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Risk factors responsible for atrial fibrillation development between symptomatic patients with concealed or manifest atrioventricular accessory pathways ☆

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ABSTRACT

Background: Patients with manifest atrioventricular accessory pathways (mAPs) have a greater tendency to develop atrial fibrillation (AF) compared with patients with concealed atrioventricular accessory pathways (cAPs). However, the risk factors of developing AF in patients with various atrioventricular accessory pathways (APs) are not clear.

Methods: This retrospective study included 460 symptomatic patients with either cAPs (n = 246) or mAPs (n = 214) who underwent electrophysiological study and successful radiofrequency catheter ablation of APs. Clinical and electrophysiological characteristics were compared between cAPs and mAPs and between AF and non-AF groups with cAPs or mAPs. Independent risk factors of AF were analyzed using multivariate logistic regression.

Results: AF was more frequent in mAPs group than in cAPs group (23.4% vs 9.8%, $p < 0.01$). Clinical features were similar between cAPs and mAPs. Anterograde conduction properties served as the major electrophysiological feature of mAPs. Multivariate analysis indicated that mAPs, hypertension, post-ablation P wave dispersion (Pd), N-terminal proB-type natriuretic peptide (NT-proBNP) and creatinine were independent risk factors of AF in the complete cohort. Hypertension, post-ablation Pd and high-sensitivity C-reactive protein (hsCRP) were independent risk factors of AF in cAPs group. Post-ablation Pd, NT-proBNP, creatinine and shorter effective refractory period of anterograde accessory pathways (AAP ERP) were independent risk factors of AF in mAPs group.

Conclusions: Results from this study demonstrate that the risk factors of AF are not homogenous between concealed and manifest APs, which might suggest heterogeneous pathogenesis of AF in these two types of APs.

1. Introduction

Atrioventricular accessory pathways (APs) are the abnormal anatomical structures responsible for atrioventricular re-entrant tachycardia (AVRT) [1]. Besides AVRT, atrial fibrillation (AF) is another common arrhythmias related to APs [2]. Previous studies reported that patients with APs had a much higher tendency to develop AF than that in general population [3–6].

APs may exhibit anterograde and (or) retrograde conduction. There are two types of APs: manifest APs (mAPs) with atrioventricular or both atrioventricular and ventriculoatrial conduction properties, and concealed APs (cAPs) with only ventriculoatrial conduction properties. Previous studies showed that patients with mAPs were more prone to develop AF than those with cAPs [7,8].

Multiple factors are related to the development of AF in patients with APs. Previous studies demonstrated that AVRT could spontaneously degenerate into AF and surgical or catheter ablation of APs could often

Abbreviations: AAP ERP, effective refractory period of anterograde accessory pathways; AF, atrial fibrillation; AP, atrioventricular accessory pathway; AVRT, atrioventricular re-entrant tachycardia; cAP, concealed atrioventricular accessory pathway; CL, cycle length of the provoked atrioventricular reentrant tachycardia; cTnI, cardiac troponin I; DAVNPs, dual atrioventricular nodal pathways; EPS, electrophysiological study; hsCRP, high-sensitivity C-reactive protein; LDL-c, low density lipoprotein–cholesterol; mAP, manifest atrioventricular accessory pathway; NT-proBNP, N-terminal proB-type natriuretic peptide; Pd, P wave dispersion; Pmax, maximum P wave duration; Pmin, minimum P wave duration; RFCA, radiofrequency catheter ablation

☆ All co-authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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reduce the recurrence of AF [9–12]. Thus, APs and AVRT might serve as one of the mechanisms responsible for the development of AF. On the other hand, AF might still persist after successful ablation of APs in some patients, suggesting the existence of AP-independent mechanisms responsible for the pathogenesis of AF [13–15]. Therefore, there were at least two pathogenesis of AF: AP-dependent and AP-independent atrial vulnerabilities [16].

This retrospective study was designed to compare the clinical and electrophysiological characteristics between cAPs and mAPs and between AF and Non-AF patients with either cAPs or mAPs. This study also aimed to identify and compare the risk factors responsible for AF development between patients of these two APs groups.

2. Methods

2.1. Patients

A total of 460 symptomatic patients [268 (58.3%) male, mean age: 42.7 ± 17.9 years old (range 5–91)] with documented AVRT, who underwent electrophysiological study (EPS) and radiofrequency catheter ablation (RFCA) from September 2004 to November 2013 in our department, were included in this study. The existence of APs was identified by EPS in all enrolled patients. There were 246 (53.5%) patients with cAPs and 214 (46.5%) with mAPs. Patients were also divided into AF group (n = 74, 16.1%) and non-AF group (n = 386, 83.9%) in the complete cohort and in patients with either cAPs or mAPs. Patients in AF group experienced at least one spontaneous episode of AF recognized on 12-lead standard electrocardiogram or 24-hour Holter monitoring.

2.2. Pre- and post-procedure management

All patients underwent standard examination procedures. A detailed medical history, physical examinations, laboratory tests and echocardiography examinations were performed before the EPS procedure. The laboratory tests included measurement of N-terminal-proB-type natriuretic peptide (NT-proBNP), cardiac troponin I (cTnI), creatinine, uric acid, high-sensitivity C-reactive protein (hsCRP), low density lipoprotein–cholesterol (LDL-c), D-dimer and thyrotropin.

After the EPS and AP ablation, a 12-leaded surface electrocardiogram was recorded immediately. Subsequently, the maximum P wave duration (Pmax) and minimum P wave duration (Pmin) were measured, and P wave dispersion (Pd) was calculated with the formula: Pmax — Pmin [17].

2.3. EPS and RFCA

All antiarrhythmic agents were discontinued for at least five half-lives prior to the EPS and RFCA. During the procedure, three electrode catheters were positioned at His bundle region, right ventricular apex and coronary sinus respectively.

The programmed stimulation protocol, including both atrial and ventricular incremental pacing and S1S2 extrastimulation, was performed before the RFCA to reveal the anatomical location and electrophysiological properties of the APs. In this study, the location of APs was classified into seven groups around the atrioventricular annulus, including the anteroseptum, the right free wall, the posteroseptum, the left posteral wall, the left lateral wall, middle septum and multiple APs located at different anatomical sites. Several electrophysiological data were measured, including anterograde and retrograde AP effective refractory period (AAP ERP and RAP ERP), anterograde and retrograde AP 1:1 conduction (AAP 1:1 conduction and RAP 1:1 conduction) and cycle lengths of the provoked AVRT (CL).

After completion of the electrophysiological study, the target site of ablation was identified. After successful ablation of the APs, another programmed stimulation protocol was performed to reveal the electrophysiological properties of atrioventricular node. The electrophysiological characteristics of atrioventricular node include both anterograde and retrograde effective refractory period of atrioventricular node (AAVN ERP and RAVN ERP), anterograde and retrograde atrioventricular nodal 1:1 conduction (AAVN 1:1 conduction and RAVN 1:1) and dual atrioventricular nodal pathways (DAVNPs), etc.

2.4. Statistical analysis

The statistical computing was performed using the package of SPSS 18.0. Continuous variables with a normal distribution were expressed as mean ± standard deviation. The intergroup differences were tested using the t test and the χ^2 test. Data with a skewed distribution were expressed as median ± interquartile range and the intergroup differences were tested using the Mann–Whitney U test and the χ^2 test. When performing multiple comparisons, the one-way ANOVA with post hoc test (Scheffe method) was also applied in Tables 3 and 4. Statistical significance was defined as a two-sided p value < 0.05. To avoid variable selection caused by spurious correlations, only variables showing an association with AF at the $p < 0.10$ level in the univariate analysis were considered as potential risk factors, and then included into the multivariate regression model. Multivariate logistic regression analysis was performed in search of independent risk factors of AF. This analysis was based on a stepwise algorithm, with the p value set at 0.05 for entering and 0.1 for exclusion. Odds ratio (OR) and 95% confidence intervals (CI) of each independent risk factor for AF in concealed or manifest APs were reported in Table 5.

3. Results

3.1. Clinical and electrophysiological characteristics of patients with concealed or manifest APs

AP ablation was successful in all patients. Incidence of AF was significantly higher in mAPs group than in cAP group. All clinical features

Table 1
Clinical characteristics in patients with concealed or manifest APs.

Clinical characteristics	Concealed APs (n = 246)	Manifest APs (n = 214)	p value
AF	24 (9.8)	50 (23.4)	<0.001
Male	150 (61.0)	118 (55.1)	0.206
Age, years	42.7 ± 17.6	42.6 ± 18.2	0.333
Duration of tachycardia, years	7.8 ± 9.2	7.6 ± 10.0	0.860
Presyncope	15 (6.1)	12 (5.6)	0.823
Syncope	6 (2.4)	3 (1.4)	0.643
Hypertension	51 (20.7)	34 (15.9)	0.182
Coronary artery disease	12 (4.9)	19 (8.9)	0.088
Valvular heart disease	1 (0.4)	4 (1.9)	0.189
Diabetes mellitus	15 (6.1)	6 (2.8)	0.091
Chronic kidney disease	176 (71.5)	151 (70.6)	0.816
CHADS2 score	0.4 ± 0.7	0.3 ± 0.6	0.065
CHA2DS2-VASc score	1.1 ± 1.0	1.0 ± 1.0	0.716
Left atrial diameter, mm	31.7 ± 4.3	32.4 ± 4.6	0.052
Left ventricular end-diastolic diameter, mm	47.3 ± 4.5	47.4 ± 4.0	0.661
Left ventricular ejection fraction, %	66.2 ± 5.6	65.6 ± 5.5	0.413
Pmax, ms	112.6 ± 11.4	113.3 ± 10.2	0.333
Pmin, ms	75.9 ± 9.3	75.8 ± 8.9	0.841
Pd, ms	36.7 ± 9.1	37.5 ± 9.7	0.445
NT-proBNP, pg/mL	49.8 ± 69.0	56.0 ± 76.0	0.229
cTnI, ng/mL	0.033 ± 0.118	0.043 ± 0.172	0.172
Creatinine, μmol/L	63.5 ± 16.9	69.9 ± 64.8	0.092
Uric acid, μmol/L	327.2 ± 84.8	311.9 ± 87.1	0.767
hsCRP, mg/L	3.22 ± 2.03	3.04 ± 2.43	0.459
LDL-c, mmol/L	2.51 ± 0.62	2.53 ± 0.61	0.991
D-dimer, ng/mL	0.16 ± 0.14	0.15 ± 0.14	0.992
Thyrotropin, mIU/L	2.45 ± 1.61	2.36 ± 1.75	0.605

All data in this table were presented as mean ± SD, median ± IQR, or n (%). Pmax, maximum P wave duration; Pmin, minimum P wave duration; Pd, P wave dispersion; NT-proBNP, N-terminal-proB-type natriuretic peptide; cTnI, cardiac troponin I; hsCRP, high-sensitivity C-reactive protein; LDL-c, low density lipoprotein cholesterol.