

# ATRIAL FIBRILLATION POST CARDIAC SURGERY: INCIDENCE, PREDISPOSING FACTORS AND PROGNOSTIC IMPLICATIONS.

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## SUMMARY

**BACKGROUND & OBJECTIVES:** Atrial fibrillation (AF) is the most common arrhythmia occurring postcardiac surgery and is associated with significant morbidity, increased overall hospital stay and cost. Anecdotal observations suggest very low incidence in Pakistani patients undergoing cardiac surgery particularly coronary artery bypass graft surgery (CABG). The objective of this study was to assess the prevalence, morbidity & mortality of post cardiac surgery AF.

**METHODS:** A prospective study of 201 consecutive patients undergoing cardiac surgery at a tertiary care center. Clinical characteristics and perioperative data was collected & analyzed. Patients were followed for presence or absence of atrial fibrillation till hospital discharge.

**RESULTS:** The overall incidence of AF post cardiac surgery was 6.9 %. AF occurred in 9 of 187 patients undergoing CABG alone, 3 of 12 patients undergoing valve replacement and 2 of 2 undergoing combined procedures. Increased left atrial (LA) size had significant association with post cardiac surgery AF ( $p = 0.01$ ) as did the use of dopamine and epinephrine post operatively ( $p = 0.03$  &  $0.002$  respectively). In addition, significant association was also noted for valvular surgery ( $p = <0.001$ ). Multiple logistic regression analysis revealed that increased LA size (odds ratio 0.08, 95% CI 0.008-0.99,  $p = 0.04$ ) was the only independent predictor of post cardiac surgery AF with borderline significance for concomitant valvular surgery (odds ratio 0.89, 95% CI 0.79-0.99,  $p = 0.05$ ). Mean hospital stay was significantly longer & overall cost was significantly higher in patients who developed AF ( $p = <0.001$ ) in addition to higher overall mortality ( $p = 0.025$ ).

**CONCLUSIONS:** The incidence of AF post cardiac surgery was quite low in this study cohort. The occurrence of atrial fibrillation, albeit for short duration, was associated with higher all cause mortality, significantly longer hospital stay and higher overall cost.

**KEY WORDS:** Atrial Fibrillation, coronary artery bypass graft, Left atrium.

## INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia occurring post cardiac surgery and is strongly associated with prolongation of hospital stay, higher overall costs and increased morbidity. Data from Western literature indicates a prevalence rates as high as 40% after CABG and 60% after valvular

surgery<sup>1,2,3</sup>. Despite improvements in surgical techniques, the incidence has not decreased over the course of time<sup>3</sup>.

Limited available data from Pakistan suggests comparatively lower rates of post cardiac surgery AF (4). However the factors responsible for this observed difference are not clearly defined. In addition, it is not

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well known whether post cardiac surgery AF in our population causes excess morbidity, mortality, prolonged hospital stay and increased overall cost. The objective of this study was to assess the prevalence, morbidity & mortality of post cardiac surgery AF

## **METHODS:**

We conducted a prospective observational study of 201 consecutive patients who underwent cardiac surgery (CABG and/or valvular surgery) at a tertiary care medical center between May 2002 and June 2004. Patients were excluded from the study if they had preexisting AF or were using class I or III anti-arrhythmic drugs. AF was defined as any episode lasting greater than 60 min, documented by a physician on either continuous telemetric monitoring or a 12 lead ECG. Patients were included in the study if they were receiving digoxin, beta-blockers or calcium channel blockers. Detailed clinical characteristics and peri-operative data was analyzed. Patients were closely followed till hospital discharge. All patients underwent standard open heart surgery via midline sternotomy utilizing cardiopulmonary bypass technique (On-pump).

**Mode Of Myocardial Protection:** All Patients had antegrade blood cardioplegia as a mode to produce cardiac arrest. In only 8 patients a combination of antegrade and coronary sinus retrograde cardioplegia was administered. In all patients cardioplegia was supplemented by topical cooling of the myocardium with ice slush. Mild systemic hypothermia of 28-30 degrees centigrade was also observed.

## **STATISTICAL ANALYSIS:**

All the data was entered in SPSS (Statistical package for Social Sciences) version 10.0 (SPSS, Chicago, Illinois-U.S.A). Univariate analysis was done to see the distribution of various variables under study. Bivariate analysis was done to compare the group of patients who did develop postoperative AF and those who did not in relation to various explanatory and confounding factors. Chi-square test (Fischer's Exact used, where appropriate) was used for categorical variables. Independent sample t-test was used for comparison between the groups for continuous

variables. Multivariate logistic regression model was used to study the association between various risk factors and outcome of interest i.e Atrial fibrillation. Variables which were thought to be associated with the risk of developing atrial fibrillation, based on prior knowledge and clinical relevance were put in the regression model. The results in table 4 present the adjusted odds ratio, 95% confidence interval and pvalue from the logistic regression model. Odds ratios and 95% confidence intervals were obtained.  $P < 0.05$  was considered statistically significant.

## **RESULTS:**

A total of 201 patients were included in the study. 187 underwent CABG, 12 had valve replacement and 2 underwent combined procedure (CABG + valve replacement). Patients were divided into two groups based on the presence or absence of postoperative AF. AF occurred in 9(4.8%) patients undergoing CABG alone, 3(25%) patients undergoing valve replacement alone and 2(100%) patients undergoing combined procedure (CABG + valve replacement).

## **CLINICAL CHARACTERISTICS:**

Table-1 shows the clinical characteristics of patients in both groups. 75% of the patients were male. Mean age was  $56 \pm 16$  years in the AF group and  $59 \pm 12$  in the no AF group. There were no statistically significant differences amongst the two groups in age ( $p = NS$ ), gender ( $p = NS$ ), presence of hypertension ( $p = NS$ ), diabetes ( $p = NS$ ), obesity ( $p = NS$ ), hyperlipidemia ( $p = NS$ ), smoking ( $p = NS$ ) or preoperative left ventricular ejection fraction ( $p = NS$ ). However, patients with AF had significantly larger LA dimensions ( $47.6 \pm 13$  mm vs.  $37.7 \pm 6$  mm,  $p = 0.01$ ).

## **DURATION OF AF & CARDIOVERSION:**

Amongst the patients who had AF, the duration of AF was quite variable. 5 patients (35.7%) had AF less than 12 hrs, 3 patients (21.4%) between 12-24 hrs and 6 patients (42.9%) had AF lasting more than 24 hrs but less than 48 hrs. 8 patients (57.1%) had spontaneous conversion to sinus rhythm. Of these patients, 3 were receiving digoxin, 3 beta-blockers and 2 patients were on both drugs. Amongst the

patients undergoing cardioversion for AF, 4 patients (28.6%) received IV amiodarone and 2 (14.3%) patients required direct current cardioversion after 24 hrs of IV amiodarone infusion. All patients requiring IV amiodarone received oral loading dose for 5-7 days and then 200 mg/day for 3-4 weeks.

### PERIOPERATIVE CHARACTERISTICS:

Table-2 shows the perioperative characteristics of patients in both groups. There were no significant differences in the two groups in bypass time ( $p = 0.5$ ), cross clamp time ( $p = 0.8$ ), no of grafts ( $p = 0.9$ ) or intra-aortic balloon pump use ( $p = 0.27$ ). Mean number of grafts in both groups was 4. The use of perioperative beta-blockers was also similar between both groups ( $p = 0.90$ ).

### PREDICTORS OF POSTOPERATIVE AF:

Univariate analysis (Table-2) showed a statistically significant association between AF and the type of cardiac surgery, valvular surgery patients being at the highest risk ( $p = <0.001$ ). In addition, both the use and duration of dopamine use were significantly associated with new atrial fibrillation ( $p = 0.03$  &  $0.04$  respectively). The use of postoperative epinephrine for more than 24 hrs was also significantly associated with atrial fibrillation ( $p = 0.002$ ). The total hospital stay (Table-3) was longer in AF vs. no AF group (15 vs. 7 days,  $p = <0.001$ ). Overall cost was also higher in patients who developed post CABG AF ( $p = <0.001$ ). There were two mortalities in the AF group.

Both patients died of nosocomial pneumonia and subsequent respiratory failure. One patient had a post CABG stroke before any documented AF occurred, though paroxysmal AF as a probable cause cannot be ruled out, leading to prolonged hospital stay. The increased overall duration of stay in most AF patients was primarily caused by prolonged intubation either because of significant pleural effusions or nosocomial pneumonias. No patient with AF developed acute renal failure after the occurrence of AF. Apart from the 5 patients who underwent valvular replacement with or without CABG, no other AF patient required anticoagulation with heparin or warfarin.

Using multivariate regression analysis (Table-4)

**Table 1 :**  
**Clinical Characteristics of patients with and without AF (n=201)**

VARIABLE	AF (n=14)	NO AF (n=187)	p-value †
Age	56.3±16.8	59.6±12.3	0.54
Gender Male/Female	8/6	142/45	0.19
Diabetes mellitus	1	7	0.8
Hypertension	1	17	0.68
Obesity	1	17	0.22
Smoking	1	2	0.06
Alcohol intake	2	14	0.1
Serum Cholesterol (mg/dl)	184.5 ± 38	184.9 ± 50	0.98
Serum Triglyceride (mg/dl)	163.4 ± 49	192.0 ± 86	0.58
Serum LDL (mg/dl)	109.4 ± 30	117.0 ± 62	0.95
Serum HDL (mg/dl)	38.4 ± 8	35.4 ± 10	0.26
Left atrial size (mm)	47.6 ± 13	37.7 ± 6	0.01
L.Vent.Ejec.Fraction %	57.2 ± 12	50 ± 15	0.1

AF: atrial fibrillation

Data is expressed as number ± 1 SD or as percentage of total

† Independent sample t-test used for continuous variables

Chi-square test used for proportions (Fisher's Exact test used where expected cell count was < 5)

increased LA size was found to be the only significant independent predictor of post operative AF ( $p = 0.04$ ) with border line significance for valvular surgery ( $p = 0.05$ ). In the multivariate model the use of perioperative dopamine and epinephrine were no longer independent predictors of post operative AF.

### DISCUSSION:

Our study has documented a fairly low incidence of post cardiac surgery AF. While unidentified factors like genetic predisposition cannot be excluded, the most obvious difference is relative younger age (mean age 56) of patients in our study. Older age is the most potent predisposing factor for AF<sup>5</sup>. The mean age of patients undergoing CABG in the United States is 65 yrs<sup>6,7</sup>. Although the exact mechanism behind this predisposition remains unidentified, it has been suggested that ageing may lead to loss of myocardial fibers and an increase in fibrosis<sup>5</sup>.

There exists a plethora of literature looking at the predisposing factors for post cardiac surgery AF. Leung et al have recently shown that enlarged LA size and impaired LA ejection fraction predispose to post CABG AF<sup>8</sup>. We have also shown that

**Table 2 :  
Perioperative data**

VARIABLE	AF (n=14)	NO AF (n=187)	p-value †
Type of Cardiac Surgery (n)	9	178	
CABG (187)	3	9	
Valvular Surgery (12)	2	0	
CABG+Valvular (2)			
By-pass time (min)	140.28±51	145.5±44.6	0.51
Cross-clamp time (min)	90.1±32.4	85.4±24	0.81
Dopamine used postoperatively	5	29	0.03
Dopamine used more than 24 hrs	4	21	0.04
Epinephrine used postoperatively	8	94	0.48
Epinephrine used more than 24 hours	7	31	0.002
Use of Beta Blockers Pre-Op	13(92.85 %)	176(98.87%)	NS
Mean No. of grafts Applied / Surgery	4.0±0.74	4.03±0.91	NS
Use of IABP*	2(14.28%)	13(7.3%)	NS
Use of Anterograde Cardioplegia	14 (100 %)	187 (100%)	NS

Data is expressed as number ± 1 SD or as percentage of total

\* Intra-aortic balloon pump

NS: not significant

AF: atrial fibrillation

† Independent sample t-test used for continuous variables

Chi-square test used for proportions (Fisher's Exact test used where expected cell count was < 5)

**Table 3 :  
Hospital stay and financial implications of  
post operative atrial fibrillation**

VARIABLE	AF (n=14)	NO AF (n=187)	p-value †
Total hospital stay (days)	15.4±10.6	7.3±1.3	<0.001*
Total cost incurred (Pak Rs)	3,22,191 ± 61,654	2,60,587 ± 15,270	<0.001*
Myocardial Infarction	0	0	
Stroke	1(7.1%)	0	0.07
All cause mortality	2 (14.2 %)	2 (1.1%)	0.025*

\*Implies significant p value

† Independent sample t-test used for continuous variables,

Fisher's Exact test for proportions

AF: atrial fibrillation

**Table 4 :  
Predictors of Post-operative atrial fibrillation  
(Multivariate Logistic regression analysis)**

Variable	Adjusted Odds ratio	95%CI	P-value
Gender	0.47	0.07-3.1	0.43
H/o Obesity	0.001	0.00-2.5	0.88
H/o Smoking	0.415	0.67-2.58	0.34
H/o Alcohol Intake	0.48	0.26-20.8	0.44
Valvular Surgery	0.08	0.008-0.99	0.05
Epinephrine duration (>24 hrs)	0.94	0.27-3.2	0.93
Dopamine used	0.9	0.12-1.73	0.29
Left atrial size (mm)†	0.89	0.79-0.99	0.04*
Left Ventricular Ejection Fraction (%)	0.97	0.91-1.02	0.26

\* Implies significant p-value

† limited data available (81 patients only)

preoperative enlarged LA dimensions predispose to AF. Although data on left atrial size was not available on all patients (81 patients only), but the available data points that left atrial size is an important determinant of atrial fibrillation. The fact that valvular surgery patients had the highest risk of postoperative AF comes as no surprise. Patients with valvular heart disease particularly mitral valve disease have enlarged left atriums and higher LA pressures which probably play a predominant role in predisposing to postoperative AF. There has been recent interest in utilizing the Off-pump technique for CABG and it has been proposed that this technique allows better myocardial protection in addition to reducing the renal and neurological complications associated with aortic clamping.

Though we did not have any patient undergoing the Off-pump technique, the existing data in the literature is far from conclusive. A meta analysis by Athanasiou et al suggested a possible benefit of Off-pump CABG in reducing postoperative AF<sup>9</sup> in elderly population. However randomized prospective data from Pakistan<sup>4</sup> as well as the West<sup>10</sup>, showed no benefit of Off-pump technique in reducing post CABG AF.

Our study also shows that routine use of postoperative IV dopamine as well as prolonged (>24

hrs) use of IV epinephrine also predispose to AF. This is not surprising in view of the proarrhythmic potential of these beta-agonist drugs. Several studies<sup>11,12</sup> have shown male gender predisposition for post-operative AF, however our data showed no gender predisposition. In their study, Leung et al<sup>8</sup> have proposed that it is not the gender but rather the body mass index (BMI) which predisposes to postoperative AF, a finding confirmed in other studies as well<sup>13</sup>. Recent studies have also looked at other possible mechanisms for post CABG AF. Cummings et al have performed a randomized trial showing that preservation of the anterior epicardial fat pad decreased the incidence of post CABG AF<sup>14</sup>. Increases in P-wave dispersion have also been shown to be predictive of post CABG AF<sup>13</sup>.

Our study also confirms that occurrence of post cardiac surgery AF, even for a relatively short duration, leads to significantly higher mortality, longer hospital stay and higher over all costs. In view of the economic constraints faced by most developing countries like Pakistan, this has major implications and calls for implementing all possible preventive measures to prevent post cardiac surgery AF. We believe that the relatively lower incidence of post cardiac surgery AF in our patients compared to other studies from Pakistan<sup>4</sup> is because of a significantly higher use of Beta blockers in both groups in our study. Several trials have definitively shown benefit of perioperative beta-blocker use in reducing the incidence of AF<sup>15</sup>. In addition, use of perioperative amiodarone has also shown to reduce the incidence of post CABG AF<sup>16</sup>.

#### CONCLUSIONS:

Our study has several limitations: The number of AF patients was rather small and short episodes of paroxysmal AF could not be definitively excluded. Also we did not look at the long term follow up of these patients.

Despite these limitations, a significantly lower incidence of post-cardiac surgery AF has been documented in this study. As pointed earlier, this very likely represents an overall low risk population (younger age, good left ventricular function, less concomitant valvular surgery) and significantly higher perioperative beta-blocker usage. In addition,

we have identified several factors predisposing to post operative AF, the recognition of which could help cardiac surgeons and cardiologists to utilize preventive strategies and reduce the morbidity and economic burden of post CABG AF.

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