Left atrial volume index as a predictor for occurrence of atrial fibrillation after ablation of typical atrial flutter

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Purpose: Radiofrequency catheter ablation of the cavitricuspid isthmus (CTI) is effective in the treatment of typical atrial flutter (AFL) and atrial fibrillation (AF). AF and AFL often coexist. However, AF often occurs following successful ablation of CTI. The aim of this study was to investigate the predictors of concomitant AF following successful ablation of AFL. Methods: We enrolled 122 patients [59.1 ± 11.3 years, male 100 (82.0%)] with typical AFL, who received successful ablation of the CTI. They were followed up at outpatient clinic (24.6 ± 25.7 months). Twelve-lead electrocardiogram and Holter monitoring were used to confirm the diagnosis of recurrent AFL or AF. We assessed prior history of AF, structural heart disease, left ventricular ejection fraction, left atrial diameter (LAD), left atrial volume index (LAVI), and AFL cycle length.
Introduction

Atrial fibrillation (AF) and atrial flutter (AFL) are the most common sustained atrial arrhythmias and often coexist. Both arrhythmias have similar pathophysiological features including electrical remodeling [1] and shortened action potential duration [2] and similar clinical predictors such as hypertension, heart failure, and pulmonary disease [3–5]. In addition, many authors reported that 30–73% patients developed AF during long-term follow up period after successful radiofrequency catheter ablation of the cavitricuspid isthmus (CTI) in patients with typical AFL [6–8].

It might be important to predict the occurrence of AF after ablation of AFL. Although several factors have been reported as predictors of an occurrence of AF during long-term follow up, few data are available on the predictive parameters of AF. Therefore, the purpose of our study was to investigate the predictors of concomitant AF following successful ablation of AFL.

Subjects and methods

Patient population

From January 1998 to April 2007, 122 consecutive symptomatic patients with typical AFL were retrospectively included in this study. CTI-dependence of AFL was diagnosed by the presence of a characteristic pattern on the surface electrocardiogram (ECG) (negative sawtooth waves in lead II, III, and aVF and usually positive waves in lead V1) and/or entrainment mapping during electrophysiologic (EP) study [9]. However, we excluded the patients with irregular interval between atrial and ventricular waves to rule out an organizing AF in our study.

Electrophysiologic testing and ablation procedure

Each patient underwent EP study and catheter ablation in the fasting, non-sedative state after written informed consent was obtained. All anti-arrhythmic drugs except amiodarone were discontinued for at least five half-lives before the study. The patients stopped their antithrombotic treatment 48 h before the procedure in order to have an international normalized ratio <1.7. CTI ablation was performed by creating a linear lesion from the tricuspid annulus to the inferior vena cava using 4- and/or 8-mm tip electrode catheters. Radiofrequency (RF) ablation was continued until either no electrogram or consistent reduction of the electrograms amplitude of at least 90% was documented across the isthmus. The end-point of the procedure was the achievement of a complete bi-directional isthmus block persisting at least 30 min after the last RF energy application [10,11].

Echocardiographic analysis

Transthoracic Doppler echocardiography was performed within 24 h of the RF ablation procedure. All echocardiographic parameters were measured according to the recommendations of the American Society of Echocardiography [12]; left ventricular ejection fraction was calculated by planimetry in the apical two- and four-chamber views with the modified Simpson rule. Measurement of left atrial (LA) diameter from M-mode was guided by parasternal short-axis image at level of aortic valve. LA volumes are calculated using either an ellipsoid model or Simpson’s rule. Left atrial long axis and short axis were obtained by planimetry of the atrial inner borders with maximized atrial chamber size at end-systole in the four- and two-chamber views.

Follow-up

Oral anticoagulation was pursued for at least 1 month. Thereafter, the need for anticoagulation was assessed according to the presence of risk factors for thromboembolism [13]. Whenever possible, anti-arrhythmic agents were stopped after the procedure in patients with lone AFL. Anti-arrhythmic agents were continued in patients with a history of prior AF. Patients attended the outpatient clinic at 1 month, and at 3, 6, and 12 months for a 12-lead ECG or a 24-h Holter recording. Also, a 12-lead ECG and a 24-h Holter recording were evaluated when patients felt symptoms suggestive of tachycardia. The development of AF or the recurrence of AFL was defined by documentation on a 12-lead ECG or a 24-h Holter monitoring.

Statistical analysis

The SPSS 15.0 (SPSS Inc., Chicago, IL, USA) statistical software package was used for all calculations. Data are presented as means ± standard deviation for continuous variables and as percentages for categorical data. The continuous variables among groups were analyzed by the unpaired Student’s t-test or analysis of variance. Categorical data and proportions were analyzed using the Chi-square test. Univariate and multivariate analysis were performed using logistic regression analyses to determine the independent predictive factors of AF after typical AFL ablation. The actuarial probability of freedom from AF after AFL ablation was calculated with the Kaplan–Meier method and the differences between the curves were tested for significance by

Results: Among the 122 ablated patients, 15 (12.3%) had recurrent AFL and 33 (27.0%) had recurrent AF. In univariate logistic analysis, LAD and LAVI could significantly predict the recurrence of AF after AFL ablation. However, multivariate logistic regression analysis found that the independent predictor of recurrent AF was LAVI. An LAVI of 42.6 mL may allow for the differentiation between only AFL and AFL with concomitant AF with 69.0% sensitivity and 69.8% specificity.

Conclusions: LAVI might be a useful predictor for occurrence of AF after ablation of typical AFL.
Table 1 Demographic characteristics.

<table>
<thead>
<tr>
<th>No. of Pt.</th>
<th>122</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.1 ± 11.3</td>
</tr>
<tr>
<td>Male (%)</td>
<td>100 (82.0%)</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>13 (10.7%)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>26 (21.3%)</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>9 (7.4%)</td>
</tr>
<tr>
<td>Congestive heart failure (%)</td>
<td>16 (13.1%)</td>
</tr>
<tr>
<td>Intracardiac Op. d/t SHD</td>
<td>15 (12.3%)</td>
</tr>
<tr>
<td>Prior AF (%)</td>
<td>48 (39.3%)</td>
</tr>
<tr>
<td>Duration of AFL (months)</td>
<td>11.3 ± 6.2</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>55.6 ± 12.5</td>
</tr>
<tr>
<td>LA diameter (cm)</td>
<td>4.40 ± 0.66</td>
</tr>
<tr>
<td>LA volume index (mL/m²)</td>
<td>43.2 ± 16.7</td>
</tr>
<tr>
<td>Mitral regurgitation (%)</td>
<td>19 (13.7%)</td>
</tr>
<tr>
<td>Follow-up duration (months)</td>
<td>24.6 ± 25.7</td>
</tr>
</tbody>
</table>

Op.: operation; SHD: structural heart disease; AF: atrial fibrillation; AAA: anti-arrhythmic agent; AFL: atrial flutter; LV: left ventricle; LA: left atrium.

log rank statistics. A p-value <0.05 was regarded as statistically significant.

Results

Demographic characteristics

Table 1 presents the demographic characteristics of the study population. There were 100 men and 22 women. Mean age was 59.1 ± 11.3 years. All patients were followed for 24.6 months after ablation. Twelve percent of the patients had corrective cardiac surgery for congenital heart disease such as atrial septal defect, ventricular septal defect, and patent ductus arteriosus. Forty percent of the patients had a history of prior AF. Transthoracic echocardiographic parameters such as left ventricular ejection fraction, LA diameter, and LA volume index were normal. Fourteen percent of the patients had mitral regurgitation more than moderate grade.

Follow-up results after CTI ablation

The mean follow-up duration was about 2 years. During follow-up, 15 patients (12.3%) and 33 (27.0%) showed recurrences of AFL and occurrence of AF, respectively. In addition, 74 (60.7%) remained in sinus rhythm. Those with occurrence of AF included 8 with early occurrence (within 3 months after ablation) and 25 with late occurrence (greater than 3 months). Among the 14 patients with prior AF, there were 5 with early occurrence and 9 with late occurrence. Among groups, there was no difference in age, proportion of prior AF, presence of intracardiac operation, medication of anti-arrhythmic agent, left ventricular ejection fraction, and incidence of mitral regurgitation (Table 2). However, LA diameter and LA volume index in patients with occurrence of AF was significantly larger in patients with sinus rhythm or recurrence of AFL (p < 0.001).

Predictors for occurrence of atrial fibrillation

Univariate analysis showed that patients who experienced occurrence of AF were more likely to have a larger LA diameter (>4.5 cm) and LA volume index (>42.6 mL/m²) than patients who sustained sinus rhythm (Table 3). However, multivariate analysis showed that only LA volume index (>42.6 mL/m²) were associated significantly with time to occurrence of AF after CTI ablation in AFL (hazard ratio 3.788, 95% confidence interval: 1.331—10.779; p = 0.013). In a subgroup analysis of patients with or without prior AF history, larger LA diameter and LA volume index were significant predictors in univariate analysis. In multivariate analysis, LA volume index might predict the occurrence of AF, even though statistically not significant (Table 4). Fig. 1 demonstrates the Kaplan–Meier analysis of survival free of AF according to LA volume index (defined as LA volume index >42.6 mL/m²).

Discussion

This study firstly demonstrated that LA volume index might be a useful predictor of AF occurrence after a CTI ablation of typical AFL. In our study, during a mean follow-up

Table 2 Results of CTI ablation in overall population.

<table>
<thead>
<tr>
<th>Sinus</th>
<th>AFL</th>
<th>AF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Pt.</td>
<td>74 (60.7%)</td>
<td>15 (12.3%)</td>
<td>33 (27.0%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.6 ± 12.3</td>
<td>62.5 ± 8.5</td>
<td>59.3 ± 9.3</td>
</tr>
<tr>
<td>Male (%)</td>
<td>69 (83.1%)</td>
<td>12 (92.3%)</td>
<td>19 (73.1%)</td>
</tr>
<tr>
<td>Prior AF (%)</td>
<td>29 (39.2%)</td>
<td>5 (38.5%)</td>
<td>14 (42.4%)</td>
</tr>
<tr>
<td>Intracardiac operation</td>
<td>10 (13.5%)</td>
<td>2 (13.3%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>History of AAA (%)</td>
<td>30 (36.1%)</td>
<td>8 (61.5%)</td>
<td>11 (42.3%)</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>54.7 ± 12.9</td>
<td>57.0 ± 14.8</td>
<td>57.3 ± 9.9</td>
</tr>
<tr>
<td>LA diameter (cm)</td>
<td>4.22 ± 0.64</td>
<td>4.46 ± 0.72</td>
<td>4.77 ± 0.53</td>
</tr>
<tr>
<td>LA volume index (mL/m²)</td>
<td>38.9 ± 12.2</td>
<td>41.0 ± 21.9</td>
<td>53.6 ± 18.7</td>
</tr>
<tr>
<td>Mitral regurgitation (%)</td>
<td>13 (15.9%)</td>
<td>1 (7.7%)</td>
<td>5 (19.2%)</td>
</tr>
<tr>
<td>Flutter cycle length (ms)</td>
<td>236.8 ± 38.8</td>
<td>246.5 ± 26.4</td>
<td>225.7 ± 38.6</td>
</tr>
<tr>
<td>Time to first AF or AFL (months)</td>
<td>15.0 ± 22.0</td>
<td>20.0 ± 21.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

CTI: cavo-tricuspid isthmus; AFL: atrial flutter; AF: atrial fibrillation; AAA: anti-arrhythmic agent; LV: left ventricle; LA: left atrium.
Table 3 Univariate and multivariate regression analysis for predictors of AF occurrence after ablation of AFL.

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>1.029</td>
<td>0.991, 1.069</td>
</tr>
<tr>
<td>Prior history of AF</td>
<td>1.143</td>
<td>0.497, 2.631</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>1.604</td>
<td>0.558, 4.605</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.999</td>
<td>0.965, 1.033</td>
</tr>
<tr>
<td>Medication of AAA</td>
<td>1.633</td>
<td>0.707, 3.774</td>
</tr>
<tr>
<td>LAD &gt; 4.5 cm</td>
<td>3.670</td>
<td>1.524, 8.838</td>
</tr>
<tr>
<td>LAVI &gt; 42.6 mL/m²</td>
<td>5.146</td>
<td>1.984, 13348</td>
</tr>
</tbody>
</table>

CI: confidence interval; AF: atrial fibrillation; AFL: atrial flutter; AAA: anti-arrhythmic agent; LV: left ventricle; LAD: left atrial diameter; LAVI: left atrial volume index.

Table 4 Univariate and multivariate regression analysis for predictors of AF occurrence after ablation of AFL.

<table>
<thead>
<tr>
<th></th>
<th>Without prior AF (n = 64)</th>
<th>With prior AF (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>p</td>
</tr>
<tr>
<td>Age</td>
<td>1.052</td>
<td>0.051</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>2.286</td>
<td>0.263</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>1.013</td>
<td>0.572</td>
</tr>
<tr>
<td>Medication of AAA</td>
<td>2.215</td>
<td>0.159</td>
</tr>
<tr>
<td>LAD &gt; 4.5 cm</td>
<td>4.513</td>
<td>0.013</td>
</tr>
<tr>
<td>LAVI &gt; 42.6 mL/m²</td>
<td>5.370</td>
<td>0.009</td>
</tr>
</tbody>
</table>

CI: confidence interval; AF: atrial fibrillation; AFL: atrial flutter; AAA: anti-arrhythmic agent; LV: left ventricle; LAD: left atrial diameter; LAVI: left atrial volume index.

Fig. 1 Kaplan–Meier analysis of freedom from atrial fibrillation (AF) after cavo-tricuspid isthmus (CTI) ablation of atrial flutter (AFL). LAVI, left atrial volume index.
of 24.6 ± 25.7 months, AFL recurred in 12.3% of patients \( (n = 15) \) and AF occurred in 27.0% of patients \( (n = 33) \) after a CTI ablation of typical AFL.

AF and AFL have been known to share common pathophysiological features including electrical remodeling [1] and shortened action potential duration [2]. Also, Ohmura et al. [14] demonstrated that a very short cycle length of AFL circuit could result in fibrillatory conduction. Conversely, Roithinger et al. [15] suggested that initiation and perpetuation of typical AFL depend on the existence of a functional line of block, which is developed during transitional rhythm preceding AF [16].

In clinical practice, this close interplay between AFL and AF also translates into a high incidence of AF following CTI ablation of typical AFL, ranging from 17 to 58% after a follow-up of 6–36 months [17–24]. In our study, AF occurred in 27.0% of patients during a mean follow-up of 24.6 ± 25.7 months, which is a similar result compared to previous studies. This various occurrence rate of AF was explained by duration of follow-up and asymptomatic AF.

Several authors reported a variety of predictors for occurrence of AF after AFL ablation. Hsieh et al. [6] demonstrated that prior history of AF and inducible AF might be predictors for the early occurrence of AF, and prior history of AF was the only predictor for late occurrence of AF. In our study, prior history of AF was not associated with occurrence of AF. This may be due to the use of anti-arrhythmic agents during follow-up. Da Costa et al. [20] showed that mitral regurgitation was the only independent predictor of AF in patients without a prior history of AF. In patients with a prior history of AF, left ventricular ejection fraction was the only independent predictor of AF following the ablation. In our study, LA volume index (>42.6 mL/m²) might predict the occurrence of AF regardless of prior AF history. This controversy could be explained by the fact that most patients had normal left ventricular function and a small number of patients had mitral regurgitation. Ellis et al. [25] also noted that LA size was a predictor of AF recurrence after AFL ablation. In our study, dilated LA dimension could predict occurrence of AF in univariate analysis. In addition, enlarged LA volume index could be the only predictor for occurrence of AF in multivariate analysis.

Our study, as well as other published studies, has pointed out a possibility of AF after AFL ablation. Therefore, several parameters including prior history and inducibility of AF, enlarged LA volume, and left ventricular dysfunction should be included in deciding on treatment for patients taking anti-arrhythmic and antithrombotic agents after AFL ablation.

The limitations of this study include the following. First, our study is limited by its retrospective analysis. Second, we may also have underestimated the patients with asymptomatic episodes of AF, or due to the anti-arrhythmic drugs treated in cases after the ablation, which may prevent AF recurrences. However, Roy et al. [26] reported that ami- dorone and propafenone could prevent recurrence of AF in 65% and 37% for 2 years, respectively. Also, in the AFFIRM study [27], AF recurrence in the rhythm control group was observed at 26.7% at 3 years even though so many underwent cardioversion. In our study, only 25% of the patients who had prior AF history and were treated with anti-arrhythmic medication were found to AF occurrence, which is not fully explained only by effect of anti-arrhythmic medication. Third, because the study included a small number of patients, large-scale and long-term follow-up studies are required to confirm this finding.

Nevertheless, in conclusion, the present results suggest that LA volume index might be a useful predictor for occurrence of AF after ablation of typical AFL.

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