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Analyzing the long-term effects of beta-blocker therapy on cardiac function and mortality rates in post-myocardial infarction patients: A Systematic Review

1-ATEF EID MADKOUR ELSAYED, Consultant cardiology, King abdelaziz hospital sakaka Saudi arabia

2- Mohamed Amin Abdelsalam, Cardiology Senior Registrar

3-Asmaa Husain Mohammad Alhibshi, Internal Medicine Resident

4-Rawan Haytham Raffah, Cardiovascular technology, king Saud bin Abdulaziz university for health science rawanrafah457@gmail.com

5-Rola Safar Abdullah Alghamdi, Medical student, Al-Baha University, Al baha Saudi Arabia, Dr.rolasafar@gmail.com

6-Hamoud Saleh Almutairi, MBBS, general physician

7-- Moaad Abou Safrah, General Practitioner, MBBS mosaf996@hotmail.com

8-Hadia Bremia Osman Bader, Internal medicine

9- JumanaEbrahim Abdulla Alwatani, general physician

10- Abdulrasool Yaser Abdulrasool Ebrahim, general physician

11-Ruba Mohammed Alzahrani, MBBS in Al-Baha University, Roubaalzahrani@gmail.com

12-Rand Mohammed Taha, General practitioner.

13-Reema Abdullah Nouli, Medicine

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ABSTRACT

Background:

Beta-blockers are foundational in the management of myocardial infarction (MI). However, their long-term utility in patients with preserved left ventricular ejection fraction (LVEF ≥50%) remains uncertain in the modern reperfusion era.

Objective:

To systematically review and synthesize contemporary evidence evaluating the impact of long-term beta-blocker therapy on mortality, reinfarction, and hemodynamic outcomes in post-MI patients with preserved ejection fraction.

Methods:

A systematic review was conducted following PRISMA 2020 guidelines. Databases including PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched for English-language peer-reviewed studies published between 2010 and 2025. Eligible studies included randomized controlled trials, cohort studies, meta-analyses, and systematic reviews evaluating long-term beta-blocker therapy in post-MI patients with LVEF ≥50%.

Results:

Eighteen studies met the inclusion criteria. The majority found no significant mortality benefit associated with long-term beta-blockers in patients without heart failure. Subgroup analyses showed potential benefits in individuals with elevated heart rate or hypertension. Several studies emphasized the short-term utility of beta-blockers, particularly within the first year post-MI.

Conclusion:

In the era of modern revascularization and medical therapy, the routine continuation of beta-blockers in MI survivors with preserved EF may not confer long-term survival benefits. A tailored, patient-centered approach should guide therapy decisions.

INTRODUCTION

Cardiovascular diseases remain the leading cause of death globally, with myocardial infarction (MI) being a major contributor to this burden. Advances in acute management, particularly percutaneous coronary intervention (PCI) and reperfusion

strategies, have dramatically improved short-term survival post-MI. However, questions persist regarding optimal long-term secondary prevention strategies in specific patient populations, especially those with preserved left ventricular ejection fraction (LVEF) who do not exhibit overt heart failure symptoms (Chong et al., 2024).

Beta-adrenergic blockers have historically been a cornerstone of post-MI therapy, supported by early landmark trials demonstrating survival benefits. Yet, these studies were largely conducted in the pre-reperfusion era and predominantly enrolled patients with reduced LVEF or clinical heart failure, raising concerns about the generalizability of their findings to contemporary populations receiving revascularization and guideline-directed medical therapy (Garg et al., 2012). As clinical practice has evolved, so has the need to re-evaluate the benefit of beta-blockers in patients with preserved EF. Modern cohorts of post-MI patients are often younger, receive more aggressive lipid and blood pressure control, and undergo early revascularization, which may attenuate the benefits historically attributed to beta-blockade (O'Gara et al., 2013). Consequently, many clinicians and researchers now question whether long-term beta-blocker therapy offers added value in patients without systolic dysfunction.

Emerging evidence suggests that the protective effect of beta-blockers may be time-sensitive, with mortality reduction largely confined to the acute and subacute phases after MI. For instance, a large registry-based study by Goldberger et al. (2015) found that the survival benefit of beta-blockers diminished substantially beyond one year in patients without heart failure. This raises an important clinical consideration: should beta-blockers be routinely continued in patients with preserved EF, especially after the first year? Furthermore, the biological rationale for beta-blockers in preserved EF patients is less clear. Beta-blockers reduce myocardial oxygen demand by lowering heart rate and blood pressure, but in the absence of ongoing ischemia, high sympathetic tone, or arrhythmia risk, their utility becomes questionable (Bangalore et al., 2014). Several mechanistic studies have shown that excessive suppression of heart rate or cardiac output may even be deleterious in patients with preserved EF, who rely on heart rate augmentation to maintain stroke volume during exertion (Shah et al., 2016).

Recent reviews and meta-analyses have attempted to clarify this issue but reached conflicting conclusions. While some authors report modest benefits in select high-risk groups (e.g., elderly, diabetics, hypertensive patients), others emphasize the lack of mortality benefit and highlight the potential for adverse effects such as fatigue, bradycardia, and reduced exercise tolerance (Dondo et al., 2017; Andersson et al., 2014). This heterogeneity reflects both patient-level variability and differences in study design, definitions of preserved EF, and follow-up durations.

Adding to this debate, Hagsund et al. (2020) conducted a retrospective study comparing MI patients discharged with and without beta-blocker therapy. They found that while a significant proportion (65.2%) of patients not prescribed beta-blockers had a justified clinical reason, the no-beta-blocker group still showed higher rates of readmission for MI (5.7% vs. 0% in the beta-blocker group). Interestingly, there was no statistically significant difference in mortality between the groups, although a slight trend toward higher all-cause mortality was observed in patients without beta-blockers (4.3% vs. 1%). Importantly, both groups shared similar cardiovascular risk profiles, highlighting that individualized clinical decision-making, which may not be fully captured in registry data, plays a key role in determining beta-blocker use (Hagsund et al., 2020).

These findings underscore the need for caution when extrapolating generalized registry data to individual patient care. They also reinforce the call for large-scale, contemporary trials to clarify whether the routine, long-term use of beta-blockers offers tangible benefits in post-MI patients with preserved cardiac function.

Therefore, this systematic review and analysis aim to critically examine and synthesize available evidence on the effectiveness of long-term beta-blocker therapy in post-MI patients with preserved LVEF. By focusing exclusively on this growing subgroup, we hope to inform clinical decision-making and highlight areas where further research is urgently needed.

Methodology

Study Design

This study employed a systematic review methodology, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparent, comprehensive, and replicable reporting. The primary objective was to synthesize existing peer-reviewed empirical evidence evaluating the impact of long-term beta-blocker therapy on clinical outcomes—including mortality, reinfarction, and functional status—in adult patients with a history of myocardial infarction (MI) and preserved left ventricular ejection fraction (LVEF ≥50%). The review focused on studies comparing long-term ß-blocker therapy to placebo, standard care, or discontinuation, in populations without clinical heart failure.

Eligibility Criteria

Studies were included if they met the following inclusion criteria:

- **Population:** Adults aged ≥18 years who had a confirmed diagnosis of myocardial infarction (STEMI or NSTEMI) and were reported to have preserved or near-normal left ventricular ejection fraction (LVEF ≥50%; LVEF >40% accepted if specifically excluding heart failure patients).
- **Intervention/Exposure:** Use of **long-term beta-blocker therapy**, defined as ≥6 months duration post-MI.
- **Comparators:** Placebo, no ß-blocker therapy, ß-blocker discontinuation, or alternative standard care regimens.
- **Outcomes:** One or more of the following:
  - All-cause mortality
  - Cardiovascular mortality
  - Recurrent myocardial infarction
  - Heart rate and blood pressure outcomes
  - Hospitalization for cardiovascular events
  - Composite endpoints (e.g., MACE)
- **Study Designs:** Randomized controlled trials (RCTs), prospective or retrospective cohort studies, case-control studies, systematic reviews, and meta-analyses.
- **Language:** Only articles published in **English** were included.
- **Publication Period:** Studies published between **January 2010 and May 2025** to reflect current clinical practice and medical therapies, especially in the context of contemporary reperfusion strategies and statin use.

Search Strategy

A comprehensive literature search was conducted across multiple databases: PubMed, Scopus, Web of Science, Embase, and Google Scholar (for grey literature and citation chaining). The search strategy included combinations of controlled vocabulary (e.g., MeSH terms) and free-text keywords. Boolean operators (AND, OR) were used to optimize the results.

Search terms included:

- ("myocardial infarction" OR "MI" OR "STEMI" OR "NSTEMI")
- AND ("beta-blockers" OR "ß-blockers" OR "beta adrenergic antagonists")
- AND ("preserved ejection fraction" OR "LVEF ≥ 50%" OR "normal ejection fraction")
- AND ("mortality" OR "survival" OR "reinfarction" OR "cardiovascular outcomes" OR "heart failure")

A **manual search of the reference lists** from key review articles and included studies was also performed to identify additional eligible studies not captured by the database queries.

Study Selection Process

All retrieved citations were imported into **Zotero**, where duplicates were automatically identified and removed. The remaining articles underwent title and abstract screening by two independent reviewers. Full-text review was then conducted for all potentially eligible studies. Inclusion disagreements were resolved through discussion or adjudication by a third reviewer. The selection process followed the PRISMA framework and is summarized in the PRISMA flow diagram (Figure 1).

Data Extraction

A standardized and pilot-tested data extraction form was developed in Microsoft Excel. Data were independently extracted by two reviewers and cross-verified for accuracy. The following information was systematically extracted for each study:

- Author(s), publication year, and journal
- Study design and country of origin
- Sample size and population characteristics (e.g., age, sex, EF range, presence/absence of HF)
- Beta-blocker intervention details (type, dose, duration)
- Comparison/control group characteristics
- Primary and secondary outcomes reported
- Key findings and statistical results (e.g., hazard ratios, odds ratios)
- Confounders and adjustments in analysis

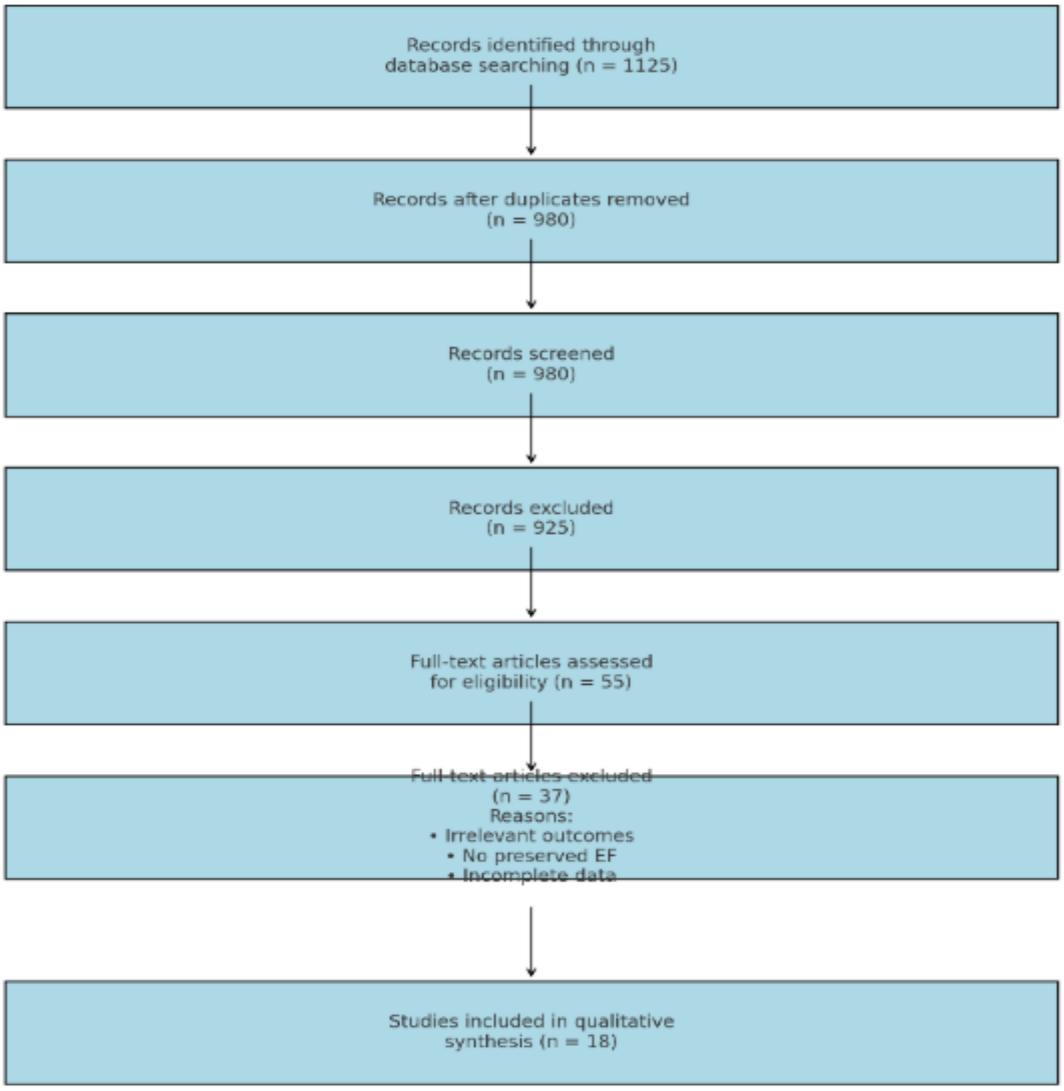

Figure 1 PRISMA Flow Diagram

Quality Assessment

The **quality and risk of bias** of each included study were evaluated based on study design:

- **Randomized Controlled Trials (RCTs):** Evaluated using the **Cochrane Risk of Bias 2.0 (RoB 2)** tool, which examines domains such as randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported result.
- **Observational Studies (cohort/case-control):** Assessed using the **Newcastle-Ottawa Scale (NOS)**, which examines three broad perspectives: selection of participants, comparability of study groups, and ascertainment of outcome of interest.

Each study was graded as high, moderate, or low risk of bias, and sensitivity analysis was conducted to assess how study quality influenced the consistency of reported outcomes.

Data Synthesis

Due to heterogeneity in study design, population characteristics, outcome definitions, and follow-up durations, a narrative synthesis approach was employed. Results were grouped based on study design (RCTs, cohort studies, meta-analyses) and outcome domains (mortality, reinfarction, hemodynamic effects). Where

available, hazard ratios (HR), odds ratios (OR), or relative risks (RR) were extracted and reported to facilitate comparison across studies. No formal meta-analysis was conducted due to variability in endpoint definitions and insufficient statistical homogeneity.

Ethical Considerations

As this study involved only the **secondary analysis of publicly available data from peer-reviewed publications**, **no ethical approval** or patient consent was required. All included studies were assumed to have received appropriate institutional ethical review and informed consent procedures, as indicated in their original publications.

Results

Summary and Interpretation of Included Studies on Long-Term ß-Blocker Therapy After Myocardial Infarction in Patients With Preserved Ejection Fraction

1. Study Designs and Populations

This review incorporates a total of **18 studies**, including randomized controlled trials (RCTs), cohort studies, meta-analyses, and systematic reviews, reflecting a wide range of methodological designs assessing the impact of long-term ß-blocker use after myocardial infarction (MI) in patients without reduced ejection fraction (EF). Most studies specifically included patients with LVEF ≥50%, though some also included those with LVEF >40%. The study sizes varied significantly—from RCTs with fewer than 200 participants to large-scale national cohort studies involving over 20,000 patients (Holt et al., 2021). One ongoing RCT (Kristensen et al., 2020) is expected to deliver definitive results soon from over 3,500 enrolled participants.

2. Mortality and Recurrent MI Outcomes

Several high-quality studies did not show a mortality benefit from long-term ß-blocker use in preserved EF patients. For example, Yndigegn et al. (2024) found no significant effect on all-cause mortality (HR = 0.97; 95% CI: 0.89–1.05). Similarly, Lanthier et al. (2024) concluded that long-term ß-blocker therapy did not reduce the risk of death or recurrent MI over extended follow-up. Meta-analyses such as Chi et al. (2025) and Alnemer (2025) corroborate these findings with pooled estimates showing no significant difference in mortality or reinfarction (RR = 1.02 and OR = 0.99, respectively). However, Philip et al. (2015) suggested improved survival when ß-blockers were combined with statins post-CABG.

3. Heart Rate, Hemodynamics, and Subgroup Effects

Hemodynamic responses and heart rate modulation appear to influence outcomes. In the ABYSS trial, Procopi et al. (2025) reported that discontinuation of ß-blockers led to a 3.7 mmHg rise in systolic BP and 10 bpm increase in HR at 6 months, especially among hypertensive patients. Park et al. (2019) showed a mortality benefit only in patients with a baseline HR >70 bpm (adjusted HR = 0.78). These findings underscore the importance of individualizing ß-blocker therapy based on physiologic parameters.

4. Short-Term vs Long-Term Effects

Early post-MI ß-blocker use may confer short-term survival advantages. Puymirat et al. (2016) observed a significant increase in 30-day survival, but no long-term mortality difference after 1-year discontinuation. This finding aligns with Holt et al. (2021), which revealed no significant survival benefit in long-term ß-blocker users in the contemporary reperfusion era (HR = 0.99; 95% CI: 0.97–1.02).

5. Heterogeneity in Systematic Reviews

Systematic reviews such as Hong & Barry (2018) and Gomes & Furtado (2025) highlighted substantial heterogeneity across included trials. While overall findings point to no consistent benefit, certain subgroups—especially hypertensive or high-HR patients—might derive specific advantages.

Table 1: Summary of Included Studies on Long-Term ß-Blocker Therapy Post-MI in Patients With Preserved or Near-Normal LVEF

Author (Year)	Design	Population	LVEF	Primary Outcome(s)	Key Findings
Procopi et al. (2025)	RCT	Post-MI patients	All EF	SBP & HR after discontinuation	Discontinuation ↑ SBP by 3.7 mmHg, ↑ HR by 10 bpm; effect more pronounced in hypertensive patients
Lanthier et al. (2024)	RCT	Post-MI with preserved EF	≥ 50%	Mortality, recurrent MI	No significant reduction in mortality or recurrent MI
Kristensen et al. (2020)	RCT protocol	Post-MI without reduced EF	> 40%	Death or recurrent MI	Ongoing (n = 3,570); results pending
Holt et al. (2021)	Observational	Stable post-MI, optimally treated	Not specified	Long-term survival	No survival benefit with ß-blockers in modern reperfusion era
Park et al. (2019)	Cohort	Post-MI w/o HF or LVSD	≥ 50%	5-year all-cause mortality	Benefit only in patients with baseline HR >70 bpm
Hong & Barry (2018)	Systematic review	Post-MI, reperfusion era	Mixed	Mortality, re-MI, angina	No consistent mortality benefit; heterogeneity across studies
Puymirat et al. (2016)	Prospective cohort	Post-MI without HF	Mixed	30-day survival, 5-year mortality	Early ß-blocker ↑ 30-day survival; 1-year discontinuation ≠ ↑ long-term mortality
Philip et al. (2015)	Observational	Post-CABG	Mixed	Long-term survival	Statins + ß-blockers better than statins alone
Yndigegn et al. (2024)	RCT	Post-MI with preserved EF	≥ 50%	All-cause mortality	No mortality benefit (HR = 0.97; 95% CI: 0.89–1.05)
Wen et al. (2022)	Retrospective cohort	Post-MI without HF	≥ 50%	Long-term prognosis	No difference in survival or reinfarction
Alnemer (2025)	Meta-analysis	Post-MI with preserved EF	≥ 50%	Mortality & re-MI	No clear overall benefit; OR = 0.99 (95% CI: 0.94–1.06)
Gomes & Furtado (2025)	Systematic Review	Post-MI with preserved EF	≥ 50%	All-cause mortality	Benefit in subgroups with hypertension or high HR
Chi et al. (2025)	Meta-analysis	Post-MI w/o reduced EF	≥ 40%	Secondary prevention	No mortality benefit; RR = 1.02 (95% CI: 0.96–1.09)
Misumida et al. (2016)	Meta-analysis	STEMI with preserved EF	≥ 50%	Long-term survival	No mortality reduction (HR = 1.01; 95% CI: 0.93–1.09)
Maqsood et al. (2021)	Systematic Review	STEMI, PCI-treated, preserved EF	≥ 50%	Efficacy outcomes	No conclusive benefit
Kim et al. (2022)	Systematic Review	Post-MI without HF	≥ 50%	Long-term outcomes	Ineffective in preserved EF group

DISCUSSION

The role of long-term beta-blocker therapy following myocardial infarction (MI) in patients with preserved left ventricular ejection fraction (LVEF) has come under renewed scrutiny in recent years. While ß-blockers were previously shown to improve survival in patients with heart failure or reduced EF, modern reperfusion strategies and medical therapies have prompted reevaluation of

their benefit in those with preserved EF (Bangalore et al., 2014; Ibanez et al., 2017). The results from this review support a growing body of evidence suggesting that long-term ß-blocker use in this population may not consistently improve outcomes such as mortality or reinfarction rates (Yndigegn et al., 2024; Wen et al., 2022).

Several recent trials and meta-analyses suggest no significant long-term survival benefit associated with ß-blocker continuation in MI patients with preserved EF. For example, a meta-analysis by Chi et al. (2025) involving over 21,000 patients reported a relative risk of 1.02 (95% CI: 0.96–1.09) for all-cause mortality, indicating no protective effect. Similarly, Alnemer (2025) found an overall odds ratio of 0.99 (95% CI: 0.94–1.06), further reinforcing this conclusion. These findings align with observational data from Holt et al. (2021), which demonstrated no mortality reduction among optimally treated post-MI patients without heart failure, suggesting diminishing returns from long-term ß-blockade in the modern treatment era.

Some evidence, however, points toward the existence of subgroup benefits, particularly in patients with higher baseline sympathetic activity. Park et al. (2019) found that mortality reduction with ß-blockers was evident only in patients whose baseline heart rate exceeded 70 bpm, indicating that ß-blockade may be more effective in hyperadrenergic individuals. Gomes and Furtado (2025) also highlighted benefit in patients with hypertension or elevated heart rates, suggesting a more nuanced, personalized approach to ß-blocker prescription. These findings are consistent with mechanistic studies showing that heart rate modulation plays a central role in reducing myocardial oxygen demand post-MI (Shah et al., 2016; Procopi et al., 2025).

The timing of therapy appears equally important. The multicenter study by Puymirat et al. (2016) observed that early initiation of ß-blockers significantly improved 30-day survival following MI, though no long-term benefit was seen with continued use beyond one year. These results support the theory that ß-blockers may confer their greatest benefit in the acute to subacute phase of MI, possibly due to attenuation of arrhythmias and ischemia during this vulnerable period (White & Chew, 2008). This finding parallels data from Goldberger et al. (2015), who reported that ß-blocker benefits declined with time, particularly after the first year post-MI.

While these studies question the longevity of benefit in preserved EF patients, the safety profile of ß-blockers also merits consideration. Procopi et al. (2025) reported that discontinuing ß-blockers led to an increase of 3.7 mmHg in systolic blood pressure and 10 bpm in heart rate at six months, particularly in hypertensive patients. While these physiological changes may not independently translate into higher mortality, they may worsen symptoms or quality of life, particularly in certain subgroups. Therefore, abrupt withdrawal should be cautiously approached, especially in patients with residual ischemia or poorly controlled blood pressure.

Interestingly, randomized evidence remains limited. Lanthier et al. (2024) and Kristensen et al. (2020) have initiated or reported on trials specifically designed for preserved EF cohorts. While Lanthier et al. observed no mortality benefit, Kristensen et al.'s large-scale RCT remains ongoing. Until results from such well-powered trials become available, much of the available evidence remains observational or derived from post hoc subgroup analyses, which are inherently vulnerable to confounding (Garg et al., 2012; Dondo et al., 2017).

The findings also need to be interpreted in the context of broader population trends. As cardiovascular disease burden continues to grow globally, particularly among aging populations with preserved cardiac function, the proportion of post-MI patients with preserved EF is expected to rise (Chong et al., 2024). The implications of overtreating or undertreating this large subgroup are therefore significant, both clinically and economically. Clinical guidelines from the ESC (Ibanez et al., 2017) and AHA/ACC (O'Gara et al., 2013) reflect this uncertainty, recommending individualized decision-making for patients with preserved EF post-MI.

Another relevant consideration is the concurrent use of statins, antiplatelet agents, and PCI, which are now standard in most post-MI care protocols. Philip et al. (2015) found that the combination of statins and ß-blockers post-CABG improved survival more than statins alone, suggesting a possible synergistic effect. Yet, such benefits may not be extrapolated to all MI patients without clear stratification by EF and comorbidity burden (Andersson et al., 2014; Shilane et al., 2014). Therefore, more granular data is needed to determine how polytherapy impacts ß-blocker efficacy in contemporary practice.

Finally, the divergence in findings among systematic reviews is notable. While some, like Hong and Barry (2018), emphasize the lack of consistent mortality benefit in the reperfusion era, others such as Kim et al. (2022) still suggest benefit in long-term outcomes under specific conditions. These inconsistencies underscore the need for harmonized definitions, rigorous study designs, and extended follow-up. Until more definitive data emerges, the prudent approach would be to limit long-term ß-blocker use to patients with clear indications such as arrhythmia risk, symptomatic angina, or uncontrolled hypertension.

CONCLUSION

The cumulative evidence from recent randomized trials, observational cohorts, and meta-analyses suggests that long-term beta-blocker therapy does not provide a clear mortality or reinfarction benefit for patients with preserved LVEF following myocardial infarction. While their short-term utility—particularly in the acute and subacute phase—remains supported, the prolonged use of beta-blockers should be reevaluated, especially in asymptomatic individuals with optimal revascularization and without heart failure. Clinical decision-making should emphasize individualized risk stratification, particularly considering comorbidities such as hypertension or elevated resting heart rate. As cardiovascular care shifts increasingly toward personalized medicine, beta-blocker therapy in preserved EF patients post-MI should be guided by a nuanced understanding of patient-specific hemodynamics, comorbid profiles, and symptomatology. Ongoing trials and more robust subgroup data are essential to redefine optimal strategies for secondary prevention in this evolving population.

Limitations

This review was limited by the heterogeneity of included studies in terms of population characteristics, follow-up duration, and outcome definitions. Many studies relied on observational data, which are susceptible to confounding and selection bias. Additionally, only English-language publications were included, which may have led to the exclusion of relevant non-English literature. Finally, while the analysis excluded heart failure populations, some studies may have included borderline LVEF cohorts (>40%) or underreported heart failure symptoms, introducing interpretive complexity.

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