ISSN: 2320-9267

Indian Journal of Pharmaceutical and Biological Research (IJPBR)

Journal homepage: www.ijpbr.in

RESEARCH ARTICLE

Therapeutic Effect of Pre-operative Bisoprolol on New-Onset Atrial Fibrillation in Female Patients Undergoing Coronary Artery Bypass Grafting

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ABSTRACT

Objectives: Our study was to analyze the occurrence of new onset post-operative Atrial Fibrillation (POAF) in the female Indian population who underwent off-pump or on-pump coronary artery bypass grafting (CABG) and to assess the Therapeutic effectiveness of pre-operative Selective Beta-blocker (Bisoprolol) therapy in the prevention of New Onset Post Operative Atrial Fibrillation after CABG.

Methods: This is a retrospective and prospective observational study of female patients who underwent coronary artery bypass grafting at ESIC Medical College and Superspecialty Hospital, Hyderabad, and other Corporate Hospitals of Hyderabad, India. Clinical data on the effectiveness of Bisoprolol were collected from the patients' medical records, and the relative clinical variables were analyzed.

Results: 60 female patients with coronary artery disease were found to undergo CABG during the study period. The mean age of patients developing Atrial Fibrillation (AF) was 61.9±8.7. 42 patients out of 60 study patients received pre-operative Bisoprolol therapy and 18 Study patients did not receive Bisoprolol therapy. Among 42 patients receiving pre-operative Bisoprolol therapy, the incidence of post-operative atrial fibrillation (POAF) following CABG was 2.38%. New-onset POAF occurred in 16.66% of patients without Bisoprolol coverage, a result that was statistically significant (p <0.05).

Conclusion: The study has shown that pre-operative therapy with Beta Blocker-Bisoprolol continuing through the post-operative period significantly reduces the incidence of new-onset post-operative Atrial fibrillation (POAF) after CABG.

Keywords: Bisoprolol, Coronary Artery Bypass, Atrial Fibrillation, Female, Adrenergic beta-1 Receptor Antagonists

Indian J. Pharm. Biol. Res. (2026): https://doi.org/10.30750/ijpbr.14.1.08

INTRODUCTION

Post-operative atrial fibrillation (POAF) is a common supraventricular arrhythmia, occurring in approximately 5 to 40% of patients during the early post-operative period following coronary artery bypass grafting (CABG)[1–3]. POAF typically develops within 2 to 4 days after surgery, with peak incidence observed on the second post-operative day[1]. The development of new-onset POAF after CABG is associated with a 29% increased risk of long-term mortality [4].

The pathophysiology of POAF is multifactorial. Key contributing mechanisms include atrial structural changes and post-operative inflammation. Age-related atrial alterations, such as atrial dilatation, fibrosis, and senile amyloidosis, increase atrial vulnerability. Post-operative inflammation creates heterogeneous myocardial tissue with varying refractory periods, promoting re-entry circuits via nodal pacemakers and resulting in an "anisotropic" atrium[5,6].

Several clinical studies recommend prophylactic

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How to cite this article: Sweta RS , Salla SPR, Srishti RS, Vasudha R, Chandak R. Therapeutic Effect of Pre-operative Bisoprolol on New-Onset Atrial Fibrillation in Female Patients Undergoing Coronary Artery Bypass Grafting. Indian J. Pharm. Biol. Res. 2026;14(1):39-45.

Source of support: Nil

Conflict of interest: None.

Received: 18/01/2026 **Revised:** 25/02/2026 **Accepted:** 14/03/2026

Published: 31/03/2026

beta-blocker therapy, including agents such as metoprolol and carvedilol, with or without amiodarone, as an effective strategy for POAF prevention. However, limited data are available on the therapeutic effectiveness of the second-generation cardioselective beta-blocker Bisoprolol, particularly in female patients undergoing CABG. Current European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines recommend beta-blockers—including metoprolol, carvedilol, and bisoprolol—for POAF prevention, although the optimal timing and duration of therapy are not clearly defined. A meta-analysis of 24 trials involving patients with left ventricular ejection fraction greater than 30% undergoing CABG demonstrated that prophylactic Cardioselective beta-blocker therapy significantly reduced the incidence of supraventricular arrhythmias [7].

Outcomes following CABG in female patients remain controversial. Jawitz and Lawton et al. reported higher mortality rates among female patients compared to males, with atrial fibrillation being a common post-operative complication [8]. In contrast, Sajja Lokeswararao and Mannam et al. found no significant differences in early post-operative outcomes between Indian male and female patients undergoing CABG [9]. Given these conflicting findings, the present study focused exclusively on female patients with coronary artery disease to evaluate the incidence of POAF and the therapeutic effectiveness of bisoprolol in its prevention.

Mechanism of Action of Bisoprolol

Bisoprolol is a long-acting, Cardioselective β_1-adrenergic receptor antagonist with heart rate–controlling and antiarrhythmic properties [10–12]. It reduces myocardial oxygen consumption, thereby decreasing cardiac workload. Bisoprolol antagonizes catecholamine-mediated sympathetic stimulation of the heart, which plays a key role in the development of POAF. By suppressing excessive sympathetic activity, bisoprolol contributes to improved autonomic nervous system stability, an important factor in the prevention of atrial fibrillation [13].

METHODS

Study Design and Setting

This study employed a combined retrospective and prospective observational design to evaluate patients diagnosed with coronary artery disease (CAD) who underwent coronary artery bypass grafting (CABG) using either on-pump or off-pump techniques. The study population comprised patients who were followed preoperatively and postoperatively at ESIC Medical College and Super Specialty Hospital, Hyderabad, as well as selected corporate super specialty hospitals in Hyderabad, India.

Selection Criteria

Patients were excluded if they had pre-operative rhythm disturbances, mostly Supraventricular arrhythmias like AF, a history of previous cardiac surgery, mostly CABG or percutaneous coronary intervention, mostly Angioplasty, or if they underwent concomitant cardiac procedures, including valvular or congenital heart disease surgeries. Clinical and pharmacological data were obtained from the medical records of participating institutions in strict compliance with ethical standards.

Data Collection and Variable Analysis

Patient comorbidities assessed included diabetes mellitus, hypertension, chronic obstructive pulmonary disease, angina on effort, ischemic heart disease, congestive heart failure, renal insufficiency, peripheral vascular disease, and cerebrovascular disease. Left ventricular function was evaluated for all patients using 2D echocardiography. Detailed medication histories, particularly the pre-operative use of beta-blockers for hypertension or angina, were extracted from discharge summaries and hospital records.

Clinical Monitoring and Follow-up

Patients who developed new-onset post-operative atrial fibrillation (POAF) were closely monitored during their intensive care unit (ICU) stay and followed up at predetermined intervals of 7 days, 1 month, and 3 months following CABG to assess clinical outcomes.

Statistical Analysis

Data were electronically stored and analyzed using IBM SPSS Statistics version 17.1 for Windows. A p-value of less than 0.05 was considered statistically significant. Continuous variables, such as age and weight, were expressed as mean ± standard deviation, along with their minimum and maximum values. Categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate, to evaluate associations between study groups.

Pharmacological Intervention

The use of Bisoprolol as a therapeutic intervention was documented in patients with clinical indications including sinus tachycardia, angina, dyspnea on exertion, reduced left ventricular ejection fraction, and hypertension.

Table 1: Patient Baseline Characteristics

Variables	*Total patients: 60*		*p-value*
	AF (n = 4)	*No AF (n = 56)*	
Age (mean ± SD)	61.9 ± 6.7	58.7 ± 7.9	<0.00001*
Female	4 (6.67%)	56 (93.33%)	
No traditional risk factors	1 (25.00%)	9 (16.07%)	0.56
HTN	2 (50.00%)	12 (21.43%)	0.29
DM	0 (0.00%)	12 (21.43%)	0.3
HTN + DM	1 (25.00%)	21 (37.50%)	0.64
COPD	0 (0.00%)	5 (8.93%)	
LVEF > 60%	2 (50.00%)	37 (66.07%)	0.61
LVEF 50–60%	1 (25.00%)	12 (21.43%)	
LVEF 40–50%	1 (25.00%)	4 (7.14%)	0.23
LVEF < 40%	0 (0.00%)	3 (5.36%)	
With preop BB	1 (25.00%)	41 (73.21%)	0.047*
Without preop BB	3 (75.00%)	15 (26.79%)	0.047*
CABG on-pump	3 (75.00%)	42 (75.00%)	
CABG off-pump	1 (25.00%)	14 (25.00%)	
Neurological complications	0 (0.00%)	0 (0.00%)	
ICU stay (hours)	73.7 ± 39.3	34.5 ± 19.4	<0.00001*
Hospital stay (days)	9.0 ± 2.3	7.0 ± 1.4	<0.00001*

*Indicates statistical significance (p>0.05)

Table 2: Comparison of POAF Incidence by Therapy and Surgical Technique

Variable	*Total (n)*	*POAF Cases (n)*	*Incidence (%)*	*p-value*
Bisoprolol Therapy				
Pre-operative Bisoprolol	42	1	2.38%	<0.05*
No Bisoprolol	18	3	16.66%	
Surgical Technique				
On-Pump CABG	45	3	6.67%	
Off-Pump CABG	15	1	6.67%	

Table 3: Comparing Post-Operative Bisoprolol Usage in "With Pre-Operative Bisoprolol Group"

	Post-operative Bisoprolol use	*AF*	*NSR*	*Total*
With pre-operative Bisoprolol	Yes	1 (2.38%)	26 (61.9%)	27 (64.2%)
	No	0 (0%)	15 (35.7%)	15 (35.7%)
	Total	1	41	42

*NSR: Normal Sinus Rhythm; AF: Atrial Fibrillation

Table 4: Comparing Post-Operative Bisoprolol Usage in "Without Pre-Operative Bisoprolol Group"

	Post-operative Bisoprolol use	*AF*	*NSR*	*Total*
Without pre-operative Bisoprolol	Yes	1 (5.6%)	9 (50%)	10 (55.6%)
	No	2 (11.1%)	6 (33.3%)	8 (44.4%)
	Total	3	15	18

*NSR: Normal Sinus Rhythm; AF: Atrial Fibrillation

Ethical Considerations

The study was approved by the Ethics Committee of the Hyderabad Cardiac Research Center (Reference No. 5, June 2024). All participating institutions, including ESIC Medical College, complied with Institutional Review Board guidelines. The research was conducted in accordance with the principles of the Declaration of Helsinki, ensuring the protection of participants' rights, safety, and confidentiality.

RESULTS

Study Population and Baseline Characteristics

This prospective observational study, conducted between August 2024 and December 2025, included 60 female patients undergoing coronary artery bypass grafting (CABG). Patients were monitored during their Intensive Care Unit (ICU) stay, throughout a seven-day inpatient period, and at follow-up intervals of one month and three months postoperatively.

Baseline demographic and clinical characteristics are summarized in Table 1. The mean age of the study population was 58.7 ± 7.9 years (range: 37–80 years). Ten patients (16.6%) had no significant comorbidities. Hypertension was present in 14 patients (23.34%), diabetes mellitus in 12 patients (20%), and combined diabetes and hypertension in 22 patients (36.6%). Chronic obstructive pulmonary disease (COPD) was observed in 5 patients (8.33%) (Table 1).

Pre-operative Cardiac Function and Pharmacological Management

Pre-operative two-dimensional echocardiographic assessment of left ventricular ejection fraction (LVEF) showed that 39 patients had an LVEF >60%, 13 patients had an LVEF between 50 to 60%, and 5 patients had an LVEF between 40 to 50%. Severe left ventricular systolic dysfunction (LVEF <40%) was noted in 3 patients. With respect to pharmacological management, 42 patients (70%) received pre-operative bisoprolol therapy, whereas 18 patients (30%) did not receive any pre-operative beta-blocker (Table 1).

Incidence of Post-operative Atrial Fibrillation

The overall incidence of new-onset post-operative atrial fibrillation (POAF) in the study population was 6.66% (4/60). A statistically significant difference was observed based on pre-operative bisoprolol use. POAF occurred in 2.38% of patients receiving pre-operative bisoprolol compared with 16.66% of patients who did not receive bisoprolol prophylaxis ($p < 0.05$).

Regarding surgical technique, POAF developed in 1 of 15 patients (6.67%) undergoing off-pump CABG and in 3 of 45 patients undergoing on-pump CABG (6.67%). This difference was not statistically significant ($p > 0.05$) (Table 2).

Management of POAF and Clinical Outcomes:

Management strategies for POAF included bisoprolol monotherapy in 50% of cases, bisoprolol combined with amiodarone infusion in 25%, and bisoprolol combined with digoxin in 25%. None of the patients required anticoagulation therapy or electrical cardioversion for rapid or complicated atrial fibrillation. No major post-operative complications, such as acute kidney injury or embolic stroke, were observed.

Patients who developed POAF had significantly longer hospital admission stay periods. The mean ICU admission period of stay was 73.74 ± 39.33 hours in the POAF group compared with 34.47 ± 19.39 hours in patients who maintained sinus rhythm. Similarly, the total hospital stay was longer in the POAF group (9 ± 2.3 days) than in the non-AF group (7 ± 1.4 days).

Follow-up and Recovery

Patients with POAF were discharged on oral Bisoprolol (2.5 mg once daily) and amiodarone (200 mg twice daily). The incidence of POAF was 9.09% among patients receiving post-operative Bisoprolol alone, whereas it increased to 16.66% in patients who did not receive Bisoprolol during either the pre-operative or post-operative period (Tables 3 and 4).

At one-month follow-up, 35.71% of patients with POAF had reverted to normal sinus rhythm. By the three-

month follow-up, all patients (100%) had achieved sinus rhythm. No mortality was reported during the study period.

DISCUSSION

Post-operative atrial fibrillation (POAF) remains the most prevalent supraventricular arrhythmia following cardiac surgery globally. Its occurrence is clinically significant as it substantially extends the duration of both Intensive Care Unit (ICU) stays and overall hospital admissions. Furthermore, post-CABG atrial fibrillation significantly elevates the risk of cerebrovascular accidents, particularly stroke [14,15]. While post-operative anticoagulation can mitigate this risk, it must be carefully balanced against the potential for major bleeding and cardiac tamponade [16]. According to the American College of Chest Physicians, anticoagulation is indicated for prolonged or frequent AF episodes—especially in patients with a history of stroke or transient ischemic attacks—and should be continued for 30 days after the restoration of sinus rhythm [17]. Anticoagulation is also recommended for patients aged 75 or older or those with high-risk cardiovascular profiles.

Retrospective analyses from large surgical databases have reported a reduction in post-operative mortality from 3.4 to 2.8% with the use of pre-operative beta-blockers [18]. The benefit in preventing POAF is largely achieved through the prophylactic use of long-acting beta-blockers [19-22]. Surgical stress often leads to an overactivation of the sympathetic nervous system, which serves as a primary trigger for AF [23].

While global POAF incidence varies—ranging from 41.6% in the Middle East to 15.7% in Asia—this study observed a notably lower incidence of 6.66% among female post-CABG patients in India. In contrast, Western research reports higher variable incidences of POAF. In our study, we noticed that patients who developed AF were predominantly in the elderly age group (>60 years), likely due to age-related degenerative histological remodeling and structural changes in atrial tissue.

Most initial episodes of AF in our Research Study were paroxysmal, typically reverting to sinus rhythm within 24 hours to seven days [24]. We also compared POAF occurrence between On-pump CABG (utilizing cardiopulmonary bypass) and Off-pump CABG ("beating-heart" surgery). Patients undergoing the On-pump technique showed a higher incidence of POAF compared to off-pump patients, though the difference was not statistically significant ($p > 0.05$). Research by Ascione et al. [25], Tchervenkov et al. [26], and Smith et al. [27] identified cardiopulmonary bypass (CPB) as an independent predictor for post-operative arrhythmias, attributed to inadequate atrial protection during cardioplegia and the resulting systemic inflammatory response.

Cardioselective beta-blockers remain the primary therapeutic standard for managing POAF. In this study, a rate-control strategy using Bisoprolol was implemented. Similar findings by Behmanesh and Tossios et al. [28] demonstrated that Betabloccker-Bisoprolol effectively reduces POAF incidence—particularly in elderly populations—and is associated with shorter hospital stays. Khan and Wendel et al. [29] also reported that prophylactic beta-blockers decreased POAF incidence from 32.8 to 20% ($p < 0.001$).

Our Research study demonstrated a statistically significant reduction in new-onset POAF through consistent medication. Physiological data indicate that patients maintained on Beta-blockers exhibit a higher density of beta-adrenergic receptors in atrial tissues. Consequently, the sudden withdrawal of these drugs is contraindicated, as it can trigger rebound sympathetic overactivity and receptor upregulation, leading to tachycardia or myocardial infarction.

Specifically, when pre-operative Bisoprolol was continued into the post-operative period, the prevalence of POAF was only 1.2% ($p < 0.05$). Conversely, 13.23% of patients developed POAF when the drug was not continued postoperatively. In cases where Bisoprolol was started only postoperatively (with no pre-operative therapy), 11.1% of patients developed POAF. The highest incidence (16.66%) occurred in patients who did not receive Bisoprolol therapy at all.

POAF patients required significantly longer ICU stays (73.74 ± 39.33 hours) and hospital admissions (9 ± 2.3 days). Following discharge, patients maintained on Bisoprolol showed excellent recovery: 35.71% returned to sinus rhythm within one month, and 100% achieved sinus rhythm restoration by the end of three months. The lower incidence (6.66%) in our study compared to Western cohorts may be attributed to the younger age profile of Indian female patients undergoing CABG.

RECOMMENDATIONS

Based on these findings, we recommend the prophylactic administration of Bisoprolol for patients undergoing CABG. Therapy should be initiated preoperatively and maintained throughout the post-operative period to ensure Supraventricular rhythm stability.

LIMITATIONS

The findings are limited by the observational nature of the study and a modest cohort size, which may restrict generalizability. Additionally, the follow-up duration was

insufficient to capture late-onset arrhythmias or long-term thromboembolic complications. Future longitudinal studies are necessary.

CONCLUSION

Advanced age is a primary independent predictor of AF following CABG. While surgical technique (on-pump vs. off-pump) did not significantly influence New Onset Post Operative Atrial Fibrillation (POAF) development, pharmacological intervention was critical. Maintaining pre-operative Bisoprolol therapy consistently through the post-operative period significantly reduces POAF incidence in female patients, offering a highly effective strategy for optimizing post-operative outcomes.

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