Risk factors of atrial fibrillation recurrence despite successful radiofrequency ablation of accessory pathway: At 11 years of follow-up

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Abstract
Background: Previous reports on patients with radiofrequency catheter ablation (RFCA) of accessory pathway (AP) and atrial fibrillation (AF) include only short follow-up periods. The aim of this study was to analyze predictors of recurrence of AF in patients after successful RFCA of APs over long term follow-up periods.

Methods: Of the 1,007 patients who underwent non-pharmacological treatment of APs (between the years 1993–2008), data of 100 consecutive patients were retrospectively analyzed (75 men, mean age 43.6 ± 14.7), with the longest period of follow-up (mean 11.3 ± 3.5 years) after successful RFCA of AP. In Group 1, there were 72 patients (54 men, mean age 40.66 ± 13.85 years) without documented episodes of AF after RFCA of AP. Group 2 consisted of 28 patients (21 men, mean age 50.79 ± 14.49 years) with AF episodes despite successful elimination of AP.

Results: In univariate analysis, patients from Group 1 were significantly younger at the time of ablation than patients from Group 2 (40.66 ± 13.85 vs. 50.79 ± 14.49 years; p = 0.002), had shorter history of AF episodes (4.11 ± 4.07 vs. 8.25 ± 7.50 years; p = 0.024) and had less frequently documented atrial tachycardia (AT) prior to ablation (3.39 vs. 20.00 years; p = 0.022). In multivariate analysis, the history of AF in years (p = 0.043) was an independent risk factor for AF recurrences.

Conclusions: Older patient age, longer history of AF and AT prior to RFCA of APs identified a subgroup of patients who required additional treatment. In the multivariate analysis, the history of AF in years (p = 0.043) was a risk factor for AF recurrence. (Cardiol J 2017; 24, 6: 597–603)

Key words: Wolff-Parkinson-White syndrome, atrial fibrillation, radiofrequency ablation, accessory pathway, follow-up

Introduction
Pre-excitation occurs in 0.1–0.3% of the general population [1–5]. Among patients with accessory pathways (APs), the incidence of atrial fibrillation (AF) has been reported to be as high as 30%, which is far greater than the incidence of AF in the general population where it is 3–4% [6, 7]. Such a high occurrence of AF in patients with APs is still a subject of debate [6–8]. Patients with
pre-excitation are at risk of sudden cardiac death (SCD). The generally accepted mechanism for SCD in Wolff-Parkinson-White syndrome (WPW) is the fast conduction of AF to the ventricles over an AP with subsequent degeneration into ventricular fibrillation (VF) [9–11]. The current guidelines recommend radiofrequency catheter ablation (RFCA) as the first line therapy in patients having AF and WPW [12–14]. Research has demonstrated that following successful surgical dissection of APs, there is an almost complete elimination of paroxysmal AF; however, the patients in these studies were young [15–17]. Less information exists concerning RFCA due to the enrollment of small groups of patients in previous studies and a short follow-up period [18–20]. Among patients with WPW and AF, ablation of AP may have a sufficient clinical impact of preventing recurrence of AF in selected patients [21]. Some patients need additional attention and treatment [19].

The aim of this study was to analyze the predictors of recurrence of AF in patients after successful RFCA of AP during long term follow-up and ascertain the impact of ablation on future AF risk [18, 19].

Methods

Study patients
Of the 1,007 patients (mean age 35.00 ± 15; 45% female) who underwent non-pharmacological treatment of APs (years 1993–2008), 281 patients (28%) had AF (Fig. 1).

Data were retrospectively analyzed for 100 consecutive patients (75 male, 25 female, mean age 43.6 ± 14.7 years, range 15–74), with the longest period of follow-up (mean 11.3 ± 3.5 years) after successful RFCA of AP in order to accomplish the longest follow-up ever published on a large group of patients. This was a retrospective analysis, nevertheless the follow-up was prospectively designed.

Patients with persistent AF prior to ablation were excluded and patients with a history of VF were the topic of a previous publication [22]. Clinical, electrocardiographic, electrophysiological, and echocardiographic data were analyzed.

Ethics
The study was conducted according to the Declaration of Helsinki. All patients provided written, informed consent for the ablation procedure and for the scientific data analysis. The consent for the procedure was approved by the Institutional Ethics Committee.

Electrophysiological study
In patients with a history of AF, the aim of the electrophysiological study was to confirm the diagnosis and to perform the ablation procedure as safely as possible. Aggressive atrial stimula-
tion was therefore avoided in order to reduce the risk of inducing life-threatening arrhythmia. As amiodarone was administered prior to admission to this institution in most patients after a VF or AF episode with fast ventricular response, the refractory periods of AP and AV node were not analyzed.

Statistical analysis
Continuous variables were expressed as means and standard deviations (SD). The Yates-corrected $\chi^2$ test was used to compare fractions of two categorical variables and the maximum-likelihood $\chi^2$ test was used when larger frequency tables were constructed. The differences in the means of continuous variables were investigated with t-test and analysis of variance (ANOVA). Post-hoc comparisons in the analysis of variance were made with Tukey’s range test. The Pearson correlation was used to investigate relationships between two continuous variables. P < 0.05 was considered statistically significant.

Definitions
The location of the AP was retrospectively described using the anatomic nomenclature proposed by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [23].

Accessory pathways were grouped into three locations: left free wall (left superior, left posterior, left postero-inferior and left inferior), septal-paraseptal region (superoparaseptal, septal and inferoparaseptal), and right free wall (right superior, right supero-ante-rior, right anterior, right antero-inferior and right inferior) [24].

Multiple APs (or an AP with multiple ventricular or atrial insertions, Fig. 2) was defined as previously described [25].

Follow-up
Patients underwent routine follow-up at 6 and 12 months after ablation in the outpatient clinic of the hospital or by the referring physician. Echocardiography was performed on all patients and they had undergone two or more Holter electrocardiogram (ECG) recordings. After 12 months, patients with no palpitation and no pre-excitation in ECG were referred to regional outpatient cardiovascular centers. There a Holter ECG recordings were performed at least once a year.

Late follow-up after a mean of 11.3 ± 3.5 years was performed by questionnaire designed by the authors or by direct telephone interviews with patients and/or via direct contact with the referring physician. During late follow-up, 73% of patients were still under cardiac supervision in a regional outpatient clinic. When patients had documented arrhythmias during the follow-up period, informa-
tion regarding these arrhythmias were obtained from the referring physicians and documentation was sought. The methodology of late follow-up contact was published previously [19].

**Results**

In Group 1, there were 72 patients (54 males, 18 females; mean age: 40.66 ± 13.85 years) without documented episodes of AF after RFCA of AP. Group 2 consisted of 28 patients (21 males, 7 females; mean age: 50.79 ± 14.49 years) with AF episodes despite the successful elimination of AP. 119 RFCA of APs in 100 patients were performed (range 1–5, mean 1.2).

**Clinical data**

Clinical data are presented in Table 1. Using univariate analysis, patients from Group 1 were found to be significantly younger, at the time of ablation, than were patients from Group 2: 40.66 ± 13.85 vs. 50.79 ± 14.49 years (p = 0.002), respectively. Furthermore, patients from Group 1 had a shorter history of AF episodes: 4.11 ± 4.07 vs. 8.25 ± 7.50 years (p = 0.024), respectively.

**Echocardiographic and electrophysiological data**

Data are presented in Table 2. In Group 1, there were significantly less patients with documented atrial tachycardia (AT) prior to ablation 3.39 vs. 20.00 (p = 0.022), respectively.

**Deaths during follow-up**

During follow-up, 2 patients died despite successful RFCA of AP. Both had a normal ejection fraction as well as hypertension and dyslipidemia. The first patient died at the age of 69, due to cancer 9 years after RFCA of AP. According to the family, the second patient died at age of 71, 6 months after RFCA, due to respiratory failure.

**Multivariate analysis**

Using multivariate analysis, only a history of AF in years (p = 0.043) were independent risk factors for AF recurrences.

**Discussion**

The present study investigated AF recurrence in one of the largest cohorts of patients with paroxysmal AF and RFCA of APs. It was sought to describe the long-term outcomes of AP and AF patients and ascertain the impact of ablation on future AF risk.

Data of patients with AF and RFCA of APs published previously reported a relatively short follow-up that lasted from 23.9 ± 12 to 35 ± 12 months [18, 19]. Research herein indicates that the present study has the longest follow-up period of 11 years. This study demonstrates that a shorter
period between the diagnosis of AF in patients with APs to the treatment and elimination of APs reduces the risk of future AF episodes. This is also observed in patients without AP [26]. The present research finds that this correlation has not yet been reported for AP and AF patients.

Moreover, one of the most important findings of this study is that patients with AF recurrence after the elimination of APs is more commonly documented in AT prior to ablation. Miyamoto et al. [20] reported a correlation of premature atrial complexes prior to ablation of atrioventricular nodal reciprocating tachycardia (AVNRT) or AP and higher recurrences of AF after a successful procedure.

More frequently documented episodes of AT in patients with AF after RFCA of AP in these patients, may suggest that, in Group 2, there were more patients with focal AF, triggers in pulmonary veins, or focal re-entry of electrical signal propagation in the left atrium [13].

### Table 2. Electrocardiographic and electrophysiological data.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documented AT [%]</td>
<td>3.39</td>
<td>20.00</td>
<td>0.022</td>
</tr>
<tr>
<td>Overt pre-excitation [%]</td>
<td>83.33</td>
<td>71.43</td>
<td>NS</td>
</tr>
<tr>
<td>Intermittent pre-excitation [%]</td>
<td>6.94</td>
<td>10.71</td>
<td>NS</td>
</tr>
<tr>
<td>Concealed AP [%]</td>
<td>9.73</td>
<td>17.86</td>
<td>NS</td>
</tr>
<tr>
<td>Documented AVRT [%]</td>
<td>79.17</td>
<td>67.86</td>
<td>NS</td>
</tr>
<tr>
<td>Documented AVNRT [%]</td>
<td>2.94</td>
<td>8.70</td>
<td>NS</td>
</tr>
<tr>
<td>Documented AF [%]</td>
<td>9.43</td>
<td>10.00</td>
<td>NS</td>
</tr>
<tr>
<td>Documented VF [%]</td>
<td>1.41</td>
<td>3.57</td>
<td>NS</td>
</tr>
<tr>
<td>Mean SPRR [ms]</td>
<td>250.00 ± 67.85</td>
<td>274.62 ± 100.88</td>
<td>NS</td>
</tr>
<tr>
<td>Mean max. AVRT [bpm]</td>
<td>220.77 ± 41.59</td>
<td>208.13 ± 28.10</td>
<td>NS</td>
</tr>
<tr>
<td>Mean min. AVRT [bpm]</td>
<td>182.32 ± 27.13</td>
<td>178.57 ± 26.85</td>
<td>NS</td>
</tr>
<tr>
<td>RFW [%]</td>
<td>12.50</td>
<td>21.43</td>
<td>NS</td>
</tr>
<tr>
<td>LFW [%]</td>
<td>61.12</td>
<td>50.00</td>
<td>NS</td>
</tr>
<tr>
<td>Midseptal/posteroseptal [%]</td>
<td>26.38</td>
<td>28.57</td>
<td>NS</td>
</tr>
<tr>
<td>MAP [%]</td>
<td>22.86</td>
<td>25.00</td>
<td>NS</td>
</tr>
<tr>
<td>ECV [%]</td>
<td>43.18</td>
<td>45.45</td>
<td>NS</td>
</tr>
</tbody>
</table>

AF — atrial fibrillation; AP — accessory pathway; AT — atrial tachycardia; AVNRT — atrioventricular nodal reciprocating tachycardia; AVRT — atrioventricular reciprocating tachycardia; ECV — electrical cardioversion; LFW — left free wall; MAP — multiple accessory pathways; NS — not significant; mean SPRR — mean shortest pre-excited RR; RFW — right free wall; VF — ventricular fibrillation

### Table 3. Echocardiographic data.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction [%]</td>
<td>66.40 ± 7.58</td>
<td>65.29 ± 5.97</td>
<td>NS</td>
</tr>
<tr>
<td>Shortening fraction [%]</td>
<td>37.88 ± 6.41</td>
<td>36.29 ± 4.69</td>
<td>NS</td>
</tr>
<tr>
<td>LA [cm]</td>
<td>3.68 ± 0.55</td>
<td>3.74 ± 0.57</td>
<td>NS</td>
</tr>
<tr>
<td>LVDD [cm]</td>
<td>4.97 ± 0.38</td>
<td>5.03 ± 0.44</td>
<td>NS</td>
</tr>
<tr>
<td>LVSD [cm]</td>
<td>3.15 ± 0.53</td>
<td>3.17 ± 0.34</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDV [mL]</td>
<td>115.91 ± 29.02</td>
<td>121.39 ± 25.34</td>
<td>NS</td>
</tr>
<tr>
<td>LVESV [mL]</td>
<td>41.05 ± 13.99</td>
<td>39.79 ± 9.62</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke volume [mL]</td>
<td>76.18 ± 19.97</td>
<td>80.14 ± 19.31</td>
<td>NS</td>
</tr>
<tr>
<td>IVSD [cm]</td>
<td>1.07 ± 0.13</td>
<td>1.07 ± 0.15</td>
<td>NS</td>
</tr>
<tr>
<td>Additional heart diseases [%]</td>
<td>8.06</td>
<td>10.00</td>
<td>NS</td>
</tr>
</tbody>
</table>

IVSD — interventricular septal diameter; LA — left atrium; LVDD — left ventricular diastolic diameter; LVSD — left ventricular systolic diameter; LVEDV — left ventricular end-diastolic volume; LVESV — left ventricular end-systolic volume; NS — not significant
These findings support the observations of Dagres et al. [19], which indicated that age is a risk factor for AF recurrence. Patients with recurrences of AF several years after elimination of AP, probably revealed a second mechanism of AF episodes, which is not connected with AP.

Limitations of the study
Data were collected on ablation procedures, retrospectively. However, long-term follow-up was prospectively designed. It is not possible to refute the theory that some patients from Group 1 were asymptomatic of or did not report experiencing AF.

Conclusions
Older patient age, longer history of AF, and the presence of AT episodes prior to RFCA of APs in patients with an AP and AF indicated the need for additional treatment. Upon multivariate analysis, only a history of AF (p = 0.043) was an independent risk factor for AF recurrence.

This data may assist physicians to advise patients properly regarding the future risk of arrhythmia as well as anticoagulation.

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References


