

Advances in understanding and managing acute coronary syndrome: Pathophysiology, diagnostic innovations, and therapeutic strategies

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ABSTRACT Acute Coronary Syndrome (ACS) encompasses unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI), which arise from acute myocardial ischemia due to coronary artery obstruction. ACS is a leading cause of global morbidity and mortality, requiring prompt diagnosis and intervention. Pathophysiology involves plaque rupture, thrombosis, and ischemic injury, exacerbated by systemic inflammation and oxidative stress. Diagnosis is guided by clinical symptoms, electrocardiography (ECG), and biomarkers like high-sensitivity troponins, complemented by imaging tools such as echocardiography and coronary computed tomography angiography (CCTA). Treatment aims to restore perfusion, reduce myocardial damage, and prevent recurrence. STEMI necessitates immediate reperfusion via primary percutaneous coronary intervention (PCI) or fibrinolysis, while NSTEMI and UA management depends on risk stratification using tools like GRACE or TIMI scores. Dual antiplatelet therapy (DAPT), anticoagulants, beta-blockers, statins, and ACE inhibitors form the cornerstone of pharmacological treatment. Recent advancements include newer antiplatelet agents (ticagrelor, prasugrel), lipid-lowering therapies (PCSK9 inhibitors), and hybrid approaches combining PCI and coronary artery bypass grafting (CABG). Challenges persist in timely diagnosis, access to advanced care, and addressing disparities in outcomes. Multidisciplinary care and cardiac rehabilitation are critical for improving long-term prognosis. Emerging technologies, including digital health and AI-driven tools, hold promise for enhancing ACS management. In summary, a comprehensive, evidence-based approach is essential for managing ACS effectively, with ongoing innovation and global efforts aimed at improving equity, access, and personalized care.

KEYWORDS acute coronary syndrome, unstable angina, NSTEMI, STEMI, myocardial infarction, revascularization, risk stratification, multidisciplinary care, pharmacological advances

1. INTRODUCTION

ACS represents an acute cardiac disease that comes as a form of acute myocardial ischemia resulting from compromised or obstructed blood flow to the coronary arteries. It essentially presents in three major clinical entities: unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) [1]. As a collective group, it contributes to morbidity and mortality in the whole world at rates that are of concern [2]. Early recognition, accurate diagnosis, and timely intervention are the keys to optimizing outcomes and minimizing complications [3].

The pathophysiology of ACS derives from the atheroscle-

rotic plaque tear or erosion culminating in the thrombus which, in due course, fills up the ostia of one or more segments of the coronaries. Subsequent mechanisms by which ischemia and myocardial injury occur encompass vasospasm, microvascular dysfunction, as well as spontaneous coronary artery dissection [4]. All these together have driven advanced diagnostic methods, and therapeutic management to make treatments more precise as well as better in management scope [5].

In the last few years, not just high-sensitivity cardiac biomarkers but also advanced imaging techniques as well as risk stratification systems transformed the approach to ACS

care [6]. Similarly, pharmacologic and interventional advancements, including dual antiplatelet therapy, drug-eluting stents, and revascularization techniques, improved the best outcomes of the patients involved [7]. Challenges persist, such as ensuring timely access to care and addressing regional disparities in healthcare resources [8].

This paper aims to discuss the current scenario of ACS, focusing on the latest developments in diagnosis, management, and prevention. By pointing out these developments, we are trying to stress the importance of a multidisciplinary, patient-centered approach in dealing with this critical public health challenge [9].

1.1. Search strategy

We conducted a literature search using the databases PubMed, Scopus, Web of Science, and Google Scholar. The keywords used included "Acute Coronary Syndrome," "STEMI," "NSTEMI," "unstable angina," "myocardial infarction," "revascularization," and "risk stratification." Studies, clinical guidelines, and systematic reviews published within the last ten years were preferred.

2. PATHOPHYSIOLOGY OF ACUTE CORONARY SYNDROME

Acute Coronary Syndrome, or ACS, is primarily driven by the disruption of acute myocardial ischemia due to an abrupt interference in coronary blood flow. Underlying mechanisms for this interference have proved to be complex and include plaque instability due to atherosclerosis, thrombus formation, vasospasm, and, rarely, spontaneous dissection of the coronary arteries.

2.1. Plaque rupture or erosion

Most initiating events for ACS is the rupture or erosion of an atherosclerotic plaque within the coronary artery [10]. This event exposes the lipid core and subendothelial matrix to circulating blood, which results in platelet activation, aggregation, and the coagulation cascade. The resulting thrombus partly or completely occludes the coronary artery leading to ischemia and myocardial injury [11].

2.2. Inflammatory processes

Inflammation plays a key role in the pathogenesis of plaque instability. Increased levels of inflammatory markers, including C-reactive protein (CRP), have been linked to increased risk of ACS [12]. Inflammatory cells, such as macrophages and T-lymphocytes, infiltrate the plaque, releasing enzymes such as matrix metalloproteinases (MMPs) that weaken the fibrous cap and predispose it to rupture [13].

2.3. Vasospasm and microvascular dysfunction

In some instances, ischemia might be caused by coronary vasospasm, that is, the sudden, transient narrowing of coronary arteries. In this mechanism, the condition Prinzmetal's angina often comes into consideration [14]. Finally, microvascular dysfunction, meaning impaired vasodilation and enhanced

vascular resistance, is another contribution to myocardial ischemia and is especially encountered in patients suffering from nonobstructive CAD [15].

2.4. Spontaneous coronary artery dissection (SCAD)

Although it is rare, SCAD is an important non-atherosclerotic cause of ACS. It occurs due to the formation of an intramural hematoma or an intimal tear within the coronary artery that leads to obstruction of blood flow. SCAD predominantly affects younger women, often in the context of pregnancy or connective tissue disorders [16].

2.5. Systemic responses to ischemia

Acute ischemia elicits systemic inflammatory and oxidative stress response, which worsens the myocardial injury. These responses invite further endothelial dysfunction, increased vascular permeability, and enhanced thrombus formation based on [17].

3. CLINICAL PRESENTATION AND DIAGNOSIS

3.1. Clinical presentation

ACS is a presentation of acute coronary syndrome that may differ from patient to patient depending on age, gender, and other comorbidities. Chest pain is the classic symptom that is often described as a sensation of pressure, tightness, or burning and radiates to the left arm, neck, jaw, or back according to cite [18]. Other symptoms include dyspnea, diaphoresis, nausea, and fatigue. Atypical presentations are more common in women, the elderly, and diabetic patients, where symptoms such as epigastric discomfort, dizziness, or syncope may dominate [19].

3.2. Diagnostic tools

Accurate and timely diagnosis of ACS is critical to optimizing outcomes. Diagnosis relies on a combination of clinical evaluation, electrocardiography (ECG), and cardiac biomarkers:

- **Electrocardiography (ECG):** ECG is the cornerstone of initial ACS diagnosis. It helps differentiate ST-elevation myocardial infarction (STEMI), which requires urgent revascularization, from non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA) [20]. Classic findings in STEMI include ST-segment elevation in two contiguous leads, while NSTEMI and UA may present with ST-segment depression or T-wave inversions [21].
- **Cardiac Biomarkers:** High-sensitivity troponins (hs-cTn) have revolutionized ACS diagnostics, enabling the detection of myocardial injury with high sensitivity and specificity. Elevated hs-cTn levels are a key criterion for diagnosing NSTEMI [22]. Serial measurements are essential to distinguish acute events from chronic elevations due to other conditions [23].
- **Imaging Modalities:** Echocardiography provides valuable information about left ventricular function, regional wall motion abnormalities, and complications such as

pericardial effusion [24]. Coronary computed tomography angiography (CCTA) is increasingly used for evaluating coronary anatomy and ruling out significant obstructions in low- to intermediate-risk patients [25].

3.3. Risk stratification

Risk stratification is a vital component of ACS management, guiding therapeutic decisions. Tools such as the GRACE (Global Registry of Acute Coronary Events) and TIMI (Thrombolysis in Myocardial Infarction) scores assess the likelihood of adverse outcomes, assisting clinicians in determining the need for invasive versus conservative approaches [26].

4. MANAGEMENT OF ACUTE CORONARY SYNDROME

4.1. Goals of management

The primary goals in managing Acute Coronary Syndrome (ACS) are to restore coronary perfusion, minimize myocardial damage, prevent complications, and reduce the risk of recurrent ischemic events [27]. Management strategies are tailored based on the ACS subtype (STEMI, NSTEMI, or UA) and the patient's clinical profile.

4.2. Revascularization strategies

- **ST-Elevation Myocardial Infarction (STEMI):** In STEMI, immediate reperfusion is critical. Primary percutaneous coronary intervention (PCI) is the preferred method, ideally performed within 90 minutes of first medical contact. PCI techniques have advanced with the use of drug-eluting stents (DES) and intravascular imaging, improving outcomes [28]. When PCI is unavailable, fibrinolysis within 30 minutes is recommended as an alternative [29].
- **Non-ST-Elevation Myocardial Infarction (NSTEMI) and Unstable Angina (UA):** Management of NSTEMI and UA depends on risk stratification. High-risk patients benefit from early invasive strategies, including angiography and PCI, while low-risk patients may be managed conservatively with close monitoring and medical therapy [30]. Complete revascularization, particularly in patients with multivessel disease, has shown to improve long-term outcomes [31].

4.3. Pharmacological therapy

Pharmacological treatment forms the backbone of ACS management, with the following key components:

- **Dual Antiplatelet Therapy (DAPT):** DAPT, consisting of aspirin and a P2Y₁₂ inhibitor (e.g., clopidogrel, ticagrelor, or prasugrel), is essential to prevent thrombosis. Newer agents like ticagrelor and prasugrel have shown superior efficacy but carry a higher bleeding risk [32].
- **Anticoagulants:** Agents such as unfractionated heparin, low-molecular-weight heparin (LMWH), or direct oral anticoagulants (DOACs) are used to reduce thrombotic complications [33].

- **Other Medications:** Beta-blockers, ACE inhibitors (or ARBs), and statins address ischemia, control blood pressure, and manage dyslipidemia. PCSK9 inhibitors are increasingly used in patients with residual lipid abnormalities despite statin therapy [34].

4.4. Adjunctive and supportive measures

Cardiac rehabilitation programs are crucial for secondary prevention, focusing on lifestyle modifications, psychological support, and adherence to pharmacotherapy. Smoking cessation, a healthy diet, and regular physical activity are integral to improving long-term outcomes [35].

4.5. Addressing disparities and timely access to care

Delays in symptom recognition, prehospital care, and access to advanced diagnostic and therapeutic modalities remain significant challenges. Streamlined care pathways, public awareness campaigns, and equitable healthcare policies are essential to bridge these gaps and improve outcomes across diverse populations [36].

4.6. Emerging therapies and future directions

Ongoing research is exploring hybrid approaches combining PCI and coronary artery bypass grafting (CABG) for complex cases. Digital health technologies, such as remote monitoring and AI-based decision-making tools, hold promise for improving care precision and efficiency [37].

5. RECENT ADVANCES AND EMERGING THERAPIES

5.1. Advancements in revascularization techniques

Revascularization remains a cornerstone in the management of Acute Coronary Syndrome (ACS). Advances in percutaneous coronary intervention (PCI) techniques, including the development of second-generation drug-eluting stents (DES) and intravascular imaging technologies, have significantly improved outcomes by reducing restenosis and ensuring precise stent placement [38]. Additionally, complete revascularization strategies, particularly in multivessel disease, have demonstrated superior long-term benefits compared to culprit-only interventions [39]. Hybrid approaches, combining PCI with coronary artery bypass grafting (CABG), are being explored for complex cases to individualize care [40].

5.2. Innovations in pharmacological therapies

- **Antiplatelet Therapy:** Newer P2Y₁₂ inhibitors, such as ticagrelor and prasugrel, have shown enhanced efficacy in reducing ischemic events compared to clopidogrel. These agents, however, require careful consideration of bleeding risks, especially in high-risk patients [41].
- **Lipid-Lowering Agents:** Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have revolutionized dyslipidemia management, providing additional LDL-C reduction in patients with residual lipid abnormalities despite statin therapy. These agents significantly lower the risk of recurrent cardiovascular events [42].

- **Anticoagulants:** Direct oral anticoagulants (DOACs) are being evaluated for their role in ACS, particularly in patients with concomitant atrial fibrillation. Early trials suggest potential benefits in specific patient subsets [43].

5.3. Digital health and artificial intelligence

The integration of digital health technologies into ACS care has gained momentum. Remote monitoring systems and wearable devices enable continuous tracking of vital parameters, enhancing early detection and management of complications [44]. Artificial intelligence (AI)-based tools are being developed to support clinical decision-making by analyzing large datasets for personalized risk stratification and treatment optimization [45].

5.4. Inflammation as a therapeutic target

Inflammation is a critical contributor to atherosclerosis and ACS pathogenesis. Targeting inflammatory pathways has shown promise, as evidenced by the success of therapies like canakinumab, an IL-1 β inhibitor, in reducing cardiovascular events in high-risk patients. Ongoing trials are exploring other anti-inflammatory agents to further refine this approach.

5.5. Regenerative and stem cell Therapies

Regenerative medicine emerges as a promising direction for the treatment of myocardial damage following an acute coronary syndrome. Stem cell-based therapies target repair or replacement of damaged cardiac tissue, although clinical use remains in the experimental stage. Initial results from early studies in the area have included some promising improvements in cardiac function and scar reduction.

5.6. Reducing health disparities, cost, and access

Recent efforts have focused on addressing inequities in ACS care. Initiatives promoting access to advanced therapies, such as mobile PCI units and telemedicine platforms, are being implemented in underserved regions. Additionally, public health campaigns emphasizing symptom recognition and early presentation are helping reduce delays in care.

5.7. Future directions

Ongoing research is exploring novel therapies, including gene-editing technologies and targeted molecular interventions, to address the underlying mechanisms of atherosclerosis and thrombosis. Personalized medicine approaches leveraging genomic and proteomic data are also being developed to optimize therapy selection and improve patient outcomes.

6. CONCLUSION

Acute Coronary Syndrome (ACS) is a leading cause of morbidity and mortality worldwide and continues to be a challenge to healthcare systems. The condition necessitates a comprehensive approach, integrating rapid diagnosis, risk stratification, and evidence-based management. Recent ad-

vances in revascularization techniques, pharmacological therapies, and diagnostic technologies have significantly improved patient outcomes. Innovations such as drug-eluting stents, high-sensitivity troponins, and PCSK9 inhibitors have further refined the management of ACS, while emerging technologies such as artificial intelligence and digital health tools promise to enhance care precision and accessibility. Despite these advances, there are still challenges such as unequal access to care, delayed recognition of symptoms, and unequal outcomes among different socioeconomic groups. Overcoming these barriers is important for equitable delivery of healthcare. Multidisciplinary care, public health awareness campaigns, and cardiac rehabilitation programs are essential for improving the long-term prognosis of patients with ACS.

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