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Postoperative Atrial Fibrillation following Open Cardiac Surgery: Predisposing Factors and Complications

Khosrow Hashemzadeh[1], Mahnaz Dehdilani[2], Marjan Dehdilani[1*]

[1]*Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[2]*Department of Cardiovascular Surgery, Tabriz University of Medical Sciences, Tabriz, Iran*

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ABSTRACT

Introduction: New-onset postoperative atrial fibrillation (POAF) is a common complication of cardiac surgery that has substantial effects on outcomes. The aim of this study is to analyze the risk factors in the pre, intra, and postoperative periods, and evaluate its impact on patients' outcome.

Methods: In this prospective study, between March 2007 and February 2011, a total of 1254 patients with preoperative sinus rhythm who underwent open cardiac surgery were included of which 177 (13.6%) had developed POAF. Many clinical variables that are associated with the development of POAF, were evaluated.

Results: The study population consisted of 1254 patients that 864 (68.9%) were male and 390 (31.1%) female, and average age was 55.1±15.7 years. POAF occurred in 171 (13.6%) of patients and most of them (68.4%) developed within the first two days after surgery. Multivariate logistic regression analysis was used to identify the following risk factors of POAF: Preoperative risk factors: age>50, smoking, Left ventricular hypertrophy, renal dysfunction, intraoperative risk factors: intraoperative inotrope use, valve surgery, atrial septal defect (ASD) surgery, bicaval cannulation, concomitant cardiac venting of pulmonary and aorta, longer cardiopulmonary time, longer cross-clamp time, postoperative use of inotropic agent after termination of cardiopulmonary bypass.

Conclusion: POAF is the most common arrhythmia after cardiac surgery and not only concerted effort should be performed to identify and to reduce the risk factors, but also effective treatment is necessary to prevent mortality and morbidity.

Introduction

Postoperative atrial fibrillation (POAF) is the most common arrhythmia after cardiac surgery. The true incidence of POAF following cardiac surgery is unclear. Reported incidences range from 10-65%, depending on patient profile, type of surgery, method of arrhythmia surveillance, and definition of arrhythmia.[1-4] POAF normally develops between days 2 and 4 after surgery. The maximum incidence of POAF was usually seen on postoperative day 2. Ninety percent of the patients who develop POAF do so by day 4 after surgery; and 94%, by the end of day 6.[5,6]

The precise pathophysiology of POAF is unknown; however, most of the evidence suggests that it is multifactorial. A common underlying factor associated with POAF induced by mechanical, metabolic or pharmacologic stimuli is the redox changes in atrial tissue associated with tachyarrhythmia.[7] POAF is often a short-lived and self-limiting condition. Around 25%-80% of patients convert within 24 hours through correction of electrolyte imbalances only.[8,9] POAF adversely affects the mortality and morbidity and consequently leads to a longer hospital stay, and more use of resources, driving up the cost of care.[10,11]

This prospective study was conducted to determine the incidence of postoperative AF in patients undergoing a variety of open cardiac surgery procedures and identify preoperative, intraoperative and postoperative factors which have significant association with the development of postoperative AF, and to evaluate its impacts on patients' outcome, and to compare the in-hospital outcome of patients who remain in sinus rhythm postoperatively.

Materials and Methods

In this prospective study, a total of 1254 patients entered the study between March 2007 and February 2011 in Shahid Madani Heart center, Tabriz, Iran. Patients with any history of preoperative AF or any other arrhythmias were excluded. POAF was defined by the documentation of AF rhythm with at least 5 minutes duration within 96 hours at

***Corresponding author:** Marjan Dehdilani, E-mail: md56422@yahoo.com

postoperative period. Patients with POAF are diagnosed using continuous electrocardiogram (ECG) monitoring and ECG and finally analyzed by a cardiologist.

Patients with POAF were treated by Amiodarone and replacement of potassium and magnesium. First for intravenous loading, Amiodarone (150 mg) was given over 10 minutes for acute therapy in adults, followed by a secondary loading infusion of 60 mg/h for 6 hours and then by a maintenance infusion of 30 mg/h to achieve a 1000 mg/d dosing, then oral administration of Amiodarone was continued 600-800 mg/d for 4-6 weeks and finally decided according to the response of treatment. Anticoagulation was instituted in only those patients who have persistent AF more than 48 hours or valve surgery.

A total of 1254 patients were included of which 171 (13.6%) developed POAF. Patients' details, medical records were surveyed. Many clinical variables that are associated with the development of PAOF were shown in Table 1. Preoperative, intraoperative and postoperative risk factors were analyzed for their association with POAF. In addition, other complications that associated with POAF were surveyed too.

Statistics

In the statistical analysis, numerical variables were presented as mean (SD). The *t*-test was used to compare values of continuous variables between patients in whom AF developed versus those in whom AF did not develop whereas categorical variables were compared with the χ^2 test. For all analyses, a $P< 0.05$ was considered significant. Multivariate logistic regression analysis was used to identify the following risk factors of POAF. The odds ratio (OR) and 95% confidence interval (CI) for each independent variable in the final regression model presented. For the statistical analysis, the statistical software SPSS 19.0 (SPSS Inc., Chicago, IL, USA) was used.

Results

The demographic characteristics of the patients included in this study are shown on Table 2.

A total of 1254 patients were included in the study. Of these patients 864 (68.9%) were male and 390 (31.1%) female, and average age was 55.1±15.7 years (range, 1 to 85). Patients younger than 50 years constituted only approximately 29.6% of the total population. Postoperative AF occurred in 171 (13.6%) of patients. The incidence of AF by type of operative procedure was listed in Table 3. Coronary artery bypass grafting (CABG) as the sole operative procedure was performed in 1007 (80.3%) of patients, CABG + valve in 48 (3.8%), and isolated valve surgery were done in 132 (10.5%) patients.

In nearly 68.4% AF occurred within the first 2 days of surgical ICU hospitalization, with a mean delay of 2.1 ± 1.5 (median, 2 days). Preoperative, intraoperative, and postoperative risk factors were presented in Table 1. POAF was more frequent in patient's > 50 years old (81.3%). POAF were characterized by higher incidence of smoking, left ventricular hypertrophy and renal dysfunction. Preoperative use of beta-blocker was not associated with a lesser incidence of AF (*P*=0.364). Intraoperatively, patients who have valve surgery, atrial septal defect (ASD) closure, use of intropic agents, longer CPB time, longer aortic cross- clamp time, concomitant venting of pulmonary vein and aorta, and bicaval cannulation increased frequency of AF. Multivariant analysis identified 12 independent factors as predictors of POAF (Table 4).

From preoperative variables left ventricular hypertrophy was the strongest predictor of AF (OR=2.373; *P*=0.009). Age, smoking and renal dysfunction were independent predictors of AF (OR=0.505, *P*=0.000, OR=0.629, *P*=0.005 & OR=1.661, *P*=0.042; respectively). From intraoperative variables, type of surgery (valve surgery, OR=0.573, *P*=0.017, ASD surgery, OR=0.171; *P*=0.028), bicaval cannulation (OR=1.833; *P*=0.020), concomitant pulmonary vein and aortic root venting (OR=0.272; *P*=0.001), aortic cross-clamp time (OR=1.012; *P*=0.040), CPB time (OR=0.984; *P*=0.000) were associated with AF. Postoperative variables associated with AF was postoperative inotrope use (OR=1.622; P=0.007). Inotropic requirement postoperatively was significantly higher in the AF group (*P*=0.007). The reintubation rate (4.7% AF *vs* 1.1% no AF), was also higher in the AF group (*P*=0.003).

In addition, length of ICU stay (6.16±7.36 AF *vs* 3.79±3.71 no AF), as well as hospital stay were significantly higher in the AF patients compared to those remaining in sinus rhythm (*P*=0.000). In this study, the rate of stroke was higher in the AF group (4.7% AF *vs* 2.0% no AF; *P*=0.041). This finding also showed that about 85.4% of POAF converted to sinus rhythm through correction of electrolyte imbalances and administration of amiodarone. In-hospital mortality was significantly greater in patients who developed AF (8.2% AF *vs* 2.1% no AF) compared to group in sinus rhythm before and after matching for patients and operative characteristics (*P*=0.000).

Discussion

POAF remains the most frequent postoperative complication of cardiac surgery.[12] Despite all the modern anti-arrhythmic drugs, the incidence of POAF remains unchanged. Patients who develop POAF show significantly worse outcome compare to those without AF. The incidence of AF in general populations and general surgical procedures are approximately 1.8% and 5% respectively.[13-15] For patients undergoing open cardiac procedures, the incidence of POAF is clearly much higher and it has been reported to be between 10 and 65%[4,16], with most large series reporting an incidence around 30%.[6,10,17-23] The current study shows an average incidence of 13.6% for POAF. Although in this study group, mean

Table 1. Pre-, intra-, and post-operative variables according to atrial fibrillation following cardiac surgery

Characteristics	Total	AF	No-AF	*P*
Preoperative risk factors				
Age(year)				0.000
≤50	371/1253(29.6%)	32/171(18.7%)	339/1082(31.3%)	
>50	882/1253(70.4%)	139/171(81.3%)	743/1082(68.7%)	
Smoking	504/1254(40.2%)	53/171(31.0%)	451/1083(41.6%)	0.005
History of cardiac surgery	27/1254(2.2%)	2/171(1.2%)	25/1083(2.3%)	0.265
Diabetes	257/1254(20.5%)	34/171(19.9%)	223/1083(20.6%)	0.462
COPD	155/1254(12.4%)	19/171(11.1%)	136/1083(12.6%)	0.348
CVA	37/1252(3.0%)	7/171(4.1%)	30/1081(2.8%)	0.232
Peripheral vascular disease	10/1254(0.8%)	3/171(1.8%)	7/1083(0.6%)	0.145
Renal failure (cr≥2.5)	12/1243(1.0%)	1/170(0.6%)	11/1073(1.0%)	0.496
Beta-blocker consumption	965/1254(77.0%)	133/171(77.8%)	832/1083(76.8%)	0.434
Hypertension≥140/90	100/1254(8.0%)	19/171(11.1%)	81/1083(7.5%)	0.074
Pulse≤70(min)	374/1254(29.8%)	47/171(27.5%)	327/1083(30.2%)	0.266
CCS>III	49/1219(4%)	5/165(3%)	44/1054(4.2%)	0.329
NYHA Function Class≥III	601/1213(49.5%)	89/163(54.6%)	512/1050(48.8%)	0.096
Cardiomegaly	230/1248(18.4%)	29/171(17%)	201/1077(18.7%)	0.339
Left ventricular hypertrophy	53/1248(4.2%)	14/171(8.2)	39/1077(3.6%)	0.009
Creatinine=1.4-2.5(mg/dl)	67/1243(5.4%)	14/170(8.2%)	53/1073(4.9%)	0.042
Hemoglobin<12 (g/dl)	178/1239(14.4%)	30/170(17.6%)	148/1069(13.8%)	0.117
Intraoperative risk factors				
Aortic cross-clamp time(min)	64.7±22.5	67.9±25.2	64.2±22.0	0.040
CPB time(min)	107.7±31.8	116.8±40.6	106.2±29.9	0.000
Cold blood cardioplegia				0.421
Antegrade	621/1254(49.5%)	80/171(46.8%)	541/1083(50.0%)	
Both(antegrade+retrograde)	630/1254(50.2%)	91/171(53.2%)	539/1083(49.8%)	
Retrograde	3/1254(0.2%)	0/171(0%)	3/1083(0.3%)	
Aortic root reperfusion	460/796(57.8%)	78/129(60.5%)	382/667(57.3%)	0.284
Topical ice slush	662/763(86.8%)	106/119(89.1%)	556/644(86.3%)	0.258
Cardiac venting techniques				0.003
Aorta	1193/1254(95.1%)	156/171(91.2%)	1037/1083(95.8%)	
Pulmonary vein	33/1254(2.6%)	5/171(2.9%)	28/1083(2.6%)	
Both	28/1254(2.2%)	10/171(5.8%)	18/1083(1.7%)	
Bicaval cannulation	93/1254(7.4%)	20/171(21.5%)	73/1083(78.5%)	0.020
Need of perioperative IABP	32/1254(2.6%)	5/171(2.9%)	27/1083(2.5%)	0.447
Type of surgery				0.014
CABG	1007/1254(80.3%)	128/171(74.9%)	879/1083(81.2%)	
CABG+Valve	48/1254(3.8%)	10/171(5.8%)	38/1083(3.5%)	
Valve	132/1254(10.5%)	27/171(15.8%)	105/1083(9.7%)	
Congenital	55/1254(4.4%)	3/171(1.8%)	52/1083(4.8%)	
Other	12/1254(1.0%)	3/171(1.8%)	9/1083(0.8%)	
Inotropic agents	350/1254(27.9%)	71/171(41.5%)	279/1083(25.8%)	0.000
Dopamine	48/1254(3.8%)	12/171(7.0%)	36/1083(3.3%)	0.023
Dobutamine	297/1254(23.7%)	58/171(33.9%)	239/1083(22.1%)	0.001
Epinephrine	31/1254(2.5%)	12/171(7.0%)	19/1083(1.8%)	0.000
Norepinephrine	18/1254(1.4%)	5/171(2.9%)	13/1083(1.2%)	0.086
Amrinone	19/1254(1.5%)	8/171(4.7%)	11/1083(1.0%)	0.002
Postoperative (ICU) risk factors				
Inotropic agents	258/1254(20.6%)	48/171(28.1%)	210/1083(19.4%)	0.007
Beta blocker use	1005/1254(80.1%)	132/171(77.2%)	873/1083(8.06%)	0.174
Red blood cell transfusion	178/1239(14.4%)	30/170(16.9%)	148/1069(83.1%)	0.117

CVA: Cerebrovascular Accident; CCS: Canadian Cardiovascular Society Angina Score; CPB: Cardiopulmonary Bypass; IABP: Intra Aortic Balloon Pump; COPD: Chronic Obstructive Pulmonary Disease; NYHA: New York Heart Association

Table 2. Demographic characteristics of patients

	Atrial fibrillation		No atrial fibrillation		
	N	%	N	%	*P*
Age (year, mean±SD)	171(59.8±11.9)	13.6	1082(54.4±16.1)	86.4	0.000
Female	55	14.1	335	85.9	0.407
Smoking	53	10.5	451	89.5	0.005
DM	34	13.2	223	86.8	0.462
COPD	19	12.3	136	87.7	0.348
CVA	7	18.9	30	81.1	0.232
Prior MI	51	15.2	284	84.8	0.185
Prior heart surgery	2	7.4	25	92.6	0.265
HTN	19	19.1	81	80.9	0.074
Renal failure (cr≥2.5)	21	18.8	91	81.3	0.071
B-blocker use	133	13.8	833	86.2	0.364
Digoxin use	20	18.9	86	81.1	0.068
Amiodarone	3	25.0	9	75.0	0.215
Diuretics	30	17.6	140	82.4	0.062
Calcium channel blocker	62	15.8	331	84.2	0.071

Cr=Creatinine; COPD = Chronic Obstructive Pulmonary Disease; CVA= Cerebrovascular Accident; DM = Diabetes Mellitus; HTN=Hypertention≥140/90; MI = Myocardial Infarction.

age (55.1±15.7) is low, but the rate of POAF is the same range of other studies. In addition in this group POAF more frequent in patient's >50 years old and this may be related to exclusion of patients with history of AF, or low mean age of coronary artery disease in our country. The influence of sex in the POAF is controversial.[24,25] No difference between sexes was observed in present study. Several risk factors are associated with the development of POAF. These risk factors can be classified as preoperative, intraoperative and postoperative variables (Table 1). From preoperative patients' variables, age, smoking, left ventricular hypertrophy and renal dysfunction, were associated with an increased of POAF. Advanced age is a major risk factor for POAF.[2,26] In the present study, 81.3% of the patients who experienced POAF were >50 years old. Smoking was also a predictor of POAF in this study and some of these smoker patients may have COPD, therefore these patients usually have a ventilation perfusion (V/Q) mismatch that can lead to arterial hypoxemia. V/Q mismatch can be aggravated after operation because of poor ventilating mechanics and atelectasis of the lung. These patients also have frequent premature atrial contractions that predispose them to POAF.[10] Our study showed left ventricular hypertrophy as predictive for POAF. The majority of these patients usually suffer from high blood pressure with secondary cardiac hypertrophy. These hearts may contain of myocardial fibrosis[27,28], that combined with senescent changes in myocardium, can provide a suitable substrate for generation of POAF.[6,29] Prior studies have shown the association between hypertension and POAF[5,30], but, in this study there was not any relation between them.

We also demonstrated preoperative renal dysfunction as a predictor of POAF. Although in other studies, renal failure was found as a predictor of POAF. Mechanisms that have been proposed for this event in these patients include ischemia, atheroembolism, and systemic inflammation.[31-33] The use of beta-blockers starting in the preoperative period has been shown to decrease the incidence of POAF.[11,17,19] The preoperative use of beta-blocker agents in our patients had no relation to the development of POAF. This may be because our study was not specifically designed to look at this issue.

Intraoperative variables associated with POAF included cardiopulmonary bypass time, aortic cross-clamp time, bicaval cannulation, valve surgery, ASD surgery and cardiac venting technique. Cardiopulmonary bypass deprives the heart of blood flow and thus could result in atrial ischemia-reperfusion injury and POAF. Some studies have demonstrated that long procedure times can increase likelihood of POAF and that aortic-cross clamp time correlates with POAF.[34] Bicaval cannulation has been shown to increase the incidence of POAF.[11,35] We also found that POAF occurs, more frequently in patients who underwent valve surgery and ASD closure. This may resulted from structural and hemodynamic abnormalities such as left atrial enlargement, pathological changes from rheumatic heart disease, increased left atrial pressure and surgical trauma.[34] On the other hand, ASD closure and most of valve surgeries mandate bicaval cannulation and this cannulation technique can also increase POAF in these patients. The present study showed concomitant venting of the left ventricle (LV) via pulmonary vein and aortic

Table 3. preoperative characteristics

	Isolated CABG			CABG + Valve surgery			Isolated Valve surgery			Other cardiac operations		
	AF (n=128)	No AF (n=879)	*P*	AF (n=10)	No AF (n=38)	*P*	AF (n=27)	No AF (n=105)	*P*	AF (n=6)	No AF (n=61)	*P*
Age (mean+SD)	63.1±8.9	58.7±10.5	0.000	58.8±8.7	58.9±9.9	0.966	49.8±12.3	35.9±18.7	0.000	37.3±21.2	20.6±19.0	0.831
Female gender	37(28.9)	229(26.1)	0.279	3(30.0)	14(36.8)	0.497	12(44.4)	55(52.4)	0.302	3(50.0)	37(61.7)	0.443
Angina class>III	3(2.4)	35(3.8)	0.264	0	3(7.9)	0.488	0	6(6.0)	0.281	2(33.3)	0	0.009
NYHA≥III	69(55.6)	427(49.6)	0.122	6(60)	27(71.1)	0.377	11(47.8)	49(49.5)	0.535	3(50.0)	9(17.3)	0.096
Recent MI	47(36.7)	274(31.2)	0.124	4(40.0)	8(21.1)	0.202	0	1(1.0)	0.795	0	1(1.6)	0.910
Current smoker	45(35.2)	403(45.8)	0.014	3(30.0)	17(44.7)	0.320	5(18.5)	26(24.8)	0.343	0	5(8.2)	0.616
Diabetes	32(25.0)	212(24.1)	0.452	1(10.0)	4(10.5)	0.724	1(3.7)	4(3.8)	0.729	0	3(4.9)	0.751
HTN	15(11.7)	74(8.4)	0.145	0	1(2.6)	0.792	3(11.1)	5(4.8)	0.208	1(16.7)	1(1.6)	0.172
COPD	15(11.7)	119(13.5)	0.343	3(30.0)	0	0.007	1(3.7)	14(13.3)	0.141	0	3(4.9)	0.751
CVA	6(4.7)	22(2.5)	0.134	0	3(7.9)	0.488	1(3.7)	5(4.8)	0.644	0	0	-
PVD	2(1.6)	4(0.5)	0.171	0	1(2.6)	0.792	0	2(1.9)	0.632	1(16.7)	0	0.090
Renal dysfunction	13(10.2)	78(9.0)	0.369	4(40.0)	3(7.9)	0.027	3(11.1)	8(7.7)	0.404	1(16.7)	4(6.6)	0.252
Prior surgery	0	10(1.1)	0.255	0	2(5.3)	0.623	1(3.7)	9(8.6)	0.352	1(16.7)	1(11.1)	0.384
Drug history	115(89.8)	793(90.2)	0.498	10(100)	36(94.7)	0.623	21(77.8)	69(65.7)	0.167	2(33.3)	20(32.8)	0.649

MI: Myocardial Infarction; PVD: Peripheral Vascular Disease; AF: Atrial Fibrillation; CVA: Cerebrovascular Accident; HTN:Hypertension≥140/90; Other cardiac operations consist surgery for congenital heart disease (n=55), Pericardial Cyst (n=2), Aneurysm (n=4), Aortic Dissection (n=3).

Table 4. Significant variables associated with atrial fibrillation

Variable	Odds ratio	95% confidence interval	*P*
Preoperative			
Age>50	0.505	0.336-0.757	0.000
Smoking	0.629	0.445-0.890	0.005
LVH	2.373	1.260-4.471	0.009
Renal dysfunction	1.661	0.988-2.790	0.042
Intraoperative			
Type of surgery			
Valve surgery	0.573	0.362-0.905	0.017
ASD closure	0.171	0.023-1.256	0.028
Intraoperative inotrope use	2.046	1.466-2.855	0.000
Aortic cross-clamp time	1.012	1.001-1.024	0.040
Cardiopulmonary bypass time	0.984	0.976-0.992	0.000
Bicaval cannulation	1.833	1.086-3.093	0.020
Concomitant venting of PV&Aorta	0.272	0.123-0.600	0.001
Postoperative(ICU)			
Inotrope use	1.622	1.125-2.339	0.007

ASD= Atrial Septal Defect; LVH= Left Ventricular Hypertrophy; PV=Pulmonary Vein; Renal Dysfunction: cr=1.4-2.5

root has also been associated with POAF, whereas, in some studies LV venting through the pulmonary vein had been associated with increased risk of POAF.[11,35] Therefore it appears that the cause of POAF with pulmonary vein venting is related to other factors.

Our data imply that the use of inotropic agent in the postoperative period is related to POAF. Several studies have suggested that a heightened sympathetic response predisposes a patient to developing POAF.[22,36,37] In this study, the postoperative morbid events were also increased with POAF. The need for reintubation was almost tripled in patients with POAF. In addition, the median length of ICU stay was significantly higher in the POAF patients (6 days) compared to these remaining in sinus rhythm (4 days). The POAF also increased the median postoperative hospital stay from 7 days to 11 days. Some other studies have found similar associations.[6,10,30,38] The POAF also increases the risk of stroke by fivefold[39] and several reports[39-41] show a significantly high stroke rate in patients developing POAF. This is largely due to circulatory stasis in the left atrum resulting in the formation of an embolus.[40] In the current study, the rate of stroke in patients with POAF (4.7%) was almost double the rate of stroke in patients without AF (2.0%) This results also revealed higher in-hospital mortality rate in patients with POAF than without AF (8.2% AF *vs* 2.1% no AF). Similar results were also observed by other investigators.[16,29,31] It is clear that a longer hospital stay and more use of resources will have significantly driven up the cost of hospitalization.

Conclusion

POAF is the most common arrhythmia after cardiac surgery and can affect the outcome and survival of the patients. We concluded that not only concerted effort should be performed to identify the risk factors, but also preventive measures should be done to reduce POAF. In addition, POAF should be treated effectively to prevent mortality and morbidity.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

Conflict of interests: The authors declare no conflicts of interest.

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