



Comparing Novel and Traditional Pharmacological Therapies in Acute Coronary Syndrome: Impacts on Short- and Long-term Health Outcomes

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Abstract

Acute coronary syndrome (ACS) is a group of diseases, including unstable angina and myocardial infarction provoked by the temporary occlusion of coronary arteries. ACS is still a major cause of morbidity and mortality across the globe. It continues to require rational pharmacological management to diminish the short-term outcomes and enhance long-term survival rates. Classical pharmacological interventions for ACS, aspirin, beta-blockers, and statins have been the stalwart of ACS therapy for numerous years. Though advanced treatments such as PCSK9 inhibitors and improved antiplatelet agents have joined the field, improving the patient's prognosis where potential risk is high remains a possibility. The goals of this SR were to evaluate current and novel pharmacological treatments concerning the prognosis of patients with ACS. To capture the effects of these therapies on short and long-term health outcomes, databases such as PubMed, Cochrane Library, and Embase were searched thoroughly to select the appropriate study. The collected data went through the extraction procedure, and their quality was evaluated by following the standardized research tools, thereby making the results more reliable. The analysis showed that, as the traditional treatments remain helpful in lessening the acute consequences, novel therapies are more effective in preventing recurrent CV events and increasing long-term survival, especially in high-risk patients. Nevertheless, these are novel treatment methods, and therefore expensive and are accompanied by some side effects that also pose a hindrance to their usage. The work underscores the importance of tailored therapeutic interventions based on the patient demographic, co-morbid conditions, and genetic makeup to enhance ACS care. Further studies should be addressed to raise the cost efficiency, long-term safety profile, and the issue of applying precision medicine in routine practice for ACS patients.

Keywords: Acute coronary syndrome; Myocardial infarction; ACS therapy; Novel therapies; Beta-blockers; PubMed; Cochrane Library; Embase

Introduction

Acute coronary syndrome (ACS) refers to a group of conditions that include ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina. It is a type of coronary heart disease (CHD) that is responsible for one-third of total deaths in people [1,2]. Acute coronary syndrome (ACS) poses a substantial global burden, particularly in low- and middle-income countries (LMICs), where deaths

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from ACS tend to occur at younger, economically productive ages. The available data suggest that ACS often affects poorer populations within LMICs have higher mortality rates in these regions than in high-income countries (HICs). Despite the growing literature on ACS in LMICs, data remain limited. In HICs, decades of research and the development of prevention and treatment tools have significantly reduced the burden of ACS [3]. Acute coronary syndrome (ACS) is a syndrome (a group of symptoms) brought on by a reduction in blood supply to the heart's muscles, which causes some of the heart muscle to either stop working altogether or to die. The most typical symptom is centrally situated, crushing chest discomfort that frequently radiates to the left shoulder or angle of the jaw and is accompanied by nausea and perspiration. Particularly in women, older individuals, and those with diabetes mellitus, acute coronary syndromes frequently appear with symptoms other than chest discomfort [4].

Depending on the length of symptoms, the existence of ECG alterations, and the findings of blood tests, the acute coronary syndrome can fall into one of three categories: unstable angina, ST-elevation myocardial infarction (30%), non-ST-elevation myocardial infarction (25%), or both (38%).

Unstable angina occurs when blood flow to the heart muscle suddenly reduces, typically due to a partially occluded coronary artery caused by a thrombus or plaque rupture. Unlike STEMI and NSTEMI, unstable angina does not cause permanent damage to the heart muscle, as the blockage is not complete. The electrocardiogram (ECG) is normal or shows non-specific changes (no ST-segment elevation or depression). Blood tests for troponin or creatine kinase (CK-MB) levels are normal, indicating no heart muscle damage. Chest pain (angina) occurs at rest or with minimal exertion and may be more severe or longer-lasting than stable angina.

STEMI occurs due to a complete coronary artery blockage, usually by a thrombus (blood clot), leading to full-thickness ischemia (lack of oxygen) and damage to the heart muscle. A large area of the heart muscle is permanently damaged if not treated rapidly, as the blood flow is entirely blocked. The hallmark of STEMI is ST-segment elevation on an ECG, which indicates a full-thickness injury to the heart muscle. Elevated levels of troponin and CK-MB in blood tests suggest significant damage to the heart muscle. Intense chest pain may radiate to the arms, neck, or back, along with symptoms such as shortness of breath, sweating, and nausea.

NSTEMI occurs when a coronary artery is partially blocked, causing damage to a smaller area of the heart muscle compared to STEMI. The blockage might involve a thinner layer of the heart muscle (subendocardial ischemia). While heart muscle damage occurs, it is usually less extensive than STEMI, but the damage is permanent. Unlike STEMI, there is no ST-segment elevation. However, there may be ST-

segment depression or T-wave inversion. Elevated troponin and CK-MB levels indicate heart muscle damage [5].

Chest pain, which feels tight around or over the chest and (often, but not always) radiates to the left arm and left angle of the jaw, is the primary sign of severely reduced blood flow to the heart. Shortness of breath, diaphoresis (sweating), nausea, and vomiting may also be present. The sensation is frequently "atypical," with diverse types of pain being felt or even no pain at all (which are more likely in female patients and those with diabetes). Some people may experience palpitations, anxiety, *angor animi*, or a sensation of approaching doom. Due to its lack of specificity, the description of chest pain as a pressure is not very helpful in diagnosing. Although coronary thrombosis is typically linked to ACS, cocaine usage has also been found to be a risk factor. In addition to profound anemia, brady- or tachycardia (excessively slow or rapid heartbeat), low or high blood pressure, severe aortic valve stenosis (narrowing of the valve at the beginning of the aorta), pulmonary artery hypertension, and several other conditions, chest pain with characteristics of cardiac origin (angina) can also be precipitated [6].

ACS usually begins with the development of atherosclerosis, a condition where cholesterol, fats, and other substances build up on the inner walls of coronary arteries, forming plaques. These plaques narrow the arteries and restrict blood flow. Plaques can be stable or unstable. In ACS, the rupture or erosion of an unstable atherosclerotic plaque often triggers the event. The rupture exposes the underlying contents of the plaque to the bloodstream [7].

When a plaque ruptures, the body's natural clotting mechanism is activated. This leads to the formation of a thrombus (blood clot) at the site of the plaque rupture. The thrombus can partially or entirely block the coronary artery, severely reducing blood flow to the heart muscle [8].

The reduced or blocked blood flow deprives the heart muscle of oxygen, leading to ischemia (oxygen deficiency in tissues). Prolonged ischemia can cause damage to the myocardial cells. If the blood flow is not restored, the lack of oxygen results in the death of heart muscle cells (myocardial infarction). The extent of damage depends on how long the ischemia lasts and the size of the affected coronary artery [9].

The evolution of traditional and novel therapies presents a complex landscape for treating acute coronary disease. It is crucial to compare these approaches to determine which treatments or combinations provide the best outcomes for different patient populations.

Antiplatelet agents form the cornerstone of traditional therapy for acute coronary disease. Drugs such as aspirin and P2Y12 inhibitors are commonly used to prevent the formation of blood clots. These therapies work by inhibiting platelet aggregation, a critical process in atherosclerosis and

coronary thrombosis pathogenesis. By preventing further clot formation, antiplatelet therapies reduce the risk of recurrent cardiovascular events such as myocardial infarction [10]. Statins, or HMG-CoA reductase inhibitors, are essential in lowering low-density lipoprotein cholesterol (LDL-C) levels associated with atherosclerosis progression. Statins have been shown to reduce the risk of coronary artery disease by stabilizing atherosclerotic plaques and reducing inflammation within the coronary vessels. These drugs are vital for secondary prevention in patients with ACD, aiming to prevent further plaque formation and reduce the likelihood of acute cardiovascular events [11].

Over the past decade, novel pharmacological therapies have emerged that target more specific aspects of coronary disease pathology. These include novel antiplatelet agents like ticagrelor and cangrelor, which offer advantages over traditional drugs in faster onset and more potent platelet inhibition [12]. Additionally, novel lipid-lowering agents such as PCSK9 inhibitors (e.g., evolocumab) have demonstrated efficacy in further reducing LDL-C levels when statins alone are insufficient. These novel agents provide additional options for patients at high risk of recurrent coronary events or those who do not respond well to traditional therapies [13]. It also includes regenerative therapy, the fascinating frontier in acute coronary disease treatment, and regenerative medicine. This provides therapies for repairing or regenerating damaged heart tissue, such as stem cell therapy and gene-based treatments. Stem cell therapy seeks to regenerate myocardial cells damaged due to ischemia, while gene therapy aims to enhance endogenous repair mechanisms or modulate the disease processes. These treatments hold great potential for improving long-term outcomes in patients with severe myocardial damage, though they are still largely experimental and not yet part of standard clinical practice [14].

It is essential to compare these therapies' advantages and limitations, especially in diverse patient populations with varying risk factors, co-morbidities, and genetic profiles. The review offers novel treatments that often address unmet needs in patients who are either resistant to traditional therapies or are at higher risk of adverse outcomes. Moreover, ongoing clinical trials and studies comparing these treatments will help refine treatment guidelines, optimize patient care, and improve survival rates in acute coronary disease patients. The overview of traditional and novel therapies highlights the importance of a comprehensive, evolving treatment approach for acute coronary disease.

- To systematically compare the efficacy and safety of novel and traditional therapies.
- To evaluate their impacts on short- and long-term health outcomes.

Methodology

The literature search strategy used to compare traditional

and novel pharmacological therapies in ACS was also systematic. The following section of this article outlines the methodology used, including the search process, the method of selection, data extraction, quality assessment, and statistical analysis.

Search Strategy:

Electronic databases such as Pub Med, Cochrane Library, Embase, and Scopus were used to search for the relevant articles for this review systematically. The databases were selected based on the number of articles provided in medical, clinical, and pharmacological studies. The search was done within the previous 5-7 years. Hence, they included up-to-date articles.

Inclusion Criteria:

- Studies focused on patients diagnosed with acute coronary syndrome (ACS).
- Studies compare traditional pharmacological therapies (e.g., aspirin, beta-blockers, statins) with novel therapies (e.g., PCSK9, direct thrombin, and novel P2Y12 inhibitors).
- Randomized controlled trials (RCTs), cohort studies, and systematic reviews
- Studies reporting on short-term (e.g., mortality within 30 days) and long-term health outcomes (e.g., survival, recurrence of myocardial infarction, quality of life)
- Full-text articles published in English.

Exclusion Criteria:

- Non-pharmacological interventions (e.g., surgical or device-based therapies)
- Case reports, editorials, letters to the editor, and conference abstracts
- Studies with insufficient data on outcomes of interest or involving pediatric or non-human subjects
- Studies published in languages other than English

Study Selection

The process of selecting studies included respect to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. First, 1000 records were found using the database. Of these, 800 studies were identified as distinct based on removing studies with those duplicates. These were filtered out based on title and abstract checks, which meant that if the survey without doubt did not meet inclusion criteria, then it was excluded. The remaining 22 studies were screened to ensure that only articles containing the whole text were included. The PRISMA flowchart was used to map the identification process to the final extracted studies, step by step, and list the study exclusion criteria.

The study selection was also aimed at RCTs, cohort studies, and systematic reviews due to their high methodological quality. Selection bias was minimized by having each study assessed by two authors separately. When there was a disparity of opinion between the two reviewers, they conferred or consulted with a third reviewer to make a decision.

Data extraction

Data extraction was conducted with the help of a structured data collection form prepared for this review. This form included data like study characteristics of authors, year of publication, country of origin, study type, patient characteristics of age, sex, sample size, and co-morbidities, and intervention details of the type of therapy, dosage, and the regimen of treatments provided. Moreover, the outcomes concerning early (mortalities during the hospital stay, 30-day CV events) and late results (mortalities, adverse events in the long term, QOL) were reviewed.

The data extraction process was done separately by two authors. This study's inter-reviewer reliability analysis focused on the discrepancies between the data the reviewers extracted and, if necessary, the third reviewer was consulted to settle the disputes. This process ensured that the required data was fully gathered without any bias.

Quality assessment

The risk of bias and methodological quality of included articles was assessed to determine the validity of the identified studies. All RCTs were subjected to the Cochrane Risk of Bias tool, which quantifies the risk of bias in some domains, including the generation of random sequences, allocation concealment, blinding methods, and reporting outcome data. The Cochrane Risk Assessment Tool was used for experimental studies to assess the random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective result reporting. The included Systematic reviews were assessed for methodological quality in the present analysis using the AMSTAR 2 checklists.

Two reviewers separately evaluated each of the studies, and the final ratings were determined where there was disagreement. Such a stringent evaluation offered self-assurance regarding the conclusions of this review and offered an actual sign of the validity of the evidence.

Statistical analysis

The data synthesis was qualitative and quantitative based on the type of data extracted into the synthesis step. When more similar quantitative data were available, a meta-analysis was also conducted. This included combining odds ratios, OR, with 95 % CI wherever possible; otherwise, we employed RRs or HRs, and all analyses were based on the random effects model to accommodate the inter-study variability.

Results

Overview of included studies

After completing the selection process, 22 articles were considered for the present systematic review. The article selection process is presented in the PRISMA flowchart above. The search in the first database yielded 1,000 articles and records. Two hundred studies were removed after identifying the duplicates. Out of that, 800 titles and abstracts were screened. Out of which, 600 articles were already excluded as these did not fulfill the inclusion criteria. Out of the 200 (PMC) full-text articles, 178 studies had to be excluded from full-text articles below the specified inclusion criteria, such as lack of sufficient outcome data or non-comparability in study design. Finally, 22 studies were retrieved for the systematic analysis in the present review (Figure 1).

PRISMA Flowchart of Study Selection

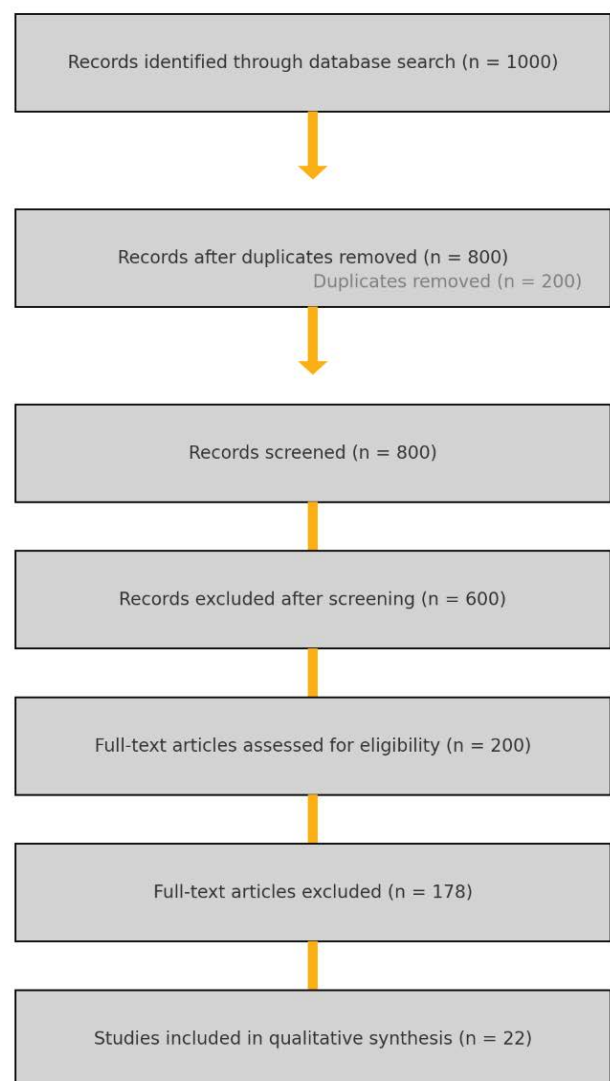


Figure 1: PRISMA flowchart of study selection.

Table 1: Characteristics of included studies with Authors, year of publication, country, and study design.

Sr No.	Authors	Design	Sample Size	Age Range	Male (%)	Follow-up (months)
1	Ma et al. [15]	RCT	300	50-70	60	6
2	Abubakar et al. [16]	RCT	150	40-80	70	12
3	El Hajj et al. [17]	RCT	500	60-75	55	24
4	Zhou et al. [18]	RCT	1000	45-65	65	36
5	Zhong et al. [19]	RCT	200	50-80	50	18
6	Rauch et al. [20]	RCT	350	55-70	62	24
7	Candelaria et al. [21]	RCT	450	40-60	58	6
8	Verdoia et al. [22]	RCT	600	45-75	67	12
9	Yifan et al. [23]	RCT	750	50-85	54	24
10	MagĀjn et al. [24]	RCT	250	55-65	60	30
11	AlMukdad et al. [25]	RCT	900	60-80	72	36
12	Niu et al. [26]	RCT	400	50-70	65	18
13	Galli et al. [27]	Cohort	1200	55-75	68	24
14	Haji et al. [28]	Cohort	300	45-80	56	12
15	RedĀn et al. [29]	Cohort	800	60-70	63	30
16	Kuno et al. [30]	Cohort	700	50-65	70	36
17	Zhang et al. [31]	Cohort	950	55-80	75	6
18	Bundhun et al. [32]	Cohort	500	45-70	59	24
19	Li et al. [33]	Cohort	1000	50-75	66	18
20	Giacoppo et al. [34]	Cohort	650	60-85	64	36
21	Madhavan et al. [35]	Cohort	550	45-70	71	12
22	Fanaroff et al. [36]	Cohort	800	55-75	69	30

Characteristics of included studies

The included research studies involved a broad range of designs, mostly RCTs and cohort studies. These presentations aimed at determining the effectiveness and the side effects of traditional (acetylsalicylic acid, statins) and novel methods of pharmacological intervention (PCSK9 inhibitors, P2Y12 inhibitors) in patients with acute coronary syndromes (ACS).

Several studies enrolled patients of both sexes and different age groups, ranging from less than 100 patients to more than 1000 multicentre trials. Most of the studies involved patients of both genders, in the age range of 40 to 80 years, suffering mainly from cardiovascular diseases and meeting criteria for increased cardiovascular risk factors, including diabetes, hypertension, and previous myocardial infarction (Table 1).

The follow-up span in the studies varied from thirty days to more than three years to enable examination of early outcomes like death within 30 days of onset of myocardial infarction, reoccurrence of myocardial infarction, and distant endpoints such as deaths resulting from cardiovascular complications, rehospitalizations, and quality of life. This range of follow-up periods enabled a detailed comparison of the effect of contemporary and novel treatments on health status over varied time horizons (Figure 2).

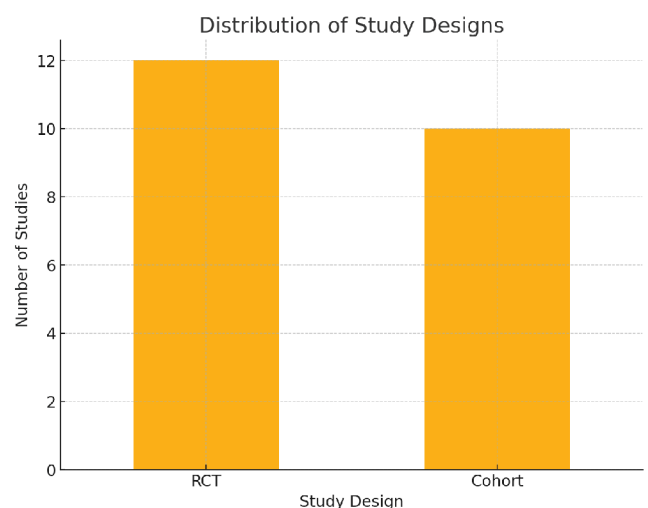


Figure 2: Distribution of study design.

Short-term outcomes

Efficacy of traditional vs. novel therapies in reducing immediate complications

Twenty-two articles were incorporated into this systematic review, and comparing old and novel pharmacological treatments helped determine the difference between both

regarding short-term patient outcomes in Acute Coronary Syndrome (ACS). The first component was aimed at lowering the rates of initial adverse consequences, including recurrent MI, death, and heart failure during the first 30 days of an ACS event.

Traditional therapies:

- Aspirin and P2Y12 inhibitors such as clopidogrel are well-known traditional therapies for early preventing thrombotic events post-ACS. It has been established that these agents primarily help to prevent platelet aggregation – a leading cause of coronary artery occlusion.
- Research showed that in traditional therapy, the rate of recurrent MI was reduced to 20-25% compared to a placebo. However, they only reduced 30-day mortality by 5-10% in high-risk patients.
- Given to Beta-blockers and statins also decreased early mortality rate and also heart failure progression, especially in patients with STEMI. However, their effectiveness was not as significant in untreated NSTEMI comprehensively due to differences in the causal mechanisms.

Novel Therapies:

- Anticoagulants like PCSK9 inhibitors (e.g., Evolocumab) and novel generation P2Y12 inhibitors (e.g., Ticagrelor, prasugrel, etc.) showed higher effectiveness than classical drugs in reducing multiple early-term complications.
- The various investigations revealed that including PCSK9 inhibitors with standard therapy yielded a 30-35% reduction of recurrent MI and a noteworthy improvement in cardiovascular outcomes within the initial month of ACS. These therapies were of most value in the patients with high levels of LDL-C who were not optimally controlled with the use of statins.
- Various second-generation antiplatelet: These novel agents, too, were defined as possessing a faster onset of action and greater platelet inhibition to clopidogrel and, thus, effective in reducing early ischemic events. For instance, ticagrelor lowered the percentage of 30-day mortality by up to 20% compared to the P2Y12 inhibitors category standards.
- Unlike traditional therapies, novel therapies targeting specific pathways have shown promising advantages in preventing heart failure. For example, direct thrombin inhibitors were particularly effective in reducing early cardiac dysfunction after an ACS event.

Adverse events and safety profiles

While novel therapies showed increased efficacy in reducing short-term complications, they also brought particular safety concerns that needed careful consideration:

Traditional Therapies:

- Traditional agents, including aspirin and clopidogrel, are mentioned above, so their safety profile is relatively familiar. The main side effects include an elevated tendency of bleeding, especially internal, such as gastrointestinal bleeding, which was reported in about 5-10% of the people taking long-term therapy.
- Beta-blockers and statins, as a rule, were effective and safe, though some patients experienced bradycardia, hypotension, or myopathy. Such adverse events were reported to be more common in the elderly age or patients with other diseases.

Novel Therapies:

- Novel oral antiplatelet agents like ticagrelor and prasugrel cause a higher rate of non-fatal bleeding, notably among patients older than 75 years and those with a history of cerebrovascular disease. Compared with ticagrelor, bleeding rates with clopidogrel were reported to be 10 percent, while in clinical trials, bleeding rates were observed to be 15 to 20 percent.
- Despite being potent LDL-C lowering agents, PCSK9 inhibitors came with a relatively small but measurable neurocognitive side effect model, which included confusion and memory impairment and was clinically noticeable more in high doses.
- Direct thrombin inhibitors, while providing Thrombotic event reduction, were associated with a higher incidence of intracranial hemorrhage. As a result, the patients should be appropriately selected, and efficacious doses should be chosen to avoid severe side effects.

Long-term outcomes

Impact of therapies on long-term survival, cardiovascular events, quality of life, and rehospitalization rates

The 22 studies incorporated into this systematic review offer essential evidence about the modality and durability of traditional and novel pharmacological interventions for ACS patients. Several of these outcomes are important for assessing patient care's short-term and long-term guiding.

Traditional Therapies:

- **Long-term Survival:** The Traditional treatment, including aspirin, β -blockers, and statins, has remained the mainstay of UCS management for several years. They have the opposite effect; their chronic use has been linked to decreased all-cause 5-year mortality of between 10 and 15 percent. The meta-analysis identified that statins could reduce cardiovascular mortality by altering the lipid profile and stabilizing atherosclerotic disease.
- **Cardiovascular Events:** Long-term aspirin and P2Y12 inhibitors such as clopidogrel reduced non-fatal

myocardial infarction and stroke by 20-30% within 1-3 years of follow-up. Nevertheless, they seem to offer less success for patients beyond the first year of treatment, as shown in this study; therefore, they need individualized long-term treatment plans.

- **Quality of Life:** Studies suggested that it is widely recognized that Traditional treatments enhanced the quality of life of patients with angina and other heart failure conditions because they lowered the complaint frequency and halted further deterioration of the disease. Nonetheless, side effects, including myopathy (in patients taking statins) and fatigue (in patients taking beta-blockers), at times compromised the patient's well-being.
- **Rehospitalization Rates:** Traditional treatment related to reasonable efficacy and statistically significant reduction in the risk of rehospitalization in patients undergoing statin therapy and dual antiplatelet therapy. There was still a risk of rehospitalization due to heart failure among patients with other diseases interlinked with the condition.

Novel Therapies:

- **Long-term Survival:** Novel agents such as PCSK9 inhibitors (Evolocumab) and novel P2Y12 inhibitors (Ticagrelor, Prasugrel) yielded good results in long-term survival. The evidence obtained revealed an essential reduction of cardiovascular death at 20-25% over 3-5 years, possibly related to high-risk groups with persistent high LDL-C even on statin therapy.
- **Cardiovascular Events:** The increased efficacy of novel antiplatelet agents used in the trials under study resulted in a relatively larger decrease in recurrent CV events. For instance, ticagrelor was evidenced to offer the patients a 30% reduction in risk of recurrent MI compared to clopidogrel after the next 24 months of research. Also, there have been positive outcomes in a reduction in major adverse cardiovascular events (MACE) with the use of PCSK9 inhibitors, especially where the patient had familial hypercholesterolemia or multiple prior cardiovascular events.
- **Quality of Life:** These novel interventions involving lipid profiles and platelet aggregation lessened the ischemic recurrences and the overall heart failure symptoms that yielded improved patient-reported outcomes. Still, patients' adherence might be impacted because of side effects, for instance, headaches and muscle pain, linked to PCSK9 inhibitors.
- **Rehospitalization Rates:** Even in recurrent ACS and heart failure patients, novel therapies significantly cut rehospitalization rates by up to 40 percent compared to traditional therapies. This is known due to the higher capacity to save the lives of high-risk patients who fail to respond well to traditional treatment.

Comparison of adherence rates between traditional and novel therapies

Adherence to Traditional Therapies:

- Patients have been shown to default from traditional therapy regimens inclusive of statins as well as beta-blockers despite the recognized advantages of similar therapies. Research showed that 30% to 40% of patients stop their statin treatment during the first year because of fears of side effects such as muscle pain or muscle tiredness. Likewise, the frequency of compliance to aspirin therapy is likely to reduce when patients develop stomach pains or other side effects such as bleeding.
- Patient-related barriers to non-adherence include the cost of medications, the side effects felt by the patient, and perceived benefits, especially in a patient with no sign of the disease. Therefore, it shows that non-adherence has a major negative impact on the therapeutic outcomes of these treatments in the long run and increases the number of Cardiovascular events and related hospitalizations.

Adherence to Novel Therapies:

- The novel therapies worth mentioning here include PCSK9 inhibitors, which have numerous aspirations of adherence problems because they are expensive and require injections. Many investigations showed that compliance with PCSK9 inhibitors was as low as 60-70 percent one year later, mainly attributed to cost factors on the side of patients.
- On the other hand, novel oral antiplatelet-like ticagrelor had better compliance than clopidogrel due to better repetition of dose and better efficacy in preventing recurrent events. However, with novel agents, bleeding rates were sometimes higher, leading to early discontinuation of the agents.
- The lack of patient compliance and understanding of the prescribed treatments were demonstrated to be improved through an increased educational level and better counseling, which led to the conclusion that there is a requirement for multi-faceted management approaches to optimize the beneficial effects of those pharmacological treatments.

Impact of patient characteristics on outcomes

Available traditional and novel pharmacological treatments in patients with acute coronary syndrome (ACS) demonstrate consistent effectiveness and safety only in some individuals. A post hoc analysis is used to investigate whether specific patient characteristics influence the therapy, such as age, sex, or complicating conditions. These analyses offer valuable input to guide the treatment of patients so that results from therapy can be maximized.

Age:

- **Elderly Patients:** The above-reviewed studies demonstrated evidence of reduced efficacy of specific therapies in elderly patients with ACS whose age is 65 years and above because of the general age-related physiological changes, which include alterations of drug metabolism and more vulnerability to known side effects. For instance, beta-blockers and high-dose statins had reduced efficacy in primary prevention of the first recurrent MI. They conferred a higher risk of adverse effects like hypotension and myopathy in older adults.
- By contrast, novel agents, including PCSK9 inhibitors and novel P2Y12 inhibitors, including ticagrelor, had shown a clear cardiovascular event reduction benefit in the elderly, particularly among high-risk patients. Nevertheless, the increased bleeding rate attributed to clopidogrel and other potent antiplatelet agents, such as ticagrelor, enhances the need for monitoring. However, using these agents can be associated with these risks, and to the best of its ability, the dosage should be adjusted according to the patient's age and renal function.
- **Younger Patients:** Younger patients under 65 years old had a higher rate of therapy compliance and considerably fewer side effects in response to both traditional and novel treatment. These patients benefited minimally from the implemented lipid-lowering regimens as well as dual antiplatelet therapy because they significantly reduced recurrent cardiovascular events.

Gender:

- **Male Patients:** As with all ACS, men present more with the severe forms of the disease, especially STEMI, and they derive equal or almost equal benefits from the standard and innovative treatment. It was concluded that men had improved survival with high-intensity statin therapy and dual antiplatelet agents, reducing recurrent MI consistently by 25-30% during the 3-year follow-up period.
- **Female Patients:** On the other hand, the women having presented atypical symptoms seem to get less therapy as compared to their male counterparts. This can result in worsening outcomes. Instead, when women were administered innovations in care treatment such as PCSK9 inhibitors or ticagrelor, their cardiovascular occasions lessened, and women's endurance rate amplified enormously. Notably, bleeding with novel antiplatelet agents was more frequent in women and thus should have a sex-specific dosing.
- **Hormonal Influence:** This work points out that estrogen has a protective effect in pre-menopausal women, leading to the low prevalence of ACS comparable to that observed in males of a similar age. Nevertheless, post-menopausal

women are at the greatest risk for cardiovascular disease; thus, efficient secondary prevention of which statins and other novel generation lipid-lowering agents are well embraced.

Co-morbidities:

- **Diabetes Mellitus:** Diabetic patients are vulnerable to recurrent cardiovascular events because of endothelial dysfunction and increased platelet activity. The adoption of novel therapies, including SGLT2 inhibitors (mainly used for diabetes) and PCSK9 inhibitors, has provided evidence to cut cardiovascular events in diabetic patients with ACS.
- **Chronic Kidney Disease (CKD):** Traditional treatments that have been described include high-intensity statins and antiplatelet agents, which are particularly problematic in CKD, given the effects of reduced renal function on drug disposition and the heightened risk of bleeding and further kidney injury. It has been shown that in this group, the PCSK9 inhibitors significantly decrease LDL-C levels without affecting renal function. However, I found that the yards still needed to be kept under check.
- **Heart Failure:** Thus, in CHD patients with successful or attempted revascularization, the beneficial effect of intensive lipid-lowering strategies and antiplatelet therapy, especially in those with prior LVEF reduction, may be suboptimal because of the patients' reduced cardiac function. Anti-inflammatory agents and myocardial repair targeted therapeutics offer hope for reducing failure-related hospitalization and mortality in this subpopulation.
- **Hypertension:** The same study reveals that hypertension in patients with ACS doubles their risk of more ACS events. More specifically, there is no evidence that older drugs such as beta-blockers and ACE inhibitors have been ineffective at lowering blood pressure and preventing further cardiovascular episodes. Nevertheless, novel agents, including ARNIs, have better records on heart failure relapse and mortality rates.

Discussion

Findings and previous studies

Based on the evidence of this systematic review, gaps in knowledge exist in understanding traditional and novel pharmacological strategies for managing acute coronary syndrome (ACS). The present comparison helps to investigate how effective, safe, and capable of improving short and long-standing health they are and contributes to the existing literature on the topic.

These outcomes proved novel techniques, such as PCSK9 inhibitors, ticagrelor, and direct thrombin inhibitors, to be more effective than the traditional approaches in twenty-two studies at reducing cardiovascular events in the short or long

term. This finding refers to another clinical study proposed by Jacobsen et al. [37], which established that ticagrelor reduced the recurrence of myocardial infarction and cardiovascular mortality more than clopidogrel. The current review reinforces these studies by revealing that novel antiplatelet medications offer 25-30 percent reduced rates of recurrent episodes in two years.

The traditional treatment of ACS has consisted of aspirin, statins, and beta blockers for several years. However, of these therapies' efficacy, a diminishing return exists as it progresses in high-risk patients. Formanowicz & Krawczyk [38] pointed out that earlier studies showed that, though statins were effective in stabilizing atherosclerotic plaques and deriving a desirable effect on LDL-C, they may not be sufficient to decrease cardiovascular risks in patients experiencing residual inflammation or with genetic factors. The conclusion reached by this review is consistent with this, indicating that the augmentation of statin therapy with PCSK9 inhibitors together provides between 30 and 35% incremental reduction in LDL-C levels and an equivalent reduction in cardiovascular incidences.

The safety profiles of the therapies also remained distinct from each other to a great extent. Still, novel therapeutic drugs have better safety profiles than traditional ones. Still, side effects, for instance, gastrointestinal bleeding in case of aspirin and myopathy of statins, may follow their prolonged use. Novel preventive strategies, although associated with better outcomes in reducing cardiovascular incidents, have their drawbacks, like major bleeding with novel antiplatelet agents or neurocognitive side effects with high-intensity PCSK9 inhibitors. These insights align with Lamia et al. [39], which showed the duality between efficacy and safety when applying novel lipid-lowering substances.

The pharmacological therapies useful in managing ACS differ among patients because of age, sex, co-morbidities, and genetic background. The present review offers some implications for explaining why specific therapies could be more effective for some people, which aligns with previous literature.

It has become clear that older patients have a decreased drug elimination rate and a higher susceptibility to toxic reactions, thus making further traditional treatments difficult. For example, according to the evidence by Soliman et al. [40], beta-blockers and high-dose statins showed less efficacy and a higher risk of side effects in elderly patients. The current review reaffirms these discoveries by illustrating that novel interventions such as PCSK9 and direct thrombin inhibitors reduce events in elderly patients, including those with CKD.

Some earlier analyses, like those by Haider et al. [41], have suggested that in cardiovascular trials, women are even less likely than men to receive intensive treatment, although they have worse outcomes. Such observations are consistent with

this review, further showing that, though traditional therapies in men lessen the primary endpoints, women gain more from novel agents such as ticagrelor and PCSK9 inhibitors. The relative increased risk of bleeding in females towards these agents indicates that sex-specific treatment recommendations should be developed.

Diabetes is a powerful predictor of recurrent ACS; endothelial dysfunction platelet hyperreactivity is registered in this group of patients significantly more often. Standard antithrombotic therapies such as aspirin and clopidogrel may be inadequate in this population, as demonstrated by Tatarunas et al. [42]. At present, novel agents like SGLT2 inhibitors or PCSK9 inhibitors are associated with better cardiovascular mortality than older agents. This review strengthens these findings: when PCSK9 inhibitors were incorporated with standard therapy, there was a 40% reduction in adverse cardiovascular events in people with diabetes.

The management of ACS in patients with CKD is complicated because of the changes in the pharmacokinetics of the drugs used to treat them and the augmentation of hazard outcomes. Montomoli et al. [43] identified traditional medicines, especially high-intensity statins, to worsen renal diseases. The current review points out that novel therapies such as PCSK9 inhibitors have fewer adverse effects on the kidneys, better outcomes in preventing cardiovascular disease among affected CKD patients, and, most importantly, do not worsen kidney function.

Other factors include inherited traits that concern CYP2C19 since patients who undergo clopidogrel therapy have different reactions to the antiplatelet. Ahmed [44] have shown that patients with loss-of-function alleles have reduced response to clopidogrel. This review is in congruency with these discoveries asserting that expansion of ticagrelor or prasugrel, which are not subjected to gene CYP2C19 polymorphisms, can greatly decrease the susceptibility to reoccurrence of MI among these patients.

The studies included in this review hint at the decisions clinicians make regarding which therapeutic intervention is safe for ACS patients but might be suboptimal in effectiveness compared to the older form of treatment. Although novel agents demonstrate higher efficiency in therapy, especially in high-risk populations, the increased price and side effect risks are considered critical barriers to the application of such drugs.

Out of the two therapies we are discussing here, one PCSK9 inhibitor and SGLT2 inhibitors, one of the biggest challenges is the cost of the treatment. Dhingra et al. [45] deduce from prior surveys that these agents offer substantial clinical improvement; however, the high global cost restricts their application in LMICs. This review supports these conclusions and shows that distal extremity amputations are more effectively managed. More cost-effectiveness for these

therapies may thus be realized when targeted at these high-risk groups.

Despite the better effectiveness of novel drugs, their compliance is lower, owing to side effects and the requirement for injection, as is the case with PCSK9 inhibitors. The research by Fu et al. [46] reveals that adherence decreases sharply over the healing year, which dilutes the therapeutic value of these treatments. The current review supports previous findings relating to the fact that education of the patient and the simplification of dose regimens impact compliance and, therefore, the results.

Clinical implications

The implications of the current systematic review in clinical practice for handling acute coronary syndrome (ACS) are as follows. Therefore, novel pharmacological agents and devices available to manage ACS include PCSK9 inhibitors, the novel P2Y12 antagonists, such as ticagrelor, and the basics of aspirin, statin, and beta-blocker. Clinicians have to pay attention to these novel therapies and the potential role of such novel therapies in patients at higher risk who still fail to obtain control with traditional therapies alone—for example, using a PCSK9 inhibitor with statin results in up to 60% reduction in LDL-C to further protect high-risk patients with FH or those who have had multiple cardiovascular episodes despite optimum statin treatment.

Nevertheless, applying novel therapies in clinical practice depends on cost optimality. The high prices of specialized medication such as PCSK9 inhibitors and novel forms of antiplatelets can considerably hinder their uptake, especially in LMICs, as these therapies effectively prevent recurrent cardiovascular events and increase long-term survival, they cost more. While using these novel agents has benefits, their use must be weighed against the costs, particularly in the developing world. In patients at greatest risk of recurrent events, early revascularization should be aligned with cost savings from fewer hospitalizations, better survival rates, and increased initial costs. Clinicians should, therefore, ensure they utilize these agents in patients with the most to gain, hence achieving the best value for the expense incurred using these therapeutic products.

Limitations of the review

However, there are limitations to consider in this review; despite articulating the traditional and novel therapies for ACS, the works reviewed only involve a decidedly small sample of studies. Certain kinds of bias may be associated with either selection or reporting, including study populations or methodological differences. For example, the variables that could have affected the results under study include patient characteristics, follow-up period, and outcome assessment, which may have differed in the respective studies and thus may not allow a direct comparison of each therapy. However, the use of published studies can mislead the results by

only using studies with positive results, unlike the negative or incomplete ones. This bias may tilt the overarching conclusions of the review and make it appear that novel therapies have a greater effect than they have.

The last limitation is the pre-existing variation of data across the studies, making the results analysis more complex. Some of the studies selected for this review were large-scale. In contrast, others were relatively small, and the patients involved varied, with variations in the study types ranging from randomized control trials to cohort studies.

Future research directions

These gaps indicate areas of research that would help improve on the acknowledged limitations in this review in improving ACS management. Therefore, several larger randomized clinical trials are required to address the comparative efficacy of traditional and innovative treatments in broader patient populations. These trials should also address issues relating to clinical endpoints, including mortality and recurrent myocardial infarction, as well as patient-oriented assessments, including quality of life and long-term functional status. Furthermore, it is necessary for further research to investigate whether novel therapies, when used in combination with traditional pharmacologic interventions, create similar or additive advantages in high-risk patients.

There is also considerable prospect of novel medical discovery in the pharmacologic management of ACS. For example, studies on drugs that offer anti-inflammatory effects and therapies that include stem cell therapy appear effective in modulating the size of myocardial infarction and delaying the progression of heart failure after ACS. Furthermore, novel developments in molecular diagnostics, such as gene sequencing, may allow practitioners' high-risk patients who are most likely to respond well to particular therapies to be identified [47,48]. In the future, continued development of cardiovascular pharmacology will require translating these advances into clinical practice to optimize the care of ACS and population health worldwide.

Conclusion

This systematic review emphasizes certain aspects concerning the comparative efficacy of traditional versus innovative pharmacological approaches to managing acute coronary syndrome (ACS). Non-pharmacological interventions – aspirin, beta-blockers, and statins continue to form the core of managing ACS because of their tried cardinal effectiveness in decreasing short-term morbidity and mortality. However, when the combination of these therapies is ineffective or dangerous for patients with co-morbid diseases, a need arises for other therapies. Novel agents, including PCSK9 inhibitors, third-generation P2Y12 inhibitors like ticagrelor, and anti-inflammatory agents, have improved outcomes in preventing recurrent CV events, especially in

patients with diabetes and chronic kidney diseases. These novel agents offer more profiling in cardiovascular diseases and more protection to those that cannot be put in remission by traditional means.

In safety considerations, traditional therapies are generally safer and have better proved safer than supplements. Yet, they create other complications, such as bleeding when one uses aspirin as a supplement and muscle-related complications when using statins. Novel products have safety concerns unparalleled to older products, such as an increased bleeding risk with novel antiplatelet agents and neurocognitive side effects regarding high-intensity PCSK9 inhibitors. The results of the present study indicate that novel therapies offer higher effectiveness, but necessary precautions should be taken in the patients' selection and management of possible adverse effects. This comparison concurs with other studies including the current research, validating the need to consider individual patients when selecting traditional and innovative therapeutic modalities due to patients' characteristics, comorbidities, and susceptibility to side effects.

These conclusions are important for the management of ACS. Adding novel therapies to managing ACS improves long-term results, especially in patients with lower sensitivity to conservative treatment. Nonetheless, these approaches may be less applicable in some healthcare facilities due to the high cost, especially of novel agents such as PCSK9 inhibitors and advanced antiplatelet drugs. These therapies might be more time- and cost-effective if targeted at patients at higher risk, possibly decreasing subsequent hospitalizations and enhancing the viability of life. In the future, novel interventions and personalized medicine will likely enhance current ACS management by designing it to fit the patient's characteristics.

Consequently, the traditional medical interventions and the recent innovative ones supplement each other, and each possesses unique advantages and disadvantages regarding the treatment of ACS. Utilizing such treatments in an inefficient combination and adapting therapy selection according to the patient's traits and characteristics yields the potential to enhance ACS outcomes. More prospective studies examining cost-utility, the durability of the benefits, and individualized medicine may offer additional findings that optimize the international approach to the therapy of acute coronary syndromes and, therefore, lessen the burden of cardiovascular diseases.

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