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ORIGINAL ARTICLE

Catheter ablation of paroxysmal atrial fibrillation in patients with sick sinus syndrome

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Abstract

Sick sinus syndrome (SSS) frequently coexists with atrial fibrillation (AF). The results of AF ablation in patients with SSS have not been fully evaluated. We retrospectively investigated 65 patients with paroxysmal AF (PAF) and SSS who underwent AF ablation using either radiofrequency ($n=50$) or cryoballoon ablation ($n=15$) in our institute. Forty-nine (75.4%) patients had a median of 5.6 (4.8–6.0) s of documented sinus pauses prior to the procedure (42 patients on antiarrhythmic drugs), and were observed when AF terminated in 47 patients. Successful pulmonary vein isolation was achieved in all, and substrate modification was added in 3 patients. Freedom from recurrent atrial arrhythmias after single procedures was 58.7, 45.2, and 38.9% at 1, 2, and 3 years after the initial procedure. During a 23.4 (11.1–40.7) month median follow-up and after 1.4 ± 0.6 sessions, 80.6% of patients were free from arrhythmia recurrence; however, permanent pacemaker implantations were required in 9 (13.8%) patients at a median of 5.3 (2.9–21.0) months after initial procedures. The average heart rate did not significantly differ before or a median of 2.5 (1.2–5.3) months post-procedure (76.7 ± 17.4 vs. 73.5 ± 14.6 bpm, $p=0.90$). Multivariate analyses revealed that larger left atrial diameters [odds ratio (OR) 1.21, 95% confidential interval (CI) 1.01–1.45, $p=0.042$] were independent predictor of AF recurrence, and SSS type 1 was the sole predictor of pacemaker implantations (OR 10.30, 95% CI 1.38–76.7, $p=0.023$), respectively. AF ablation obviated permanent pacemaker implantations in the majority of the patients with SSS and PAF, and SSS type 1 was a sole factor predicting pacemaker implantations.

Keywords Sick sinus syndrome · Pulmonary vein isolation · Atrial fibrillation · Catheter ablation · Pacemaker

Introduction

Atrial fibrillation (AF) frequently coexists with sick sinus syndrome (SSS), and sinus node dysfunction is manifested or worsened by the use of antiarrhythmic drugs, limiting their use [1, 2]. Although prolonged sinus pauses on AF termination are generally an indication of a permanent pacemaker implantation, the elimination of atrial arrhythmias by catheter ablation could lead to the disappearance of termination pauses [3, 4]. Therefore, the latest guidelines of AF ablation state that it is reasonable to offer AF ablation as an alternative to a pacemaker implantation in patients with bradycardia tachycardia syndrome (BTS) [5]. In the present study, we sought to (1) investigate the freedom from permanent pacemaker implantations after AF ablation in patients with SSS and paroxysmal AF, and (2) explore the clinical factors predicting the requirement of a pacemaker implantation.

Methods

Study population

This study consisted of 65 consecutive patients with documented SSS and paroxysmal AF who underwent AF ablation. No patients received a pacemaker implantation prior to the procedure. All patients had symptoms or suspected

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symptoms related to bradyarrhythmia at least once. AF was classified according to the latest guidelines [5]. SSS types 1, 2 and 3 were defined as sinus bradycardia with a heart rate of less than 50 bpm, documented episodes of sinus arrest or sinoatrial block with junctional or ventricular escape beats, and sinus pauses following the termination of the AF episodes, respectively [1]. All patients gave their written informed consent. The study protocol was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki.

Mapping and ablation protocol

All antiarrhythmic drugs were discontinued for at least five half-lives prior to the procedure. The procedure was performed under minimal or moderate sedation obtained with dexmedetomidine. A 100 IU/kg body weight of heparin was administered immediately following the venous access, and heparinized saline was additionally infused to maintain the activated clotting time at 300–350 s. In radiofrequency ablation, the left- and right-sided ipsilateral PVs were circumferentially ablated guided by a 3-D mapping system (CARTO3, Biosense Webster, Diamond Bar, CA) [6, 7]. In cryoballoon ablation, PV isolation was performed with a 28-mm second-generation cryoballoon (Arctic Front Advance, Medtronic, Minneapolis, MN) using a single 3-min freeze strategy [8]. During the repeat procedure, the previous lesion set was evaluated and consolidated first.

Follow-up

No antiarrhythmic drugs were prescribed after the procedure. The patients underwent continuous, in-hospital ECG monitoring for 2–4 days following the procedure. The first outpatient clinic visit was 3 weeks after the ablation procedure. Subsequent follow-up visits consisted of a clinical interview, ECGs, and/or 24 h Holter monitoring every 2–3 months at our cardiology clinic. Patients with palpitations were encouraged to use a patient activated event recorder for 1 month. Recurrence was defined according to the patient's symptoms, and/or if an arrhythmia lasting longer than 30 s was documented beyond a 3-month blanking period following the latest guidelines [5]. A pacemaker implantation was considered when the patients had any symptoms or suspected symptoms related to bradyarrhythmias even after the AF ablation.

Statistical analysis

Continuous data are expressed as the mean ± standard deviation for normally distributed variables or as the median (25th, 75th percentiles) for non-normally distributed variables, and were compared using a Student's *t* test or Mann–Whitney *U* test, respectively. Categorical variables were compared using the Chi square test. Parameters with a significance of <0.05 in the univariate analysis were entered into a multiple logistic regression analysis to identify the factors associated with arrhythmia recurrence and the requirement of a pacemaker implantation. A Kaplan–Meier analysis was used to determine the percentage of patients free from recurrence and pacemaker implantations. A probability value of $p<0.05$ indicated statistical significance.

Results

Patient characteristics and procedural results

The baseline patient characteristics are presented in Table 1. Twelve (18.5%) patients had sinus bradycardia with a heart rate of less than 50 bpm (type 1), and 54 (83.1%) had sinus pauses following the termination of the AF episodes (type 3) [1]. The longest pause was a median of 5.6 (4.8–6.0) s. In 42 patients, a post-termination pause manifested during antiarrhythmic drug therapy. In the index procedure, a PV isolation was successfully achieved in all patients with either radiofrequency ($n=50$) or cryoballoon ablation ($n=15$). Additional substrate modification and cavo-tricuspid isthmus ablation were performed in 3 and 24 patients, respectively. The total procedure time and fluoroscopic time were 118 (101–146) and 27 (21–36) min, respectively.

The freedom from recurrent atrial arrhythmias after a single procedure was 55.5, 49.5 and 43.3% at 1, 2, and 3 years after the initial procedure (Fig. 1a). Twenty-four, 4, and 1 patients underwent 2nd, 3rd, and 4th procedures at a median of 4.3 (2.5–9.2), 22.8 (12.9–34.6), and 45.2 months after the index procedure. PV reconnections were observed in 20/24, 1/4, and 0/1 patients during the 2nd, 3rd, and 4th procedures, respectively, and all conduction resumption were successfully eliminated. Freedom from recurrent atrial arrhythmias after the last procedure was 88.3, 85.0 and 79.3% at 1, 2, and 3 years (Fig. 1b). Antiarrhythmic drugs were prescribed in 15 (23.1%) patients at the last follow-up. Among a total of

Table 1 Characteristics of the study population

n	65
Age, year	70 (66–76)
Male, *n* (%)	45 (69.0)
LA diameter, mm	39 (34–44)
LV ejection fraction, %	67 (63–71)
SSS type 1, *n* (%)	12 (18.5)
SSS type 3, *n* (%)	54 (83.1)

AF atrial fibrillation, *LA* left atrial, *LV* left ventricular, *SSS* sick sinus syndrome

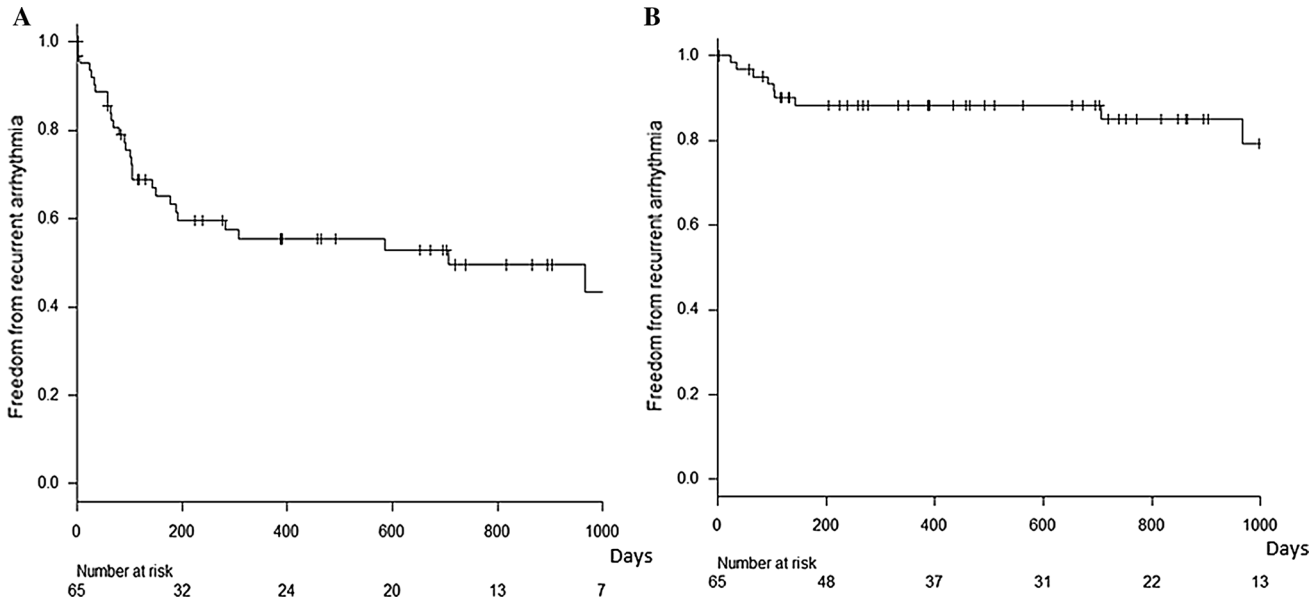

Fig. 1 The freedom from recurrent atrial arrhythmias after a single (**a**) and the last AF ablation procedure (**b**) is shown

94 ablation procedures, cardiac tamponade, right phrenic nerve injury, and pneumothorax during the subclavian vein puncture were observed in 3 (3.2%), 1 (1.1%), and 1 (1.1%) patients, respectively. A multivariate logistic regression analysis revealed that a larger left atrial diameter (odds ratio 1.21, 95% confidential interval 1.01–1.45, $p = 0.042$) was the independent predictor of an AF recurrence (Table 2).

Pacemaker implantations and the factors associated with those pacemaker implantations

Among 17 patients who underwent 24-h Holter monitoring both before and a median of 2.5 (1.2–5.3) months after the procedure, the mean heart rate did not significantly differ (76.7 ± 17.4 vs. 73.5 ± 14.6 bpm, $p = 0.90$). There was no significant difference in the heart rate change between SSS type 1 and type 3 patients (-3.7 and -3.1 bpm, $p = 0.886$). During a median of 23.4 (11.1–40.7) months of follow-up

Table 2 Predictors of arrhythmia recurrence after AF ablation

	Univariate analysis			
	Odds ratio	95% CI		*p* value
Age, year	1.04	0.93	1.17	0.451
Female	1.15	0.26	5.13	0.858
SSS type 1	1.31	0.24	7.29	0.755
Pause without antiarrhythmic drugs	0.29	0.03	2.48	0.256
Left atrial diameter, mm	1.20	1.03	1.41	0.022
Left ventricular ejection fraction, %	0.89	0.77	1.02	0.096
Cryo ablation use	0.38	0.04	3.27	0.375
Substrate modification	3.37	0.27	41.60	0.343
Early recurrence of AF	9.60	1.12	82.10	0.039
	Multivariate analysis			
	Odds ratio	95% CI		*p* value
Early recurrence of AF	5.98	0.62	57.60	0.122
Left atrial diameter, mm	1.21	1.01	1.45	0.042

AF atrial fibrillation, *CI* confidential interval, *SSS* sick sinus syndrome

period, 9 (13.8%) patients underwent permanent pacemaker implantations at a median of 5.3 (2.9–21.0) months after the index ablation procedure. Among the 9 patients who required a pacemaker implantation, 6 patients had SSS type 1 and 5 patients had drug-induced SSS at baseline, and 4 patients had arrhythmia recurrence at the time of pacemaker implantation. The freedom from a permanent pacemaker implantation at 1, 2, and 3 years from the initial procedure was 89.9, 87.0 and 77.0, respectively (Fig. 2). The patients who required a pacemaker implantation were significantly older, had lower left ventricular ejection fraction, and had more likely type 1 SSS. A multivariate logistic regression analysis revealed that type 1 SSS (odds ratio 10.30, 95% confidential interval 1.38–76.70, $p = 0.023$) was the sole independent predictor of a permanent pacemaker implantation (Table 3).

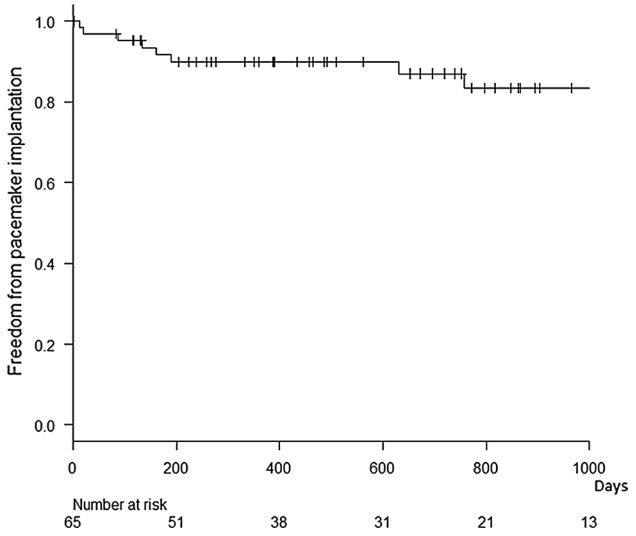

Fig. 2 The freedom from a permanent pacemaker implantation after the index AF ablation procedure is shown

Discussion

The main findings of the present study were that (1) although the single procedure AF freedom was limited, the majority of the patients were free from permanent pacemaker implantation during a median of 23.4 (11.1–40.7) months of follow-up, and (2) type 1 SSS was the sole factor predicting the requirement of a permanent pacemaker implantation even after AF ablation in the patients with SSS and paroxysmal AF.

SSS is used to define the constellation of a slow sinus rate or frank sinus arrest [1]. The patients commonly suffer from presyncope, syncope, and palpitations if it is coupled with AF. A number of etiologies have been thought to explain the occurrence of sinus node dysfunction; however, the vast majority of the patients have no identifiable causes. Pathology studies have revealed fibrous tissue

Table 3 Predictors of a permanent pacemaker implantation

	Univariate analysis			
	Odds ratio	95% CI		*p* value
Age, years	1.19	1.02	1.39	0.028
Female	3.42	0.808	14.40	0.095
SSS type 1	16.70	3.28	84.60	< 0.001
Pause without antiarrhythmic drugs	1.37	0.30	6.17	0.685
Left atrial diameter, mm	0.96	0.85	1.09	0.519
Left ventricular ejection fraction, %	0.84	0.72	0.98	0.028
Cryoballoon use	0.37	0.04	3.27	0.375
Substrate modification	3.37	0.27	41.60	0.343
Early recurrence of AF	1.21	0.29	4.97	0.796
AF recurrence after 1st session	0.92	0.22	3.80	0.912
Number of sessions ≥ 2	1.31	0.49	3.51	0.593
AF recurrence after final session	2.00	0.34	11.60	0.440
	Multivariate analysis			
	Odds ratio	95% CI		*p* value
Age, years	1.15	0.92	1.43	0.227
Left ventricular ejection fraction, %	0.90	0.76	1.06	0.205
SSS type 1	10.30	1.38	76.70	0.023

AF atrial fibrillation, *CI* confidential interval, *SSS* sick sinus syndrome

infiltration of the sinus node and surrounding area [2]. On the contrary, experimental studies have shown that sinus node dysfunction could be produced by pacing induced AF [9]. These data suggest that SSS is a phenotype and consists of diverse mechanisms. In a part of the patients, SSS is presumed to be the result of the senescence of the sinus node and likely reflects an underlying atrial disease that may be involved as a substrate of AF.

In clinical practice, pacing therapy is the sole effective treatment for patients with SSS, and placement of a permanent pacemaker is a Class 1 indication for the treatment of symptomatic SSS. Moreover, it has long been recognized that patients with SSS are more prone to developing AF [1, 2]. The clinical implication of the combination of a tachycardia and bradycardia is a limitation imposed on the use of negative chronotropic agents without the concomitant use of cardiac pacing. Thus, the use of antiarrhythmic drugs is often restricted by the risk of further worsening the bradycardia in clinical practice. Symptomatic sinus pauses on cessation of an atrial arrhythmia are also considered an indication for cardiac pacing followed by antiarrhythmic therapy to control AF [2]. Since AF ablation can eliminate or considerably reduce the AF burden, AF ablation could be a reasonable therapeutic option for BTS [3, 4, 10]. Indeed, in the present study, a permanent pacemaker implantation could be obviated in the majority of the patients with SSS. This was because of the disappearance of the AF episodes causing post-termination pauses and also because there was no need for antiarrhythmic drug therapy owing to the considerable reduction in the AF burden after the procedure. The present study results suggested that sinus pauses may be a manifestation of tachycardia-mediated remodeling of the sinus node. The incidence of an AF recurrence was relatively high in our study, which was consistent with a previous report [11], presumably because our study included patients with more advanced atrial disease. On the other hand, type 1 SSS was the significant predictor of the requirement of a pacemaker implantation. Since a prior report [12] showed that the mean heart rate significantly increased after PV isolation and continued during 1-year of follow-up, we expected that AF ablation might lead to the avoidance of a pacemaker implantation in patients with type 1 SSS. However, half of the type 1 SSS patients required a pacemaker implantation even after the AF ablation. These cases presumably had advanced sinus node remodeling regardless of the tachycardia episodes.

Study limitations

The study was a single-center non-randomized study and the population was relatively small. The sinus node function was not evaluated by an electrophysiological study.

Conclusion

The majority of the patients with SSS and paroxysmal AF may benefit from catheter ablation of AF, obviating the need for antiarrhythmic drugs and a permanent pacemaker implantation. SSS type 1 was the sole factor predicting the requirement for a pacemaker implantation. It seems to be reasonable to consider AF ablation earlier in the management of patients with BTS.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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