Right atrial overdrive pacing does not prevent atrial fibrillation after coronary artery bypass surgery


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Abstract
The purpose of this prospective randomized study was to investigate the efficacy of atrial overdrive pacing (AOP) and bradycardia prevention pacing (BPP) in the prophylaxis of atrial fibrillation (AF) after coronary artery bypass surgery (CABG).

Methods
One hundred and twenty-four on-pump CABG patients were randomized into three groups: AOP, BPP, and NP (no pacing). AOP patients were paced via epicardial wires using an atrial preference pacing algorithm, and BPP patients were paced in the AAI mode with a base rate of 60/min. Patients were paced for 48 h starting on the first postoperative day. The endpoint of the study was the first onset of AF lasting longer than 5 min.

Results
Preoperative risk factors and surgical data of patients did not differ between the AOP, BPP and NP groups. Pacing was technically successful in 80.5% of patients in the AOP and in 92.7% in the BPP groups. The incidence of AF in the AOP (26.8%), BPP (19.5%) and NP (28.6%) groups did not differ significantly. In the AOP group, AF in three patients was probably induced by inappropriate pacing due to sensing failure.

Conclusions
Atrial overdrive pacing and bradycardia prevention pacing were not effective in the prevention of AF after CABG.

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia to occur after coronary artery bypass grafting (CABG). Incidences ranging from 20% to 40% have been reported, with a peak occurring between the second and fourth postoperative days [1–4]. AF is associated with postoperative complications, including increased risk of stroke, gastrointestinal complications, patient discomfort, and need for additional treatment, as well as prolonged hospital stay and increased costs [4–6].

Atrial pacing has been studied for the prophylaxis of AF after CABG. The trials, however, have used different pacing algorithms and pacing sites, and the results of the studies are conflicting [7–17]. Two studies [10,11] evaluated the efficacy of atrial overdrive pacing algorithms in the prevention of postoperative AF but their results were divergent.

This prospective controlled trial studied the effects of atrial overdrive pacing (AOP) and bradycardia prevention pacing (BPP) algorithms in the prevention of AF after CABG.

Methods

The study protocol was approved by the Kuopio University Ethical Committee, and all patients gave informed consent. From September 2002 to November 2003, 124 patients (non-consecutive) who were scheduled to undergo first isolated (no accompanying procedures) on-pump CABG were enrolled into the study. Patients were excluded from the study if they had a history of AF or atrial flutter paroxysms, and if they used other antiarrhythmic medication than beta-blockers. Patients were excluded if they had to stay in the intensive care unit longer than the first postoperative day. Patients were also excluded if they had AF occurrence during the first 24 h after the operation before randomization and commencement of the pacing protocols.

Patients underwent CABG on standard cardiopulmonary bypass, and antegrade cold crystalloid cardioplegia was used. Epicardial temporary pacing wires (Ethicon Inc., Somerville, New Jersey) were sutured to the epicardium of the right atrium, one near the site of the sinus node and the other on the lateral wall of the right atrium, 2 cm apart. In the first postoperative morning patients were randomly assigned to one of the three groups: (AOP), (BPP), or no atrial pacing (NP). Treatment allocations were sealed in numbered envelopes in a blinded randomized manner. Each enrolled subject was assigned to a treatment or the control group according to the allocation designated in the next envelope opened in sequence. In the AOP group, a specific algorithm, as described by Blommaert et al. [10], was used. A pacemaker (Medtronic AT500, Medtronic Inc., Minneapolis, USA) was connected to the atrial wires and paced in AAI mode with a base rate of 60/min. When a spontaneous beat was sensed, the algorithm increased the heart rate by shortening its escape interval by 50 ms. The pacemaker then gradually decreased the interval by 5 ms per stimulus, reducing the heart rate until a new spontaneous beat was detected. In the BPP group, the pacemaker was connected to the atrial wires and paced in AAI mode with a rate of 60/min. In both the pacing groups, the sensitivity was set to 0.15 mV and output to 6.0 V/1.0 ms.

In accordance with the randomization protocol, pacing was started on the first postoperative morning (ca. 24 h after the operation) and continued for 48 h or until the first occurrence of AF (i.e. pacing was discontinued 72 h after the operation unless the occurrence of AF). All patients were on beta-blockers. Metoprolol was given orally from the first postoperative morning, with the dosage titrated according to the heart rate. The target heart rate was 60–90/min. ECG was continuously recorded during the study period. The ECG data were stored for 24 h and reviewed off-line on a daily basis.

The endpoint of the study was the occurrence of AF lasting longer than 5 min or the completion of the 48 h pacing protocol. After the first episode of AF, atrial pacing was discontinued.

All continuous variables were expressed as mean ± standard deviation (SD). Data were primarily analyzed on the basis of intention-to-treat, and also on an on-treatment basis. Continuous variables were compared by means of the Kruskall–Wallis test. Categorized variables were analyzed with the Pearson chi-square test. *P* < 0.05 was considered statistically significant. All the statistical procedures were performed with the SPSS 9.0 statistical package (SPSS Inc., Chicago, Illinois, USA).

Results

Of the 124 patients, 41 were assigned to the AOP group, 41 to the BPP group, and 42 to the NP group. The mean age of the patients was 63.3 ± 8.9 years, with no statistical difference between the study groups. Neither was there any
difference between the groups with respect to other preoperative risk factors or operative data (Table 1). The patient’s serum potassium concentration at the time when AF occurred did not differ between the groups. Adequate pacing during the whole study period or until the occurrence of AF was possible in 33/41 (80.5%) of patients in the APP group and 38/41 (92.7%) in the BPP group. Pacing was discontinued prematurely due to an increase in pacing threshold and/or a decrease in sensing. No complications were associated with the placement or removal of the atrial electrodes.

A total of 31 patients developed AF, giving an incidence of 25% (Table 2). The incidence in the AOP group (26.8%), BPP group (19.5%) and the NP group (28.6%) did not differ statistically significantly. The mean time from surgery to the onset of AF (44 h for the AOP, 52 h for the BPP and 48 h for the NP groups,) did not differ between the groups. Of the 11 patients who developed AF in the AOP group, review of the continuous ECG recording showed that in three patients AF was probably induced by inappropriate pacing due to sensing failure.

When the data were analyzed using on-treatment analysis, the results did not differ from those obtained by intention-to-treat analysis. The incidence of AF in patients with technically successful pacing was 21.2% in the AOP and 18.4% in the BPP groups, with no significant difference when compared with the AF incidence in NP group ($P = 0.47$ and $P = 0.29$, respectively).

### Discussion

We compared the efficacy of atrial overdrive pacing and prevention of bradycardia in the prophylaxis of AF after CABG. The results of our study suggest that neither atrial overdrive pacing nor bradycardia prevention is effective in AF prophylaxis after CABG. Blommaert et al. found atrial dynamic overdrive pacing to be an effective algorithm in the prevention of AF after CABG [10], but we were not able to replicate this finding. Schweikert et al. [11] were also unable to show the effectiveness of dynamic atrial overdrive pacing in the prevention of AF after CABG in their study. The preoperative characteristics of the patients in the study of Blommaert et al. and in ours were quite similar. One difference between the studies is that we administered beta-blockers postoperatively to all patients, whereas Blommaert et al. did not give beta-blockers to any patient. It is possible that beta-blockers reduced the incidence of AF in all groups in our study, and atrial pacing did not give any further efficacy in the AF prophylaxis. Our

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical characteristics and surgical data of the patients</th>
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</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
<td><strong>Control (n = 42)</strong></td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>32 (76.2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.2 ± 8.6</td>
</tr>
<tr>
<td>CCS class, n (%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1 (2.4)</td>
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<tr>
<td>II</td>
<td>10 (23.8)</td>
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<tr>
<td>III</td>
<td>17 (40.5)</td>
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<tr>
<td>IV</td>
<td>13 (31.0)</td>
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<tr>
<td>Smoking, n (%)</td>
<td>7 (16.7)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>26 (61.9)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td>8 (19.0)</td>
</tr>
<tr>
<td>History of TIA or stroke, n (%)</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td>Unstable angina, n (%)</td>
<td>12 (29.3)</td>
</tr>
<tr>
<td>3-vessel disease, n (%)</td>
<td>39 (92.9)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>64 ± 12</td>
</tr>
<tr>
<td>Preoperative use of β-blockers, n (%)</td>
<td>39 (95.1)</td>
</tr>
<tr>
<td>Number of peripheral anastomoses, n</td>
<td>4.1 ± 0.9</td>
</tr>
<tr>
<td>RCA bypass, n (%)</td>
<td>37 (90.2)</td>
</tr>
<tr>
<td>Pump time (min)</td>
<td>86 ± 20</td>
</tr>
<tr>
<td>Aorta cross clamp time (min)</td>
<td>75 ± 17</td>
</tr>
<tr>
<td>Postop. CKMβm (µg/l)</td>
<td>28.9 ± 16.6</td>
</tr>
</tbody>
</table>

Abbreviations: AOP = atrial overdrive pacing, BPP = bradycardia prevention, CKMβm = creatinine kinase-MB mass, CCS = Canadian Cardiovascular Society, RCA = right coronary artery, TIA = transient ischaemic attack.
results are also in agreement with those of Chung et al. [16]. In a prospective randomized trial they reported that AAI atrial pacing at 10 beats/min or more above the resting heart rate had no influence on the incidence of AF after CABG. Paradoxically, Chung et al. [16] found that the frequency of atrial ectopy was significantly higher in the paced than in the control group, suggesting a potential for proarrhythmia with that form of pacing.

Bradyarrhythmia has been suggested to increase vulnerability to AF [18]. From the theoretical point of view, prevention of bradycardia by atrial pacing prevents the arrhythmogenic consequences of bradycardia [19]. In our study bradycardia prevention reduced the incidence of AF by 32% with intention-to-treat analysis and by 36% with on-treatment analysis. However, it did not reach the level of statistical significance. Even if bradycardia might contribute to the development of postoperative AF after CABG, our study demonstrated that other mechanisms play a more dominant role. Indeed, it is known that increased sympathetic nervous activity increases the susceptibility to postoperative AF. The mean postoperative norepinephrine level (reflecting sympathetic nervous activity) was significantly higher in the patients who developed AF compared with patients who remained in sinus rhythm [20]. Correspondingly, the efficacy of beta-blockers has been demonstrated in the prophylaxis of AF after CABG [17].

It is interesting that in spite of the fact that a pacemaker designed for permanent pacing was connected to temporary epicardial electrodes, effective pacing was achieved in a high number of patients, 80.5% in the AOP group and 92.7% in the BPP group. The reasons for prematurely discontinuing pacing were elevation of the pacing threshold or sensing failure. The percentage of patients in whom pacing was prematurely discontinued in our study is around the same as reported in other studies [8,9,12]. Three patients in the AOP group developed AF presumed due to inappropriate pacing. Atrial activation was not sensed and pacing occurred shortly after a QRS complex. It may have happened during an atrial vulnerable period and induced AF. Our data and the study of Chung et al. [16] indicate the potential proarrhythmic effect of this kind of pacing in the case of sensing failure.

The main limitation of our study is small number of patients in the study groups. The sample size determination was based on the assumption that the incidence of AF can be diminished from 35% to 10% with treatment. However, the incidence of AF turned out to be lower than expected, only 28%, and the treatment effect was also lower than expected. Thus our study became as such underpowered to detect reduction in the incidence of AF. Another limitation is that severity of AF episodes were not estimated.

We conclude that neither atrial overdrive pacing nor bradycardia prevention were effective in preventing AF after CABG. The algorithms based on the sensed atrial rhythm are also vulnerable to sensing failure, and thus may be potentially proarrhythmic.
Acknowledgement

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References