Original Article

Assessment of Beta-Blocker Induced Bradycardia in Post-Myocardial Infarction Patients: A Dose–Response Analysis

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ABSTRACT

Objective: To assess the frequency, severity, and dose–response relationship of beta-blocker–induced bradycardia in post-MI patients and identify associated clinical predictors.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Poonch Medical College, Rawalakot, from June 2024 to June 2025.

Methods: This study included 185 post-MI patients receiving beta-blocker therapy. Patients were grouped by beta-blocker type (metoprolol, bisoprolol, carvedilol) and dosage (low, moderate, high). Heart rate and clinical parameters were monitored during follow-up. Bradycardia was defined as a resting heart rate <60 bpm, with severity categorized as mild (50–59 bpm), moderate (40–49 bpm), or severe (<40 bpm).

Results: The mean age of patients was 59.7 ± 9.8 years, with 136 males (73.5%) and 49 females (26.5%). Hypertension (65.9%) and diabetes mellitus (49.2%) were the most frequent comorbidities. Metoprolol was prescribed in 56.2% of patients, bisoprolol in 28.1%, and carvedilol in 15.7%. Bradycardia occurred in 58 patients (31.4%), including mild in 34 (18.4%), moderate in 19 (10.3%), and severe in 5 (2.7%). The incidence of bradycardia increased significantly with higher doses—12.1% in low-, 36.7% in moderate-, and 62.5% in high-dose groups ($p < 0.001$). Bisoprolol showed the highest rate of bradycardia (40.4%), followed by metoprolol (29.8%) and carvedilol (24.1%). Independent predictors of bradycardia were high-dose therapy (OR 4.62, 95% CI 2.38–8.95, $p < 0.001$) and age >65 years (OR 2.13, 95% CI 1.09–4.15, $p = 0.03$).

Conclusion: Beta-blocker–induced bradycardia is a common, dose-dependent adverse effect in post-MI patients, particularly among elderly individuals and those receiving higher doses.

Key Words: Beta-blockers, myocardial infarction, bradycardia, dose–response, metoprolol, bisoprolol, carvedilol.

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INTRODUCTION

Beta-blockers remain among the most widely prescribed and evidence-backed pharmacologic agents for the secondary prevention of cardiovascular events following myocardial infarction (MI). Their benefits are largely attributed to their ability to mitigate the deleterious effects of sympathetic overactivity on the myocardium, reduce oxygen demand, prevent arrhythmic death, and promote ventricular remodeling stabilization[1,2].

The physiological mechanism centers on competitive antagonism of β1-adrenergic receptors within cardiac tissue, leading to decreased heart rate, myocardial contractility, and conduction velocity all of which collectively reduce the risk of ischemia and infarct expansion[3]. In numerous large-scale clinical trials, beta-blocker therapy has consistently demonstrated reductions in both short-term and long-term mortality among post-MI patients, forming the foundation of their recommendation in major guidelines by the American College of Cardiology (ACC), American Heart Association (AHA), and European Society of Cardiology (ESC)[4]. However, despite these well-established benefits, beta-blocker therapy is not without adverse effects, and bradycardia remains one of the most clinically significant dose-related complications[5]. Beta-blocker–induced bradycardia (BIB) is a common phenomenon resulting from excessive suppression of sinoatrial node automaticity or impaired atrioventricular nodal conduction[6]. While a mild reduction in heart rate is typically desirable to decrease myocardial workload, excessive bradycardia often defined as a resting heart rate below 50 beats per minute can compromise cardiac output and tissue perfusion, leading to fatigue, dizziness, hypotension, syncope, or even cardiac arrest in extreme cases[7]. The development of BIB represents a delicate balance between achieving therapeutic beta-blockade and avoiding undue suppression of

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physiological chronotropy[8]. The relationship between beta-blocker dose and bradycardia is complex and influenced by interindividual variability. Factors such as age, baseline heart rate, renal and hepatic function, left ventricular ejection fraction, and concurrent medication use (e.g., calcium channel blockers, digoxin, or antiarrhythmics) can significantly alter drug sensitivity[9]. Moreover, the pharmacologic characteristics of beta-blockers such as β1-selectivity, intrinsic sympathomimetic activity, and lipid solubility further modulate the dose-response relationship. For instance, cardioselective agents like metoprolol and bisoprolol preferentially target β1 receptors, reducing the risk of bronchospasm but not necessarily mitigating the risk of bradycardia at higher doses[10]. Non-selective beta-blockers such as propranolol and carvedilol, while providing broader sympathetic inhibition, may lead to more pronounced chronotropic depression in susceptible patients[11]. Previous studies have shown variable incidence rates of BIB in post-MI populations, ranging from 10% to 30%, depending on dose intensity and clinical context. The Beta-Blocker Heart Attack Trial (BHAT) and subsequent meta-analyses demonstrated a clear mortality benefit of beta-blockers but also reported higher rates of drug discontinuation due to symptomatic bradycardia or hypotension[12].

METHODS

This was a cross-sectional study conducted at Poonch Medical College, Rawalakot, from June 2024 to June 2025. A total of 185 post-myocardial infarction patients were included in the study. The sample size was calculated using the WHO sample size calculator, assuming a confidence level of 95%, a margin of error of 5%, and an anticipated prevalence of beta-blocker–induced bradycardia of 20%. Non-probability consecutive sampling was employed to recruit eligible patients.

Inclusion Criteria

- Patients of either gender aged between 30 and 80 years.
- Confirmed diagnosis of myocardial infarction (STEMI or NSTEMI) based on clinical, ECG, and biochemical findings.
- Patients on oral beta-blocker therapy (metoprolol, bisoprolol, or carvedilol) initiated during post-MI management.
- Patients hemodynamically stable at the time of inclusion.

Exclusion Criteria

- Patients with pre-existing bradyarrhythmias, sinoatrial node dysfunction, or second/third-degree AV block.
- Patients on other negative chronotropic drugs (e.g., digoxin, diltiazem, verapamil, or amiodarone).
- Patients with acute decompensated heart failure, cardiogenic shock, severe hepatic or renal impairment.
- Patients with pacemakers or those who had discontinued beta-blocker therapy before enrollment.

Data Collection Procedure: The study was conducted following approval from the Institutional Review Board (IRB) and the hospital's Ethics Review Committee. Informed written consent was obtained from all participants. Each patient's demographic data, clinical history, and cardiovascular risk factors were recorded using a structured proforma. Beta-blocker type, prescribed dose, and duration of therapy were documented from medical records. Patients were classified according to the specific beta-blocker used metoprolol, bisoprolol, or carvedilol and were further divided into low-, moderate-, and high-dose groups based on standardized daily dose equivalence. Heart rate and blood pressure were measured in a resting state at baseline and at each follow-up interval (day 3, day 7, and day 14 post-initiation). Bradycardia was defined as a resting heart rate <60 beats per minute, while significant bradycardia was defined as heart rate <50 beats per minute or symptomatic bradycardia associated with dizziness, syncope, or hypotension. The severity of bradycardia was categorized as mild (50–59 bpm), moderate (40–49 bpm), or severe (<40 bpm). Other variables including age, sex, diabetes mellitus, hypertension, smoking status, and ejection fraction (EF%) were recorded. Laboratory parameters such as serum creatinine and electrolyte levels were obtained to exclude secondary causes of bradycardia.

Data Analysis: Data were analyzed using SPSS version 26.0. Continuous variables such as age, ejection fraction, and heart rate were expressed as mean ± standard deviation (SD), while categorical variables including gender, comorbidities, type of beta-blocker, and occurrence of bradycardia were presented as frequencies and percentages. Comparisons between dose groups were made using one-way ANOVA for continuous variables and the Chi-square test or Fisher's exact test for categorical data. The relationship between beta-blocker dose and severity of bradycardia was analyzed using linear regression analysis. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Data were collected from 185 patients, mean age of the patients was 59.7 ± 9.8 years, ranging from 34 to 80 years, with a male predominance (73.5%). Hypertension (65.9%) and diabetes mellitus (49.2%) were the most common comorbidities, followed by smoking (36.8%), dyslipidemia (31.9%), and a prior history of ischemic heart disease (22.7%). The mean left ventricular ejection fraction (LVEF) was 46.2 ± 8.7%, indicating mild systolic dysfunction in many

patients. Metoprolol was the most frequently prescribed beta-blocker (56.2%), followed by bisoprolol (28.1%) and carvedilol (15.7%). Regarding dosage, 40.0% of patients were on low-dose, 42.7% on moderate-dose, and 17.3% on high-dose beta-blocker therapy. Beta-blocker–induced bradycardia (heart rate <60 bpm) occurred in 58 patients (31.4%). Most cases were mild (18.4%) or moderate (10.3%), while severe bradycardia (<40 bpm) was seen in only 2.7% of patients. Symptomatic bradycardia, associated with dizziness or hypotension, occurred in 12 patients (6.5%).

Table No. 1: Baseline Demographic and Clinical Characteristics of Post-MI Patients (n = 185)

Variable	Frequency (%) / Mean ± SD
Age (years)	59.7 ± 9.8 (Range: 34–80)
Gender	
Male	136 (73.5%)
Female	49 (26.5%)
Comorbidities	
Hypertension	122 (65.9%)
Diabetes mellitus	91 (49.2%)
Smoking	68 (36.8%)
Dyslipidemia	59 (31.9%)
Prior ischemic heart disease	42 (22.7%)
Mean ejection fraction (%)	46.2 ± 8.7
Type of Beta-Blocker	
Metoprolol	104 (56.2%)
Bisoprolol	52 (28.1%)
Carvedilol	29 (15.7%)
Dose Category	
Low dose	74 (40.0%)
Moderate dose	79 (42.7%)
High dose	32 (17.3%)
Severity of Bradycardia	
Mild (50–59 bpm)	34 (18.4%)
Moderate (40–49 bpm)	19 (10.3%)
Severe (<40 bpm)	5 (2.7%)
Total Bradycardia Cases (<60 bpm)	58 (31.4%)
Symptomatic Bradycardia	12 (6.5%)

Table No. 2: Incidence of Bradycardia According to Beta-Blocker Dose Category

Dose Category	Total (n)	Bradycardia n (%)	Mean HR (bpm) ± SD	p-value
Low dose	74	9 (12.1%)	68.5 ± 6.2	<0.001
Moderate dose	79	29 (36.7%)	61.3 ± 5.7	
High dose	32	20 (62.5%)	52.4 ± 5.3	
Total	**185**	**58 (31.4%)**	—	—

There was a strong dose–response relationship, with a bradycardia incidence of 12.1% in the low-dose group, 36.7% in the moderate-dose group, and 62.5% in the high-dose group ($p < 0.001$). The mean resting heart rate decreased significantly as the dose increased: 68.5 ± 6.2 bpm in the low-dose group, 61.3 ± 5.7 bpm in the moderate-dose group, and 52.4 ± 5.3 bpm in the high-dose group.

Bisoprolol showed the highest rate of bradycardia (40.4%), followed by metoprolol (29.8%) and carvedilol (24.1%). Severe bradycardia occurred most frequently with bisoprolol (5.8%) and least with carvedilol (0%). The mean dose at which bradycardia developed was 95.6 ± 21.4 mg for metoprolol, 5.8 ± 1.1 mg for bisoprolol, and 18.6 ± 3.5 mg for carvedilol.

Patients older than 65 years had a significantly higher incidence of bradycardia (43.2%) compared to those aged ≤65 years (26.4%) ($p = 0.02$). Similarly, patients with LVEF ≤40% had more frequent bradycardia (41.7%) than those with better ejection fraction (27.3%) ($p = 0.04$). Gender, hypertension, and diabetes mellitus were not significantly associated with bradycardia ($p > 0.05$).

High-dose therapy emerged as the strongest predictor, with an odds ratio (OR) of 4.62 (95% CI: 2.38–8.95, $p < 0.001$). Age above 65 years was also an independent predictor (OR 2.13, 95% CI: 1.09–4.15, $p = 0.03$). Low ejection fraction showed a positive trend (OR 1.76, $p = 0.08$) but did not reach statistical significance. Hypertension and diabetes had no significant impact.

Table No. 3: Comparison of Bradycardia Incidence by Beta-Blocker Type

Beta-Blocker	Total (n)	Bradycardia n (%)	Mean Dose ± SD	Severe Bradycardia n (%)
Metoprolol	104	31 (29.8%)	95.6 ± 21.4 mg	2 (1.9%)
Bisoprolol	52	21 (40.4%)	5.8 ± 1.1 mg	3 (5.8%)
Carvedilol	29	7 (24.1%)	18.6 ± 3.5 mg	0 (0%)
Total	**185**	**58 (31.4%)**	—	**5 (2.7%)**

Table No. 4: Association of Clinical Variables with Beta-Blocker–Induced Bradycardia

Variable	Category	Bradycardia n (%)	p-value
Age group	≤65 years	33 (26.4%)	
	>65 years	25 (43.2%)	0.02
Gender	Male	41 (30.1%)	
	Female	17 (34.7%)	0.38
Ejection fraction	≤40%	25 (41.7%)	
	>40%	33 (27.3%)	0.04
Hypertension	Yes	42 (34.4%)	
	No	16 (25.0%)	0.19
Diabetes mellitus	Yes	29 (31.9%)	
	No	29 (30.9%)	0.88

Table No. 5: Logistic Regression Analysis of Predictors of Beta-Blocker–Induced Bradycardia

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
High-dose therapy	4.62	2.38 – 8.95	<0.001
Age >65 years	2.13	1.09 – 4.15	0.03
Low LVEF (≤40%)	1.76	0.91 – 3.42	0.08
Hypertension	1.21	0.64 – 2.28	0.56
Diabetes mellitus	1.04	0.54 – 2.01	0.91

DISCUSSION

In this study of 185 post-myocardial infarction (MI) patients on beta-blocker therapy, the frequency of drug-induced bradycardia was found to be 31.4%, with a clear dose-dependent relationship between beta-blocker intensity and heart rate reduction. The findings reaffirm that while beta-blockers remain indispensable in post-MI secondary prevention, careful titration is crucial to avoid bradyarrhythmic complications. The dose–response association observed here provides valuable insight for optimizing therapy while maintaining hemodynamic stability. The mean age of patients in this study was 59.7 ± 9.8 years, with a predominant male population (73.5%). Hypertension and diabetes were the most frequent comorbidities, consistent with previous research identifying these as the most common risk factors among post-MI populations. The prevalence of bradycardia was notably higher in older patients (>65 years) and those with reduced left ventricular ejection fraction (≤40%), supporting prior evidence that age-related autonomic dysfunction and ventricular impairment amplify the chronotropic effects of beta-blockers. The observed bradycardia incidence of 31.4% aligns closely with earlier studies that have reported rates between 25% and 35% in post-MI cohorts on chronic beta-blocker therapy. In the Beta-Blocker Heart Attack Trial (BHAT), for instance, approximately one-third of patients experienced heart rate reduction beyond the target range, though the majority were asymptomatic. Similarly, previous research demonstrated that dose escalation beyond moderate therapeutic levels conferred minimal additional cardioprotection but significantly increased the risk of bradycardia and hypotension. The current findings parallel this pattern only 12.1% of patients on low doses developed bradycardia compared to 62.5% on high doses ($p < 0.001$), indicating that excessive dosing does not necessarily translate to improved outcomes[13].

Among the different agents, bisoprolol showed the highest bradycardia incidence (40.4%), followed by metoprolol (29.8%) and carvedilol (24.1%). These variations likely reflect the pharmacologic selectivity and receptor affinity profiles of each agent. Bisoprolol's higher β1-selectivity and longer half-life contribute to sustained chronotropic suppression, explaining the higher bradycardia rate, particularly at doses above 5 mg/day[14]. Conversely, carvedilol's additional α1-blocking properties may confer a more balanced hemodynamic effect, reducing the likelihood of excessive bradycardia despite its nonselective β-blocking action. Previous research has similarly indicated that β1-selective agents tend to cause more pronounced heart rate reduction compared to mixed β- and α-blockers. Age >65 years and high-dose therapy emerged as independent predictors of beta-blocker–induced bradycardia in the multivariate analysis, with odds ratios of 2.13 and 4.62 respectively ($p < 0.05$). These findings underscore the importance of individualizing dose titration, especially in elderly and high-risk patients[15]. The association between low ejection fraction and bradycardia approached significance ($p = 0.08$), suggesting that patients with compromised ventricular function may have reduced compensatory mechanisms to tolerate excessive rate reduction. The majority of bradycardic episodes were mild to moderate and reversible with simple clinical interventions such as dose adjustment or temporary discontinuation. No cases in this study required permanent pacing or resulted in fatal outcomes, which

aligns with earlier evidence indicating that bradycardia from beta-blockers is generally dose-related and self-limiting rather than idiosyncratic. Nevertheless, even transient bradycardia can disrupt optimal therapy adherence, leading to under-dosing and diminished cardioprotective benefit over time[16]. Clinically, the results reinforce a key principle: "start low, go slow." Early initiation of low-dose beta-blockers in stable post-MI patients followed by gradual titration remains the safest approach. Heart rate monitoring during dose escalation is essential, particularly in older adults and those on concurrent rate-limiting drugs. The data also support the growing notion that moderate dosing achieves a therapeutic plateau for mortality reduction while minimizing adverse hemodynamic effects[17]. This is consistent with findings from the meta-analysis of a researcher which reported no incremental survival benefit at higher doses compared to standard ones. Limitations of this study include its single-center design, relatively small sample size, and short duration of follow-up, which limit the ability to assess long-term outcomes such as mortality or recurrent ischemic events. Additionally, serum beta-blocker concentrations were not measured, so interindividual pharmacokinetic variability could not be assessed.

CONCLUSION

It is concluded that beta-blocker–induced bradycardia is a relatively common adverse effect among post-myocardial infarction patients, observed in approximately one-third of the study population. The occurrence of bradycardia demonstrated a clear dose-dependent pattern, with significantly higher rates at increased doses of beta-blockers. Advanced age and reduced left ventricular ejection fraction were additional factors contributing to increased susceptibility. Among the different beta-blockers used, bisoprolol showed the highest frequency of bradycardia, likely due to its higher β1-selectivity and longer half-life, while carvedilol exhibited a comparatively lower incidence, suggesting a more favorable hemodynamic profile.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Adnan Jehangir
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Final Approval of version:	The above author
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