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Atrial fibrillation prevalence and atrial vulnerability analysis in paroxysmal supraventricular tachycardia patients after radiofrequency ablation

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Abstract. – OBJECTIVE: Paroxysmal supraventricular tachycardia (PSVT) patient has higher prevalence ratio of atrial fibrillation (AF), while AF recurrence remains a high ratio after radiofrequency ablation (RFCA). This study explored AF prevalence and atrial vulnerability in PSVT patients after RFCA, using ROC curve to analyze atrial effective refractory period dispersion (dERP) on postoperative AF in the prediction of PSVT.

PATIENTS AND METHODS: The PSVT patients were enrolled and divided into three groups and received RFCA treatment between January 2010 and December 2014. Group A, AF was induced by programmed electrical stimulation (PES) under isopropyl epinephrine (ISO) perfusion; group B, AF was induced by PES or PES under ISO perfusion; group C, no AF was generated by PES or PES under ISO perfusion. Ultrasonic cardiogram was applied to detect intra, inter, atrial electromechanical delay and dERP. ROC curve was adopted to analyze the prediction effect of dERP on postoperative AF recurrence.

RESULTS: dERP, group B > A > C; inter and intra: group B > A (p<0.05). Logistic regression analysis showed that age, gender, sympathetic nerve stimulation, and left/right atrial diameter were independent risk factors of postoperative AF in PSVT patients (p<0.05). Of note, dERP cut-off value at 75.5 msec can effectively predict AF recurrence in PSVT patients after RFCA (p<0.05).

CONCLUSIONS: Atrial vulnerability index dERP could be applied to evaluate AF recurrence in PSVT patients after RFCA.

Key Words:
Atrial fibrillation, Paroxysmal supraventricular tachycardia, Atrial vulnerability, dERP.

Introduction

Atrial fibrillation (AF) is a common arrhythmia in clinic. Paroxysmal supraventricular tachycardia (PSVT) patients show higher AF morbidity than healthy individuals. About 18% of atrioventricular reentrant tachycardia (AVNRT) and atrioventricular reentrant tachycardia (AVRT) patients are complicated with AF[1,2]. AF recurrence rate in PSVT patients complicated by AF after atrioventricular bypass (AP) or radiofrequency ablation (RCFA) remains to be high[3,4], suggesting that non-atrioventricular bypass or atrioventricular node slow path mechanism plays an important role in AF occurrence in PSVT patients[5,6]. Research showed that cardiac autonomic nervous system was strictly associated with AF occurrence[7,8]. It was reported that paroxysmal AF was related to atrial fibrillation and ectopic excited foci in pulmonary vein sleeve. Atrial electrical remodeling and multiple-wavelet maintain ectopic excited foci. Ganglion contains a large amount of sympathetic nerve and vagus nerve. Vagus nerve excitement shortens atrial effective refractory period, while sympathetic nerve excitement increases trigger activity by early afterdepolarization. Sympathetic nerve and vagus nerve are synergized during ganglion excitement, inducing and maintaining ectopic excited foci in pulmonary vein[9,10]. The stimulation of cardiac sympathetic nerve increased calcium ion concentration in myocardial sarcoplasmic reticulum, leading to AF. The difficulty in the assessment of AF occurrence with electrophysiological property index is the atrial vulnerability. The indications of atrial electrical machinery delay and atrial effective refractory period dispersion (dERP) are commonly used in the evaluation, high levels of which are considered to have a close correlation with atrial vulnerability. However, clinical cut-off value remains to be further clarified[11,12]. Additionally, there is still a lack of investigation about the relationship between cardiac sympathetic nerve stimulation and AF pre-

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valence in PSVT patients. Efficacy evaluation of PSVT patients with atrioventricular bypass or slow atrioventricular node path radiofrequency ablation (RFCA) showed that AF can only be induced by programmed electrical stimulation (PES) (S1S1 and S1S2) under isopropyl epinephrine (ISO) perfusion[13]. This study thus explored the correlation between cardiac sympathetic nerve stimulation and AF prevalence in PSVT, and analyzed its role in the process of AF in PSVT patients.

Patients and Methods

Clinical Information

A total of 854 cases of PSVT patients enrolled in Zhengzhou People's Hospital received RFCA treatment between January 2010 and December 2014. All patients were confirmed to have an atrioventricular bypass or slow atrioventricular node path by cardiac electrophysiological examination. This research was approved by Zhengzhou People's Hospital Ethics Committee and received informed consent. Inclusion criteria: all patients had atrioventricular bypass or slow atrioventricular node path, suitable for RFCA treatment, and possessed complete clinical data. Exclusion criteria: calcium channel blockers, amiodarone and digoxin drug withdrawal time less than 5 drug half-life before the operation, diabetes, heart failure, hyperthyroidism, heart valve disease, hypertension, body mass index (BMI) ≥ 25 kg/m^2, smoking, alcoholic, atrial tachycardia, preoperative AF diagnosed by ECG.

Observation Index and Method

All patients received preoperative ultrasonic cardiogram and ECG examination to test atrial electromechanical delay and dERP[14]. The value was tested for three times at each time point.

Intra: intra-atrial electromechanical delay = T2-T3. Inter: interatrial electromechanical delay = T1-T3. T1 means the time interval between P wave start point to anterior mitral valve late diastolic blood flow spectrum A peak start point. T2 means the time interval between P wave start point to posterior mitral valve late diastolic blood flow spectrum A peak start point. T3 means the time interval between P wave start point to tricuspid valve late diastolic blood flow spectrum A peak start point. dERP: the difference between the maximum and minimum values of four parts of the atrial effective refractory period (AERP) (HRA: high right atrium, LRA: low right atrium, CS1-2: distal coronary sinus electrode, CS9-10: proximal coronary sinus electrode).

AF Induction and Grouping

ISO perfusion: ISO drips heart rate ≥ 30% basic heart rate. Intraoperative evoked AF: rapid atrial rhythm, duration > 30 s with a different period. The patients were grouped based on PSVT ablation efficacy. Group A, AF was induced by programmed electrical stimulation (PES) under ISO perfusion; group B, AF was induced by PES or PES under ISO perfusion; group C, no AF was generated by PES or PES under ISO perfusion.

Follow-up

AF recurrence was followed up at 1, 3, 6, 12, 18, 24 months after discharge. ROC curve was adopted to analyze dERP prediction effect on postoperative AF recurrence. End point events: AF was observed by ECG. There were 7 patients loss to follow-up (2 cases in group A, 2 cases in group B, 3 cases in group C), 9 patients appeared PSVT recurrence (2 cases in group A, 3 cases in group B, 4 cases in group C), and 1 cases in group C died of cerebral apoplexy.

Statistical Analysis

All statistical analysis was performed on SPSS 19.0 (IBM, Armonk, NY, USA). Enumeration data was presented as rate and compared by χ^2-test or correct χ^2-test. Measurement data accorded with normal distribution was presented as mean ± standard deviation ($\bar{\chi}\pm S$) and compared by one-way ANOVA or LSD test. The abnormal distribution data was presented as median and percentiles and compared by rank sum test. ROC curve was adopted to analyze dERP prediction effect on postoperative AF recurrence. Youden index J (J = sensitivity + specificity - 1) was calculated to obtain the best sensitivity and specificity value as cut-off value. $p<0.05$ was considered statistically significant.

Results

Clinical Information Comparison

The clinical information was listed in Table I. No significant difference was observed among three groups except index of age.

AERP Comparison at Different Atrium Loci

AERP at different atrium loci showed no significant difference among three groups ($p>0.05$) (Figure 1). The value of dERP presented as group

Table I. PSVT patients' clinical information.

Group	A	B	C	D	t/χ^2 value	*p*-value
Case (N)	45	81	711	53	-	-
Gender (male: female)	22:23	41:40	354:357	25:28	0.177	0.98
Mean age (year)	42.54±1.42	58.48±3.26	53.61±2.16	52.43±1.87	5.971	0.00
Systolic pressure (mmHg)	118.58±17.21	117.81±16.92	117.71±17.41	115.71±16.41	0.325	0.74
Diastolic pressure (mmHg)	78.14±7.14	79.83±7.86	79.74±7.12	78.74±6.12	1.462	0.14
Total cholesterol (mmol/L)	3.89±0.73	3.88±-0.54	4.01±0.82	3.95±0.45	0.958	0.34
Triglyceride (mmol/L)	1.15±0.51	1.06±0.41	1.08±0.32	1.11±0.47	0.909	0.37
HDL (mmol/L)	1.15±0.31	1.23±0.36	1.18±0.28	1.20±0.34	0.692	0.49
LDL (mmol/L)	2.83±0.41	2.76±0.27	2.74±0.24	2.75±0.31	1.457	0.15
FBG (mmol/L)	4.78±0.38	4.69±0.27	4.68±0.21	4.69±0.27	1.838	0.07
Left atrial diameter (mm)	38.16±7.91	39.41±6.34	38.44±4.65	39.12±6.14	0.235	0.82
Right atrial diameter (mm)	40.36±6.77	39.84±6.79	39.61±5.37	42.01±8.13	0.729	0.47

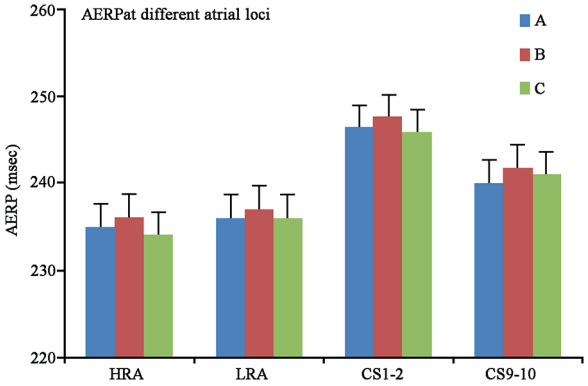

Figure 1. AERP comparison among different groups.

B > A > C; inter and intra-atrial electromechanical delay as group B > A (p<0.05), while no statistical difference was observed between group A and C (p>0.05) (Figure 2).

Follow-up AF Prevalence Comparison

After 3, 6, 12, 18, 24 months, AF morbidity in-group A and B was significantly higher than that in-group C (p<0.05). After 12, 18, 24 months, a statistically higher AF morbidity in-group A was found than that in-group C (p<0.05) (Figure 3).

Influence Factor Analysis of Postoperative AF in PSVT Patients

Parameters of age, gender, left and right atrial diameter, FBG, blood lipid, and sympathetic nerve stimulation were enrolled for logistic regression analysis. The results showed that age, gender, sympathetic nerve stimulation, and left/right atrial diameter were independent risk factors of postoperative AF in PSVT patients (p<0.05) (Table II).

dERP Prediction Effect on AF Recurrence in PSVT Patients after RFCA

ROC curve revealed that dERP cut-off value was 75.5 msec, and area under the curve was 0.896 (95% CI: 0.833~0.959, p<0.05), suggesting that dERP might be used to effectively predict AF recurrence in PSVT patients after RFCA (Figure 4).

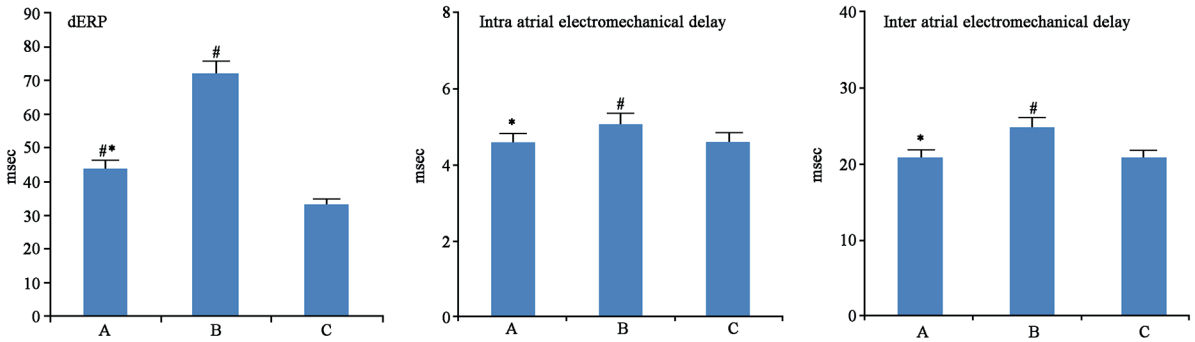

Figure 2. Atrial vulnerability comparison. HRA: high right atrium, LRA: low right atrium, CS1-2: distal coronary sinus electrode, CS9-10: proximal coronary sinus electrode. $^{\#}p$<0.05, compared with group C; $^{*}p$<0.05, compared with group B.

Table II. Influence factor analysis of postoperative AF in PSVT patients.

Relevant factor	β	S	χ^2 value	*p*-value	OR value	95% CI
Age	0.704	0.258	7.469	0.010	2.022	1.220~3.350
Sympathetic nerve stimulation	0.963	0.333	8.358	0.002	2.620	1.363~5.032
Gender	0.453	0.205	5.125	0.034	1.573	1.053~2.350
Left atrial diameter	0.487	0.219	4.927	0.033	1.627	1.059~2.502
Right atrial diameter	0.411	0.170	5.856	0.036	1.508	1.081~2.104

Discussion

Studies showed that AF recurrence in PSVT patients after RFCA was related to atrial diameter increase, atrial effective refractory period shorten, atrial electromechanical delay, and vagus nerve tension enhancement[15]. The electrical physiological basis of AF occurrence and maintenance is local reentry. The increase of dERP leads to atrial local reentry formation. dERP elevation and atrial effective refractory period declination can reflect atrial electrical remodeling and atrial vulnerability augment. It has been demonstrated that age, Kir2.1 gene and adhesion 40 gene polymorphism, autonomic nerve stimulation, and atrial pressure were associated with atrial vulnerability[16,17]. Atrial mechanical stimulation and atrial effective refractory period dispersion are used to assess atrial vulnerability, but clinical reference value is seldom determined. This study used ROC curve to analyze dERP on postoperative AF prediction effect in PSVT. The results proposed that dERP could be employed to predict AF recurrence in PSVT patients after RFCA.

Autonomic nervous system vagus and sympathetic nerve composition were widely distributed in the myocardial tissue. Myocyte sarcoplasmic reticulum calcium release increases under the stimulation of cardiac sympathetic nerve, inducing AF. Accumulative evidence[18,19] showed that RFCA eliminated atrioventricular bypass or retarded the atrioventricular node path, whereas cardiac sympathetic nerve stimulation factors cannot be eradicated. This report observed AF prevalence in PSVT patients after RFCA, and found that values of dERP and inter and intra in-group of AF induced by PES or PES under ISO perfusion were significantly higher than that in other groups. AF prevalence in PSVT patients sensitive to sympathetic nerve stimulation after RFCA was higher than those individuals insensitive to the stress. High AF prevalence in PSVT patients after RFCA was associated with cardiac sympathetic nerve stimulation. Logistic regression analysis showed that age, gender, sympathetic nerve stimulation, and left/right atrial diameter were independent risk factors of postoperative AF in PSVT patients, which was consistent with the previous result that senile has been considered as a risk factor of AF, though its impact on AF vulnerability is still controversy[19-21].

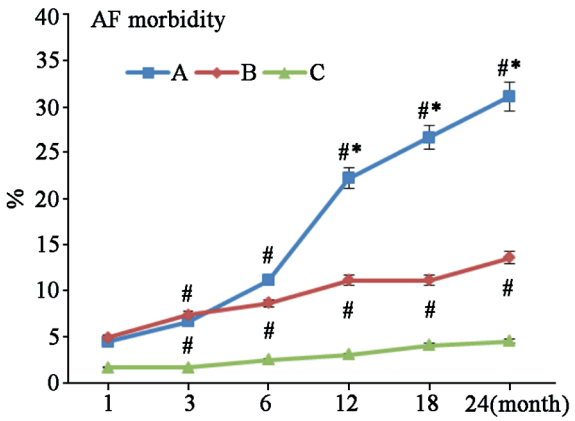

Figure 3. AF morbidity during follow-up.

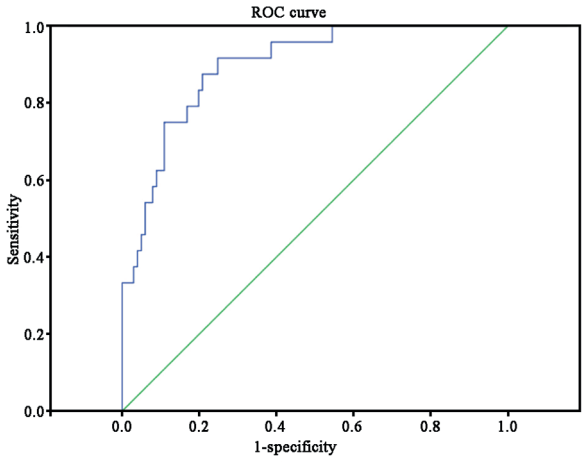

Figure 4. dERP prediction effect on AF recurrence in PSVT patients after RFCA.

The clinical trial reported that during PES (S1S2) induced AF, elder group showed longer aERP than younger group did. Premature extra-stimuli AF induction rate decreased in elder group, suggesting that different AF mechanism may exist between younger and elder group, and high AF morbidity in elder group may be related to non-physiological factors. Atrial vulnerability electrophysiological index during AF included slow conduction velocity, atrial electromechanical delay, and aERP. Atrial size, vagus nerve stimulation, atrial tension, age, and connexin may affect atrial vulnerability in AF. Though it is widely used in electrical physiology examination, atrial vulnerability application in AF treatment and prognosis still needs further study.

Conclusions

Age, gender, sympathetic nerve stimulation, and left/right atrial diameter were independent risk factors of postoperative AF in PSVT patients. Atrial vulnerability index dERP could contribute as an evaluation factor of AF recurrence in PSVT patients after RFCA.

Conflict of interest

The authors declare no conflicts of interest.

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