evaluate the retrograde conduction of Aps, electrical cardioversion was applied for patients with atrial fibrillation.

The initial bidirectional blockage of Ap conduction was set as the end point of the procedure in

105 group S. Free wall Aps in group M were addressed by an additional ablation for 60 seconds on either side of the site of initial success (within the interelectrode space). Aps of the septal wall in group M were treated with an additional ablation for 60 seconds on the side adjacent to the first successful site but away from the septum. **Figure 1 (A, B, C)** shows the strategies used in the two procedures.
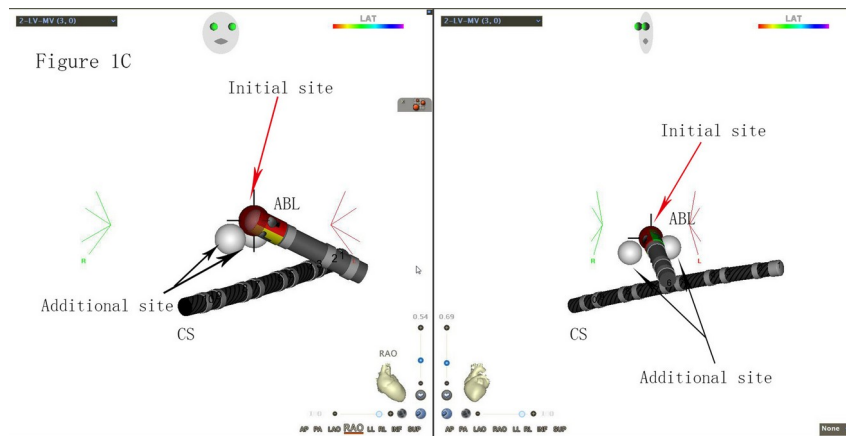
Figure 1

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Figure 1. A1 shows the localization of the ablation site for the free wall Ap in group S (red arrow refers to the initial site of ablation success), A2 shows additional ablation sites on both sides adjacent to the initial site of ablation success for the free wall Ap (white point refers to the additional ablation site), and septal wall Aps in group M were treated with an additional ablation on the side adjacent to the first successful site and away from the septum (B1, B2); Figure 1.C shows 3D mapping for patients in S group and M group.

All patients were routinely monitored for 24 hours after the EP procedure. The puncture site in the femoral vein was compressed for two hours, while the femoral artery was compressed for 6 hours. All procedures were performed by an experienced electrophysiologist, and all patients signed informed consent forms.

1.3 Follow-up strategy: The main complications and incidence of recurrence after EP procedures were all recorded. Follow-up was conducted in the form of a clinical intervention or a telephone call after discharge. In the first month after the EPS procedure, routine review of 12-lead electrocardiograms was performed, and the longest observation period was set at 24 months or the time of relapse. The interphase of the last two episodes before the EP procedure was recorded as the frequency of tachycardia. The interphase of WPW was recorded as 0 (only a small number of cases). We attempted to reduce the medical expenses associated with the additional procedure to avoid the loss of information about patients with recurrence as much as possible. The cumulative recurrence rates at the 1st, 3rd, 6th, 12th, and 24th months after ablation and the incidence of perioperative complications, including chest pain, overactive vagus reflex, thromboembolic events, pericardial tamponade, tissue vaporization (steam pop), valve damage, angina pectoris, and myocardial infarction, were observed.

2. Statistical analysis:

Normally distributed continuous data are expressed as the means ± standard deviations and were compared with independent sample t tests, and non-normally distributed continuous data are expressed as the median (Q1, Q3) and were compared with Mann-Whitney U tests. Enumeration data are expressed as the count and rate, and Fisher's test or Pearson's X^2 test was used for comparisons. Recurrence rates were estimated with the Kaplan-Meier method. Cox proportional hazards models were used to determine factors associated with the risk of recurrence. SPSS 23 software was used for the statistical analysis, and p=0.05 was set as the level of significance for two-sided tests.

3. Results:

3.1 Baseline characteristics:

145 Preoperative and intraoperative baseline data were compared (**Table 1**), as in other reports[11-15], including age, sex, Ap location, number of Aps, frequency of tachycardia episodes, number of initial ineffective ablations, catheter approach, concomitant coronary artery disease (CAD), concomitant atrial fibrillation, concomitant heart failure (ejection fraction (EF)%<35%), and other factors related to prognosis and complications. There were 882 patients with 898 Aps in the S
150 group, ranging in age from 10 to 80 years (mean age, 47±16 years), consisting of 365 females and 517 males. Among all 898 Aps, 688 (76.6%) were left-sided, 210 (23.4%) were right-sided, and 164 (18.3%) were septal. The mean age of group M was 48±17 years old, with females accounting for 40.7%. There were 843 Aps in group M, with 642 (76.2%) Aps on the left, 149 (16.7%) involving the septum, and 201 (23.8%) on the right. The median frequency of tachycardia was 1
155 (1, 3) month in group S and 1 (1, 2) month in group M. In total, 28.6% of the patients in group S and 27.4% of the patients in group M were successfully ablated on the atrial aspect. Additionally, 6.2% of the patients in group S and 7.2 % in group M underwent EP procedure with a 3D mapping system. In group S, 1.4% of the patients had a history of coronary heart disease, 2.4% had pre-excitation with atrial fibrillation, and 0.2% had an EF <35%. In group M, 0.8% of the patients had
160 a history of coronary heart disease, 1.5% had pre-excitation with atrial fibrillation, and 0.4% had an EF <35%. There was no significant difference in any presented factor between the two groups.

Table 1. Main clinical features stratified by different ablation methods.

Basic characteristics	Group S (882 patients)	Group M (830 patients)	*P*
Age (years)	47±16	48±17	0.119
Sex (female)	365(41.4%)	338(40.7%)	0.781
Ap number	898	843	
Multiple Aps	16(1.8%)	13(1.6%)	0.691
Initial ineffective ablation	1.72±0.80	1.68±0.83	0.379
Left Aps	688 (76.6%)	642(76.2%)	0.822
Septal wall	123(13.7%)	119(14.1%)	0.801
Free wall	565 (62.9%)	523 (62%)	0.706
WPW	67 (7.5%)	61 (7.2%)	0.857
Right Aps	210 (23.4%)	201(23.8%)	0.822
Free wall	169 (18.8%)	171 (20.3%)	0.441
Septal wall	41(4.6%)	30 (3.6%)	0.288
WPW	23 (2.6%)	19 (2.3%)	0.676
Episode frequency (month)	1(1, 3)	1(1, 2)	0.885
Ablation site			
Atrial aspect	257 (28.6%)	231 (27.4%)	0.572
Ventricular aspect	641	612	--
Transeptal approach	13 (1.5%)	15(1.8%)	0.227
3D mapping	55(6.2%)	60(7.2%)	0.41
WPW with AF	22 (2.4%)	13 (1.5%)	0.177
CAD* history	13 (1.4%)	7 (0.8%)	0.227

EF*<0.35%	2(0.2%)	3(0.4%)	0.607

* EF: Ejection fraction, CAD: Coronary artery disease

165 3.2 Post-procedure characteristics:

3.2.1 Efficacy analysis: The immediate success rate in both groups was 100%. All patients were observed for 1-24 months, with a median follow-up of 24 months. There were 45 cases of recurrence in group S and 7 cases in group M. The cumulative recurrence rate in each observation period was significantly lower in group M than in group S, and the cumulative number of 170 recurrences (rates) at months 1, 3, 6, 12 and 24 were 4 (0.5%) and 17 (1.9%), $p<0.05$; 5 (0.6%) and 27 (3.0%), $p<0.05$; 6 (0.7%) and 34 (3.8%), $p<0.05$; 6 (0.7%) and 43 (4.8%), $p<0.05$; and 7 (0.8%) and 45 (5.0%), $p<0.05$, in group M and group S, respectively. More than 90% of the recurrences occurred within 1 year after ablation in both groups. The cumulative recurrence rate in group M was lower than that in group S during the entire follow-up period (**Table 2, Figure 2**). 175 Among all 52 Aps involved in recurrence, 19 were left-sided, and 33 were right-sided (**Table 3**).

Table 2. Cumulative recurrence after ablation

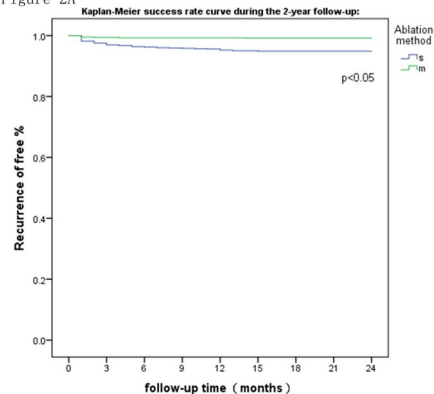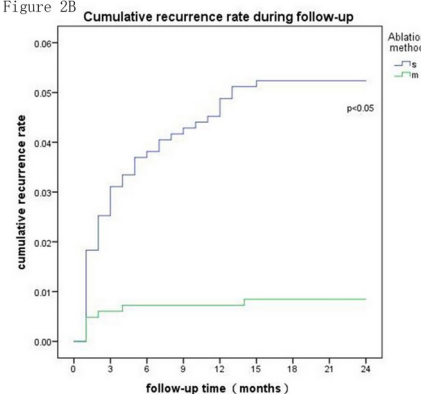| Recurrence time	No. of Patients (%)		*P*
	Group S	Group M	
a. Immediately	0	0	--
b. 1 month	17 (1.9%)	4(0.5%)	p<0.05
c. 3 months	27(3.0%)	5(0.6%)	p<0.05
d. 6 months	34 (3.8%)	6(0.7%)	p<0.05
e.12 months	43 (4.8%)	6(0.7%)	p<0.05
f. 24 months	45(5.0%)	7(0.8%)	p<0.05

FIG. 2A shows the survival curves of the two groups during the 2-year observation period. During the 2-year 180 observation period, the cumulative recurrence rate at every observation timepoint was significantly lower in group M than in group S. Group M showed an advantage in terms of a high ablation success rate (log-rank test (Mantel-Cox) p value<0.05). FIG. 2B shows that the cumulative recurrence rate in the S group was higher than that in the M group at all observation time points after ablation. The cumulative recurrence rate in the 2-year follow-up in the S group was 5%, while that in the M group was only 0.8% (P value <0.05).

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Table 3. Characteristics of recurrence

Ap location of recurrence	No. of Patients (%)		P
	Group S	Group M	
Right side	16	3	p<0.05
Left side	29	4	p<0.05

3.2.2 Procedure safety analysis (**Table 4**): A total of 41 patients in group S (51 in group M)
190developed ablation-related chest pain, which was relieved immediately by ceasing the energy
delivery. Three patients (1 in group M) complained of chest tightness with transient changes in ST-
T morphology on electrocardiography (ECG). One patient in group M complained of chest pain in
the pre-cardiac area with continuously typical ST-segment elevation during the initial energy
delivery, and instant coronary angiography confirmed a coronary artery occlusion located at the
195site of the ablation target. No myocardial infarction occurred in group S. There was no significant
difference in the incidence of an excessive vagal response between the two groups (19 (2.2%) vs
15 (1.85%), p=0.607). Steam pops occurred infrequently in both groups (3 (0.3%) vs 2 (0.2%)
p=0.707). Only a few patients in the two groups were found to have a small amount of pericardial
effusion on routine ultrasound after the EP procedure (11 (1.2%) vs 9 (1.1%), p=0.754). One
200patient suffered from pulmonary embolism (confirmed by CT angiography) after lower limb
braking and vascular compression in group S, with sudden dyspnea accompanied by a decrease in
blood pressure, while no pulmonary embolisms occurred in group M. Only a few patients suffered
from lower extremity venous thrombotic-associated edema (2 (0.2%) vs 1 (0.1%), p=0.559) in
both groups. No cardiac tamponade, peripheral arterial embolization, valvular injury, or
205perioperative deaths occurred in either group.

Table 4 Main complications

Complication Type	No. of Pts (%)		P
	group S	group M	
a. Chest pain	47(5.3%)	51(6.1%)	0.468
b. Angina	3 (0.3%)	1(0.1%)	0.347
c. Overactive vagal response	19 (2.2%)	15(1.85%)	0.607
d. Pericardial effusion	11(1.2%)	9(1.1%)	0.754
e. Myocardial infarction	0	1(0.1%)	0.302
f. Steam pop	3(0.3%)	2(0.2%)	0.707
g. Pulmonary embolism	1 (0.1%)	0	0.332
h. Deep vein thrombosis	2(0.2%)	1(0.1%)	0.559

Separate Cox proportional hazards models were used to assess the risk of recurrence, and 2
predictors, namely, the ablation method and Ap location, were independent significant predictors
(p<0.05). **Table 5** shows that ablation of right-sided Aps was associated with a 6.16-fold increased
210risk of recurrence compared to ablation of left-sided Aps. Complementary ablation reduced the
risk of recurrence by 83.8%.

Table 5. Stepwise multivariate Cox proportional hazards model: recurrence

Predictor	Partial Risk Ratio	95% CI	Model P
AP on right side（19/52）	1.835	(1.043, 3.228)	0.035
Ablation in group M	0.162	(0.073, 0.36)	<0.05

Table 5 shows that ablation of right-sided Aps was associated with a 6.16-fold–increased risk of recurrence compared with ablation of left-sided Aps. Complementary ablation reduced the risk of recurrence by 83.8%.

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4. Discussion:

RFCA is a highly effective curative treatment for AVRT (>95%). Initially successful RF ablation is generally persistent, but late recurrence of Ap conduction after ablation is not uncommon (5%). Given the technical expertise required to map arrhythmias accurately and maintain adequate
220 catheter-tissue contact to achieve the necessary tissue heating, it is perhaps not unexpected that success is more likely at more experienced ablation centers.

As reports have shown, most insertions of Aps are typically discrete in size (1 to 3 mm) and close to the mitral annulus. The ventricular insertion site tends to be located over the region of interest but could be displaced a small distance away from the mitral annulus[16-18]. Theoretically, complete
225 blockage could be achieved by single-point ablation for most Aps. However, 60-80% of Aps are oblique across the valve annulus[19,20], which results in mapping pitfalls. In addition, the insertion cannot always be accurately located due to unique anatomical factors, such as a wide Ap or dendritic[21] insertion far away from the valve annulus, resulting in incomplete bypass damage and recurrence. Mapping pitfalls are largely related to inaccurate localization of an Ap that has an
230 oblique course. This is more likely to occur when retrograde atrial activation mapping is performed with the ablation catheter positioned at the ventricular side of the annulus. Because of the oblique course of the Ap, the site of earliest atrial activation recorded from the ventricular aspect of the annulus does not correspond to the ventricular insertion site. Similar situations can occur when the ablation catheter is positioned on the atrial aspect of the annulus and RF ablations
235 are delivered where the earliest ventricular activation is recorded. In these situations, mapping the earliest atrial activation site with the catheter on the atrial side of the annulus or mapping the earliest ventricular activation site with the catheter on the ventricular side of the annulus should be undertaken. Occasionally, ablation at an atrial site proximal to the actual Ap atrial insertion site can cause a substantial shift in the atrial activation sequence, simulating the presence of a second
240 Ap. Our study showed a higher recurrence rate after ablation of the right free wall and septal Aps than after ablation of left free wall Aps, which was similar to previous reports[15]. These findings can be explained by the increasingly well-recognized target-dependent differences that exist in the ease of mapping and the effectiveness of tissue heating. Catheter shift reduces the effective damage depth of the target site and hinders further effective heat diffusion. We assumed that
245 performing an additional ablation in the vicinity of to the initial site of success was advantageous for distributing the energy to the correct depth from the side.

The transaortic approach is best suited for mapping anterograde Ap activation (i.e., pre-excitation). Mapping retrograde activation from the subannular position is more difficult than anterograde mapping because of the obscuration of the low-amplitude atrial electrogram after the large
250 ventricular electrogram. The transseptal approach is primarily used for mapping the Ap atrial

insertion site during retrograde Ap conduction (orthodromic AVRT or ventricular pacing). However, the transseptal approach provides less catheter stability and is associated with a higher risk of cardiac perforation and air embolism. Furthermore, the transseptal approach entails a higher cost. VA/AV fusion and pseudo-disappearance of A in the process of mapping leads to the phenomena of unrecognized EVA and EAA and makes it difficult to precisely locate the Ap insertion site, which is also considered to be a factor involved in relapse after single-target ablation. We attempted rapid pacing on the side of the target to identify A or V activation, which sometimes failed to identify EAA or EVA. In addition, we found that in many cases, EAA and EVA were widely distributed, suggesting the possibility of a wide pathway and increasing the difficulty of ablation. Mccleland et al[22] reported a group of bypass ducts, of which 18% required ablation within the range of 3 cm along the CS to achieve a completely bidirectional block.

The initial success of immediate ablation indicates that the catheter tip is positioned at or near the insertion site of the Ap, but whether the bypass has been irreversibly damaged cannot be determined. Therefore, we proposed performing an additional ablation near the initial successful target to reduce the recurrence rate. Earlier reports[23,24] showed that the effective ablation depth of conventional 4-mm-tip ablation catheters is 4-6 mm, and we selected a distance within the interelectrode space of the CS catheter (<4 mm) next to the initial successful target along the CS as the site of the additional ablation. Theoretically, continuous fusion and effective heat penetration in target tissues can be achieved. Through this ablation strategy, the success rate of AVRT ablation in our center has been significantly improved.

New mapping systems that work with artificial intelligence (AI) and a good energy delivery catheter (e.g., irrigation catheter) are expected to improve the accuracy of Ap localization and increase the stability of the catheter. This will enlarge the ablation lesions but entail a higher cost. Conventional mapping and catheter manipulation under fluoroscopic guidance is still the main method for the EP assessment of PSVT, and a modification of the ablation strategy to reduce the recurrence rate is necessary.

Additional ablation entails added X-ray exposure and EP procedure time. Theoretically, there is a possibility of an increased risk of complications, including myocardial infarction, myocardial perforation, and cardiac tamponade, especially for patients undergoing atrial aspect ablation. Repeated sub-valvular ablation increases the risk of steam pop, and repeated catheter manipulation may increase the risk of thrombosis, embolism, and valve damage. It is necessary that all of the above factors be considered. Our study showed that the incidence of complications was similar in both groups, and no complications occurred during the additional ablation in group M. The incidence rates of various complications in our center were lower than those reported by other EP centers[11,25,3]. We suggest that if the initial mapping and ablation are successful, the level of increased risk associated with performing an additional ablation is acceptable.

Limitations: In our retrospective study, data were collected from different periods, leading to inevitable bias in the two groups and possibly affecting the results. A longer ablation time, operator experience and technology advances may comprise the reasons for improved outcomes in group M. A prospective randomized multicenter study is needed to verify the results.

Conclusion: Compared to conventional ablation, the EP procedural time was only extended by an average of 5-10 minutes in the additional ablation group, and the complication rate did not increase. However, the recurrence rate decreased significantly. The results of this study may serve as a reference for clinicians considering therapeutic options in patients.

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