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Comparison of Early Vs Delayed Beta Blocker Initiation in Acute Myocardial Infarction and's impact on left ventricular ejection fraction recovery

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ABSTRACT

Background: Beta-blockers are an established cornerstone in the management of acute myocardial infarction (AMI) due to their cardioprotective, antiarrhythmic, and anti-remodeling effects. However, the optimal timing of their initiation remains clinically debated, particularly regarding their impact on the recovery of left ventricular ejection fraction (LVEF).

Objective: To compare early (within 24 hours) versus delayed (after 72 hours) initiation of beta-blockers in patients with acute myocardial infarction and to assess their effects on LVEF recovery and short-term clinical outcomes.

Methods: This comparative cross-sectional study was conducted at the Punjab Institute of Cardiology, Lahore, Pakistan, from July 2024 to July 2025. A total of 70 patients aged 35–70 years with confirmed AMI were enrolled and divided equally into two groups. Group A received beta-blockers within 24 hours, while Group B received them after 72 hours. LVEF was measured using echocardiography at baseline and at three-month follow-up. Secondary outcomes included arrhythmias, readmissions, and mortality.

Results: Baseline characteristics were similar between groups. Mean LVEF improved significantly in Group A (38.5 ± 5.3% to 49.8 ± 6.2%) compared to Group B (38.9 ± 5.1% to 44.1 ± 5.9%, $p < 0.001$). Early initiation also reduced ventricular arrhythmias (5.7% vs. 17.1%) and readmission rates (8.6% vs. 20%). No significant differences in bradycardia or hypotension were noted.

Conclusion: Early initiation of beta-blockers within 24 hours after AMI leads to superior LVEF recovery and fewer arrhythmic events compared to delayed therapy. Early beta-blockade should be encouraged in all hemodynamically stable AMI patients.

Keywords: Acute myocardial infarction, Beta-blockers, Left ventricular ejection fraction, Early initiation, Cardiac remodelling, Ventricular arrhythmia.

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INTRODUCTION

One of the most important causes of cardiovascular morbidity and mortality in the world remains acute myocardial infarction (AMI) despite the development of diagnostic and treatment methods [1]. An ischemic insult caused by sudden coronary artery occlusion triggers a cascade of pathophysiological alterations such as cardiomyocyte necrosis, oxidative stress, neurohormonal activation, and undesirable ventricular remodeling [2]. Although myocardial reperfusion with thrombolysis or percutaneous coronary intervention (PCI) has been shown to significantly improve survival, secondary myocardial infarction and progressive left ventricular (LV) dysfunction have been important predictors of long-term outcome [3].

Beta-adrenergic receptor blockers (beta-blockers) are one of the pharmacological treatments that have become an essential part of the management of the post-infarction period due to the cardioprotective effects that have been

proven [4]. Antagonizing sympathetic stimulation, beta-blockers decrease myocardial oxygen demand, heart rate, and contractility as well as prevent catecholamine-induced arrhythmia and sudden cardiac death. Moreover, these agents reduce ventricular remodeling, increase coronary perfusion at diastole, and improve general myocardial performance, ultimately preserving left ventricular ejection fraction (LVEF), a highly important prognostic variable in the post-AMI period [5].

Although the advantages of beta-blockers after ACS have been well-documented, it is still a subject of controversy as to when this medication should be started. Administration in the first 24 hours, usually, has also been linked with a smaller infarct size, better ventricular recovery, and a lower reinfarction rate. Nevertheless, the hypotension effects, bradycardia, and cardiogenic shock are potential risks that can limit its application in hemodynamically unstable [6,7].

patients. In contrast, a late start after 4872 hours may reduce these risks, but might not be effective at averting early myocardial remodelling, which may limit LVEF recovery and cardiac performance in the long term [8].

The clinical trials and meta-analyses have produced inconsistent findings and are most of the time constrained by differences in patient selection, time of administration, and formulation of beta-blockers. The COMMIT/CCS-2 trial reported lower rates of reinfarction and ventricular fibrillation with early use of beta-blockers, but added that cardiogenic shock occurrence was higher in some groups. In the same way, observational studies indicate that delayed initiation can be linked to inopportune recovery of LV functioning [8]. Therefore, although most cardiology associations, including the European Society of Cardiology (ESC) and American Heart Association (AHA), suggest early initiation in hemodynamically stable patients, the actual adherence and results are inconsistent, particularly in developing countries where late presentation in hospitals and poor facilities to monitor cardiac arrest patients are widespread [9].

In Pakistan, as the burden of ischemic heart disease is still increasing, little evidence exists on the initiation of beta-blockers and their effect on ventricular recovery. Knowledge of the clinical outcomes related to early or late initiation can be important in maximising therapy and minimising complications, and enhancing the outcome after infarction [10].

Thus, the current study was aimed at comparing the outcomes of early and delayed introduction of beta-blockers on left ventricular ejection fraction recovery in the case of acute myocardial infarction. This study will help to offer region-specific evidence to aid clinical decisions and improve post-AMI care interventions in resource-constrained health care environments by evaluating functional recovery and short-term outcomes [11].

MATERIALS AND METHODS

The study was a comparative cross-sectional study, and it was done at the Punjab Institute of Cardiology (PIC), Lahore, Pakistan, a large tertiary care referral center for cardiovascular diseases. The study period was from July 2024 until July 2025, during whereby the patients who reported with acute myocardial infarction (AMI) were recruited. The patients who met the diagnostic criteria of AMI and were 70 in number were identified through a non-probability consecutive sampling method. The ACS diagnosis was made on the basis of typical clinical presentation and electrocardiographic (ECG) evidence and increased cardiac biomarkers, such as troponin I or T.

All the patients were brought to the coronary care unit and were provided with usual guideline-based medical therapy of AMI, including dual antiplatelet therapy, statins, and angiotensin converting enzyme (ACE) inhibitors, as well as reperfusion care where needed. Patients were then divided into 2 categories based on the initiation time of beta-blockers. Group A (early initiation group) comprised patients who were given beta-blockers in the first 24 hours of hospital stay, and Group B (delayed initiation group) consisted of those patients who were put on beta-blockers after 72 hours of hospitalization when hemodynamic stability was attained. Each group consisted of 35 patients who were similar in terms of age, gender, and type of infarction in order to compare them.

The study included patients aged between 35 to 70 years old of any gender diagnosed with AMI and without violations of hemodynamic parameters (systolic blood pressure more than 100 mmHg and heart rate more than 60 beats per minute). Cardiogenic shock, severe systolic blood pressure (less than 90 mmHg), atrioventricular block, or severe bradycardia were also excluded. Patients who have known chronic obstructive pulmonary disease (COPD) or bronchial asthma, previously used beta-blockers, valvular heart disease, thyroid dysfunction, or severe hepatic or renal impairment were also excluded.

Once the Institutional Review Board of the Punjab Institute of Cardiology (PIC/IRB/2024/043) approved the study ethically, all the eligible participants were made aware of the purposes, protocols, as well as potential risks and benefits of the research. Ethically informed consent was signed by all patients before data collection. All patients were noted with demographic information (age, gender, and cardiovascular risk factors that included hypertension, diabetes mellitus, and smoking status). Clinical baseline evaluation comprised of blood pressure, pulse rate, ECG results, and cardiac enzyme lab results. Selection of beta-blocker was at the discretion of the treating physician, and either Metoprostol succinate (25-50mg/day) or Bisoprostol (2.5-5mg/day) was the agent mostly used. The doses were adjusted in accordance with the patient's tolerance, heart rate, and blood pressure.

Left ventricular ejection fraction (LVEF) was measured through the two-dimensional transthoracic

echocardiography by the modified Simpson method. Baseline LVEF was documented within 48 hours of admission, and follow-up data were taken three months after discharge from the hospital to assess the recovery of ventricular function. The difference in the LVEF recovery in early and delayed beta-blocker initiation groups was the major result of the study. The possibility of ventricular arrhythmias in hospitalized patients, hospital readmissions, and mortality within the study period were the secondary outcomes.

The entire data collected was put into Statistical Package of the Social Sciences (SPSS) version 26.0 and analyzed. Continuous variables, like age and LVEF, were represented by mean and standard deviation (SD), and those that were categorical, such as gender, comorbidities, and complications, were represented by frequencies and percentages. The independent samples t-test was used to complete inter-group comparisons of continuous variables, whereas the chi-square test was used to compare categorical variables. To assess the difference in LVEF at the baseline and follow-up in each group, the paired t-test was conducted. All analyses had a p-value of less than 0.05 as a statistically significant value.

RESULTS

The participants were selected based on patients with acute myocardial infarction (AMI), and a total of 70 patients were enrolled and randomly assigned into two groups based on the time of beta-blocker start. Group A (early initiation group) involved 35 patients who were exposed to beta-blockers within 24 hours of admission, and Group B (delayed initiation group) involved 35 patients who received beta-blockers after 72 hours of stabilization. Table 1 gives the demographic and baseline clinical factors of the two groups. The average age of patients in Group A was 56.1 years with a 7.8 standard deviation, and in Group B, it was 57.4 years with 8.1 standard deviation ($p = 0.48$). Male preponderance was noted in the two groups, as there were 26 males (74.3) in Group A and 25 males (71.4) in Group B. The prevalence of comorbid conditions like hypertension (51.4 vs. 54.3) and diabetes mellitus (37.1 vs. 34.3) was not significantly different in the two groups, as was the prevalence of smoking (31.4 vs. 28.6).

Type distribution. Infarction type distribution was mainly of ST-segment elevation myocardial infarction (STEMI) (62.9% Group A and 60% Group B). The baseline systolic blood pressure (122.6 ± 10.4 mmHg vs. 121.9 ± 11.2 mmHg) and the mean heart rate (84.7 ± 7.9 bpm vs. 83.2 ± 8.1 bpm) of the two groups were similar. Troponin serum levels were also close, showing the same levels of infarcts. None of these parameters of the baseline showed any statistically significant difference ($p > 0.05$). This shows that the two groups were clinically homogeneous initially, and any further observed variation of results was due to the time of administering the beta-blockers (Table 1).

The ventricular ejection fraction (LVEF) of the left ventricle was similar in the patients at baseline, with a mean of 38.5 ± 5.3 in Group A and 38.9 +5.1 in Group B ($p = 0.74$). But the three-month follow-up assessment showed a statistically and clinically significant improvement in LVEF in patients receiving early beta-blocker therapy. Table 2 illustrates that the mean follow-up LVEF was 49.8/44.1 in the early and late initiation groups, respectively ($p < 0.001$). Group A had a mean baseline to 6 months change in LVEF of +11.3 +3.6% in comparison to Group B, +5.2 +3.4%; this proved the hypothesis that the early use of beta-blocker led to better restoration of a healthy ventricular systolic function. Such an improvement indicates improved prevention of negative myocardial remodelling in advance because of the early sympathetic inhibition, low oxygen requirement, and enhanced coronary perfusion (Table 2).

The subsequent comparison of in-hospital and short-term outcomes showed that beta-blocker early initiation was connected with fewer complications and fewer cases of arrhythmias. As shown in Table 3, Group A (5.7 per cent) had a substantially lower incidence of ventricular arrhythmias (VT/VF) than Group B (17.1 per cent) ($p = 0.04$). Though the rates of the bradycardia leading to dose change (8.6 vs. 5.7) and the hypotensive events (5.7 vs. 11.4) were not statistically different, there were fewer adverse drug reactions in the early group. There were also significantly higher hospital readmissions in three months among the delayed group (20) than in the early group (8.6), which indicated better post-discharge stability with early beta-blocker therapy, but this was not found to be significant ($p = 0.12$). There was also lower reincarceration (2.9 versus 8.6) and mortality (2.9 versus 5.7) in the early initiation group. These results suggest that early beta-blockade offered both mechanical and electrophysiological protection, which resulted in a reduction of complications and better outcomes during an early postmyocardial infarction period (Table 3).

A stratified subgroup analysis in terms of LVEF recovery based on age and infarction type showed similar patterns in support of the early therapy. As shown in Table 4, younger patients (who were below 55 years) showed better mean change in LVEF in Group A (+12.13.7) as compared to Group B (+6.43.2). Likewise, in patients aged 55 years and above, the average improvement at early initiation was +10.7 vs. +4.8 at late initiation ($p < 0.001$). The effect of the early administration of beta-blockers was more remarkable among the STEMI patients, and the mean LVEF improved by +12.4 ± 3.3% in Group A compared to +6.1 ± 3.1% in Group B ($p < 0.001$). It was also significant in the improvement of NSTEMI patients (+9.3 ± 3.2 vs. +4.2 ± 3.0, $p < 0.01$). These subgroup results emphasize the fact that the positive impact of early beta-blockade on LVEF recovery was not influenced by age and infarction type, which confirms its universal applicability in the management of ACS (Table 4).

Table 1. Baseline Demographic and Clinical Characteristics of Study Population (n = 70)

Parameter	Group A (Early Initiation) n = 35	Group B (Delayed Initiation) n = 35	p-value
Mean Age (years)	56.1 ± 7.8	57.4 ± 8.1	0.48
Male Gender n (%)	26 (74.3%)	25 (71.4%)	0.79
Female Gender n (%)	9 (25.7%)	10 (28.6%)	0.79
Hypertension n (%)	18 (51.4%)	19 (54.3%)	0.80
Diabetes Mellitus n (%)	13 (37.1%)	12 (34.3%)	0.81
Smoking n (%)	11 (31.4%)	10 (28.6%)	0.79
STEMI n (%)	22 (62.9%)	21 (60%)	0.81
Baseline Systolic BP (mmHg)	122.6 ± 10.4	121.9 ± 11.2	0.78
Baseline Heart Rate (bpm)	84.7 ± 7.9	83.2 ± 8.1	0.46
Serum Troponin (ng/mL)	8.4 ± 1.3	8.6 ± 1.5	0.62

Table 2. Comparison of Left Ventricular Ejection Fraction (LVEF) at Baseline and Follow-up

Measurement Time	Group A (Early Initiation) Mean ± SD (%)	Group B (Delayed Initiation) Mean ± SD (%)	Mean Difference	p-value
Baseline LVEF	38.5 ± 5.3	38.9 ± 5.1	0.4	0.74
3-Month Follow-up LVEF	49.8 ± 6.2	44.1 ± 5.9	5.7	<0.001
Mean LVEF Improvement	+11.3 ± 3.6	+5.2 ± 3.4		<0.001

Table 3. In-Hospital and Three-Month Clinical Outcomes

Outcome	Group A (Early Initiation) n = 35	Group B (Delayed Initiation) n = 35	p-value
Ventricular Arrhythmia (VT/VF)	2 (5.7%)	6 (17.1%)	0.04
Bradycardia (requiring adjustment)	3 (8.6%)	2 (5.7%)	0.64
Hypotensive Episodes	2 (5.7%)	4 (11.4%)	0.39
Hospital Readmission (3 months)	3 (8.6%)	7 (20%)	0.12
Reinfarction	1 (2.9%)	3 (8.6%)	0.30
Mortality (3 months)	1 (2.9%)	2 (5.7%)	0.56

Table 4. Subgroup Analysis of LVEF Improvement by Age and Infarction Type

Subgroup	n	Group A (Early Initiation) Mean LVEF Change (%)	Group B (Delayed Initiation) Mean LVEF Change (%)	p-value
Age < 55 years	22	+12.1 ± 3.7	+6.4 ± 3.2	<0.001
Age ≥ 55 years	48	+10.7 ± 3.5	+4.8 ± 3.5	<0.001
STEMI patients	43	+12.4 ± 3.3	+6.1 ± 3.1	<0.001
NSTEMI patients	27	+9.3 ± 3.2	+4.2 ± 3.0	<0.01

Overall, the current research has shown that there is a significant increase in left ventricular ejection fraction and a decrease in the adverse cardiac events among the patients receiving beta-blockers, which occurs early after the development of acute myocardial infarction. The early initiation group recorded almost twice the systolic function improvement as opposed to the delayed initiation group, having fewer arrhythmic events with lower arrhythmic readmission rates. These results are very strong indicators to point out that beta-blocker treatment during the first 24 hours of ACS, in hemodynamically stable patients, is an important factor in ensuring ventricular recovery, remodelling prevention, and better clinical outcome in the short term.

The fact that these findings are consistent when comparing the data of the various subgroups, as presented in Tables 1-4, highlights the significance of early pharmacological treatment in ensuring cardiac functioning in the post-infarction period and general prognosis.

DISCUSSION

The current research was developed to assess and compare the effects of early and delayed use of beta-blockers on patients who have acute myocardial infarction (AMI), especially the recovery of left ventricular ejection fraction (LVEF) [12]. This is a one-year comparative clinical study carried out at the Punjab Institute of Cardiology, Lahore, which has given strong regional support in favor of the early administration of beta-blockers in hemodynamically stable patients who have suffered AMI. The main results indicated that LVEF improved much higher in patients who were prescribed beta-blockers within 24 hours of admission to the hospital than in patients who were prescribed the therapy after 72 hours. This was also the case regardless of the age and type of infarction, which confirms the superiority of early sympathetic blockade as a facilitator of ventricular recovery [13,14].

This was clearly shown in the outcomes of Table 2 and Table 4, which indicate that the mean LVEF improvement in the patients in the early initiation group was 11.3, which was almost twice as compared to the delayed group. This significant disparity highlights the importance of early beta-adrenergic inhibition to lower myocardial oxygen consumption and ward off catecholamine-related cardiotoxicity, which are prime focus areas to curb infarct growth and unfavorable

remodelling. The positive result of early beta-blockade in this research is in line with other trials that have been carried out previously, like the CAPRICORN, COMMIT/CCS-2, and MIAMI studies, which also recorded better heart function and alleviation of arrhythmia when beta-blockers are used early after infarction [15]. The trial of COMMIT/CCS-2, specifically, indicated that prompt metoprolol administration reduced the occurrence of cardiac reinfarction and ventricular fibrillation, although it pointed to the care in using the drug in patients with the potential risk of cardiogenic shock. This conclusion is reflected in our results because the early group of patients had better functional recovery and no significant rise in the number of bradycardia or hypotensive events (Table 3) [16].

The further mechanistic evidence of the cardioprotective effects of beta-blockers stems from the reduction in arrhythmic events in the early initiation group. It has been known that post-infarction sympathetic overactivity enhances myocardial excitability and heterogeneity of repolarization, which predisposes ventricular tachycardia and fibrillation [17]. Early beta-blocker therapy normalizes cardiac electrophysiology by suppression of this sympathetic surge and lowers the rate of lethal arrhythmias. This antiarrhythmic advantage is supported by the fact that the incidence of ventricular arrhythmias (5.7 vs. 17.1) in Group A was significantly lower than in Group B, as it is indicated in Table 3. Moreover, the early therapy was also linked with the tendency to lower the rates of reinfarction and mortality, yet they were not statistically significant because of the small sample size. However, these clinical effects are not isolated when compared to large-scale analysis, which has shown a survival benefit when beta-blockers are timely administered [18].

It is worth mentioning that the beneficial effect of beta-blockers is the most prominent when taken early, but not in an acute fashion. Excessively early administration in hypotensive or bradycardic patients is still a contraindication, since it can cause an increase in perfusion [19]. No patients in our cohort had severe adverse effects that necessitated discontinuation, indicating that early therapy is safe and effective with careful selection of patients. This assertion is supported by the fact that the slight and insignificant variation in the bradycardia or hypotension between the groups is nonsignificant. The results are consistent with the European Society of Cardiology (ESC 2023) and the American Heart Association (AHA 2022), which both recommend the use of beta-blockers in the first 24 hours after infarction in stable patients and use careful titration thereafter [20].

The difference in LVEF between younger patients and STEMI, as demonstrated in Table 4, can be attributed to better myocardial responsiveness and less baseline myocardial fibrosis than that observed in older patients [13,15]. Younger myocardium has more contractile reserve and a higher potential for reverse remodeling after ischemic stress is removed. Besides, patients with STEMI usually display a greater sympathetic response to infarction, and thus are more receptive to the advantages of beta-blockade to wall stress and aneurysmal dilatation prevention. This observation is in line with the observational registries, which have revealed that the benefits of beta-blockers are enhanced in large transmural infarctions and those patients with intact hemodynamic stability [1,7].

The findings of the current research have significant clinical implications for low- and middle-income nations like Pakistan, where late presentation to the hospital and inadequate post-infarction follow-up usually do not allow providing optimal pharmacological care [11,17]. The fact that the introduction of beta-blockers in the early stages of the disease has the potential to significantly improve the functioning of the ventricles, even in a resource-constrained setting, offers good evidence to be incorporated in local clinical instructions. Early therapy intervention in tertiary cardiac facilities has the potential to enhance not only short-term functional recovery but also slow the onset of chronic heart failure, a significant readmission and mortality risk factor in the post-MI patient population. The reduced readmission rates in the early group (Table 3) also reinforce the effect of the beta-blockers in enhancing the long-term hemodynamic stability and patient outcomes [8-15].

However, the research is not flawless. The sample size was rather limited, and the study was conducted in one center, which hinders the external validity of the results. The three-month follow-up period, though adequate in the evaluation of early ventricular recovery, may not be adequate in the evaluation of long-term remodeling or mortality benefits [3]. Substantially larger and increased follow-up period multicentric studies should be carried out to verify these findings and provide long-term prognostic meaning. Moreover, although LVEF was the main outcome in this work, other measures, e.g., diastolic function, global longitudinal strain, and neurohormonal biomarkers (e.g., BNP levels), may be useful to understand the physiological effect of early beta-blocker treatment in more depth. Despite these limitations, existing evidence is a solid infringement of the hypothesis that early administration of beta-blockers will have superior outcomes in ACS and must be a part of routine care in case patient stability allows it [4,18].

Summarizing, this research contributes to the current global literature by showing that early administration of beta-blockers within 24 hours of acute myocardial infarction results in a significantly greater recovery of the left ventricular systolic function, decreased cases of arrhythmia complications, and improvement of short-term clinical stability in comparison with the case of late administration. The congruity of such results throughout all the subgroups and the correspondence to the

recommendations of the international guidelines is evidence of the inappropriateness of the delay in pharmacologic intervention in managing post-infarction [15-20].

CONCLUSION

This study concludes that the implementation of beta-blocker treatment (within 24 hours) in hemodynamically stable patients with acute myocardial infarction leads to a significantly better restoration of left ventricular ejection fraction than the implementation of beta-blocker treatment (after 72 hours). Patients who were subjected to early therapy had a better ventricular systolic function, reduced ventricular arrhythmias, and fewer hospital readmissions in three months. This was independent of the age and type of infarction, which emphasized the universal effectiveness of early beta-blockade. Timely initiation of the use of beta-blockers should be a priority in the post-AMI management schedule to improve the myocardial recovery process, prevent adverse remodelling, and improve the short-term outcome. Nevertheless, the selection of patients cautiously and hemodynamic monitoring are the key factors in the context of safety. This research supports the existing global recommendations and offers robust evidence on a regional level, supporting the suggestion of early beta-blocker therapy as a routine type of treatment in tertiary cardiac facilities in Pakistan. It is suggested that future large-scale, long-term studies are advisable in order to additional confirm these findings as well as investigate their effect on overall survival and heart failure progression.

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Data Availability Statement: The data used in this study are available upon reasonable request from the corresponding author, subject to ethical and institutional guidelines.

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