Frequency and Outcome of Postoperative Atrial Fibrillation Following Mitral Valve Replacement for Mitral Stenosis

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ABSTRACT

Objective: To determine the frequency and outcome of postoperative atrial fibrillation (POAF) in terms of in-hospital and 30-day mortality and morbidity after mitral valve replacement (MVR).

Study Design: Observational study.

Place and Duration of the Study: Department of Cardiac Surgery, Northwest General Hospital and Research Centre, Peshawar, Pakistan, from September 2017 to March 2023.

Methodology: A total of 186 patients between the ages of 20 and 70 years, who had severe mitral stenosis and normal sinus rhythm and underwent MVR surgery, were included in the study. The frequency of POAF within 7 days following surgery and outcomes in terms of in-hospital and 30-day mortality / morbidity were recorded.

Results: POAF occurred in 19.4% patients. Patients with POAF were predominantly male ($p = 0.01$), aged over 50 years ($p = 0.002$), diabetic ($p = 0.02$), hypertensive ($p = 0.02$), had impaired LV function ($p < 0.001$), enlarged LA ($p = 0.003$), pulmonary hypertension ($p = 0.009$), previous PMBV ($p < 0.001$), and previous infective endocarditis ($p < 0.001$). In-hospital and 30-day mortality rates were 7% and 8.6%, respectively. POAF patients had prolonged ICU stays ($p < 0.001$), hospital stays ($p = 0.04$), and higher mortality rates ($p < 0.001$). Persistent AF (22%) contributed to 30-day morbidity in the form of embolic stroke, limb ischaemia, and congestive heart failure.

Conclusion: POAF commonly occurs following the MVR surgery and significantly impacts perioperative and 30-day morbidity and mortality.

Key Words: *Postoperative atrial fibrillation, Mitral stenosis, Mitral valve replacement.*

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INTRODUCTION

Mitral stenosis (MS) commonly results from rheumatic heart disease but may have non-rheumatic aetiologies such as mitral annular calcification, endomyocardial fibroelastosis, and malignant carcinoid syndrome.[1] Severe MS is managed with percutaneous mitral balloon valvotomy (PMBV), mitral commissurotomy, or mitral valve replacement (MVR).[2]

Postoperative atrial fibrillation (POAF) is a common tachyarrhythmia following open-heart surgery, ranging between 10-50%.[3,4] Various risk factors contribute to its occurence, including advanced age, obesity, coronary artery disease, heart failure, atrial dilation, hypertension, myocardial dysfunction, preoperative leukocytosis, prolonged cardiopulmonary and cross-clamp time, poor myocardial protection, increased catecholamine use, and postoperative pericarditis.[5,6]

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Inflammation plays a key role in its multifactorial pathogenesis triggered by surgical trauma, prolonged cardiopulmonary bypass, and ischaemia/reperfusion injury.[7,8] Pericardial disruption causes increased production of pericardial fluid and local inflammation. Pericardial inflammation causes apoptosis of cardiac myocytes, altering electrical activity, and arrhythmia formation.[7,9] Electrolyte abnormalities (hypomagnesaemia, hypokalaemia) also increase the risk of POAF.[10,11]

Typically, POAF is self-limiting and benign. However, it can result in haemodynamic instability, congestive heart failure, renal or respiratory morbidities, embolic events, and extended stays in the ICU or hospital, leading to higher overall costs.[12,13] Studies have shown the association of POAF with short- and long-term cardiovascular morbidity and mortality, as well as reduced long-term survival.[6] Thrombolytic events are serious complications that additionally raise the risks of morbidity and mortality.[5,12]

This study aimed to assess the frequency of POAF and its associated factors following MVR. Limited data are available in Pakistan regarding the post-MVR POAF. This study will determine the local burden of POAF and common factors. Moreover, the study will provide a roadmap for future research and clinical practice.

METHODOLOGY

This retrospective observational study was conducted at the Department of Cardiac Surgery, Northwest General Hospital and Research Centre in Peshawar, Pakistan. It involved patients undergoing MVR surgery between September 2017 and March 2023. Data were obtained from the cardiac surgery database and hospital electronic records following approval from the Ethical Committee (IRB&EC/2023-GH/041; Dated 16-08-2023).

The study included all patients, regardless of gender, aged between 20 to 70 years, diagnosed with severe mitral stenosis and normal sinus rhythm, and those who underwent MVR surgery in accordance with the AHA guidelines for valvular heart disease.[2] Patients with incomplete record, chronic AF, use of anti-arrhythmic drugs other than beta-blockers, severely impaired LV (EF <40%), congestive heart failure (NYHA III-IV), LA thrombus, severe mitral regurgitation, moderate-severe aortic or tricuspid regurgitation, PAH >50mm Hg, LA size >5.5cm, coronary artery disease, previous stroke or TIA, active infective endocarditis, emergency or redo surgery, and concomitant heart procedure were excluded from the study.

All patients underwent comprehensive preoperative assessment, including baseline labs, electrocardiogram (ECG), and echocardiography (transthoracic or trans-oesophageal). Coronary angiography was performed if age was >40 years. Standard midline sternotomy with cardiopulmonary bypass and trans-atrial approach was performed. Either mechanical (St. Jude Medical; SJM™ Master series) or tissue valve (St. Jude Medical Biocor) was used. No systemic intravenous prophylaxis was given to any patient. However, beta-blockers were introduced / reintroduced within 24 hours after surgery. Postoperative anticoagulation with warfarin ± LMWH (target INR 2.5 - 3.5) was introduced after pericardial drain control.

POAF was defined as "any sustained episode recorded during hospitalisation (within seven days) following MVR that required medical and / or electrical cardioversion". The heart rhythm of all patients was thoroughly monitored using continuous ambulatory ECG. Any suspected dysrhythmia observed during ambulatory ECG was confirmed by standard ECG with a rhythm strip. POAF was managed pharmacologically with amiodarone-infusion or electrical-cardioversion according to established ICU-protocols. Thirty-day follow-up of all POAF patients were searched for any incidence of embolic complications (i.e., stroke or limb ischaemia), congestive heart failure, and death.

Data were analysed using Microsoft Excel 2019 and IBM-SPSS (26.0). Continuous variables were expressed as mean ± SD and categorical variables as frequencies and percentages. Statistical comparisons were performed using Chi-square tests for categorical variables and t-tests for numerical variables, with significance defined as a p-value <0.05.

RESULTS

Results are detailed in Table I-III. Males were 53.8% and females were 46.2% with a mean age of 43.92 ± 8.5 years. Diabetes was present in 21.5%, hypertension in 10.8%, and 20.4% of the patients were smokers. The majority (73%) had rheumatic heart disease, while 15.6% had prior PMBV, and 8.6% had a history of infective endocarditis. The SJM™ Master Series was implanted in 65.6% of patients, while the St. Jude Biocor tissue valve was used in 34.4%. Mean cross-clamp time was 59.62 ± 11.9 minutes, and mean CPB time was 81.36 ± 12.6 minutes. Intraoperative-cardioversion was required in 41.4%, and 9.7% needed transient-pacing for bradyarrhythmia. The majority (67.7%) were extubated within 24 hours. ICU and hospital stays ranged from 20 to 24 hours and 4 to 17 days, respectively. Extended ICU-stays were observed in 26.3% of patients, while 20.4% experienced a prolonged duration of hospitalisation. The 30-day stroke rate was 3.2% ($p = 0.08$, Table III). In-hospital mortality was 7% (n = 13), with an overall 30-day mortality of 8.6% (n = 16). The frequency of postoperative complications is summarised in Table III.

Table I: Preoperative characteristics.

Variables	Total n (%) 186	NSR n (%) 150 (80.6%)	POAF n (%) 36 (19.4%)	p-value χ^2 test for categorical t-test for numerical
Gender				
Male	100 (53.8%)	74 (74%)	26 (26%)	0.01
Female	86 (46.2%)	76 (88.4%)	10 (11.6%)	
Age (range)	24 - 67 years	24 - 63 years	26 - 67 years	
Age (mean)	43.92 ± 8.5 years	42.77 ± 8.3 years	48.72 ± 7.9 years	<0.001
Age <50 years	138 (74.2%)	119 (86.2%)	19 (13.8%)	0.002
Age >50 years	48 (25.8%)	31 (64.6%)	17 (35.4%)	
Diabetes mellitus	40 (21.5%)	27 (67.5%)	13 (32.5%)	0.02
Hypertension	20 (10.8%)	12 (60%)	8 (40%)	0.02
Smoking	38 (20.4%)	35 (92.1%)	3 (7.9%)	0.06
Rheumatic heart disease	136 (73.1%)	106 (77.9%)	30 (22.1%)	0.14
Ejection fraction				
LV-EF ≥60%	95 (51.1%)	88 (92.6%)	7 (7.4%)	
LV-EF 50 - 59%	52 (28%)	39 (75%)	13 (25%)	
LV-EF 40 - 49%	39 (21%)	23 (59%)	16 (41%)	<0.001
Mitral regurgitation				
No MR	33 (17.7%)	30 (90.9%)	3 (9.1%)	
Mild MR	81 (43.5%)	59 (72.8%)	22 (27.2%)	
Moderate MR	72 (38.7%)	61 (84.7%)	11 (15.3%)	0.04
LA Dimension				
≤4.4cm	60 (32.3%)	56 (93.3%)	4 (6.7%)	
4.5 - 5.5cm	126 (67.7%)	94 (74.6%)	32 (25.4%)	0.003
Pulmonary Hypertension				
≤40mmHg	61 (32.8%)	56 (91.8%)	5 (8.2%)	
41 - 50mmHg	125 (67.2%)	94 (75.2%)	31 (24.8%)	0.009
Previous PMBV	29 (15.6%)	12 (41.4%)	17 (58.6%)	<0.001
Infective endocarditis	16 (8.6%)	6 (37.5%)	10 (62.5%)	<0.001

Table II: Operative characteristics.

	n	%
Type of valve		
Tissue valve	64	34.4%
Mechanical valve	122	65.6%
Size of Valve		
27mm SJM	33	17.7%
29mm SJM	49	26.3%
31mm SJM	64	34.4%
33mm SJM	40	21.5%
Chordal preservation		
Complete preservation	42	22.6%
Partial preservation	91	48.9%
No preservation	53	28.5%
Left atrial appendage complication	40	21.5%
CPB-time: 81.36 ± 12.6 minutes (Range 54 - 115 minutes)		
Cross-clamp time: 59.62 ± 11.9 minutes (Range 39 - 88 minutes)		
Intraoperative cardioversion	77	41.4%
Temporary pacing requirement	18	9.7%

POAF was noted in 19.4% of cases, with the highest occurence (52.8%) on the first postoperative day (Table III). Normal sinus rhythm was restored using intravenous amiodarone (80.6%) or DC-shock (19.4%). Persistent AF was found in 22.2% of cases. Patients with POAF were more likely to be male (26% *vs.* 11.6%, p = 0.016), over 50 years of age (35.4% *vs.* 13.8%, p = 0.002), diabetic (32.5%, p = 0.02), hypertensive (40%, p = 0.02), had impaired EF (41%, p <0.001), moderate MR (15.3%, p = 0.04), enlarged LA (25.4%, p = 0.003), pulmonary hypertension (24.8%, p = 0.009), previous PMBV (58.6%, p <0.001), and previous infective endocarditis (62.5%, p <0.001, Table I). Factors such as prolonged ventilation (p <0.001), re-intubation (p = 0.02), LCOS (p = 0.002), postoperative pneumonia (p = 0.01), pericardial effusion (p <0.001), more blood transfusions (p = 0.001), prolonged ICU stay (p <0.001), and extended hospital stay (p=0.04) were significantly associated with POAF (Table III). During the 30-day follow-up, two cases of congestive heart failure and three embolic complications were noted in patients with persistent AF. Patients with POAF had higher mortality rates both in-hospital (61.5% *vs.* 38.5%, p <0.001) and at 30-day (68.8% *vs.* 31.3%, p <0.001, Table III).

DISCUSSION

The observed incidence of POAF in this study falls within the lower range (19.4%) compared to international studies (20-50%), likely due to variations in patient populations and selection criteria.[5] Patients with specific exclusion criteria, such as severe comorbidities or concomitant procedures, may have contributed to this difference. Increasing age is a recognised predictor of atrial fibrillation.[4,13,14] In this study, the population aged above 50 years constituted 25.8%, showing a notable incidence of POAF (p = 0.002, Table I). Similarly, the mean age of the POAF group (48.72 ± 7.9 years) was significantly higher (p <0.001) than the NSR group (42.77 ± 8.3 years) (Table I). While the literature supports a higher occurence of POAF in rheumatic pathologies,[1] the observed incidence of POAF in this study was noted as non-significant (73%, p = 0.14, Table I), possibly due to the study's small sample size.

Table III: Postoperative characteristics.

Variable	n (%)	NSR n (%) 150 (80.6%)	POAF n (%) 36 (19.4%)	p-value (χ^2 test)
Ventilation time:				
Extubation <24 hours	126 (67.7%)	111 (88.1%)	15 (11.9%)	
Extubation >24 hours	60 (32.3%)	39 (65%)	21 (35%)	<0.001
Re-intubation	7 (3.8%)	3 (42.9%)	4 (57.1%)	0.02
Reopening	9 (4.8%)	6 (66.7 %)	3 (33.3%)	0.37
Perioperative MI	3 (1.6%)	2 (66.7%)	1 (33.3%)	0.47
Low cardiac output syndrome (LCOS)	12 (6.5%)	5 (41.7%)	7 (58.3%)	0.002
Ventricular arrhythmias	6 (3.2%)	3 (50%)	3 (50%)	0.08
Acute kidney injury	14 (7.5%)	9 (64.3%)	5 (35.7%)	0.15
Blood transfusion (RCC >1unit)	68 (36.6%)	46 (67.6%)	22 (32.4%)	0.001
Postoperative pneumonia	6 (3.2%)	2 (33.3%)	4 (66.7%)	0.01
Pericardial effusion	13 (7%)	3 (23.1%)	10 (76.9%)	<0.001
Sternal wound infection	4 (2.2%)	2 (50%)	2 (50%)	0.16
Stroke				
In-hospital	5 (2.7%)	3 (60% of stroke) and (3% of NSR)	2 (40% of stroke) and (5.6% of POAF)	0.24
All 30-days	6 (3.2%)	3 (50% of stroke) and (2% of NSR)	3 (50% of stroke) and (8.3% of POAF)	0.08
ICU stay: Range 20 - 264 hours				
Stay <48 hours	137 (73.7%)	132 (96.4%)	5 (3.6%)	
Stay >48 hours	49 (26.3%)	18 (36.7%)	31 (63.3%)	<0.001
Hospital stay: Range 4 - 17 days				
Stay <7days	148 (79.57%)	124 (83.8%)	24 (16.2%)	
Stay >7days	38 (20.4%)	26 (68.4%)	12 (31.6%)	0.04
Mortality				
In-hospital	13 (7%)	5 (38.5% of mortality) and (3.3% of NSR)	8 (61.5% of mortality) and (22.2% of POAF)	<0.001
30-days	16 (8.6%)	5 (31.3% of mortality) and (3.3% of NSR)	11 (68.8% of mortality) and (30.6% of POAF)	<0.001

Enlarged left atrial size (>5cm) increases the risk of both immediate POAF and late-onset atrial fibrillation.[14,15] An enlarged LA produces elevated atrial pressures and subsequently impaired atrial systolic dysfunction. This chronically elevated pressure and dysfunction can induce electrical remodelling and predispose to an increased propensity for POAF. The more accurate determination of LA size is the left atrial volume index (LAVI) and the global longitudinal strain (GLS) of LA.[15,16] Mohamed Sabry *et al.* showed in their research that LAVI was an independent predictor for POAF and LAVI >36 ml/m^2 had a sensitivity of 84.6% and specificity of 68.6% in predicting POAF.[17] Reduced GLS of LA assessed by 2D echocardiography is an independent predictor of POAF. It reflects passive stretching of the LA during LV systole and is an accurate measure of LA reservoir function. The LA-GLS ≤23.1 had a sensitivity of 85% and a specificity of 66% in predicting POAF.[17-19] In the present study, LAVI and LA-GLS were not calculated. Patients with an LA diameter >4.5cm had an increased incidence of POAF (p = 0.003, Table I). Diastolic dysfunction and reduced LV function are recognised as the risk factors for POAF after cardiac surgery, and the incidence increases with the degree of diastolic dysfunction.[16,20] Global left ventricular longitudinal strain (LV-GLS) decreases with decreasing LV function, and studies have shown that LV-GLS ≤-14.4 is a strong predictor of POAF with 70% sensitivity and 85% specificity.[17] This study excluded severe LV dysfunction, yet mild-to-moderate LV dysfunctions was present in 20.9% of cases, showing a significantly high POAF (p <0.001, Table I).

Patients whose ventilation exceeded 24 hours (32.3%) experienced POAF at a rate of 35% compared to 11.9% (p <0.001). Likewise, individuals who required reintubation (3.8%) exhibited POAF at a rate of 57.1% (p = 0.02, Table III). Prolonged invasive ventilation and ventilation settings (elevated peak pressures, plateau pressures, and respiratory rate) cause increased intra-thoracic pressure and reduced intra-thoracic vascular flow / volume and LV-filling. Reduced LV-filling leads to increased myocardial stress *via* extra-cardiac pressure. Schnaubelt *et al.* observed a significantly higher POAF incidence (p = 0.019) in patients having higher plateau pressure (adjusted OR 1.199 [1.0381.661], p = 0.019), driving pressure (adjusted OR 1.244 [1.1031.713], p = 0.021), and peak respiratory rate (adjusted OR 1.206 [1.0051.601], p = 0.040).[21]

A significantly high incidence of POAF at 76.9% (p <0.001) was noted in patients who developed postoperative pericardial effusion (Table III). The presence of pericardial effusion or blood can provoke localised inflammation within the pericardial space, potentially triggering POAF. Several studies have shown that shed mediastinal blood and breakdown products have pro-inflammatory and pro-oxidant properties, which may provoke POAF in susceptible individuals.[22] Two key points regarding pericardial effusion are noteworthy. Firstly, patients undergoing MVR who receive anticoagulation are more susceptible to developing a pericardial collection. Secondly, in MVR patients, the pleural cavity remains unopened, increasing the likelihood of pericardial effusion. The posterior-left pericardiotomy for the prevention of POAF after cardiac surgery has been shown to be effective.[23] Additionally, the current study also supports an association between increased POAF (32.4%, p = 0.001) and higher blood transfusion rates.[24]

The study has several inherent limitations. Firstly, it was conducted at a single institution with a relatively small patient cohort. Secondly, due to its retrospective nature, observations were limited to the first month following MVR, and long-term outcomes were not investigated. Additionally, the study excluded patients with severe comorbidities and those undergoing concomitant cardiac procedures such as combined valvular and coronary artery bypass grafting.

CONCLUSION

Several important conclusions can be drawn from this study. Firstly, POAF following MVR is a prevalent complication, occurring in 19.4% of cases. Secondly, comorbidities such as diabetes, hypertension, impaired left ventricular function, significant mitral regurgitation, left atrial enlargement, pulmonary hypertension, previous PMBV, and previous infective endocarditis contribute to the incidence of POAF. Thirdly, postoperative complications including prolonged ventilation, re-intubation, LCOS, postoperative pneumonia, pericardial effusion, and increased blood transfusion are associated with a higher likelihood of POAF. Lastly, POAF significantly correlates with prolonged stays in ICU, prolonged hospitalisation, and increased 30-day mortality.

ETHICAL APPROVAL:

An approval was obtained from the Institutional Review Board and Ethical Committee of the Hospital, before starting the research. (Ref No: IRB&EC/2023-GH/041; Dated 16-08-2023).

PATIENTS' CONSENT:

As a retrospective observational study, informed consent of patients was not required by the Ethical Committee. Patient confidentiality and data anonymisation were strictly maintained.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

KUK: Concept and design, data collection, and manuscript writing.
TI: Concept and design, software and statistical analysis, and manuscript writing.
AT, MA: Data collection, analysis, and manuscript writing.
NA: Guidance and revision of the manuscript.
All authors approved the final version of the manuscript to be published.

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