Efficacy of Catheter Ablation for Atrial Fibrillation in Patients with a Permanent Pacemaker for Sick Sinus Syndrome

Jin-Tao Wu¹,², Jian-Zeng Dong¹, Cai-Hua Sang¹, Ri-Bo Tang¹, Xiao-Hong Li¹ and Chang-Sheng Ma¹

Abstract

Objective To study the clinical efficacy of catheter ablation for paroxysmal atrial fibrillation (AF) in patients with a permanent pacemaker (PM) for sick sinus syndrome (SSS).

Methods Our prospectively established database of patients who underwent circumferential pulmonary vein (PV) ablation for paroxysmal AF was retrospectively reviewed. A total of 41 patients with a permanent PM for the treatment of SSS (SSS+PM group) and 123 age- and gender-matched control subjects (on a 1:3 basis) without SSS or a permanent PM (no-SSS+no-PM group) were included in this study. AF recurrence was defined as the occurrence of confirmed atrial tachyarrhythmia lasting more than 30 seconds beyond three months after catheter ablation in the absence of any antiarrhythmic treatment.

Results During a mean follow-up period of 18.3±10.6 months (range 3-30 months), 50 patients (30.5%) developed recurrence of AF. The recurrence rate was higher in the SSS+PM group than in the no-SSS+no-PM group (43.9% vs. 26.3%, p=0.011). A Cox regression analysis adjusted for age, valvular heart disease, left atrial (LA) diameter and PV isolation identified only SSS and the use of a PM together as an independent predictor of recurrence of AF (hazard ratio 2.02, 95% confidence interval 1.10-3.69, p=0.023).

Conclusion Patients with a permanent PM for SSS are at an increased risk of recurrence of AF after catheter ablation.

Key words: atrial fibrillation, catheter ablation, pacemaker, sick sinus syndrome

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Introduction

Cardiac pacing is the only effective treatment for patients with symptomatic sick sinus syndrome (SSS). Patients with SSS can be treated with any kind of commercially available pacemaker (PM) (1), such as a dual-chamber PM (DDD), single-chamber ventricular PM (VVI) or single-chamber atrial PM (AAI). Recent studies have shown that atrial fibrillation (AF) is the most frequent tachyarrhythmia in patients with a permanent PM, occurring in up to 65% of patients with a PM for the treatment of SSS (2, 3). The exact mechanisms underlying the increased incidence of AF are unknown. It has long been recognized that patients with SSS are more prone to developing AF (4, 5). In addition, multiple studies and meta-analyses have demonstrated that, in patients with SSS, cardiac pacing is associated with an increased incidence of AF (6-10).

Catheter ablation has been established to be an effective therapy for drug-refractory paroxysmal AF and is recommended as the treatment of choice for many patients, including those with a permanent PM. However, there is little information available about the clinical efficacy of catheter ablation for paroxysmal AF in SSS patients with a permanent PM. In patients with SSS and a permanent PM, most pathogenic factors for AF persist after ablation, and it is therefore
reasonable to hypothesize that patients with a permanent PM for SSS have an increased risk of recurrence of AF. This retrospective study evaluated the clinical efficacy of catheter ablation for paroxysmal AF in SSS patients with a permanent PM.

Materials and Methods

Study subjects

We reviewed the records of 1,593 consecutive patients with symptomatic paroxysmal AF refractory to at least one antiarrhythmic drug who had been prospectively entered into our database. All patients were referred to Beijing An Zhen Hospital, Capital Medical University for first-time circumferential pulmonary vein (PV) radiofrequency ablation between January 2008 and December 2012. Of the patients, 41 had undergone prior permanent PM implantation for the treatment of SSS, including 28 patients (68.3%) with a VVI PM, 11 patients (26.8%) with a DDD PM and two patients (4.9%) with an AAI PM. These patients were enrolled in the study (SSS+PM group) along with 123 age- and gender-matched patients (on a 1:3 basis) without SSS or a permanent PM (no-SSS+no-PM group). All patients provided their written informed consent, and the study protocol was approved by the local institutional review board. Transesophageal and transthoracic echocardiography were performed prior to ablation to measure the left atrial (LA) anteroposterior diameter, left ventricular (LV) end-diastolic diameter, LV end-systolic diameter and LV ejection fraction and to exclude intra-atrial thrombosis.

Electrophysiological study and catheter ablation

The ablation procedure was performed in a postabsorptive state under conscious sedation. All antiarrhythmic drugs, with the exception of amiodarone, were discontinued for at least five half-lives. We employed the technique of circumferential PV ablation guided by three-dimensional LA mapping, which has been previously described in detail (11, 12). Briefly, the left atrium was explored using a trans-septal approach. The LA geometry was reconstructed with a 3.5-mm tip ablation catheter (Navi-Star ThermoCool, Biosense-Webster, USA) in a CARTO system. Continuous irrigated radiofrequency ablation was performed along each PV antrum in order to encircle the ipsilateral PVs (target temperature: 43°C, maximum power: 35W, infusion rate: 17 mL/min). The procedural end points were the completeness of the continuous circular lesions and the electrical isolation of all PVs identified using a decapolar circumferential mapping catheter (Lasso, Biosense-Webster). If a typical atrial flutter was documented before the procedure, the tricuspid isthmus responsible for the tachycardia was identified and ablated. Following ablation, programmed stimulation of the right atrium and right ventricle was conducted separately.

Postablation management and follow-up

After the procedure, all patients received antiarrhythmic drugs if there were no contraindications or intolerance. If no recurrent atrial tachyarrhythmia occurred after two to three months, the drug treatment was discontinued. All asymptomatic patients were followed up with a 12-lead electrocardiogram and 24-hour Holter recordings at the 1st, 3rd, 6th and 12th months and every six months beyond one year after the ablation procedure. If the patient was symptomatic, then a new electrocardiogram or 24-hour Holter recording was obtained. Recurrence was defined as the occurrence of confirmed atrial tachyarrhythmia lasting more than 30 seconds beyond three months after the catheter ablation in the absence of any antiarrhythmic treatment. The diagnosis of recurrence in both groups was based on atrial tachyarrhythmia documented on electrocardiography or Holter monitor recordings, not on a PM. This means that asymptomatic recurrence of AF was not recorded in either group.

Statistical analysis

All analyses were performed using the SPSS software package version 17.0. Continuous data are presented as the mean ± standard deviation. A univariate analysis was conducted to assess the predictive value of clinical variables on AF recurrence using the unpaired independent samples t-test for continuous variables and the χ² test and Fisher’s exact test if necessary for categorical variables. A Kaplan-Meier estimation with a log-rank test was used to perform the unadjusted analysis of the impact of SSS and a PM together on the recurrence of AF. A Cox proportional hazards regression analysis was employed to examine the risk factors for recurrence. Age, valvular heart disease, LA diameter and PV isolation were adjusted in the Cox analysis. All probability values were two-sided, and a p value of less than 0.05 was considered to be significant.

Results

Patient clinical characteristics

The clinical characteristics of the patients in the SSS+PM and no-SSS+no-PM groups are shown in Table 1. The prevalence of hypertension and valvular heart disease was significantly higher in the SSS+PM group than in the no-SSS+no-PM group. The LA diameter was significantly larger in the SSS+PM group than in the no-SSS+no-PM group. Age, gender and the AF duration, LV ejection fraction, LV end-diastolic dimension and LV end-systolic dimension were not significantly different between the two groups. The prevalence of diabetes mellitus and coronary artery disease was not significantly different between the two groups. The prevalence of medication use (antiarrhythmic agents, β-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and statins) immediately before hospitalization for catheter ablation for AF was not
Table 1. Characteristics of Patients in SSS+PM and No-SSS+no-PM Groups

<table>
<thead>
<tr>
<th></th>
<th>SSS+PM(n=41)</th>
<th>No-SSS+no-PM(n=123)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64±9</td>
<td>65±9</td>
<td>0.606</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>26(63.4%)</td>
<td>78(63.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>AF duration (years)</td>
<td>7.8±5.5</td>
<td>7.3±4.7</td>
<td>0.595</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>9(22.0%)</td>
<td>18(14.6%)</td>
<td>0.274</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>20(48.9%)</td>
<td>37(30.1)</td>
<td>0.029</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>6(14.6%)</td>
<td>7(5.7%)</td>
<td>0.133</td>
</tr>
<tr>
<td>Valvular heart disease, n (%)</td>
<td>10(24.4%)</td>
<td>12(9.8%)</td>
<td>0.017</td>
</tr>
<tr>
<td>CAD, n (%)</td>
<td>6(14.6%)</td>
<td>16(13.0%)</td>
<td>0.791</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>39.5±5.1</td>
<td>37.5±5.1</td>
<td>0.032</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>49.8±5.0</td>
<td>48.3±4.9</td>
<td>0.103</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>32.8±5.1</td>
<td>32.4±4.8</td>
<td>0.646</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>59.7±10.4</td>
<td>62.1±10.3</td>
<td>0.193</td>
</tr>
<tr>
<td>No medication, n (%)</td>
<td>10 (24.4%)</td>
<td>34 (27.6%)</td>
<td></td>
</tr>
<tr>
<td>Class I, n (%)</td>
<td>8 (19.5%)</td>
<td>18 (14.6%)</td>
<td></td>
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<tr>
<td>Amiodarone, n (%)</td>
<td>23 (56.1%)</td>
<td>67 (54.4%)</td>
<td></td>
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<tr>
<td>Sotalol, n (%)</td>
<td>0</td>
<td>4 (3.3%)</td>
<td></td>
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<tr>
<td>β-blockers, n (%)</td>
<td>13 (31.7%)</td>
<td>25 (20.3%)</td>
<td>0.135</td>
</tr>
<tr>
<td>ACEI/ARB, n (%)</td>
<td>13 (31.7%)</td>
<td>34 (27.6%)</td>
<td>0.618</td>
</tr>
<tr>
<td>Statins, n (%)</td>
<td>7 (17.1%)</td>
<td>16 (13.0%)</td>
<td>0.516</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>158±42</td>
<td>155±40</td>
<td>0.668</td>
</tr>
<tr>
<td>X-ray time (min)</td>
<td>31±9</td>
<td>30±7</td>
<td>0.588</td>
</tr>
<tr>
<td>Pulmonary vein isolation, n (%)</td>
<td>39(95.1%)</td>
<td>121(98.4%)</td>
<td>0.559</td>
</tr>
<tr>
<td>Complications, n(%)</td>
<td>1(2.4%)</td>
<td>2(1.6%)</td>
<td>0.737</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation, DM: diabetes mellitus, CAD: coronary artery disease, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, ACEI: angiotensin-converting enzyme inhibitors, ARB: angiotensin receptor blockers, PM: pacemaker, SSS: sick sinus syndrome

Recurrence of atrial fibrillation in the patients with SSS and a cardiac pacemaker

During the mean follow-up period of 18.3±10.6 months (range: 3-30 months), 50 patients (30.5%) developed recurrence of AF. The recurrence rate was 43.9% in the SSS+PM group and 26.0% in the no-SSS+no-PM group (p=0.011) (Figure). The characteristics of the patients with and without recurrence are shown in Table 2. The univariate analyses found that SSS and a PM together was the only predictor of recurrence of AF. The Cox regression analysis adjusted for age, valvular heart disease, LA diameter and PV isolation identified only SSS and a PM together as an independent predictor of recurrence of AF (hazard ratio 2.02, 95% confidence interval 1.10-3.69, p=0.023)(Table 3).

Procedure outcomes and complications

There were no significant differences in the procedural time, fluoroscopy time or PV isolation rate between the SSS+PM and no-SSS+no-PM groups (Table 1). Atrioventricular node reentrant tachycardia and the atrioventricular accessory pathway were excluded in all patients in both groups based on the electrophysiological study. No adverse effects of radiofrequency on the PM function were observed during or after the ablation procedures. The complication rate was not significantly different between the SSS+PM and no-SSS+no-PM groups (2.4 vs. 1.6%, p=0.737) (Table 1).

Discussion

The main finding of the present study is that patients with a permanent PM for SSS have an increased risk of recurrence of AF after catheter ablation. It has long been recognized that SSS is associated with an...
increased risk of AF (4, 5). SSS is primarily a disease of the elderly and is presumed to be due to senescence of the sinus node and atrial muscle (1). Therefore, SSS likely reflects an underlying atrial disease that may be involved as a substrate of AF. In our study, of the 41 patients with a permanent PM for SSS, 14 (34.1%) had bradycardia and tachycardia syndrome before PM implantation. This finding also supports the results of previous studies (4, 5) showing that SSS is associated with an increased LA size (24). In the present study, the patients in the SSS+PM group had a larger LA size than those in the no-SSS+no-PM group. The LA size is associated with AF (17). A previous study (18) and a meta-analysis (10) reported that atrial pacing also increases the incidence of AF. These findings may be related to the non-physiological propagation and conduction time of atrial depolarization during atrial pacing (10). The subsequent delay in LA contraction can diminish LV filling, leading to higher atrial pressures and thus increasing the risk of AF. In addition, the electrical dispersion caused by atrial appendage pacing and scar tissue formation around the implanted atrial lead may act as a trigger for the formation of reentrant pathways, particularly in patients with atrial disease.

In patients with SSS and a PM, most of the pathogenic factors causing AF remain after ablation. It is therefore reasonable to believe that patients with a PM for SSS have a lower success rate of catheter ablation for AF. In this study, we evaluated the clinical efficacy of catheter ablation for paroxysmal AF in patients with a PM for SSS. The univariate and multivariate analyses found that SSS and a PM together were associated with recurrence of AF. Here, there exist two factors together: SSS and a PM. SSS likely reflects an underlying atrial disease, such as atrial fibrosis. Atrial fibrosis (19-21) is associated with an increased rate of recurrence of AF after catheter ablation. The presence of a PM may further contribute to the development of AF recurrence. Atrial and ventricular pacing secondary to PM implantation results in an increased LA pressure. An increased LA pressure is associated with arrhythmogenic remodeling (16) and mechano-electric feedback (22), which may promote recurrence of AF. In addition, as mentioned above, right ventricular pacing has recently been demonstrated to cause endothelial dysfunction (17). Endothelial dysfunction is an important predictor of recurrence of AF after catheter ablation (23).

Geske et al. reported that an increased LA pressure is associated with an increased LA size (24). In the present study, the patients in the SSS+PM group had a larger LA size than those in the no-SSS+no-PM group. The LA size is a well-known predictor of recurrence of AF after catheter ablation.
ablation (23, 25). However, after adjusting for the LA diameter, SSS and a PM together was identified as an independent predictor of recurrence of AF. This may be explained by the findings of a recent study (19) that showed that, while patients with a severely enlarged left atrium may be accurately identified as ‘high risk’ for AF recurrence, patients with mild-to-moderate LA enlargement exhibit a varying response to catheter ablation. Another likely explanation for this phenomenon is that when LA dilation inclines to asymmetry, the LA volume is superior to the LA diameter in predicting recurrence of AF (26, 27).

Several limitations of this study should be noted. First, two factors exist together: SSS and a PM. The relative impact of each of these factors on the recurrence of AF was not evaluated in this study. However, it is difficult to determine this information, as patients with SSS and AF usually undergo PM implantation before catheter ablation for AF, and there are virtually no patients with SSS without a PM who have undergone catheter ablation for AF to serve as controls. Second, pacing modes are associated with the incidence of AF. It has been demonstrated that VVI pacing in patients with SSS is associated with a higher incidence of AF than DDD or AAI pacing (5, 8). The pacing modes were not changed after ablation in this study. Therefore, the predominance of VVI pacing (68.3%) in our study population limits the generalizability to DDD or AAA pacing. Third, the cumulative percentages of atrial or ventricular pacing before ablation were not available for all patients in this retrospective study. Therefore, it is not clear whether there were differences in the percentages of pacing between the patients with recurrence of AF and those without; this should be corrected in future studies. Fourth, a recent post hoc analysis of the Danish multicenter randomized trial on single-lead atrial pacing versus dual-chamber pacing in patients with sick sinus syndrome (DANPACE trial) reported that a longer baseline PQ interval, but not the percentage of ventricular pacing or the programmed AV delay, is associated with an increased risk of AF in patients with SSS and dual-chamber rate modulated pacing (DDDR) (28). This study did not evaluate whether the baseline PQ interval was associated with the rate of recurrence of AF after catheter ablation in the SSS+PM group because data for the baseline PQ interval were not available for all patients. Fifth, pulmonary vein reconnection is a known cause of recurrence of AF (29, 30). The rate of pulmonary vein isolation did not differ between the SSS+PM and no-SSS+no-PM groups; however, this study did not determine whether SSS and a PM together increased the likelihood of pulmonary vein reconnection. Another limitation is that the diagnosis of recurrence was based on symptoms and ECG and Holter-ECG findings. Therefore, the rate of recurrence of AF may have been underestimated because some patients were asymptomatic. Furthermore, the patients in the SSS+PM group may have undergone more frequent ECG and Holter-ECG monitoring during follow-up, which may have increased the chance of detecting AF in the SSS+PM group compared with the no-SSS+no-PM group. Finally, the small sample size, with only 41 patients in the SSS+PM group, may have introduced statistical bias. Further studies of larger numbers of patients are needed to further evaluate the effects of SSS and a PM together on the outcomes after catheter ablation for AF.

**Conclusion**

Radiofrequency catheter ablation for AF in patients with SSS and a permanent PM is safe; however, these patients have an increased risk of recurrence of AF.

The authors state that they have no Conflict of Interest (COI).

**References**


13. Prinzen FW, Hunter WC, Wyman BT, McVeigh ER. Mapping of


