Influence of External Temporary Biatrial Pacing on the Prevention of Atrial Fibrillation after Coronary Artery Bypass without Extracorporeal Circulation

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Summary
Background: Atrial fibrillation is the most common complication after myocardial revascularization, and it increases morbidity/mortality.

Objective: The purpose of this prospective randomized study was to test the hypothesis that temporary biatrial pacing is effective in reducing the incidence of postoperative atrial fibrillation after myocardial revascularization.

Methods: Ninety-eight non-consecutive patients who had undergone off-pump myocardial revascularization received two temporary electrodes attached to the right and left atria, which were connected to either pair of atrial pacemaker electrodes, in addition to the leads implanted in the right ventricle. Two groups of patients were randomized (control: 49 patients with no biatrial pacing; therapeutic: 49 patients with biatrial pacing). The variables of interest were atrial fibrillation (present or absent) and length of hospital stay.

Results: The incidence of atrial fibrillation was 36.73% in the control group and 14.29% in the therapeutic group (p=0.0194). Length of hospital stay was 7.00 ± 2.82 days for patients with no atrial fibrillation (n=73) and 9.20 ± 2.87 days for patients with atrial fibrillation (n=25) (p=0.0001). Age was an important predictor of arrhythmia and ranged between 62.34 ± 9.00 years in the group with no atrial fibrillation and 67.20 ± 7.42 years in the group with atrial fibrillation (p=0.0170).

Conclusion: Compared to controls, prophylactic temporary biatrial pacing is effective in preventing atrial fibrillation. Hospital stay was longer for patients who developed postoperative atrial fibrillation, and age was an important predictor for the development of arrhythmia. (Arq Bras Cardiol 2008; 90(2):80-85)

Key words: Atrial fibrillation; cardiac pacing, artificial; myocardial revascularization.

Introduction
Atrial fibrillation is the most common complication in patients undergoing cardiovascular surgery, with an incidence of approximately 35% to 50% after myocardial revascularization that reaches its peak in the 2nd and 3rd postoperative days. Postoperative atrial fibrillation has significant implications in morbidity and use of hospital resources. Although atrial fibrillation is not life-threatening and its clinical significance in the postoperative phase varies from patient to patient, it is frequently associated with multiple comorbidities such as thromboembolic events, hemodynamic deterioration, exacerbation of heart failure, renal failure, and infection, and prolongs the stay of patients both in intensive care units and the hospital.

The pathogenesis of postoperative atrial fibrillation remains uncertain and is likely to be multifactorial. Several authors have suggested that the initial mechanism of atrial fibrillation in this population of patients consists of multiple reentry circuits propagating through the atria, often initiated by an atrial extrasystole originating in areas of slow conduction and unidirectional block.

Although prophylactic therapy with beta-adrenergic antagonists, amiodarone, and sotalol may reduce the incidence of postoperative atrial fibrillation after myocardial revascularization, this condition remains an important cause of prolonged hospital stay.

Patients who have undergone myocardial revascularization can serve as a model for evaluating the impact of prophylactic atrial pacing on the occurrence of atrial fibrillation (provided they have temporary pacemaker electrodes implanted during the operation). This technique can be very useful in reducing hospital costs and comorbidities associated with this arrhythmia.
By means of this prospective randomized study, we hope to establish an acceptable, safe, and at the same time effective intervention capable of reducing the incidence of postoperative atrial fibrillation after myocardial revascularization.

Method

From May 2004 to March 2005, 98 non-consecutive patients treated with betablockers and diagnosed with obstructive coronary artery disease with indication to undergo cardiac surgery were selected at the Irmãode da Santa Casa de Misericórdia de Curitiba – Aliança Saúde – PUCPR. Inclusion criteria were: patients 18 years of age or older, indication for elective surgery for isolated myocardial revascularization, and written informed consent. Exclusion criteria were: presence of atrial fibrillation or any type of arrhythmia at the time of recruitment, treatment with antiarrhythmic drugs (except digoxin, beta-blockers, or calcium-channel blockers), 2nd- or 3rd-degree AV block, bradycardia defined as a heart rate less than 60 bpm (with no active sinus or atrioventricular node agents), previous cardiac surgery, need for additional surgical procedures along with the myocardial revascularization, contraindication of beta-blocker use, and left atrium larger than 5.0 cm.

Study protocol - This study was approved by PUCPR's Institutional Review Board, under number 342. Patients who complied with all inclusion criteria were randomized to two groups, using extractions from a random numerical table:

- **Control group:** with no temporary biatrial electrical stimulation;
- **Therapeutic group:** with temporary biatrial electrical stimulation.

“Pacebox” - The “pacebox” was especially designed for this study and it consisted of two pairs of atrial stimulation connectors and one pair of ventricular stimulation connectors. The electrical stimulation system was a cardiac pacing Integrity™ DR+(St Jude Medical – USA) model, with a “AF Suppression™” algorithm (St Jude Medical – USA) (fig. 1).

**Features of the “AF Suppression™” algorithm** - This algorithm dynamically adjusts the pacing frequency to stimulate the heart slightly above the intrinsic atrial rates, regardless of the patient being active or at rest. Stimulation with the “AF Suppression™” algorithm releases atrial stimuli according to the programmed number of overdrive stimulation cycles. If two natural P waves are detected before the programmed overdrive cycle is completed or during the period of recovery, the stimulated atrial rate is then automatically increased.

Surgical technique and implantation of temporary epicardial pacing system - All patients underwent off-pump myocardial revascularization. With the patient under general anesthesia and in the supine position, the left subclavian vein and radial artery were punctured, and median sternotomy and longitudinal pericardiotomy were performed. Arterial and venous grafts were dissected according to the coronary arteries to be treated. Patients were anticoagulated with unfractioned heparin (2 mg per kilogram of body weight). After identification of the vessels and anastomosis site, the Lima stitch was used to help position the tissue stabilizing device, a proximal tourniquet was positioned, and suture of the graft was started following longitudinal arteriotomy. Once the suture was completed, the tourniquet and stabilizer were removed. The venous graft was anastomosed to the aorta using lateral clamping. After hemodynamic stabilization, 75% of the initial dose of heparin was neutralized and hemostasis was checked. All surgical planes were sutured.

Following completion of the surgical procedure, two pacemaker electrodes (Ethicon™ multifilament steel wire coated with a layer of blue polyethylene) were placed in the left atrial ceiling between the aorta and the superior cava, as well as two electrodes in the right atrium, one of them in the right atrial auricle and the other in the lateral wall, and two electrodes in the right ventricle, as is commonly done in cardiac surgeries (figure 1 – Panel B). The extremities of the epicardial leads were introduced through the skin and connected to the “pacebox” which had been programmed according to the specifications of the patient’s treatment group.

Pacemaker electrodes were implanted in both groups (control and therapeutic).
**Patient management** - At the end of the operation, the patient was transferred to the cardiovascular intensive care unit where he was continuously monitored until being released to the surgical ward. In the therapeutic group, the electrodes were connected to the “pacebox” 12 hours after surgery and remained for 96 hours. At discharge from the intensive care unit, which usually took place around 36 to 48 hours after the surgery, a dynamic 24-hour electrocardiogram system was installed for continuous monitoring. Data from daily 12-lead electrocardiograms obtained up until hospital discharge were evaluated by at least two independent investigators, along with data from the dynamic electrocardiogram. Patients who developed atrial fibrillation during the postoperative phase (control and therapeutic groups) were treated as per the atrial fibrillation guidelines set by the Brazilian Society of Cardiology, taking in consideration their hemodynamical profiles (stability and instability). Patients with hemodynamical stability were treated with amiodarone (bolus 300 mg IV followed by 900 mg IV within 24 hours). At the same time, they were started on an anticoagulant (enoxaparin or unfractioned heparin) and continuously monitored for possible bleeding. Patients with hemodynamic instability underwent electrical cardioversion (200 – 360 J), as did those who did not respond to chemical cardioversion (amiodarone).

**Statistical analysis** - Categorical variable results were expressed as frequencies and percentages, and quantitative variables as means and standard deviations. Fisher’s exact test was used to compare the groups as to their categorical variables. Student’s t test for independent samples or the non-parametric Mann-Whitney test was used to compare the groups as to quantitative variables, as appropriate. For the multivariate analysis, a logistic regression model was adjusted considering atrial fibrillation as the response variable and the other ones as explanatory variables. In this analysis, decisions were based on Wald’s test. For all tests, p < 0.05 values indicated statistical significance.

**Results**

**Population** - This study consisted of 98 patients, 67 men and 31 women, aged 44 to 78 years (mean age 63.58 ± 8.84 years and median age 64 years). Patients underwent off-pump myocardial revascularization, and 1 to 5 arterial and venous grafts were made (average 2.61 ± 0.82 and median 3.00); size of the left atria ranged from 2.90 to 5.00 cm, (average 4.02 ± 0.45 and median 4.10); size of the left ventricle varied from 3.60 to 6.50 cm, (average 5.06 ± 0.72 and median 5.15); ventricular function ranged from 26.00 to 70.00, (average 58.13 ± 10.07 and median 60.00). Patients were randomized to two groups with the aid of a random numerical table extraction, with even numbers designating the group with no heart stimulation, and odd numbers the group with stimulation. Determination of the initial line and columns for this procedure was made by drawing numbered balls from an urn. Control Group – no stimulation (n=49) and Therapeutic Group – with biatrial stimulation (n=49). Variables of interest were atrial fibrillation (presence or absence) regardless of duration (nonsustained, paroxysmal, short duration) and several demographic and clinical characteristics of the patient. All patients provided informed consent.

**Clinical and demographic patient characteristics** - Table 1 shows the results of the comparison of several clinical and demographic variables between control and therapeutic groups.

**Atrial fibrillation** - Table 2 shows the results of the comparison between the control group (patients with no biatrial stimulation) and the therapeutic group (patients with biatrial stimulation) as to the primary variable of the study, i.e., the presence or absence of atrial fibrillation. There was a statistically significant difference between the therapeutic group and controls (p: 0.0194).

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**Table 1** - Patients’ clinical and demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=49)</th>
<th>Therapeutic (n=49)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.02 ± 8.29</td>
<td>62.14 ± 9.22</td>
<td>0.1077*</td>
</tr>
<tr>
<td>Male gender</td>
<td>31 (63.27%)</td>
<td>36 (73.47%)</td>
<td>0.3651*</td>
</tr>
<tr>
<td>Smoking</td>
<td>14 (28.57%)</td>
<td>20 (40.82%)</td>
<td>0.2886*</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>31 (63.27%)</td>
<td>27 (55.10%)</td>
<td>0.5378</td>
</tr>
<tr>
<td>Previous MI</td>
<td>27 (55.10%)</td>
<td>24 (48.98%)</td>
<td>0.6861</td>
</tr>
<tr>
<td>SAH</td>
<td>47 (95.92%)</td>
<td>42 (85.71%)</td>
<td>0.1591*</td>
</tr>
<tr>
<td>DM</td>
<td>22 (44.00%)</td>
<td>26 (53.06%)</td>
<td>0.5446</td>
</tr>
<tr>
<td>CRF</td>
<td>1 (2.04%)</td>
<td>3 (6.12%)</td>
<td>0.6171</td>
</tr>
<tr>
<td>Grafts: 3 or more</td>
<td>28 (57.14%)</td>
<td>27 (55.10%)</td>
<td>1</td>
</tr>
<tr>
<td>LA</td>
<td>4.04 ± 0.50</td>
<td>4.00 ± 0.40</td>
<td>0.6726*</td>
</tr>
<tr>
<td>LV</td>
<td>4.90 ± 0.74</td>
<td>5.22 ± 0.66</td>
<td>0.0239*</td>
</tr>
<tr>
<td>LVEF</td>
<td>59.02 ± 10.79</td>
<td>57.24 ± 9.32</td>
<td>0.3857*</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>7.47 ± 2.52</td>
<td>7.65 ± 3.41</td>
<td>0.6661</td>
</tr>
</tbody>
</table>

*a* - Student’s t test for independent samples; *b* - Fisher’s exact test; *c* - Nonparametric Mann-Whitney test; MI - myocardial infarction; SAH - systemic arterial hypertension; DM - diabetes mellitus; CRF - chronic renal failure; LA - left atrium; LV - left ventricle; LVEF - left ventricular ejection fraction.
The null hypothesis that the distribution of patients according to the time free from atrial fibrillation in the therapeutic group is equal to this distribution in the control group was tested against the alternative hypothesis of different distributions. The results are displayed in Graphic 1 (Kaplan-Meier).

Relative risk calculations indicate that patients with no stimulation are 2.57 times more likely to develop atrial fibrillation within the 96 hours following surgery than patients with stimulation. Moreover, patients ≥ 65 years of age are 2.31 times more prone to develop atrial fibrillation than those aged up to 65 years. The potential effect of these two characteristics, for patients with no pacemaker and ages ≥ 65 years, is a probability of developing atrial fibrillation 4.63 times greater than for patients with a pacemaker and under 65 years of age.

With regard to hospital stay, it was noted that the presence of atrial fibrillation significantly increases length of hospitalization. In this study, patients with no atrial fibrillation stayed an average of 7.00 ± 2.82 days in hospital, whereas patients with atrial fibrillation were hospitalized for an average of 9.20 ± 2.87 days (p=0.0001).

Discussion

The pathogenesis of postoperative atrial fibrillation remains uncertain and is likely to be multifactorial.

Several authors have suggested that the initial mechanism of atrial fibrillation in this population of patients consisted of multiple reentry circuits propagated internally through the atria, often initiated by an atrial extrasystole originating in areas of unidirectional conduction blocks. Other authors have demonstrated that the surgical technique employed, i.e., myocardial revascularization with or without extracorporeal circulation, plays a significant role in the presence or absence of atrial fibrillation. The former is in itself associated with a systemic vascular inflammatory response contributing to the increased incidence of postoperative morbidity, whereas the latter is associated with a significant decrease in the inflammatory response and release of myocardial necrosis markers. I wish to emphasize that our study was conducted with this technique (without extracorporeal circulation). These authors concluded that the cardioplegic solution and extracorporeal circulation are the main independent predictors of this arrhythmia.

At the institution where this study was conducted, the off-pump technique for myocardial revascularization is routinely used with potential benefits in comparison with conventional technique, such as: shorter procedure time, quicker recovery, shorter ICU and hospital stay, early extubation and reduced need for hemoderivates.

Several authors have shown the impact of this arrhythmia on clinical and economic profiles, which represents a significant increase in hospital costs of more than 16%. i.e., $8,000 per case.

This study clearly shows the marked relationship between atrial fibrillation and a longer hospital stay.

A few drugs such as beta-adrenergic antagonists, sotalol and amiodarone have been used as prophylactic agents to try to reduce the incidence of atrial fibrillation following myocardial revascularization; however, this strategy may
have limited use due to its side effects and contraindications for some patients, and also because it needs to be initiated a few days before surgery. Despite the use of such a scheme, a significant incidence of this arrhythmia was observed in this population.

Due to the limitations and poor efficacy of this pharmacological approach, new options are needed in order to reduce the incidence of this arrhythmia in this population of patients.

In non-pharmacological prevention, two mechanisms may explain how temporary biaatrial stimulation can prevent atrial fibrillation in this population. The first mechanism refers to the fact that the dispersion of atrial refractivity is reduced with the use of a biaatrial pacemaker. Clinical studies have shown that atrial extrasystoles result from the dispersion of atrial refractivity. This difference in atrial electrophysiology is essential for the reentry that facilitates the start of atrial fibrillation.

The second possible mechanism through which biaatrial stimulation may prevent atrial fibrillation is the suppression of atrial extrasystoles. Atrial fibrillation is frequently initiated by an early atrial beat, especially during the period of sinus bradycardia.

In this study, the biaatrial stimulation mode has been chosen to ensure early activation of the atrial myocardium as a response to the early atrial contraction, thus reducing atrial dispersion. When the dynamic atrial overdrive (DAO) algorithm is programmed, the device adjusts the stimulation frequency of the pacemaker, increasing it or reducing it, according to the variation in the patient's intrinsic atrial rate.

According to literature, several studies conducted with single and biaatrial pacemakers (with a variety of algorithms) have been published showing results generally favourable for reducing the incidence of atrial fibrillation in the period after myocardial revascularization. This was demonstrated in this study in which the presence of atrial fibrillation in the control group (with no artificial stimulation) was 36.73%, and in the therapeutic group (with artificial stimulation) it was 14.29%, with high statistical significance (p = 0.0194).

However, in a recent meta-analysis, Ronald and Dunning concluded that only the biaatrial pacemaker is effective as a prophylactic measure in preventing atrial fibrillation in this population, and that use of an isolated right or left atrial pacemaker is not effective.

On the other hand, temporary cardiac stimulation to prevent postoperative atrial fibrillation has also been evaluated, according to the guidelines on atrial fibrillation set by the Brazilian Society of Cardiology. Ten studies analyzed the effects of pacemaker, employing temporary epicardial electrodes in the postoperative period of cardiac surgeries, mostly myocardial revascularization. The techniques of stimulating the right atrium, left atrium and both (simultaneously) were compared with the control group. The three techniques evaluated reduced the incidence of atrial fibrillation relative to the control group.

Concerning safety, no complications were observed during implantation or removal of pacemaker electrodes. No patient from the therapeutic group needed to have the treatment interrupted. According to data from literature, the rate of complications is significantly lower when compared with the control group, and were observed in patients who developed atrial fibrillation.

**Conclusions**

The use of temporary biaatrial stimulation in patients...
undergoing off-pump myocardial revascularization significantly reduces the incidence of atrial fibrillation when compared to the control group, the presence of arrhythmia significantly increases the length of hospitalization, and age is a marked predictor for the incidence of this arrhythmia.

Potential Conflict of Interest
Supply and assembly of the “pacebox” according to our instructions

References


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Study Association
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