Radiofrequency Catheter Ablation of Atrial Fibrillation: A Cause of Silent Thromboembolism?

Magnetic Resonance Imaging Assessment of Cerebral Thromboembolism in Patients Undergoing Ablation of Atrial Fibrillation

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Background—Radiofrequency left atrial catheter ablation has become a routine procedure for treatment of atrial fibrillation. The aim of this study was to assess with preprocedural and postprocedural cerebral magnetic resonance imaging the thromboembolic risk, either silent or clinically manifest, in the context of atrial fibrillation ablation. The secondary end point was the identification of clinical or procedural parameters that correlate with cerebral embolism.

Methods and Results—A total of 232 consecutive patients with paroxysmal or persistent atrial fibrillation who were candidates for radiofrequency left atrial catheter ablation were included in the study. Pulmonary vein isolation or pulmonary vein isolation plus linear lesions plus atrial defragmentation with the use of irrigated-tip ablation catheters was performed. All of the patients underwent preprocedural and postablation cerebral magnetic resonance imaging. A perioperative symptomatic cerebrovascular accident occurred in 1 patient (0.4%). Postprocedural cerebral magnetic resonance imaging was positive for new embolic lesions in 33 patients (14%). No clinical parameters such as age, hypertension, diabetes mellitus, previous history of stroke, type of atrial fibrillation, and preablation anti-thrombotic treatment showed significant correlation with ischemic cerebral embolism. Procedural parameters such as activated clotting time value and, in particular, electric or pharmacological cardioversion to sinus rhythm correlated with an increased incidence of cerebral embolism. Cardioversion was also associated with an increased risk of 2.75 (95% confidence interval, 1.29 to 5.89; P = 0.009).

Conclusions—Radiofrequency left atrial catheter ablation carries a low risk of symptomatic cerebral ischemia but is associated with a substantial risk of silent cerebral ischemia detected on magnetic resonance imaging. Independent risk factors for cerebral thromboembolism are the level of activated clotting time and, in particular, the electric or pharmacological cardioversion to sinus rhythm during the procedure.

Key Words: ablation ■ arrhythmia ■ fibrillation ■ magnetic resonance imaging ■ stroke

Atrial fibrillation (AF) is the most frequent supraventricular arrhythmia, with a high prevalence in the elderly population. AF is not a benign arrhythmia; the risk of stroke in people with AF is 5 times higher than those in sinus rhythm. Furthermore, different studies have shown a cognitive decline in patients with AF, with an increased risk of dementia. It is generally believed that the cognitive impairment is a result of silent cerebral embolism, which correlates with symptomatic cerebral infarcts in patients with AF. One of the main objectives of the treatment of AF is the maintenance of sinus rhythm to reduce the incidence of ischemic cerebral events. Because pharmacological treatment has limited efficacy, various nonpharmacological therapies have been proposed, and left atrial (LA) catheter ablation has become a routine procedure in many laboratories. However, catheter ablation has an inherent risk of stroke that is increased to 1.8% to 2% when ablation is performed on the left side of the heart. The incidence of symptomatic thromboembolic complications in the context of AF ablation has been reported to range from 0.5% to 0.9% according to worldwide surveys and retrospective studies. In contrast to clinically evident stroke, few data exist on the possibility of...
experiencing a silent cerebral embolism in the context of AF ablation.9,10 Because of these considerations, knowledge of the incidence of silent cerebral embolism as well as clinically manifest stroke in the context of AF ablation is important. These data will enable us to fully comprehend the clinical implications of AF ablation and to better assess the risk profile of the procedure.

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The primary end point of our study was to evaluate the incidence of cerebral embolism, either silent or clinically evident, assessed by cerebral magnetic resonance imaging (MRI) in a large population of AF patients undergoing LA radiofrequency catheter ablation. In addition, the secondary end point was the identification of clinical or procedural parameters that correlate with cerebral embolism.

Methods

Study Population

Two hundred thirty-four consecutive patients from 3 different experienced centers who were undergoing radiofrequency catheter ablation for symptomatic, paroxysmal, or persistent AF defined according to the American Heart Association guidelines, refractory to at least 2 antiarrhythmic drugs, were enrolled in the study. Two patients were excluded because an ablation procedure was not performed after the transesophageal echocardiogram showed atrial thrombus.

Exclusion criteria were as follows: age <21 years or >80 years, valvular heart disease with surgical indication, acute coronary syndrome <3 months, previous pacemaker implantation, or other contraindications for MRI.

A second group of 65 patients with persistent AF and indications for electric cardioversion was enrolled as a control group to compare preablation MRI with postablation MRI of the brain. Two hundred thirty-four consecutive patients from 3 different centers were included in the study: the University Hospitals of Cleveland, Cleveland, Ohio; Mayo Clinic, Rochester, Minn; or SL0, St. Jude). The sheath was perfused with heparinized solution (3000 U of heparin in 500 mL of NaCl 0.9%) at 180 mL/h. A multipolar catheter was inserted through the long sheath to map the pulmonary vein ostia. An irrigated-tip ablation catheter was advanced into the LA through the same hole whenever possible; otherwise, a second transseptal puncture was performed. After transseptal puncture, intravenous unfractionated heparin was given as a bolus (50 U/kg), and additional boluses were given throughout the procedure to maintain an activated clotting time (ACT) of at least 250 to 300 seconds, in accordance with the suggestions of the Venice Chart International Consensus.11

Once the catheters in the LA were positioned, the venous sheath was moved into the right atrium and continuously perfused with heparinized 0.9% NaCl. ACT was determined 30 minutes after the transseptal puncture and subsequently every 30 minutes. Deep sedation was achieved by means of intravenous fentanyl, midazolam, and propofol.

A 3-dimensional reconstruction of the LA and pulmonary vein (PV) ostia, with the use of an electroanatomic mapping system (Carto, Biosense Webster, Diamond Bar, Calif; or Nav-X, St. Jude) was performed in all patients, and PV electric activity was assessed with a multipolar ring catheter (Orbiter PV, Bard; Lasso, Biosense Webster; Optima, St. Jude; or Reflexion, St. Jude). For paroxysmal AF, the end point of the ablation procedure was to obtain a complete electric PV; if a repeat procedure was necessary, PV1 plus the addition of linear lesions was performed. For persistent AF or long-standing persistent AF, PV1 plus the creation of linear lesions interconnecting the upper PV ostia (roof line) and the left inferior PV down to the mitral annulus and, when necessary, ablation of fragmented atrial electrograms was performed. Radiofrequency was applied with the use of an open irrigated-tip catheter (Navistar Thermocool, Biosense Webster; or Coolpath, St. Jude) with power output up to 30 W close to the PV ostia and up to 40 W while creating the roof line and the left mitral isthmus line, with an irrigation rate of 20 to 35 mL/min (0.9% saline infused with the Cool Flow Pump, Biosense Webster) to maintain a tip temperature of <45°C. If AF persisted, all patients were converted to sinus rhythm either pharmacologically or electrically at the end of the procedure. In addition, all patients underwent radiofrequency ablation of the cavotricuspid isthmus. Sheaths were removed after the procedure once ACT was <200 seconds.

Echoangiography was performed soon after the patient was transferred to the ward. If echocardiography was negative for pericardial effusion, heparin was given intravenously. The heparin infusion was started at ∼30 to 45 minutes from the sheath removal and was titrated according to the partial thromboplastin time, which was kept between 60 and 80 seconds. The day after the procedure, intravenous heparin was stopped, and the patient was restarted on low-molecular-weight heparin twice daily at a weight-adapted dose (80 U/kg) and oral anticoagulation with warfarin. Low-molecular-weight heparin was continued until the international normalized ratio was >2.

Cerebral MRI

MRI of the brain was performed the day before and the day after the procedure with a 1.5-T scanner (1.5-T Magnetom Avanto, Siemens, Erlangen, Germany) to compare preablation MRI with postablation MRI to identify new procedure-related ischemic cerebral lesions.

The imaging protocol included a sagittal T1-weighted spin echo sequence to obtain a better definition of the anterior and posterior cerebral commissures. The parameters of the T1-weighted spin echo sequence were as follows: repetition time/echo time 400/13; slice thickness 5 mm; distant factor 0%; field of view 230 mm; matrix 192 × 256; and acquisition time 59 seconds. An axial fluid-attenuated inversion recovery (FLAIR) sequence was then used. The parameters of the FLAIR sequence were as follows: repetition time/echo time
8500/112; TI 2500 ms; slice thickness 5 mm; distant factor 30%; field of view 240 mm; matrix 154×256; and acquisition time 3.24 seconds. A diffusion-weighted (DW) sequence, with the use of a single-shot spin echo with echo-planar imaging technique that combined the motion-probing gradient before and after the 180° pulse with echo-planar imaging readout, was obtained; fat was suppressed by placing a frequency-selective radiofrequency pulse before the pulse sequence. The parameters of the DW sequence were as follows: repetition time/echo time 3200/99; slice thickness 5 mm; distant factor 30%; field of view 230 mm; matrix 128×128; bandwidth 1502 Hz; gradient strength 22 mT; duration of diffusion gradients 31 ms; gradient separation 42 ms in 3 orthogonal directions; and acquisition time 43 seconds. For each DW sequence, the apparent diffusion coefficient map was obtained.

Both sequences were centered on the axis defined by a line passing between the anterior and posterior cerebral commissures. The definition of this line was important to allow reproducibility of the MRI sequences before and after the procedure.

On the postablation MRI, an acute embolic lesion was defined as a focal hyperintense area detected by the FLAIR sequence, corresponding to a restricted diffusion signal in the DW sequence, confirmed by apparent diffusion coefficient mapping to rule out a shine-through artifact. The size and localization of the focal lesions were evident after the procedure. Postprocedural cerebral MRI was positive for asymptomatic new ischemic lesions in 33 of 232 patients (14%): In 25 patients a single lesion was present, in 3 patients 2 lesions were found, and in 5 patients 3 new lesions were evident. The dimensions of the lesions varied from 3 to 35 mm in diameter. The lesions were cortical in 25 cases, and 7 were localized in the cerebellum and 1 in the basal ganglia (Figure). In all 33 patients with a positive MRI, a neurological examination performed by an experienced neurologist was negative. In these 33 patients, a carotid Doppler examination was negative as well.

No clinical parameters such as age, hypertension, diabetes mellitus, previous history of stroke, type of AF, and preablation antithrombotic treatment were found to show a significant correlation with ischemic cerebral embolism by the univariate models (Table 2). On the other hand, procedural parameters such as electric or pharmacological conversion to sinus rhythm during the procedure and the ACT value correlated significantly with the incidence of cerebral embolism (Table 2). Specifically, electric or pharmacological conversion to sinus rhythm during the procedure conferred a significantly increased risk for thromboembolism (odds ratio=2.75; confidence interval, 1.29 to 5.89; \( P=0.009 \)). Sixty-two patients underwent cardioversion at the end of ablation (53 electric and 9 pharmacological cardioversion). Sixteen of 62 (26%) had evidence of new cerebral embolism (1 transient ischemic attack and 15 silent ischemic emboli). In the group of patients without cardioversion, ischemic events occurred in 18 of 170 patients (11%). Ischemic events occurred in 10 of 112 patients (9%) who presented sinus rhythm throughout the procedure (group A), in 8 of 58 patients (14%) in whom sinus rhythm was restored by catheter ablation (group B), and in 62 patients (26%) in whom electric or pharmacological conversion to sinus rhythm was necessary at the end of the procedure (group C). The results showed that group A and group B can be considered equal (\( P=0.331 \)), whereas group C is statistically different (\( P=0.004 \)) from the other 2 groups. We found that for ACT <250 seconds, 17% of the patients were evident after the procedure. Postprocedural cerebral MRI was positive for asymptomatic new ischemic lesions in 33 of 232 patients (14%): In 25 patients a single lesion was present, in 3 patients 2 lesions were found, and in 5 patients 3 new lesions were evident. The dimensions of the lesions varied from 3 to 35 mm in diameter. The lesions were cortical in 25 cases, and 7 were localized in the cerebellum and 1 in the basal ganglia (Figure). In all 33 patients with a positive MRI, a neurological examination performed by an experienced neurologist was negative. In these 33 patients, a carotid Doppler examination was negative as well.

No clinical parameters such as age, hypertension, diabetes mellitus, previous history of stroke, type of AF, and preablation antithrombotic treatment were found to show a significant correlation with ischemic cerebral embolism by the univariate models (Table 2). On the other hand, procedural parameters such as electric or pharmacological conversion to sinus rhythm during the procedure and the ACT value correlated significantly with the incidence of cerebral embolism (Table 2). Specifically, electric or pharmacological conversion to sinus rhythm during the procedure conferred a significantly increased risk for thromboembolism (odds ratio=2.75; confidence interval, 1.29 to 5.89; \( P=0.009 \)). Sixty-two patients underwent cardioversion at the end of ablation (53 electric and 9 pharmacological cardioversion). Sixteen of 62 (26%) had evidence of new cerebral embolism (1 transient ischemic attack and 15 silent ischemic emboli). In the group of patients without cardioversion, ischemic events occurred in 18 of 170 patients (11%). Ischemic events occurred in 10 of 112 patients (9%) who presented sinus rhythm throughout the procedure (group A), in 8 of 58 patients (14%) in whom sinus rhythm was restored by catheter ablation (group B), and in 62 patients (26%) in whom electric or pharmacological conversion to sinus rhythm was necessary at the end of the procedure (group C). The results showed that group A and group B can be considered equal (\( P=0.331 \)), whereas group C is statistically different (\( P=0.004 \)) from the other 2 groups. We found that for ACT <250 seconds, 17% of the patients
had a positive MRI, whereas for ACT value >250 seconds, 9% of the patients were positive for silent embolism.

When we assessed the patients who underwent intraprocedural electric or pharmacological cardioversion, the incidence of cerebral embolism was 29% for ACT value <250 seconds, whereas in patients with ACT >250 seconds, the risk decreased to 21%. In patients in whom electric or pharmacological cardioversion was not performed, asymptomatic cerebral thromboembolism occurred in 13% of patients with ACT value <250 seconds, whereas it decreased to 4% when ACT value was >250 seconds.

In the multivariable analysis, we also found that the ACT value (\( P = 0.0087 \)) and electric or pharmacological conversion to sinus rhythm (\( P = 0.0025 \)) were independently associated with a risk of periprocedural cerebral thromboembolism.

In regard to the 65 patients with persistent AF who underwent electric cardioversion without ablation, the mean age was 66±9 years, systemic hypertension was found in 71% of the patients, and diabetes mellitus was found in 17% (11 patients). Structural heart disease was present in 38% of the patients. A CHADS score was calculated for each patient, and it was 0 in 15%, 1 in 54%, 2 in 25%, and >2 in 6% of the patients. In 5 patients (8%), previous symptomatic thromboembolic cerebral events were demonstrated. The postcardioversion cerebral MRI was negative for new acute cerebral ischemic lesions in all patients.

**Discussion**

This is the first large prospective study that sought to detect silent and clinically evident cerebral embolism, assessed with MRI before and after the procedure, in patients undergoing LA catheter ablation for AF. The major findings are as follows: (1) LA transcatheter ablation for AF is associated with silent cerebral thromboembolism; (2) periprocedural symptomatic cerebral thromboembolism (transient ischemic attack) represents only a minimal part of the thromboembolic risk (0.4% symptomatic versus 14% asymptomatic; odds ratio=40.53); (3) the thromboembolic risk is independent from clinical parameters such as age, hypertension, and diabetes mellitus and from the type of AF, occurrence of previous cerebral thromboembolic events, preprocedural antithrombotic treatment, and the ablation strategy used; and (4) in univariate and multivariable analyses, the most important factor that correlated with cerebral embolism was electric or pharmacological conversion to sinus rhythm during the procedure, with a significantly increased odds ratio of 2.75.

AF is an independent risk factor for stroke, resulting in an 3- to 5-fold excess risk.\(^1\) Anticoagulant therapy has been shown to reduce this risk, although thromboembolic events, either symptomatic or silent, may occur even during antithrombotic treatment (1.2% and 14.7%, respectively).\(^{12,13}\)

In recent years, radiofrequency catheter ablation has evolved as an effective nonpharmacological treatment for AF. The main objective of the therapy is not only to improve symptoms but also to maintain sinus rhythm with the hope of reducing the incidence of thromboembolism. Today, in fact, the possibility of discontinuation of antithrombotic treatment if catheter ablation is successful is a matter of debate. However, similar to drug therapy, a balance of the risk-benefit ratio of a therapeutic act should always be considered. Our assessment of retrospective studies and worldwide surveys has revealed that ablation per se may be responsible for symptomatic stroke, with the incidence ranging from 0.5% to 0.9%.\(^{7,8}\) Few data exist relative to the incidence of silent ischemic embolism in the context of AF ablation, whereas rates of silent ischemia after other cardiovascular interventions, including carotid stenting and retrograde catheterization of the aorta, are well described.\(^{14,15}\) To our knowledge, only a small study of 53 patients assessed with only postablation cerebral MRI showed the possibility of occurrence of silent cerebral embolism during AF ablation.\(^{10}\)
Our study is the first large prospective study that sought to assess, with cerebral MRI before and after ablation, the incidence of symptomatic and silent cerebral embolism in patients undergoing AF ablation. The incidence of symptomatic cerebral embolism was 0.4%, comparable to the previous series. Most importantly, symptomatic cerebral embolism represented only the “tip of the iceberg” because the incidence of MRI-documented silent cerebral embolism was 14%. This difference can be attributed to the possibility that an ischemic lesion even of large dimension may be localized in silent areas of brain.

Certainly, the occurrence of symptomatic stroke is dramatic for both the risk of death and the social and economic impact of the disease, but the evidence of silent embolic lesions is worrisome because these lesions add a dimension of further cerebral damage in a population at high risk for cerebral embolism and dementia. Awareness of these complications is crucial to physicians because patients who are candidates for AF ablation undergo >1 ablation procedure in 30% to 50% of cases,16–18 raising the possibility of cumulative damage. Periprocedural cerebrovascular accidents may be caused by preexisting LA thrombus not seen on transesophageal echocardiography, char formation on radiofrequency ablation catheters or ablated tissue, thrombus formation on LA catheters and sheaths, air embolus, or periprocedural development of new atrial thrombus after conversion of AF to sinus rhythm.19,20 All of the measures commonly used to minimize the risk of periprocedural stroke were taken routinely during the procedure: a preprocedural transesophageal echocardiogram, anticoagulation before the procedure, intraprocedural use of heparin, continuous flushing of the sheaths, and use of irrigated-tip catheters.

Table 2. Clinical and Procedural Parameters Considered for Univariate Analysis

<table>
<thead>
<tr>
<th>Patients With Periprocedural Silent Cerebral Ischemic Lesion</th>
<th>Patients Without Periprocedural Cerebral Ischemic Lesion</th>
<th>OR</th>
<th>95% CI, Lower Limit of OR</th>
<th>95% CI, Upper Limit of OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>33</td>
<td>198</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age, y</td>
<td>60±8</td>
<td>58±10</td>
<td>1.02</td>
<td>0.98</td>
<td>1.06</td>
</tr>
<tr>
<td>Male gender</td>
<td>24 (73)</td>
<td>156 (79)</td>
<td>0.74</td>
<td>0.32</td>
<td>1.72</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (52)</td>
<td>95 (48)</td>
<td>1.08</td>
<td>0.52</td>
<td>2.24</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0</td>
<td>10 (5)</td>
<td>0.00</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>6 (18)</td>
<td>24 (12)</td>
<td>1.55</td>
<td>0.58</td>
<td>4.13</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>8 (24)</td>
<td>49 (25)</td>
<td>0.93</td>
<td>0.39</td>
<td>2.20</td>
</tr>
<tr>
<td>Previous stroke or transient ischemic attack</td>
<td>2 (6)</td>
<td>13 (7)</td>
<td>1.37</td>
<td>0.37</td>
<td>5.11</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>20 (61)</td>
<td>117 (59)</td>
<td>0.89</td>
<td>0.42</td>
<td>1.88</td>
</tr>
<tr>
<td>Persistent</td>
<td>13 (39)</td>
<td>81 (41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antithrombotic drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>23 (70)</td>
<td>154 (78)</td>
<td>0.68</td>
<td>0.30</td>
<td>1.54</td>
</tr>
<tr>
<td>Aspirin</td>
<td>10 (30)</td>
<td>44 (21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHADS score</td>
<td></td>
<td></td>
<td>Base</td>
<td>Base</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>15</td>
<td>92</td>
<td>Base</td>
<td>Base</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>83</td>
<td>1.18</td>
<td>0.55</td>
<td>2.53</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>16</td>
<td>0.38</td>
<td>0.04</td>
<td>3.10</td>
</tr>
<tr>
<td>&gt;2</td>
<td>2</td>
<td>7</td>
<td>2.04</td>
<td>0.37</td>
<td>11.08</td>
</tr>
<tr>
<td>Spontaneous echo contrast</td>
<td>3</td>
<td>5</td>
<td>3.86</td>
<td>0.87</td>
<td>16.99</td>
</tr>
<tr>
<td>Mean ACT value during the procedure, s</td>
<td>269±28</td>
<td>282±32</td>
<td>0.98</td>
<td>0.97</td>
<td>0.99</td>
</tr>
<tr>
<td>Type of procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV isolation</td>
<td>95 (48)</td>
<td>73 (37)</td>
<td>0.75</td>
<td>0.33</td>
<td>1.73</td>
</tr>
<tr>
<td>PV+linear lesion</td>
<td>12 (37)</td>
<td>30 (15)</td>
<td>1.42</td>
<td>0.53</td>
<td>3.79</td>
</tr>
<tr>
<td>PV+linear lesion+atrial fragmented potential</td>
<td>8 (24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transseptal approach</td>
<td>27 (79)</td>
<td>169 (85)</td>
<td>0.58</td>
<td>0.24</td>
<td>1.40</td>
</tr>
<tr>
<td>Patent foramen ovale</td>
<td>6 (21)</td>
<td>29 (15)</td>
<td>1.5</td>
<td>0.60</td>
<td>3.79</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>196±96</td>
<td>180±80</td>
<td>1.00</td>
<td>0.99</td>
<td>1.00</td>
</tr>
<tr>
<td>Radiofrequency time, min</td>
<td>50±20</td>
<td>47±20</td>
<td>1.00</td>
<td>0.99</td>
<td>1.00</td>
</tr>
<tr>
<td>Electric or pharmacological cardioversion during ablation</td>
<td>15 (45)</td>
<td>46 (23)</td>
<td>2.75</td>
<td>1.29</td>
<td>5.89</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. OR indicates odds ratio.
Independent factors that correlated with the thromboembolic risk were intraprocedural cardioversion and, to a lesser extent, the level of anticoagulation, whereas clinical parameters were not associated with an increased risk of thromboembolism. In fact, the thromboembolic risk increased to 26% in patients in whom conversion to sinus rhythm was necessary at the end of the procedure compared with 9% risk in patients in sinus rhythm throughout the procedure. In patients in whom sinus rhythm was restored by means of catheters, the thromboembolic risk increased to 14%. In regard to the value of ACT combined with conversion to sinus rhythm, it has been shown that an ACT value >250 seconds conferred only a small protective effect; in fact, the risk of thromboembolism decreased only from 29% to 21% in patients who underwent electric or pharmacological cardioversion. These results may be important because, in most centers, cardioversion is utilized at the end of the procedure if sinus rhythm is not restored after the ablation.

In regard to the mechanisms by which cardioversion may constitute a higher risk, different hypothesis can be postulated. First, cardioversion itself might be the cause of silent embolism. Cardioversion has been associated with both symptomatic cerebral embolism21–23 and silent ischemia.24 To validate this hypothesis, a separate group of 65 patients who were candidates for electric cardioversion for persistent AF underwent transesophageal echocardiography and cerebral MRI the morning of electric cardioversion and a repeat cerebral MRI 24 hours after cardioversion. Interestingly, in none of these patients were new asymptomatic lesions found on the cerebral MRI. It seems therefore that conversion to sinus rhythm is not risky per se but becomes significantly risky in the context of the ablation procedure. This evidence corroborates the possibility that the endothelial lesion determined by the application of radiofrequency energy may play a significant role. Potential mechanisms of thrombogenesis during ablation procedures are multiple and include endothelial disruption, electroporation injury, and heating of circulating blood elements by radiofrequency energy. The aforementioned mechanisms can cause activation of the cascade of events that ultimately results in thrombin generation and platelet activation.19,20 The mechanical trauma due to electric cardioversion or the restored atrial contractility after AF may dislocate LA microthrombi, causing cerebral embolism. On the other hand, we cannot exclude that a group of patients at high risk of thromboembolism because of underlying substrate resistant to ablation have been selected, and further ablation may increase the risk of thromboembolism.

Consistent with the results of other studies, the level of anticoagulation during the procedure showed a significant correlation with a higher incidence of thromboembolic complications. In fact, with ACT values <250 seconds, the incidence of silent thromboembolism is 17%. However, with ACT values ranging from 250 to 400 seconds, the risk of silent thromboembolism is still 9%. It has already been reported that thromboembolic risk decreases as the ACT is maintained at >300 seconds.25 We followed the recommendations of the Venice Chart International Consensus,11 which suggests an ACT target of at least 250 to 300 seconds to also reduce the risk of cardiac tamponade.

On the basis of the results of the study, a few issues about LA catheter ablation must be raised. First, patients must be informed of the possibility of silent cerebral ischemia. Second, intraprocedural cardioversion represents a relevant risk factor for thromboembolism, with a significantly increased odds ratio of 2.75.

Therefore, the issue of postponing intraprocedural cardioversion once the radiofrequency lesions are healed is a possibility to consider that needs to be confirmed in further studies. Other possibilities may be (1) to be more aggressive during ablation to restore sinus rhythm with catheters or (2) to continue the anticoagulant therapy with warfarin during the procedure.26

Limitations

The results of the study apply only to patients undergoing radiofrequency ablation with irrigated-tip catheters, which is the most frequently used form of energy for AF ablation. Studies of ablation in which other forms of energy are used may show different results.27 Another limitation is the lack of a repeat 3-month cerebral MRI in the case of positive MRI results after ablation, which does not allow assessment of evolution of the ischemic lesions in the long term. In addition, the study lacks performance of routine carotid Doppler before the ablation. However, in all cases of positive MRIs, a carotid Doppler was performed, with negative results.

Conclusions

LA catheter ablation has today become a routine procedure to cure AF. This procedure carries a small risk of symptomatic cerebral ischemia, but a substantial risk of silent cerebral ischemic emboli detected on MRI is associated with the procedure. Independent risk factors for cerebral thromboembolism are the level of ACT and, in particular, conversion to sinus rhythm during the procedure.

Disclosures

None.

References


CLINICAL PERSPECTIVE

Atrial fibrillation is a common arrhythmia and an important cause of strokes, which can be clinically silent. Left atrial radiofrequency catheter ablation has emerged as an important therapy for atrial fibrillation in selected patients. The ablation procedure has a risk of stroke reported to be ≈0.5%, but few data exist on the association between silent cerebral embolism and atrial fibrillation ablation. This study performed magnetic resonance imaging before and after atrial fibrillation ablation to assess cerebral infarcts. Heparin and low-molecular-weight heparin were used during transition to and from warfarin, and the activated clotting time goal for anticoagulation during the procedure was 250 to 300 seconds. Only 1 patient (0.4%) had a symptomatic cerebral embolism, but 14% had magnetic resonance imaging evidence of a new embolic lesion. Lower activated clotting times and the need for electric cardioversion at the end of the procedure, performed when ablation failed to restore sinus rhythm, were associated with embolism risk. Thus, with this anticoagulation and procedural regimen, the risk of symptomatic embolism is low, but there is a substantial risk of silent cerebral emboli.
Radiofrequency Catheter Ablation of Atrial Fibrillation: A Cause of Silent Thromboembolism?: Magnetic Resonance Imaging Assessment of Cerebral Thromboembolism in Patients Undergoing Ablation of Atrial Fibrillation

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심방세동의 도자질제술, 뇌경색의 위험도는 안심할 만한가?

최기준 교수 서울아산병원 심장내과

Summary

배경
심방세동 치료 시 최상방 내시에서의 도자질제술은 많이 시행되고 있으나, 혈전성병증의 위험은 갈 알려져 있지 않다. 본 연구에서는 심장 전과 후에 뇌 자기공명영상(IS)를 시행하여 증상이 있는 경우뿐만 아니라, 무증상의 뇌경색 위험을 평가하였다. 그리고 이자적인 연구목표로는 뇌경색의 진단과 치료에 관한 의사의 의료안전과 심장 전후의 위험인자를 분석하였다.

방법 및 결과
232명의 연속적인 발작성 혹은 지속성 심방세동의 도자질제술 환자들을 대상으로 하였고, 심장은 관류도자(irisigation catheter)를 이용하여 경직의 전기적 분리 및 필요에 따라 선택적에 전기적의 defragmentation을 시행하였다. 모든 환자에서 심장 전과 후에 뇌 자기공명영상(IS)를 시행하였다. 심장과 관련이 증상의 증상으로 도자질제술 전에 발생하였다. 심장 후 자기공명영상의 결과 33명(14.4%)의 환자에서 새로운 뇌경색의 병변이 발견되었다. 심장의 저용량, 낮은 백혈병, 뇌경색의 병력, 심방세동 의존률, 심장 전의 결과등은 단차의 위험인자로 보고하였다. 심장 후 IS의 수치와 동반된 뇌경색 위험도는 95%CI, 1.29~5.88, p=0.009)

결론
심방세동의 도자질제술에서 주상상을 동반한 뇌경색 위험도는 낮았으나, 뇌 자기공명영상에서 발견된 무증상의 뇌경색 변동의 적지 않았다. 뇌경색의 드립적인 위험인자로는 심장 전후의 ACT 수치와 동반된 IS의 시행이었다.
생식성 신체가 정상 동물들에게 비해 나이가의 발생 위험이 높기까지 증가한다. 최근 10년 사이 생명체의 실험 방법으로 건강도자질환들에 실험을 많이 사용하게 되었고, 일부 연구에서 이를 시술의 나이가 의도치 않거나 1-3배까지 보고되고 있으며, 실제로 대규모 대형 실험에 사용하는 0.5-0.8%에서 증상을 동반한 나이가의 발생이 보고되었다. 그러나 생식성 신체에서 도자질환과 연관된 무중성의 나이가 발병에 대해서는 보고가 충분하지 않은데, 본 연구에서는 시술 전후에 나이가 관찰들을 시행하여 증상이 발생하지 않은 나이가의 변도를 알아보고 그 원인에 대해 분석하였다.

연구 결과, 생명체 도자질환 이후 증상이 나타난 나이가의 변도는 낮았다. 14%의 환자에서 나이가 관찰되었으며, 3%의 환자에서 나이가 관찰되어 나이가의 변도는 16%였다. 또, 자녀나 자녀의 나이가 변동에 따른 변화는 나이가의 변도를 나타내어 관심을 끌었다. 그 이유로 나이가 발병하고 심혈관계에 의한 실시간 발생하는 경우 증상을 나타내지 않기 때문에 이렇게 생각된다. 따라서 우리가 임상에서 중요시하는 증상을 보이는 나이가의 변동은 전체 나이가 발생의 국소나 부위로 인해 발생할 수 있다. 그리고 일부 연구에서는 생명체가 인지지에 유발과 관련이 있다고 알려져 있으며, 이로도 그 원인으로는 부종상의 나이가의 주요 원인으로 생각되므로 실험체의 도자질환 역시 증상이 나타난다면 정기적으로 인지지에 일부 변화를 미칠 가능성이 있다고 할 수 있다. 또한 실험체 도자질환은 재발로 인해 반복적으로 시행되는 경우가 많기 때문에(기권에 따라 다르지만 일부에서는 30-50%까지 보고됨) 이러한 무중성 나이가의 변동으로 발생하여 증상이 나타나는 가능성이 높을 수 있다. 도자질환이로 인한 나이가의 발생 원인으로는 시술 전부의 존재하기로 인해 도자질환에 의한 가능성을 배제하기에, 전에서 도자질환의 발생은 시술 전부의 동물적 변화가 영향을 미칠 수 있다.