A prospective randomized controlled trial on the incidence and predictors of late-phase postoperative atrial fibrillation up to 30 days and the preventive value of biatrial pacing

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BACKGROUND Postoperative atrial fibrillation (POAF) is considered to be a transient arrhythmia in the first week after cardiac surgery.

OBJECTIVE To determine the 30-day incidence and predictors of POAF and the value of postoperative overdrive biatrial pacing in the prevention of POAF.

METHODS Patients (n = 148) without a history of atrial fibrillation undergoing aortic valve replacement or coronary artery bypass graft (CABG) were randomized into a pacing group (n = 75) and a control group. Patients were treated with standardized sotalol postoperatively. Rhythm was continuously monitored for 30 days by a transtelephonic event recorder.

RESULTS POAF occurred in 73 (49.3%) patients, of whom 60 (40.5%) patients showed POAF during postoperative days (PODs) 0–5 and 37 (25%) patients during PODs 6–30. Prolonged aortic cross-clamp time was an important univariate predictor of 30-day and of late POAF (PODs 6–30; $P = .017$ and $P = .03$, respectively). Best-fit model analysis using 15 predetermined risk factors for POAF showed different positive interactive effects for early POAF (ie, baseline C-reactive protein levels with a history of myocardial infarction or low body mass index) and late POAF (ie, high body mass index, diabetes mellitus, baseline C-reactive protein, early POAF, creatinine levels, type of operation, smoking, and male gender). Biatrial pacing reduced the late POAF incidence in patients with aortic cross-clamp time >50 minutes ($P = .006$).

CONCLUSION POAF is not limited to the first week after cardiac surgery but also occurs frequently in the postoperative month. It is desirable to regularly follow patients with POAF for atrial fibrillation recurrences after discharge.

KEYWORDS Postoperative atrial fibrillation; Biatrial pacing; Late POAF

ABBREVIATIONS **ACCT** = aortic cross-clamp time; **AF** = atrial fibrillation; **AVR** = aortic valve replacement; **BMI** = body mass index; **CABG** = coronary artery bypass graft; **CRP** = C-reactive protein; **DM** = diabetes mellitus; **MI** = myocardial infarction; **POAF** = postoperative atrial fibrillation; **POD** = postoperative day; **SR** = sinus rhythm

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Introduction

Historically, postoperative atrial fibrillation (POAF) has been defined as a transient arrhythmia in the first week after cardiac surgery, with a peak incidence between the second and third postoperative days (PODs). A growing body of evidence has identified POAF as an important risk factor for increased late mortality.[1,2] Data on the incidence of POAF after discontinuation of in-hospital continuous telemetric monitoring are rare but increasingly important because POAF may show later occurrences.[3]

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In addition, despite the several treatment and preventive strategies, the reported incidence of POAF remains high.[4,5] Overdrive atrial pacing has shown conflicting results in previous studies when tested for POAF prevention.[6–9] To our knowledge, long-term effects of strategies to prevent POAF have not yet been studied. We hypothesize that episodes of atrial fibrillation (AF) frequently recur after the first postoperative week and aimed to determine the preventive value of synchronized biatrial overdrive pacing on the 30-day POAF incidence.

Methods

Population

Between October 2009 and July 2011, patients undergoing elective coronary artery bypass graft (CABG) or aortic valve

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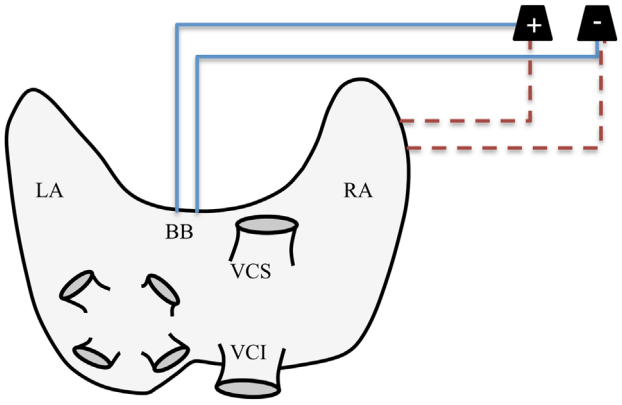

Figure 1 Schematic representation of the electrode placement. The right atrial (red line) and the Bachmann bundle (blue line) wire placement. BB = Bachmann bundle; LA = left atrium; RA = right atrium; VCI= inferior caval vein; VCS = superior caval vein.

replacement (AVR) without a known history of AF or any treatment for that purpose were enrolled in the study. Exclusion criteria were a history of AF, sick sinus syndrome, or atrioventricular block. The local medical ethics committee approved this trial.

Study protocol

All patients underwent an elective CABG or AVR using cardiopulmonary bypass, through a median sternotomy, with the use of cold crystalloid antegrade cardioplegia support. Perioperatively 2 pairs of unipolar temporary atrial pacemaker wires (Flexon^{TM}) were placed on the epicardium of the right atrial wall and on the Bachmann bundle in all patients (Figure 1). Patients were randomized into a pacing and a nonpacing group, and all were treated with sotalol during the first postoperative week, unless contraindicated (dosage and discontinuation were left to the discretion of the attending resident and the cardiologist).

The rhythm of patients was monitored by daily review of the continuous telemetric monitoring (PODs 0–3). Twelve-lead electrocardiograms were obtained on the first, second, and fourth postoperative days. In addition, from the moment of cessation of in-hospital telemetric monitoring, continuous transtelephonic monitoring was started for a total of 4 weeks. For this purpose, an external 1-lead transtelephonic loop recorder (Vitaphone 3100 BT) with an autotrigger for AF was used. It detects conversion of sinus rhythm (SR) into AF and AF into SR. Clinical and rhythm-monitoring data were collected and analyzed by blinded investigators.

Pacing protocol

After arrival at the cardiovascular intensive care unit, pacing wires in the pacing group were connected to the output of an external pacemaker and pacing protocol was initiated. The sensing and stimulus threshold of all wires were tested before chest closure and on a daily basis after surgery. The output was set at 2 times greater than the stimulation threshold of the pacing site with the highest threshold (ie, Bachmann bundle or right atrium). The sensitivity was set at half of the sensing threshold of the location with the lowest threshold. Pacing was maintained for 72 hours in AAI mode, with 10 beats/min above the intrinsic heart rate (minimum of 80 beats/min and maximum of 120 beats/min). Pacing was discontinued during AF or sinus tachycardia (>110 beats/min) and resumed after conversion to normal SR to complete the 72-hour protocol. Uniatrial right atrial pacing in the nonpacing group (POD 0) in response to bradycardia was not considered a protocol violation (n = 7). In case of loss of capture and/or failure of sensing, the anode and cathode connections to the pacemaker were exchanged. The same was done when phrenic nerve pacing occurred.

All pacemaker wires were removed after 72 hours.

Outcomes

AF was defined as an irregular RR interval during at least 10 seconds, without a detectable P wave.[10,11] The event rate and duration of POAF were compared between study groups for early POAF (PODs 0–5), late POAF (PODs 6–30), and total POAF (PODs 0–30). In addition, we aimed to determine demographic and clinical risk factors confounding the net effect of pacing on all outcome measures.

Statistical analysis

Metric variables are characterized by means and SDs if they are normally distributed, as tested by using the Shapiro-Wilk test. Baseline patient characteristics between both randomized groups were tested by using the Student *t* test (if normally distributed), the Mann-Whitney test (if not), or the log-likelihood χ^2 test (for categorical data).

To examine the relationship of risk factors or variables with early POAF, late POAF, and overall 30-day POAF, a univariate analysis was performed in terms of absolutes and percentages, log-likelihood χ^2 statistics (χ^2_L), *P* values of χ^2_L, odds ratios, and 95% confidence intervals of odds ratios. Multivariate analysis on the 3 POAF incidence measures (early, late, and total POAF) was performed by using the Cox regression model. At first, a univariate Cox regression analysis was performed using the experimental groups factor (nonpacing vs pacing) in addition to a per-protocol analysis for 3 groups (nonpaced vs sufficiently paced vs insufficiently paced). Next, a direct-effects Cox regression model with only statistically significant effects on each of the 3 outcome measures was searched for by means of the backward elimination log-likelihood χ^2 technique using a predetermined list of 15 risk factors for POAF in addition to the experimental factor. All first-order interactive effects of these risk factors between themselves and those of each risk factor with the experimental groups factor (nonpacing vs pacing) were groupwise and hierarchically tested by means of the backward elimination log-likelihood χ^2 technique. Finally, for each of the 3 measures separately, a final Cox regression model was searched for containing only statistically significant effects. A *P* value of $<.05$ was considered statistically significant. All types of analyses were performed using SPSS version 20.0 for Windows PC.