Metoprolol Versus Amiodarone in the Prevention of Atrial Fibrillation After Cardiac Surgery
A Randomized Trial
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Background: Current guidelines recommend β-blockers as the first-line preventive treatment of atrial fibrillation (AF) after cardiac surgery. Despite this, 19% of physicians report using amiodarone as first-line prophylaxis of postoperative AF. Data directly comparing the efficacy of these agents in preventing postoperative AF are lacking.

Objective: To determine whether intravenous metoprolol and amiodarone are equally effective in preventing postoperative AF after cardiac surgery.

Design: Randomized, prospective, equivalence, open-label, multicenter study. (ClinicalTrials.gov registration number: NCT00784316)

Setting: 3 cardiac care referral centers in Finland.

Patients: 316 consecutive patients who were hemodynamically stable and free of mechanical ventilation and AF within 24 hours after cardiac surgery.

Intervention: Patients were randomly assigned to receive 48-hour infusion of metoprolol, 1 to 3 mg/h, according to heart rate, or amiodarone, 15 mg/kg of body weight daily, with a maximum daily dose of 1000 mg, starting 15 to 21 hours after cardiac surgery.

Measurements: The primary end point was the occurrence of the first AF episode or completion of the 48-hour infusion.

Results: Atrial fibrillation occurred in 38 of 159 (23.9%) patients in the metoprolol group and 39 of 157 (24.8%) patients in the amiodarone group (P = 0.85). However, the difference (-0.9 percentage point [90% CI, -8.9 to 7.0 percentage points]) does not meet the prespecified equivalence margin of 5 percentage points. The adjusted hazard ratio of the metoprolol group compared with the amiodarone group was 1.09 (95% CI, 0.67 to 1.76).

Limitations: Caregivers were not blinded to treatment allocation, and the trial evaluated only stable patients who were not at particularly elevated risk for AF. The withdrawal of preoperative β-blocker therapy may have increased the risk for AF in the amiodarone group.

Conclusion: The occurrence of AF was similar in the metoprolol and amiodarone groups. However, because of the wide range of the CIs, the authors cannot conclude that the 2 treatments were equally effective.

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We aimed to directly compare intravenous metoprolol and amiodarone and determine whether they are equally effective in preventing AF after cardiac surgery.

Methods
Study Overview
We conducted a randomized, prospective, equivalence, open-label, multicenter trial to compare the efficacy and safety of intravenous metoprolol with that of intravenous amiodarone in preventing AF after cardiac surgery. The study was done in 3 cardiac centers in Finland: 1 secondary referral hospital and 2 tertiary referral hospitals. At each hospital, 300 to 900 cardiac surgeries are performed each
β-Blockers and amiodarone are used to prevent atrial fibrillation after cardiac surgery, although data directly comparing the 2 drugs are lacking.

In this study, β-blocker and amiodarone therapy started within 24 hours and continued for 48 hours after cardiac surgery resulted in similar rates of atrial fibrillation, but the CIs could not rule out a difference between the groups.

The study could not definitively establish the equivalence of the 2 treatments.

Additional studies are warranted.

—The Editors

year. Study enrollment took place between October 2006 and January 2009. The study protocol was approved by the local ethics committees, and all patients gave written informed consent.

Participants

The study population consisted of 316 consecutive ethnic Finnish patients scheduled to have their first on-pump CABG surgery, aortic valve replacement, or combined CABG and aortic valve surgery. The patients were receiving β-blocker therapy before the surgery, which was discontinued on the day of surgery.

Patients with previous episodes of AF or flutter, the sick sinus syndrome, second- or third-degree atrioventricular block, acute ST-segment elevation myocardial infarction, severe asthma, chronic obstructive pulmonary disease, thyroid dysfunction, or allergy to iodine were excluded. In addition, patients receiving thioridazine, erythromycin, pentamidine, terfenadine, or cisapride were excluded because the use of amiodarone is contraindicated in combination with these medications. All eligible patients gave informed consent before surgery.

To be included in the study, patients had to be hemodynamically stable and free of AF. Accordingly, patients were excluded if AF had occurred at the time of randomization (15 to 21 hours after surgery); they had already received β-blockers; or they were receiving vasoactive therapy, had a heart rate less than 60 beats/min, or had systolic blood pressure lower than 100 mm Hg. Furthermore, enrolled patients were excluded after the surgery if they developed a new second- or third-degree atrioventricular block, temporary pacing was not functioning properly, the operation had been unexpectedly performed off pump, or they stayed longer than 24 hours in the intensive care unit for any reason. Figure 1 presents the study flow diagram.

Patients had cardiac surgery on standard cardiopulmonary bypass. Intermittent blood or cold crystalloid cardio-

plegia solution was administered through the antegrade or retrograde route. The cardioplegia solution consisted of 32 mEq/L of magnesium, and no extra magnesium substitution was administered.

After surgery, patients were followed up in the intensive care unit and were weaned off mechanical ventilation when they were hemodynamically stable, had a temperature greater than 32 °C, were awake and cooperative, and did not have major bleeding. Chest drains were removed 15 to 21 hours after surgery, and patients were referred to the surgical ward. No vaspressors were administered in the surgical ward. Patients did not receive any other medication that might have affected heart rate.

All patients were connected to 3-channel ward monitors for continuous electrocardiographic monitoring for the 48-hour study period. The ward monitors stored 24-hour electrocardiographic recordings for subsequent analysis, and 12-lead electrocardiography was performed if necessary to confirm the rhythm. The electrocardiograms were reviewed by the cardiologist on duty. The rhythm was defined as AF when there were no consistent P waves before each QRS complex and ventricular rate was irregular. Atrial fibrillation episodes lasting longer than 5 minutes were recognized.

Interventions

The study protocol started on the first postoperative morning before the referral to the surgical ward, 15 to 21 hours after the surgery. The study period was 48 hours. Patients in the intravenous metoprolol group received an infusion of 1 mg/h for a heart rate of 60 to 70 beats/min, 2 mg/h for a heart rate of 70 to 80 beats/min, or 3 mg/h for a heart rate greater than 80 beats/min. If heart rate decreased below 60 beats/min or systolic blood pressure decreased below 100 mm Hg during treatment, slow bolus infusion of 1 mg/h for a heart rate of 60 to 70 beats/min, or 2 mg/h for a heart rate greater than 80 beats/min. If heart rate decreased below 60 beats/min or systolic blood pressure decreased below 100 mm Hg during treatment, intravenous metoprolol administration was discontinued for 1 hour and then continued according to heart rate, as described. Patients in the intravenous amiodarone group received amiodarone, 15 mg per kg of body weight, with a maximum daily dose of 1000 mg. Amiodarone therapy was discontinued for 1 hour if heart rate decreased below 60 beats/min or systolic blood pressure decreased below 100 mm Hg during treatment and was restarted at the same dose after interruption.

Outcomes

The primary end point of the study was the occurrence of a first AF episode or completion of the 48-hour infusion. The study protocol was discontinued after the first AF episode. Adherence was assessed by how many randomly assigned patients discontinued the study before the designated end point.

The secondary end points were death, stroke, thrombophlebitis, hypotension, and bradycardia. Stroke was defined as a new neurologic symptom verified by correlative changes on computed tomography. Thrombophlebitis was defined as local pain, tenderness, redness, and bulging of a
vein. Ultrasonography was not used in the diagnosis of thrombophlebitis. Hypotension was defined as systolic blood pressure less than 100 mm Hg, and bradycardia as heart rate less than 60 beats/min. In addition, perioperative myocardial infarction was defined as the development of new Q waves. Resternotomy was defined as reoperation because of bleeding. Creatine kinase-MB mass was measured after surgery when patients arrived at the intensive care unit.

Sample Size
The study was planned as an equivalence, open-label study. We calculated the sample size by using the formula presented by Pocock (27). On the basis of previous studies, we assumed an incidence of AF of 15% in both groups (8, 17, 21) and defined “equivalence” as a difference in the treatment effect less than 5 percentage points in both directions. At an \( \alpha \) level of 0.10 with a power greater than 80%, the sample size was calculated to be 158 patients in each group.

Randomization
Block randomization was performed centrally by the coordinating center with a block size of 30. The study group, metoprolol or amiodarone, was printed on a sheet of paper, which was then sealed in numbered envelopes in a blinded, randomized manner. The randomization envelopes were kept by a secretary in each participating hospital and opened by investigators at the time of randomization. The patients were assigned to the intravenous metoprolol or intravenous amiodarone groups according to the allocation designated in the next envelope opened in sequence.

Blinding
The study was open-label. The participants, caregivers, and investigators assessing the outcomes were not blinded to the treatment allocation.

Statistical Analysis
We analyzed the difference in continuous variables by using the unpaired \( t \) test. We tested dependencies between the treatment groups and categorical variables by using the chi-square test for independence or, in the case of low expected frequencies, the Fisher exact test. Kaplan–Meier curves were plotted for the development of AF after cardiac surgery. In addition, we used a multivariate Cox proportional hazards model to determine the hazard ratio (HR) of AF in the metoprolol group compared with the amiodarone group. Possible confounders (age, sex, left ventricular ejection fraction, type of operation, unstable angina pectoris, chronic obstructive pulmonary disease, and right coronary artery bypass) were adjusted in the model. We verified the assumptions of the Cox proportional hazards regression analysis with log-minus-log plots. The limit for statistical significance was a \( P \) value less than 0.05. All statistical procedures were performed with SPSS for Windows, release 14.0 (SPPS, Chicago, Illinois).

Role of the Funding Source
This study was funded by the Finnish Foundation for Cardiovascular Research and the Kuopio University EVO Foundation. The funding sources had no role in the design, conduct, analysis, or publishing policy of this study.

RESULTS
A total of 159 and 157 patients were randomly assigned to the metoprolol and amiodarone groups, respectively. All patients received the allocated treatment for the efficacy analysis and received complete courses until the designated end points were reached (Figure 1).

Figure 1. Study flow diagram.

* Reasons for exclusions: >24 h in the intensive care unit (n = 18), atrial fibrillation occurred before randomization (n = 6), temporary pacing was not functioning properly (n = 40), the operation was unexpectedly performed off pump (n = 7), patients had new second- or third-degree atrioventricular block (n = 13), heart rate <60 beats/min (n = 15), systolic blood pressure <100 mm Hg at randomization (n = 34), and patient received metoprolol before randomization (n = 6).
Table 1. Preoperative and Perioperative Patient Characteristics

| Characteristic                        | Metoprolol Group (n = 159) | Amiodarone Group (n = 157) |
|---------------------------------------|-----------------------------|-----------------------------|
| Preoperative                          |                             |                             |
| Mean age (SD), y                      | 63.8 (9.0)                  | 64.5 (9.3)                  |
| Men, n (%)                            | 117 (73.6)                  | 140 (89.2)                  |
| Mean LVEF (SD)                        | 0.57 (0.11)                 | 0.59 (0.10)                 |
| History of diabetes mellitus, n (%)   | 48 (30.2)                   | 33 (21.0)                   |
| History of COPD, n (%)                | 5 (3.1)                     | 2 (1.3)                     |
| Unstable angina pectoris, n (%)       | 43 (27.0)                   | 41 (26.1)                   |
| Hypertension, n (%)                   | 106 (66.7)                  | 101 (64.3)                  |
| Three-vessel disease, n (%)           | 123 (77.4)                  | 130 (82.8)                  |
| CCS class, n (%)                      |                             |                             |
| I                                      | 2 (1.3)                     | 2 (1.3)                     |
| II                                     | 44 (28.0)                   | 53 (33.8)                   |
| III                                    | 63 (40.1)                   | 67 (42.7)                   |
| IV                                     | 47 (29.9)                   | 35 (22.3)                   |
| Current smoker, n (%)                 | 23 (14.5)                   | 28 (17.8)                   |
| History of stroke or TIA, n (%)       | 11 (6.9)                    | 7 (4.5)                     |
| Use of statins, n (%)                 | 125 (80.5)                  | 122 (83.0)                  |
| Use of ACE inhibitors, n (%)          | 62 (42.2)                   | 69 (46.9)                   |
| History of claudication, n (%)        | 10 (6.3)                    | 11 (7.0)                    |
| Perioperative                          |                             |                             |
| Mean number of distal anastomoses (SD)| 4.1 (1.3)                   | 4.0 (1.2)                   |
| Mean pump time (SD), min              | 94.5 (31.8)                 | 92.8 (33.3)                 |
| Mean cross-clamp time (SD), min       | 80.3 (27.3)                 | 79.7 (29.2)                 |
| Right coronary artery bypass, n (%)   | 133 (84.7)                  | 128 (82.1)                  |
| Type of operation, n (%)              |                             |                             |
| Isolated CABG                         | 144 (90.6)                  | 146 (93.0)                  |
| Isolated AVR                          | 7 (4.5)                     | 3 (1.9)                     |
| Combined CABG and AVR                 | 8 (5.0)                     | 8 (5.1)                     |

ACE = angiotensin-converting enzyme; AVR = aortic valve replacement; CABG = coronary artery bypass graft; CCS = Canadian Cardiovascular Society; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

Table 1 presents the baseline demographic, clinical, and perioperative characteristics of the study groups. In general, the groups were well matched, although more patients in the amiodarone group were men. Most of the surgeries in both groups were isolated CABGs.

A total of 75 patients (23.7%) had AF during the 48-hour study period. Atrial fibrillation occurred in 38 of 159 (23.9%) patients in the metoprolol group and 39 of 157 (24.8%) patients in the amiodarone group (P = 0.85) (Figure 2 and Table 2). However, the difference between treatments (−0.9 percentage point [90% CI, −8.9 to 7.0 percentage points]) did not satisfy the prespecified definition of equivalence that the treatment effect would be between −5 and 5 percentage points. The HR of the metoprolol group compared with the amiodarone group was 0.99 (95% CI, 0.63 to 1.56). This remained unchanged after adjustment for potential confounders (age, sex, left ventricular ejection fraction, type of operation, unstable angina pectoris, chronic obstructive pulmonary disease, and right coronary artery bypass) (adjusted HR, 1.09 [95% CI, 0.67 to 1.76]). Atrial fibrillation occurred significantly earlier in patients in the metoprolol group than in those in the amiodarone group (mean time to onset of AF, 21.1 hours [SD, 11.3] vs. 27.0 hours [SD, 10.2]; P = 0.020). The incidence of AF in the metoprolol group and amiodarone group at each of the 3 participating centers was 22.2% and 23.4% (228 enrolled patients), 30.0% and 30.2% (83 enrolled patients), and 0% and 0% (5 enrolled patients), respectively. In addition, after the study period but before hospital discharge, an additional 28 (17.7%) patients in the metoprolol group and 26 (16.9%) patients in the amiodarone group developed AF (P = 0.85). The mean time to hospital discharge or transfer to the referring hospital (after cardiac surgery) was 5.6 days (SD, 3.5) in the metoprolol group and 5.4 days (SD, 2.7) in the amiodarone group (difference, 0.23 day [95% CI, −0.43 to 0.89 day]).

One patient in the amiodarone group died of cardiac arrest (ventricular fibrillation) 9 hours after the start of the infusion (Table 3). The patient had amiodarone infusion without temporary pauses until ventricular fibrillation occurred. One patient in the metoprolol group developed cardiac tamponade and died on the fifth postoperative day. One patient in the metoprolol group developed AF 30 hours after the start of the infusion and had a stroke 38 hours later. One patient in the metoprolol group was readmitted to the intensive care unit for respiratory failure during the study period.

Figure 2. Kaplan–Meier curves of the cumulative proportion of patients with atrial fibrillation after cardiac surgery.
Amiodarone caused thrombophlebitis of the infusion vein in 11 patients, whereas no thrombophlebitis was observed in the metoprolol group (7.0% vs. 0%; \( P = 0.001 \)) (Table 3). The study medication was temporarily discontinued because of hypotension more frequently in the metoprolol group than in the amiodarone group (14.5% vs. 3.8%; \( P = 0.001 \)). In addition, bradycardia occurred more often in the amiodarone group than in the metoprolol group (10.8% vs. 5.0%; \( P = 0.056 \)). Episodes of hypotension and bradycardia did not result in clinically important adverse events but were transient and asymptomatic. The infusion of study medication could be restarted after the interruption in all patients. Resternotomy was needed in 8 patients in the metoprolol group and 5 patients in the amiodarone group (5.0% vs. 3.2%; \( P = 0.41 \)).

**DISCUSSION**

We found no difference in the occurrence of postoperative AF in patients treated with intravenous metoprolol or amiodarone after cardiac surgery. Atrial fibrillation occurred in 23.9% and 24.8% of patients in the metoprolol and amiodarone groups, respectively. However, the wide range of the CIs does not satisfy the hypothesized definition of equivalence (between −5 and 5 percentage points) and therefore does not allow us to conclude that the 2 treatments are equally effective in preventing AF after cardiac surgery.

According to current guidelines, \( \beta \)-blockers should be the first-line preventive treatment of AF in patients having cardiac surgery. Amiodarone should be reserved for patients in whom \( \beta \)-blocker therapy fails or is contraindicated (25). Despite this, according to a recent survey, 19% of physicians reported using amiodarone as the first-line prophylactic strategy for postoperative AF (26). This nonadherence to guidelines may be because amiodarone is considered to be the most potent drug in the prevention of AF (21) and data directly comparing the efficacy and safety of intravenous \( \beta \)-blockers and amiodarone in preventing postoperative AF are lacking.

Several studies (8, 13, 14, 22, 23) have demonstrated the effectiveness of \( \beta \)-blockers in preventing AF after cardiac surgery. A meta-analysis of 27 prospective randomized trials and 3840 patients reported a 61% decrease in the incidence of postoperative AF with \( \beta \)-blocker therapy (13). In the largest randomized trial, oral amiodarone decreased the incidence of postoperative AF after CABG by 39% compared with placebo (28). In a meta-analysis of 18 randomized trials, amiodarone decreased the incidence of postoperative AF by 62% (14).

\[ \text{Table 2. Postoperative Characteristics} \]

| Characteristic | Metoprolol Group | Amiodarone Group | Univariate \( P \) Value | Treatment Difference (95% CI) |
|---------------|------------------|------------------|------------------------|-------------------------------|
| AF during 48-h protocol, n (%) | 38 (23.9) (n = 159) | 39 (24.8) (n = 157) | 0.85* | −0.94 (−10 to 8.5) |
| Mean time to onset of AF after randomization (SD), h† | 21.1 (11.3) (n = 37) | 27.0 (10.2) (n = 38) | 0.020‡ | −5.9 (−11 to −0.98) |
| Mean ventricular rate during AF (SD), beats/min† | 119.6 (26.5) (n = 34) | 113.8 (20.0) (n = 37) | 0.29‡ | 5.9 (−5.2 to 17) |
| Mean serum potassium level before AF (SD), mmol/L† | 4.4 (0.45) (n = 35) | 4.2 (0.44) (n = 38) | 0.22‡ | 0.13 (−0.079 to 0.33) |
| AF after 48 h but before discharge, n (%) | 28 (17.7) (n = 158) | 26 (16.9) (n = 154) | 0.85* | 0.04 (−7.6 to 9.3) |
| Mean first postoperative CK-MBm concentration (SD), μg/L | 21.9 (12.4) (n = 157) | 21.8 (10.6) (n = 155) | 0.95‡ | −0.078 (−2.5 to 2.6) |

\[ \text{Table 3. Adverse Events} \]

| Adverse Event | Metoprolol Group (n = 159, n (%) | Amiodarone Group (n = 157, n (%)) | Group Difference (95% CI), percentage points |
|---------------|----------------------------------|-----------------------------------|---------------------------------------------|
| Death | 1 (0.63) | 1 (0.64) | −0.008 (−1.8 to 1.7) |
| Any adverse event | 42 (26) | 41 (26) | 0.30 (−9.4 to 10) |
| Serious adverse event | 2 | 1 | 0.62 (−1.5 to 2.8) |
| Adverse events | | | |
| Postoperative stroke | 1 (0.63) | – | 0.63 (−0.61 to 1.9) |
| Perioperative MI | 1 (0.63) | 2 (1.3) | −0.64 (−2.8 to 1.5) |
| Thrombophlebitis of arm vein | – | 11 (7.0) | −7.0 (−11 to −3.0) |
| Bradycardia | 8 (5.0) | 17 (10.8) | −5.8 (−12 to 0.16) |
| Hypotension | 23 (14.5) | 6 (3.8) | 11 (4.3 to 17) |
| Resternotomy because of bleeding | 8 (5.0) | 5 (3.2) | 1.8 (−2.5 to 6.2) |
| New conduction disturbances (RBBB, LAHB, LPHB, LBBB) | 3 (1.9) | 2 (1.3) | 0.61 (−2.1 to 3.4) |
| New atrioventricular block (I–III degree) | 1 (0.63) | – | 0.63 (−0.61 to 1.9) |

MI = myocardial infarction; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LPHB = left posterior hemiblock; RBBB = right bundle branch block.
Only a few studies have compared \(\beta\)-blockers and amiodarone in a head-to-head setting. In a recent report by Sleiaty and colleagues (29), oral bisoprolol and amiodarone were equally effective for prophylaxis against AF after CABG. Auer and coworkers (30) compared oral amiodarone plus metoprolol with oral sotalol, oral metoprolol, and placebo in patients having cardiac surgery. The combination of amiodarone and metoprolol reduced the incidence of AF significantly (44%) compared with placebo, whereas no significant differences were found between the active-treatment groups. In these trials, the study drugs were administered orally, whereas drugs were given intravenously in our study. The bioavailability of drugs is markedly reduced when they are administered in oral form during the early phase after CABG (24). Only 1 earlier trial compared intravenous \(\beta\)-blockers with intravenous amiodarone (31). Solomon and colleagues (31) randomly assigned patients to either intravenous amiodarone for 48 hours followed by oral amiodarone until discharge or intravenous propranolol for 48 hours followed by oral propranolol until discharge in 102 patients having cardiac surgery. Amiodarone was superior to propranolol in preventing postoperative AF; however, \(\beta\)-blocker treatment was continued throughout the study in the patients assigned to amiodarone who took \(\beta\)-blockers before surgery. Thus, in many cases, the true comparison was amiodarone plus \(\beta\)-blocker versus \(\beta\)-blocker alone rather than amiodarone versus \(\beta\)-blocker.

With regard to serious adverse events, in our study, 1 patient in each group died during the 48-hour follow-up. In addition, 1 patient in the metoprolol group had a stroke. In all of these cases, the study medication was unlikely to be related to these adverse events. Both treatments seemed to be well tolerated. No patients required crossover to the other treatment. The only symptomatic adverse effect was venous thrombophlebitis in 11 patients in the amiodarone group. The study drug infusion was temporarily interrupted because of hypotension more often in the metoprolol group than in the amiodarone group and because of bradycardia more often (although nonsignificantly) in the amiodarone group than in the metoprolol group. These findings are in line with those of an earlier study reporting that amiodarone infusion was associated with bradycardia and interruption of the infusion in 18% of patients (32).

An obvious limitation of our study is that although the incidence of AF was similar in the study groups (38 and 39 patients in the metoprolol and amiodarone groups, respectively), we lacked sufficient power to demonstrate equality. Even after adjustment for potential confounders, the wide range in the 95% CIs (0.67 to 1.76) does not allow us to conclude that the 2 treatments were equally effective in preventing postoperative AF. Thus, we cannot exclude the possibility that true differences in efficacy exist between amiodarone and \(\beta\)-blockers in the prevention of AF.

For example, withdrawal of established \(\beta\)-blocker therapy for patients allocated to amiodarone therapy may have precipitated AF. Although we doubt this was the case, because amiodarone has \(\beta\)-blocking properties (33), we cannot exclude the possibility that this may have biased our results against amiodarone. The \(\beta\)-blocking effect of amiodarone is supported by our finding that bradycardia (heart rate = 60 beats/min) developed more frequently in patients treated with amiodarone than in those treated with metoprolol.

Our patients were not considered to be at particularly elevated risk for AF and were hemodynamically stable, were not receiving pressors, and were free of mechanical ventilation within 24 hours of cardiac surgery. Thus, our results cannot be safely applied to sicker patients or those at higher risk for AF, such as patients with a history of AF or undergoing mitral valve repair.

The study period of 48 hours starting from the first postoperative morning may be argued to be too short. The incidence of AF is highest on the second and third postoperative days (5, 11). Most of this period was well covered in our study. As many as 17% of the patients developed AF after the study period but before hospital discharge. However, the occurrence of AF after the study period did not differ between the groups (17.7% vs. 16.9%).

It could also be argued that the amiodarone dose in our study was insufficient. Amiodarone has been shown to be efficient in various doses and in oral and intravenous administration (13, 14, 19, 20, 28, 34). In the largest randomized trial, the amiodarone dose was 10 mg/kg, whereas it was 50% more in our study, that is, 15 mg/kg per day (28). Thus, an insufficient dose is unlikely to explain our results.

Although we did not find any difference in the incidence of AF, larger multicenter trials or meta-analyses are needed to confirm the equality of metoprolol and amiodarone in preventing postoperative AF. In addition, comparisons of metoprolol and amiodarone are needed in patient cohorts with higher risk for AF, for example, patients undergoing mitral operation, those with a history of AF, and those who are not hemodynamically stable after surgery. Until more data are available, we recommend adherence to current guidelines: the use of \(\beta\)-blockers as first-line prophylaxis of postoperative AF.

We conclude that although the observed incidence of AF during 48 hours of treatment with intravenous metoprolol or amiodarone after cardiac surgery was similar, we cannot conclude that the treatments are equally effective.

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