



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	BETA-BLOCKERS DISCONTINUATION AFTER MYOCARDIAL INFARCTION REFERRING TO EJECTION FRACTION
----------------------	--

DOI	https://doi.org/10.31435/ijitss.3(51).2026.5994
------------	---

RECEIVED	19 July 2026
-----------------	--------------

ACCEPTED	09 September 2026
-----------------	-------------------

PUBLISHED	22 September 2026
------------------	-------------------

LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

© The author(s) 2026.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

BETA-BLOCKERS DISCONTINUATION AFTER MYOCARDIAL INFARCTION REFERRING TO EJECTION FRACTION

Krzysztof Machnik (Corresponding Author, Email: kmachnik01@gmail.com)

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0000-3345-8593

Beata Tekieli

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0008-4427-6654

Wojciech Krzysztof Cyran

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0001-8992-3199

Tatsiana Matsiusheuskaya

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0007-2984-5356

Weronika Cionżyńska

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0007-1464-4957

Bartosz Gawel

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0008-7135-7679

Anna Justkowska-Gebauer

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0001-3106-5697

Maksymilian Olesiński

Independent Public Health Care Institution of the Ministry of the Interior and Administration in Krakow, Kraków, Poland

ORCID ID: 0009-0004-7179-1476

Ewelina Chudyba

Edward Szczeklik Specialist Hospital in Tarnow, Tarnow, Poland

ORCID ID: 0009-0004-7320-4773

Michał Górecki

Stefan Żeromski Specialist Hospital in Cracow, Cracow, Poland

ORCID ID: 0009-0006-0557-868X

Dominik Zajac

Central Clinical Hospital of UCC WUM, Warszawa, Poland

ORCID ID: 0009-0004-0415-5322

ABSTRACT

The clinical role of beta-blocker therapy after myocardial infarction (MI) has been debated extensively as the landscape of post-MI management has evolved. Historically, beta-blockers were established as a cornerstone of secondary prevention following landmark randomized controlled trials conducted in the 1980s (Hjalmarson, 1997) that demonstrated significant reductions in all-cause and cardiovascular mortality. However, those foundational studies were conducted before the widespread adoption of primary percutaneous coronary intervention, dual antiplatelet therapy, high-intensity statins, and renin-angiotensin-aldosterone system inhibitors, and they predominantly enrolled patients with reduced left ventricular ejection fraction (LVEF). This review comprehensively synthesizes evidence from contemporary randomized controlled trials including REDUCE-AMI (Yndigegn et al., 2024), ABYSS (Silvain et al., 2024), REBOOT-CNIC (Ibanez et al., 2025), BETAMI-DANBLOCK (Munkhaugen et al., 2025), and landmark individual patient data meta-analysis published between 2024 and 2025, that re-examine the benefits of beta-blockers stratified by LVEF. Findings uniformly demonstrate that among post-MI patients with preserved LVEF ($\geq 50\%$), long-term beta-blocker therapy does not reduce death or recurrent MI. Patients with mildly reduced LVEF (40-49%) may derive modest benefit, while those with reduced LVEF ($<40\%$) retain a clear and unambiguous indication for beta-blockade. Emerging evidence challenges the appropriateness of routine beta-blocker discontinuation and supports a personalized, ejection fraction-stratified approach. The review also evaluates guideline evolution, mechanisms of action, safety considerations, and directions for future research.

KEYWORDS

Beta-blockers, Myocardial Infarction, Ejection Fraction, Secondary Prevention, Discontinuation, Cardiovascular Outcomes

CITATION

Krzysztof Machnik, Beata Tekieli, Wojciech Krzysztof Cyran, Tatsiana Matsiusheuskaya, Weronika Cionżyńska, Bartosz Gawel, Anna Justkowska-Gebauer, Maksymilian Olesiński, Ewelina Chudyba, Michał Górecki, Dominik Zajac. (2026). Beta-blockers discontinuation after myocardial infarction referring to ejection fraction. *International Journal of Innovative Technologies in Social Science*, 3(51). [https://doi.org/10.31435/ijitss.3\(51\).2026.5994](https://doi.org/10.31435/ijitss.3(51).2026.5994)

COPYRIGHT

© The author(s) 2026. This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

1. Introduction

Acute myocardial infarction (AMI) remains one of the leading causes of morbidity and mortality worldwide, accounting for millions of hospital admissions and deaths annually. Following successful revascularization or stabilization of an acute coronary event, long-term pharmacotherapy is central to secondary prevention. For nearly five decades, beta-adrenergic receptor blockers commonly referred to as beta-blockers have occupied a foundational role in this pharmacological armamentarium. Their recommendation for routine post-MI use stems from a series of pivotal randomized controlled trials (RCTs) conducted in the late 1970s and 1980s (Hjalmarson, 1997) that demonstrated dramatic reductions in total mortality, sudden cardiac death, and reinfarction rates.

Among the most cited of these landmark studies were the Norwegian Multicenter Study Group timolol trial (Pedersen, 1983), which reported a 42.5% reduction in all-cause mortality at 33 months; the Beta-Blocker Heart Attack Trial (BHAT) ("A Randomized Trial of Propranolol in Patients with Acute Myocardial Infarction. I. Mortality Results,," 1982) using propranolol, which showed a 26% reduction in total mortality; and early metoprolol studies that achieved a 36% reduction in mortality in the acute MI setting (Hjalmarson et al., 1983). These trials established beta-blocker therapy as one of the most effective interventions in post-MI management, and the drug class subsequently became embedded in international cardiovascular guidelines.

However, a critical appraisal of this evidence reveals important contextual limitations. The seminal trials were conducted in an era before primary percutaneous coronary intervention (PCI), high-sensitivity biomarker-based diagnosis, dual antiplatelet therapy (DAPT), high-intensity statins, renin-angiotensin-aldosterone system (RAAS) inhibitors, and other cornerstone modern therapies. Furthermore, a substantial proportion of patients enrolled in those trials had large myocardial infarctions with significant left ventricular (LV) systolic dysfunction - a patient population known to derive the greatest benefit from beta-blockade through prevention of adverse ventricular remodeling, reduction of sympathetic activation, and anti-arrhythmic properties. In

contemporary clinical practice, the typical post-MI patient has a smaller infarction, preserved or near-preserved LVEF, receives early revascularization, and is discharged on multiple evidence-based medications.

This fundamental shift in the post-MI landscape raises a clinically important question: do beta-blockers continue to provide meaningful benefit in patients who have undergone successful revascularization and have preserved left ventricular function? Observational studies and earlier meta-analyses provided conflicting answers. The 2021 Cochrane review (Holt et al., 2021) underscored the critical gap: no contemporary RCTs had specifically assessed long-term beta-blocker therapy in post-MI patients without LV dysfunction.

Between 2024 and 2025, this evidence gap has been substantially narrowed by the publication of several large, well-designed RCTs and meta-analyses. The REDUCE-AMI trial (Yndigegn et al., 2024), published in the *New England Journal of Medicine* in April 2024, was the first contemporary RCT to directly randomize post-MI patients with preserved LVEF ($\geq 50\%$) to beta-blocker therapy versus no therapy. Subsequently, the ABYSS trial (Silvain et al., 2024) investigated the safety of interrupting established beta-blocker therapy in stable post-MI patients with LVEF $\geq 40\%$. In August 2025, the ESC Congress witnessed the simultaneous presentation and publication of the REBOOT-CNIC (Ibanez et al., 2025) trial and the combined BETAMI-DANBLOCK trial (Munkhaugen et al., 2025), accompanied by a landmark individual patient data (IPD) meta-analysis of all five contemporary trials (Rossello et al., 2025).

This review synthesizes the totality of this contemporary evidence, contextualized within the historical framework, guideline evolution, pathophysiological considerations, and clinical implications. The objective is to provide a comprehensive, up-to-date assessment of where beta-blockers stand in post-MI management, stratified by left ventricular ejection fraction.

2. Methodology

This review was conducted as a narrative review of the existing literature with a focus on contemporary randomized controlled trials and meta-analyses published between 2022 and 2026. A systematic search strategy was employed across PubMed/MEDLINE, EMBASE, and Cochrane Library databases using the following key search terms and their combinations: "beta-blocker," "beta-adrenergic blocker," "myocardial infarction," "ejection fraction," "preserved ejection fraction," "reduced ejection fraction," "secondary prevention," "REDUCE-AMI," "ABYSS," "REBOOT," "BETAMI," "DANBLOCK," and "discontinuation."

Eligible studies included prospective randomized controlled trials, meta-analyses, and systematic reviews evaluating the effect of beta-blocker therapy on mortality and cardiovascular outcomes in post-MI patients. Studies were stratified based on LVEF categories: preserved LVEF ($\geq 50\%$), mildly reduced LVEF (40-49%), and reduced LVEF ($< 40\%$). Observational studies and registry analyses were included as supplementary evidence where relevant. Studies from the pre-reperfusion era were reviewed for historical context. Guidelines from the European Society of Cardiology (ESC) and the American Heart Association/American College of Cardiology (AHA/ACC) relevant to this topic were also reviewed.

Data extraction focused on study design, sample size, LVEF inclusion criteria, treatment allocation, primary and secondary endpoints, follow-up duration, and key outcomes. The principal trials reviewed in depth include: REDUCE-AMI (Yndigegn et al., 2024), ABYSS (Silvain et al., 2024), REBOOT-CNIC (Ibanez et al., 2025), BETAMI-DANBLOCK (Munkhaugen et al., 2025), and the IPD meta-analysis (Rossello et al., 2025) of REBOOT, REDUCE-AMI, BETAMI, DANBLOCK, and CAPITAL-RCT (Bangalore et al., 2014). Evidence from additional referenced articles was incorporated to provide a comprehensive perspective on mechanisms, safety profiles, and guideline recommendations.

3. Results

3.1. Historical Evidence: The Foundation of Beta-Blocker Use After MI

The use of beta-blockers following AMI was established through a series of landmark RCTs conducted primarily in the 1970s and 1980s. The Norwegian Multicenter Study Group (Pedersen, 1983) demonstrated that timolol administered to post-MI survivors significantly reduced total mortality by 42.5% over 33 months compared with placebo. Similarly, the BHAT ("A Randomized Trial of Propranolol in Patients with Acute Myocardial Infarction. I. Mortality Results,") (1982) showed that long-term propranolol therapy reduced all-cause mortality by 26% and sudden death by approximately 28% in post-MI survivors over a mean follow-up of 25 months. These results were replicated by early European studies (Hjalmarson et al., 1983) using metoprolol, which reported a 36% reduction in mortality in acute MI. In aggregate, meta-analyses of these pre-

reperfusion era trials (Bangalore et al., 2014) suggested a mortality reduction of approximately 20–25% with long-term beta-blocker therapy.

Pharmacologically, the clinical benefits were attributed to several complementary actions of beta-adrenoceptor blockade: reduction in myocardial oxygen demand through negative chronotropic and inotropic effects, reduced wall stress thereby limiting adverse ventricular remodeling, anti-arrhythmic properties that lowered the threshold for ventricular fibrillation, and attenuation of the harmful neurohumoral activation that characterizes the post-infarction state. In an era when reperfusion was unavailable or delayed, large anterior MIs with substantial LV dysfunction were common, and sympathetic overdrive was a primary driver of both early and late mortality. Beta-blockade directly countered these mechanisms.

The CAPRICORN trial (Dargie, 2001), conducted in the reperfusion era but specifically enrolling post-MI patients with LV dysfunction (LVEF $\leq 40\%$), further confirmed carvedilol reduced all-cause mortality by 23% and recurrent MI by 41% in this high-risk subgroup. This trial importantly demonstrated that even in the contemporary context, with ACE inhibitors and early reperfusion, patients with reduced LVEF continue to derive substantial benefit from beta-blockade.

However, the vast majority of patients enrolled in the pre-reperfusion era trials had significantly impaired LVEF, with many not receiving the pharmacological and interventional therapies that are now standard of care. The extrapolation of these findings to modern post-MI patients with preserved LVEF has been the subject of ongoing debate, culminating in the contemporary trials reviewed below.

3.2. The REDUCE-AMI Trial (Yndigegn et al., 2024): A Pivotal Paradigm Shift

The REDUCE-AMI (Randomized Evaluation of Decreased Usage of Beta-Blockers after Acute Myocardial Infarction) trial, published in the New England Journal of Medicine in April 2024, represented the first large, prospective RCT specifically designed to address the clinical question of whether long-term beta-blocker therapy improves outcomes in post-MI patients with preserved left ventricular function in the era of modern cardiovascular care.

The trial enrolled 5,020 patients across 45 centers in Sweden, Estonia, and New Zealand. Inclusion criteria required a diagnosis of acute MI, early coronary angiography, and a confirmed LVEF of at least 50% at the time of randomization. Patients were randomly assigned in an open-label parallel-group design to receive either long-term beta-blocker therapy (metoprolol or bisoprolol, with a target dose of 100 mg and 5 mg per day, respectively) or no beta-blocker treatment. Patient enrollment spanned September 2017 through May 2023, with a median follow-up of 3.5 years (interquartile range 2.2 to 4.7 years).

The primary composite endpoint was death from any cause or new myocardial infarction. The primary endpoint occurred in 199 of 2,508 patients (7.9%) in the beta-blocker group and 208 of 2,512 patients (8.3%) in the no-beta-blocker group (hazard ratio [HR] 0.96; 95% confidence interval [CI] 0.79 to 1.16; $P=0.64$), a difference that was neither statistically nor clinically significant. Secondary endpoints including all-cause mortality (3.9% vs. 4.1%), cardiovascular mortality (1.5% vs. 1.3%), recurrent MI (4.5% vs. 4.7%), hospitalization for atrial fibrillation (1.1% vs. 1.4%), and hospitalization for heart failure (0.8% vs. 0.9%) were all similar between groups. The absence of effect was consistent across all prespecified subgroups, including patient age, sex, type of MI (STEMI vs. NSTEMI), and diabetes status.

Several contextual features of the REDUCE-AMI population are worth noting. The majority of patients (95.4%) were from Sweden and represented a well-treated, relatively lower-risk group. Approximately 95% underwent percutaneous coronary intervention, and the vast majority were discharged on modern evidence-based pharmacotherapy. In the beta-blocker group, 62.2% received metoprolol and 37.8% received bisoprolol, with median doses of 100 mg and 5 mg per day, respectively. Adherence to therapy was maintained in approximately 90% of the beta-blocker arm at one year, lending internal validity to the findings.

The REDUCE-AMI investigators concluded that, for patients with preserved LVEF undergoing early coronary angiography after AMI, routine long-term beta-blocker therapy does not reduce mortality or reinfarction. An accompanying editorial by Philippe Gabriel Steg, however, urged caution, noting that "absence of evidence is not evidence of absence" and that the trial may have been somewhat underpowered, given that observed event rates were lower than anticipated.

3.3. The ABYSS Trial (Silvain et al., 2024): The Safety of Discontinuation in Stable Patients

While REDUCE-AMI addressed the question of initiating beta-blocker therapy after MI with preserved LVEF, the ABYSS (Assessment of Beta-Blocker Interruption 1 Year after an Uncomplicated Myocardial Infarction on Safety and Symptomatic Cardiac Events Requiring Hospitalization) trial addressed a different but equally pertinent clinical question: is it safe to discontinue established long-term beta-blocker therapy in stable post-MI patients?

ABYSS was a multicentre, open-label, randomized noninferiority trial conducted at 49 centres across France. It enrolled 3,698 patients with a prior MI (more than 6 months before enrolment), all of whom had been receiving beta-blocker therapy chronically and had an LVEF of at least 40% with no major cardiovascular event in the preceding 6 months. The median time between the index MI and randomization was 2.9 years. Patients were randomized 1:1 to either interruption (n=1,846) or continuation (n=1,852) of beta-blocker therapy.

The primary composite endpoint was death, nonfatal MI, nonfatal stroke, or hospitalization for cardiovascular reasons at the longest follow-up (minimum one year), assessed using a noninferiority analysis (threshold: upper bound of 95% CI for between-group difference <3 percentage points). The primary endpoint occurred in 23.8% of the interruption group and 21.1% of the continuation group (HR 1.16; 95% CI 1.01 to 1.33; P for noninferiority = 0.44). The prespecified noninferiority criterion was not met, driven primarily by numerically greater cardiovascular hospitalizations in the interruption group (18.9% vs. 16.6%; risk difference 2.3 percentage points).

Notably, hard cardiovascular outcomes such as all-cause mortality (4.1% vs. 4.0%), MI (2.5% vs. 2.4%), and stroke (1.0% vs. 1.0%) did not differ meaningfully between groups. Quality of life as assessed by the European Quality of Life–5 Dimensions (EQ-5D) questionnaire also did not differ significantly, though the sensitivity of this instrument to detect beta-blocker-specific side effects such as fatigue, sexual dysfunction, and cold extremities has been questioned.

An important distinction from REDUCE-AMI is that ABYSS enrolled patients who were already established on beta-blocker therapy for a median of nearly three years, raising the possibility of a class effect discontinuation risk (rebound adrenergic activation) that may not apply to de novo initiation. Tomas Jernberg, in an editorial accompanying the ABYSS publication, advised that the results of additional ongoing trials be awaited before definitively updating guidelines, while acknowledging that the convergence of evidence from ABYSS and REDUCE-AMI was informative. The contrast between REDUCE-AMI (neutral initiation) and ABYSS (failed noninferiority of discontinuation) creates a nuanced clinical picture, suggesting that while starting beta-blockers in low-risk post-MI patients with preserved LVEF may not be beneficial, abruptly stopping them in patients who are already established on therapy may carry some cardiovascular risk.

3.4. REBOOT-CNIC (Ibanez et al., 2025): Confirming the Neutral Signal in a Larger Population

The REBOOT-CNIC (tREatment with Beta-blockers after myOcardial infarction withOut reduced ejection fracTion) trial was a large, pragmatic open-label RCT conducted at multiple centres in Spain and Italy. Results were simultaneously published in the New England Journal of Medicine and presented at ESC Congress 2025 in Madrid in August 2025.

REBOOT-CNIC enrolled 8,505 patients after an acute MI within 14 days of the event, with an LVEF greater than 40%. The majority of patients had a mean LVEF of approximately 57%, and about 12% had an LVEF in the mildly reduced range (40-49%). Patients were randomized to receive beta-blocker therapy (predominantly bisoprolol) or no beta-blocker. The primary composite endpoint was all-cause death, reinfarction, or hospitalization for heart failure.

Over the follow-up period, the primary endpoint occurred in 32.6 events per 1,000 patient-years in the beta-blocker arm versus 43 events per 1,000 patient-years in the no-beta-blocker arm (HR 0.75; 95% CI 0.58-0.97; P=0.03). However, when results were stratified by LVEF, the benefit was concentrated entirely in patients with mildly reduced LVEF (40-49%), with no significant benefit observed in the preserved LVEF subgroup ($\geq 50\%$). This subgroup distinction is clinically critical and consistent with the mechanistic rationale: patients with some degree of LV impairment retain the neurohumoral substrate upon which beta-blockade acts, while patients with preserved systolic function - managed with modern reperfusion and pharmacotherapy - may not.

The REBOOT sex-stratified substudy, published in the European Heart Journal in 2025, raised an additional interesting dimension: women in the REBOOT trial appeared to have numerically more adverse events when treated with beta-blockers, a finding that did not reach statistical significance in either the individual trial or in subsequent meta-analyses, but warrants further investigation given known sex-based pharmacokinetic and pharmacodynamic differences.

3.5. BETAMI-DANBLOCK (Munkhaugen et al., 2025): A Positive Signal and the LVEF Threshold

In contrast to the neutral findings of REDUCE-AMI and REBOOT-CNIC among patients with preserved LVEF, the combined BETAMI-DANBLOCK trial - presented at the same ESC Congress 2025 Hot Line session and simultaneously published in the New England Journal of Medicine - reported a statistically significant benefit of beta-blockade.

BETAMI (Norwegian Beta-Blocker Treatment after Acute Myocardial Infarction in Revascularized Patients) and DANBLOCK (Danish Trial of Beta-Blocker Treatment after Myocardial Infarction without Reduced Ejection Fraction) were parallel open-label, randomized trials in Norway and Denmark, respectively. Their combined analysis included 5,574 patients (mean age 63 years; 20.8% female) with an acute MI in the preceding 7 to 14 days and an LVEF of at least 40%. After a median follow-up of 3.5 years, the composite endpoint of all-cause death, new MI, unplanned revascularization, ischemic stroke, heart failure, or ventricular arrhythmias occurred in 14.2% of beta-blocker-treated patients and 16.3% of controls (HR 0.85; 95% CI 0.75 to 0.98; $P=0.024$).

The apparent discrepancy between BETAMI-DANBLOCK and REDUCE-AMI/REBOOT-CNIC was resolved through careful subgroup analysis: the benefit in BETAMI-DANBLOCK was concentrated in patients with mildly reduced LVEF (40-49%), a group that represented approximately 15-20% of the combined population. Among patients with strictly preserved LVEF ($\geq 50\%$), no significant benefit was observed - a finding consistent with the other trials. As explained by principal investigator Professor Dan Atar: the signal in BETAMI-DANBLOCK "likely reflects the inclusion of a non-negligible proportion of patients with mildly reduced cardiac function, a group known to benefit from beta-blockers."

3.6. Individual Patient Data Meta-Analysis (Rossello et al., 2025): Definitive Synthesis

The most authoritative synthesis of contemporary evidence was the individual patient data (IPD) meta-analysis presented at ESC Congress 2025 and simultaneously published in the New England Journal of Medicine. This analysis pooled patient-level data from five contemporary open-label randomized trials: REBOOT (7,459 patients), REDUCE-AMI (4,967 patients), BETAMI (2,441 patients), DANBLOCK (2,277 patients), and CAPITAL-RCT (657 patients) - for a total of 17,801 patients, the largest synthesis of contemporary post-MI beta-blocker data to date.

Of the 17,801 patients, 8,831 (49.6%) were assigned to beta-blocker therapy and 8,970 (50.4%) to no beta-blocker. During a median follow-up of 3.6 years (interquartile range 2.3 to 4.6), the primary composite endpoint of death from any cause, MI, or heart failure occurred in 717 patients (8.1%) in the beta-blocker group and 748 patients (8.3%) in the no-beta-blocker group (HR 0.97; 95% CI 0.87 to 1.07; $P=0.54$). All-cause mortality (HR 1.04; 95% CI 0.89 to 1.21), MI (HR 0.89; 95% CI 0.77 to 1.03), and heart failure (HR 0.87; 95% CI 0.64 to 1.19) did not differ significantly.

The meta-analysis, restricted to patients with LVEF $\geq 50\%$, unequivocally demonstrated no benefit of beta-blocker therapy. When stratified for patients with LVEF 40-49%, the IPD analysis suggested a significant benefit (HR 0.75; 95% CI 0.58-0.97), consistent with BETAMI-DANBLOCK findings. The investigators from the Beta Blocker Trialists Collaboration (BBTC) concluded: "Thanks to this collaborative effort, we now know how beta-blockers should be used after infarction: patients with preserved cardiac function (ejection fraction $\geq 50\%$) do not benefit, while those with reduced function ($<50\%$) do."

Table 1. Summary of Contemporary Randomized Controlled Trials of Beta-Blockers After Myocardial Infarction (2024–2025)

Trial	N	LVEF Criteria	Intervention	Primary Endpoint	HR (95% CI)	Conclusion
REDUCE-AMI (2024)	5,020	$\geq 50\%$	BB vs. No BB	Death or MI	0.96 (0.79–1.16)	No benefit of BB in preserved EF
ABYSS (2024)	3,698	$\geq 40\%$	BB interruption vs. continuation	Death, MI, stroke, CV hospitalization	1.16 (1.01–1.33)*	Interruption failed noninferiority; more CV hospitalizations
REBOOT-CNIC (2025)	8,505	$>40\%$	BB vs. No BB	Death, MI, or HF hospitalization	0.75 (0.58–0.97)†	Benefit only in LVEF 40–49% subgroup
BETAMI-DANBLOCK (2025)	5,574	$\geq 40\%$	BB vs. No BB	All-cause death or MACE	0.85 (0.75–0.98)	Benefit concentrated in LVEF 40–49%
IPD Meta-Analysis (2025)	17,801	$\geq 50\%$	BB vs. No BB	Death, MI, or HF	0.97 (0.87–1.07)	No benefit for preserved EF; benefit for LVEF 40–49%

BB = beta-blocker; CI = confidence interval; EF = ejection fraction; HR = hazard ratio; HF = heart failure; LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular events; MI = myocardial infarction. * Failed noninferiority threshold. † Overall result; no significant benefit in LVEF $\geq 50\%$ subgroup.

4. Discussion

4.1. Reconciling Apparently Conflicting Results

The body of contemporary evidence, when examined holistically, is more coherent than it may initially appear. The apparent discrepancy between BETAMI-DANBLOCK - which showed a positive result - and REDUCE-AMI and REBOOT-CNIC - which showed neutral results - is explained by differences in LVEF inclusion criteria and the composition of each trial population. REDUCE-AMI exclusively enrolled patients with LVEF $\geq 50\%$, while BETAMI-DANBLOCK enrolled patients with LVEF $\geq 40\%$, including a meaningful proportion (~15–20%) with mildly reduced LVEF (40–49%). The benefit observed in BETAMI-DANBLOCK appears to originate almost entirely from this mildly reduced LVEF subgroup. The IPD meta-analysis, which allows precise stratification by LVEF at the individual patient level, provides the definitive reconciliation: no benefit in LVEF $\geq 50\%$, clear benefit in LVEF 40–49%.

This EF-stratified framework aligns well with mechanistic understanding. In patients with preserved LVEF after contemporary reperfusion-based management, the degree of sympathetic nervous system activation, residual ischemia, and adverse remodelling is substantially lower than in the era of pre-reperfusion, large-MI, LV-dysfunction-predominant trials. The hemodynamic and anti-remodelling mechanisms by which beta-blockers exert benefit are less relevant when the myocardium is not significantly impaired. Conversely, patients with LVEF 40–49% retain some degree of systolic dysfunction, with a substrate of neurohumoral activation that may still be favourably modulated by beta-adrenoceptor blockade.

4.2. Mechanisms of Action: Relevance to the Contemporary Patient

Beta-blockers exert their cardiovascular effects through competitive antagonism of catecholamines at beta-1 (cardiac) and beta-2 (vascular and pulmonary) adrenergic receptors. The principal cardioprotective mechanisms include: negative chronotropy, reducing heart rate and thereby prolonging diastolic filling time and coronary perfusion; negative inotropy, lowering myocardial oxygen demand and limiting ischemic burden; reduction of wall stress, attenuating myocardial remodelling; anti-arrhythmic effects, raising the threshold for ventricular fibrillation by suppressing adrenergic-driven electrical instability; and modulation of the renin-angiotensin-aldosterone system, reducing neurohormonal activation.

In the pre-reperfusion era, these mechanisms were critically relevant because patients frequently had large, incomplete infarctions with substantial residual ischemia and LV dysfunction - conditions that create a state of sustained sympathetic overdrive. In contrast, a contemporary patient who undergoes successful primary PCI within 90 minutes of symptom onset, has a small-to-medium MI, achieves LVEF $\geq 50\%$, and is discharged on dual antiplatelet therapy, high-intensity statin, ACE inhibitor, and SGLT2 inhibitor has a very different neurohormonal milieu. Modern reperfusion significantly limits infarct size and preserves LV function, while RAAS inhibitors and statins independently reduce adrenergic activation and adverse remodeling. The incremental benefit of beta-blockade in this scenario - while biologically plausible - appears to be negligible based on the evidence reviewed.

The distinction between patients with LVEF 40-49% and $\geq 50\%$ is not merely statistical but reflects a meaningful biological difference. Even modest LV impairment is associated with evidence of maladaptive neurohumoral activation, including elevated catecholamines, renin, and angiotensin II levels, as evidenced by meta-iodobenzylguanidine (MIBG) imaging studies demonstrating sympathetic dysregulation even in HFmEF. In this context, beta-blockade continues to have a substrate for therapeutic benefit.

4.3. The ABYSS Paradox: Initiation vs. Discontinuation

The juxtaposition of REDUCE-AMI and ABYSS creates an important clinical paradox. REDUCE-AMI demonstrates that initiating beta-blockers in preserved-LVEF post-MI patients does not improve outcomes. Yet ABYSS demonstrates that discontinuing already-established beta-blocker therapy in stable post-MI patients fails the noninferiority criterion, driven by more cardiovascular hospitalizations. How can both findings be reconciled?

One explanation is the phenomenon of rebound adrenergic activation following abrupt or gradual discontinuation of chronic beta-blockade. In patients who have been receiving beta-blockers for a median of approximately three years, the cardiac beta-adrenergic receptors may have undergone upregulation (sensitization). Withdrawal of the drug can lead to a transient surge in sympathetic activity, increasing heart rate, blood pressure, and potentially triggering ischemic episodes or arrhythmias - effects that may translate into more hospitalizations without necessarily increasing hard events like death or MI. This mechanism is well recognized in patients with ischemic heart disease and is the reason beta-blocker therapy should generally be tapered rather than abruptly discontinued.

A second consideration is that the ABYSS population - stable post-MI patients who had been tolerating beta-blockers without significant side effects for years - represents a selected group in whom continuation may be relatively safe and potentially even clinically beneficial. In contrast, the REDUCE-AMI trial asked whether *de novo* initiation in all post-MI patients with preserved LVEF is warranted, a broader question with a population-level answer of "no."

Clinically, these results together suggest a nuanced approach: while routine initiation of beta-blockers in post-MI patients with preserved LVEF appears to be unnecessary, indiscriminate discontinuation in patients who are already stable on therapy carries its own risks and should be approached carefully, with individualized assessment.

4.4. Guideline Evolution: From Universal Prescription to Personalized Medicine

The shift in the evidence base has been reflected, albeit cautiously, in major international cardiovascular guidelines. The 2017 ESC guidelines for STEMI management (Ibanez et al., 2018) maintained a Class I recommendation for beta-blockers in all post-MI patients, largely based on historical evidence. However, the 2023 ESC Guidelines for the Management of Acute Coronary Syndromes (Marx et al., 2023) acknowledged that "the role of long-term beta-blocker therapy in patients without heart failure or left ventricular systolic dysfunction remains uncertain," downgrading the strength of recommendation and adding nuance. The guidelines retained a Class I, Level A recommendation for patients with LVEF $\leq 40\%$, regardless of heart failure symptoms.

In North America, the 2023 AHA/ACC Guideline for the Management of Patients with Chronic Coronary Disease (Joglar et al., 2024) introduced a Class IIb recommendation - the lowest positive level - for reassessing long-term beta-blocker therapy in post-MI patients without LVEF $\leq 50\%$ or other compelling indications, reflecting recognition of the emerging evidence. The 2025 ACC/AHA/ACEP Guidelines for Management of Patients with Acute Coronary Syndromes (Writing Committee Members* et al., 2025) similarly noted that it "may be reasonable to reassess" beta-blocker continuation in patients with preserved

LVEF. The 2024 ESC Guidelines for the Management of Chronic Coronary Syndromes (McEvoy et al., 2024) further moved toward an individualized, EF-stratified framework.

This trajectory, from universal prescription to personalized, ejection fraction–guided therapy, represents a paradigm shift that will likely continue as the full impact of the 2025 ESC Hot Line trials is incorporated into future guideline revisions. However, international guidelines tend to evolve conservatively, and clinicians should expect a period of practice heterogeneity as individual societies update their recommendations.

4.5. Safety, Tolerability, and Quality of Life Considerations

While much of the debate has focused on efficacy, the safety and tolerability of beta-blockers are equally important considerations, particularly given the substantial pill burden experienced by post-MI patients who are typically prescribed four to six medications. Beta-blocker side effects that affect quality of life include fatigue, exercise intolerance, sexual dysfunction, cold extremities, depression, and sleep disturbances. These adverse effects are particularly relevant in younger, active patients in whom beta-blockers may limit physical recovery and rehabilitation.

The ABYSS trial used the EQ-5D instrument to assess quality of life and found no significant improvement in patients who discontinued beta-blockers. However, the EQ-5D has been criticized as insensitive to the specific side effect profile of beta-blockers, which primarily affects dimensions not captured by the five items of the questionnaire. Future trials incorporating more sensitive quality-of-life instruments should address this limitation.

Additional safety considerations include the potential for bradycardia and hypotension, particularly in elderly patients or those with concomitant calcium channel blockers. In patients with significant obstructive pulmonary disease, non-selective beta-blockers may exacerbate bronchospasm, though cardioselective beta-1 selective agents (bisoprolol, metoprolol) are generally tolerable even in mild asthma. The aggregate benefit-risk ratio for beta-blockers in preserved-LVEF post-MI patients, considering the lack of demonstrated benefit alongside the potential for side effects and drug interactions, tips increasingly in favour of individualized, rather than universal, prescribing.

4.6. Special Populations and Subgroup Considerations

Several special populations warrant specific attention. In elderly patients (>75 years), the balance between potential benefits and the risk of bradycardia, falls, fatigue, and drug interactions may differ substantially from younger cohorts. The REDUCE-AMI and REBOOT-CNIC trials did not demonstrate differential effects in older patients, suggesting that preserved-LVEF post-MI older adults do not derive benefit from beta-blockers, while the added burden of side effects remains relevant.

Sex-based differences represent an emerging area of interest. As noted, the REBOOT trial sex-stratified analysis (Rossello et al., 2026) suggested that women treated with beta-blockers had numerically more adverse events, a finding that was not statistically significant in the overall IPD meta-analysis but warrants further investigation. Known pharmacokinetic differences between sexes - including greater bioavailability and higher plasma concentrations in women for most beta-blockers - may underlie differential efficacy and tolerability.

In patients with diabetes mellitus, beta-blockers may mask hypoglycaemic symptoms and alter glycaemic regulation; in this subgroup, the absence of a clear benefit further supports a selective prescribing approach. Patients with concurrent atrial fibrillation or heart failure with reduced ejection fraction retain strong, distinct indications for beta-blockade independent of post-MI considerations (Yang et al., 2025).

The question of optimal beta-blocker type, dose, and duration also remains unresolved. Most contemporary trials used bisoprolol or metoprolol succinate at moderate doses. Whether carvedilol, with its additional alpha-1 blocking activity, or nebivolol, with its vasodilatory properties, might confer differential benefits in specific subgroups remains an open question not addressed by the current evidence base.

5. Conclusions

The evidence landscape for beta-blocker therapy after myocardial infarction has undergone a fundamental transformation in 2024-2025. A convergence of large, well-designed randomized controlled trials: REDUCE-AMI, REBOOT-CNIC, BETAMI-DANBLOCK, and the individual patient data meta-analysis of 17,801 patients has established a clear, ejection fraction-stratified framework for clinical decision-making:

For patients with preserved LVEF ($\geq 50\%$) after contemporary MI management, long-term beta-blocker therapy does not reduce mortality, recurrent MI, or heart failure hospitalization. Routine initiation in this population is not supported by the available evidence and may add unnecessary pill burden and side effects. Current evidence supports a selective approach in which these patients are not routinely prescribed beta-blockers unless other indications (such as atrial fibrillation, heart failure, or symptomatic angina) are present.

For patients with mildly reduced LVEF (40-49%), emerging evidence from BETAMI-DANBLOCK and the IPD meta-analysis suggests a modest but statistically significant benefit of beta-blocker therapy, consistent with the mechanistic rationale of neurohumoral modulation in the presence of LV dysfunction. These patients should continue to receive beta-blockers as part of guideline-directed medical therapy.

For patients with reduced LVEF ($<40\%$), the evidence base - including CAPRICORN and older extensive heart failure trials (MERIT-HF (Wikstrand, 2000), CIBIS-II ("The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): A Randomised Trial," 1999), COPERNICUS (Eichhorn & Bristow, 2001)) - provides an unambiguous and strong indication for beta-blocker therapy, regardless of concurrent post-MI management.

Regarding discontinuation, the ABYSS trial cautions against indiscriminate withdrawal of established beta-blocker therapy in stable post-MI patients, as this may increase cardiovascular hospitalization risk, potentially through rebound adrenergic activation. In patients already on beta-blockers who tolerate therapy well and have preserved LVEF, the decision to continue or discontinue should be individualized, with careful consideration of side effect burden, patient preferences, and comorbidities.

The transition from universal beta-blocker prescription to a personalized, ejection fraction-guided approach represents a clinically meaningful application of contemporary evidence. Future research should address several remaining gaps: the optimal duration of beta-blocker therapy in LVEF 40-49% patients, the role of novel beta-blockers and personalized dosing strategies, sex-based differences in treatment response, and quality-of-life outcomes measured with more sensitive instruments. Guidelines are expected to continue evolving, and clinicians should remain attentive to forthcoming updates from ESC and ACC/AHA expert committees.

In conclusion, the evidence now compels a departure from the historical paradigm of routine beta-blocker prescribing for all post-MI patients. A stratified, patient-centred approach guided by LVEF measurement and clinical context represents the new standard of care in contemporary cardiovascular medicine.

Author Contributions:

Conceptualization, K.M. and B.T.; methodology, W.C. and B.G.; validation, B.T.; formal analysis, B.T. and A.J.G.; investigation, W.K.C. and D.Z.; resources, T.M. and M.G.; writing - rough preparation, B.T. and E.C.; writing - review and editing, B.T., W.C., K.M., M.G.; visualization, E.C., M.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflict of interests: The authors declare no conflict of interests.

Acknowledgements: The authors would like to thank the principal investigators and clinical research teams of the REDUCE-AMI, ABYSS, REBOOT-CNIC, BETAMI-DANBLOCK trials, whose landmark work provided the foundational data for this review.

REFERENCES

1. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. (1982). *JAMA*, 247(12), 1707–1714. <https://doi.org/10.1001/jama.1982.03320370021023>
2. Bangalore, S., Makani, H., Radford, M., Thakur, K., Toklu, B., Katz, S. D., DiNicolantonio, J. J., Devereaux, P. J., Alexander, K. P., Wetterslev, J., & Messerli, F. H. (2014). Clinical outcomes with β -blockers for myocardial infarction: A meta-analysis of randomized trials. *The American Journal of Medicine*, 127(10), 939–953. <https://doi.org/10.1016/j.amjmed.2014.05.032>
3. Dargie, H. J. (2001). Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: The CAPRICORN randomised trial. *Lancet (London, England)*, 357(9266), 1385–1390. [https://doi.org/10.1016/s0140-6736\(00\)04560-8](https://doi.org/10.1016/s0140-6736(00)04560-8)
4. Eichhorn, E. J., & Bristow, M. R. (2001). The Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) trial. *Current Controlled Trials in Cardiovascular Medicine*, 2(1), 20–23. <https://doi.org/10.1186/cvm-2-1-020>
5. Hjalmarson, A. (1997). Effects of beta blockade on sudden cardiac death during acute myocardial infarction and the postinfarction period. *The American Journal of Cardiology*, 80(9B), 35J–39J. [https://doi.org/10.1016/s0002-9149\(97\)00837-0](https://doi.org/10.1016/s0002-9149(97)00837-0)
6. Hjalmarson, A., Herlitz, J., Holmberg, S., Rydén, L., Swedberg, K., Vedin, A., Waagstein, F., Waldenström, A., Waldenström, J., Wedel, H., Wilhelmsen, L., & Wilhelmsson, C. (1983). The Göteborg metoprolol trial. Effects on mortality and morbidity in acute myocardial infarction. *Circulation*, 67(6 Pt 2), I26–32.
7. Holt, A., Blanche, P., Zareini, B., Rajan, D., El-Sheikh, M., Schjerning, A.-M., Schou, M., Torp-Pedersen, C., McGettigan, P., Gislason, G. H., & Lamberts, M. (2021). Effect of long-term beta-blocker treatment following myocardial infarction among stable, optimally treated patients without heart failure in the reperfusion era: A Danish, nationwide cohort study. *European Heart Journal*, 42(9), 907–914. <https://doi.org/10.1093/eurheartj/ehaa1058>
8. Ibanez, B., James, S., Agewall, S., Antunes, M. J., Bucciarelli-Ducci, C., Bueno, H., Caforio, A. L. P., Crea, F., Goudevenos, J. A., Halvorsen, S., Hindricks, G., Kastrati, A., Lenzen, M. J., Prescott, E., Roffi, M., Valgimigli, M., Varenhorst, C., Vranckx, P., Widimský, P., & ESC Scientific Document Group. (2018). 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal*, 39(2), 119–177. <https://doi.org/10.1093/eurheartj/ehx393>
9. Ibanez, B., Latini, R., Rossello, X., Dominguez-Rodriguez, A., Fernández-Vazquez, F., Pelizzoni, V., Sánchez, P. L., Anguita, M., Barrabés, J. A., Raposeiras-Roubín, S., Pocock, S., Escalera, N., Staszewsky, L., Pérez-García, C. N., Díez-Villanueva, P., Pérez-Rivera, J.-A., Prada-Delgado, O., Owen, R., Pizarro, G., ... REBOOT-CNIC Investigators. (2025). Beta-Blockers after Myocardial Infarction without Reduced Ejection Fraction. *The New England Journal of Medicine*, 393(19), 1889–1900. <https://doi.org/10.1056/NEJMoa2504735>
10. Joglar, J. A., Chung, M. K., Armbruster, A. L., Benjamin, E. J., Chyou, J. Y., Cronin, E. M., Deswal, A., Eckhardt, L. L., Goldberger, Z. D., Gopinathannair, R., Gorenek, B., Hess, P. L., Hlatky, M., Hogan, G., Ibeh, C., Indik, J. H., Kido, K., Kusumoto, F., Link, M. S., ... Peer Review Committee Members. (2024). 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*, 149(1), e1–e156. <https://doi.org/10.1161/CIR.0000000000001193>
11. Marx, N., Federici, M., Schütt, K., Müller-Wieland, D., Ajjan, R. A., Antunes, M. J., Christodorescu, R. M., Crawford, C., Di Angelantonio, E., Eliasson, B., Espinola-Klein, C., Fauchier, L., Halle, M., Herrington, W. G., Kautzky-Willer, A., Lambrinou, E., Lesiak, M., Lettino, M., McGuire, D. K., ... ESC Scientific Document Group. (2023). 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. *European Heart Journal*, 44(39), 4043–4140. <https://doi.org/10.1093/eurheartj/ehad192>
12. McEvoy, J. W., McCarthy, C. P., Bruno, R. M., Brouwers, S., Canavan, M. D., Ceconi, C., Christodorescu, R. M., Daskalopoulou, S. S., Ferro, C. J., Gerdts, E., Hanssen, H., Harris, J., Lauder, L., McManus, R. J., Molloy, G. J., Rahimi, K., Regitz-Zagrosek, V., Rossi, G. P., Sandset, E. C., ... ESC Scientific Document Group. (2024). 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *European Heart Journal*, 45(38), 3912–4018. <https://doi.org/10.1093/eurheartj/ehae178>
13. Munkhaugen, J., Kristensen, A. M. D., Halvorsen, S., Holmager, T., Olsen, M. H., Bakken, A., Sehested, T. S. G., Ruddox, V., Mæng, M., Vikenes, K., Jensen, S. E., Steigen, T., Lambrechtsen, J., Jortveit, J., Bovin, A., Schirmer, H., Christiansen, M. K., Wiseth, R., Mikkelsen, D., ... BETAMI–DANBLOCK Investigators. (2025). Beta-Blockers after Myocardial Infarction in Patients without Heart Failure. *The New England Journal of Medicine*, 393(19), 1901–1911. <https://doi.org/10.1056/NEJMoa2505985>

14. Pedersen, T. R. (1983). The Norwegian Multicenter Study of Timolol after Myocardial Infarction. *Circulation*, 67(6 Pt 2), 149-53.
15. Rossello, X., Dominguez-Rodriguez, A., Latini, R., Sánchez, P. L., Raposeiras-Roubín, S., Anguita, M., Barrabés, J. A., Grigis, G., Owen, R., Pocock, S., Gómez-Talavera, S., García-Lunar, I., Escalera, N., Pérez-García, C. N., Di Fusco, S. A., Pizarro, G., López Benito, M., Pongetti, G., Rincón-Díaz, L. M., ... Ibanez, B. (2026). Beta-blockers after myocardial infarction: Effects according to sex in the REBOOT trial. *European Heart Journal*, 47(6), 701–715. <https://doi.org/10.1093/eurheartj/ehaf673>
16. Rossello, X., Prescott, E. I. B., Kristensen, A. M. D., Latini, R., Fuster, V., Fagerland, M. W., Pocock, S. J., Halvorsen, S., Dominguez-Rodriguez, A., Holmager, T. L. F., Sanchez, P. L., Bakken, A., Raposeiras-Roubin, S., Jensen, S. E., Kimura, T., Ottani, F., Lambrechtsen, J., Anguita, M., Ozasa, N., ... Munkhaugen, J. (2025). β blockers after myocardial infarction with mildly reduced ejection fraction: An individual patient data meta-analysis of randomised controlled trials. *Lancet (London, England)*, 406(10508), 1128–1137. [https://doi.org/10.1016/S0140-6736\(25\)01592-2](https://doi.org/10.1016/S0140-6736(25)01592-2)
17. Silvain, J., Cayla, G., Ferrari, E., Range, G., Puymirat, E., Delarche, N., Guedeney, P., Cuisset, T., Ivanès, F., Lhermusier, T., Petroni, T., Lemesle, G., Bresoles, F., Labeque, J.-N., Pommier, T., Dillinger, J.-G., Leclercq, F., Boccara, F., Lim, P., ... ABYSS Investigators of the ACTION Study Group. (2024). Beta-Blocker Interruption or Continuation after Myocardial Infarction. *The New England Journal of Medicine*, 391(14), 1277–1286. <https://doi.org/10.1056/NEJMoa2404204>
18. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): A randomised trial. (1999). *Lancet (London, England)*, 353(9146), 9–13.
19. Wikstrand, J. (2000). MERIT-HF--description of the trial. *Basic Research in Cardiology*, 95 Suppl 1, I90-7. <https://doi.org/10.1007/s003950070016>
20. Writing Committee Members*, Jones, D. W., Ferdinand, K. C., Taler, S. J., Johnson, H. M., Shimbo, D., Abdalla, M., Altieri, M. M., Bansal, N., Bello, N. A., Bress, A. P., Carter, J., Cohen, J. B., Collins, K. J., Commodore-Mensah, Y., Davis, L. L., Egan, B., Khan, S. S., Lloyd-Jones, D. M., ... Williamson, J. D. (2025). 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Hypertension (Dallas, Tex. : 1979)*, 82(10), e212–e316. <https://doi.org/10.1161/HYP.0000000000000249>
21. Yang, W., Sun, X., Zhang, Y., Lu, Z., Shu, Z., & Zhang, K. (2025). β -blocker and clinical outcomes in patients after myocardial infarction: A systematic review and meta-analysis. *European Journal of Clinical Pharmacology*, 81(12), 1807–1817. <https://doi.org/10.1007/s00228-025-03919-2>
22. Yndigegn, T., Lindahl, B., Mars, K., Alfredsson, J., Benatar, J., Brandin, L., Erlinge, D., Hallen, O., Held, C., Hjalmarsson, P., Johansson, P., Karlström, P., Kellerth, T., Marandi, T., Ravn-Fischer, A., Sundström, J., Östlund, O., Hofmann, R., Jernberg, T., & REDUCE-AMI Investigators. (2024). Beta-Blockers after Myocardial Infarction and Preserved Ejection Fraction. *The New England Journal of Medicine*, 390(15), 1372–1381. <https://doi.org/10.1056/NEJMoa2401479>