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Atrial Fibrillation Following Surgical Management of Ischemic Heart Disease; One Year, Single Center, Single Surgeon Results

İskemik Kalp Hastalığı Cerrahi Tedavisi Sonrası Gelişen Atriyal Fibrilasyon; Bir Yıllık, Tek Merkez, Tek Cerrah Sonuçlarımız

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ABSTRACT

Introduction: *Postoperative atrial fibrillation is the most common arrhythmia following bypass surgery with significant morbidity, mortality and increased healthcare costs. The aim of this study is to determine the incidence and timing of atrial fibrillation, identify the risk factors covering preoperative and intraoperative periods, evaluate rate of return to sinus rhythm by disharge, and explore the impact on postoperative outcomes in a large group of patients operated in a single center by a single surgeon.*

Patients and Methods: *Between January 2011 and January 2012, 418 patients on preoperative sinus rhythm were operated for ischemic heart disease and associated complications (left ventricle aneurysm repair and ischemic mitral insufficiency) in a single center, by a single surgeon. The preoperative, intraoperative and postoperative variables were studied.*

Results: *The mean age of the patients were 61.92 ± 10.05, and 77.5% were male. Atrial fibrillation developed in 68 (16.3%) patients. The incidence peaked at second day. Patients with atrial fibrillation were older (p< 0.001). Gender, preoperative comorbidities, ejection fraction, left atrial diameter, preoperative beta-blocker use, leukocyte count, type of operation and intraoperative variables did not affect its occurence. Intensive care unit and hospital length of stay were longer (p< 0.05). 95.5% (n= 65) of patients were in normal sinus rhythm at discharge.*

Conclusion: *Postoperative atrial fibrillation is a popular subject with unknowns and controversial results which may lead to wrong interpretations. We believe that every center has its own risk*

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factors related with the population of that region. Discussion will last, but simple precautions and close monitoring will help to minimize adverse outcomes.

Key Words: *Atrial fibrillation; coronary artery disease; risk factors*

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ÖZET

Giriş: *Postoperatif atriyal fibrilasyon, koroner baypas sonrası en sık görülen; ciddi morbidite, mortalite ve artmış sağlık harcamalarına neden olan bir ritim bozukluğudur. Bu çalışmanın amacı; tek merkez, tek cerrah tarafından yapılan geniş bir hasta grubunda atriyal fibrilasyon insidansının ve zamanlamasının belirlenmesi, preoperatif ve intraoperatif risk faktörlerinin belirlenmesi, taburculukta sinüs ritmine dönüşün saptanması ve postoperatif sonuçlara etkisinin değerlendirilmesidir.*

Hastalar ve Yöntem: *Ocak 2011-Ocak 2012 tarihleri arasında, preoperatif sinüs ritminde olan 418 hasta iskemik kalp hastalığı ve komplikasyonları için (sol ventrikül anevrizma tamiri, iskemik mitral yetmezliği) tek merkezde, tek cerrah tarafından opere edilmiştir. Preoperatif, intraoperatif ve postoperatif değişkenler çalışılmıştır.*

Bulgular: *Hastaların ortalama yaşı 61.92 ± 10.05 yıldı ve %77.5'i erkekti. Altmış sekiz (%16.3) hastada atriyal fibrilasyon gelişti, ikinci günde pik yaptı. Atriyal fibrilasyon gelişen hastalar daha yaşlı idi (p< 0.001). Cinsiyet, preoperatif komorbiditeler, ejeksiyon fraksiyonu, sol atriyum çapı, preoperatif beta-bloker kullanımı, beyaz küre sayısı, operasyon tipi ve intraoperatif değişkenler atriyal fibrilasyon oluşumunu etkilemedi. Atriyal fibrilasyon gelişen hastalarda yoğun bakım ve hastanede kalış süreleri daha uzundu (p< 0.05). Taburculukta hastaların %95.5 (n= 65)'i sinüs ritminde idi.*

Sonuç: *Postoperatif atriyal fibrilasyon çok bilinmeyenli, çelişkili sonuçlara sahip ve halen popülerliğini koruyan bir konudur, bu sebeple yanlış yorumlara açıktır. Biz her ülkenin ve her merkezin kendine has risk faktörleri olduğunu düşünüyoruz. Bu konu ile ilgili tartışmalar hiç sona ermeyecektir, ancak basit önlemler ve yakın takiple olumsuz sonuçlardan kaçınılabilir.*

Anahtar Kelimeler: *Atriyal fibrilasyon; koroner arter hastalığı; risk faktörleri*

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INTRODUCTION

Postoperative atrial fibrillation (POAF) is the most commonly encountered rhythm disturbance following coronary artery bypass grafting (CABG) surgery with significant in-hospital and future morbidity, future mortality and increased health care costs. The incidence is reported in a wide range in different studies, but POAF occurs approximately in 30% of cases following isolated CABG procedures[1-3]. Despite recent advances in surgical and anesthesiological applications, its incidence has increased and is expected to rise more in future due to aging of the population. It mostly occurs within two to four days following surgery and peaks on second day[1,4]. It is defined as a major morbid event due to increased incidence of minor and major thromboembolic events, hemodynamic disturbances, ventricular dysrhythmias, iatrogenic complications related to therapeutic interventions, increased intensive care unit and hospital length of stay and mortality[1].

There are innumerous documented and speculated risk factors for occurence of POAF. The most consistent ones are the age, male gender, history of prior atrial fibrillation, inceased left atrial diameter, decreased ejection fraction, chronic obstructive pulmonary disease (COPD), chronic renal failure, diabetes mellitus, obesity and concomitant valvular surgery[4-6].

The aim of this study is to determine the incidence and timing of POAF; identify the risk factors associated with its occurence covering the preoperative and intraoperative periods; evaluate percentage of return to sinus rhythm by discharge; and find out the impact on postoperative outcomes in a large group of patients undergoing surgery for ischemic heart disease management, in a single center, by a single surgeon.

MATERIALS and METHODS

Four hundred and twenty two patients were operated for ischemic heart disease and associated complications (left ventricular aneurysm and ischemic mitral insufficiency) between January 2011 and January 2012. Four patients were excluded due to preoperative existing atrial fibrillation atrial fibrillation in whom radiofrequency ablation during surgery was performed. The Hospital Ethics Committee approved the study based on retrospective data retrieval, waiving for individual consent. The patients were

retrospectively divided into two groups; atrial fibrillation and non-atrial fibrillation.

All patients were premedicated with oral diazepam, 10 mg on the night prior to surgery. Anesthesia was induced with etomidate 2 mg/kg, fentanyl 1 μg/kg, vecuronium 1 mg/kg and maintained with isofluorane 1 MAC.

For on-pump cases, the cardiopulmonary bypass (CPB) circuit was primed with 1.500 mL Isolyte-S® (Eczacıbaşı-Baxter, Istanbul) which is a balanced electrolyte solution, and 5,000 units of heparin was added. After anticoagulation with heparin (300 U/kg), activated clotting time (ACT) was kept over 400 seconds. Cardiopulmonary bypass was established using a roller pump with a membrane oxygenator (Dideco Compactflo Evo, Sorin Group, Mirandola Modena, Italy). The average flow rate varied from 2.3 to 2.4 L/min/m^2. Surgery was performed under mild hypothermia (33°C). Mean arterial pressure was kept between 45 to 70 mmHg. All patients were rewarmed to 37°C (nasopharyngeal temperature) before weaning from CPB. Heparin was neutralized with 1:1 protamine sulfate.

1000 mL of cold (4-8°C) blood cardioplegia (25 mEq/L potassium) was administered after aortic cross clamping, and 500 mL repeat doses were given every 15 to 20 minutes (antegrade and from venous bypass grafts; retrograde in patients with left main coronary disease). Terminal warm blood cardioplegia (36-37°C) was given prior to aortic clamp release.

The operation room temperature was kept at 20-21°C.

For off-pump cases, 5000 U heparin was administered and ACT was kept around 200 seconds. Deep pericardial suture was employed. Estech® tissue stabilizer system (Estech, Danville, Ca, USA) was routinely used for left anterior descending (LAD) and right coronary artery (RCA) anastomoses. Starfish® (Medtronic, MN, USA) heart positioner was used for circumflex system bypass. Intravenous metoprolol was administered to decrease heart rate and inotropic agents were used to increase blood pressure when necessary.

In postoperative period rate of fluid infusions were adjusted according to hemodynamic measurements. Central venous pressure was maintained between 8-12 mmHg.

Packed red blood cells (RBC) were given if the hematocrit level fell below 25%. Fresh frozen plasma (FFP) and platelet concentrates (PC) were administered in cases of documented postoperative coagulation abnormalities (international normalized ratio > 1.5, activated prothrombin time > 60 s and platelet count < 80.000/mm^3), postoperative platelet dysfunction and factor deficiency.

The decision for re-exploration for hemorrhage was made when 200 mL/hour of drainage was documented on two consecutive hours despite measures taken or more than 300 mL/hour drainage.

On postoperative day 1, all patients were administered metoprolol (50 mg/day) or carvedilol (3.125-6.25 mg/day) and N-acetylcysteine (NAC) (oral: creatinine < 1.3 mg/dL; intravenous: creatinine > 1.3 mg/dL) and continued. All patients were routinely administered low molecular weight heparin in prophylactic dose.

Atrial fibrillation was diagnosed based on electrocardiogram (ECG). All patients were ECG monitored continiously during the intensive care unit (ICU) and for the first 48 hours in the ward. Soon ECG was immediately performed in cases of irregular pulse, palpitation or symptoms related with possible atrial fibrillation.

In cases with POAF, if required intravenous metoprolol was administered. For rhythm control, intravenous amiodarone was administered as intravenous 300 mg loading dose in 1 hour, followed by 900 mg in 24 hours, followed by oral amiodarone 200 mg three times a day. In refractory cases 450 mg additional intravenous infusion was given in 12 hours period. If no response was noted after 48 hours, electrical cardioversion was employed. Low molecular weight heparin dosage was switched to therapeutic interval. In cases of permanent atrial fibrillation development, oral warfarin was administered.

Primary outcome variables included mean time to extubation, ICU and postoperative hospital length of stay, incidence of renal dysfunction (based on the finding that peak creatinine value was 1.5 or greater times the preoperative value), postoperative stroke, postoperative total amount of blood loss, postoperative exploration for hemorrhage, number of used packed RBC, FFP and PC, and inhospital mortality.

Statistical Analysis

The data were analyzed using software SPSS version 17.0 (version 17.0, Statistical Package for the Social Sciences Inc, Chicago, IL, USA). Continuous variables were presented as “mean ± SD” and, categorical variables were presented as “numbers and percentages”. The continuous variables were compared, between AF and non-AF groups, using “two independent samples t-test” and, categorical variables were compared using Chi-square and Fisher’s exact test. Statistically significance was set as p values < 0.05.

RESULTS

After four cases with preoperative atrial fibrillation were excluded, 418 patients were included in the study. Postoperative atrial fibrillation developed in 68 (16.3%) patients. The incidence of atrial fibrillation peaked at second day and declined soonafter in the postoperative period (Figure 1).

The mean age of patients were 61.92 ± 10.05. There were 324 (77.5%) male patients. Patients with POAF were older than patients without atrial fibrillation (65.94 ± 8.92 vs. 61.14 ± 10.08, p< 0.001). Gender was not found to have any effect on occurence of POAF.

Different operative procedures were performed for ischemic heart disease management (Table 1). The occurence of atrial fibrillation was not significantly different in different types of operations; isolated CABG or concomitant procedures. Moreover, there was no difference between off-pump CABG and isolated on-pump CABG cases, 15% and 16.1% respectively (p> 0.05).

The preoperative characteristics of patients are given in Table 2. Left atrial diameter (mm), left ventricular ejection fraction and preoperative coexisting morbidities did not affect occurence of POAF. The basal heart rate of the patients were noted upon admittance. There was no difference between atrial fibrillation and non-atrial fibrillation groups (p> 0.05). Leukocyte count recorded prior to operation was not significantly different between groups (p> 0.05) .

The intraoperative variables of patients are given in Table 3. The number of grafts anastomozed, CPB time, CPB time/graft and aortic cross clamp time did not affect occurence of POAF. Defibrillation after aortic cross clamp release was required in 55 (13.8%) patients. Defibrillation requirement did not differ between the groups (p> 0.05).

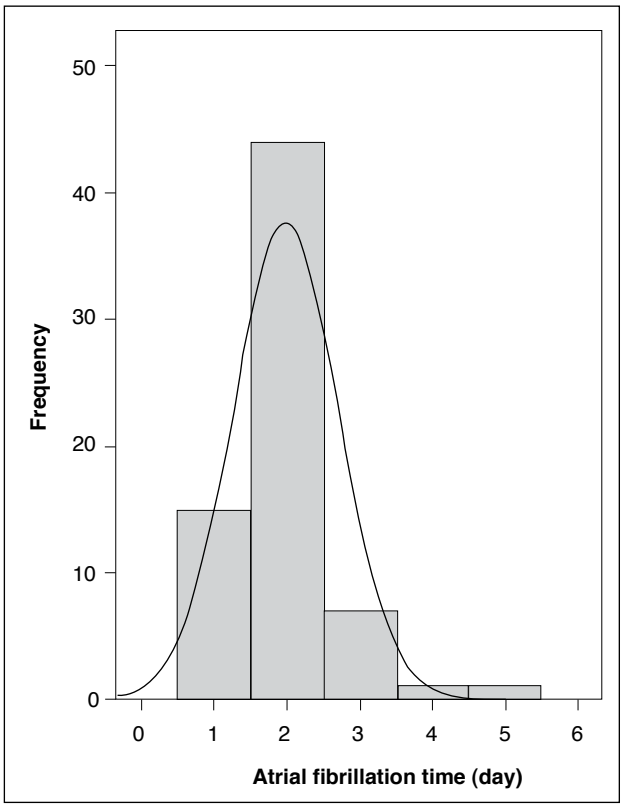

Figure 1. Time scale for occurence of atrial fibrillation; it peaks at postoperative second day.

All patients with atrial fibrillation were given pharmacologic treatment consisting of only rate control agents in 2 (2.9%) patients, only antiarrhythmic agents in 60 (88.2%) patients and both in 6 (8.8%) patients. Metoprolol was the only rate control agent and amiodarone was the only rhythm control agent used. Electrical cardioversion was employed in 8 (11.7%) patients who were refractory to pharmacologic treatment.

Table 1. Operative procedures

Operation	Total n (%)	AF (-) n (%)	AF (+) n (%)	p*
On-pump CABG	374 (89.5)	313 (83.7)	61 (16.3)	
Off-pump CABG	20 (4.8)	17 (85.0)	3 (15.0)	
CABG + LV Aneurysm Repair	14 (3.3)	13 (92.9)	1 (7.1)	
CABG + MRA	6 (1.4)	4 (66.7)	2 (32.3)	0.518
CABG + LV Aneurysm Repair + MRA	2 (0.5)	1 (50.0)	1 (50.0)	
Redo-CABG	2 (0.5)	2 (100.0)	-	
Total	418 (100)	350 (83.7)	68 (16.3)	

* Chi-square test.
AF: Atrial fibrillation, CABG: Coronary artery bypass grafting, LV: Left ventricle, MRA: Mitral ring annuloplasty.

Table 2. Preoperative characteristics of patients

Factor	Total Mean ± SD	AF (-) Mean ± SD	AF (+) Mean ± SD	p[a]
Age	61.92 ± 10.05	61.14 ± 10.08	65.94 ± 8.92	< 0.001
BMI (kg/m^2)	28.41 ± 5.91	28.58 ± 6.13	27.53 ± 4.55	0.182
LVEF (%)	52.48 ± 12.05	52.75 ± 12.11	51.06 ± 11.72	0.290
LA diameter (cm)	3.59 ± 0.45	3.58 ± 0.45	3.63 ± 0.45	0.418
Heart rate upon admittance (bpm)	74.64 ± 11.13	74.93 ± 11.57	73.12 ± 8.87	0.219
Preoperative WCC (/mm^3)	8385.77 ± 2281.74	8436.03 ± 2322.96	8127.06 ± 2052.84	0.307
	n (%)	**n (%)**	**n (%)**	**p[b]**
Sex				
Male	324 (77.5)	273 (84.3)	51 (15.7)	0.588
Female	94 (22.5)	77 (81.9)	17 (18.1)	
Preoperative beta-blocker therapy				
Yes	183 (43.8)	149 (81.4)	34 (18.6)	0.256
No	235 (56.2)	201 (85.5)	34 (14.5)	
Smoking				
Current/Ex-smoker	296 (70.8)	251 (84.8)	45 (15.2)	0.358
Non-smoker	122 (29.2)	99 (81.1)	23 (18.9)	
Diabetes mellitus				
Yes	166 (39.7)	137 (82.5)	29 (17.5)	0.589
No	252 (60.3)	213 (84.5)	39 (15.5)	
Hypertension				
Yes	273 (65.3)	225 (82.4)	48 (17.6)	0.318
No	145 (34.7)	125 (86.2)	20 (13.8)	
Peripheral arterial disease[c]				
Yes	11 (2.6)	9 (81.8)	2 (18.2)	0.696[d]
No	407 (97.4)	341 (83.8)	66 (16.2)	
Stroke				
Yes	8 (1.9)	6 (75.0)	2 (25.0)	0.622[d]
No	410 (98.1)	344 (83.9)	66 (16.1)	
Carotid disease[e]				
Yes	16 (3.8)	15 (93.8)	1 (6.3)	0.488[d]
No	402 (96.2)	335 (83.3)	67 (16.7)	
COPD/Asthma				
Yes	33 (7.9)	27 (81.8)	6 (18.2)	0.756
No	385 (92.1)	323 (83.9)	62 (16.1)	
Chronic renal failure				
Yes	12 (2.9)	11 (91.7)	1 (8.3)	0.700[d]
No	406 (97.1)	339 (83.5)	67 (16.5)	
Emergent surgery				
Yes	11 (2.6)	11 (100.0)	-	0.224[d]
No	407 (97.4)	201 (85.5)	34 (14.5)	

[a] Independent samples t-test.
[b] Chi-square test.
[c] History of therapeutic vascular intervention, history of claudication, angiography/non-invasive proven peripheral arterial disease.
[d] Fisher's exact test.
[e] History of carotid intervention or angiographic/non-invasive proven > 40% stenosis of either carotid.
AF: Atrial fibrillation, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, LA: Left atrium, LVEF: Left ventricular ejection fraction, WCC: Blood cell count.

Table 3. Intraoperative characteristics of patients

	Total	AF (-)	AF (+)	
Factor	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**p[a]**
Number of grafts[b]	2.99 ± 1.05	2.95 ± 1.06	3.22 ± 0.96	0.051
Cross-clamp time (min)	54.16 ± 20.27	53.95 ± 20.35	55.23 ± 20.00	0.642
CPB time (min)	81.30 ± 28.20	80.74 ± 28.47	84.22 ± 26.81	0.364
CPB time/graft (min)	28.32 ± 11.22	28.56 ± 11.50	27.11 ± 9.64	0.342
	n (%)	**n (%)**	**n (%)**	**p[c]**
Defibrillation after aortic clamp release				
Yes	55 (13.8)	47 (85.4)	8 (14.5)	0.699
No	343 (86.2)	286 (83.4)	57 (16.6)	

[a] Independent samples t-test.
[b] On-pump and off-pump cases.
[c] Chi-square test.
AF: Atrial fibrillation, CPB: Cardiopulmonary bypass.

At discharge 95.5% (65/68) of patients with POAF were in normal sinus rhythm. Normal sinus rhythm was not maintained in 3 (4.4%) cases who were discharged with oral warfarin and metoprolol. Two of those patients were in normal sinus rhythm on first postoperative month.

Patients in whom atrial fibrillation developed postoperatively, ICU stay was longer (48.79 ± 17.63 hours) than those who did not develop atrial fibrillation (45.22 ± 10.04 hours) ($p< 0.05$) (Figure 2a). Similarly, patients with POAF had longer postoperative hospital length of stay (6.19 ± 2.43 days) compared to ones without atrial fibrillation (5.53 ± 1.50 days) ($p= 0.003$) (Figure 2b). The postoperative characteristics of patients are summarized in Table 4. Postoperative renal failure was observed in 6.9% (29/406) of

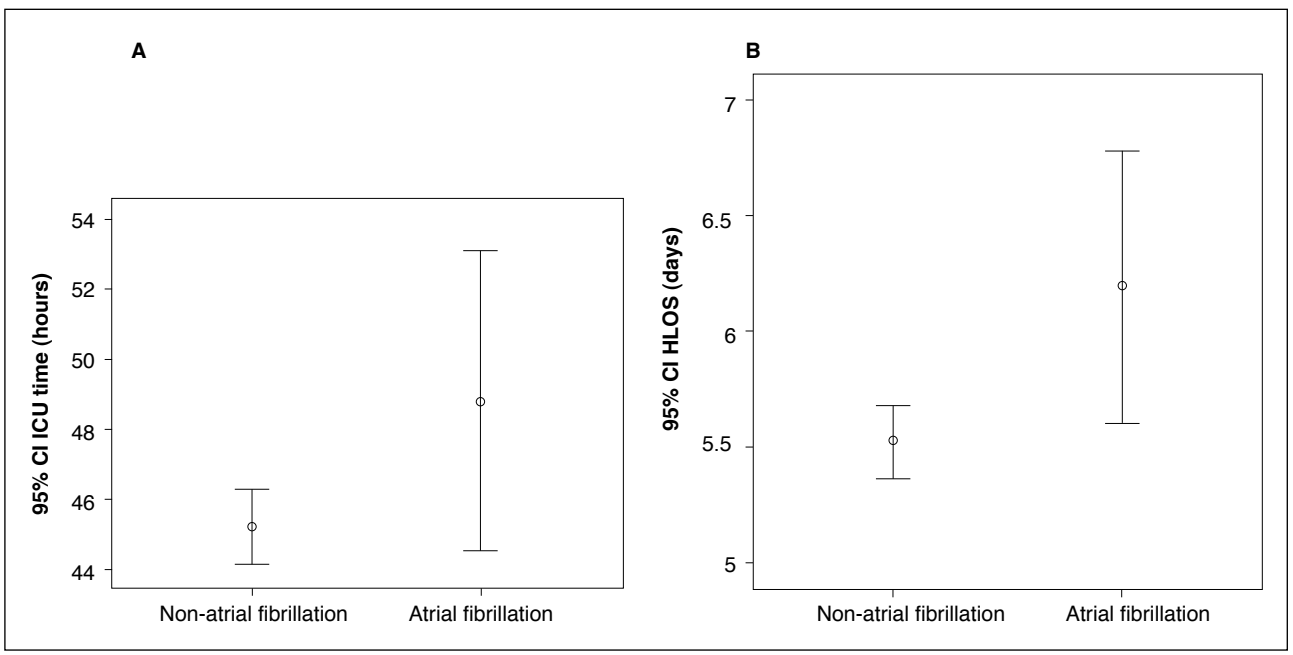

Figure 2. (a) Length of intensive care unit stay (hours); atrial fibrillation vs. non-atrial fibrillation patients. (b) Length of postoperative hospital stay (days); atrial fibrillation vs. non-atrial fibrillation patients.

Table 4. Comparison of the two groups by postoperative variables

	Total	AF (-)	AF (+)	
	Mean ± SD	Mean ± SD	Mean ± SD	p[a]
ICU intubation time, hours	9.25 ± 5.47	9.14 ± 5.82	9.83 ± 3.06	0.346
Length of stay				
ICU, hours	45.80 ± 11.67	45.22 ± 10.04	48.79 ± 17.63	0.021
Postoperative, days	5.63 ± 1.70	5.53 ± 1.50	6.19 ± 2.43	0.003
Drainage tubes removed, hours	36.68 ± 10.97	36.50 ± 11.26	37.62 ± 9.41	0.442
Total amount of drainage, mL	697.44 ± 395.34	690.49 ± 392.12	733.24 ± 412.66	0.415
Number of FFP used	1.41 ± 1.73	1.33 ± 1.65	1.82 ± 2.06	0.033
Number of packed RBC used	1.75 ± 1.74	1.69 ± 1.75	2.06 ± 1.68	0.112
Number of PC used	0.50 ± 1.75	0.50 ± 1.79	0.49 ± 1.55	0.94
	n (%)	n (%)	n (%)	p[b]
Postoperative exploration for hemorrhage				
Yes	11 (2.6)	9 (81.8)	2 (18.2)	0.696
No	407 (97.4)	341 (83.8)	66 (16.2)	
Renal failure[c]				
Yes	27 (7.1)	22 (81.5)	5 (18.5)	0.788
No	379 (93.3)	317 (83.6)	62 (16.4)	
Postoperative stroke				
Yes	3 (0.7)	3 (100.0)	-	1.000
No	415 (99.3)	347 (83.6)	68 (16.4)	

[a] Independent samples t-test.
[b] Fisher's exact test.
[c] Out of 406 patients with preoperative normal renal functions.
AF: Atrial fibrillation, ICU: Intensive care unit, FFP: Fresh frozen plasma, PC: Platelet concentrate, RBC: Red blood cell.

patients (12 patients had chronic renal failure). Only one patient who was in the non-atrial fibrillation group required hemodialysis in the postoperative period, which was transient. When blood and blood products use were explored, number of FFP used was higher in patients with POAF (1.82 ± 2.06) than in patients with normal sinus rhythm (1.33 ± 1.65) ($p< 0.05$).

Sternal dehiscence was observed in 4 (1%) patients. There was only one case with mediastinitis (0.2%) in whom operative debridement with Robicsek procedure and intravenous antibiotic administration was adequate.

There were two mortalities during the study period. One patient with CABG concomitant with left ventricular aneurysm repair and mitral ring annuloplasty died due to low cardiac output in the postoperative third day. The other patient was operated for ischemic mitral insufficiency together with surgical revascularization. Recurrent mitral regurgitation developed in the postoperative third week with severe hemolysis. Mitral valve replacement surgery was performed, but the patient died on the postoperative second day.

DISCUSSION

Atrial fibrillation is the most common rhythm disturbance and most frequent complication following cardiac surgery[1,7]. The pathophysiology of atrial fibrillation is still an unanswered question. The most possible explanation is that the patients with a preoperative predisposition are more vulnerable to atrial electrical re-entry, thus to fluctuations in every intra and postoperative variable including surgery itself. Specifically CPB, related with its undesired systemic inflammatory response may adversely affect whole process.

Age is a very well documented risk factor for occurence of POAF. Mathew et al. reported a 75% increase in odds ratio for developing POAF in every advancing decade[4].

Nisanoglu et al. found POAF incidence to be higher in patients over 65 years of age[8]. The structural changes of the atrium developing with advancing age like atrophy, dilatation, fibrosis and decreased conductive tissue are the probable causative mechanisms[9]. In this study, the age of patients with POAF was also higher. Age itself will gain more importance in near future as the life expectancy of the population increases as well as the age of patients undergoing cardiac surgery, mainly the octogenarian and nanogenarian population.

Beta-blockers are probably the most studied drugs in prevention of POAF. Crystal et al. performed a meta-analysis of 3840 patients based on 27 randomized clinical trials and reported POAF incidence as 19% in cases on beta-blocker therapy while 33% in control group[10]. In a spesific systematic review on pharmocologic prophylaxis of POAF, Koniari et al. emphasized the importance of preoperative administration of beta-blocker drugs in prevention of POAF[11]. Similarly in a very recent review on POAF, Echadidi et al. documented the very effective role of beta-blockers in prophylaxis, and also the adverse effects of beta-blocker withdrawal on incidence[1]. Chronic use of beta-blockers provide pharmacologic remodelling and act as anti-reentrant agents[12]. Our study consists of only ischemic heart disease patients, but the percentage of preoperative beta-blocker therapy can be considered as low. The study was carried out in a single center which is a private hospital. Most of the patients are transferred to cardiovascular surgery ward soon after coronary angiography is performed and surgical decision is made, so most of the patients are immediately diagnosed with ischemic heart disease. Time interval between angiography and surgery is quite short, which is the main explanation for low rate of preoperative beta-blocker treatment. Despite, this low percentage, preoperative use of beta-blockers had no effect on incidence of POAF which is contrary to majority of the published data.

Amiodarone is probably the most commonly administered drug for treatment and also the prophylaxis of POAF. Studies with different timing and administration routes were made. The PAPABEAR trial (Prophylactic Oral Amiodarone for the Prevention of Arrhytmias that Begin Early After Revascularization, Valve Replacement or Repair) demonstrated the efficiency of preoperative oral amiodarone treatment in prophylaxis of postoperative atrial tachyarryhthmias, decreasing its incidence to 16.1% compared to 29.5% in placebo[13]. Bagshaw et al. in their 19 clinical trial consisting meta-analysis also documented a decrease in incidence of POAF with prophylactic perioperative amiodarone use[14]. The efficiency of amiodarone in treatment of POAF is also very well documented and its pharmacological remodelling effect is proven[12]. Conversely, Cicekoglu et al. revealed that postoperative amiodarone was not effective enough in new onset atrial fibrillation following CABG[15]. Our protocol did not include preoperative amiodarone prophylaxis, but the first choice in treatment of POAF was amiodarone for rhythm control. Normal sinus rhythm could be maintained in 95.5% of patients at discharge and 98.5% on first postoperative month. Considering the finding that 97% of patients received amiodarone in treatment of POAF, the success of normal sinus rhythm maintainance can be attributed to amiodarone.

The use of CPB provides a steady and bloodless field during operation. But it leads to a series of inflammatory reactions. The association between atrial fibrillation and postoperative inflammatory reaction is reviewed. Cardiopulmonary bypass and cardioplegic arrest were indicated as main predictors of atrial fibrillation. The positive impact of off-pump surgery on incidence of POAF was noticably observed in elderly patients and in patients with preoperative comorbidities that are risk factors for occurence of atrial fibrillation[16]. Conversely, the occurrence of POAF was not different in off-pump CABG cases compared to on-pump cases in a study among 822 patients[17]. Our study consisted only 20 off-pump cases (4.8%) which makes up the minor part of whole group. The use of CPB did not affect occurence of CABG. In on-pump cases, total CPB time, CPB time per graft and aortic cross-clamp time also did not have any effect on occurence of POAF.

Related with the inflammatory mechanisms, the relationship between preoperative white blood cell count (WCC) and occurence of POAF was studied. It was postulated that increased preoperative WCC may indicate a preexisting inflammatory state which may contribute to occurence of POAF. A 3.8 fold higher risk of development of POAF in patients with preoperative WCC over 7.000/mm^3 was documented[18]. Sood et al. also reported a relationship between increased postoperative WCC and POAF[19]. In 2012, as a part of Framingham Heart Study, the relationship between WCC and occurence of atrial fibrillation was studied in a 936 participant population during 5 year follow-up, and increased risk of atrial fibrillation with higher WCC was documented[20]. We think that this is a very general and basic assumption, because many factors affect the WCC including every single variable related with the disease and timing of the operation. In our study, the mean

number of WCC among whole group of patients was 8385/mm^3 which is itself a risk factor if the study by Fontes et al. is considered[18]. This so-called increased WCC may be related to the previously mentioned short time interval between the angiography and surgery, but still WCC was not higher in the POAF group.

Atrial ischemia is another notable factor for occurence of POAF and is closely related with aortic cross-clamp time and recovery of atrial activity after cardioplegia[21]. In this study, the percentage of patients recovering spontaneous normal sinus rhytm after aortic cross-clamp release was 86.1% (343/398 on-pump cases). There was no difference between defibrillated patients and patients with spontaneous normal sinus rhythm after aortic clamp release.

Since the beginning of cardiac surgery era, use of blood and blood products use have been blamed for occurence of adverse outcomes including atrial fibrillation. Postoperative use have been linked to occurence of every kind of arrhythmia. Direct relationship (odds ratio: 1.89) between transfusion and POAF was revealed[19]. An 18% increase in odds ratio for developing POAF per unit of red blood cell transfused was documented in another study[22]. The mechanism was explained by inflammation in both studies. We also explored the relationship between transfusion of each blood product separately and POAF and number of FFP used was higher in patients with POAF. This finding may also be attributed to the occurence of inflammation related with the use of blood products.

Atrial fibrillation leads to multiple adverse events which leads to an increase in hospital length of stay. In a series of 822 cases increased length of stay was documented[17]. In a retrospective study including 15.580 patients undergoing first cardiac surgery, similar results were found[23]. This increase in hospital length of stay can be attributed to increased requirement for monitorization, additional therapeutics administered necessitating closer follow-up, sometimes in ICU, requirement for further imaging modalities like echocardiography and longer time needed for treatment strategies directed against complications related with atrial fibrillation. Close follow-up also includes additional blood tests, all make up the increased health care costs. We documented increased stay in intensive care unit and also increased postoperative hospital length of stay, but we did not observe any minor or major thromboembolic events related with POAF. This study did not examine the costs and resource utilization, but a direct relationship between them and increased length of stay can easily be done.

An interesting inference from the study may be the possible positive effect of postoperative routine use of NAC and occurence of POAF. Ozaydin et al. studied the effects of NAC in prevention of POAF and found positive results[24]. In our study incidence of POAF was 16.3% which can be considered as moderately low compared to upto 30% values in literature. Occurence of POAF is multifactorial, but since we could not document relationship with many of the risk factors published, NAC may be considered as a protective agent given its many proven antioxidant effects[25].

Absence of C-reactive protein values which objectively defines preoperative inflammatory status and absence of health care cost analysis are the main limitations of this study.

Postoperative atrial fibrillation is a very popular subject and still many unknowns are being studied. Many controversial results are published in the literature which may lead to serious wrong interpretations. We believe that every center has its own defined risk factors related with the surgical team, the instutional protocols and most importantly the factors related with the diseased population of that region. Ongoing discussion on POAF does not seem to end, but simple precautions and close monitoring will help to minimize the adverse outcomes.

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