Suppression of Atrial Fibrillation by Atrial Pacing

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Background Atrial fibrillation (AF) is a common arrhythmia in patients with an implanted pacemaker, but the role of atrial pacing in preventing AF is still unclear.

Methods and Results Sixty-six patients (67.8 ± 12.1 years) were enrolled: 54 with sick sinus syndrome (SSS), 11 with atrioventricular blocks (AVB), and 1 with SSS and AVB. The prevalence of AF was investigated. In 22 patients with AF, the AF burden was estimated under “back-up pacing” (40–50 beats/min), then under “atrial pacing” (60–85 beats/min). The prevalence of AF in the SSS group tended to be higher than that in the AVB group (48.1% vs 18.2%, $p=0.06$). The AF burden in patients with a percentage of atrial pacing (% atrial pacing) $<50\%$ was significantly greater than that in patients with % atrial pacing $\geq 50\%$ ($12.5 \pm 21.1\%$ vs $4.2 \pm 10.3\%$, $p<0.05$). AF disappeared immediately after “atrial pacing” in 4 patients (18.2%). In 9 patients (40.9%), the AF burden decreased gradually, and AF disappeared in 6 patients (27.3%) after 207.9 ± 130.2 days.

Conclusion The prevalence of AF may be higher in patients with SSS than in those with AVB. Atrial pacing has a preventive effect on AF, and the effect of atrial pacing is not always immediate but is progressive in some patients. (Circ J 2006; 70: 1398–1401)

Key Words: Atrial fibrillation; Pacemaker; Pacing

Paroxysmal atrial fibrillation (AF) is a common arrhythmia in patients with an implanted pacemaker. Previous studies have suggested that atrial pacing in patients with sick sinus syndrome (SSS) is associated with a lower frequency of AF. Some studies have investigated the long-term effect of atrial pacing in AF suppression. Most of these studies compared physiological pacing with non-physiological pacing.^{1–3} The role of atrial pacing itself in preventing AF still remains unclear. For patients with an implanted pacemaker, atrial tachyarrhythmia detection with the implanted pacemaker is useful. However, atrial far-field oversensing from the ventricle is one of the greatest problems in the automatic interpretation of memory functions in DDD pacemakers.⁴ In many studies of AF suppression using pacing, far-field oversensing was not excluded. We examined the prevalence of AF in SSS and atrioventricular block (AVB), and the beneficial effect of atrial pacing itself, compared with “back-up pacing”, not with ventricular pacing. Moreover, we investigated the long-term effect of continued atrial pacing in AF suppression.

Methods

Patients

Between May 1998 and July 2002, 67 patients who underwent implantation of a dual-chamber pacemaker (Vitatron, Selection®, Dieren, NL) for bradycardia were

recruited. Far-field R wave oversensing was observed in 7 patients. In 6 patients, it could be avoided by changing the pacemaker's programming. They were subsequently included in the present study. However, one patient, in whom far-field oversensing could not be avoided, was excluded. Thus, 66 patients, of which 33 were male, with a mean age of 67.8 ± 12.1 years, were enrolled after giving informed consent. The indication for pacing was SSS in 54 patients, AVB in 11 and SSS with AVB in one. Although some patients were taking antiarrhythmic agents during the study period, the drugs all patients were already receiving were left unchanged.

Study Protocol

We investigated the prevalence of AF in all patients during the 28 days immediately after implantation. Twenty-two (21 with SSS, 1 with AVB) had paroxysmal AF. The pacemakers were programmed for “back-up pacing” (40–50 beats/min) at first. Subsequently, the pacemakers were programmed for “atrial pacing” (60–85 beats/min). The follow-up period for each program was 3 months. The AF burden (%) was estimated under “back-up pacing” (40–50 beats/min) and “atrial pacing” (60–85 beats/min). Afterwards, all patients were left with their pacemaker programmed to “atrial pacing”. The AF burden (%) was followed continuously in these patients. The follow-up time was more than 15 months. The AF burden (%) was calculated as the proportion of the total duration of AF detected during the follow-up period.

Statistical Analysis

The values are given as mean $\pm$ standard deviation. Data were compared using Student's t-test. A p value <0.05 was considered significant.

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Fig 1. Percentage atrial pacing under “atrial pacing” was significantly higher than that under “back-up pacing” ($67.3 \pm 32.1\%$ vs $10.8 \pm 20.7\%$, $p < 0.001$).

Fig 2. Atrial fibrillation (AF) burden in patients with % atrial pacing $< 50\%$ was significantly greater than that in patients with % atrial pacing $\geq 50\%$ ($12.5 \pm 21.1\%$ vs $4.2 \pm 10.3\%$, $p < 0.05$).

Fig 3. Time course changes in atrial fibrillation (AF) burden after physiological pacing. In 4 cases, AF slowly decreased and disappeared at a maximum of 390 days after starting atrial pacing. In 2 cases, AF did not disappear; however, the AF burden (%) continued to decrease 450 days after starting atrial pacing.

Results

Prevalence of AF

The prevalence of AF during the 28 days after enrollment tended to be higher in the SSS group than in the AVB group (48.1% (26/54) vs 18.2% (2/11), $p = 0.06$).

AF Burden

The pacing % under “atrial pacing” was significantly higher than that under “back-up pacing” ($67.3 \pm 32.1\%$ vs $10.8 \pm 20.7\%$, $p < 0.001$) (Fig 1). Of the patients who had AF, the AF burden in those with an atrial pacing (%) percentage of $< 50\%$ was significantly greater than that in those with % atrial pacing $\geq 50\%$ ($12.5 \pm 21.1\%$ vs $4.2 \pm 10.3\%$, $p < 0.05$) (Fig 2).

AF Suppression by Atrial Pacing

AF disappeared immediately after “atrial pacing” in 4 of the 22 patients (18.2%). In 9 patients (40.9%), the AF burden decreased to less than 50% in 174.3 ± 155.3 days, and AF completely disappeared in 6 of them (27.3%) in 207.9 ± 130.2 days.

Long-Term Effect of Atrial Pacing

In 4 cases, the AF burden slowly decreased and disappeared, the longest interval after which AF disappeared was 390 days from starting atrial pacing. In 2 cases, AF did not disappear, but the AF burden (%) decreased by less than half and still continued to decrease 450 days after starting atrial pacing (Fig 3).

Discussion

The first major finding in the present study was that the prevalence of AF tended to be higher in SSS patients than in AVB patients. Second, atrial pacing in patients with a % atrial pacing of more than 50% had a preventive effect on AF. The preventive effect of atrial pacing on AF did not always seem to be immediate; it was progressive in some patients.

In present study, AF tended to be more prevalent with SSS patients than AVB patients. A previous report on the histological findings of SSS demonstrated that the atrium was likely to consist of fibrosis or fatty infiltration.⁵ A recent study has demonstrated that atrial fibrosis can provide a pathophysiologic substrate for AF, which results in increased conduction heterogeneity associated with the inducibility of AF.⁶ Therefore, it is of concern that SSS patients with fibrosis in the atrium have substrate for AF. It is likely to induce the occurrence and maintenance of AF. A previous study showed that the prevalence of supra-ventricular arrhythmias was higher, but not significantly, in AVB than in sinus node disease and sinus node disease with AVB;⁷ however, far-field oversensing was not excluded in the previous study. When we interpret the Holter memory in an implanted pacemaker, we should distinguish far-field oversensing from atrial high rate episodes. Some studies have reported the incidence of far-field oversensing. It was reported that the incidence of inappropriate mode switching caused by atrial preventricular oversensing related to near-field P wave or far-field R wave oversensing in a dual chamber pacemaker is up to 10%.^{4,8} Therefore, atrial far-field oversensing from the ventricle is one of the greatest problems in the evaluation of atrial pacing for the prevention of AF. We examined the prevalence of AF in SSS and AVB, after excluding far-field oversensing.

High atrial pacing (%) was associated with a reduction in the AF burden (%). Previous studies suggested that atrial pacing may have a preventive effect on AF. However, most of them compared physiological pacing with non-physiological pacing. Physiological pacing can be performed using 2 methods; single chamber atrial pacing and dual chamber pacing. One study showed that single chamber atrial pacing was associated with a lower frequency of AF, though not significant, than single chamber ventricular pacing in patients who had SSS for 3 years.¹ Moreover, a study with extended follow-up period of up to 8 years showed a beneficial effect from atrial pacing on the incidence of AF.⁹ In a prospective randomized study that examined the risk of AF, dual chamber pacing significantly decreased the risk of AF compared to single chamber ventricular pacing in patients with sinus node dysfunction.³ In those studies, the effect of atrial or dual chamber pacing was often compared to that of ventricular pacing. However, it has been reported that ventricular pacing is associated with cardiac function abnormalities and enlargement of the left atrium. Ventricular pacing might cause a proarrhythmic effect due to impaired ventricular function and atrial stretch from valvular regurgitation.^{10–12} Therefore, the effect of atrial pacing alone for preventing AF in patients with symptomatic bradycardia still remains unclear. It is important that we investigate the preventive effect of atrial pacing compared with no pacing on the occurrence or frequency of AF. Some previous studies examined whether physiological pacing would prevent AF when compared with no pacing.¹³ In one study, it was demonstrated that

physiological pacing prevented AF compared to no pacing.¹⁴ On the other hand, another study failed to demonstrate that physiological pacing prevented AF compared to no pacing in patients with frequent paroxysmal AF. However, there was no symptomatic bradycardia in the study population.¹⁵ The % atrial pacing may be low in such a situation. Physiological pacing cannot be performed sufficiently using the usual pacemaker settings with a base rate of 60 beats/min in patients without bradycardia. The role of physiological pacing in preventing AF may not be significant in patients without symptomatic bradycardia. In such a study population, the % atrial pacing should be low. On the other hand, in a study examining the benefit of atrial overdrive pacing in the prevention of AF in patients with SSS, there was no significant benefit of atrial overdrive pacing when compared to atrial pacing with a base rate of 60 beats/min.¹⁶ However, there was no significant difference in the % atrial pacing between the 2 groups. The % atrial pacing with a base rate of 60 beats/min was $60 \pm 26\%$ and that with atrial overdrive pacing was $72 \pm 7\%$. We consider that the total duration of atrial pacing is important in obtaining a beneficial effect in the prevention of AF. We investigated the effect of atrial pacing, not compared with ventricular pacing, in relation to % atrial pacing, and there was a significant difference between AF burden with % atrial pacing $<50\%$ and that with % atrial pacing $\geq 50\%$. Moreover, we investigated the long-term effect of continued atrial pacing for AF suppression. No study has investigated the disappearance of AF using atrial pacing in the long term. Our findings suggest that atrial pacing is effective in AF suppression, and the benefits can appear immediately or gradually. Some recent clinical and experimental studies have shown that AF alters the electrical and mechanical remodeling of the atrium, which results in the maintenance and recurrence of AF.^{17,18} In the study of an experimental model of AF, it was reported that reverse remodeling of atrial electrical properties following conversion to AF occurred.¹⁹ In humans, the AF cycle length as a measure of atrial refractoriness and the shortest coupling interval of atrial premature beats as a separate measure of atrial refractoriness were examined before the initial cardioversion and at the time of the first AF recurrence to investigate the reversibility of atrial electrical remodeling.²⁰ It was shown that the changes in atrial electrophysiology associated with chronic AF were reversible after cardioversion and that the extent of this reversal was dependent on the duration of sinus rhythm after cardioversion. There are some reports about atrial mechanical remodeling. The maintenance sinus rhythm using cardioversion with implantable atrial defibrillator reduced the total burden of AF and the left atrial size. That is, it was shown that maintaining sinus rhythm caused a reversed atrial mechanical remodeling in the patients with persistent AF.²¹ Furthermore, in another study, it was reported that the recovery of left atrial mechanical function was related to the duration of AF before chemical or direct current cardioversion.²² From the results of these reports, prompt cardioversion of AF reduces AF burden and reverses atrial remodeling, and prevents subsequent AF recurrence. In present study, AF disappeared in the long term after the implantation of pacemaker in some patients. The mechanism of the progressive role in the suppression of AF using atrial pacing may be similar to the mechanism of maintaining of sinus rhythm using repetitious cardioversion. The maintenance of sinus rhythm using atrial pacing may also cause reverse atrial remodeling of the electrophysiological and mechani-

cal properties, and result in reduction of AF burden.

In conclusion, the prevalence of AF is higher in SSS patients than in AVB patients. Atrial pacing has a preventive effect on AF, and the preventive effect is not always immediate but is progressive in some patients.

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