Evaluation of Bi-Atrial Pacing and Single Site Right Atrial Pacing for the Prevention of Atrial Fibrillation

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Atrial resynchronization resulting from simultaneous pacing of the atria may adjust inter- or intra-atrial asynchrony and prevent atrial fibrillation (AF). The purpose of this study was to assess the efficacy of bi-atrial pacing (BAP) in preventing AF, and the safety of this system. The effect of BAP was compared with single site right atrial pacing (RAP) in 6 patients with sick sinus syndrome and paroxysmal AF in a prospective switchover trial. P wave duration was significantly reduced during BAP (p<0.01). Pacing threshold, atrial wave amplitude and the lead impedance presented no significant differences at implant, 1 week and 3 months after implantation, respectively (NS). The number of AF episodes significantly decreased during both RAP and BAP compared with the control (p<0.01). Although the number of premature atrial contractions was significantly less during BAP than RAP (p<0.05), there were no significant differences of AF episodes between the two. The percentage of pacing was achieved in only 70% during both pacing modes. BAP was safe and reliable in this follow-up period and can prevent AF. These findings provide encouragement for further study and observation of BAP to prevent AF.
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Key Words: Atrial fibrillation; Bi-atrial pacing; Coronary sinus; Prophylactic effect

Atrial fibrillation (AF) is the most commonly occurring arrhythmia with an incidence that increases 2-fold with every decade after 55 years of age. It is also associated with a 2-fold increase in cardiac mortality and is a major contributor to stroke. The antiarrhythmic drug therapy for the prevention of AF is limited and has adverse effects when used chronically. Pacing therapy is a promising new alternative non-pharmacological therapy for the prevention of AF.

Although retrospective studies have demonstrated that atrial pacing reduced the incidences of AF by preventing pauses in patients with bradycardia, single site right atrial pacing (RAP) does not prevent AF in patients without symptomatic bradycardia. Inter- or intra-atrial conduction delays are associated with a high incidence of AF, so permanent atrial resynchronization resulting from simultaneous pacing of both the atria may adjust the inter- or intra-atrial asynchrony and prevent AF. However, multi-site atrial pacing, such as bi-atrial pacing (BAP) and dual-site right atrial pacing (DAP) is a novel concept for the prevention of AF recurrence, so the efficacy of this method is still under investigation. There are few prospective controlled studies to support the benefit of permanent atrial pacing, so we performed a prospective switchover trial that compared the preventive effect of BAP with that of RAP for AF, as well as the safety and reliability of this new pacing manner.

Methods

Patient Selection (Table 1)
Six patients with sick sinus syndrome and paroxysmal AF were enrolled (5 females, 1 male; age range, 72–89 years). All patients fulfilled the following criteria: (1) symptomatic drug refractory AF; (2) more than one episode of AF in the week before enrollment; (3) pacemaker implantation was required because of coexisting bradycardia; and (4) written informed consent for implantation of the pacemaker and 2 atrial leads was given. The protocol and the device implantation was approved by the ethical committee of Toho University Ohashi Hospital.

Study Design
Patients were evaluated for arrhythmia events for 1 week before device implantation by monitor recording, 12-lead electrocardiogram (ECG), 24-h Holter ambulatory monitoring and clinical symptoms. Next, 6 consecutive patients underwent pacemaker implantation with 2 atrial leads, one in the right atrial appendage (Medtronic model 5554) and the other in the coronary sinus (CS) (Medtronic model 2188), and one ventricular lead (Medtronic model 5054) if necessary (Fig 1). The Medtronic model 2188 lead is a bipolar pacing electrode without tines at the distal end and is specifically designed to perform permanent left atrial pacing over the CS. The tip electrode is first canted at 45° in the distal part of the lead to ensure close contact with the CS wall and then the distal end is preshaped into another 45° angle to facilitate catheterization of the CS ostium and to optimize positioning in the CS (Fig 2). The 2 atrial leads were connected by a Y-adapter (Medtronic model 5866-38M) and inserted into the atrial port of the device (Medtronic kappa DR731 or SR701). The right atrial lead

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was connected to the cathode port of the Y-adapter, and the CS lead to the anode. In this system, simultaneous BAP was achieved in a bipolar fashion and RAP in a unipolar fashion (Fig 2). Patients entered the trial 1 month after pacemaker implantation. During the first 3 months, the pacemaker was set to BAP, then switched to RAP for the next 3 months. The set rate was programmed to 70–80 beats/min with the intention of acquiring almost complete pacing. Pacing amplitude was set to 3 times the diastolic threshold. If the threshold was high, the pulse width was lengthened instead of increasing the pulse amplitude. Antiarrhythmic drug therapy was continued if the patient had taken it prior to pacemaker implantation. To evaluate the safety and reliability of this new pacing method, the pacing threshold, sensing amplitude and lead impedance were measured at implantation, and 1 week and 3 months after implantation. The pacing threshold of the CS was defined as the pacing output just when the sudden change of P wave configuration or the loss of capture without the change of P wave configuration was seen when decreasing the pacing output gradually. The effect of the pacing on the atrial conduction was compared among the controls, during BAP and during RAP by measuring the P wave duration of lead II recorded at 50 mm/s. Also to clarify the preventive effect for atrial arrhythmia, the number of AF episodes and premature atrial contractions (PAC) were compared during both BAP and RAP. The episodes of AF were counted according to the clinical symptoms, 12-lead ECG, 24-h Holter ambulatory recording and the store of events in the device.
Data are presented as the mean ± SD. Data within a group were first compared by one-way ANOVA and then by the t-test with the Bonferroni correction. A p value less than 0.05 was considered statistically significant.

Results

Device Parameters (Table 2)
The pacing thresholds of the right atrium measured in a unipolar fashion were 0.4±0.2, 0.5±0.2 and 0.6±0.1 V (0.5 ms) at implant, 1 week and 3 months after implantation, respectively (NS). The pacing threshold of the CS measured in a bipolar fashion were 2.2±1.7, 2.1±1.6 and 3.5±2.5 V (0.5 ms), respectively (NS). Sensing amplitudes measured by bipolar recording between the right atrium and CS were 4.6±3.5, 5.3±2.5 and 5.5±2.3 mV, respectively (NS). Lead impedances measured in a bipolar fashion were 968±295, 1,019±241 and 972±182 Ω, respectively (NS). The percentage of pacing was only achieved 71±11% during BAP, and
67±20% during RAP (NS) even though the pacing rate was set high to almost 70–80 beats/min.

Effect of Pacing on Atrial Conduction Time
The P wave duration decreased significantly during BAP (0.08±0.01 s) compared with the control (0.14±0.02 s) and during RAP (0.13±0.03 s) (p<0.01) (Table 1, Fig 3).

Efficacy of Pacing on AF Prevention
Table 3 shows the number of PAC and AF episodes among the control, RAP and BAP groups. The number of PAC was significantly reduced during BAP compared with the control (p<0.05). There was a tendency for the number of PAC to be less during BAP than during RAP, but not significantly. Also, the number of AF episodes was less during both BAP and RAP than in the control (p<0.01), but not significantly.

Case Presentation
An AF episode was documented in the monitor recording of one patient 2 days after pacemaker implantation and was followed by a PAC. The configuration of the P wave varied beat to beat just before and after the AF episode, which indicated the loss of CS capture (Fig 4). The CS threshold increased to a high level (approximately 5–6 V), so we had to reposition the CS lead.

Discussion
There were several reports concerning the preventive efficacy of a pacing method for AF. Delfaut et al7 and Fan et al8 reported that BAP significantly reduced AF occurrence after open-heart surgery, although Greenberg et al9 and Edward et al10 reported no significant difference in AF prevention between BAP and RAP. However, those reports were comparisons of each pacing method just after open-heart surgery, and the follow-up periods were short.

In contrast, Saksena et al11 reported excellent efficacy of DAP compared with RAP, and D’Allonnes et al12 also reported long-term favorable effects of BAP for AF prevention, but theirs was not a comparison between BAP and RAP in the same patient. In the present prospective switchover trial, a prevention of AF was equally observed during both BAP and RAP, and the number of PAC episodes was also decreased during both pacing methods. Although the AF episodes and the number of PAC were less during BAP compared with RAP, there were no significant differences between the two.

There are several mechanisms whereby pacing prevents AF. One is to control the heart rate regularity, which reduces the bradycardia-dependent refractoriness dispersion13. The second is to suppress the occurrence of PAC, which trigger AF by overdrive pacing. The third is to prevent the pauses so as to avoid the long–short or short–long–short cycle phenomenon that promotes arrhythmogenic circumstances. However, although these 3 mechanisms are obtained with RAP, there is no evidence that RAP prevents AF in patients without bradycardia. On the other hand, BAP or DAP may prevent AF by different mechanisms. It is well known that in patient with AF, there is an inter- or intra-atrial conduction disturbance and BAP or DAP can re-synchronize these conduction disturbances, which may reduce the refractoriness dispersion and prevent macro-reentry. In our study, the atrial conduction disturbances were judged by the P wave duration on the 12-lead ECG and according to this the P wave duration ranged from 0.12 to 0.16 s (mean 0.14±0.02 s), then decreased significantly in all patients during BAP compared with the control or RAP, which might contribute to the favorable effect of BAP on the prevention of PAC and AF.

The main reason for the lack of significant differences in the prevention of AF between BAP and RAP may be attributed to the fact that in both pacing methods we could not achieve almost complete pacing even though the pacing rate was set to high. We did not use specific pacing algorithms permitting permanent atrial resynchronization, neither in paced cycles nor in spontaneous rhythm. Therefore, using a specifically designed algorithm to achieve almost complete pacing would enable an even better preventive effect to be obtained.

Study Limitations
In our study, the AF episodes were judged using a 12-lead ECG, 24-h ambulatory Holter recording, the store of events recorded on the device and the clinical symptoms. Therefore, we might have missed asymptomatic AF episodes.

Second, we performed a prospective comparison between BAP and RAP, but all the patients started BAP first, and RAP second, so we cannot rule out the effect of electrical remodeling by pacing the effective method constantly. Wijffels et al14 reported that treatment that effectively prevented arrhythmia recurrence promoted an electrical remodeling that subsequently enhanced the preventive effect of the original treatment. If this hypothesis is applied to pacing therapy, BAP might affect the favorable effect of RAP on AF prevention, so for a future study the patients should be randomized and compared with either BAP or RAP as the first pacing method.

Third, the P wave duration was shortened during BAP in all of the 6 patients, which showed its favorable effects on the inter- or intra-atrial conduction, but there were no significant differences during spontaneous rhythm. Also, there were no patients who had a remarkably long P wave duration. Therefore, we need to compare the relationship between AF prevention and the improvement of P wave duration during BAP in more patients.

Conclusion
Not only BAP but also RAP can prevent AF in patients with sick sinus syndrome. Further observation is required of these 2 pacing methods to assess their overall preventative effect and in addition, a new algorithm to achieve almost complete pacing is required to enhance the outcome.

References


