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Additional material is published online only. To view please visit the journal online.

Cite this as: Saheed E. Sanyaolu, Diana O. Wilson, Blessing A. Oguntolu, Mautin S. Salako and Rukayat O. Adeyemi. Current Evidence on the Clinical Management of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review. Premier Journal of Cardiology 2025;4:100011

DOI: <https://doi.org/10.70389/PJC.100011>

Received: 15 June 2025

Revised: 17 July 2025

Accepted: 18 July 2025

Published: 26 July 2025

Ethical approval: N/a

Consent: N/a

Funding: No industry funding

Conflicts of interest: None

Author contribution:

Saheed E. Sanyaolu, Diana O. Wilson, Blessing A. Oguntolu, Mautin S. Salako and Rukayat O. Adeyemi – Conceptualization, Writing – original draft, review, and editing

Guarantor: Saheed Ekundayo Sanyaolu

Current Evidence on the Clinical Management of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review

Saheed E. Sanyaolu¹, Diana O. Wilson², Blessing A. Oguntolu¹, Mautin S. Salako¹ and Rukayat O. Adeyemi¹

ABSTRACT

Coronary artery disease (CAD) and acute coronary syndrome (ACS) share a pathophysiological basis of myocardial ischemia, primarily driven by atherosclerosis, plaque rupture, and thrombogenesis. Despite advancements in diagnosis and treatment, CAD and ACS continue to pose significant clinical challenges due to variable patient responses, limitations in pharmacological and interventional therapies, and gaps in long-term safety data. Current pharmacologic management integrates conventional agents such as aspirin, clopidogrel, anticoagulants, beta-blockers, and angiotensin-converting enzyme inhibitors. Furthermore, emerging therapies, such as proprotein convertase subtilisin kexin type 9 inhibitors, sodium-glucose co-transporter two inhibitors, RNA-based therapies, and anti-inflammatory agents such as canakinumab, offer innovative approaches to improving patient outcomes and addressing the limitations of traditional therapies. However, adherence remains a challenge, particularly in high-risk patients. Lifestyle modifications and interventional strategies, including percutaneous coronary intervention, coronary artery bypass grafting, transcatheter aortic valve replacement, and hybrid revascularization, provide tailored approaches based on disease severity. Mechanical circulatory support devices, such as Impella pumps, are also critical in managing cardiogenic shock. To optimize CAD and ACS management, a multidisciplinary approach that integrates pharmacological innovations, surgical expertise, algorithm-based interventions, and precision medicine is essential. Improving adherence strategies and refining individualized treatment regimens will be key to advancing cardiovascular care globally.

Keywords: Atherosclerosis, Myocardial ischemia, Pharmacologic management, Coronary revascularization, Precision medicine

Highlights

- Pharmacologic approaches for CAD and ACS comprise aspirin, clopidogrel, anticoagulants, beta-blockers, and angiotensin-converting enzyme inhibitors.
- Emerging therapies, including PCSK9 inhibitors, sodium-glucose cotransporter-2 inhibitors, RNA-based therapies, and anti-inflammatory agents, offer innovative approaches to improving patient outcomes
- A multidisciplinary approach integrating pharmacologic innovations, surgical expertise, AI-assisted interventions, and precision medicine is essential for the management of ACS and CAD

Background

Cardiovascular diseases, including coronary artery disease (CAD) and acute coronary syndrome (ACS), remain a leading cause of death worldwide. In 2021, approximately 20.5 million deaths were attributed to cardiovascular disorders, accounting for 32% of all global mortality.^{1,2} CAD, also known as coronary heart disease, is a condition characterized by reduced or obstructed blood flow to the heart muscles due to atherosclerotic plaque buildup in the coronary arteries. The blood flow impairment reduces oxygen delivery to the myocardium, potentially leading to angina or myocardial infarction.³ Correspondingly, ACS is a manifestation of CAD, involving three serious heart conditions resulting from sudden blockage or restricted blood flow in the coronary arteries: unstable angina, non-ST-elevation myocardial infarction, and ST-elevation myocardial infarction.⁴ These conditions often lead to severe complications, requiring the urgent need for timely diagnosis and intervention.

Several risk factors contribute to the development of CAD and ACS, including hypertension, diabetes mellitus, hyperlipidemia, smoking, overweight, and advanced age (>65 years). Furthermore, a family history of premature CAD significantly elevates an individual's risk of the disease.⁵ Although global trends in cardiovascular disease show a decline in the prevalence of CAD and ACS since 1990, they continue to impose a significant burden on global health. In particular, CAD and ACS remain widely prevalent and account for one-third of total deaths in people older than 35 years.⁶ Despite medical advancements, progress in reducing mortality from the disease has stalled, especially in low- and middle-income countries, where four out of five cardiovascular deaths occur.² The American Heart Association similarly estimated that CAD affects about 15.5 million individuals in the United States, with the classic hallmark symptom being substernal chest pain, often described as crushing or pressure-like, radiating to the jaw or left arm.⁴ Moreover, recent epidemiological data from 2022 indicate an estimated 315 million prevalent cases of CAD globally, with Central Europe, Eastern Europe, and Central Asia exhibiting the highest age-standardized prevalence.⁷

The management of these arteriosclerotic diseases requires an interdisciplinary approach that integrates pharmacological therapy, lifestyle modifications, and interventional procedures to reduce the risk of heart attack and improve patient outcomes.⁸ However, the role of early intervention and precision medicine in tailoring treatment for individuals with varying genetic, metabolic, and inflammatory profiles remains underexplored. As treatment strategies continue to

Provenance and peer-review:
Unsolicited and externally
peer-reviewed
Data availability statement:
N/a

evolve with a stronger emphasis on antithrombotic therapy, revascularization, and secondary prevention, it becomes important to review the current evidence on the clinical management of ACS and CAD, as this understanding can guide holistic and long-term patient care. By integrating new evidence into practice, clinicians can offer more personalized, effective, and comprehensive care, ultimately improving patient quality of life and long-term prognosis. This study, therefore, aimed to review current evidence on the clinical management of CAD and ACS.

Pathophysiology and Etiologies

CAD and ACS both share a fundamental pathophysiology characterized by reduced myocardial perfusion; however, their pathogenesis exhibits notable distinctions. CAD is predominantly caused by atherosclerosis, a pathological process marked by the gradual accumulation of lipids, inflammatory mediators, and fibrous tissue within the coronary arteries.⁹ The atherosclerosis cascade begins with an endothelial dysfunction,

facilitating the uptake of low-density lipoprotein (LDL), connective tissues, and leukocyte trafficking into the subintimal space; all of which contribute to the formation of susceptible plaques in the coronary arteries.¹⁰ This progressive arterial narrowing impairs myocardial perfusion, leading to ischemia and subsequent functional deterioration of cardiac tissue. The increased plaque buildup in the arteries is facilitated by an etiology of both modifiable and non-modifiable risk factors (Figure 1). While modifiable factors, such as obesity, sedentary lifestyle, smoking, and high blood pressure, can be changed through lifestyle modifications or medications, non-modifiable risk factors, including age, gender, family history, and genetics, remain inherent contributors to disease susceptibility.¹¹

While CAD manifests as a chronic and gradual atherosclerotic plaque buildup, ACS is an acute condition, often triggered by abrupt plaque disruptions, which leads to severe manifestations (Figure 2). The underlying pathophysiologic mechanism in the development of ACS involves plaque rupture, plaque erosion, and calcified nodule formation, each of which contributes to the thrombotic occlusion of coronary vessels.¹⁰ Pathophysiologic contributors, such as diabetes and smoking, can activate plaque inflammation and rupture, a critical mechanism of coronary thrombosis, accounting for up to 75% of all ACS. This resultant thrombogenesis can lead to either partial or complete luminal obstruction, culminating in varying degrees of myocardial ischemia and infarction.¹²

The etiological factors contributing to CAD and ACS extend beyond atherosclerosis. Underestimated etiologies, such as coronary artery vasospasm, can also induce transient ischemia by causing temporary constriction of the coronary arteries.¹³ Similarly, embolic occlusion, arising from thrombotic or atheromatous debris from a distal site, may abruptly obstruct coronary blood flow; in the same vein, systemic inflammatory disorders, which compromise endothelial integrity and vascular function, further augment the risk of acute ischemic events.¹⁴ However, the severity of ACS is contingent upon its etiology and the extent and stability of the thrombus.

Risk Factors of Atherosclerosis

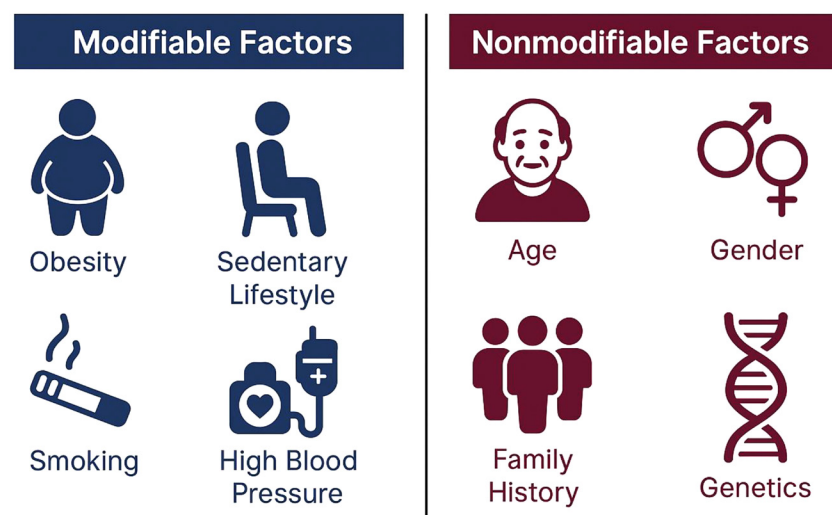


Fig 1 | Modifiable and non-modifiable risk factors of atherosclerosis

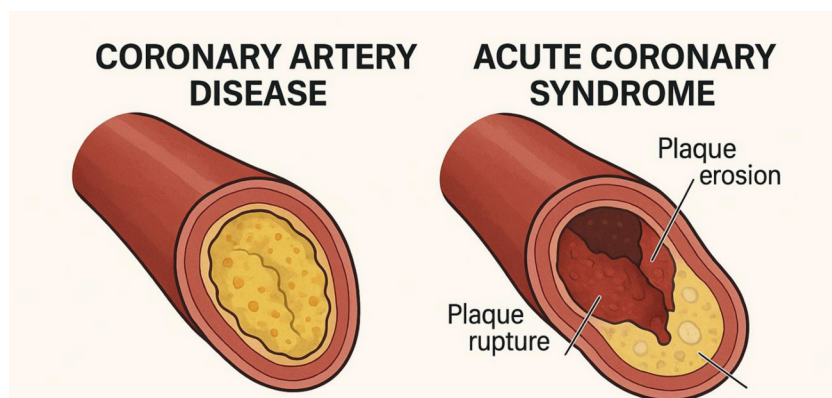


Fig 2 | CAD and ACS

Signs and Symptoms of CAD and ACS

ACS and CAD manifest as a spectrum of symptoms arising from impaired myocardial perfusion. Angina is the hallmark symptom of CAD, with exertional chest discomfort being the most common presentation. However, in cases where coronary artery stenosis exceeds 90%, angina may occur even at rest.¹⁵ The disease progression is further complicated by plaque rupture, which exposes tissue factor and initiates thrombosis, potentially leading to subtotal or total occlusion of the coronary lumen. Such acute obstruction frequently precipitates ACS, presenting as unstable angina, non-ST-elevation myocardial infarction,¹⁶ or ST-elevation myocardial infarction,¹⁷ depending on the degree of vascular insult. Additional symptoms include dyspnea, dizziness, nausea, and excessive sweating. Notably, CAD symptoms tend to be insidious and persist over extended periods, whereas ACS is characterized

by sudden-onset, intense substernal chest pain or pressure that may radiate to the arms, neck, jaw, or back and is frequently accompanied by dyspnea.¹⁵

Complications

The complications of arteriosclerotic diseases can be severe and life-threatening. CAD increases the risk of chronic kidney disease and end-stage renal disease,^{18,19} whereas ACS may lead to left ventricular dysfunction, cardiogenic shock, recurrent ischemia and infarction, pericardial effusion, pericarditis, arrhythmias, and venous thromboembolism.²⁰ Structural complications, including left ventricular aneurysm, thrombus formation, and arterial embolism, further exacerbate the disease burden. According to a previous study,²¹ patients with these comorbidities face a substantially increased risk of recurrent events, with an annual mortality rate five to six times higher. Owing to these complications, the global impact of CAD remains profound, accounting for 8.9 million deaths and 164.0 million disability-adjusted life years in 2015.¹⁷

Prognosis

The prognosis of CAD and ACS depends on several factors, including the extent of arterial obstruction, the presence of comorbidities, and the timeliness of medical intervention. Early implementation of revascularization strategies, lifestyle modifications, and pharmacologic therapies significantly improves outcomes; however, the risk of recurrent ischemia and progressive heart failure remains a long-term concern. In a study by Shibata et al.,²² deaths and new myocardial infarctions occurred in 22% and 10%, respectively, at 6 months, and in 60% and 20%, respectively, at 4 years in patients with ACS managed with angiotensin-converting enzyme inhibitors (ACEIs) after discharge. Several demographic and clinical variables have been identified as independent predictors of poor prognosis, including advanced age and a high burden of comorbidities. Gender disparities further influence outcomes, with Wada et al.²³ reporting that women experience poorer prognoses compared to men following percutaneous coronary intervention (PCI). Moreover, gender differences in symptom presentation complicate early diagnosis, as women are more likely to exhibit atypical symptoms, which can contribute to misdiagnosis or delayed recognition of ischemia, leading to adverse clinical outcomes.

Diagnosis and Clinical Assessments

Differentiating between CAD and ACS is fundamental for accurate diagnosis and treatment. Given the chronic and progressive nature of CAD, coronary angiography is commonly employed to assess the severity of arterial stenosis, determining the extent of vascular obstruction. Clinical evaluation for CAD encompasses a range of diagnostic approaches, including electrocardiography, stress testing, and echocardiography, which facilitate a functional assessment of myocardial perfusion. Additionally, clinical prediction models for CAD diagnosis undergo continuous validation, updates, and extensions to improve diagnostic accuracy.^{24,25}

Conversely, ACS usually presents as a medical emergency requiring immediate intervention to mitigate complications. Hence, the ability to detect plaque rupture in clinical practice has constituted a significant challenge.²⁶ Advanced intravascular imaging modalities, such as intravascular ultrasonography and optical coherence tomography, have therefore been used in recent times to provide detailed insights into plaque morphology, structural instability, and rupture characteristics, aiding in precise diagnosis.²⁷

Despite advances in the distinct diagnostic modalities for ACS and CAD, several factors, including atypical symptoms and silent ischemia, complicate the diagnosis, often resulting in delayed or missed detection. Atypical symptom presentation, frequently observed in women, older adults, and individuals with diabetes, presents a significant challenge. While classic symptoms include exertional chest pain, atypical manifestations such as nausea, fatigue, and dyspnea may obscure clinical suspicion, increasing the risk of underdiagnosis.²⁸ Similarly, silent ischemia, characterized by myocardial ischemic episodes without noticeable symptoms, is particularly prevalent in individuals with diabetes due to autonomic dysfunction, leading to underdiagnosis and elevated morbidity rates.²⁹ This underscores the critical need for effective differentiation between these conditions to ensure timely intervention for improved patient outcomes and mitigation of the disease progression. An integrated, multimodal approach that incorporates advanced imaging techniques, biochemical markers, and refined clinical prediction models is therefore warranted to enhance diagnostic accuracy.

Methods

Search Strategy

A comprehensive literature search was conducted to identify relevant studies on the clinical management of CAD and ACS published in the last 15 years (January 1, 2010–April 30, 2025). The databases searched included PubMed, Embase, Scopus, and the Cochrane Library. Both Medical Subject Headings and free-text keywords were used to ensure comprehensive coverage. Search terms included combinations of “coronary artery disease,” “acute coronary syndrome,” “clinical management,” “treatment,” “PCI,” “CABG,” and “evidence-based practice.” Boolean operators were applied to appropriately structure the search queries.

Boolean operators (AND, OR) were used to structure the search. For example, a sample search string in PubMed was: (“coronary artery disease” OR “coronary heart disease” OR “CAD”) AND (“acute coronary syndrome” OR “ACS”) AND (“clinical management” OR “treatment” OR “therapy” OR “intervention”) AND (“current evidence” OR “recent advances” OR “updated guidelines”). Similar adaptations of these terms and filters were applied in other databases.

Selection Criteria

Regarding inclusion criteria, articles were considered eligible if they were published in English between April 2010 and April 2025, focused on human populations,

and addressed the clinical management of CAD and ACS. Priority was given to studies that explored both pharmacological and procedural treatment approaches. The study designs of the reviewed articles included randomized controlled trials, observational studies, and official clinical guidelines. For the exclusion criteria, studies were excluded if their primary focus involved animal or laboratory-based research without direct clinical application. Similarly, work that focused on basic science, genetics, or pathophysiological mechanisms without providing insights into patient care was excluded.

The literature search, study selection, and reporting for this narrative review were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidance. 30 The full PRISMA flow diagram detailing the identification, screening, eligibility, and inclusion of records is provided (Figure 3).

Quality Grading

A formal risk of bias appraisal using standardized tools, such as ROBIS, was not conducted, as this review followed a narrative design rather than a systematic one. However, to ensure the credibility of the evidence presented, an informal grading approach was used based

on the hierarchy of evidence. Studies were assessed in terms of their design, with greater interpretive weight given to high-quality evidence such as randomized controlled trials (RCTs),³¹ clinical guidelines, and systematic reviews. Observational studies and other study designs were included to enrich context but were interpreted with appropriate caution.

Results

A total of 1,314 records were identified through database searches. After applying the inclusion and exclusion criteria, seven studies were included in the final review. The study selection process is summarized in the PRISMA flow diagram (Figure 3). The management of atherosclerotic diseases requires an interdisciplinary approach that integrates medical therapy, lifestyle modifications, cardiac rehabilitation, and interventional procedures to reduce the risk of heart attack and improve patient outcomes

Lifestyle Modifications

In recent times, lifestyle modifications have become increasingly recognized as an essential intervention in the prevention and management of cardiovascular diseases, including CAD and ACS. These interventions exert a cumulative long-term effect on cardiovascular health, significantly reducing the risk of complications and adverse events.³² A 6-month follow-up study by Gaudel et al.³³ shows that behavioral interventions play a significant role in mitigating cardiometabolic risks and enhancing a patient's quality of life. Similarly, Lehman et al.³⁴ conducted a 3-year follow-up trial, which demonstrated the impact of lifestyle interventions in reducing blood pressure, heart rate, and dosages of anti-ischemic medications. Hence, lifestyle modifications such as smoking cessation, regular physical activity, and adherence to a heart-healthy diet have become fundamental in preventing and managing CAD and ACS progression.

A major lifestyle intervention for cardiovascular health hinges on dietary modifications. Heart-healthy diets, including the Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and plant-based diets, have been extensively recommended for preventing and managing cardiovascular disease.³⁵ These dietary patterns emphasize the consumption of fruits, vegetables, legumes, whole grains, and lean protein sources while minimizing or avoiding processed foods, trans fats, and sugar-sweetened beverages. Prevention guidelines strongly advocate these diets as effective strategies for improving cardiovascular health.³⁶ However, other emerging dietary patterns, such as the ketogenic diet and intermittent fasting, require further long-term investigation to determine their efficacy and safety in cardiovascular disease prevention.

Additionally, regular physical activity represents a major lifestyle intervention for cardiovascular health. Exercises such as brisk walking, strength training, flexibility exercises, and aerobic workouts have been reported to significantly improve heart health by increasing physiological cardiac hypertrophy and

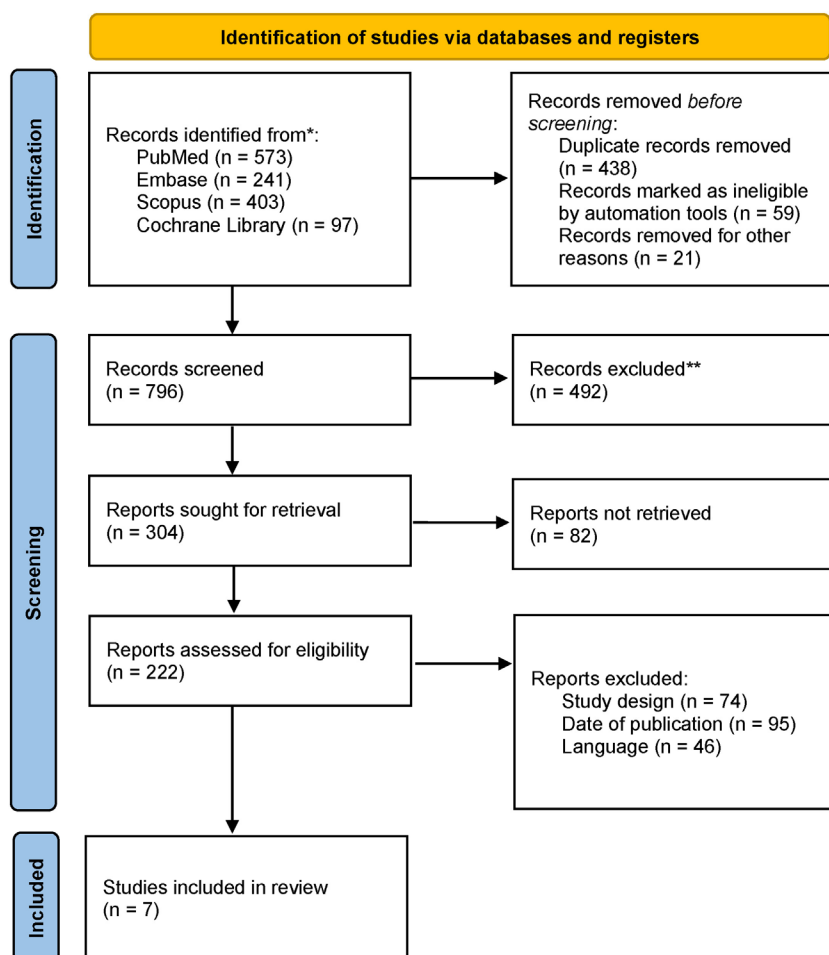


Fig 3 | PRISMA flow diagram. PRISMA, Preferred reporting items for systematic reviews and meta-analyses

decreasing resting heart rate, blood pressure, and atherogenic markers.³⁷ This intervention has been further implicated in the reduction of depression and in enhancing the quality of life in patients with heart disease following a major coronary event. The benefits of physical exercise appear to be independent of age or gender. A 2023 report by Jepma et al.³⁸ demonstrated that improved management of lifestyle-related risk factors in older adults was comparable to that observed in younger counterparts. This reinforces the importance of ensuring equal access to lifestyle modifications, regardless of demographic factors, while also ensuring that interventions are tailored to meet individual needs. Additionally, stress management techniques such as mindfulness and relaxation therapies, as well as smoking cessation, also contribute significantly to cardiovascular health. Further studies examining the influence of these psychosocial and socioeconomic factors on lifestyle adherence are therefore crucial for providing valuable insights into optimizing strategies for diverse populations.

Pharmacological Management

Conventional Drug Management

Current evidence in the pharmacologic management of ACS and CAD involves a combination of conventional drugs and emerging therapies to reduce myocardial ischemia, prevent recurrent events, and improve long-term survival (Figure 4). Clinical guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology emphasize a multifaceted therapeutic regimen tailored to each patient's profile.³⁹ Based on these guidelines, standard treatment approaches include antiplatelet agents, anticoagulants, lipid-lowering medications, and hemodynamically active agents such as beta-blockers, ACEIs, or angiotensin receptor blockers, all of which collectively improve outcomes when applied judiciously on a case-by-case basis.

To inhibit thrombus propagation in ACS, anticoagulant therapy, encompassing unfractionated heparin or low-molecular-weight heparins, plays a central role; however, these therapies are associated with bleeding risks. More recent advances with direct thrombin inhibitors, such as bivalirudin, which have more predictable pharmacokinetics, have therefore been shown to address the significant bleeding limitation of heparins, especially during invasive procedures.⁴⁰ Similarly, aspirin remains the first-line antiplatelet therapy against thrombus propagation due to its irreversible inhibition of platelet cyclooxygenase-1, thereby mitigating thromboxane A₂-A₂-mediated aggregation.⁴¹ When combined with a P2Y₁₂ receptor antagonist such as clopidogrel, prasugrel, or ticagrelor in dual antiplatelet therapy (DAPT), this approach reduces the incidence of thrombotic events post-ACS and PCI.⁴²

A critical challenge to DAPT remains the uncertain optimal duration after carotid artery stenting, bleeding risks, and the ambiguity in choosing the appropriate and patient-specific P2Y₁₂ receptor antagonist.⁴³ For instance, while certain individuals may develop resistance to clopidogrel, thus posing an incremental risk of deleterious cardiovascular events and stroke, the selection of ticagrelor addresses this gap. However, although ticagrelor demonstrates superior efficacy over clopidogrel according to the PLATO trial, the risk of increased bleeding persists.⁴⁴ The selection and duration of antiplatelet therapy in CAD and ACS, therefore, requires careful consideration of both efficacy and safety outcomes. The TWILIGHT trial⁴⁵ investigated whether ticagrelor monotherapy after 3 months of DAPT could reduce bleeding risk in high-risk patients following PCI. The study found that patients on ticagrelor alone had a significantly lower incidence of clinically relevant bleeding (4.0%) compared to those on ticagrelor plus aspirin (7.1%).

Unlike antiplatelet agents, beta-blockers do not interfere with coagulation pathways, making them a safer option for patients with high bleeding propensity. Beta-blockers, such as metoprolol, atenolol, and carvedilol, play a crucial role in addressing the gaps in DAPT by reducing myocardial oxygen demand, stabilizing heart rate, and preventing arrhythmias, thereby lowering the risk of recurrent ischemic events without increasing the risk of bleeding.^{46,47} In ACS, beta-blockers contribute to plaque stabilization, reducing the likelihood of rupture and subsequent thrombus formation. In contrast, ACEIs, such as ramipril or lisinopril, limit adverse ventricular remodeling and improve survival post-myocardial infarction.⁴⁸ The complementary mechanism of ACEIs and beta blockers on the sympathetic nervous system and the renin-angiotensin-aldosterone axis presents a compelling rationale for combination therapy. Recent studies, including the PRIDE observational study,⁴⁹ suggest that single-pill combinations such as bisoprolol and perindopril yield enhanced blood pressure control, symptom relief, and greater adherence, thus offering a promising strategy to achieve treatment targets more efficiently. However, patients may be susceptible to vasospasms or intolerant to beta-blockers.

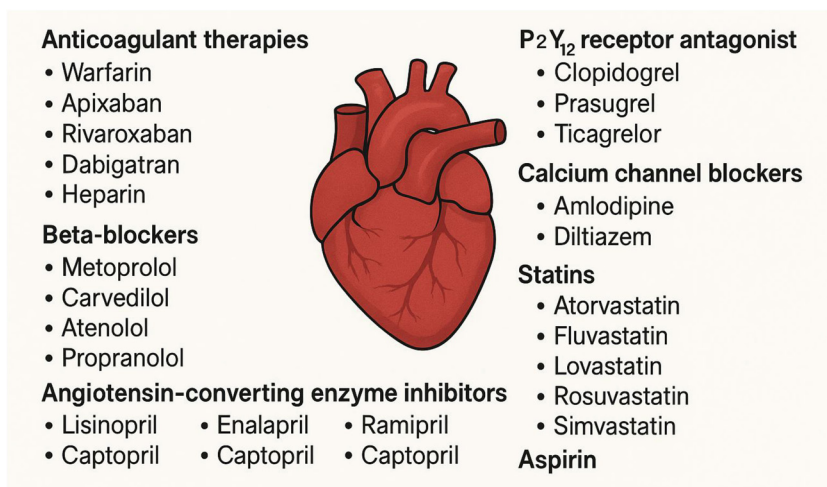


Fig 4 | Pharmacologic treatment options for CAD and ACS. CAD, Coronary artery disease; ACS, Acute coronary syndrome

In select patients, calcium channel blockers such as amlodipine and diltiazem are employed to address vasospasm or intolerance to beta-blockers.⁵⁰ Correspondingly, statins remain a mainstay for lipid management, with high-intensity agents like atorvastatin and rosuvastatin shown to significantly reduce LDL cholesterol (LDL-C) and plaque instability, as evidenced in the PROVE-IT TIMI 22 trial.⁵¹

Novel Pharmacologic Treatments

As treatment goals evolve, emerging therapies have begun to reshape the therapeutic landscape for persons with familial hypercholesterolemia or those unable to achieve LDL targets with statins alone. Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors, including alirocumab and evolocumab, represent new advances in the pharmacotherapy of ACS and have demonstrated profound LDL-lowering capabilities with substantial cardiovascular benefits as reported in the ODYSSEY OUTCOMES⁵² and FOURIER trials.⁵³ These monoclonal antibodies work by inhibiting PCSK9, a protein that facilitates LDL receptor degradation. By preventing receptor loss, more LDL can be removed from circulation, leading to a dramatic reduction of up to 60% in LDL-C levels. However, the long-term safety profile of these therapies remains under evaluation, with the most reported adverse effect being mild injection site reactions and, in rare instances, neurocognitive complaints.⁵⁴

Canakinumab, another novel monoclonal antibody therapy for atherosclerotic diseases, including ACS and CAD, is reported in the CANTOS trial.⁵⁵ Canakinumab exerts its anti-inflammatory effect by specifically inhibiting interleukin-1 β (IL-1 β), thereby reducing systemic inflammation that contributes to plaque destabilization.⁵⁶ According to the CANTOS trial, a 15% reduction in recurrent cardiovascular events among patients who received canakinumab is observed with canakinumab compared to placebo, reinforcing the role of inflammation in coronary pathology. Interestingly, the study also noted a potential reduction in lung cancer incidence among participants receiving the drug, hinting at broader applications beyond cardiovascular disease. However, the immunosuppressive

effects of IL-1 β blockade result in an increased risk of infections and neutropenia, which can limit the widespread adoption of canakinumab in routine cardiovascular care.⁵⁶ Further research is, however, needed to improve patient selection and ensure safety.

Other novel therapies undergoing trial include RNA-based therapies such as inclisiran, which utilize small interfering RNA to suppress hepatic PCSK9 synthesis, thus offering biannual dosing and sustained LDL reduction.⁵⁷ Clinical trials have demonstrated LDL-C reductions of approximately 50%, with sustained effects over 6 months, presenting a promising alternative to frequent subcutaneous monoclonal antibody injections.^{58,59} While the safety profile of inclisiran appears favorable and its ease of use and sustained LDL reduction make it an appealing option for patients struggling with adherence to traditional lipid-lowering therapies, evidence of its long-term systemic effects remains lacking.

Similarly, sodium-glucose cotransporter-2 (SGLT2) inhibitors like dapagliflozin and empagliflozin, which were initially developed for glycemic control, have demonstrated significant reductions in cardiovascular events, particularly in patients with CAD.⁶⁰ These drugs have been shown to improve cardiac function by promoting natriuresis and diuresis; these alleviate fluid overload. In the DAPA-HF trials,⁶¹ dapagliflozin was reported to lower heart failure hospitalizations by 26%, highlighting the role of SGLT2 inhibitors in cardiovascular risk reduction regardless of the presence or absence of diabetes. While SGLT2 inhibitors are generally well-tolerated, adverse effects such as urinary tract infections, euglycemic ketoacidosis, and hypotension in volume-depleted patients have also been observed. Table 1 provides a comparative overview of key clinical decision points in the management of stable CAD and ACS.

Clinical Procedures and Surgery

In cases of severe CAD or ACS, especially when pharmacologic therapy alone is insufficient, interventional strategies such as PCI with stent placement or coronary artery bypass grafting (CABG) are utilized to restore blood flow in affected arteries. With the 2023 ESC Guidelines²⁴ highlighting the advantages of an early

Table 1 | Clinical decision checklist for CAD and ACS management

	Stable CAD	ACS
Clinical Presentation	Exertional chest pain, stable angina, no acute ECG or biomarker changes	Chest pain at rest, ECG changes, troponin elevation
Initial Risk Stratification	Functional testing Coronary CTA or stress imaging	TIMI/GRACE score Immediate ECG + troponin
Antiplatelet Therapy	Aspirin P2Y ₁₂ inhibitor	DAPT: Aspirin + P2Y ₁₂ inhibitor
Bleeding Risk Assessment	PRECISE-DAPT ARC-HBR	Adjust DAPT duration based on bleeding and ischemic risk
Lipid Management	LDL-C goal: <70–<55 mg/dL	High-intensity statin Ezetimibe and PCSK9 inhibitor
Revascularization Decision	Based on symptoms or ischemia burden	Emergent PCI or other early invasive strategy

CAD, Coronary artery disease; ACS, Acute coronary syndrome; DAPT, Dual antiplatelet therapy; CTA, Computed tomography angiography; ECG, Electrocardiogram; TIMI, Thrombolysis in myocardial infarction; GRACE, Global registry of acute coronary events; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; LDL-C, Low-density lipoprotein cholesterol; PRECISE-DAPT, Predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy; ARC-HBR, Academic Research Consortium for High Bleeding Risk.

invasive strategy for high-risk individuals with atherosclerotic diseases, revascularization with PCI has been identified as a critical therapy for most patients with ACS.⁶² This minimally invasive procedure involves threading a catheter through the femoral or radial artery to reach the site of arterial narrowing, followed by balloon inflation to widen the artery. Stent placement often accompanies this procedure to prevent restenosis. PCI offers the advantage of immediate restoration of blood flow, shorter recovery times, and a lower risk of complications compared to surgical alternatives.⁶³ Recent trials reporting the use of the SYNTAX II PCI strategy have reported outcomes in complex CAD, showing improved survival rates compared to traditional invasive techniques.⁶⁴

For patients with extensive arterial blockages, CABG remains the gold standard surgical approach. CABG is a major surgical operation where atheromatous blockages in a patient's coronary arteries are bypassed with harvested venous or arterial conduits.⁶⁵ This procedure is particularly advantageous for patients with ACS or CAD complicated with morbidities such as diabetes or left main coronary artery involvement, as it offers superior long-term survival and lower rates of repeat interventions compared to PCI. The ART trial, which assessed the outcomes of single versus bilateral internal mammary artery grafting, found better long-term survival in patients who underwent bilateral grafting, thereby reinforcing the efficacy of CABG.⁶⁶ Furthermore, the EXCEL trial compared CABG to PCI in left main CAD and demonstrated the superiority of CABG in complex cases where multiple stents would otherwise be required.⁶⁷ Additionally, hybrid coronary revascularization presents an innovative strategy to address complex cases of CAD by combining PCI and CABG in a single treatment plan. This approach optimizes management for patients with complex coronary anatomy, leveraging the benefits of minimally invasive PCI for accessible lesions while utilizing CABG for more severe obstructions. As highlighted by Ullman et al.,⁶⁸ hybrid revascularization therapy results in improved recovery times and reduced hospital stays compared to

standalone CABG procedures, suggesting its potential to be widely adopted as a surgical and interventional cardiology technique tailored to meet the complex manifestation of CAD.

In cases where CAD coexists with severe aortic stenosis, transcatheter aortic valve replacement (TAVR) serves as an effective alternative to conventional open-heart valve replacement. Unlike surgical aortic valve replacement, TAVR is performed via catheter insertion, allowing for the implantation of a prosthetic valve without the need for a sternotomy or cardiopulmonary bypass.⁶⁹ This approach is particularly beneficial for elderly and high-risk surgical candidates, significantly reducing perioperative complications and hospital stays. Studies have also reported TAVR's superiority over surgical valve replacement in younger or low-risk patients, demonstrating comparable outcomes.⁷⁰ In more severe cases, such as in critically ill patients experiencing cardiogenic shock or severe ACS, mechanical circulatory support devices such as Impella pumps, intra-aortic balloon pumps, and extracorporeal membrane oxygenation may be employed to provide temporary cardiac support.⁷¹ These devices help stabilize patients by improving cardiac output and oxygenation, particularly in high-risk surgical or post-ACS scenarios. While these devices improve hemodynamic stabilization and procedural success, adverse events have been reported more significantly with Impella pumps than with intra-aortic balloon pumps.⁷² However, combining these procedural advancements offers a range of options tailored to individual patient profiles, ensuring optimal revascularization strategies while minimizing adverse outcomes.

Table 2 provides a summary of key clinical trials highlighting evidence-based approaches to the management of CAD and ACS.

Quality Grading

All seven studies included in this review were RCTs, representing the highest level of primary evidence for evaluating clinical interventions.³¹ These trials were generally well-conducted, with clearly defined

Table 2 | Summary of key clinical trials on the management of CAD and ACS

Trial	Therapy	Study Design	Number of Participants	Outcome	Effect Size
TWILIGHT ⁴⁵	Ticagrelor monotherapy post-PCI in high-risk patients	RCT	7,119	Reduced incidence of BARC type 2, 3, or 5 bleeding	4.0% vs. 7.1% (HR, 0.56; 95% CI, 0.45–0.68; P < 0.001)
PROVE-IT TIMI 22 ⁵¹	Intensive versus moderate lipid lowering with statins after ACS	RCT	4,162	Intensive therapy provided greater protection against MACE and death	16% reduction in the HR (P = 0.005; 95% CI, 5–26%)
ODYSSEY OUTCOMES ⁵²	Alirocumab	RCT	18,924	Lower incidence of MACE and death	9.5% vs. 11.1% (HR, 0.85; 95% CI, 0.78–0.93; P < 0.001)
FOURIER ⁵³	Evolocumab	RCT	27,564	Reduced risk of MACE and death	9.8% vs. 11.3% (HR, 0.85; 95% CI, 0.79–0.92; P < 0.001)
CANTOS ⁵⁵	Canakinumab (50 mg, 150 mg, and 300 mg, every 3 months)	RCT	10,061	Lower rate of recurrent cardiovascular events (lowest with 150 mg dose)	Placebo, 4.50; 50 mg, 4.11; 150 mg, 3.86; and 300 mg, 3.90 events/100 person-years
ART ⁶⁶	Bilateral vs. Single Internal-Thoracic-Artery Grafts	RCT	3,102	No significant between-group difference in the rate of death	20.3% vs. 21.2% (HR, 0.96; 95% CI, 0.82–1.12; P = 0.62)
EXCEL ⁶⁷	PCI or CABG for Left Main Coronary Disease	RCT	1,905	No significant difference in the rates of death and MACE occurrence	22.0% vs. 19.2% (95% CI, –0.9–6.5; P = 0.13)

RCT, Randomized controlled trial; PCI, Percutaneous coronary intervention; CAD, Coronary artery disease; ACS, Acute coronary syndrome; CABG, Coronary artery bypass grafting; BARC, Bleeding Academic Research Consortium; MACE, Major adverse cardiovascular events; HR, Hazard ratio; CI, Confidence interval.

inclusion criteria, intervention protocols, outcome measures, and follow-up durations. Although a formal risk of bias assessment was not conducted due to the narrative design of the review, the rigorous methodological characteristics typical of RCTs improve the credibility and reliability of the findings presented.

To provide a comprehensive understanding of current clinical management strategies for CAD and ACS, findings from the RCTs were supplemented with supporting evidence from additional peer-reviewed studies, including observational studies, expert consensus statements, and updated clinical guidelines. These supplementary sources were used to provide context and clarify variations in clinical practice.

Discussion

Challenges in the Management of CAD and ACS

Despite significant advancements in the clinical management of CAD and ACS, several limitations persist in both pharmacologic and interventional strategies. One major challenge is the heterogeneity of patient responses to treatment. Although dual DAPT continues to be a common strategy for ACS management, the best duration of treatment is still debated, especially for patients at high risk of bleeding. The balance between ischemic protection and hemorrhagic complications continues to pose a clinical challenge, necessitating individualized treatment approaches and larger-scale research. However, many studies focus on relatively homogeneous cohorts, limiting the generalizability of findings to broader patient populations. Moreover, long-term safety data for newer pharmacologic therapies, including PCSK9 inhibitors, RNA-based lipid-lowering agents, and anti-inflammatory treatments such as canakinumab, remain incomplete. While short-term effectiveness is well established, concerns about potential adverse effects from long-term use require further research.

From an interventional perspective, revascularization strategies such as PCI and CABG, while highly effective, have inherent drawbacks. PCI, despite its minimally invasive nature, carries a higher risk of restenosis and late thrombosis, particularly in complex coronary lesions. Whereas, CABG offers superior long-term outcomes but is associated with higher perioperative morbidity, especially among older adult patients. The challenge remains in optimizing patient selection for hybrid approaches, where PCI is combined with CABG to achieve favorable outcomes while minimizing procedural risks.

Finally, adherence to long-term cardiovascular therapy continues to be a significant barrier. Polypharmacy, socioeconomic limitations, and patient engagement in preventive care continue to pose a challenge. The development of fixed-dose combination therapies and personalized medicine may enhance compliance; however, further translational research is needed to achieve this goal.

Future Directions

Addressing the limitations in the clinical management of ACS and CAD requires an integrated approach,

leveraging precision medicine, advanced imaging, and artificial intelligence–driven risk prediction models. Future studies targeting large-scale populations, long-term effects of newer pharmacologic medications, and patient-specific therapies are warranted to advance knowledge in optimizing patient care. This underscores the critical need for effective differentiation between patient peculiarities to ensure timely and individualized interventions, thereby improving outcomes and mitigating disease progression. Specifically, while RNA-based therapies, such as inclisiran, represent a major shift in lipid management with significant implications for improving patient adherence and reducing the lifelong burden of statin therapy, the uncertainty surrounding their long-term adverse effects needs to be clarified. Recent advancements in gene-editing technologies, including CRISPR-based interventions,⁷³ may offer novel solutions for bridging current treatment gaps and should therefore be explored. CRISPR-Cas9 has shown early promise in targeting key regulators of lipid metabolism, including PCSK9 and ANGPTL3, which are involved in the modulation of LDL-C and triglyceride levels.⁷⁴ However, while these developments are exciting, long-term safety data remain limited, and concerns persist regarding off-target gene edits and immune reactions.⁷⁴

Furthermore, future research should investigate the psychosocial and socioeconomic factors that influence lifestyle adherence, as these elements are crucial for optimizing treatment strategies for diverse populations. While dietary plans like the Mediterranean, DASH, and plant-based diets are well-supported in preventing cardiovascular disease, new dietary patterns, such as the ketogenic diet and intermittent fasting, require further long-term studies to verify their safety and effectiveness. Likewise, examining how various physical activity routines affect ACS and CAD, along with demographic factors like age and gender, can help develop more tailored exercise programs.

Equitable access to lifestyle modifications remains essential, ensuring that interventions are inclusive and adaptable across different demographic groups. In parallel, the integration of wearable technology and digital health solutions is expected to transform the management of CAD and ACS. Continuous cardiac monitoring, combined with AI-engineered therapies, can facilitate early detection and proactive intervention, ultimately reducing hospitalizations and improving long-term patient outcomes. Awasthi et al.⁷⁵ utilized digital data from more than 7 million patients from hospitals across five states in the US to develop a deep learning model for analyzing electrocardiograms and providing clinical decision support. The model was trained to detect the presence of key indicators of CAD, including high coronary artery calcium, obstructive CAD, and left ventricular akinesis, among patients who had no history of atherosclerosis. The model demonstrated strong predictive performance, with an AUROC of 0.88 for coronary artery calcium ≥ 300 Agatston units, 0.85 for obstructive CAD, and 0.94 for akinesis. These AI-based innovations can ensure more

precise therapeutic strategies tailored to individual patient profiles and need to be explored extensively. However, the deployment of AI-based innovations in clinical settings must adhere to stringent regulatory standards. Consistent with the 2024 EU AI Act,⁷⁶ which classifies AI systems in healthcare as high-risk, AI systems and their use must be guided by transparent and guided by human oversight.

Future research should address medication adherence. Digital tools, including mobile apps and remote monitoring, can support adherence and personalize follow-up care. Evaluating the cost-effectiveness of both current and emerging therapies is crucial for guiding the sustainable adoption and allocation of resources. Given the need for these interventions in low- and middle-income countries, future research should prioritize affordable interventions tailored to local health systems.

Study Limitations

This review has certain limitations that should be acknowledged. As a narrative review, this study did not follow a systematic methodology for article selection and data synthesis, which may introduce selection bias and limit reproducibility. Moreover, the search was restricted to English-language publications, potentially overlooking relevant evidence published in other languages and contributing to language bias. Furthermore, while emerging therapies such as CRISPR-based lipid editing and novel antiplatelet strategies are considered promising areas for future research, many of these interventions currently lack long-term safety and outcome data, which limits their immediate applicability in routine clinical practice. These factors should be considered when interpreting the findings and implications of this review.

Conclusion

This review provides current evidence on the clinical management of ACS and CAD, which is crucial for advancing comprehensive and long-term care for patients. As new evidence emerges, clinical practice must remain adaptable, ensuring that evolving therapies translate into meaningful improvements in survival and quality of life for individuals affected by CAD and ACS. The management of CAD and ACS has evolved significantly, incorporating pharmacologic, interventional, and digital health innovations to improve outcomes. Conventional therapies such as statins, antiplatelet agents, and revascularization procedures remain the cornerstone of cardiovascular care. Nonetheless, challenges persist, particularly in optimizing DAPT duration, improving adherence, and refining patient selection for emerging therapies. Newer approaches, including PCSK9 inhibitors, RNA-based lipid-lowering therapies, and anti-inflammatory agents, have emerged with significant potential for expanding individualized patient care while addressing the limitations of traditional therapies.

Interventional advancements, such as hybrid coronary revascularization and AI-assisted therapies,

offer promising solutions to reduce procedural complications and improve long-term outcomes in patients with the represented atherosclerotic disease. These interventions can significantly improve real-time cardiac monitoring, offering a proactive approach to CAD and ACS management. Despite these advancements, continued research is essential to refine treatment protocols, integrate personalized medicine, and expand equitable healthcare access worldwide. Future directions should prioritize multidisciplinary collaboration, leveraging pharmacologic innovation, surgical expertise, and AI-assisted tools to enhance cardiovascular care in patients with ACS and CAD.

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