

## EDITORIAL COMMENT

# Prevention of Postoperative Atrial Fibrillation: What Is the Best Approach?\*

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Atrial fibrillation is the most frequent complication after coronary artery bypass surgery, occurring in up to 40% of patients (1). It is even more common in those undergoing valvular surgery, especially of the mitral valve, occurring in as many as 64% of patients (2). Most episodes of atrial fibrillation occur within the first few days after surgery, with a peak incidence on postoperative days 2 to 3 (3). Although postoperative atrial fibrillation is not usually associated with significant morbidity and is often self-limited, it has a major economic effect, increasing the length of hospital stay by up to three days, with an additional cost of several thousand dollars per patient (4,5).

A number of risk factors associated with an increased risk of postoperative atrial fibrillation have been identified and include age; atrial infarction and trauma resulting from cannulation; postoperative electrolyte shifts, including potassium and magnesium; pericarditis; right coronary artery grafting; valvular heart disease; heightened postoperative sympathetic tone; beta-adrenergic blocking agent withdrawal; and chronic obstructive heart disease (5,6).

Despite the identification of a number of risk factors for postoperative atrial fibrillation, prevention of this arrhythmia has been problematic, and many prophylactic therapies, including digoxin and calcium channel blocking agents, have been found ineffective. Exceptions are the beta-blockers, or drugs with beta-blocking activity, and a number of studies have shown that beta-blockers, administered before or immediately after surgery, are very effective for preventing atrial fibrillation (7-9). Two meta-analyses have confirmed that beta-blockers, regardless of the agent used, the time of initiation or the dose administered, are an effective prophylactic therapy, reducing the incidence of atrial fibrillation from 34% and 20% to 8.7% and 9.8%, respectively (10,11). Unfortunately, none of these trials evaluated the influence of beta-blocking therapy on length of stay or hospital cost.

Amiodarone, a class III antiarrhythmic drug that also has beta-blocking activity, has also been shown to be an effective prophylactic therapy, and in one trial of 124 patients

preoperative therapy begun at least seven days before surgery reduced the incidence of atrial fibrillation compared with placebo (53% vs. 25%) (12). Amiodarone therapy reduced the duration of hospitalization (7.9 vs. 6.5 days), translating into a decrease in hospital costs of \$8,000. A second trial of 300 patients (ARCH), reported in 1998 at the American College of Cardiology Annual Sessions, found that intravenous amiodarone, administered immediately after surgery, reduced the incidence of postoperative atrial fibrillation compared with placebo (35.4% vs. 47.2%); however, length of hospital stay was not reduced by amiodarone therapy.

Several studies have found that sotalol, another class III agent with beta-blocking activity, begun after surgery is an effective agent for preventing postoperative atrial fibrillation when compared with placebo or metoprolol (13,14). The study by Gomes et al. (15) published this month in the *Journal*, in which oral sotalol therapy was administered preoperatively, confirms and extends these observations.

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This study randomized 85 patients to sotalol or placebo; therapy was begun 24 to 48 h before surgery and was continued for four days after surgery. Compared with placebo or a standard beta-blocker, which was administered to 47% of patients in the placebo group, sotalol significantly reduced the incidence of postoperative atrial fibrillation (37.5% and 38.0% vs. 12.5%, respectively). It is important to note that there were no episodes of torsades de pointes as a result of sotalol therapy. However, the reduction in the occurrence of atrial fibrillation with sotalol did not translate into a reduction in hospital length of stay, which was identical to that of placebo patients.

These results confirm the data from other studies in which sotalol was administered postoperatively, that is, sotalol is an effective therapy for preventing postoperative atrial fibrillation and appears to be more effective than other beta-blockers, perhaps because of its class III antiarrhythmic activity. However, when the results of this and other trials are compared, there does not appear to be a difference in the effectiveness of sotalol when administered before or immediately after surgery, as the incidence of atrial fibrillation with sotalol (12.5%) is similar to that reported by other studies in which sotalol therapy was administered postoperatively (range 10% to 16%).

Before these results are put into widespread clinical practice, there are many issues to consider.

1. Many patients who undergo bypass surgery and are at high risk for the development of atrial fibrillation were excluded from this trial, including those with a left ventricular ejection fraction <28% or clinically evident congestive heart failure, chronic obstructive pulmonary

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disease, impaired renal disease or first-degree or higher atrioventricular block. Therefore, the data can only be applied to a selected group of patients.

2. The role of conventional beta-blockers in the Gomes study is uncertain, despite the finding in a small number of patients that sotalol was more effective than conventional beta-blockers. This is an important concern in view of the substantial data from a number of other studies suggesting that the incidence of postoperative atrial fibrillation with prophylactic therapy using conventional beta-blockers is low (8% to 10%) and is equivalent to that seen in the current trial with sotalol (10,11). It is therefore not clear that sotalol is more effective than a standard beta-blocker.

An additional concern is that the doses of beta-blockers administered in the Gomes trial were relatively low. Without comparative data about the degree of beta blockade achieved with conventional beta-blockers and sotalol, such as the resting sinus heart rate, which is a marker of beta blockade, it is unclear if the findings in this trial are due to differences in the intensity of beta blockade achieved in the different groups. As an example, one study found that, compared with low doses of propranolol and sotalol, higher doses of these drugs were more effective for reducing the incidence of atrial fibrillation; moreover, there was no difference between these two agents when they were administered at equivalent doses (16).

3. There were more patients who underwent valve replacement in the placebo group (18% vs. 10% in the sotalol group). The incidence of postoperative atrial fibrillation, even in those receiving therapy, is higher in patients with valvular heart disease compared with those with coronary artery disease (2). It is possible that this may account for some of the observed differences in outcome.
4. Although the incidence of atrial fibrillation in the placebo group was 38%, the arrhythmia was paroxysmal in 56% of these patients (duration 0.5 to 73 h). Because paroxysmal atrial fibrillation is unlikely to be associated with morbidity or to prolong hospitalization, it is uncertain if such patients would derive benefit from any prophylactic antiarrhythmic therapy.
5. It is not clear why there were no episodes of atrial fibrillation after discontinuation of sotalol on day 4, whereas those receiving placebo continued to have episodes after this period of time. Sotalol has a half-life of 8 to 12 h in patients without renal disease, and therefore a prolonged drug effect is unlikely.
6. Although there were no cases of torsade de pointes in this small study, this remains an important concern in postoperative patients who often have electrolyte abnormalities, especially hypokalemia, which is an important risk factor for drug-induced torsade de pointes (17).
7. Most importantly, the reduction in postoperative atrial

fibrillation in the present study did not translate into a reduction in the length of hospitalization, which is the most important reason for the prevention of this arrhythmia. Another important potential benefit from the reduction in the incidence of atrial fibrillation is the decreased risk for embolic stroke. However, the risk of this complication associated with postoperative atrial fibrillation is unknown, although likely to be low; nevertheless, this study did not address this issue.

Since postoperative atrial fibrillation is often paroxysmal, and it may revert spontaneously within several weeks in those with arrhythmia that is still present at hospital discharge, an alternative approach is initial rate control and anticoagulation with pharmacologic or electric reversion at a later time if atrial fibrillation persists (18). This strategy has been found to reduce the duration and cost of hospitalization and is safe, without a risk of bleeding complications or thromboembolic events. It is possible that this may be the best and safest approach to the management of postoperative atrial fibrillation, reducing length of stay and hospital cost and eliminating the potential risks associated with antiarrhythmic drug therapy. It is hoped that future studies will evaluate this approach and compare it with strategies that involve arrhythmia prevention with antiarrhythmic drugs.

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