Atrial Fibrillation After Cardiac Surgery: Incidence, Risk Factors, and Economic Burden

Atrial Fibrillation After Cardiac Surgery: Incidence, Risk Factors, and Economic Burden

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Objective: **To evaluate the incidence of postoperative atrial fibrillation (POAF), the predisposing factors, the results of treatment before discharge, and the impact on duration and costs of hospitalization.**

Design: **A prospective observational study.**

Methods: **Patients who underwent cardiac surgery from January 1, 2007 to December 31, 2007.**

Interventions: **Electrocardiography was continuously monitored after surgery. Patients with symptomatic new-onset atrial fibrillation or lasting >15 minutes were treated with amiodarone and with DC shock in prolonged cases.**

Results: **POAF occurred in 29.7%, with the higher incidence between the 1st and 4th postoperative day. Age ($p < 0.001$), atrial size >40 mm ($p < 0.001$), previous episodes of AF ($p < 0.001$), female sex ($p = 0.010$), and combined valve and bypass surgery ($p = 0.012$) were multivariate predictors of POAF at logistic regression. Sinus rhythm was restored by early treatment in 205 of 215 patients. This was associated with a low incidence of cerebrovascular events (<0.5%) and with a limited increase of average length of hospitalization (24 hours) in patients with POAF.**

Conclusions: **The overall incidence of POAF in the authors' center is close to 30%; 95.3% of patients were discharged in sinus rhythm. The increase in length and costs of hospitalization (on average, 1.0 day with a burden of about €1,800/patient) were significantly lower than in previous investigations.**

KEY WORDS: atrial fibrillation, perioperative complications, cardiac surgery, amiodarone

THE INCIDENCE OF atrial arrhythmias after cardiac surgery ranges between 10% and 65%.[1,2] A meta-analysis comprising 24 studies reported postoperative atrial fibrillation (POAF) in 30% of cases after coronary artery bypass graft (CABG) surgery.[3] The increasing age of patients undergoing cardiac surgery is significantly associated with an increased risk of POAF.[4-6] Several factors, including the type of surgical procedure, patient demographics, criteria used for diagnosis, and methods of electrocardiographic (ECG) monitoring, may account for the wide range of POAF incidence reported in the literature.[7-9] POAF is near 10% when the diagnosis is based on scheduled 12-lead ECGs, but more than 40% when continuous ECG recording or Holter monitoring are used and episodes lasting less than 10 minutes[7,8] are included in the analysis. Otherwise, the incidence of POAF has been reported to range between 16% and 30% when the diagnosis is made on the basis of patients' symptoms.[10,11] At present, there is no definite evidence regarding the clinical weight of POAF-related clinical complications in patients suffering from symptomatic versus asymptomatic atrial fibrillation (AF), and further studies are needed to clarify the question.

Previous investigations suggested that POAF is associated with increased hospital mortality and morbidity, in particular a higher incidence of stroke, up to 3 times more in comparison with patients with stable sinus rhythm, and an increase in the length of hospitalization.[12-14] Heart rate control instead of an early attempt to restore sinus rhythm is usually the strategy of choice in patients with POAF, and little information exists on the effects of early recovery of sinus rhythm on POAF-related complications.[7] Therefore, to improve POAF management, the authors set out to (1) determine the prevalence and timing of perioperative AF, (2) identify its risk factors, (3) evaluate treatment strategies, (4) assess return to sinus rhythm by hospital discharge, (5) investigate its impact on outcomes, and (6) evaluate its economic implications.

PATIENTS AND METHODS

A 1-year survey was planned. Among 822 patients who underwent cardiac surgery between January 2007 and December 2007, 28 patients who died during the perioperative period and 69 suffering from chronic AF and/or undergoing the maze procedure were excluded from the analysis. In the study, 725 patients, 482 men and 243 women (mean age, 67.4 ± 12 years), were finally included. Surgical procedures are shown in Figure 1. Echocardiographic evaluation was performed 48 hours before surgery using a Sequoia Acuson Instrument (Siemens Medical Solution, CA) according to the guidelines of the American Society of Echocardiography.[15]

Table 1 shows baseline clinical and echocardiographic patient characteristics. Oral drugs were administered up to 12 hours before surgery and resumed 12 hours after intensive care unit (ICU) admission, clinical conditions permitting, through a nasogastric tube if necessary.

The primary endpoint was the development of AF. All patients had continuous ECG monitoring in the ICU and were subsequently discharged to a monitored unit throughout their hospital stay. Atrial arrhythmias were identified according to the Society of Thoracic Surgeons' definition as those that were clinically documented or treated. Observed atrial arrhythmias were AF and atrial flutter, and, unless otherwise stated, the authors use "AF" to mean either. Indeed, all symptomatic episodes of AF confirmed by ECG recording or asymptomatic AF revealed by continuous ECG monitoring lasting more than 10 minutes were considered as POAF and included in the analysis.

Secondary endpoints included discharge rhythm, length of postoperative stay, and incidence of postoperative complications. Discharge rhythm was identified as normal sinus rhythm (NSR), AF, or atrial flutter.

Transient electric stimulation through epicardial wires was used for severe bradycardia or atrioventricular block until the restoration of heart rhythm or definitive pacemaker implant. Patients who did not

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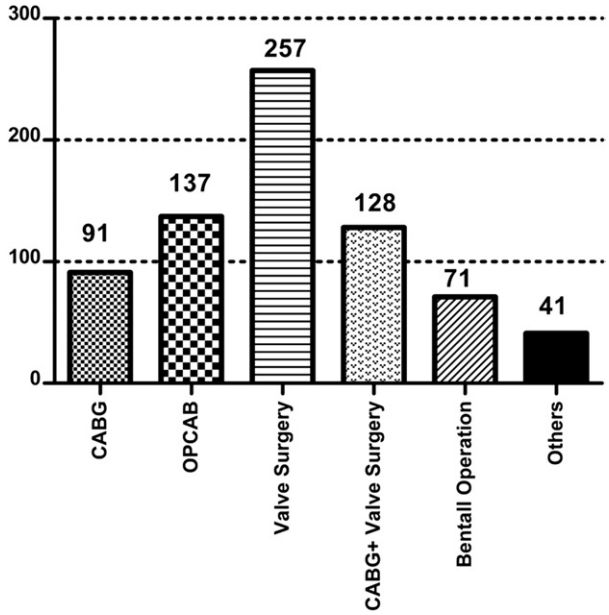

Fig 1. The number of interventions performed in the period under investigation.

recover NSR within 30 minutes usually were treated with intravenous amiodarone (300 mg in 1 hour followed by 900 mg/24 hours IV continuous infusion) to control heart rate. Propafenone was used in cases of known previous amiodarone-related side effects. Electrical cardioversion by biphasic DC shock was considered when sinus rhythm was not restored after 24 hours of pharmacologic treatment. Electrical cardioversion was performed on a selective basis in 39 patients. Cardioversion was begun at 200 J and was performed according to American College of Cardiology recommendations.[16]

In-hospital costs were obtained from the hospital's financial accounting department. All billed items associated with the occurrence of POAF were assigned to one of the following categories: anesthesia: cost of anesthetics, equipment, and disposables used by anesthesiologists during electric cardioversion; intensive care unit: cost/day of nursing, equipment, and space in the ICU (total = cost/d × number of extra days); **s**ubintensive care unit **+w**ard: cost of nursing, equipment, and space in the **s**ubintensive care unit and in the ward (total = cost/d × number of extra days); laboratory: cost of blood tests; cardiology laboratory: cost of electrocardiograms and echocardiograms; pharmacy: cost of pharmacy; therapies: cost of physical and occupational therapies; and others: unknown and nonspecified costs.

Following the World Medical Association Guidelines concerning ethical principles for medical research involving human subjects,[5] the study was approved by the Institutional Ethics Boards. Furthermore, all patients gave their informed consent.

Variables were tested for normal distribution by the Kolmogorov-Smirnov test. Continuous variables were presented as mean and standard deviation, categoric variables as percentage, and non-normally distributed variables as median and interquartile range. The timing of AF was calculated as the interval from the date of surgery to the date of developing AF. The time-related risk of AF was estimated parametrically by a multiphase hazard decomposition method.[17]

Categoric variables were compared with the chi-square or Fisher exact test. Student *t* tests (unpaired) were used to compare continuous variables except when data were skewed; in which case, the Wilcoxon test was used. Variables reaching statistical significance or borderline (<0.1) were introduced in multivariate analysis.

Multivariate logistic regression analysis by means of a backward stepwise algorithm (cutoff for entry 0.05, for removal 0.10) was performed to select independent predictors of early death and postoperative events. Categoric variables with more than 2 levels in the regression model were converted into dummy variables. Thirty-eight variables (Appendix 1) were chosen based on existing Society of Thoracic Surgeons risk-adjustment models and investigated for their predictive value. Nonetheless, to enhance the accuracy of the model, the number of variables were reduced using variable clustering[18] (PROC-VARCLUS;SAS/STAT, release 9; SAS Institute, Cary, NC). The appropriateness of fit of the final logistic regression models was assessed with the Hosmer-Lemeshow statistic, and predictive accuracy was assessed by the concordance index.[19] Internal validation of predictors generated by multivariate logistic regression was performed by means of bootstrapping techniques, with 1,000 cycles and generation of odds ratios and bias-corrected 95% confidence interval.[20] SPSS 12.0 (SPSS, Chicago, IL) and Stats Direct 2.5.7 (Stats Direct, Sale, UK) were used for these calculations. Significance for hypothesis testing was set at the 0.05 2-tailed level.

RESULTS

POAF developed in 215 patients (29.7%). Thirty-nine (4.1%) had preoperative episodes of AF. The incidence of AF peaked 2 days after the procedure (4.14%/d [standard error of the mean, 3.47-4.90]) and declined steadily thereafter (Fig 2).

Patients with POAF were older than patients without arrhythmic complications (71.0 ± 8.9 years *v* 66.4 ± 6.5 years, $p < 0.001$). Furthermore, POAF was more frequent in females (106/243 [33.3%]) than in males (134/482 [27.8%], $p = 0.049$). In addition, POAF was significantly less frequent in patients undergoing isolated CABG surgery (23.5%) than in patients undergoing associated CABG surgery and valve procedures (42.2%, $p < 0.001$). The occurrence of POAF was not significantly different in off-pump coronary artery bypass grafting compared with on-pump CABG surgery (23.4% and 22%, respectively; $p = 0.9$). Moreover, patients developing POAF had more frequent episodes of AF in the preoperative period (18.4% *v* 37.3%, $p < 0.001$).

In addition, subjects who experienced POAF had a larger left atrial diameter (38.2 ± 1.4 *v* 43.3 ± 2.6, $p < 0.001$) and a lower left ventricular ejection fraction (42.4% ± 12% *v* 54.2% ± 15%, $p = 0.005$). Regarding postoperative variables, patients with POAF underwent prolonged use of catecholamines in the ICU (2.5 ± 0.9 hours *v* 5.9 ± 1.2 hours, $p < 0.001$). Preop-

Table 1. Baseline Clinical and Echocardiographic Characteristics

Sex M/F	482/243 (66.5/33.5)
Age (years ± standard deviation)	67.4 ± 12.3
Hypertension	428 (59%)
PAF history	39 (5.37%)
LA diameter (mm)	41.65 ± 6.3
LVEF (%)	52.26 ± 10.5
β-Blockers	288 (39.72%)
ACE inhibitors or AT_1 blocker	469 (64.69%)
Statins	276 (38.06%)

NOTE. Continuous variables are presented as mean ± standard deviation. Discrete variables are presented as percentage (parentheses).

Abbreviations: M/F, male/female; PAF, preoperative AF; LA, left atrium; LVEF, left ventricular ejection fraction.

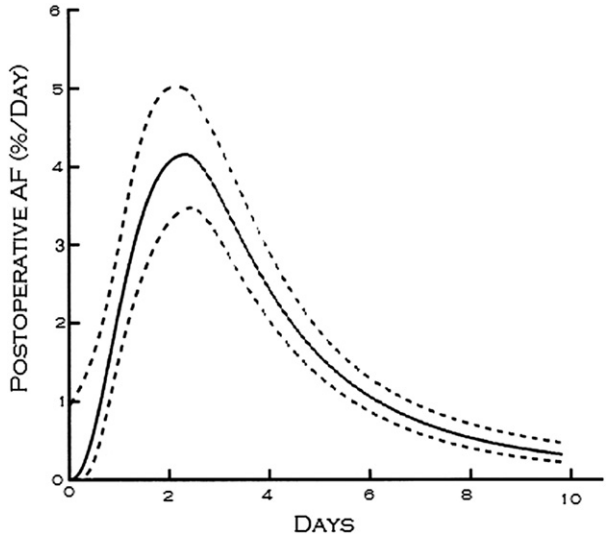

Fig 2. The incidence of AF after cardiac surgery (hazard function). The solid line is the parametric estimate, and dashed lines are 68% confidence limits, equivalent to ±1 standard error.

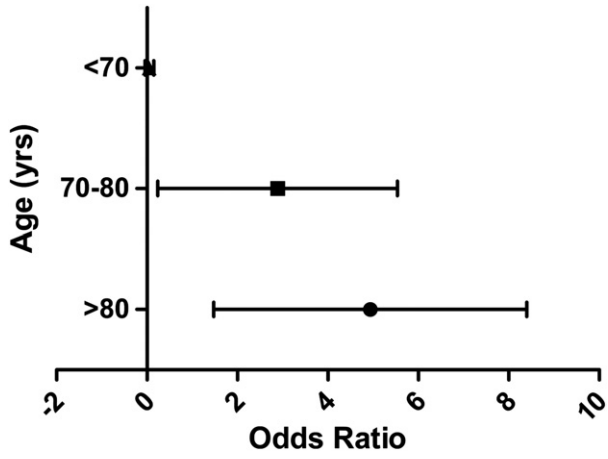

Fig 3. The predictive value of age at multivariate logistic regression. Data are expressed as odds ratio and 95% bias-corrected confidence interval.

erative use of β-blockers ($p = 0.06$), angiotensin-converting enzyme (ACE) inhibitors (or AT_1-receptor blockers, $p = 0.4$) or statins ($p = 0.2$) failed to show a predictive value on POAF for univariable analysis.

For multivariate analysis, age was a strong predictor of POAF ($p < 0.001$, Table 2). Indeed, patients older than 80 years had 39.3% higher probability than patients aged 70 to 80 years and 98.4% higher probability than patients younger than 70 years (Fig 3). In addition, atrial size >40 mm ($p < 0.001$) and previous episodes of AF in the preoperative period ($p < 0.001$) significantly increased the likelihood of developing POAF. Finally, female sex ($p = 0.010$) and combined valve and bypass surgery ($p = 0.012$) were multivariate predictors of POAF at logistic regression.

One hundred ninety patients (92.7%) underwent pharmacologic treatment consisting of rate-control agents only in 4 (2.1%), antiarrhythmics only in 163 (85.8%), and both in 23 (12.1%). Rate-control agents included metoprolol, carvedilol, diltiazem, propafenone, and digoxin; amiodarone was the only rhythm-control agent used. Electrical cardioversion was used in 67 patients (31.1%), of whom 28 (41.7%) had undergone previous unsuccessful pharmacologic treatment.

At discharge, 95.3% (205/215) of patients with POAF were in NSR. In 15 (7.3%), sinus rhythm was restored spontaneously within 30 minutes. Among patients who required pharmacologic treatment, 85.8% (140/163) receiving only amiodarone and 73.9% (17/23) undergoing combined rate control and antiarrhythmic therapy recovered sinus rhythm.

Among patients undergoing cardioversion, 59.7% (40/67) required 1 DC shock, 25.4% (17/67) 2, and 14.9% (10/67) 3 or more attempts. The overall cardioversion success rate was 94% (63/67). Ten patients (4.6%) were discharged in atrial fibrillation. Among them, 4 had only pharmacologic therapy, whereas 6 had cardioversion after unsuccessful pharmacologic treatment. All these patients had undergone valve surgery and were discharged with antiarrhythmic therapy associated with digoxin and warfarin.

Patients in whom AF developed postoperatively had a longer median length of hospital stay (7.9 days; interquartile range, 4.5-9.5) than those who did not have AF (5.7 days; interquartile range, 3.6-7.1; $p < 0.001$ [Fig 4]). No difference in hospital incidence of cerebrovascular events was found between patients with POAF compared with patients with stable sinus rhythm (0.45% *v* 0.41%, $p > 0.9$).

Total costs (Table 3) were higher in the POAF group (plus €;1,800 [1,599-2,302], $p < 0.001$), with the largest increases in the ICU ($p = 0.02$), subintensive care unit + ward ($p < 0.001$), laboratory ($p = 0.004$), and cardiology laboratory ($p = 0.01$).

Table 2. Multivariate Predictors of POAF

Variable	B	St. Err	Wald	*p*	Ex(B)	95% CI
Intercept	1.648	0.57	8.339	0.004	—	—
Age >80 y	1.516	0.309	24.109	<0.001	4.552	2.486-8.335
Atrial size >40 mm	1.429	0.296	23.388	<0.001	4.175	2.339-7.451
Valve surgery + CABG	1.010	0.403	6.276	0.012	2.746	1.246-6.055
Preoperative episodes of AF	1.516	0.309	24.109	<0.001	4.512	2.486-8.335
Female sex	0.988	0.393	6.378	0.010	2.685	1.243-5.798

NOTE. Hosmer and Lemeshow = 0.729; concordance index = 0.8.
Abbreviations: B, regression coefficient; CI, bias-corrected confidence interval.

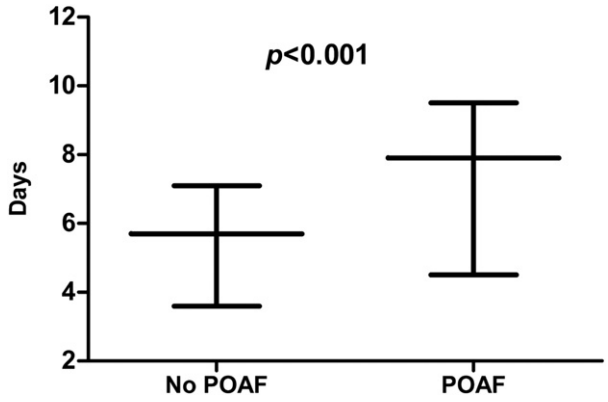

Fig 4. The length of hospital stay in patients with and without POAF. (Data are expressed as median and interquartile range.)

DISCUSSION

AF is the most frequent complication after cardiac surgery.[2] Previous investigations reported increased morbidity and mortality related to POAF.[3,21] Moreover, POAF was associated with significant increases in duration and the overall costs of hospitalization.[14,22] Mathews et al[21] reported that the overall incidence of POAF was 27% in 2,417 patients undergoing CABG surgery with or without concurrent valve surgery. In a study by the Department of Veterans Affairs,[23] similar results were reported. Mitral valve repair or replacement significantly increased the risk of AF (odds ratio = 2.88 and 2.33, respectively).

In the present investigation, the overall incidence of POAF was close to 30%, which was not significantly different from that reported in previous studies.[24,25] With multivariate logistic regression analysis, the present results suggest that age, atrial size >40 mm ($p < 0.001$), previous episodes of AF ($p < 0.001$), female sex ($p = 0.010$), and combined valve and bypass surgery ($p = 0.012$) significantly increased the likelihood of developing POAF.

Patients undergoing valve surgery, in particular when associated with coronary revascularization, were twice as likely to develop POAF compared with patients undergoing CABG surgery, which is in agreement with previously reported data.[26] In patients undergoing surgical revascularization, the authors did not find any significant difference between patients undergoing cardiopulmonary bypass (CPB) surgery versus off-pump surgery (23.4% *v* 22%). It has been hypothesized that intraoperative ischemia related to hemodynamic changes during CBP plays a role in the development of POAF; it was suggested that the decreased risk of ischemic damage in beating-heart CABG surgery reduced its incidence. Initial favorable results[27,28] were not confirmed by other authors who failed to find a relation between the techniques of CABG surgery.[29,30]

Independent predictors of POAF included advanced age, female sex, a history of AF or of congestive heart failure, and the incidence of POAF.[21-23] Age is the independent variable most consistently associated with POAF.[31-33] In the present investigation, 62.6% of POAF patients were aged >70 years. Aranki et al[34] report an 18% incidence of POAF in patients aged <60 years versus 52% for those aged >80 years. The probability of developing POAF increases by about 25% for every 5-year increase in age,[32] with a plateau after 80 years.[13] Because the incidence of AF also increases with age in "medical" AF, age-related degenerative and inflammatory changes in atrial anatomy may induce modifications of electophysiologic properties of atrial myocytes that may advance the onset of the arrhythmia.[35,36]

Surgical variables that may advance atrial ischemia, such as the duration of aortic cross-clamping and the time of the recovery of atrial electrical activity after cardioplegia, have been shown to be independently related to the risk of POAF.[12,37,38] In accordance with previous studies,[38,39] a history of paroxysmal AF was associated with a 2 to 3 times higher risk of POAF. An increased left atrial diameter and a lower LVEF were significantly associated with an increased risk of POAF as suggested previously.[40] Several studies, however, failed to find a clear relation between atrial enlargement and postoperative AF.[41,42]

Acute stretching of atrial fibers caused by an abrupt increase in left atrial pressure may favor dispersion of refractoriness with a higher risk of AF.[43] Chronic atrial dilation caused by valvular disease or left ventricular dysfunction is associated with anatomic changes, mainly foci of fibrosis, which may lead to atrial "electric remodeling."

Almassi et al[18] showed that the use of inotropic agents for more than 30 minutes after the termination of CPB was associated with a higher incidence of arrhythmias; the risk of POAF exceeded 50% in patients with cardiogenic shock undergoing surgical revascularization.[44] In the present study, 14% of patients with POAF had severe postoperative hemodynamic impairment requiring prolonged administration of catecholamines, in comparison to 5.7% of patients without arrhythmia complications ($p = 0.005$). The relative proarrhythmic effect of a severe hemodynamic impairment per se and that of sympathicomimetic drugs in the development of POAF remain to be clarified. POAF has been reported to be associated with a longer hospital stay and with a higher risk of infectious, renal, and neurologic complications.[45-47] Moreover, discharge from the hospital before the restoration of sinus rhythm has

Table 3. Extra Costs in Patients With POAF (in Euros)

Anesthesia	80 (30-95)
Intensive care unit	180 (138-223)
Subintensive care unit + ward	830 (770-1,030)
Laboratory	293 (250-328)
Cardiology laboratory	265 (235-312)
Pharmacy	130 (102-175)
Therapies	78 (46-84)
Other	44 (28-55)
Total cost	1,800 (1,599-2,302)

NOTE. Costs are presented as median and interquartile range. Anesthesia: cost of anesthetics, equipment, and disposables used by anesthesiologists during electric cardioversion; intensive care unit: cost/d of nursing, equipment, and room in the intensive care unit (total= cost/d × number of extra days); subintensive care unit + ward: cost of nursing, equipment, and room in the subintensive care unit and in the ward. Total = cost/d × number of extra days; laboratory: cost of blood examinations; cardiology laboratory: cost of electrocardiograms and echocardiograms; pharmacy: cost of pharmacy; therapies: cost of physical and occupational therapies; others: unknown and nonspecified costs.

been associated with a high incidence of persistence of arrhythmia. In the study of Loubani et al,[46] 39% still had AF 6 months after surgery despite the use of antiarrhythmic medication. This observation emphasizes the need for a close follow-up in patients discharged in AF and a scheduled attempt at electrical cardioversion after an adequate period of anticoagulation in the case of persistence of AF.

Early restoration of sinus rhythm before discharge, usually within 24 hours from the onset of the arrhythmia, avoids the need for transesophageal echocardiography before DC shock and reduces the risk and the costs of prolonged anticoagulation and those for rehospitalization for elective electrical cardioversion. According to the authors' protocol, all patients in whom AF lasted >30 minutes were treated with amiodarone and, in the case of failure of drug treatment, with DC shock. Less than 5% (10/214) of patients were discharged in AF. Prompt restoration of sinus rhythm may account for the low incidence of neurologic complications (only 1 stroke was observed in each group). Moreover, early restoration of NSR is likely to decrease the lengthening and overall costs of hospitalization independently attributable to POAF. Aranky et al[34] reported a duration of hospitalization in patients with POAF an average of 3 to 4 days longer than in patients in NSR, which is on average 2 days more than that observed in the present study. Similar results were reported by other authors, with additional attributable costs associated with POAF ranging from $5,000 to $12,000 per patient.[14,22,47]

A recent investigation has shown that an exaggerated inflammatory response is associated with a higher risk of POAF.[48,49] The release of cytokines and an increase in oxidative stress with elevated atrial levels of peroxynitrite may affect the activity of sodium channels,[50] whereas interleukin 2 and free radicals decrease the upstroke velocity of the action potential by reducing sodium currents.[51] Finally, the tumor necrosis factor downregulates gap junction proteins and reduces cell coupling.[52] These electrophysiologic changes may result in nonhomogeneity of atrial conduction and favor POAF. The present authors failed to find any relationship between clinical and ECG signs of pericardial involvement and the risk of POAF, although the role of inflammation may be significantly underestimated by simple clinical evaluation.

Several investigations evaluated the effectiveness of pharmacologic and nonpharmacologic interventions for the prevention of AF, with the main purpose of decreasing the length of hospital stay and the risk of POAF-related stroke.[53,54] β-Blocker withdrawal before surgery was associated with a higher risk of POAF; conversely, continuation of treatment decreased the incidence of arrhythmic complications.[21] Similarly, Mathew et al[26] suggested that preoperative treatment with inhibitors of the renin-angiotensin system was associated with a decreased risk of postoperative AF. Contrasting results were reported by Coleman et al.[55]

Results from the present investigation failed to show that POAF incidence was influenced by perioperative treatment with β-blockers, ACE inhibitors, or AT_1 blockers or statins. It must be emphasized that prophylactic treatment with β-blockers has been investigated extensively in patients undergoing cardiac surgery without contraindications to the drugs[53]; the incidence of POAF was decreased by active treatment from 33% in the control group to 19% in the β-blockers group. Even if single studies showed a marked heterogeneity in the type and dosage of drugs used, the administration protocol, size of the sample under study, and criteria used for the diagnosis of AF, clinical results were not significantly influenced by these variables. Regarding the effects of ACE inhibitors or AT_1-blockers in the prevention of postsurgery AF, no randomized studies have been published. Finally, it has been suggested that POAF was less frequent and its duration shorter in patients treated with statins in comparison with a nonstatin group,[56,57] and associated with a decrease in inflammatory markers.

The exact mechanisms by which statins may reduce POAF are unclear. Modulation of remodeling of the cardiac extracellular matrix and of the inflammatory response as shown by decreased markers of inflammation, including C-reactive protein, serum amyloid A, tumor necrosis factor α, and interleukin-6, may play a role in the statin protective action.[58,59] Recently, the ARMYDA-3 study[60] randomized 200 patients without a history of AF undergoing CPB surgery with atorvastatin, 40 mg/d, or placebo, starting 7 days before surgery. Statins decreased POAF incidence from 57% to 35%, as they did the length of hospitalization. The contribution of oxidative stress in the pathogenesis of POAF is strengthened by the observation of a 50% decrease in AF in patients treated with vitamin C for 5 days after surgery.[61]

CONCLUSIONS

Results from the present investigation confirm that despite the progress in anesthesiology and surgical techniques the incidence of POAF has not shown significant changes in the last 2 decades. Conversely, the present data support the hypothesis that early treatment enables the restoration of sinus rhythm before discharge in more than 95% of patients, and this factor is associated with decreases in clinical complications and economic costs related to the development of the arrhythmia. The present results, although not comparable with randomized studies, failed to show any significant difference in POAF incidence in patients treated with β-blockers, ACE inhibitors, or AT_1 blockers or statins. Further studies are needed to evaluate if combined treatment aimed at decreasing oxidative stress and stabilizing membrane channels could decrease the incidence of postoperative AF.

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APPENDIX 1 VARIABLES TESTED IN UNI- AND MULTIVARIATE ANALYSIS

Preoperative Variables

Age >80 years, age 70 to 80, age <70, sex, previous episodes of AF, body surface area $\geq$1.95 m^2, obesity, smoking, hypertension, diabetes mellitus, impaired renal function (plasma creatinine >2 mg/dL), hemodialysis, chronic obstructive pulmonary disease, need for preoperative intra-aortic balloon pump, left ventricular ejection fraction $\leq$35%, left atrial di-

mension >40 mm, preoperative use of β-blockers, use of β-blockers, ACE inhibitors or statins, preoperative serum K^+.

Operative Variables

Urgent/emergent operation, CABG surgery, off-pump CABG surgery, complete arterial revascularization, isolated valve procedures, valve procedures and CABG surgery, other procedures, aortic cross-clamp time ≥90 minutes, cardiopulmonary bypass time ≥120 minutes.

Postoperative Variable

Return to the intensive care unit, reoperation, prolonged mechanical ventilation (>24 hours), anemia, bleeding complications, postoperative use of intra-aortic balloon pump, prolonged use of catecholamines in the intensive care unit, prolonged electrical stimulation by epicardial wires for bradycardia, or transient AV block.

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