Effects of Right Atrial Pacing Preference in Prevention of Paroxysmal Atrial Fibrillation

Atrial Pacing Preference Study (APP Study)

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Background Several preliminary studies have indicated that atrial pacing can prevent atrial tachyarrhythmias. The suggested mechanisms by which pacing may be effective include suppression of premature atrial beats.

Methods and Results The Atrial Pacing Preference™ (APP; Guidant, St Paul, MN, USA) algorithm allows the pacemaker to maintain a pacing rate slightly higher than the sinus rate. The preventive effects of APP on paroxysmal atrial fibrillation (AF) were studied in 51 patients (70±11 years). Nine patients did not complete the protocol. The pacemaker was programmed in random order to APP off and APP on at 3 different settings (ie, 8, 16 and 32 cycles) for 4 weeks each, using a cross-over design. Percentage atrial pacing was lower in APP off than at the other settings. Premature beat counts were greater in APP off than at the other settings. There was a significant difference in mode switch episode counts between APP off and the most effective setting (3,818±15,356 vs 596±1,719; p<0.01).

Conclusions The APP algorithm is a promising method for preventing atrial tachyarrhythmia in patients with an implanted pacemaker and AF. Optimizing the setting of the APP algorithm is an important issue in the prevention of AF. (Circ J 2008; 72: 700–704)

Key Words: Atrial fibrillation; Overdrive pacing; Pacemaker; Pacemaker algorithm
Effect of Atrial Pacing Preference

APP maximum pacing rate. When a PAC is detected, the APP algorithm does not change the V–A interval. PAC was defined by a spontaneous atrial sense interval <750 ms and an adjacent atrial sense interval shortened by 25% or less. As a result, a high percentage of atrial pacing is achieved. The pacemaker Holter monitor was reset before each study period and interrogated at the end of a 1-month pacing period to assess the number and total duration of AF episodes. The pacemaker was programmed in random order to APP off (setting a) and APP with 3 different search interval settings (ie, 8 cycles for setting b, 16 cycles for setting c, and 32 cycles for setting d) for 4 weeks each, using a cross-over design.

A total of 51 patients participated. The indications for pacing were atrio-ventricular block in 4 patients, and SSS in 47 patients. The pacemaker and algorithm programming settings for the patients included in the analysis are shown in Table 1. The pacemaker was programmed in random order to APP off (setting a) and APP on with 3 different search interval settings (ie, 8 cycles at setting b, 16 cycles at setting c, and 32 cycles at setting d) for 4 weeks each, using a cross-over design. The overall design is shown in Fig 1.

Table 1 Programmed Parameters

<table>
<thead>
<tr>
<th>Setting</th>
<th>Basic setting only</th>
<th>APP search interval 8 cycles</th>
<th>APP search interval 16 cycles</th>
<th>APP search interval 32 cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Basic setting only</td>
<td>APP search interval 8 cycles</td>
<td>APP search interval 16 cycles</td>
<td>APP search interval 32 cycles</td>
</tr>
<tr>
<td>b</td>
<td>Basic setting + APP</td>
<td>APP search interval 16 cycles</td>
<td>APP search interval 32 cycles</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>Basic setting + APP</td>
<td>APP search interval 16 cycles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>Basic setting + APP</td>
<td>APP search interval 32 cycles</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AV, atrio ventricular; ATR, atrial tachycardia response; APP, atrial pacing preference.

Comparing APP off with APP on, atrial pacing percentage was lower in APP off (setting a) than in any of the APP on settings (ie, settings b, c and d) (45.6±30.7 vs 86.8±16.7, p<0.01, 86.6±20.3, p<0.01; 86.2±21.3, p<0.01 for each setting, respectively).

Statistical Analysis

Baseline descriptive statistical data are presented as the mean±SD. Differences between groups were evaluated using Friedman or non-parametric tests, Wilcoxon or Mann–Whitney’s U-test.

Results

Forty-two patients completed the 5-month follow up (mean age, 70±11 years; 17 men). Nine patients did not complete the protocol. The reasons for withdrawal from the study were persistent AF in 4 cases, far-field sensing in 4 cases, and 1 patient decided to discontinue. No major adverse clinical events were observed. Antiarrhythmic therapy included sodium channel blockers in 13 patients, potassium channel blockers in 5 patients, β-blocking agents in 4 patients, calcium channel blockers in 2 patients, and digitalis in 7 patients. Comparing APP off with APP on, atrial pacing percentage was lower in APP off (setting a) than in the APP on settings (ie, settings b, c and d) (45.6±30.7 vs 86.8±16.7, p<0.01; 86.6±20.3, p<0.01; 86.2±21.3, p<0.01 for each setting, respectively; Fig 2).

Ventricular pacing percentage was 88% in setting a, and more than 94% in each of settings b, c, and d. There was no
significant difference of ventricular pacing percentage in each setting. Premature beat counts were greater in atrial pacing preference (APP) off (setting a) than in the APP on settings (i.e., settings b, c and d) (72,034±157,237 vs 40,507±89,714, p<0.01; 39,363±99,668, p<0.01; 41,380±104,381, p<0.01 for each setting, respectively).

Fig. 3. Comparison of number of premature atrial contraction among 4 settings. Premature beat counts were greater in atrial pacing preference (APP) off (setting a) than in the APP on settings (i.e., settings b, c and d) (72,034±157,237 vs 40,507±89,714, p<0.01; 39,363±99,668, p<0.01; 41,380±104,381, p<0.01 for each setting, respectively). (Fig 3)

Fig. 4. Comparison of number of atrial tachyarrhythmia response among 4 settings. The number of atrial tachyarrhythmias tended to be reduced by atrial pacing preference on, but the reduction did not reach statistical significance (setting a: 3,720±15,006; setting b: 1,382±3,823; setting c: 1,653±3,564; setting d: 1,644±3,926). (Fig 4)

Discussion

We considered that the optimal APP search interval setting would be different for each patient. We compared APP off with the most effective APP search interval setting. There was a significant difference in mode switch episode counts between APP off and the most effective setting (3,818±15,356 vs 596±1,719; p<0.01). ATR total time corresponds approximately to AF burden. However, ATR is not specific for AF because it may occur after a few premature atrial beats or as the result of far-field sensing. Therefore, all recordings from the event recorders were analyzed manually. We examined electrograms and ruled out ATR events by far-field sensing. AF is associated with significant morbidity and mortality. It is found to be a risk factor for death independent of other cardiovascular conditions. There are several mechanisms for the development of AF. The Pacemaker Selection in the Elderly (PASE) trial has reported that AF is not affected significantly by pacing mode or the indication for pacing (SSS vs atrioventricular block). In contrast, the Canadian Trial of Physiological Pacing (CTOPP) showed a significant reduction in AF with physiological pacing. The differences in outcome between these studies might be attributable to differences in design. Atrial pacing could reduce AF by pre-
venting the changes in refractoriness caused by pauses or bradycardia, reducing intra-atrial conduction time, reducing dispersion of atrial refractoriness or reducing atrial ectopy. The results of many prospective and retrospective studies have shown significant antiarrhythmic effects. Nonetheless, some patients require relatively faster atrial pacing at a rate of 90 beats/min, which may be poorly tolerated on a long-term basis. Basic rate programming does not usually allow atrial pacing percentages higher than 80%. When a preventive effect on AF is expected by overdrive pacing, a high pacing percentage is needed. The role of a true overdrive atrial pacing algorithm was first evaluated by Murgatroyd et al, who found that the APP algorithm provides additional benefit. This algorithm allows the pacemaker to maintain a pacing rate slightly higher than the sinus rate. As a result, a high percentage of atrial pacing is achieved. The APP algorithm has been developed to perform continuous atrial overdrive pacing so that pacing percentages greater than 85% can be obtained. A high percentage of atrial pacing is important to produce a clinical effect. No major adverse effects were observed.

In the current study, the total duration of atrial tachyarrhythmia tended to be reduced by APP, but the reduction did not reach statistical significance during 4 settings (ie, APP off and APP on with 3 different search intervals). We hypothesized that the optimal APP search interval setting was different for each patient, and then compared APP off with the most effective search interval setting in each individual. The total duration of atrial tachyarrhythmia was reduced significantly by the most effective APP search interval setting. It is not yet apparent as to how to decide the optimal overdrive setting. The arrival time interval to basic sinus rate may be different for each person. The APP search interval setting may influence the effect of APP, so the most effective APP search interval setting should be selected.

Conclusions

The results of this prospective clinical trial show that the APP algorithm is safe in patients with paroxysmal AF. The APP algorithm is a promising method for preventing atrial tachyarrhythmia in patients with an implanted pacemaker and AF. The optimal APP search interval setting is an important issue in the prevention of AF.

References