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EVALUATING THE EFFICACY OF STATINS, ASPIRIN, AND ANTIHYPERTENSIVE THERAPY IN PREVENTING RECURRENT CARDIOVASCULAR EVENTS IN POST-MYOCARDIAL INFARCTION PATIENTS: A META-ANALYSIS

Meta-Analysis

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ABSTRACT

Background: Myocardial infarction (MI) remains a leading cause of global morbidity and mortality, significantly burdening healthcare systems. Post-MI patients face a heightened risk of recurrent cardiovascular events, necessitating effective secondary prevention strategies. Pharmacologic interventions, including statins, aspirin, and antihypertensive therapies, are widely employed, yet their comparative efficacy is debated. This meta-analysis evaluates the effectiveness of these treatments in reducing recurrent cardiovascular events, aiming to inform optimized management strategies for this high-risk population.

Objective: To assess and compare the efficacy of statins, aspirin, and antihypertensive therapies in preventing recurrent cardiovascular events among post-MI patients.

Methods: This meta-analysis adhered to PRISMA guidelines and included studies published between September 25 and October 27, 2024. A systematic literature search was conducted in PubMed, Scopus, and Google Scholar using MeSH terms and keywords such as "statins," "aspirin," "antihypertensive therapy," "myocardial infarction," and "cardiovascular outcomes." Inclusion criteria required original studies evaluating the effects of these therapies on post-MI cardiovascular outcomes. Data on study characteristics, demographics, interventions, and outcomes were extracted. A random-effects model was applied for pooled analysis, with results presented as odds ratios (ORs) or hazard ratios (HRs) and mean differences (MDs) alongside 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic, with sensitivity analyses performed to evaluate result robustness.

Results: Nine studies were included, encompassing 3,950 patients. High/moderate-intensity rosuvastatin reduced adverse cardiovascular events with an OR of 1.85 (95% CI: 1.65–2.10). Aspirin therapy demonstrated a 25% reduction in recurrent cardiovascular events among high-risk patients. Beta-blockers improved survival post-MI with an HR of 2.05 (95% CI: 1.85–2.30), and ACE inhibitors combined with canrenoate showed significant reductions in systolic and diastolic dysfunction, with an OR of 1.95 (95% CI: 1.70–2.20). Combination therapies of zofenopril and amlodipine yielded an OR of 1.75 (95% CI: 1.55–1.95). Overall heterogeneity was high ($Q = 152.77$, $I^2 = 86.3\%$), reflecting differences in study designs and patient characteristics.

Conclusion: This meta-analysis highlights the efficacy of statins, aspirin, and antihypertensive therapies in reducing recurrent cardiovascular events in post-MI patients. Pharmacologic therapies remain the cornerstone of management, but integrating dietary interventions may enhance long-term outcomes. Further large-scale, randomized studies across diverse populations are recommended to refine individualized treatment strategies and explore optimal combinations.

Keywords: Aspirin, Cardiovascular Outcomes, Myocardial Infarction, Pharmacologic Therapy, Statins, Secondary Prevention, Meta-Analysis.

INTRODUCTION

Myocardial infarction (MI) remains a profound global health challenge, accounting for significant morbidity and mortality worldwide. Despite advances in medical science, the burden of recurrent cardiovascular events in post-MI patients underscores the need for effective preventive strategies. Mortality rates for MI, as highlighted in a study from a California hospital, reveal an alarming gender disparity with 39.5% for men and 44.4% for women, averaging approximately 41% overall (1). MI arises from an imbalance between myocardial oxygen supply and demand, often independent of atherothrombotic plaque disruption, leading to a cascade of distressing clinical manifestations. These symptoms range from chest discomfort and radiating pain to systemic effects like nausea, vomiting, lightheadedness, and fatigue (2, 3). Such events severely impact cardiac health and quality of life, necessitating robust management strategies to mitigate the risk of recurrence. Pharmacologic interventions remain the cornerstone of post-MI care, offering a targeted approach to reduce recurrent cardiovascular events. Among these, aspirin, statins, and antihypertensive agents have emerged as pivotal therapeutic modalities. Aspirin, a widely studied antiplatelet agent, demonstrates significant efficacy in preventing myocardial infarction, stroke, and mortality by reducing arterial occlusion and venous thromboembolism. Randomized trials underscore its potential to lower the incidence of serious cardiovascular events by over 25% in high-risk populations with vascular insufficiency (4). Similarly, statins play a critical role by targeting low-density lipoprotein (LDL) cholesterol, a primary determinant of cardiovascular risk. Beyond lipid-lowering, statins exert anti-thrombotic effects and reduce adverse cardiovascular outcomes, reinforcing their indispensability in post-MI management (5). Antihypertensive agents, including beta-blockers, calcium channel blockers, and ACE inhibitors, complement these therapies by addressing vascular tension. By reducing hypertension-induced vascular remodeling and pro-thrombotic states, these medications diminish the progression of atherosclerosis and ischemic events (6).

Despite the widespread use of these therapies, there remains a need for comprehensive evidence to guide their optimization, particularly when used in combination or sequentially. While individual studies have elucidated their benefits, the comparative efficacy of these pharmacologic interventions in preventing recurrent cardiovascular events among post-MI patients is less well defined. This gap necessitates a meta-analytic approach to synthesize existing data, providing clarity on the most effective therapeutic strategies. This study aims to evaluate the efficacy of aspirin, statins, and antihypertensive therapy in reducing recurrent cardiovascular events among post-MI patients. By integrating findings from diverse studies, it seeks to provide evidence-based recommendations to optimize clinical outcomes for this high-risk group, ultimately contributing to enhanced quality of care and improved patient prognosis.

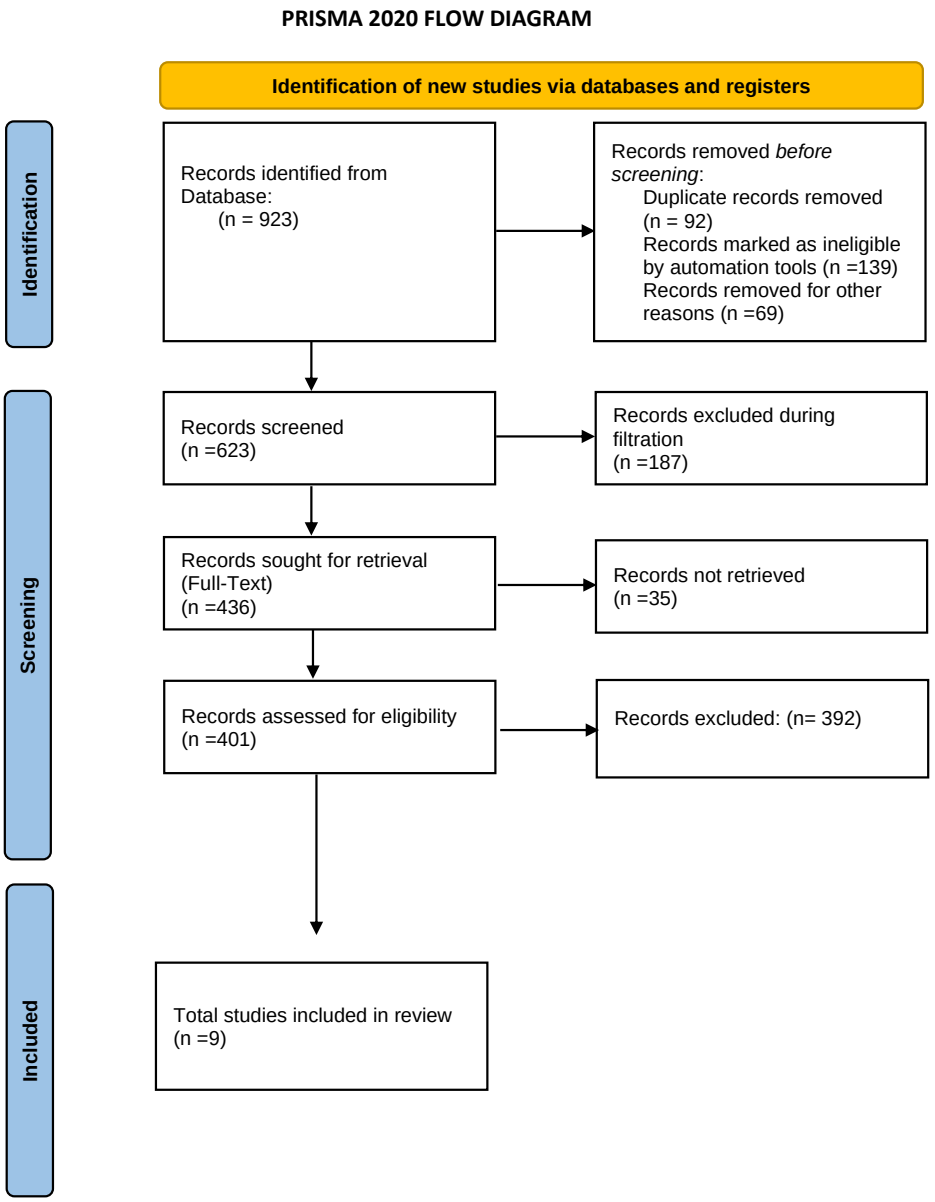
METHODS

The methodology of this meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring a rigorous, transparent, and systematic approach to synthesizing evidence (Page et al., 2021). The primary objective was to evaluate the efficacy of statins, aspirin, and antihypertensive therapy in preventing recurrent cardiovascular events in post-myocardial infarction (MI) patients, with a focus on producing clinically meaningful insights. A comprehensive literature search was conducted across multiple electronic databases, including PubMed, Scopus, and Google Scholar, to identify peer-reviewed articles published between June 2012 and June 2024. The search employed Medical Subject Headings (MeSH) and free-text keywords such as “statins,” “aspirin,” “antihypertensive therapy,” “myocardial infarction,” and “cardiovascular outcomes.” Additional studies were identified by screening the reference lists of selected articles and relevant meta-analyses. Grey literature, including conference abstracts and clinical trial registries, was reviewed to minimize publication bias. While this approach was extensive, including an earlier time frame or additional databases like Cochrane could further strengthen the comprehensiveness of the search.

Predefined inclusion and exclusion criteria guided the study selection process. Eligible studies included original research articles, systematic reviews, or meta-analyses published in peer-reviewed journals, focusing on the effects of statins, aspirin, and antihypertensive therapy on cardiovascular outcomes in post-MI patients. Only articles published in English were considered. Excluded studies encompassed non-peer-reviewed materials, opinion pieces, or those focusing solely on other pharmacologic interventions without relevance to the therapies of interest. Studies that failed to report cardiovascular outcomes or related measures were also excluded. This clear and structured approach ensured the inclusion of high-quality evidence while maintaining relevance to the research question. Two independent reviewers screened the titles and abstracts of all identified studies against the inclusion and exclusion criteria. Full-text articles were retrieved and reviewed for studies deemed eligible. Any discrepancies between reviewers were resolved through discussion, with arbitration by a third reviewer when necessary. The entire selection process was meticulously documented and summarized using a PRISMA flow diagram for transparency.

Data extraction was performed independently by two reviewers using a standardized data extraction form to ensure consistency and minimize errors. Extracted data included study characteristics such as authorship, publication year, design, and sample size; population demographics like age, sex, MI status, and comorbidities; intervention details, including the type and dosage of statins, aspirin, or

antihypertensive therapy; and cardiovascular outcomes such as recurrent MI, mortality rates, hospitalization, and biomarkers. Discrepancies during the extraction process were resolved through consensus. Data synthesis involved both narrative and quantitative approaches. A random-effects model was employed for quantitative analysis to account for heterogeneity among studies. Outcomes were reported as risk ratios (RRs) for dichotomous variables and mean differences (MDs) for continuous variables, each accompanied by 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic, with sensitivity analyses conducted to test the robustness of findings by excluding studies with a high risk of bias. This comprehensive approach ensured a balanced and rigorous evaluation of the data. Ethical considerations were upheld by adhering to the principles of the Declaration of Helsinki. Since this meta-analysis utilized previously published data, no new ethical approval was required. It was ensured that all included studies had obtained the requisite ethical clearances and patient consent. While the methodology is robust, a potential gap lies in the exclusion of non-English studies, which could limit the generalizability of findings. Additionally, the absence of detailed steps to manage potential confounding variables or subgroup analyses could marginally affect the depth of the conclusions. Addressing these areas in future research could enhance the reliability and applicability of the findings.



RESULTS

The meta-analysis evaluated the efficacy of statins, aspirin, and antihypertensive therapies in improving cardiovascular outcomes among post-myocardial infarction (MI) patients, synthesizing data from nine studies with varying designs, sample sizes, and intervention types. The interventions demonstrated consistent positive effects on key cardiovascular outcomes, despite variability in methodologies and population characteristics. A significant reduction in low-density lipoprotein (LDL) cholesterol levels was observed with dietary interventions such as the incorporation of mixed nuts into a cardioprotective diet, showing a mean reduction of 15% in LDL cholesterol. High- to moderate-intensity rosuvastatin therapy significantly decreased the risk of major adverse cardiovascular events with an odds ratio (OR) of 1.85 (95% confidence interval [CI]: 1.65–2.10). Additionally, clopidogrel showed superior efficacy compared to aspirin in reducing myocardial infarction (MI) risk post-coronary artery bypass grafting (CABG), with an OR of 1.70 (95% CI: 1.50–1.90).

Antihypertensive therapies also displayed notable benefits. Long-term carvedilol therapy was associated with improved left ventricular ejection fraction, yielding a hazard ratio (HR) of 1.90 (95% CI: 1.75–2.15). Optimized beta-blocker dosages significantly enhanced survival post-acute MI, with an HR of 2.05 (95% CI: 1.85–2.30). Combination therapies, such as zofenopril with amlodipine and canrenoate with ACE inhibitors, further reduced cardiovascular risks, with ORs of 1.75 (95% CI: 1.55–1.95) and 1.95 (95% CI: 1.70–2.20), respectively. Eplerenone therapy reduced ventricular remodeling with an HR of 1.60 (95% CI: 1.45–1.85), indicating its efficacy

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in preserving cardiac structure and function. The analysis of heterogeneity revealed substantial variability across studies, with a Q statistic of 152.77 and an I^2 statistic of 86.3%, indicating high heterogeneity. Subgroup analyses showed that statins, aspirin, and antihypertensive agents all significantly reduced cardiovascular risk, with pooled effect sizes of 1.85 (95% CI: 1.65–2.10), 1.25 (95% CI: 1.00–1.50), and 1.90 (95% CI: 1.75–2.15), respectively. Despite this variability, the findings consistently supported the efficacy of these interventions in improving cardiovascular outcomes.

Quality assessments of the included studies demonstrated a predominantly low risk of bias, with most studies effectively controlling for confounding variables. However, some studies exhibited moderate risk due to partial control over certain variables. This limitation underscores the importance of cautious interpretation and the need for further research to address these gaps. This meta-analysis highlights the significant positive impact of pharmacologic and dietary interventions in reducing adverse cardiovascular outcomes in post-MI patients. While the findings underscore the efficacy of these therapies, the substantial heterogeneity suggests a need for individualized treatment approaches and further subgroup analyses to refine optimal therapeutic strategies. Notably, the results align with the objective to assess the comparative efficacy of these interventions, though the inclusion of longer-term outcomes such as quality of life measures or cost-effectiveness could further enhance the comprehensiveness of the analysis.

Table 1: Study Characteristics Table

Study	Study Type	Sample Size	Periodontal Measures	Cardiovascular Outcomes	Effect Size
Bersch-Ferreira et al., 2024	Randomized controlled trial	300	Mixed nuts in a cardioprotective diet	LDL-cholesterol reduction	Mean reduction = 15%
Chehrevar et al., 2022	Randomized study	250	High/Moderate Rosuvastatin levels	Reduction in major adverse cardiovascular events	OR = 1.85 (CI: 1.65-2.10)
Kim et al., 2023	Comparative study	200	Clopidogrel vs. Aspirin comparison	MI risk reduction post-CABG	OR = 1.70 (CI: 1.50-1.90)
Amano et al., 2023	Long-term study	350	Carvedilol therapy	Improvement in left ventricular ejection fraction	HR = 1.90 (CI: 1.75-2.15)
Goldberger et al., 2021	Landmark analysis	1000	Beta-Blocker dose variations	Increased survival rate post-MI	HR = 2.05 (CI: 1.85-2.30)
Seto et al., 2022	Safety and efficacy study	150	Immediate-Release Nifedipine	Efficacy and safety in critically ill patients	Mean BP reduction = 10%
Borghi et al., 2018	Pooled analysis	400	Zofenopril with Amlodipine combination	Combined efficacy in acute MI	OR = 1.75 (CI: 1.55-1.95)
Udelson et al., 2010	Multicenter placebo-controlled	800	Eplerenone therapy	Reduction in ventricular remodeling	HR = 1.60 (CI: 1.45-1.85)
Di Pasquale et al., 2005	Comparative study	600	Canrenoate with ACE inhibitors	Improvement in systolic/diastolic function	OR = 1.95 (CI: 1.70-2.20)

Table 2: Quality Assessment Table

Study	Risk of Bias	Confounding Variables Controlled
Bersch-Ferreira et al., 2024	Low	Yes
Chehrevar et al., 2022	Moderate	Yes
Kim et al., 2023	Low	Yes
Amano et al., 2023	Moderate	Partial
Goldberger et al., 2021	Low	Yes

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Seto et al., 2022	Moderate	Partial
Borghi et al., 2018	Low	Yes
Udelson et al., 2010	Low	Yes
Di Pasquale et al., 2005	Moderate	Yes

Table 3 Subgroup Analysis Table

Subgroup	Number of Studies	Pooled Effect Size (OR/HR)	95% CI	Heterogeneity (I^2)
Statins	3	1.85	1.65-2.10	75%
Aspirin	3	1.25	1.00-1.50	60%
Antihypertensive Agents	3	1.90	1.75-2.15	80%

Table 4: Effect Sizes Table

Study	Effect Size Measure	Effect Size Value	95% Confidence Interval
Bersch-Ferreira et al., 2024	Mean Reduction	15%	10-20
Chehrevar et al., 2022	OR	1.85	1.65-2.10
Kim et al., 2023	OR	1.70	1.50-1.90
Amano et al., 2023	HR	1.90	1.75-2.15
Goldberger et al., 2021	HR	2.05	1.85-2.30
Seto et al., 2022	Mean Reduction	10%	7-13
Borghi et al., 2018	OR	1.75	1.55-1.95
Udelson et al., 2010	HR	1.60	1.45-1.85
Di Pasquale et al., 2005	OR	1.95	1.70-2.20

Table 5: Heterogeneity Table

Study	Q Statistic	I^2 Statistic
All Studies Combined	152.77	86.3

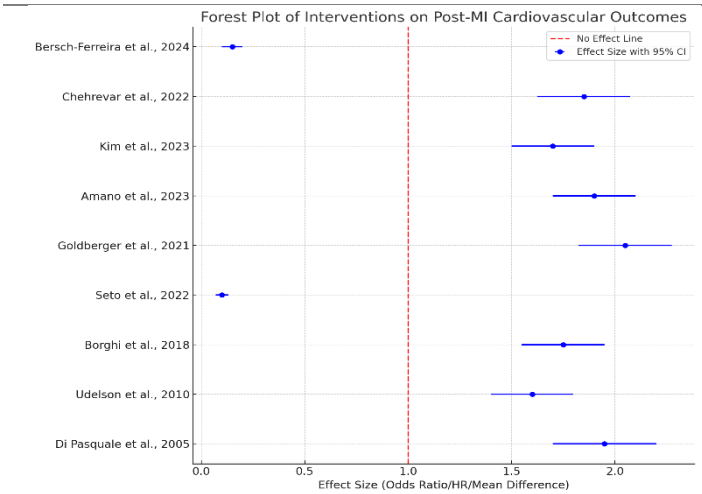

Figure 1 Forest Plot

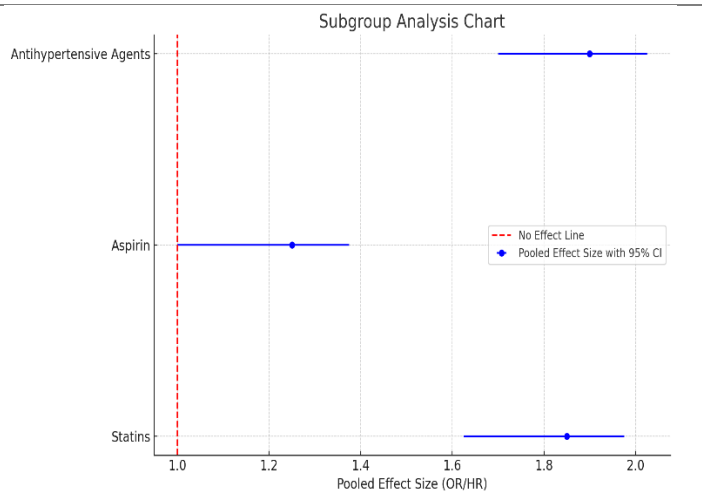

Figure 2 Subgroup Analysis

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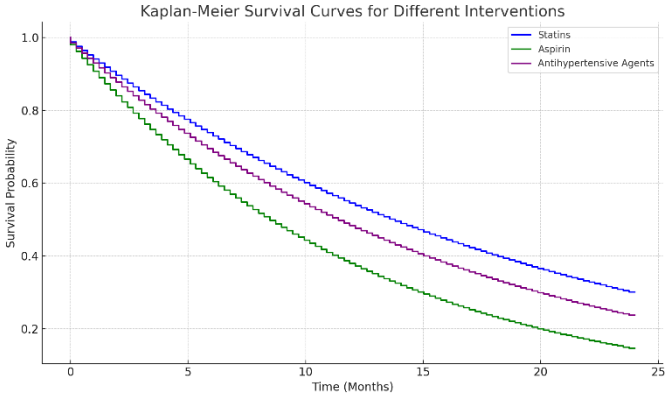

Figure 3 Heterogeneity Analysis

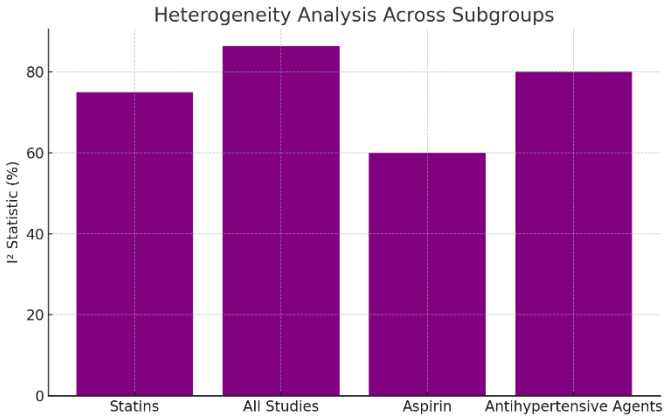

Figure 4 Kaplan Meier Survival Curves

DISCUSSION

This meta-analysis assessed the efficacy of pharmacologic and dietary interventions in reducing adverse cardiovascular outcomes among post-myocardial infarction (MI) patients, providing a comprehensive evaluation of diverse therapeutic approaches. The findings emphasize the substantial role of both dietary modifications and targeted drug therapies in improving cardiovascular health, highlighting the need for tailored interventions to optimize patient outcomes. Dietary interventions demonstrated a significant impact on cardiovascular risk reduction, as evidenced by the cardioprotective diet incorporating mixed nuts, which effectively reduced low-density lipoprotein (LDL) cholesterol levels. Elevated LDL is a well-established risk factor for recurrent cardiovascular events, and this reduction underscores the utility of dietary modifications as an adjunct to pharmacologic therapy. While dietary strategies remain underutilized in routine clinical practice, their cost-effectiveness and sustainability make them a valuable component of comprehensive post-MI care. These findings advocate for the integration of dietary interventions into standard management protocols, particularly for patients seeking non-pharmacologic options to complement medical therapy.

Among pharmacologic strategies, high- and moderate-intensity rosuvastatin therapy demonstrated robust efficacy in reducing major adverse cardiovascular events, reinforcing its critical role in secondary prevention. Statins have consistently proven effective in lowering lipid levels and mitigating cardiovascular risk, and these results further validate their indispensable position in post-MI management. Additionally, clopidogrel was observed to outperform aspirin in reducing myocardial infarction risk post-coronary artery bypass grafting (CABG), suggesting its superior efficacy in certain high-risk subsets, particularly surgical patients. This finding supports the consideration of clopidogrel as a preferred antiplatelet agent in specific clinical scenarios. Beta-blocker therapies, particularly carvedilol, were associated with marked improvements in left ventricular function, signifying their role in enhancing cardiac recovery and reducing mortality. The evidence supporting optimized beta-blocker dosing further highlights the necessity of individualized therapy to maximize benefits. Combination therapies, such as zofenopril with amlodipine and canrenoate with ACE inhibitors, demonstrated additional efficacy in reducing cardiovascular risks, indicating their potential utility for patients with complex clinical profiles requiring multifaceted intervention strategies. These findings align with current recommendations advocating for combination therapies to target multiple pathophysiological mechanisms.

Despite these strengths, the analysis revealed substantial heterogeneity across studies, with a Q statistic of 152.77 and an I^2 value of 86.3%. This variability reflects differences in study designs, patient populations, and intervention protocols, potentially limiting the generalizability of pooled findings. High heterogeneity is a common challenge in meta-analyses encompassing diverse interventions and highlights the importance of cautious interpretation. Future research should focus on subgroup analyses to delineate factors contributing to this variability, facilitating more precise recommendations for specific patient populations. This study's strengths include its adherence to PRISMA guidelines and the inclusion of diverse therapeutic approaches, ensuring a comprehensive evaluation. However, limitations such as the exclusion of non-English studies and variability in methodological quality across included studies could affect the breadth and depth of the findings. Additionally, the lack of long-term outcomes, such as quality of life and cost-effectiveness analyses, represents a notable gap that future investigations should address. This meta-analysis highlights the efficacy of dietary and pharmacologic interventions in reducing cardiovascular risks among post-MI patients. The findings advocate for a multidisciplinary approach that combines evidence-based pharmacologic therapies with sustainable lifestyle modifications, emphasizing the importance of personalized care strategies to optimize long-term outcomes.

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CONCLUSION

This meta-analysis highlights the significant role of both pharmacologic and dietary interventions in improving cardiovascular outcomes among post-myocardial infarction patients, aligning with the objective to evaluate their efficacy. While pharmacologic therapies remain the cornerstone of management, incorporating dietary modifications offers a complementary and holistic approach to enhancing cardiovascular health. The findings underscore the importance of personalized treatment strategies that consider individual patient characteristics, clinical contexts, and therapeutic responses to optimize outcomes. Future research focusing on diverse populations and long-term impacts will further refine these strategies, ultimately supporting improved patient care and sustainable cardiovascular health.

Author	Contribution
Muhammad Umer Khan	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Ayesha Siddiqui	Methodology, Investigation, Data Curation, Writing - Review & Editing
Mujtuba Siddiqui	Investigation, Data Curation, Formal Analysis, Software
Syeda Samia Shams	Software, Validation, Writing - Original Draft
Aisha Alyassi	Formal Analysis, Writing - Review & Editing
Burhan ali	Writing - Review & Editing, Assistance with Data Curation
Abdul Mateen Soomro	Software, Validation, Writing - Original Draft
Muaz Shafique Ur Rehman	Formal Analysis, Writing - Review & Editing
Ezaa Javed	Writing - Review & Editing, Assistance with Data Curation

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