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Revisiting Long-Term B-Blocker Therapy After Myocardial Infarction in the Contemporary Era: A Contemporary Review of the Evidence

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Abstract **Review Article**

Background: β-blockers have long been a cornerstone of secondary prevention after myocardial infarction (MI), based largely on randomized trials conducted in the pre-reperfusion era. However, major advances in acute coronary care, including early revascularization, optimized antithrombotic therapy, and widespread statin use, have raised uncertainty regarding the role of long-term β-blocker therapy in contemporary post-MI patients, particularly those with preserved left ventricular ejection fraction (LVEF). ***Objective:*** This review aims to reassess the evidence supporting long-term β-blocker therapy after MI in the modern era, with particular focus on patient subgroups defined by left ventricular systolic function. ***Methods:*** Reviewed contemporary randomized controlled trials, meta-analyses, and international guideline recommendations evaluating the impact of β-blocker therapy after MI in the reperfusion era. Special emphasis was placed on recent individual-patient data (IPD) meta-analyses pooling major randomized trials. ***Results:*** Historical trials demonstrated clear mortality benefits of β-blockers after MI; however, these findings may not be fully applicable to current practice. Contemporary evidence suggests that the prognostic benefit of β-blockers is largely confined to patients with impaired or mildly reduced LVEF. A recent IPD meta-analysis pooling the REBOOT, BETAMI, DANBLOCK, and CAPITAL-RCT trials demonstrated a significant reduction in major cardiovascular events among patients with mildly reduced LVEF (40–49%), while no consistent benefit was observed in patients with preserved LVEF (≥50%). These findings help reconcile previously conflicting trial results and support a stratified, phenotype-driven approach to β-blocker therapy after MI. ***Conclusion:*** In the contemporary era of myocardial infarction management, long-term β-blocker therapy should no longer be considered universal. While β-blockers remain strongly indicated in patients with reduced or mildly reduced LVEF and in those with heart failure, their routine long-term use in stable post-MI patients with preserved systolic function should be individualized. Integration of modern randomized evidence into future guideline updates is warranted to better reflect this risk-based approach.

Keywords: β-blockers, myocardial infarction, left ventricular ejection fraction, secondary prevention, reperfusion era, cardiovascular outcomes.

INTRODUCTION:

Beta-blockers have long been a mainstay of post-myocardial infarction (MI) management, their benefit in terms of prognostic having been demonstrated in historical trials conducted in the pre-reperfusion era [1]. These data largely underpinned current recommendations, which advocate their routine use after MI. However, the major evolution of therapeutic strategies, including early reperfusion, optimization of antithrombotic therapies, and the widespread use of statins, calls into question the extrapolation of these results to patients treated in the contemporary setting.

Recent observational and randomized studies suggest that the benefit of beta-blockers after myocardial infarction (MI) may be primarily limited to patients with left ventricular dysfunction or heart failure [2]. Conversely, in stable, revascularized patients with preserved systolic function, these studies did not demonstrate a significant reduction in mortality or major cardiovascular events. This growing discrepancy between contemporary data and current recommendations underscores the need to reassess the role of beta-blockers after MI, favoring a more individualized approach based on the patient's risk profile.

DISCUSSION:

The use of beta-blockers in the management of myocardial infarction became established in the 1970s and 1980s, following several randomized clinical trials that demonstrated a significant reduction in mortality and ischemic recurrence. Pioneering studies such as the Beta-Blocker Heart Attack Trial (BHAT) evaluating propranolol, and the Norwegian trial on timolol, showed a decrease in all-cause mortality and sudden death in patients treated after an MI [3]. These benefits were attributed primarily to the reduction of myocardial ischemia, heart rate, and the risk of ventricular arrhythmias in a context where reperfusion strategies and concomitant treatments were limited.

In myocardial infarction (MI) and the post-acute phase, the use of beta-blockers should now be considered in a more targeted manner, distinguishing between symptomatic control (antianginal/chronotropic) and prognostic benefit. The 2024 ESC guidelines reaffirm that, in the majority of patients with symptomatic chronic coronary artery disease, initial treatment with a beta-blocker and/or calcium channel blocker is recommended to control heart rate and symptoms (Class I), with the possibility of escalation to a beta-blocker-dihydropyridine calcium channel blocker combination if control is insufficient (Class IIa) [4]. At the same time, the ESC highlights the contemporary uncertainty regarding the systematic maintenance of beta-blockers after an uncomplicated stroke/MI when ventricular function is preserved, recalling that the impact of stopping between 6 and 12 months in patients with LVEF ≥40% is currently being evaluated in randomized trials. [4].

In the United States, the AHA/ACC guidelines specify that long-term beta-blocker therapy has no prognostic benefit in the absence of an MI within the past year, an LVEF ≤50%, or another formal indication, and encourage reassessment of the indication for treatment beyond one year in patients prescribed beta-blockers for an MI without LV dysfunction (Class IIb). [5].

Conversely, a prognostic benefit is clearly established when the LVEF is impaired: a beta-blocker is recommended to reduce the risk of major cardiovascular events in patients with an LVEF ≤40% (Class I), with a preference for extended-release metoprolol succinate, carvedilol, or bisoprolol when the LVEF is <50%.[5]

A major advance in this field has been the publication of an individual-patient data (IPD) meta-analysis pooling four contemporary randomized controlled trials REBOOT, BETAMI, DANBLOCK, and CAPITAL-RCT all conducted in the reperfusion era and enrolling post-MI patients without overt heart failure [6,7]. This approach enabled harmonized subgroup analyses and improved statistical power, particularly for clinically relevant LVEF strata.

Benefit concentrated in mildly reduced LVEF (40–49%)

The IPD meta-analysis demonstrated that among patients with mildly reduced LVEF (40–49%), β-blocker therapy was associated with a significant reduction in a composite endpoint of all-cause mortality, recurrent MI, or hospitalization for heart failure [6]. This observation offers a biologically plausible explanation for previously conflicting results, as patients within this LVEF range share pathophysiological features with those who have reduced systolic function and may therefore benefit from the anti-ischemic, anti-arrhythmic, and heart rate–lowering effects of β-blockers.

Reconciling neutral and positive trial results

The pooled results help reconcile the divergent findings of individual contemporary trials. The REBOOT trial, which enrolled post-MI patients with LVEF ≥40%, did not demonstrate a significant reduction in cardiovascular death, reinfarction, or heart failure hospitalization with β-blocker therapy in the overall population [8]. However, subgroup analyses suggested that treatment effects may vary according to LVEF category.

Conversely, the combined BETAMI-DANBLOCK trials reported a modest but statistically significant reduction in major cardiovascular events among patients with LVEF ≥40%, driven primarily by fewer recurrent non-fatal myocardial infarctions, although no clear reduction in all-cause mortality was observed [9,10]. Differences in baseline risk, inclusion criteria, and the proportion of patients with mildly reduced versus preserved LVEF likely contributed to these discrepancies. By pooling individual-level data, the meta-analysis clarified that the most consistent benefit was confined to patients with LVEF 40–49%, whereas uncertainty increased as LVEF approached normal values [6].

Preserved LVEF: limited and inconsistent benefit

In contrast, patients with preserved LVEF (≥50%) did not show a clear prognostic benefit from β-blocker therapy in the pooled analysis [6]. These findings are consistent with results from other contemporary randomized trials and meta-analyses, suggesting that in low-risk, optimally treated post-MI patients, the incremental value of β-blockers on hard clinical outcomes may be limited [11]. Collectively, these data challenge the historical paradigm of systematic long-term β-blocker prescription for all post-MI patients irrespective of ventricular function.

Safety and subgroup considerations

Emerging evidence also suggests potential heterogeneity of treatment effect, particularly according to sex. A secondary analysis of the REBOOT trial reported a possible signal of harm among women treated with β-blockers, especially at higher doses, although this

finding remains hypothesis-generating and requires further confirmation [12]. These observations reinforce the need for individualized treatment decisions and careful dose titration in clinical practice.

Clinical implications

Taken together, the pooled evidence from REBOOT, BETAMI, DANBLOCK, and CAPITAL-RCT supports a stratified approach to β-blocker therapy after MI. β-blockers remain strongly indicated in patients with reduced LVEF or clinical heart failure, while patients with mildly reduced LVEF (40–49%) appear to derive a meaningful prognostic benefit according to contemporary randomized evidence [6,7]. In contrast, for stable patients with preserved LVEF, routine long-term β-blocker therapy should be reconsidered and individualized based on symptoms, comorbidities, heart rate, blood pressure, and treatment tolerance.

CONCLUSION

Recent contemporary randomized evidence, including the individual-patient data meta-analysis pooling REBOOT, BETAMI, DANBLOCK, and CAPITAL-RCT, substantially refines the role of β-blockers after myocardial infarction in the modern era of reperfusion and optimized secondary prevention [6]. This pooled analysis demonstrates that the clinical benefit of long-term β-blocker therapy is largely confined to patients with mildly reduced left ventricular ejection fraction (40–49%), whereas no consistent prognostic benefit is observed in stable patients with preserved LVEF (≥50%) who are free from heart failure [6].

These findings are closely aligned with current European Society of Cardiology (ESC) recommendations, which strongly endorse β-blockers in patients with reduced LVEF or clinical heart failure while acknowledging weaker evidence for their routine long-term use in patients with preserved LVEF after MI [13]. The contemporary meta-analysis strengthens the European position by providing robust randomized evidence supporting β-blocker therapy in the intermediate LVEF range (40–49%), a subgroup previously less clearly defined in guidelines.

In contrast, American guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA) continue to recommend β-blocker therapy for up to three years after MI, even in patients with preserved LVEF, largely based on historical trials conducted before current revascularization and pharmacological strategies were standard [14,15]. However, the absence of a clear mortality or reinfarction benefit in preserved LVEF populations in contemporary trials challenges the universal applicability of these recommendations and suggests that future guideline updates may adopt a more selective, risk-based approach.

Overall, integration of modern randomized evidence with existing guidelines supports a phenotype-driven strategy for β-blocker therapy after MI. While β-blockers remain indispensable in patients with reduced or mildly reduced LVEF, heart failure, or other compelling indications, their routine long-term use in patients with preserved LVEF should be individualized, balancing potential benefits against tolerability and patient preference. Future European and North American guideline revisions are likely to increasingly reflect this nuanced, evidence-based approach.

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