

The occurrence of postoperative atrial fibrillation according to different surgical settings in cardiac surgery patients

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Abstract

OBJECTIVES: Atrial fibrillation is the most common arrhythmia after cardiac surgery. The pathogenesis of postoperative atrial fibrillation is multifactorial. The aim of the study was to analyse preoperative, intraoperative and postoperative factors and their relationships with the occurrence and duration of atrial fibrillation.

METHODS: One hundred and ninety-six patients with coronary heart disease (152 men, age 62.7 ± 10.1 years) underwent surgical revascularization. Extracorporeal circulation was used in 64 patients and minimal extracorporeal circulation was used in 75 patients. Fifty-seven patients underwent surgery without extracorporeal circulation. During the first three postoperative days, subjects were monitored for the duration and incidence of atrial fibrillation, laboratory markers of inflammation (C-reactive protein, leucocytes) and serum potassium.

RESULTS: Demographic data and associated cardiovascular diseases in the groups were not statistically different. The overall incidence of atrial fibrillation was 56% (110 patients). The highest incidence of atrial fibrillation was found in the extracorporeal circulation subgroup, with a significantly lower incidence using minimal extracorporeal circulation, and in patients operated on without extracorporeal circulation (75 vs 47 vs 46%, $P < 0.001$). The longest duration of atrial fibrillation was found in patients operated on with extracorporeal circulation compared with minimal extracorporeal circulation, and without extracorporeal circulation (9.7 ± 11.6 vs 4.9 ± 8.3 vs 3.1 ± 5.2 , $P \leq 0.001$). The incidence of postoperative atrial fibrillation significantly correlated with elevation of inflammatory markers (C-reactive protein, leucocytes) compared with patients who were free of atrial fibrillation ($P \leq 0.001$, $P \leq 0.05$). The values of serum potassium were not significantly different. The relationship between postoperative atrial fibrillation and echocardiographic parameters was not confirmed.

CONCLUSIONS: The use of extracorporeal circulation leads to a higher incidence of postoperative atrial fibrillation compared with the use of minimal extracorporeal circulation or with surgery without extracorporeal circulation, probably due to enhanced systemic inflammatory response.

Keywords: Atrial fibrillation • Extracorporeal circulation • Cardiac operation • Minimal extracorporeal circulation • Systemic inflammatory response syndrome

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia after cardiac surgery, with its incidence ranging between 10 and 65%. AF usually occurs between the second and fourth postoperative days [1]. AF is often temporary and disappears after the recovery of mechanical and metabolic functions [2]. It is more frequent after valvular cardiac surgery than after isolated coronary artery bypass graft (CABG) surgery [1]. The pathogenesis of postoperative AF is complex and multifactorial, and includes

preoperative, intraoperative and postoperative factors. These involve excessive catecholamine production, postoperative autonomic imbalance, mobilization of interstitial fluid resulting in changes in intravascular volume status and neurohumoral changes. The leading causes of postoperative AF include ischaemic myocardial injury due to hypotension and inadequate cardioprotection [3], postincision surgical trauma and handling of the heart, local inflammation, temporarily reduced left ventricular (LV) function after surgery and increased left atrial (LA) pressure due to anaesthesia [2].

The use of extracorporeal circulation (ECC) is another possible risk factor for postoperative AF. The contact of blood with the synthetic surfaces of the ECC system leads to the activation of protein and cellular blood components of the systemic inflammatory response syndrome (SIRS) [4]. Inflammation is one of the predictors of postoperative AF [2, 5] and affects atrial conduction. Inflammatory markers including IL-6, IL-8, C-reactive protein (CRP), tumour necrosis factor- α and indices of neutrophil and platelet activation [5, 6] are significantly increased in the systemic bloodstream after CABG. It has been proposed that electrical remodelling plays a role in the high incidence of early AF after ischaemic-reperfusion myocardial injury caused by cardioplegic arrest. Atrial ischaemia may play a role in the development of postoperative AF. Electrolyte abnormalities also have been implicated as a precipitating factor [2].

PATIENTS AND METHODS

The incidence of postoperative AF after CABG was assessed in 196 patients (152 men, age 62.7 ± 10.1 year) undergoing isolated elective coronary revascularization for single-, double-, triple- or more vessel disease. Patients had coronary artery disease and were acceptable candidates for elective operation with cardiopulmonary bypass (CPB). They were divided into three groups according to the type of ECC:

- (1) Classic ECC, $n = 64$.
- (2) Minimal ECC (mini ECC), $n = 57$.
- (3) Without ECC (off-pump), $n = 75$ (control group).

Coronary angiography verified (1)–vessel coronary artery disease in 27 patients (14%), (2)–vessel coronary artery disease in 34 patients (17.3%), (3)–vessel coronary artery disease in 131 patients (66.8%) and more-vessel coronary artery disease in 4 patients (2%). Patients were preoperatively treated according to the currently applicable guidelines. They took ACE-inhibitors (142 patients/72%), sartans (23 patients/11.7%), beta blockers (169 patients/86.2%), calcium channel blockers (51 patients/26%) and statins (172 patients/87.7%).

Arrhythmia incidence and duration were monitored during the first three postoperative days using 72-h Holter ECG recording.

Exclusions

Patients were selected at the Clinic of Cardiac Surgery by individual surgeon decision.

Exclusion criteria for all three groups were the presence of preoperative arrhythmias, the presence of heart failure, severe valvular disease requiring surgical repair before cardiac surgery, dialysis, markedly elevated baseline (preoperative) CRP (>10 mg/l) or leucocytosis ($>10 \times 10^9/l$), and intake of corticosteroids. The 'mini ECC' group contained more stringent exclusion criteria such as reoperation, acute endocarditis, acute coronary syndrome within 10 days before the procedure, stenosis of an internal carotid artery $>70\%$ and previous cerebrovascular accident. The 'off-pump' group contained patients with ECC risk. Patients who met all other criteria and were not included in 'mini ECC' and 'off-pump' group were included in 'ECC group'.

Anaesthesia and operative technique

The induction of intravenous anaesthesia was preloaded with propofol (150 ± 35 mg) combined with sufentanyl ($15\text{--}25$ μ g) and midazolam ($2\text{--}5$ mg bolus). Skeletal muscle relaxation was achieved by atracurium (50 mg bolus). The lungs were ventilated to normocapnia with air and oxygen and anaesthesia was maintained with combined intravenous-inhalatory anaesthesia according to the anaesthesiologist's preference, usually sevoflurane with minimal alveolar concentration $0.6\text{--}1.1$. All patients had peripheral venous lines and a central venous line. A radial artery line was established after the induction of anaesthesia. Heparin was administered at a dose of $300\text{--}400$ IU/kg to achieve a target-activated clotting time from 300 to 480 s (classic ECC 480 s or above, mini ECC and off-pump above 300 s). Sevoflurane minimal alveolar concentration $0.6\text{--}1.0$, sufentanyl (0.62 ± 0.12 μ g/kg/min) and atracurium (1.2 ± 0.3 mg/kg/hod.) were used during ECC. Heparin was injected into the central venous line 10 min before the initiation of CPB. CPB was established after a standard median sternotomy. After achieving sufficient heparinization, the CPB was introduced with an arterial cannula in the ascending aorta and single- or double-atrial cannulation for venous return. Normothermic body temperature was maintained during CPB. Body temperature was measured at the rectal site. Antegrade intermittent cold blood cardioplegia was used. The ECC circuit was primed with 1500 ml of solution (500 ml volulyte 6%, 500 ml inf. manitoli 20% and 500 ml plasmalyte). The pump used was a roller system (Terumo 1), with a biocompatible treatment (x-coating). The mini ECC circuit was primed with 1000 ml of saline solution. The pump used was centrifugal (Terumo). The oxygenator was a membrane oxygenator (Terumo Caplox 25RX). The target pump flow was set to ~ 2.8 l/min/m², and the target mean arterial pressure was set to $50\text{--}70$ mmHg. A standard arterial blood gas analysis was performed on the arterial blood of the CPB circuit immediately after establishing CPB and every 20 min thereafter. Additional arterial blood gas analyses were done according to the perfusionist's needs and in case of hyperlactataemia.

Classic ECC consisted of a rotatory pump, a membrane oxygenator and a cardiotomy reservoir. Mini ECC (RocSafe) included a centrifugal pump and a membrane oxygenator. The circuit had no cardiotomy reservoir and the priming volume was 1000 ml. Protamine sulphate was used at the end of the procedure to reverse the effect of heparin (in ratio $1:1\text{--}1:1.5$) and return the activated clotting time to preoperative levels.

Measurement of laboratory markers

Serum concentration of inflammatory markers (CRP, leucocytes, potassium and myocardial enzymes [creatin kinase (CK), CK-MB and troponin]) was measured. Leucocyte count and serum potassium were measured on the day of surgery and 24 , 48 and 72 h after surgery. CK, CK-MB and troponin were assessed 24 h after surgery, and CRP was measured 24 and 48 h after cardiac surgery.

Measurement of echocardiographic parameters

Transthoracic echocardiography (Siemens Sequoia, with $2.5\text{--}3.5$ MHz probe) was used to assess the structural and functional

condition of the heart preoperatively. We evaluated the LA dimension in systole, thickness of the interventricular septum (IVS) and posterior LV wall in diastole, and end-diastolic LV dimension (LVEDD) using M-mode and 2D images from parasternal and apical projections. The LV ejection fraction (LVEF) was calculated by biplanar Simpson's method and regional kinetic disorders were evaluated.

Postoperative protocol

Patients were weaned off the ventilator when the patients' respiratory function was stable. Potassium supplementation was given as necessary to maintain electrolyte balance within the normal range. Patients were continuously monitored in the postoperative period. Arrhythmia incidence and duration were monitored using 72-h Holter ECG recording. Evaluations of ECG recordings were done in patients hospitalized at the Clinic of Anaesthesiology and Intensive Care Medicine during the first three postoperative days. We focused attention on the presence of postoperative AF and the duration of AF, or for any other arrhythmia. The results were recorded in the daily protocol. Postoperative AF was evaluated for duration if it lasted for at least 1 h.

Statistical analysis

All normally distributed measurements are presented as mean \pm standard deviation (SD). The mean values of age, duration of

hospitalization, body mass index (BMI), biochemical variables and measures of cardiac function were analysed using between-group analysis of covariance (ANOVA) with three levels corresponding to the three types of circulation used during revascularization surgery. The contrasts between groups of patients were tested using the post-hoc Scheffé test. As the major dependent variable was the presence of post-surgery arrhythmias, the ANOVA was used. A 95% confidence level was always employed.

RESULTS

Demographic data and prevalence of associated diseases were not statistically different in ECC, mini ECC and off-pump groups ($P > 0.05$). AF in the postoperative period was recorded in 110 patients (56%). The highest incidence was found in patients operated on using ECC (75%), compared with patients using mini ECC (47%) and patients operated off-pump (46%).

To analyse the differences between the three types of circulation used during revascularization surgery, one-way ANOVAs (three levels) were used in each of the dependent variables. The factors affecting the AF after cardiac surgery (the P and F values, as well as the mean values \pm SDs) are shown in table 2. Importantly, the duration of AF in the first postoperative day was significantly longer using ECC compared with those using mini ECC or off-pump. The mean values of total duration of AF are shown in Table 1.

Table 1: The average values of basic haematological and biochemical parameters, echocardiographic parameters, duration of postoperative atrial fibrillation and extracorporeal circulation

	ECC (n = 64)	Mini ECC (n = 57)	Off-pump (n = 75)	F	Statistical significance
Potassium day 0 (mmol/l)	3.9 \pm 0.4	3.8 \pm 0.2	3.7 \pm 0.4	6.4	$P \leq 0.005$
Potassium day 1 (mmol/l)	3.9 \pm 0.3	3.9 \pm 0.3	3.8 \pm 0.2	3.8	NS
Potassium day 2 (mmol/l)	3.9 \pm 0.3	3.9 \pm 0.3	3.9 \pm 0.3	2.9	NS
Potassium day 3 (mmol/l)	3.8 \pm 1.8	3.8 \pm 1.9	3.8 \pm 1.9	2.5	NS
Creatine kinase (μ kat/l)	11.2 \pm 10.7	11.1 \pm 6.5	7.9 \pm 5.9	3.9	$P \leq 0.05$
MB fraction of creatine kinase (μ kat/l)	1.3 \pm 2.8	0.8 \pm 0.6	0.7 \pm 1.1	1.8	NS
Troponin T (μ g/l)	4.1 \pm 5.6	1.7 \pm 3.2	2.4 \pm 3.4	5.4	$P \leq 0.01$
Leucocytes day 0 ($\times 10^9/l$)	13.1 \pm 3.7	10.8 \pm 2.9	11.3 \pm 3.8	7.1	$P \leq 0.005$
Leucocytes day 1 ($\times 10^9/l$)	14.2 \pm 4.1	11.3 \pm 3.1	12.5 \pm 3.7	9.9	$P \leq 0.001$
Leucocytes day 2 ($\times 10^9/l$)	13.1 \pm 3.9	10.9 \pm 2.9	11.7 \pm 3.3	6.4	$P \leq 0.005$
Leucocytes total ($\times 10^9/l$)	13.5 \pm 3.4	10.9 \pm 2.7	11.8 \pm 3.4	9.4	$P \leq 0.001$
C-reactive protein average (mg/l)	149.6 \pm 53.6	114.6 \pm 44.3	113.8 \pm 47.5	27.9	$P \leq 0.001$
The average values of basic echocardiographic parameters					
LVEDD PLAX (mm)	51.1 \pm 0.5	49.2 \pm 0.5	51.3 \pm 0.6	2.9	NS
LA PLAX (mm)	42.6 \pm 0.5	41.6 \pm 0.6	42.1 \pm 0.6	0.8	NS
IVS PLAX (mm)	12.8 \pm 0.2	12.8 \pm 0.1	12.1 \pm 0.2	0.7	NS
RWLV PLAX (mm)	11.3 \pm 0.1	11.3 \pm 0.1	10.8 \pm 0.1	0.4	NS
LVEF (%)	43.8 \pm 8.1	47.3 \pm 7.9	43.4 \pm 8.4	0.8	NS
Duration of postoperative atrial fibrillation (h)					
Postoperative day 0	1.5 \pm 4.0	0.4 \pm 1.3	0.6 \pm 2.9	2.9	NS
Postoperative day 1	3.6 \pm 5.0	1.6 \pm 3.3	0.7 \pm 1.8	12.3	$P \leq 0.001$
Postoperative day 2	3.2 \pm 6.0	2.1 \pm 4.1	1.5 \pm 3.1	2.4	NS
Postoperative day 3	1.3 \pm 3.7	0.8 \pm 3.0	0.3 \pm 1.6	1.9	NS
Total duration of atrial fibrillation	9.7 \pm 11.6	4.9 \pm 8.3	3.1 \pm 5.2	10.4	$P \leq 0.001$
Duration of extracorporeal circulation (min)	62.8 \pm 21.4	56.4 \pm 16.0	NA	321.0	$P \leq 0.001$
Duration of cross clamp (min)	37.4 \pm 16.3	33.3 \pm 13.4	NA	9.3	$P \leq 0.05$
Length of hospitalization—anaesthesiology department (days)	4.8 \pm 2.3	3.9 \pm 1.4	4.1 \pm 1.4	4.7	$P \leq 0.01$

LVEDD: left ventricle end diastolic diameter; LA: left atrium; IVS: interventricular septum; RWLV: rear wall of the left ventricle; LVEF: ejection fraction of left ventricle.

Table 2: The factors affecting the atrial fibrillation after cardiac surgery

Factors	F	Statistical significance
Age	4.4	$P \leq 0.05$
Body mass index	0.1	NS
Atrial fibrillation day 0	18.6	$P \leq 0.001$
Potassium day 0	0.1	NS
Potassium min total	0.3	NS
C-reactive protein		
Max	0.3	$P \leq 0.05$
Min	1.8	$P \leq 0.05$
Average	0.3	$P \leq 0.05$
Extracorporeal circulation	10.1	$P \leq 0.001$
Aortic clamp	9.3	$P \leq 0.051$
Creatin kinase	4.3	$P \leq 0.05$
MB fraction of creatin kinase	1.3	NS
Leucocytes (all)	4.4	$P \leq 0.05$
Type of ECC	0.6	NS

The occurrence of postoperative AF was significantly associated with prolonged hospitalization in patients operated under ECC compared with those with mini ECC and off-pump. The ECC group of patients also showed the highest values of CRP and leucocyte counts white blood cells (Table 1). There were significant differences during the entire hospitalization when comparing laboratory values of leucocytes in patients operated under ECC and mini ECC. Leucocyte counts also significantly differed in patients operated with ECC and off-pump on the day of operation, postoperative day 1 and in the overall examination. The LVEF was significantly higher in patients operated with mini ECC compared with those operated in ECC and off-pump (47.28 ± 7.85 vs 43.79 ± 8.14 vs $43.44 \pm 8.38\%$, $P \leq 0.05$). There was no difference in postoperative AF rate between single- and double-atrial cannulation.

To analyse the contributions of the type of circulation, patient age, and a number of biochemical and cardiac parameters, ANOVA was used with the total AF count as the dependent variable. Table 2 gives the list of covariates used and their *F* and *P* covariate effects. The total AF count was significantly associated with the type of circulation, patient age, duration of aortic clamp, CRP and leucocyte count.

DISCUSSION

Postoperative AF has been noted by several authors [1, 2] as the most common postoperative arrhythmic complication. The incidence of postoperative AF in our study was 56%, corresponding to the data in the literature ranging from 10 to 65% [1, 2]. The incidence of postoperative AF was high in this study. It was probably caused by recording each postoperative arrhythmia paroxysm (longer than 1 h). Electrolyte imbalance, especially hypokalaemia, is considered to be a triggering factor of postoperative AF [1, 3]. In this study, there was no statistically significant relationship between serum potassium and the incidence of postoperative AF. This may be explained by normal serum potassium levels in all subgroups due to routine supplementation of potassium in all patients after surgery.

Aranki *et al.* [7] showed that the duration of cross clamp represents an independent predictor of AF. Our study showed that aortic clamp duration represents a significant predictor of postoperative AF. Although previous studies have shown a relationship between postoperative AF and markers of intraoperative ischaemic/reperfusion myocardial injury [7, 8], we found significant differences among study groups only in total CK values, but not in troponin and CK-MB, which are more substrate specific (Table 1). The lowest values of total CK were found in the SECC group, suggesting less ischaemic/reperfusion injury. However, Butler *et al.* [8] showed that the incidence of AF in non-cardioplegic operations with short ischaemia time was the same as in cardioplegic procedures with an extended ischaemia time.

Echahidi *et al.* [9] observed a 2.36-fold increased risk of postoperative AF in the presence of metabolic syndrome with the risk of postoperative AF 1.4 times higher in mild obesity and 2.3 times higher in severe obesity. In our study, patients operated on using ECC and having higher risk of postoperative AF had a significantly higher BMI, but statistical analysis did not confirm BMI as an independent risk factor for AF.

The data in the literature show a relationship between the occurrence of postoperative AF and increasing age in patients undergoing cardiac surgical intervention [10]. The relatively high mean age of our patients has a significant inherent risk of postoperative AF, and further analysis confirmed age as an independent predictive factor for AF. Although some authors describe a higher incidence of postoperative AF in men than in women [2, 11], this study did not find differences between gender and the occurrence of postoperative AF.

Structural changes of the heart, (e.g. LA dilation and LV hypertrophy) have been found to be other factors contributing to postoperative AF [11, 12]. We found diminished LV systolic function with LVEF <50% in all three groups of patients. The subgroups receiving a different type of ECC showed no differences in echocardiographic parameters of the left ventricle (end diastolic diameter and thickness of the IVS and posterior wall of the left ventricle). The left atrium in all groups was rated as borderline to slightly dilated, but no relationship between LA size and AF was found. Only one dimension of the LA was assessed in the patients and volume of the LA was not evaluated. No other single echocardiographic parameter independently predicting the occurrence of postoperative AF was found. This suggests another mechanism of postoperative arrhythmia.

Surgical myocardial revascularization using ECC is still the therapeutic gold standard for multivessel coronary involvement. However, this procedure is associated with the occurrence of SIRS, which may lead to postoperative AF and postoperative organ failure. Possible causes of SIRS include the protracted contact of blood with the non-endothelial surface of ECC, tissue injury during surgery, microbial contamination, the effect of heparin and protamine, the duration of tissue ischaemia and subsequent reperfusion, hypothermia, relative anaemia and the negative side effects mediated by blood products [4].

Inflammatory markers such as CRP and leucocyte count have also been observed as predictors of postoperative AF [6, 13]. When comparing patients on ECC or mini ECC with those off-pump, we found significantly lower leucocyte counts and CRP values in the latter group (Table 1). It follows that the inflammatory processes initiated by ECC might alter intra-atrial

conduction and other electrophysiological properties of the atria leading to postoperative AF [14]. One way to reduce the occurrence of SIRS and the incidence of postoperative AF is minimizing the use of ECC. Mini ECC, a new technology and alternative to classic ECC, is characterized by a reduced inner surface of the system, which thus decreases the filling volume. It represents a completely closed system in which the tubing, cannula and oxygenator are coated with heparin, providing biocompatible protection of all blood components. Unlike classic ECC, mini ECC does not have a venous reservoir, resulting in diminished haemodilution during the use of this pump [15, 16]. Given the better biocompatibility of mini ECC, blood cells are not as damaged as in the standard ECC. Immer *et al.* [15] found significantly less need for inotropic circulatory support when using mini ECC compared with classic ECC in patients undergoing cardiac surgery. Mini ECC also has been associated with a shorter length of hospitalization, lower values of inflammatory markers and a lower incidence of postoperative arrhythmias [16–18], all of which were confirmed in this study.

Another possibility of diminishing the negative consequences of ECC is performing cardiac surgery without ECC (off-pump). Off-pump is associated with reduced early mortality and morbidity compared with patients operated on using ECC and is less demanding for high-risk patients with associated cardiovascular diseases [19, 20]. Some authors have described reduced blood loss and decreased need for blood transfusions [21]. Athanasiou *et al.* [22] observed reduced handling of the heart, better LV contractility and greater endocardial blood supply in those patients undergoing surgery off-pump. Some authors [17, 20] reported a lower incidence of postoperative AF in off-pump patients. Similarly, this study showed that postoperative AF duration in the off-pump group was significantly shorter than in patients operated on using ECC (Table 1).

Development of postoperative AF is usually associated with longer hospitalization. This was confirmed in this study where patients operated on using off-pump or mini ECC had a lower incidence of AF and shorter hospitalization than patients operated on with ECC. The patients who developed postoperative AF were treated according to the current guidelines, including maintaining oxygen saturation above 95%, maintenance and correction of electrolyte imbalances, and treatment of hypovolaemia or hypervolaemia during surgery and in the early postoperative period. Conventional treatment strategies also include ventricular rate control (beta-blockers and cordarone), restoration and maintenance of sinus rhythm (electrical cardioversion is preferred in symptomatic patients) and prevention of thromboembolic events (postoperative LMWH in therapeutic doses) [23].

CONCLUSION

Despite advances in surgical techniques, postoperative AF still remains the most frequent arrhythmic complication after cardiac surgery. ECC plays an important role in the activation of the inflammatory cascade during cardiac surgery. Our results show that the use of mini ECC or surgery without ECC were both associated with reduced systemic inflammatory response and lower incidence of postoperative AF compared with the use of ECC. Proper choice of surgical strategy and modulation of inflammation may represent a therapeutic target in the short-term prevention of postoperative AF. The authors had full control of

study design, methods used, outcome parameters, analysis of data and production of the written report.

Conflict of interest: none declared.

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