Characterization of post-discharge atrial fibrillation following open-heart surgery in uncomplicated patients referred to an early rehabilitation program

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Key words:
Atrial fibrillation; β-blockers; Cardiac hypertrophy; Heart surgery; Valve disease.

Background. **Atrial fibrillation (AF) is frequently observed after open-heart surgery, following discharge from the cardiac surgery clinic. Compared to those usually reported in the early postoperative period, this arrhythmia is delayed in onset and is often a cause of re-hospitalization. Post-discharge AF has never been characterized in the literature.**

Methods. **We retrospectively analyzed post-discharge AF occurring within 30 days of coronary artery bypass graft or of valvular procedures in 376 patients referred to an early postoperative rehabilitation program. To investigate the probability of the persistence of post-discharge AF, we prospectively examined 232 patients who had undergone valvular procedures.**

Results. **An arrhythmia was recognized in 61/376 patients (16%), resulted in worsening of the NYHA functional class in 27 (44%) and in life-threatening hemodynamic effects requiring urgent cardioversion in 5 (8%). Events were predicted by the occurrence of postoperative AF (6-fold higher risk), left ventricular hypertrophy, an enlarged left atrium and valvular pathology (3-fold) and by the lack of β-blocker protection (5-fold). AF persisted in 20/232 (9% of the study population, 18% of patients who had post-discharge AF) and had a relevant impact on the patient's clinical status. Predictors of events were older age, an enlarged left atrium and a lower left ventricular ejection fraction.**

Conclusions. **Post-discharge AF following open-heart surgery is frequent in patients undergoing valvular procedures and often persists over time. The clinical impact of the arrhythmia is relevant, it might cause re-hospitalizations in many circumstances and, consequently, may have an impact on hospital resources. Events are much less frequent in patients taking β-blockers than in those who do not, and they can be predicted by simple variables observed in the early stages after surgery.**

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Introduction

Atrial fibrillation (AF) is a frequent complication of open-heart surgery occurring mostly within the cardiac surgery clinic between the second and fourth postoperative days[1-3]. Because of differences in the definition and methods used to recognize the arrhythmia, the reported incidence varies considerably[1-6] and has apparently increased in the last decades[4,7,8]. Although it has been shown that postoperative AF is associated with a higher incidence of systemic embolism[4,7,9-11] and with an increased duration and cost of hospitalization[4,7,8,12], antiarrhythmic prophylaxis is not routinely recommended[2,3,13].

The occurrence of AF after discharge from the cardiac surgery clinic is a frequent event. Compared to those usually reported in the early postoperative period, its onset is delayed. Such a "delayed" postoperative complication has never been characterized although it represents a frequent cause of rehospitalization within the first month of surgery[14,15].

A possible evolution of post-discharge AF is the persistence of the arrhythmia over time, an outcome frequently observed in our clinical practice, in particular among patients who had undergone valvular procedures. In these patients, indeed, the rates of postoperative AF and of the lack of effective cardioversion are much higher than in those

submitted to other surgical procedures[2,4,16,17]. In such patients, the incidence and the predictors of the persistence of post-discharge AF are largely unknown.

Accordingly, this study was performed to characterize post-discharge AF in patients who had undergone open-heart surgery. Having assessed the risk pattern in relation to the underlying disease, we also evaluated the prevalence and predictors of the persistence of post-discharge AF for more than 30 days in high risk patients.

Methods

Design and study population. The study population comprised patients who had recently undergone open-heart surgery with cardioplegic arrest, and who were randomly referred from the main cardiac surgery clinics of Northern Italy to our Rehabilitation Center where they stayed for an expected period of 3 weeks. Training in the Rehabilitation Center included a number of early post-operative controlled physical exercises. Two populations have been analyzed.

Step 1 (retrospective analysis). Three hundred and seventy-six patients were retrospectively examined in order to characterize the episodes of post-discharge AF. Criteria for eligibility were: ascertained sinus rhythm at the time of discharge from the cardiac surgery clinic, a recent coronary artery bypass graft (CABG), mitral or aortic valve replacement or mitral valve repair. Patients taking antiarrhythmic drugs at the time of surgery or with a history of amiodarone therapy within 4 months before the procedure, and those who experienced severe post-operative complications requiring more than 1 week stay in the intensive care unit were excluded. Patients with documented episodes of AF occurring within 4 months before surgery were also ineligible for this study, whereas those in whom such episodes occurred more than 4 months before surgery were included. The recruitment period lasted from March 1996 to December 1997.

Step 2 (prospective analysis). To assess the incidence and the predictors of the persistence of AF over 30 days after surgery, we selected patients at higher risk for post-operative AF because their underlying disease was valvular (based on the results of step 1). Hence, from January 1998 to March 1999 we recruited 232 consecutive patients who had undergone open-heart surgery for mitral or aortic valve replacement or mitral valve repair, and who were in sinus rhythm at the time of discharge from the cardiac surgery clinic. Exclusion criteria were the same as those in step 1.

Follow-up. During their stay in the Rehabilitation Center patients underwent daily clinical evaluation. Unless contraindicated, low-dose β-blocker therapy (atenolol 25 mg, bisoprolol 5 mg, metoprolol 100 mg daily) was generally administered to patients with a heart rate > 90 b/min. Anticoagulant treatment was administered to patients who had undergone valvular surgery. As recommended, the dose of anticoagulant drugs was titrated in order to keep the prothrombin time at values ranging between 2 and 3 of the International Normalized Ratio (INR) for the first 2 weeks after surgery (moderate-intensity regimen)[18], and in patients with mechanical prosthetic valves it was then adjusted to maintain a higher range (INR 2.5-3.5)[19].

Electrocardiographic monitoring. At the beginning of our observation, a standard 12-lead ECG was performed and then repeated every 7 days, at the time of discharge or whenever the attending cardiologist suspected the presence of an arrhythmia. Twenty-four hour Holter monitoring was performed in all patients using a two trace (V_1 and V_5 leads) Traker Recorder (Reinolds Medical System, Hertford, UK). Recordings were subsequently analyzed by the Autosurveyor Lector, Reinolds Medical model (Hertford, UK). Using a telemetric system, one electrocardiographic lead (D_2) was continuously recorded during the two daily sessions of exercise training scheduled for all patients.

Echocardiography. Standard transthoracic echocardiographic evaluation was performed using a commercially available machine (SIM 7050 Esaote Biomedical System, Florence, Italy) equipped with a 2.5-3.5 MHz annular-array transducer. Left ventricular chamber dimensions, septal and posterior wall thickness and the left atrial diameter were measured according to the recommendations of the American Society of Echocardiography[20]. The Penn Convention was used to calculate the left ventricular mass on the basis of data obtained from two-dimensional-guided M-mode echocardiograms[21]. The left ventricular mass was then normalized for the patient's height to the power of 2.7, as previously reported[22]. The relative wall thickness was used as a measure of concentric geometry and calculated by dividing the posterior wall thickness by the left ventricular end-diastolic radius[23]. The left ventricular volumes and ejection fraction were computed by the area-length method using data from apical 2- and 4-chamber views[24].

Definition and management of post-discharge atrial fibrillation. All documented episodes of AF, atrial flutter and atrial tachycardia (for the purposes of this study, no distinction was made between the three types of arrhythmia) lasting > 2 min were considered in this analysis[25]. Paroxysmal AF, defined according to Levy's criteria[25], and AF lasting > 7 days and then cardioverted to sinus rhythm were defined as reversible AF. Patients in whom cardioversion failed and in whom AF persisted

until the end of follow-up, and those in whom serial electrocardiographic documentation proved recurrence of the arrhythmia after an initially successful cardioversion were considered as having persistent AF. When AF was occasionally discovered in asymptomatic patients, no drug was given for 48 hours. In symptomatic patients and in those in whom AF persisted > 2 days quinidine or propafenone was administered in an attempt to restore sinus rhythm. Anticoagulant treatment was started in patients who had undergone CABG in whom AF lasted > 48 hours.

Statistical analysis. *Step 1 (retrospective analysis).* At this stage the prevalence and the clinical characteristics of post-discharge AF in 376 patients were retrospectively analyzed. Using an SPSS/PC 7.5 Release (SPSS Inc., Chicago, IL, USA) software, multiple logistic regression analysis was performed by a stepwise forward-conditional procedure to identify the independent predictors of events. Because the risk factors were influenced by the etiology of cardiac disease, analysis was adjusted for the type of surgical procedure. A subanalysis was finally performed to verify the incidence and the effect of the distinct subsets of the arrhythmias on the outcome.

Step 2 (prospective analysis). As for the retrospective phase, the variables of 232 patients who had undergone valvular procedures were tested by multiple logistic regression analysis in order to investigate the persistence of AF 30 days after open-heart surgery.

Data are reported as mean values ± 1 SD. The unpaired Student's t-test and χ^2 test were used for descriptive statistics. The null hypothesis was rejected at a two-tailed $\alpha \leq 5\%$.

Results

The study patients were discharged from the cardiac surgery clinic 7.3 ± 2.4 days (range 4-11 days) after surgery. In both phases of the study, our observations lasted from the time of discharge to 30 ± 3 days after surgery (mean time 21 ± 4 days). Echocardiographic evaluation and ECG Holter monitoring were performed 9 ± 2 and 10 ± 3 days after surgery respectively.

Step 1 (376 patients - retrospective analysis). *Prevalence and clinical course of post-discharge atrial fibrillation.* The main clinical characteristics of 376 patients are reported in table I. During follow-up, 61 patients (16%) presented with at least one documented episode of post-discharge AF. The relative incidence of the arrhythmias was 78% for atrial fibrillation, 21% for atrial flutter and 1% for atrial tachycardia. The onset of AF occurred most frequently between the eighth to the sixteenth postoperative days (average time 12 ± 4 days) (Fig. 1). Post-discharge AF resulted in acute hemodynamic impairment in 5 patients (8% of events; hypotension in 2 patients and heart failure in 3 patients) and in worsening of the NYHA functional class in 27 patients (44%). In 29 patients (48%), the arrhythmia was not associated with any symptoms. Patients with symptoms exhibited a higher ventricular rate than patients who remained asymptomatic (135 ± 18 vs 103 ± 9 b/min respectively, p = 0.001). No other variable differed between the two groups. No association was found between the type of arrhythmia and the variations in the patients' clinical picture; furthermore, the relative incidence of these arrhythmias was not related to the surgical procedure performed or to any other considered variable. Post-discharge AF was neither associated with death nor with clinical or ECG signs of myocardial ischemia.

Table I. Characteristics of 376 study patients (retrospective analysis).

Clinical	
Sex (M/F)	270/106
Age (years)	62 ± 10
NYHA class (score 1-4)	1.7 ± 0.6
Diabetes mellitus (n)	55 (15%)
Anticoagulant therapy (n)	150 (40%)
Preoperative myocardial infarction (n)	138 (37%)
Preoperative episode of acute pulmonary edema (n)	33 (9%)
Preoperative AF (foregoing 4 months from surgery) (n)	11 (3%)
Surgical	
Coronary artery bypass graft (n)	275 (73%)
Aortic valve replacement (n)	57 (15%)
Mitral valve replacement (n)	19 (5%)
Double valve replacement (n)	9 (2%)
Mitral valve repair (n)	16 (4%)
Perioperative myocardial infarction (n)	21 (5%)
Postoperative AF (n)	93 (25%)

AF = atrial fibrillation.

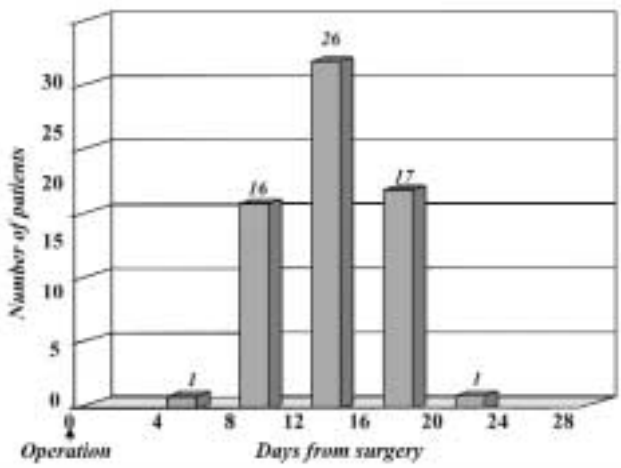

Figure 1. *Distribution over time of episodes of post-discharge atrial fibrillation diagnosed during follow-up.*

Predictors of post-discharge atrial fibrillation. The characteristics of patients grouped according to the occurrence of post-discharge AF are reported in table II. Arrhythmia was associated with older age, female gender, valvular etiology, previous acute pulmonary edema, preoperative episodes of AF, postoperative AF, a higher left ventricular mass, a left ventricular concentric geometry and with a larger left atrium. Therapy was similar in the two groups, but β-blockers were administered less frequently in patients with events.

One hundred and sixteen patients (31% of the study group) were indeed receiving β-blockers at the time of entry: 112 had undergone CABG, while valvular procedures had been performed in 4. Fifty-seven of the 260 patients (22%) who were not taking β-blockers developed post-discharge AF as compared to 5 of 116 patients (4%) on β-blockers (odds ratio 6.3, 95% confidence intervals 2.5-16.2, $p < 0.0001$). The incidence of post-discharge AF was higher in patients not taking β-blockers both in the group submitted to CABG (4.5 vs 12%, odds ratio 2.84, 95% confidence interval 1.03-7.86, $p < 0.05$) and in the group submitted to valvular procedures (0 vs 39%).

Table II. Clinical, surgical, electrocardiographic and echocardiographic characteristics of patients with and without post-discharge atrial fibrillation (AF) during follow-up.

	Post-discharge AF (n=61)	Stable sinus rhythm (n=315)	p
Clinical			
Sex (M/F%)	58/42	74/26	0.02
Age (years)	64 ± 10	61 ± 10	0.03
Body mass index (kg/m^2)	25.7 ± 3.1	26.5 ± 3.4	NS
Systolic blood pressure (mmHg)	118 ± 14	120 ± 12	NS
Diastolic blood pressure (mmHg)	78 ± 9	76 ± 8	NS
Hypertension (n)	19 (31%)	100 (32%)	
Diabetes mellitus (n)	7 (11%)	48 (15%)	NS
NYHA class (score 1-4)	1.9 ± 0.6	1.7 ± 0.6	NS
Ischemic/valvular etiology (%)	38/62	80/20	0.0001
Preoperative myocardial infarction (n)	14 (23%)	124 (39%)	NS
Preoperative acute pulmonary edema (n)	11 (18%)	22 (7%)	0.004
Preoperative episode of atrial fibrillation (foregoing 4 months from surgery) (n)	7 (11%)	4 (1%)	0.0001
Surgical			
Coronary artery bypass graft (n)	23 (38%)	252 (80%)	0.01
Grafts (number per person)	2.6 ± 1.1	3.1 ± 1.3	NS
Mitral replacement (n)	12 (20%)	7 (2%)	0.0001
Aortic replacement (n)	16 (26%)	41 (13%)	0.0001
Double valve replacement (n)	4 (7%)	5 (2%)	0.01
Mitral repair (n)	6 (10%)	10 (3%)	NS
Perioperative myocardial infarction (n)	1 (2%)	20 (6%)	NS
Aortic cross-clamp time (min)	77 ± 19	99 ± 37	NS
Postoperative atrial fibrillation (n)	35 (57%)	58 (18%)	0.0001
ECG 24-hour Holter monitoring			
P wave duration (ms)	84 ± 19	84 ± 20	NS
P wave amplitude (mm)	11.3 ± 3.4	11.7 ± 3.9	NS
Heart rate (b/min)	82 ± 13	83 ± 13	NS
Supraventricular ectopic beats (n/24 hours)	261 ± 42	285 ± 44	NS
Ventricular ectopic beats (n/24 hours)	578 ± 75	358 ± 52	NS
Complex ventricular ectopic beats (n)	6 (10%)	30 (8%)	NS
Echocardiographic			
Left ventricular end-diastolic diameter (mm)	51 ± 7	49 ± 6	NS
Left ventricular ejection fraction (%)	54 ± 7	53 ± 7	NS
Relative wall thickness	0.44 ± 0.08	0.41 ± 0.07	0.01
Left ventricular mass (g/m$^{2.7}$)	47 ± 16	37 ± 15	0.0001
Left atrial diameter (mm)	42 ± 7	39 ± 5	0.02
Drugs			
Digitalis (n)	25 (40%)	135 (43%)	NS
Nitrates (n)	17 (28%)	113 (36%)	NS
β-blockers (n)	5 (8%)	111 (35%)	0.0001
Calcium antagonists (n)	11 (18%)	79 (25%)	NS
ACE-inhibitors (n)	3 (5%)	25 (8%)	NS

Table III shows the results of multiple logistic regression analysis. The likelihood of developing post-discharge AF was more than 6-fold higher in patients who experienced postoperative AF, 5-fold higher in the absence of β-blocker therapy, 3-fold higher in patients with left ventricular hypertrophy and 3-fold greater for valvular procedures than for CABG. The risk of post-discharge AF independently increased even in the presence of left atrial dilation.

Clinical outcome of post-discharge atrial fibrillation. In 21 patients (34% of events) post-discharge AF converted to sinus rhythm spontaneously (within 460 ± 392 min), whereas 37 patients (61%) were given antiarrhythmic drugs and sinus rhythm was restored in 27 cases (73%). In 1 patient, sinus rhythm was restored after external electrical cardioversion, in 2 after overdrive suppression by transesophageal pacing. Restoration of sinus rhythm was obtained more frequently in patients who had been submitted to CABG than in those submitted to valvular procedures (22 of 23 patients, 96% vs 29 of 38 patients, 76% respectively, $p < 0.01$). The clinical outcome was not influenced by the type of arrhythmia. At the end of the period of observation, AF persisted in 10 patients (16% of events, 2.7% of the study population). The risk of persisting post-discharge AF was more than 22-fold higher in patients who had undergone a valvular procedure (9 of 101, 8.9%) than in those in whom a CABG had been performed (1 of 275, 0.4%, $p < 0.00001$).

Step 2 (232 patients with valvular disease - prospective analysis). *Prevalence and clinical course of the persistence of postoperative atrial fibrillation.* As a consequence of the previous observation, we prospectively studied 232 patients who had been submitted to open-heart surgery due to valvular disease (the condition identified to be at high risk in the step 1 analysis). The main clinical characteristics of the studied population are reported in table IV. During the rehabilitation period, post-discharge AF occurred in 113 of 232 patients (49%). In 60 patients (53%) arrhythmia recurred 2 or more times. AF converted to sinus rhythm spontaneously in 35 patients (31%) whereas pharmacological or external electrical cardioversion was effective in 55 (49%) and 3 (3%) patients respectively.

At the end of follow-up (30 ± 4 days after surgery), AF persisted despite the attempt at cardioversion in 20 patients (9% of study population, 18% of the patients in whom AF developed after surgery) (Fig. 2). Among 113 patients with post-discharge AF, the distribution of events according to the type of surgery performed was as follows: 16% (10 of 64 patients) after aortic valve replacement, 25% (6 of 24 patients) after mitral valve replacement, 10% (1 of 10 patients) after double valve replacement, and 20% (3 of 15 patients) after mitral valve repair. None of the patients with persistent AF were receiving β-blocker protection, while in all treated patients (n = 13, 14%) AF resolved spontaneously during the period of observation. The persistence of AF was associated with hemodynamic deterioration (hypotension) in 1 patient, worsening of the NYHA functional class in 11 patients, whereas in 8 patients the arrhythmia was not associated with any symptoms. Similarly to the findings shown in the retrospective analysis, a higher ventricular rate was the only variable which differed between the patients who were or were not symptomatic (105 ± 10 vs 85 ± 9 b/min respectively, $p < 0.0001$).

Table IV. Principal characteristics of 232 patients who had undergone valvular procedure (prospective analysis).

Clinical	
Male (n)	128 (55%)
Age (years)	62 ± 12
NYHA class (score 1-4)	1.9 ± 0.6
Diabetes mellitus (n)	12 (5%)
Preoperative episode of acute pulmonary edema (n)	40 (17%)
Preoperative AF (foregoing 4 months from surgery) (n)	21 (9%)
Surgical	
Aortic valve replacement (n)	133 (57%)
Mitral valve replacement (n)	48 (21%)
Double valve replacement (n)	21 (9%)
Mitral valve repair (n)	30 (13%)
Perioperative myocardial infarction (n)	3 (1%)
Postoperative AF (n)	88 (38%)

AF = atrial fibrillation.

Table III. Multiple regression logistic analysis for odds ratio's generation as independent measures of the post-discharge atrial fibrillation (AF) risk and forecast of likelihood of global risk.

	B coefficient and standard error	OR	95% CI	p
LV hypertrophy	1.18 ± 0.41	3.24	1.45-7.23	0.004
No β-blocker	1.56 ± 0.66	4.8	1.30-17.57	0.03
Valvular etiology	1.06 ± 0.38	2.88	1.36-6.13	0.006
Postoperative AF	1.82 ± 0.37	6.19	2.99-12.79	0.0001
Left atrial dimension	0.07 ± 0.03	1.07/cm	1.01-1.14	0.03
Constant	-6.15 ± 1.43	–	–	0.001

CI = confidence interval; LV = left ventricular; OR = odds ratio.

Anticoagulants were given to all patients. No major hemorrhagic event occurred during follow-up. Intrapericardial bleeding requiring elective pericardiocentesis was diagnosed in 2 patients and minor bleeding which did not need any intervention occurred in 35 patients (15%). On the other hand, despite warfarin, 2 of 20 patients (10%) who had persistent AF (mean INR 2.3) and 1 (INR 2.2) of 93 patients in whom AF was reversible developed an episode of systemic thromboembolism (1%, p = 0.001). All events occurred during the second postoperative week.

Predictors of persistent atrial fibrillation. Patients who had post-discharge AF were divided into two groups: one group consisting of patients with persistent AF at the end of follow-up (n = 20) and a group consisting of patients with reversible AF (n = 93). Older age, a lower left ventricular ejection fraction, a larger left atrial diameter and the lack of β-blocker protection were strongly associated with the persistence of the arrhythmia at univariate analysis (Table V). The risk did not significantly differ in patients undergoing aortic or mitral surgery, or both. Multiple logistic regression analysis revealed that an enlarged left atrium, a low ejection fraction and older age were independent predictors of the persistence of AF 30 days after open-heart surgery (Table VI).

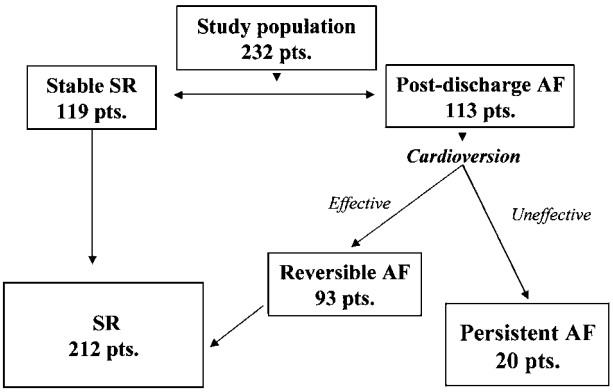

Figure 2. *Flow chart showing the occurrence of atrial fibrillation (AF) during follow-up in 232 patients who had undergone valvular surgery in ascertained stable sinus rhythm (SR). Episodes of post-discharge AF were diagnosed in 113 patients. AF was converted to SR in 93 patients, while in 20 patients cardioversion was unsuccessful. These patients had the arrhythmia at the end of follow-up (30 ± 4 days after surgery).*

Table V. Characteristics of the 113 patients who had undergone valvular procedure divided according to the development of persistent atrial fibrillation (AF) at 30 days after surgery.

	Persistent AF (n=20)	Reversible AF (n=93)	p
Clinical			
Male gender (n)	11 (55%)	49 (53%)	NS
Age (years)	70 ± 8	64 ± 11	0.02
Body mass index (kg/m^2)	25 ± 3	26 ± 3	NS
Systolic blood pressure (mmHg)	116 ± 15	119 ± 13	NS
Diastolic blood pressure (mmHg)	77 ± 9	75 ± 8	NS
Hypertension (n)	3 (13%)	8 (9%)	NS
Diabetes mellitus (n)	1 (5%)	3 (3%)	NS
Preoperative variables			
NYHA class (score 1-4)	2.3 ± 0.5	2.1 ± 0.6	NS
Acute pulmonary edema (n)	4 (20%)	10 (11%)	NS
Systemic thromboembolism (n)	1 (5%)	2 (2%)	NS
Postoperative variables			
Heart rate (b/min)	89 ± 13	87 ± 12	NS
Supraventricular ectopic beats (n/24 hours)	103 ± 71	236 ± 162	NS
Ventricular ectopic beats (n/24 hours)	801 ± 521	416 ± 271	NS
Complex ventricular ectopic beats (n)	3 (18%)	8 (10%)	NS
Left ventricular end-diastolic diameter (mm)	52 ± 6	49 ± 7	NS
Left ventricular ejection fraction (%)	50 ± 10	58 ± 9	0.0008
Left ventricular mass (g/m$^{2.7}$)	55 ± 19	54 ± 17	NS
Relative wall thickness	0.47 ± 0.05	0.46 ± 0.06	NS
Left atrial diameter (mm)	49 ± 7	41 ± 6	0.000001
β-blockers (n)	0	13 (14%)	0.02
Surgical			
Aortic replacement (n)	10 (50%)	54 (58%)	NS
Mitral replacement (n)	6 (30%)	18 (19%)	NS
Double valve replacement (n)	1 (0.5%)	9 (10%)	NS
Mitral repair (n)	3 (15%)	12 (13%)	NS
Perioperative myocardial infarction (n)	0	1 (1%)	NS

Table VI. Factors independently related to the persistence of atrial fibrillation at 30 days after open-heart surgery (valvular procedure) by multiple logistic regression analysis.

	B coefficient and standard error	OR	95% CI	p
Left atrial dimension	0.39 ± 0.019	5.51/cm	2.12-14.24	0.001
LV ejection fraction	-0.27 ± 0.02	1.42	1.14-2.17	0.02
Age	0.25 ± 0.03	1.31	1.05-2.99	0.03

Abbreviations as in table III.

Discussion

A number of studies have defined the incidence, clinical characteristics and outcome of postoperative AF following open-heart surgery. It is well known that this early complication is frequent, rarely produces adverse hemodynamic effects and generally has a good prognosis[1-8,26]. In contrast, post-discharge AF has not been well characterized in the literature. In two recent papers, Pfisterer et al.[27] and Yilmaz et al.[28] documented, in patients submitted to open-heart surgery, a post-discharge incidence of AF of 4 and 6% respectively. Beggs et al.[14] pointed out that AF was the main reason for re-hospitalization within 30 days of discharge after CABG in 13% of patients. More recently, Daoud et al.[29] reported that a home nurse diagnosed post-discharge AF in 12% of patients who had received no prophylactic treatment against postoperative arrhythmias.

Results from the present study demonstrate that post-discharge AF is frequent, might be a cause of re-hospitalization in many circumstances and, consequently, may have an impact on hospital resources. To our knowledge, this is the first study specifically designed to investigate the clinical characteristics and outcome of post-discharge AF, conducted on a large group of patients who had undergone open-heart surgery (without major complications) and including a close follow-up. Since during our recruitment period, some patients were addressed from the referring cardiac surgery hospital to other rehabilitation centers or went home, a possible selection bias should be borne in mind (severity of the baseline cardiac disease, postoperative clinical status) when interpreting our results.

The present study documented that the incidence of post-discharge AF might be as high as 16% of a cohort of consecutive patients admitted to a rehabilitation program and, with regard to those patients operated on for valvular disease, included a closer and longer follow-up than those previously reported[27-29]. Results from this study indicated that post-discharge AF often occurred without any clinical warning and spontaneously converted to sinus rhythm but, in 15% of cases, the arrhythmia persisted and in 8% of patients its occurrence resulted in acute hemodynamic impairment requiring urgent cardioversion.

Predisposing factors and prevention. A number of previous studies investigated the risk of postoperative AF, and results were often irreconcilable[4-8,26,30-33]. Age was the only variable which universally emerged as the most important risk factor. Conversely, no data are available about other factors that might increase the risk of developing post-discharge AF.

The present study identified older age as a predictor even of delayed post-discharge AF at univariate analysis, but this was not confirmed in the final logistic model which included other markers. It is possible that the latter contributed, at least in part, to the effect of age. The large differences in the selection criteria (in particular the inclusion of patients with valve diseases), the lower range of age and different duration of the interval from surgery are other factors which justify the different characteristics of postoperative AF.

Two associated markers for post-discharge AF emerging from the present study were the occurrence of postoperative AF and preoperative episodes of AF. This is consistent with reports of previous studies including very large series of patients[8]. Our results suggest that postoperative episodes of AF are a sign of increased vulnerability to the development of post-discharge AF. Besides, while preoperative episodes of AF emerged as a risk factor for post-discharge AF at univariate analysis, they were not confirmed as an independent predictor at the final multivariate analysis when left ventricular hypertrophy was included. Our data are in line with the results of the Framingham Heart Study which demonstrated that left ventricular hypertrophy was a strong predictor of supraventricular arrhythmias[34]. More recently, a number of biopsy studies[35,36] documented increased myocardial fibrosis and other structural changes in the hypertrophied heart of patients with a history of supraventricular arrhythmias associated with electrophysiological abnormalities that predispose to arrhythmias[32,33,36]. Unfortunately, we were not able, in this study, to investigate electrophysiological variables such as atrial automaticity and conduction times which might be involved in the genesis of AF.

Consistent with previous studies[4], in patients with coronary artery disease who had undergone CABG, the risk of developing post-discharge AF was lower (23 of 275 patients, 8%) than in those submitted to valvular procedures (38% of events). However, β-blocker protection

reduced the risk of AF independently of the underlying heart disease. This finding is in line with several studies[6,37-40] reporting the successful use of β-blockers even for the prevention of postoperative AF. Furthermore, recent studies have shown the long-term effectiveness of β-blocker prophylactic treatment after successful cardioversion of AF in preventing the recurrences of the arrhythmia both in the general population and in patients who had undergone open-heart surgery[41,42]. In particular, the postoperative period is characterized by a marked increase in the adrenergic tone[43,44]. The latter is sufficient to suppress vagal activity and cause the activation of an arrhythmogenic substrate[45]. Although in our patients β-blocker treatment was not randomized (this imposes caution in interpreting the results), the very low rate of events in the subgroup of patients taking β-blockers strongly suggests that the documented postoperative variations in autonomic tone[46,47] might persist for a relatively long time after open-heart surgery and that even post-discharge AF might be primarily triggered by a loss of vagal tone and an increased sympathetic tone. Appropriate randomized controlled trials should be performed to confirm this initial observation.

Persistence of postoperative atrial fibrillation. Due to evidence of a valve surgery-associated risk of AF, we prospectively evaluated the persistence of the arrhythmia in a group of patients with valve diseases. We show that the persistence of the arrhythmia is frequent in these patients. Indeed, despite the attempt at cardioversion, once AF occurred it persisted in 18% of subjects.

It is well known that the loss of the contribution of atrial systole and the increased irregular ventricular rate produced by AF impair left ventricular filling and reduce cardiac output. This results in symptoms of heart failure and affects morbidity and survival[34,48]. However, several studies[7,17] have recently proposed early hospital discharge for patients who had persistent AF following open-heart surgery, in view of the evidence that this decision could be safe and cheap if patients had a controlled ventricular rate and received an effective anticoagulant treatment. On the other hand, Beggs et al.[14] and D'Agostino et al.[15] reported that AF was a frequent cause of re-hospitalization within 30 days of discharge after open-heart surgery. In our study, the persistence of the arrhythmia had a clear influence on the patient's clinical conditions. About 60% of patients with persistent AF had a worsening in functional class, and in one hemodynamic deterioration necessitated urgent cardioversion.

Consistent with our retrospective analysis and with previous available studies[17], older age is a potent independent predictor of the persistence of the arrhythmia over time. The age-related structural changes of the atrium and coexisting morbid conditions can influence the cardiac electrophysiological balance and predispose the patient to sustained AF. An enlarged left atrium and a low left ventricular ejection fraction are other independent predictors and, together with age, provide a potentially useful tool for the identification of high-risk patients in the early stages of the postoperative period. This could be of help in implementing a preventive therapeutic strategy. And, again, the persistence of AF was significantly associated with the lack of β-blocker protection. We observed, indeed, that no patient receiving β-blockers had the arrhythmia at the end of follow-up, while AF persisted in 20% of patients who did not take the drug. The usefulness of β-blockers after valvular procedures has never been investigated, and our study suggests that they could be indicated and beneficial even for this subgroup of patients.

Conclusions. The present study demonstrated that post-discharge AF following open-heart surgery has a clinically relevant incidence. The occurrence of postoperative AF, left ventricular hypertrophy, valvular procedures and an enlarged left atrium identifies patients at high risk of events who might be considered for a possible prophylactic treatment. The patients who had undergone CABG experienced few events and had to be considered at low risk for the development of post-discharge AF. The likelihood of the persistence of AF at 30 days from surgery is particularly high in patients who are submitted to valvular procedures, and it can be predicted in the early postoperative stages by the presence of the older age, an enlarged left atrium and a low left ventricular ejection fraction.

Although it was not a specific objective of this study, preliminary results of the present analysis also suggest that the use of β-blockers in high-risk patients may be justified. In the subgroup of high-risk patients, the mechanisms inducing post-discharge AF should be better characterized and prophylactic strategies explored in appropriate randomized clinical trials.

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References

1. Lauer MS, Eagle KA, Buckley MJ, De Sanctis RW. Atrial fibrillation following coronary artery bypass surgery. Prog Cardiovasc Dis 1989; 31: 367-78.
2. McAlister HF, Luke RA, Whitlock RM, Smith WM. Intravenous amiodarone bolus versus oral quinidine for atrial flutter and fibrillation after cardiac operation. J Thorac Cardiovasc Surg 1990; 99: 911-8.
3. Davison R, Hartz R, Kaplan K, Parker M, Feiercisel P, Michaelis L. Prophylaxis of supraventricular tachyarrhythmia after coronary artery bypass surgery with oral verapamil: a randomized, double-blind trial. Ann Thorac Surg 1985; 39: 336-9.

4. Creswell LL, Schuessler RB, Rosenbloom MR, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 1993; 56: 539-49.
5. Hashimoto K, Ilstrup DM, Schaff HV. Influence of clinical and hemodynamic variables on risk of supraventricular tachycardia after coronary artery bypass. J Thorac Cardiovasc Surg 1991; 101: 56-65.
6. Andrews TC, Reimold SC, Berlin JA, Antman EM. Prevention of supraventricular arrhythmias after coronary artery bypass surgery. Circulation 1991; 84 (Suppl III): 236-44.
7. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Circulation 1996; 94: 390-7.
8. Mathew JP, Parks R, Savino JS, et al. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. JAMA 1996; 276: 300-6.
9. Reed GL, Singer DE, Picard EH, De Sanctis RW. Stroke following coronary artery bypass surgery: a case control estimate of the risk from carotid bruits. N Engl J Med 1988; 319: 246-50.
10. Taylor GJ, Malik SA, Colliver JA, et al. Usefulness of atrial fibrillation as a predictor of stroke after isolated coronary artery bypass grafting. Am J Cardiol 1987; 60: 905-7.
11. Lynn GM, Stefanko K, Reed JF III, Gee W, Nicholas G. Risk factors for stroke after coronary artery bypass. J Thorac Cardiovasc Surg 1992; 104: 1518-23.
12. Taylor GJ, Mikell FL, Moses HW, et al. Determinants of hospital charges for coronary artery bypass surgery: the economic consequences of postoperative complications. Am J Cardiol 1990; 65: 309-13.
13. Page PL, Pym J. Atrial fibrillation following cardiac surgery. Can J Cardiol 1996; 12 (Suppl A): 40-4.
14. Beggs VL, Birkemeyer NJ, Nugent WC, Dacey LJ, O'Connor GT. Factors related to rehospitalization within thirty days of discharge after coronary artery bypass grafting. Best Pract Benchmarking Healthc 1996; 1: 180-6.
15. D'Agostino RS, Jacobson J, Clarkson M, Svensson LG, Williamson C, Shahian DM. Readmission after cardiac operations: prevalence, patterns, and predisposing factors. J Thorac Cardiovasc Surg 1999; 118: 823-32.
16. Gentili C, Giordano F, Alois A, Massa E, Bianconi L. Efficacy of intravenous propafenone in acute atrial fibrillation complicating open-heart surgery. Am Heart J 1992; 123: 1225-8.
17. Solomon AJ, Kouretas PC, Hopkins RA, Katz NM, Wallace RB, Hannan RL. Early discharge of patients with new-onset atrial fibrillation after cardiovascular surgery. Am Heart J 1998; 135: 557-63.
18. Malouf JF, Alam S, Gharzeddine W, Stefadouros MA. The role of anticoagulation in the development of pericardial effusion and late tamponade after cardiac surgery. Eur Heart J 1993; 14: 1451-7.
19. Hirsh J, Fuster V. Guide to anticoagulant therapy. Part 2: oral anticoagulants. Circulation 1994; 89: 1469-80.
20. Sahn DJ, DeMaria A, Kisslo J, Weyman A. The Committee on M-Mode Standardization of the American Society of Echocardiography: recommendations regarding quantitation in M-mode echocardiography. Results of a survey study of echocardiographic measurements. Circulation 1978; 58: 1072-83.
21. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. Circulation 1977; 55: 613-8.
22. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and of the impact of overweight. J Am Coll Cardiol 1992; 20: 1251-60.
23. Ganau A, Devereux RB, Roman MJ, et al. Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol 1992; 19: 1550-8.
24. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989; 2: 358-67.
25. Levy S, Novella P, Ricard P, Paganelli F. Paroxysmal atrial fibrillation: a need for classification. J Cardiovasc Electrophysiol 1995; 6: 69-74.
26. Pires LA, Wagshal AB, Lancey R, Huang SKS. Arrhythmias and conduction disturbances after coronary artery bypass graft surgery: epidemiology, management, and prognosis. Am Heart J 1995; 129: 799-808.
27. Pfisterer ME, Kloter-Weber UC, Huber M, et al. Prevention of supraventricular tachyarrhythmias after open heart operation by low-dose sotalol: a prospective, double-blind, randomized, placebo-controlled study. Ann Thorac Surg 1997; 64: 1113-9.
28. Yilmaz AT, Demirkilic U, Arslan M, et al. Long-term prevention of atrial fibrillation after coronary artery bypass surgery: comparison of quinidine, verapamil and amiodarone in maintaining sinus rhythm. J Card Surg 1996; 11: 61-4.
29. Daoud EG, Strickberger SA, Man KC, et al. Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. N Engl J Med 1997; 337: 1785-91.
30. Caretta Q, Mercanti CA, De Nardo D, et al. Ventricular conduction defects and atrial fibrillation after coronary artery bypass grafting. Multivariate analysis of preoperative, intraoperative and postoperative variables. Eur Heart J 1991; 12: 1107-11.
31. Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary bypass grafting. Is it a disorder of the elderly? J Thorac Cardiovasc Surg 1989; 97: 821-5.
32. Buxton AE, Josephson ME. The role of P wave duration as a predictor of postoperative atrial arrhythmias. Chest 1981; 80: 68-73.
33. Lowe JE, Hendry PJ, Hendrickson SC, Weells R. Intraoperative identification of cardiac patients at risk to develop postoperative atrial fibrillation. Ann Surg 1991; 231: 338-42.
34. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol 1998; 82: 2-9.
35 Toyoshima H, Park YD, Ishikawa Y, et al. Effect of ventricular hypertrophy on conduction velocity of activation front in the ventricular myocardium. Am J Cardiol 1982; 49: 1938-45.
36. Topol EJ, Traill TA, Fortuin NJ. Hypertensive hypertrophic cardiomyopathy in the elderly. N Engl J Med 1985; 312: 277-83.
37. Ali IM, Sanalla AA, Clark V. Beta-blocker effects on postoperative atrial fibrillation. Eur J Cardiothorac Surg 1997; 11: 1154-7.
38. Babin-Ebell J, Keith PR, Elert O. Efficacy and safety of low-dose propranolol versus diltiazem in the prophylaxis of supraventricular tachyarrhythmia after coronary artery bypass grafting. Eur J Cardiothorac Surg 1996; 10: 412-6.
39. Daudon P, Corcos T, Gandjbakhch I, Levasseur JP, Cabrol A, Cabrol C. Prevention of atrial fibrillation or flutter by acebutolol after coronary bypass grafting. Am J Cardiol 1986; 58: 933-6.
40. White HD, Antman GM, Glynn MA, et al. Efficacy and safety of timolol for prevention of supraventricular tachyarrhythmias after coronary artery bypass surgery. Circulation 1984; 70: 479-84.
41. Kuhlkamp V, Schirdewan A, Stangl K, et al. Use of metoprolol CR/XL to maintain sinus rhythm after conversion from persistent atrial fibrillation: a randomized, double-blind, placebo-controlled study. J Am Coll Cardiol 2000; 36: 139-46
42. Cioffi G, Cemin C, Russo TE, et al. Post-discharge recurrences of new-onset atrial fibrillation following cardiac surgery:

impact of low-dose amiodarone and beta-blocker prophylaxis. Ital Heart J 2000; 1: 691-7.
43. Reeves JF, Karp RB, Buttner EE. Neuronal and adrenomedullary catecholamine release in response to cardiopulmonary bypass in man. Circulation 1982; 66: 49-55.
44. Kalman JM, Munawar M, Howes LG, et al. Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. Ann Thorac Surg 1995; 60: 1709-15.
45. Coumel P. Autonomic influences in atrial tachyarrhythmias. J Cardiovasc Electrophysiol 1996; 7: 999-1007.
46. Dimmer C, Tavernier R, Gjorgov N, Van Nooten G, Clement DL, Jordaens L. Variations of autonomic tone preceding onset of atrial fibrillation after coronary artery bypass grafting. Am J Cardiol 1998; 82: 22-5.
47. Wen ZC, Chen SA, Tai CT, Huang JL, Chang MS. Role of autonomic tone in facilitating spontaneous onset of typical atrial flutter. J Am Coll Cardiol 1998; 31: 602-7.
48. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg 1997; 226: 501-11.