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Effectiveness of Triple-Site Triggered Atrial Pacing for Prevention of Atrial Fibrillation after Coronary Artery Bypass Graft Surgery

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Summary

Background: Recently, several temporary multisite pacing methods have been developed for prevention of postoperative atrial fibrillation (AF).

Hypothesis: In this study, we evaluated the effect of triple-site temporary triggered pacing in the AAT mode on the development of AF in patients undergoing coronary artery bypass graft (CABG) at high risk for developing postoperative AF.

Methods: A total of 70 patients undergoing CABG were randomly assigned either to pacing group (study group, n = 35 patients) or to no pacing group (control group, n = 35 patients). The external pacemaker was programmed to pace at the atrial triggered mode at a lower rate of 40 beats/min for 4 days.

Results: Atrial fibrillation, defined as lasting > 30 s, occurred in 4 patients (11.4%) in the study group and in 16 patients (45.7%) in the control group (p = 0.003). Sustained AF, defined as AF lasting > 10 min, also was observed less frequently in the study group than in the control group (11.6 vs. 37.1%, p = 0.024). Triple-site triggered atrial pacing was observed to reduce the incidence of AF by 75% and the incidence of sustained AF by 69%.

Conclusions: We believe that multiple-site temporary pacing in the triggered mode is an effective way of preventing postoperative AF. This technique may be used especially in patients at high risk of developing AF.

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Introduction

Atrial fibrillation (AF) is the most common arrhythmic complication of coronary artery bypass graft (CABG), occurring in 10–40% of patients.[1–4] It has been shown that postoperative AF is associated with an increased risk of stroke, prolonged hospital stay, and worsened cardiac function.[5–9] Incidence of AF remains unacceptably high in high-risk patients receiving optimal medical therapy.[10–13] Recently, several pacing therapies for prevention of postoperative atrial fibrillation have been developed.

The exact mechanisms leading to postoperative AF have not been fully elucidated, but the pathophysiologic factors leading to nonsurgical AF are believed to operate in the genesis and maintenance of this arrhythmia as well. It is hypothesized that AF results from "leading circle" reentry in the atria.[14] Depolarization heterogeneity, dispersion of refractoriness, and slow conduction in the atria constitute a substrate for reentry, and triggers, such as appropriately timed atrial premature depolarizations, initiate AF.[15, 16] Atrial premature depolarizations also may result in nonuniform conduction and dispersion of refractoriness.[17, 18]

We hypothesized that triggered pacing from three different atrial sites in patients undergoing CABG might prevent depolarization heterogeneity and improve conduction speed in the atria. We thus evaluated the effect of triple-site temporary pacing in the AAT mode on the development of AF in patients undergoing CABG who are at high risk for developing postoperative AF.

Methods

Patients

From November 2001 to December 2004, patients aged > 18 years, in normal sinus rhythm, scheduled for their first

CABG surgery at our institute, were screened for the study. Patients carrying high risk for the development of postoperative AF (one or more of the following: age > 70, long-standing hypertension, associated valvular heart diseases, depressed left ventricular function, previous atrial arrhythmias, increased left atrial size, or presence of chronic obstructive lung disease) were considered eligible for the study. Patients were excluded if they had a permanent pacemaker implanted, were using class I or III antiarrhythmic medication, or if they were undergoing concomitant valvular surgery. All participants gave written informed consent. The study was approved by the ethical committee of our university.

A total of 70 patients (42 men) were included in the study. Patients continued taking their medications (including beta blockers) at the discretion of their personal surgeons. Patients were randomized blindly to either the triple-site triggered atrial pacing group (study group) or to the no pacing group (control group).

Study Protocol

All patients underwent surgery with standard cardiopulmonary bypass with cooled cardioplegia. In the study group, after completion of the surgical procedure, three epicardial wires (Ethicon® FEP13, Edinburgh, U.K.) were placed: one in the high right lateral atrium, one in the left lateral atrium, and one in the left atrium in the center of the triangle formed by the superior and inferior right pulmonary veins and coronary sinus. The threshold and sensitivity of the leads were assessed within 6 h of the patients' arrival to the intensive care unit. Immediately after this assessment, the three leads from the atria were connected to the positive end and a skin electrode was connected to the negative end of an external pacemaker pulse generator (Osypka Pace 202, Berlin, Germany). The external pacemaker was programmed to pace at the atrial triggered mode with a lower rate of 40 beats/min and an output of twice the capture threshold of the highest of any of the three atrial leads.

All patients were followed for 4 days either by telemetry or continuous ambulatory electrocardiographic recording. Capture thresholds for each lead were checked every day. An irregular rhythm with no prominent P waves was defined as AF, and the persistence of this rhythm for > 10 min or the requirement of an urgent cardioversion for this rhythm was defined as sustained AF.

Statistical Analysis

All data were analyzed on an intention-to-treat basis. Continuous variables are expressed as means ± standard deviation (SD). Continuous variables were compared using the unpaired Student's *t*-test. For categorical variables, the chi-square test was used. A p value < 0.05 was considered statistically significant. The Statistical Package for the Social Sciences, version 9.0 (SSPS Inc., Chicago, Ill., USA) was used for statistical analyses.

TABLE I Demographic and clinical characteristics of patients

	Pace n = 35	Control n = 35	p Value
Age, year (SD)	62 (8)	63 (10)	0.842
Male, n (%)	23 (66)	19 (54)	0.465
LVEF, % (SD)	42 (9)	45 (10)	0.172
Hypertension, n (%)	21 (60)	25 (71)	0.437
Diabetes mellitus, n (%)	17 (49)	18 (51)	1.0
COPD, n (%)	3 (9)	3 (9)	1.0
Smoking, n (%)	14 (40)	12 (34)	0.619
Previous MI, n (%)	19 (54)	14 (40)	0.225
Mitral regurgitation, n (%)	26 (74)	28 (80)	0.751
Left atrial diameter, cm (SD)	3.9 (0.4)	4.0 (0.5)	0.835

Abbreviations: MI = myocardial infarction, COPD = chronic obstructive pulmonary disease, LVEF = left ventricular ejection fraction, SD = standard deviation.

Results

The demographic and clinical characteristics of the patients were similar (Table I). No complications related to pacing wire implantation or removal were observed. Atrial fibrillation was observed in 4 patients (11.4%) in the study group and in 16 patients (45.7 %) in control group (p = 0.003). The incidence of sustained AF was also significantly lower in the study group than in the control group [4 patients (11.4%) vs. 13 patients (37.1%), p = 0.024]. Triple-site triggered atrial pacing reduced the incidence of AF by 75% and the incidence of sustained AF by 69%.

At least one of the pacing leads failed in six patients at some time during the course of the study. In two patients, capture thresholds became unacceptably high in all three leads on the third postoperative day. In three patients, one of the leads failed to capture the atrium (one on the second, the other on the third postoperative day). In another patient, the left atrial lead started to sense the ventricle on the second postoperative day, and the lead was disconnected from the pacemaker.

Lengths of hospital and intensive care unit stay, as well as postoperative complications, were similar between the groups (Table II).

Discussion

Our results demonstrate that triple-site atrial pacing in the triggered mode is an effective way of preventing AF after CABG. In contrast to similar studies reporting a preventive effect of multisite pacing, it seems that the preventive effect of our pacing technique is entirely due to more homogeneous atrial depolarization.

Multisite atrial pacing for prevention of atrial arrhythmias was first introduced by Daubert *et al.*[19] Since then, numerous studies have been performed that show that chronic dual-site atrial pacing is effective in reducing recurrences of the arrhythmia in patients with drug-refractory paroxysmal or permanent

TABLE II Surgical data and complications

	Pace, n = 35	Control, n = 35	p Value
Postoperative beta blocker, n (%)	17 (49)	24 (69)	0.215
Bypass pump time, min, mean (SD)	76 (19)	71 (20)	0.323
Number of grafts/patient, mean (SD)	3.4 (0.9)	3.0 (1.0)	0.060
Aorta cross-clamp time, min, mean (SD)	37 (11)	34 (11)	0.363
Intubation length, h, mean (SD)	12.0 (3.7)	11.6 (4.2)	0.662
Length of hospital stay, day, mean (SD)	7.9 (2.2)	9.8 (6.0)	0.091
Repeat surgery for bleeding, n (%)	0	2 (6)	0.493
Renal impairment (creatinine > 2.0 mg/dl), n (%)	2 (6)	3 (9)	1.0
Stroke, n (%)	2 (6)	1 (3)	0.608
Myocardial infarction, n (%)	0	1 (3)	1.0

Abbreviation: SD = standard deviation.

AF.[20–23] Recently, several reports have shown that multisite temporary atrial pacing via epicardial electrodes placed during surgery might be effective in preventing postoperative AF.[24–32] In a double-blind, randomized study, Daoud *et al.* evaluated the effects of different pacing modes in 118 patients who had undergone open heart surgery.[28] In this study, patients were randomized to one of the following three groups: right atrial pacing with an inhibited mode at a rate of 45 beats/min; right atrial overdrive pacing with a triggered mode ≥ 10 beats greater than the patient's intrinsic (but not < 85 beats/min) rate; and biatrial overdrive pacing with a triggered mode ≥ 10 beats greater than the patient's intrinsic (but not < 85 beats/min) rate. Biatrial pacing was associated with reduced incidence of postoperative AF compared with the other two pacing strategies (10, 28, and 32%, respectively; p = 0.02).

Recently, in a meta-analysis including 776 patients, Daoud *et al.*[30] found that overdrive biatrial pacing (odds ratio [OR] 2.6, confidence interval [CI] 1.4–4.8), fixed high-rate biatrial pacing (OR 2.5 CI 1.3–5.1), and overdrive right atrial pacing (OR 1.8 CI 1.1–2.7) were effective in the prevention of postoperative AF. Archbold and Schilling[31] analyzed the data on epicardial atrial pacing and concluded that prophylactic biatrial pacing in patients undergoing CABG appears to be effective in the prevention of AF.

Our study also demonstrated that multisite temporary pacing in the AAT mode in patients undergoing CABG reduced the incidence of postoperative AF. There are several proposed mechanisms for the beneficial prophylactic action of multisite pacing in surgical patients:[33] First, pacing at a rate higher than the intrinsic rate prevents bradycardia, compensatory pauses, and irregular heart rates that might facilitate development of AF. Second, suppression of atrial ectopic depolarizations by overdrive pacing may reduce the number of triggers that can initiate AF. Third, pacing from multiple sites in the atria may prevent nonuniform activation and depolarization heterogeneity in the atria.

In all of the above-mentioned trials, overdrive pacing was used to suppress atrial ectopy and prevent pause-related changes in atrial refractoriness. Although overdrive pacing may have some advantages, it is not physiological and may cause adverse hemodynamic effects in patients with intact sinus node function. In our study, we programmed the pacing rate at 40 beats/min and let the heart rate of the patient be determined by his or her own sinus node. By doing so, we were not able to prevent atrial ectopy, bradycardia, or pause-induced changes in atrial refractoriness. Still, triggered triple-site atrial pacing caused a 75% reduction in the incidence of postoperative AF in our study.

There are several theoretical explanations for the beneficial effects of triggered atrial pacing. Nonuniform and anisotropic conduction, as well as dispersion of refractoriness, play an important role in the genesis of AF. We believe that triple-site triggered pacing may prevent AF by depolarizing both atria earlier rather than simultaneously. Premature atrial depolarizations result in dispersion of refractoriness and anisotropic conduction that facilitate development of AF.[18,34] With the pacing strategy used in the current study, an atrial premature depolarization would be sensed by any of the three leads in a very short time, and both atria would be paced from three different sites as soon as this premature depolarization is sensed. Hypothetically, this would result in activation of atrial sites from at least three different directions and prevent development of structural or functional unidirectional blocks. This strategy also may lead to improved conduction and lesser degrees of dispersion of refractoriness both during sinus rhythm and after atrial premature depolarizations.

Limitations of the Study

We believe that the sample size is the most important limitation of our study. Another one is the technical difficulties in obtaining and maintaining good thresholds for the pacing sites; this factor has been a problem in other studies as well. Daoud *et al.* reported that 60% of right and 80% of left atrial electrodes failed to perform by the fifth postoperative day.[28] In our study, effective triple-site atrial pacing could not be performed in six patients. This may also have limited the value of our findings.

Because of the limited number of patients used in the current study, we could not form another group of patients with

triple overdrive atrial pacing from three different sites and compare this group with the other patients. We also did not have the chance to compare our patients with patients in whom dual-site atrial pacing was performed. This would have provided more insight into the mechanisms of the preventive role of pacing strategies in AF. Finally, our sample size did not allow us to analyze the effects of this pacing strategy on mortality, morbidity, length of hospital stay, and cost of hospitalizations.

Conclusions

Multiple-site temporary pacing in the triggered mode is a safe and effective way of preventing postoperative AF. This technique may be used especially in patients at high risk for developing AF.

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