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Understanding Acute Coronary Syndrome
Symptoms, Causes, and Treatment Options

Edited by Umashankar Lakshmanadoss

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Cardiology and Cardiovascular Medicine

Volume 10

Aims and Scope of the Series

Today, since molecular science on structural causes of oncological pathologies and their molecular treatments are developing at an unbelievable rate, the primary medical cause of death in the twenty-first century will be cardiovascular disease. Neither pandemics that threaten all humanity nor deterioration in the ecosystem will be able to change this fact. Especially, this century seems poised to witness an incredible struggle against atherosclerotic disease, which develops in the arterial walls and results in narrowing and occlusion of the arterial lumen. In addition to this disease, there has been an increasing prevalence of heart rhythm problems, deterioration of heart valves due to aging, and heart failure. Serious vascular pathologies such as stenosis and occlusion, dissection and rupture, and aneurysmal enlargement are also major concerns. Medical and invasive treatment methods may work to save human lives, but they will never provide a real solution. All kinds of medical, technological, and genetic engineering developments obtained in these processes have not yet been sufficient to alleviate or eliminate cardiovascular disease. This book series, Cardiology and Cardiovascular Medicine, includes three topics. The first, Cardiovascular Diseases and Health, reviews important cardiovascular diseases and the developments in their prognosis. The second topic, Cardiovascular Electrophysiology, illuminates the abnormal functioning of the cardiac conduction system, which is caused by all heart pathologies and negatively affects prognosis. The third topic in this series, Cardiovascular Surgery, details treatment for cardiovascular pathologies and how to regulate normal physiological functions with percutaneous or extracorporeal interventions.

Meet the Series Editor

After completing his studies at the Medicine Faculty of Istanbul University in 1990, Prof. Kaan Kırali fulfilled his mandatory medical service and commenced his residency training at Koşuyolu Heart and Research Hospital in 1992. Following five years of assistant education, he pursued further training in England and the USA in 1998. Specializing in laparoscopic and minimally invasive cardiac surgery, he earned the titles of consultant cardiovascular surgeon in 1998, Assistant Professor in 1999, Associate Professor in 2002, and Chief in 2005 at the same hospital. Prof. Kırali also developed an interest in preventive medicine, obtaining an MSc in Public Health from Istanbul University in 2000. Over the past two decades, he has concentrated his scientific pursuits on cardiovascular repairs requiring specialized experience. With his expertise in coronary artery surgery, minimally invasive cardiac surgery, valve repair, and aortic root surgery, he has established new methods for awake coronary bypass revascularization, a new surgical approach for AVR during first and re-operations, aortic valve-sparing procedure, and radiofrequency ablation. Notably, he pioneered awake complete coronary artery bypass grafting (CABG) with bilateral internal mammary arteries (BIMA) and played a crucial role in advancing aortic root surgery with a new aortotomy incision, simplifying aortic valve interventions. Since the year 2000, Prof. Kırali has expanded his interests to heart transplantation, and in recent years, to left ventricular assist devices. He has served as the head of the transplantation department since 2015 and currently continues his work as the director of Koşuyolu High Specialization Education and Research Hospital in Istanbul, Turkey. In his prolific career, he has authored numerous papers in SCI journals, contributed to various book chapters, and served as an editor and reviewer for multiple academic journals. Additionally, he has edited several international books in the field of cardiovascular medicine.

Meet the Volume Editor

Dr. Umashankar Lakshmanadoss completed his medical training at the University of Rochester, NY, USA. He previously served as Director of the Inpatient Medical Consult Service at Johns Hopkins University School of Medicine before joining the Division of Cardiovascular Medicine at the Guthrie Clinic in Sayre, PA. He went on to complete fellowship training in cardiac electrophysiology at William Beaumont School of Medicine, followed by advanced training at the Mayo Clinic in Rochester, MN. Dr. Lakshmanadoss later held the position of Assistant Professor of Medicine in the Division of Cardiology at Louisiana State University, Shreveport, where he also directed the Complex Arrhythmia Ablation Program. His primary research interests focus on cardiac electrophysiology. He currently serves as the Director of Cardiac Electrophysiology at Mercy Health in Cincinnati, USA.

Contents

Preface

Acute Coronary Syndrome (ACS) represents one of the most urgent and complex medical conditions encountered in clinical practice today. With its spectrum ranging from unstable angina to myocardial infarction, ACS demands timely recognition, accurate diagnosis, and effective treatment strategies. The challenges posed by ACS are manifold, not only due to its potentially life-threatening nature but also because of its heterogeneous presentation in various patient populations. The purpose of this textbook, *Understanding Acute Coronary Syndrome – Symptoms, Causes, and Treatment Options*, is to provide healthcare professionals—ranging from medical students to experienced clinicians—a comprehensive resource on the intricacies of ACS. This book is written to bridge the gap between current scientific understanding and practical, patient-centered care, offering both foundational knowledge and advanced insights.

The text begins by examining the pathophysiology of ACS, laying a solid foundation for understanding the disease process at the molecular and cellular levels. From there, the book delves into the complex and multifactorial causes of ACS, highlighting the key risk factors, such as atherosclerosis, inflammation, and platelet aggregation. By exploring both established and emerging scientific perspectives, we aim to present an up-to-date understanding of ACS that empowers clinicians to make informed decisions in managing their patients. The chapters are carefully curated to reflect not only the core clinical aspects of ACS but also the nuances that arise in special populations, including women, diabetic patients, and the elderly. These groups exhibit unique clinical presentations, responses to treatment, and outcomes; understanding these differences is crucial for tailoring interventions that optimize patient care. Advancing to more innovative aspects of ACS treatment, we examine the evolving role of cardiac MRI in diagnosis and monitoring. This cutting-edge imaging technique has become increasingly integral in understanding the structural and functional impact of ACS on the heart, particularly in identifying myocardial injury and guiding therapeutic decisions. Further expanding the scope of this textbook, we consider the role of Traditional Chinese Medicine in the management of ACS. While conventional Western medicine remains the primary treatment modality, the integration of complementary therapies continues to gain attention, and this chapter explores the evidence supporting their potential benefits in ACS care.

In addition, we explore the arrhythmic complications associated with ACS, one of the most critical challenges in managing these patients. The potential for life-threatening arrhythmias underscores the importance of early recognition and timely intervention, and this chapter aims to provide valuable insight into their pathophysiology, diagnosis, and management. As ACS management has become increasingly protocol-driven, our chapter on protocol-driven treatment outlines evidence-based guidelines and treatment algorithms that inform the care of ACS patients, ensuring standardized, high-quality management in emergency and inpatient settings. Finally, this textbook is designed not only as an educational tool but also as a practical reference guide. It encourages healthcare professionals to think critically about each patient encounter, to recognize the complexity of ACS, and to apply evidence-based, individualized approaches to treatment. We hope this textbook serves as a comprehensive, accessible resource that enhances your understanding of ACS and empowers you to provide optimal care for patients affected by this challenging condition.

I want to express my deepest gratitude to all those who have contributed to the successful completion of this textbook. First, I sincerely thank the publisher, IntechOpen, for their exceptional organizational support throughout this entire process. Their commitment and expertise have been essential in bringing this work to fruition. A special note of appreciation goes to Ms. Tea Jelaca, the publishing process manager, whose timely and invaluable assistance has been instrumental in every stage of the publication journey. I also extend my heartfelt thanks to the talented designers, technical staff, and information technology team who have worked tirelessly behind the scenes to ensure that this book is both visually appealing and technically sound. Their efforts have been crucial in creating a seamless and professional product.

Additionally, I want to recognize and express my profound appreciation to the marketing representatives who have worked continuously to promote this book across various platforms, ensuring that it reaches the hands of those who will benefit from its content. A very special acknowledgement goes to the esteemed contributing authors. Their excellence, dedication, and tireless commitment to their respective chapters have made this textbook a comprehensive and valuable resource. Each of them generously took time out of their busy personal and professional lives to contribute their expertise, and I am deeply grateful for their collaboration and hard work.

Finally, I would like to dedicate this book to my son, Shawn. His love, support, and constant inspiration make my life a joyous and blissful experience. It is his unwavering belief in me that has encouraged me to persevere and complete this project.

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Section 1

Clinical Evaluation of Acute Coronary Syndrome

Chapter 1

ACS in Special Populations: Women, Diabetic, and Elderly Patients

Andrew Ndakotsu and Gabriel Ariyo

Abstract

This chapter explores the unique challenges and clinical variations in diagnosing and managing Acute Coronary Syndrome (ACS) in special populations, including women, elderly patients, and individuals with comorbidities such as diabetes. It highlights the impact of biological, physiological, and social factors on symptom presentation, disease progression, and treatment outcomes. Special attention is given to gender differences, including the atypical presentation of ACS in women and their increased risk of adverse outcomes. Additionally, the chapter discusses the complexities of managing ACS in older adults and patients with multiple comorbid conditions. Through evidence-based insights and case examples, readers will gain an in-depth understanding of how to tailor their diagnostic and therapeutic approaches for diverse patient populations.

Keywords: acute coronary syndrome, cardiovascular disease, gender differences, diabetes, elderly, treatment strategies

1. Introduction

Acute coronary syndrome (ACS) remains a leading cause of morbidity and mortality worldwide, affecting diverse patient populations with distinct risk factors and disease presentations [1]. Despite advances in cardiovascular care, significant disparities exist in the epidemiology, pathophysiology, clinical presentation, diagnosis, and management of ACS in women, diabetic patients, and the elderly. Women often exhibit atypical symptoms and unique coronary pathophysiology and receive less aggressive treatment compared to men [2]. Diabetic individuals experience accelerated atherosclerosis, microvascular dysfunction, and prothrombotic states that increase their risk of recurrent cardiovascular events [3, 4]. Aging is associated with structural and functional cardiovascular changes, frailty, and atypical symptomatology, making ACS diagnosis and management more challenging in elderly patients [5]. Understanding these sex-, diabetes-, and age-related differences is critical for optimizing patient outcomes and ensuring equitable cardiovascular care.

2. Acute coronary syndrome in women

2.1 Epidemiology and risk factors

2.1.1 The burden of ACS in women

Cardiovascular disease (CVD) remains the leading cause of death in women worldwide, surpassing mortality from all cancers combined [2]. While ACS incidence has declined in men over recent decades due to improved preventive strategies and treatment, reductions in women have been less pronounced [2]. Women tend to present with ACS approximately 7–10 years later than men, often postmenopause, when the cardioprotective effects of estrogen diminish [6]. This delay contributes to an increased prevalence of comorbidities at presentation, further complicating disease management [2, 6].

Key epidemiological insights include:

- Age-related differences: Younger women (<55 years) with ACS have worse short-term outcomes than age-matched men [6].
- Under-recognition: Women with ACS are less likely to be diagnosed early and treated aggressively [2].
- Racial disparities: Black and Hispanic women have higher ACS-related mortality than White women [7].

Racial and ethnic disparities significantly impact ACS outcomes, with Black, Hispanic, and South Asian populations exhibiting higher rates of cardiovascular mortality compared to White populations. Studies indicate that Black patients are less likely to receive timely revascularization and high-intensity statins, despite comparable or greater cardiovascular risk. Additionally, pharmacogenomic differences influence antiplatelet therapy response [8]. East Asian patients demonstrate higher rates of CYP2C19 polymorphisms, leading to clopidogrel resistance and an increased preference for ticagrelor or prasugrel in these populations. Culturally tailored interventions, improved access to cardiovascular care, and race-conscious prescribing of lipid-lowering and antiplatelet therapies can help bridge these gaps in ACS management [8].

2.2 Sex-specific risk factors

While traditional cardiovascular risk factors affect both sexes, their impact and prevalence differ in women. Additionally, unique female-specific risk factors contribute to the development of ACS [9].

2.2.1 Traditional risk factors

- Hypertension: More prevalent in women and associated with higher cardiovascular risk.
- Diabetes mellitus: Confers a greater relative risk for ACS in women than in men.
- Dyslipidemia: Low HDL-C is a stronger predictor of ACS in women.

- Smoking: Women smokers have a 25% higher risk of ACS compared to men.

- Obesity and metabolic syndrome: More common in women and strongly linked to ACS development [9].

2.2.2 Female-specific and female-predominant risk factors

- Premature menopause (<40 years): Doubles the risk of ACS due to early estrogen loss.

- Pregnancy-associated conditions: Preeclampsia, gestational hypertension, and gestational diabetes increase long-term cardiovascular risk.

- Polycystic ovary syndrome (PCOS): Associated with insulin resistance, dyslipidemia, and increased ACS risk.

- Autoimmune diseases (e.g., SLE, RA): More common in women and linked to endothelial dysfunction and accelerated atherosclerosis.

- Psychosocial factors: Depression, anxiety, and social stressors disproportionately affect women and are associated with worse ACS outcomes [10, 11].

3. Pathophysiological differences in women with ACS

Sex-specific biological and pathophysiological differences influence ACS development, progression, and outcomes in women. These include distinct coronary artery disease (CAD) phenotypes, vasomotor dysfunction, thrombotic variations, and hormonal influences.

3.1 Coronary artery disease (CAD) phenotypes

- Non-obstructive CAD (NOCAD): Women more frequently present with NOCAD, where angiography reveals <50% stenosis despite ACS symptoms. This phenotype is associated with plaque erosion rather than rupture, contributing to distinct ACS pathogenesis [2, 10].

- Microvascular dysfunction: More prevalent in women, leading to myocardial ischemia in the absence of epicardial stenosis. This dysfunction is characterized by reduced coronary flow reserve and endothelial dysfunction.

3.2 Coronary vasomotor dysfunction

- Coronary microvascular dysfunction (CMD): CMD involves reduced coronary flow reserve and endothelial dysfunction, contributing to ischemia despite the absence of significant CAD.

- Coronary vasospasm: More frequently seen in women, leading to Prinzmetal's angina and ischemia [10, 11].

3.3 Spontaneous coronary artery dissection (SCAD)

- Prevalence: SCAD is five times more common in women and a significant cause of ACS, particularly in younger women without traditional risk factors. It is often associated with hormonal changes, pregnancy, and fibromuscular dysplasia (FMD) [2, 11].

3.4 Takotsubo cardiomyopathy (stress-induced cardiomyopathy)

- Often misdiagnosed as ACS, this syndrome is more prevalent in postmenopausal women and linked to catecholamine surges [10, 11].

3.5 Thrombotic and hemostatic differences

- Platelet reactivity: Women have higher platelet reactivity and a greater pro-thrombotic state, increasing ACS risk despite less obstructive CAD. Estrogen fluctuations influence endothelial function and coagulation pathways, contributing to thrombotic events [10, 11].

4. Clinical presentation and diagnostic challenges

4.1 Atypical symptomatology

Women with ACS frequently present with atypical symptoms, leading to delays in recognition and treatment.

4.1.1 Typical ACS symptoms in women

- Chest discomfort (often described as pressure, burning, or tightness, rather than the classic "crushing pain").
- Radiation to the neck, jaw, or back.
- Dyspnea, nausea, vomiting, and unusual fatigue.
- Palpitations or syncope, which are often misattributed to anxiety or gastrointestinal distress.

4.2 Underdiagnosis and delayed recognition

- Women are less likely to receive early ECGs, biomarker testing, or urgent revascularization.
- Troponin levels may be lower in women, leading to potential underdiagnosis of myocardial infarction (MI).
- High-sensitivity troponin assays (sex-specific cutoffs) improve ACS detection in women.

Risk stratification in ACS has evolved with the integration of novel imaging modalities and biomarkers. Coronary CT angiography (CTA) plays a critical role in evaluating patients, particularly women, with suspected non-obstructive ACS, helping to differentiate between microvascular dysfunction, plaque erosion, and spontaneous coronary artery dissection (SCAD) [2, 9, 11].

5. Treatment and outcomes in women with ACS

5.1 Pharmacologic management

5.1.1 Antiplatelet therapy

- Women derive similar benefits from dual antiplatelet therapy (DAPT) but have a higher bleeding risk, requiring careful selection of P2Y12 inhibitors [7, 10].

- Aspirin resistance is more prevalent in women, necessitating adequate dosing strategies [7, 10].

5.1.2 Antithrombotic therapy

- Higher bleeding risk with anticoagulants requires weight-adjusted dosing, especially in elderly women [7, 9].

5.1.3 Lipid-lowering therapy

- Statins remain first-line therapy; however, women are less likely to receive high-intensity statins despite similar benefits.

- PCSK9 inhibitors are underutilized in high-risk women [9, 11].

5.1.4 Beta-blockers and ACE inhibitors

- Underprescribed in women post-MI despite comparable benefits [9, 11].

5.2 Revascularization strategies

- Percutaneous Coronary Intervention (PCI) vs. Coronary Artery Bypass Grafting (CABG): Women have higher in-hospital mortality and complications post-PCI or CABG [9, 10].

- Radial vs. Femoral Access: Radial access is preferred in women due to lower bleeding risks [9, 10].

- Underutilization of Invasive Management: Women are less likely to receive coronary angiography, PCI, or CABG [9, 11].

5.3 Outcomes and prognosis

- Women with ACS have higher mortality and complications, particularly younger women.

- Increased risk of heart failure and recurrent ischemic events post-MI.
- Psychosocial and socioeconomic factors impact long-term adherence and outcomes [2, 9, 11].

6. Acute coronary syndrome in diabetic patients

6.1 Impact of diabetes on coronary artery disease

Diabetes mellitus profoundly influences the development and progression of coronary artery disease (CAD). Chronic hyperglycemia promotes inflammation, oxidative stress, endothelial dysfunction, and dyslipidemia, all of which contribute to plaque formation, progression, and instability (**Table 1**) [12–14].

6.2 Key pathophysiological mechanisms linking diabetes to cardiovascular disease

A summary of how endothelial dysfunction, accelerated atherosclerosis, microvascular dysfunction, a prothrombotic state, and autonomic neuropathy contribute to increased cardiovascular risk in diabetic patients.

7. Diabetes and coronary plaque characteristics

Diabetic patients exhibit more extensive and diffuse atherosclerosis, characterized by:

- Greater plaque burden with multi-vessel involvement [12].
- Higher prevalence of high-risk plaques, prone to rupture [13].
- Increased coronary calcification, making revascularization more challenging [14].
- More frequent microvascular dysfunction, impairing myocardial perfusion [12–14].

Mechanism	Impact on diabetic patients
Endothelial dysfunction	Impaired nitric oxide (NO) production leads to reduced vasodilation and increased vascular stiffness [12, 13].
Accelerated atherosclerosis	Increased LDL oxidation, foam cell formation, and chronic inflammation promote plaque progression [12, 14].
Microvascular dysfunction	Impaired coronary microcirculation contributes to ischemia even in the absence of significant epicardial stenosis [12, 13].
Prothrombotic state	Elevated fibrinogen, platelet hyperreactivity, and increased PAI-1 levels lead to a higher risk of thrombus formation [13, 14].
Autonomic neuropathy	Alters pain perception, contributing to atypical ACS presentations and silent myocardial infarctions (MIs) [2, 12].

Table 1.
Key pathophysiological mechanisms.

7.1 Clinical significance

- Diabetic patients have a 2–4 times higher risk of MI compared to non-diabetic individuals [2].
- The presence of diabetes doubles the risk of recurrent cardiovascular events post-ACS [12].
- Diabetic women have disproportionately worse outcomes following ACS than men [13].

7.2 Atypical presentations and diagnostic challenges

ACS in diabetic patients is frequently underdiagnosed or misdiagnosed due to altered pain perception, silent ischemia, and atypical symptoms (**Table 2**) [12].

7.3 Atypical acute coronary syndrome (ACS) presentation in diabetic patients

Comparison of classic ACS symptoms with the atypical manifestations often seen in diabetic patients, including dyspnea, fatigue, syncope, and nonspecific ECG changes.

7.3.1 Silent Myocardial Infarction (SMI) in diabetes

- Up to 25% of MIs in diabetic patients are silent, with no chest pain due to autonomic neuropathy.
- Diabetic patients may present only with heart failure, fatigue, or hemodynamic instability at the time of MI.
- Silent ischemia leads to delayed diagnosis and worse prognosis due to late intervention (**Table 3**) [12–15].

Typical ACS symptoms (Non-Diabetic)	Atypical symptoms in diabetic patients
Crushing chest pain	Dyspnea, nausea, vomiting
Radiating pain (arm, jaw, back)	Unusual fatigue, weakness
Diaphoresis, palpitations	Syncope, confusion
Typical ST-elevation on ECG	Subtle or nonspecific ECG changes

Table 2.
Atypical ACS symptoms in diabetic patients.

Diagnostic tool	Limitations in diabetes
ECG	Atypical or nonspecific findings increased false negatives [2].
Troponins	May be elevated in chronic kidney disease (common in diabetes), complicating MI diagnosis [12].
Coronary angiography	More challenging due to diffuse CAD rather than focal lesions [13].
Stress testing	Reduced sensitivity due to autonomic dysfunction and microvascular disease [14].

Table 3.
Challenges in ACS diagnosis in diabetic patients.

8. Challenges in diagnosing acute coronary syndrome (ACS) in diabetic patients

Overview of diagnostic limitations in diabetes, including nonspecific ECG changes, troponin elevation in chronic kidney disease (CKD), diffuse CAD on angiography, and reduced stress test sensitivity due to autonomic dysfunction and microvascular disease.

8.1 Key diagnostic strategies

- High-sensitivity troponin (hs-Tn) testing improves MI detection in diabetic patients [12, 13].
- Coronary CT angiography (CTA) is useful for evaluating non-obstructive CAD and microvascular disease [2, 13].
- Cardiac MRI may help detect ischemia, fibrosis, or infarction when conventional tests are inconclusive [12, 14].

Advanced imaging modalities are increasingly utilized for precise risk stratification in ACS. Fractional Flow Reserve Computed Tomography (FFR-CT) has emerged as a non-invasive tool for assessing the functional significance of intermediate coronary stenoses, reducing the need for invasive coronary angiography in select patients. In patients with suspected microvascular angina, cardiac MRI with perfusion imaging can identify subendocardial ischemia and microvascular dysfunction, enhancing diagnostic accuracy. Additionally, artificial intelligence-assisted echocardiography and coronary CTA interpretation are being developed to improve detection of high-risk plaque features, further refining risk assessment and individualized ACS management [2, 12, 13].

9. Management strategies and outcomes

9.1 Pharmacological therapy

Diabetic patients derive significant benefits from intensive medical therapy but are also at higher risk for adverse effects such as bleeding and hypoglycemia (**Table 4**).

10. Pharmacologic considerations for ACS management in diabetic patients

A summary of key medication considerations in diabetes, including careful use of DAPT and anticoagulation due to bleeding risk, the importance of high-intensity statins, beta-blocker caution in autonomic dysfunction, and the cardioprotective benefits of SGLT2 inhibitors and GLP-1 receptor agonists.

Recent trials, including EMPA-REG OUTCOME and LEADER, have demonstrated that sodium-glucose cotransporter-2 (SGLT2) inhibitors (e.g., empagliflozin) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) (e.g., liraglutide) confer significant cardiovascular benefits independent of glycemic

Medication	Diabetes-specific considerations
Antiplatelet therapy	Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor (e.g., ticagrelor) is recommended, but increased bleeding risk necessitates careful monitoring [12].
Anticoagulation	Higher risk of thrombotic events warrants aggressive anticoagulation, but dose adjustments are needed to prevent bleeding [13].
Lipid-lowering therapy	High-intensity statins (e.g., atorvastatin 80 mg) should be used in all diabetic ACS patients; PCSK9 inhibitors may be needed for high-risk individuals [14].
Beta-blockers	Improve survival, but caution is needed in patients with autonomic dysfunction to avoid severe bradycardia [12].
ACE inhibitors/ARBs	Essential for cardiovascular and renal protection, particularly in diabetic patients with hypertension or proteinuria [13].
SGLT2 inhibitors and GLP-1 RAs	These newer diabetes medications confer cardioprotective benefits, reducing MI and heart failure risk [14].

Table 4.
Pharmacologic considerations for ACS management in diabetic patients.

Trial	Medication	Primary outcome	Key findings
EMPA-REG OUTCOME [16]	Empagliflozin (SGLT2i)	3P-MACE (CV death, nonfatal MI, nonfatal stroke)	14% reduction in MACE, 38% reduction in CV mortality, and 35% reduction in heart failure hospitalization (HHF).
LEADER [17]	Liraglutide (GLP-1 RA)	3P-MACE	13% reduction in MACE and 15% reduction in all-cause mortality.
DAPA-HF [18]	Dapagliflozin (SGLT2i)	HF worsening or CV death	26% reduction in HF hospitalizations, independent of diabetes status.
DECLARE-TIMI 58 [19]	Dapagliflozin (SGLT2i)	MACE + HHF	Significant reduction in HF hospitalization, but no effect on MACE.

Table 5.
Key findings from major trials.

control. These agents reduce major adverse cardiovascular events (MACE), lower heart failure hospitalization rates, and improve renal outcomes in diabetic ACS patients. The 2023 European Society of Cardiology (ESC) now recommends early initiation of these agents in diabetic patients post-ACS, particularly those with heart failure or chronic kidney disease, as part of guideline-directed medical therapy (GDMT) (**Table 5**) [16–20].

11. Key cardiovascular outcomes trials in diabetes and heart disease

Summary of major clinical trials evaluating SGLT2 inhibitors and GLP-1 receptor agonists, highlighting their impact on major adverse cardiovascular events (MACE), heart failure hospitalizations (HHF), and cardiovascular mortality.

11.1 Revascularization strategies

Diabetic patients often require aggressive revascularization due to diffuse and complex CAD (**Table 6**).

Strategy	Considerations in diabetes
Percutaneous Coronary Intervention (PCI)	Higher rates of in-stent restenosis and thrombosis necessitate the use of drug-eluting stents (DES) [21].
Coronary Artery Bypass Grafting (CABG)	Preferred over PCI in patients with multi-vessel CAD due to better long-term survival [12].
Radial vs. Femoral Access	Radial access is preferred to reduce bleeding risk [13].

Table 6.
Revascularization strategies in diabetic patients with ACS.

12. Revascularization strategies in diabetic patients with ACS

Key considerations include the preference for drug-eluting stents (DES) in PCI due to higher restenosis risk, the superiority of CABG for multi-vessel disease, and the use of radial access to minimize bleeding complications.

12.1 Long-term outcomes and prognosis

- Diabetic patients have worse short- and long-term ACS outcomes due to persistent endothelial dysfunction and prothrombotic states [2, 12–14].
- Higher rates of heart failure and recurrent MI post-ACS [12, 13, 18].
- Poor adherence to secondary prevention strategies contributes to adverse outcomes [2, 22].
- Early initiation of guideline-directed medical therapy significantly improves prognosis [16, 17].

12.2 Multidisciplinary care and lifestyle modifications

See (**Table** 7).

Intervention	Benefits in diabetic ACS patients
Aggressive glycemic control (HbA1c <7%)	Reduces microvascular complications but should avoid hypoglycemia [13].
Smoking cessation	Critical for preventing recurrent ACS events [12].
Cardiac rehabilitation	Improves functional capacity and survival [14].
Weight loss and diet modification	Mediterranean or DASH diets reduce cardiovascular risk [23].

Table 7.
Lifestyle and secondary prevention strategies in diabetic ACS patients.

13. Key lifestyle and secondary prevention strategies in diabetic ACS patients

Aggressive glycemic control minimizes microvascular complications, smoking cessation reduces recurrent ACS risk, cardiac rehabilitation enhances survival, and dietary modifications like the Mediterranean or DASH diets lower cardiovascular risk.

Physiological change	Impact on elderly patients
Arterial stiffness	Increased systolic blood pressure, left ventricular hypertrophy (LVH), and higher myocardial oxygen demand [24].
Endothelial dysfunction	Reduced nitric oxide (NO) availability leads to impaired vasodilation and increased vascular resistance [25].
Coronary artery calcification	Greater plaque burden with increased likelihood of complex, multi-vessel CAD [26].
Decreased myocardial compliance	Higher risk of diastolic dysfunction and heart failure with preserved ejection fraction (HFpEF) [27].
Autonomic dysfunction	Blunted heart rate and blood pressure responses may contribute to atypical ACS presentations [24].
Prothrombotic state	Increased platelet aggregation and coagulation factor activation elevate thrombosis risk [26].

Table 8.
Key age-related cardiovascular changes.

13.1 Acute coronary syndrome in elderly patients

13.1.1 Age-related cardiovascular changes

Aging leads to progressive alterations in cardiac structure and function, which increase susceptibility to ACS and worsen ischemic tolerance. These changes impact plaque stability, vascular compliance, and myocardial response to stress (**Table 8**).

14. Lifestyle and secondary prevention strategies in diabetic ACS patients

Optimal management includes tight glycemic control to prevent complications, smoking cessation to reduce ACS recurrence, cardiac rehabilitation for improved survival, and heart-healthy diets like the Mediterranean or DASH to lower cardiovascular risk.

Aging is associated with increased arterial stiffness due to collagen deposition and elastin degradation in the arterial wall. This results in elevated systolic blood pressure and left ventricular hypertrophy (LVH), increasing myocardial oxygen demand and predisposing to ischemia. Endothelial dysfunction, characterized by reduced nitric oxide (NO) availability, impairs vasodilation and increases vascular resistance, further exacerbating ischemic risk [24–26].

Coronary artery calcification is more prevalent in the elderly, contributing to a greater plaque burden and increased likelihood of complex, multi-vessel coronary artery disease (CAD). Decreased myocardial compliance leads to diastolic dysfunction and heart failure with preserved ejection fraction (HFpEF), conditions commonly seen in older adults. Autonomic dysfunction, with blunted heart rate and blood pressure responses, may result in atypical ACS presentations, complicating diagnosis. Additionally, a prothrombotic state, characterized by increased platelet aggregation and coagulation factor activation, elevates the risk of thrombosis [24–26].

14.1 Clinical implications

- Elderly patients have a higher prevalence of multi-vessel and diffuse CAD [24].

- Myocardial ischemia is poorly tolerated, leading to greater hemodynamic instability and heart failure [25].
- Reduced physiological reserve and frailty increase post-ACS complications and mortality [26].

15. Diagnostic considerations in older adults

15.1 Atypical ACS presentations in elderly patients

Older adults frequently exhibit non-classical ACS symptoms, leading to delayed diagnosis and mismanagement (**Table 9**).

15.2 Atypical ACS presentation in elderly patients

Compared to younger adults, elderly patients often present with dyspnea, syncope, fatigue, or gastrointestinal symptoms rather than classic chest pain, with ECG findings that may be subtle or nonspecific.

Elderly patients often present with atypical symptoms such as dyspnea, dizziness, confusion, syncope, fatigue, generalized weakness, and gastrointestinal discomfort (nausea, vomiting, bloating). Up to 30% of elderly patients with ACS present without chest pain ("silent MI"), complicating timely diagnosis. Cognitive impairment and communication difficulties may further obscure symptom recognition, leading to delays in treatment (**Table 10**) [2, 24–26].

Typical ACS symptoms (Younger adults)	Atypical ACS symptoms (Elderly Patients)
Crushing chest pain	Dyspnea, dizziness, confusion [24].
Radiation to arm, jaw, back	Syncope, fatigue, generalized weakness [25].
Diaphoresis, nausea, palpitations	Gastrointestinal discomfort (nausea, vomiting, bloating) [26].
ST-elevation on ECG	Subtle or nonspecific ECG changes [24].

Table 9.
Atypical ACS symptoms in elderly patients.

Diagnostic tool	Limitations in elderly patients
Electrocardiogram (ECG)	High rates of baseline abnormalities (e.g., left bundle branch block, atrial fibrillation) can obscure ischemic changes [24].
Troponin biomarkers	May be chronically elevated in chronic kidney disease (CKD) or heart failure, complicating MI diagnosis [25].
Coronary angiography	Higher risk of contrast-induced nephropathy and procedural complications [26].
Echocardiography	Essential for evaluating diastolic dysfunction, wall motion abnormalities, and heart failure [25].
Stress testing	Often not feasible due to limited mobility or frailty, pharmacologic stress imaging is preferred [25].

Table 10.
Diagnostic challenges and strategies.

16. Diagnostic challenges of ACS in elderly patients

Coronary angiography poses a higher risk of contrast-induced nephropathy, echocardiography is crucial for assessing cardiac function, and pharmacologic stress testing is preferred due to mobility limitations.

High rates of baseline ECG abnormalities, such as left bundle branch block and atrial fibrillation, can obscure ischemic changes in elderly patients. Troponin biomarkers may be chronically elevated in conditions like chronic kidney disease (CKD) or heart failure, complicating the diagnosis of myocardial infarction (MI). Coronary angiography carries a higher risk of contrast-induced nephropathy and procedural complications in older adults. Echocardiography is essential for evaluating diastolic dysfunction, wall motion abnormalities, and heart failure. Stress testing is often not feasible due to limited mobility or frailty; pharmacologic stress imaging is preferred [25–26].

16.1 Key diagnostic considerations

- High-sensitivity troponin (hs-Tn) assays improve MI detection in elderly patients with subtle presentations.

- Coronary CT angiography (CTA) is useful in high-risk patients who are not candidates for invasive angiography.

- Comprehensive geriatric assessment (CGA) should be integrated into ACS diagnosis to evaluate frailty, cognition, and functional status.

17. Treatment strategies and prognosis

17.1 Pharmacological therapy in elderly ACS patients

Elderly patients benefit from evidence-based medical therapy but are also at higher risk for adverse effects, necessitating individualized treatment (**Table 11**).

Medication	Considerations in elderly patients
Antiplatelet therapy	Dual antiplatelet therapy (DAPT) is recommended, but higher bleeding risk requires careful selection of P2Y12 inhibitors (prefer clopidogrel over prasugrel) [24, 25].
Anticoagulation	Dose-adjustment is required to minimize bleeding risk, particularly in patients with CKD [24].
Lipid-lowering therapy	Statins reduce mortality, but tolerability (myalgia, liver dysfunction) must be monitored [20, 21].
Beta-blockers	Effective but use caution in frail, bradycardic, or hypotensive patients [26].
ACE inhibitors/ ARBs	Mortality benefit, especially in those with hypertension or heart failure, but the risk of hyperkalemia should be assessed [24, 26].
Diuretics	Used in heart failure but can cause electrolyte imbalances and hypotension [27].

Table 11.
Pharmacological therapy in elderly ACS patients.

18. Pharmacologic considerations for ACS management in elderly patients

DAPT requires careful P2Y12 inhibitor selection due to bleeding risk; anticoagulation dosing must be adjusted for CKD; statin therapy should be monitored for tolerability; and beta-blockers, ACE inhibitors, and diuretics should be used cautiously to prevent hypotension and electrolyte imbalances [24].

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is recommended for elderly ACS patients, but the higher bleeding risk necessitates careful selection of P2Y12 inhibitors, with clopidogrel preferred over prasugrel. Anticoagulation requires dose adjustment to minimize bleeding risk, particularly in patients with CKD [24]. Statins reduce mortality, but tolerability issues such as myalgia and liver dysfunction must be monitored [20, 21]. Beta-blockers are effective but should be used with caution in frail, bradycardic, or hypotensive patients [24, 26]. ACE inhibitors or ARBs provide a mortality benefit, especially in those with hypertension or heart failure, but the risk of hyperkalemia should be assessed. Diuretics are used in heart failure but can cause electrolyte imbalances and hypotension [27].

18.1 Revascularization strategies

See (**Table 12**).

Strategy	Considerations in elderly patients
Percutaneous Coronary Intervention (PCI)	Preferred in older adults with single-vessel disease or high bleeding risk [24].
Coronary Artery Bypass Grafting (CABG)	Higher perioperative risk, best for multi-vessel CAD with preserved functional status [25].
Radial vs. Femoral access	Radial access is preferred due to a lower bleeding risk [24].

Table 12.
Revascularization strategies in elderly patients.

19. Revascularization strategies in elderly patients with ACS

PCI is preferred for single-vessel disease or in those with high bleeding risk, while CABG is considered for multi-vessel CAD in patients with good functional status. Radial access is favored to minimize bleeding complications.

Invasive management should be individualized, considering frailty, cognitive function, and overall prognosis. Percutaneous coronary intervention (PCI) is preferred in older adults with single-vessel disease or high bleeding risk. Coronary artery bypass grafting (CABG) carries a higher perioperative risk but is best for multi-vessel CAD with preserved functional status. Radial access is preferred over femoral access due to lower bleeding risk. Early invasive strategy improves survival in fit elderly patients, but conservative management may be preferable in frail individuals [24–25].

20. Frailty-driven decision-making in ACS: PCI vs. CABG vs. conservative management

Frailty is a critical determinant of *treatment strategy* in elderly patients with *acute coronary syndrome (ACS)*. The *Clinical Frailty Scale (CFS)* is widely used to assess physiological reserve, guide risk stratification, and tailor invasive vs. conservative approaches. Patients with *higher frailty scores (CFS ≥ 5)* exhibit increased vulnerability to procedural complications, prolonged hospital stays, and worse long-term outcomes, necessitating an individualized approach to management [24–26].

20.1 PCI vs. CABG in frail ACS patients (CFS 5–6)

- In moderately frail patients (CFS 5–6), PCI is generally preferred over CABG due to its lower perioperative risks and faster recovery time.
- CABG, though beneficial in multi-vessel disease, is associated with higher perioperative stroke risk, prolonged mechanical ventilation, and increased mortality in frail individuals.
- The 2024 ACC/AHA guidelines recommend a heart team approach for these patients, prioritizing less invasive strategies when revascularization is needed.

20.2 Conservative management in severely frail patients (CFS ≥7)

- In severely frail patients (CFS ≥7), the risks of invasive revascularization (PCI or CABG) often outweigh the benefits.
- A conservative approach emphasizing guideline-directed medical therapy (GDMT), symptom control, and palliative care principles may be more appropriate.
- These patients have a high risk of post-procedural delirium, functional decline, and loss of independence, making procedural interventions less desirable.
- Goals of care discussions should involve patients, families, and the multidisciplinary team, focusing on quality of life, symptom relief, and shared decision-making (**Table 13**) [24–26].

21. Integrating frailty assessment into ACS management

For fit to mildly frail patients (CFS 1–4), standard ACS treatment, including PCI or CABG, is appropriate. In moderate frailty (CFS 5–6), PCI is preferred over CABG with individualized risk assessment. For severe frailty (CFS ≥7), a conservative approach focusing on GDMT and symptom management is recommended.

Frailty level (CFS Score)	Recommended ACS management strategy
CFS 1–4 (Fit to mild frailty)	Standard ACS management, PCI/CABG as indicated
CFS 5–6 (Moderate frailty)	PCI preferred over CABG, individualized risk assessment
CFS ≥7 (Severe frailty)	Conservative management, GDMT, symptom control

Table 13.
Practical application of frailty in ACS treatment.

21.1 Long-term prognosis and outcomes

- Elderly ACS patients have higher short- and long-term mortality rates than younger patients.
- Frailty, multimorbidity, and cognitive impairment negatively impact recovery and treatment adherence.
- Comprehensive cardiac rehabilitation is underutilized in elderly patients but significantly improves functional outcomes and quality of life.

22. Treatment strategies and prognosis (continued)

22.1 Multidisciplinary care and lifestyle modifications

See (**Table 14**).

Intervention	Benefit in elderly ACS patients
Frailty assessment	Helps guide treatment intensity and post-ACS care [24].
Cognitive screening	Essential for assessing medication adherence and decision-making capacity [25].
Smoking cessation	Reduces recurrent MI risk; counseling and nicotine replacement therapy are beneficial [26].
Cardiac rehabilitation	Improves functional capacity and survival but is often underprescribed in older adults [24].
Nutritional optimization	Mediterranean diet reduces cardiovascular risk [23].
Physical activity	Light-to-moderate exercise prevents functional decline [27].

Table 14.
Multidisciplinary care and lifestyle modifications in elderly ACS patient.

23. Multidisciplinary care and lifestyle modifications in elderly ACS patients

Frailty assessment guides treatment decisions, cognitive screening ensures adherence, and smoking cessation lowers MI risk. Cardiac rehabilitation enhances survival but is underutilized, while a Mediterranean diet and regular physical activity help prevent cardiovascular and functional decline.

Frailty assessment is crucial in guiding treatment intensity and post-ACS care. Frailty assessment is now central to ACS management in elderly patients, guiding treatment intensity and invasive vs. conservative approaches [27]. The FRAIL scale and the Clinical Frailty Scale (CFS) are validated tools that assess functional independence, comorbidities, and overall physiological reserve [24, 27]. The TFI (Tilburg Frailty Indicator) and gait speed tests provide additional insight into post-ACS rehabilitation potential [25]. Integrating frailty assessment into clinical decision-making helps balance the benefits of revascularization with the risks of procedural

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complications, ensuring personalized, patient-centered care. Cognitive screening is essential for assessing medication adherence and decision-making capacity, ensuring that elderly patients can manage their treatment regimens effectively. Smoking cessation is critical for preventing recurrent MI, with counseling and nicotine replacement therapy being beneficial [24–26]. Cardiac rehabilitation, although often underprescribed in older adults, significantly improves functional capacity and survival. Nutritional optimization, such as adopting a Mediterranean diet, reduces cardiovascular risk [24]. Encouraging light-to-moderate physical activity helps prevent functional decline and improves overall health [24, 26].

23.1 Special considerations in management

Effective management of Acute Coronary Syndrome (ACS) necessitates specialized considerations for different patient populations, particularly women, diabetic individuals, and the elderly. Each group presents unique challenges that impact disease progression, treatment response, and clinical outcomes.

23.2 Gender-based differences

Women with ACS often experience delayed diagnosis and underutilization of guideline-directed therapies. They are more likely to present with atypical symptoms such as nausea, fatigue, and dyspnea, and have a higher prevalence of non-obstructive coronary artery disease (NOCAD) and microvascular dysfunction. Increased awareness of these atypical presentations, the use of high-sensitivity troponin assays with sex-specific thresholds, and tailored antiplatelet and anticoagulant strategies are essential for improving outcomes in women. Encouraging adherence to secondary prevention measures, including lifestyle modifications, medication compliance, and cardiac rehabilitation, is critical.

The management of ACS has evolved with updated guidelines emphasizing high-risk populations. According to the 2023 European Society of Cardiology (ESC) guidelines and the 2024 American College of Cardiology (ACC)/American Heart Association (AHA) updates, sex-specific troponin cutoffs should be systematically used in women to improve diagnostic sensitivity. Additionally, in diabetic patients, sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been integrated into secondary prevention strategies to reduce myocardial infarction recurrence and heart failure hospitalizations. For elderly ACS patients, frailty assessment is now a cornerstone of treatment decision-making, guiding invasive vs. conservative management strategies.

23.3 Diabetes-specific challenges and considerations

Diabetic patients with ACS face worse outcomes due to accelerated atherosclerosis, increased thrombogenicity, and microvascular dysfunction. These patients benefit from prolonged dual antiplatelet therapy (DAPT), intensive glucose control, and aggressive lipid-lowering therapy with high-intensity statins and PCSK9 inhibitors. Coronary artery bypass grafting (CABG) is often preferred over percutaneous coronary intervention (PCI) in multi-vessel disease due to better long-term survival. In diabetic patients, high-sensitivity C-reactive protein (hsCRP) and lipoprotein(a) levels provide additional prognostic insights, guiding aggressive lipid-lowering strategies. Emerging cardioprotective therapies, such as SGLT2 inhibitors and GLP-1 receptor agonists, should be incorporated into secondary prevention strategies to reduce myocardial infarction recurrence and heart failure hospitalizations.

23.4 Elderly patient considerations

Elderly patients with ACS present unique challenges due to frailty, polypharmacy, cognitive impairment, and reduced physiological reserve. Atypical symptoms such as dyspnea, confusion, and syncope are common, requiring a high index of suspicion for timely diagnosis. Lower initial doses of antiplatelets, beta-blockers, and anticoagulants are recommended to reduce bleeding risk. Radial access for PCI is preferred to minimize bleeding, and CABG should be considered cautiously in frail patients. Comprehensive geriatric assessment (CGA) and frailty scoring can guide individualized management decisions. Multidisciplinary care involving geriatricians, cardiologists, and family members ensures appropriate treatment goals, while tailored cardiac rehabilitation improves mobility, functional status, and quality of life.

23.5 Disparities in cardiac rehabilitation

Despite strong evidence supporting its benefits, cardiac rehabilitation (CR) remains underutilized, particularly among women, racial and ethnic minorities, and elderly patients. Studies indicate that women are 30–50% less likely than men to be referred to or complete CR, often due to caregiving responsibilities, lower perceived risk, or lack of physician encouragement. Black and Hispanic patients also face significant barriers, including socioeconomic constraints, limited access to CR facilities, and language or cultural differences. Additionally, elderly ACS patients often experience mobility limitations, cognitive impairment, or transportation difficulties, further reducing participation rates. Strategies to improve CR participation include automatic referral systems, home-based and virtual CR programs, community-based interventions, and culturally tailored patient education to enhance engagement and adherence in these high-risk groups. Expanding insurance coverage and increasing provider awareness of these disparities are crucial to optimizing outcomes.

24. Conclusion

In conclusion, the management of Acute Coronary Syndrome (ACS) requires a nuanced understanding of the unique challenges faced by women, diabetic patients, and the elderly. Tailored diagnostic and therapeutic strategies are essential for improving outcomes in these populations. Women often present with atypical symptoms and non-obstructive coronary artery disease, necessitating the use of sex-specific diagnostic tools and treatment protocols. Diabetic patients require aggressive management of their metabolic and cardiovascular risk factors, with a focus on novel therapies such as SGLT2 inhibitors and GLP-1 receptor agonists. Elderly patients benefit from a comprehensive geriatric assessment to guide treatment decisions, balancing the benefits of invasive procedures with the risks associated with frailty and comorbidities. Future research should aim to refine these personalized approaches, incorporating emerging technologies and therapies to further enhance patient care. By addressing these specific needs, we can achieve better clinical outcomes and improve the quality of life for patients with ACS.

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Conflict of interest

The authors declare no conflict of interest related to this chapter. All opinions and recommendations are based on current evidence and clinical guidelines, with the sole aim of improving patient care and outcomes.

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References

[1] Pratesi A. Sex and gender differences in patients with acute coronary syndromes. International Journal of Cardiology: Cardiovascular Risk and Prevention. 2024;**21**:200276. Published 2024 May 6. DOI: 10.1016/j.ijcrp.2024.200276

[2] Canto JG et al. Symptom presentation of women with acute coronary syndromes: Myth vs reality. JAMA Internal Medicine. 2007;**167**(22):2405-24134

[3] Marso SP, Safley DM, House JA, Tessendorf T, Reid KJ, Spertus JA. Suspected acute coronary syndrome patients with diabetes and normal troponin-I levels are at risk for early and late death: Identification of a new high-risk acute coronary syndrome population. Diabetes Care. 2006;**29**(8):1931-1932. DOI: 10.2337/dc06-0660

[4] Diabetic patients with acute coronary syndromes in contemporary European registries: characteristics and outcomes

[5] Ratcovich H, Joshi FR, Palm P, et al. Prevalence and impact of frailty in patients ≥70 years old with acute coronary syndrome referred for coronary angiography. Cardiology. 2024;**149**(1):1-13. DOI: 10.1159/000535116

[6] Haider A, Bengs S, Luu J, et al. Sex and gender differences in acute coronary syndrome. European Heart Journal. 2020;**41**:1328-13361

[7] Alder MR, Adamek KE, Lowenstern A, Raj LM, Lindley KJ, Sutton NR. Acute coronary syndrome in women: An update. Current Cardiology Reports. 2024;**26**(5):293-301. DOI: 10.1007/s11886-024-02033-6

[8] Srivastava G, Alhuneafat L, Jabri A, Omar YA, Abdolall A, Beleny DO, et al. Racial and ethnic disparities in acute coronary syndrome: A nationally representative sample. Journal of the Society for Cardiovascular Angiography & Interventions. 2022;**1**(6):100451. DOI: 10.1016/j.jscai.2022.100451

[9] Mehilli J, Presbitero P. Coronary artery disease and acute coronary syndrome in women. Heart. 2020;**106**(7):487-4942

[10] Jackson EA et al. Sex and gender differences in acute coronary syndrome. European Heart Journal. 2020;**41**:1328-13361

[11] Alder MR et al. Acute coronary syndrome in women: An update. Current Cardiology Reports. 2024;**26**:293-3013

[12] Fuster V, Farkouh ME. Acute coronary syndromes and diabetes mellitus. Circulation. 2008;**118**:1607-16086

[13] Mäenpää M et al. The impact of diabetes on the relationship of coronary artery disease and outcome: A study using multimodality imaging. Cardiovascular Diabetology. 2023;**22**:1295

[14] Arnold SV, Kosiborod M. Discharge Management of Patients with Diabetes and ACS. Cardiac Interventions Today. 2015;**13**(2):58-61. Available from: https://citoday.com/articles/2015-mar-apr/discharge-management-of-patients-with-diabetes-and-acs

[15] Perona M et al. Symptoms, outcomes and risk factors of ACS without cardiac chest pain: Scoping review. European Cardiology Review. 2024;**19**:e127

[16] Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. The New England Journal of Medicine. 2015;**373**(22):2117-2128. DOI: 10.1056/NEJMoa1504720

[17] Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. The New England Journal of Medicine. 2016;**375**(4):311-322. DOI: 10.1056/NEJMoa1603827

[18] McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. The New England Journal of Medicine. 2019;**381**(21):1995-2008. DOI: 10.1056/NEJMoa1911303

[19] Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. The New England Journal of Medicine. 2019;**380**(4):347-357. DOI: 10.1056/NEJMoa1812389

[20] Marx N, Federici M, Schütt K, et al. ESC guidelines for the management of cardiovascular disease in patients with diabetes. European Heart Journal. 2023;**44**(39):4043-4140. DOI: 10.1093/eurheartj/ehad192

[21] Sabatine MS, Bergmark BA, Murphy SA, et al. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: An individual patient data meta-analysis. Lancet. 2021;**398**(10318):2247-2257. DOI: 10.1016/S0140-6736(21)02334-5

[22] Green JB, Bethel MA, Armstrong PW, et al. Effect of Sitagliptin on cardiovascular outcomes in type 2 diabetes. The New England Journal of Medicine. 2015;**373**(3):232-242. DOI: 10.1056/NEJMoa1501352

[23] Pi-Sunyer X. The look AHEAD trial: A review and discussion of its outcomes. Current Nutrition Reports. 2014;**3**(4):387-391. DOI: 10.1007/s13668-014-0099-x

[24] Damluji AA, Forman DE, Wang TY, et al. Management of acute coronary syndrome in the older adult population: A scientific statement from the American Heart Association. Circulation. 2023;**147**(20):1607-1630. DOI: 10.1161/CIR.0000000000001112. Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001112

[25] Aranzulla TC, De Benedictis M, Magro VM. Acute coronary syndrome in elderly and frail patients. Cardiopraxis, Council for Cardiology Practice (ESC). 15 Jan 2024. Available from: https://www.escardio.org/Councils/Council-for-Cardiology-Practice-(CCP)/Cardiopractice/acute-coronary-syndrome-in-elderly-and-frail-patients

[26] Verardi R et al. Management of Acute Coronary Syndrome in elderly patients: A narrative review through decisional crossroads. Journal of Clinical Medicine. 2024;**13**(20):603412

[27] Afilalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: The FRAILTY-AVR study. Journal of the American College of Cardiology. 2017;**70**(6):689-700. DOI: 10.1016/j.jacc.2017.06.024

Chapter 2

Pathophysiology of Acute Coronary Syndrome

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Abstract

Acute coronary syndrome (ACS) encompasses a spectrum of conditions caused by the sudden, reduced blood flow to the myocardium, leading to myocardial ischemia and, in severe cases, infarction. The primary pathophysiological mechanism involves the rupture of an atherosclerotic plaque within a coronary artery, resulting in thrombus formation. Plaque rupture exposes subendothelial elements, activating platelets and initiating a coagulation cascade that leads to clot development. The extent and stability of the thrombus determine the severity of coronary obstruction, with partial blockage causing unstable angina and complete occlusion leading to myocardial infarction. Other contributory factors include coronary vasospasm, endothelial dysfunction, and inflammation. The ischemic damage caused by ACS disrupts myocardial cell membranes, releasing cardiac biomarkers such as troponin into the bloodstream. Early recognition and intervention are critical in ACS management to restore perfusion and minimize myocardial injury.

Keywords: acute coronary syndrome, plaque rupture, myocardial ischemia, thrombus formation, coronary artery, atherosclerosis

1. Introduction

Myocardial infarction (MI) refers to myocardial cell necrosis resulting from an imbalance between oxygen supply and demand due to various causes. The universal definition of MI classifies it into five main types (**Table 1**) [1]. The term myocardial injury is defined as a condition where at least one elevated cardiac troponin measurement is detected. In contrast, myocardial infarction requires evidence of acute myocardial injury combined with clinical signs of acute myocardial ischemia.

In the presence of symptoms suggestive of unstable ischemia, acute coronary syndromes (ACS) should be considered. ACS encompasses three distinct clinical entities:

- Unstable angina pectoris (UA)
- Non-ST elevation myocardial infarction (NSTEMI)
- ST elevation myocardial infarction (STEMI)

Criteria for acute myocardial infarction (types 1, 2, and 3 MI)
The term acute myocardial infarction should be used when there is an acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following:
• Symptoms of myocardial ischemia
• New ischemic ECG changes
• Development of pathologic Q waves
• Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology
• Identification of a coronary thrombus by angiography or autopsy (not for type 2 or 3 MIs)

Table 1.
Fourth universal definition of myocardial infarction.

This chapter aims to provide an in-depth overview of the pathophysiology, diagnosis, and management of myocardial infarction, with a particular emphasis on acute coronary syndromes and their clinical implications.

2. Pathology of acute coronary syndromes

The majority of acute coronary syndromes (ACS) result from coronary thrombosis due to rupture or erosion of atherosclerotic lesions. With the widespread use of statins, the incidence of erosion-related coronary thrombosis has been increasing [2, 3].

2.1 Plaque formation

ACS typically occurs as a consequence of fibrous cap rupture, superficial erosion, or, in rare cases, vasospasm or disruption of calcified nodules within coronary atherosclerotic plaques. Vulnerable plaques are primarily characterized by thin-capped fibroatheromas. However, several other morphological features are associated with plaques prone to rupture, including:

- Expansive remodeling that reduces luminal obstruction, often resulting in only mild stenosis on angiography
- Neovascularization and angiogenesis
- Plaque hemorrhage
- Adventitial inflammation
- A "spotty" pattern of calcification

These pathophysiological features underscore the complexity of plaque dynamics and their role in the development of ACS [2, 3].

2.1.1 Atherosclerosis

Atherosclerosis is a key underlying factor in the pathogenesis of coronary, cerebral, and peripheral vascular diseases. The development of atherosclerosis can be influenced by both acquired risk factors, such as cholesterol levels, smoking, and hypertension, as well as hereditary risk factors, including mutations in the low-density lipoprotein (LDL) receptor gene. Additionally, gender and age play a significant role in determining the likelihood of developing atherosclerosis.

Atheromas, or atherosclerotic plaques, refer to intimal lesions that protrude into the vascular lumen. In simple terms, atherosclerotic plaques can be thought of as having a soft lipid core primarily composed of cholesterol and cholesterol esters, surrounded by a fibrous cap. The most feared complication of plaques that protrude into the lumen, causing narrowing, is rupture, which can lead to obstructive vascular thrombosis.

Furthermore, these changes in the vessel wall increase the diffusion distance, which can facilitate ischemic damage. This weakening of the vessel wall may also create an environment conducive to the formation of aneurysms [4].

2.1.2 Risk factors

Risk factors for atherosclerosis can broadly be classified into two categories: structural and modifiable.

2.1.2.1 Structural risk factors

The most prominent structural risk factor is genetic predisposition. Among these, family history is considered the most important independent risk factor for atherosclerosis. Since the formation of atherosclerotic plaques is a progressive process, their clinical onset increases with age. The incidence of myocardial infarction increases fivefold between the ages of 40 and 60. Gender is also considered a structural risk factor. When comparing premenopausal women to men of the same age, atherosclerosis and its complications are less commonly seen in women. However, following menopause, the incidence of atherosclerosis-related diseases increases in women, surpassing that of men. This has been attributed to the protective effects of estrogen; however, hormone replacement therapy has not been proven beneficial, and in fact, cardiovascular risk is higher in women undergoing hormone replacement therapy compared to those of the same age without treatment.

2.1.2.2 Modifiable risk factors

Among the modifiable risk factors, hyperlipidemia, particularly hypercholesterolemia, is a major contributor to atherosclerotic plaque formation. Hypertension is also strongly associated with increased risk, with a 60% higher risk compared to normotensive individuals. Smoking has a cumulative effect, with risk increasing over time, although cessation leads to a gradual reduction in this risk. Diabetes mellitus contributes to the development of hypercholesterolemia, setting the stage for plaque formation.

Other important modifiable risk factors include inflammation, which is present in all stages of atherogenesis and is closely linked to plaque formation. Metabolic syndrome, particularly central obesity, induces a systemic hypercoagulable and proinflammatory state, further promoting atherosclerosis. Sedentary lifestyle, a stressful lifestyle (type A personality), and obesity are also risk factors for plaque formation.

2.1.3 Pathogenesis

Although many hypotheses have been proposed for the pathogenesis of atherosclerosis, the most widely accepted model attributes it to a chronic inflammatory process in response to endothelial injury in the arterial wall. The formation of lesions involves the interaction of modified lipoproteins, macrophages, T lymphocytes, smooth muscle cells (SMCs), and endothelial cells (ECs). A detailed examination of this process can be outlined as follows:

1. Endothelial injury and dysfunction

   Endothelial injury leads to increased vascular permeability, leukocyte adhesion, and thrombosis.

2. Lipoprotein accumulation in the arterial wall

   Primarily low-density lipoproteins (LDL) and their oxidized forms accumulate in the vascular wall.

3. Monocyte adhesion and migration into the intima

   Following monocyte adhesion to the endothelium, these cells migrate into the intima and differentiate into foam cells through interaction with macrophages.

4. Platelet adhesion

   Platelets adhere to the site of endothelial injury.

5. Release of growth factors by activated platelets, macrophages, and smooth muscle cells

   These cells release various factors that contribute to the inflammatory and healing processes.

6. Smooth muscle cell proliferation and extracellular matrix (ECM) production

   SMCs proliferate and secrete ECM components, while T lymphocytes are recruited to the site of injury.

7. Intracellular and extracellular lipid accumulation

   The accumulation of lipids both within cells and in the extracellular space plays a crucial role in lesion formation.

8. Calcification of the ECM and necrotic debris

   As lesions progress, calcification of the ECM and accumulation of necrotic debris are seen.

Endothelial injury is considered the cornerstone of the response-to-injury hypothesis. Early lesions begin in intact endothelial tissue exhibiting characteristics of endothelial dysfunction, including increased permeability and enhanced leukocyte adhesion. Contributing factors to endothelial dysfunction may include cigarette smoke toxins, homocysteine, and locally produced inflammatory cytokines. However, the three most significant causes of endothelial dysfunction are hemodynamic disturbances, hypercholesterolemia, and inflammation.

2.1.3.1 Hemodynamic disturbances

When examining atherogenesis, the distribution of plaques is not random; they tend to form in areas with nonlaminar flow, such as at branch points or ostia of vessels. In contrast, regions with laminar, non-turbulent flow, especially those influenced by transcription factors like Krüppel-like factor-2 (KLF2), exhibit atheroprotective gene activation and suppression of inflammatory genes.

2.1.3.2 Hypercholesterolemia

Increased LDL cholesterol levels, reduced HDL cholesterol levels, and elevated abnormal lipoprotein (a) are observed in many ACS patients. This condition can be secondary to underlying diseases like nephrotic syndrome, alcoholism, hypothyroidism, or diabetes mellitus. It can also result from mutations in lipoprotein receptors or apoproteins. Genetic mutations can reduce the breakdown of LDL and other lipid molecules, leading to accumulation. A significant relationship exists between LDL and total cholesterol levels and the severity of atherosclerosis. Reducing cholesterol levels through medications or lifestyle changes has been shown to reduce cardiovascular risk.

Hypercholesterolemia is directly linked to endothelial dysfunction. Increased production of reactive oxygen species (ROS) leads to membrane and mitochondrial damage. Modified LDL, resulting from chronic hyperlipidemia, accumulates in the intima and is oxidized by free radicals produced by inflammatory cells. Modified LDL is then engulfed by macrophages via scavenger receptors, forming foam cells. Similarly, smooth muscle cells (SMCs) take up modified LDL, transforming into lipid-laden foam cells. Early lesions with foam cells are referred to as fatty streaks.

2.1.3.3 Chronic inflammation

Chronic inflammation plays a pivotal role in initiating and progressing atherosclerotic lesion formation. Cholesterol crystals and free fatty acids accumulating in macrophages trigger an immune response, contributing to the formation of inflammasomes. Activation of inflammasomes leads to the release of pro-inflammatory cytokines, such as interleukin-1 (IL-1), which triggers mononuclear cell activation. Macrophage and T lymphocyte activation results in the local production of cytokines and chemokines. Activated macrophages produce ROS, supporting LDL oxidation and smooth muscle cell proliferation. Activated T lymphocytes also contribute to inflammation by activating macrophages, endothelial cells, and smooth muscle cells.

2.1.3.4 Smooth muscle cell proliferation and ECM deposition

SMC proliferation and ECM synthesis convert fatty streaks into mature atheromas, contributing to the progressive growth of atherosclerotic lesions. Growth factors such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and transforming growth factor-α (TGF-α) are secreted by activated platelets, macrophages, endothelial cells, and smooth muscle cells. In contrast, inflammation in atheromas can increase the breakdown of ECM components, leading to unstable plaques.

2.1.3.5 Process

In summary, chronic inflammatory responses and vascular "healing" are influenced by various factors, including endothelial injury, lipid oxidation, lipid accumulation, and inflammation. Atherosclerotic lesions consist of dysfunctional endothelial cells, proliferating smooth muscle cells, T lymphocytes, and macrophages. These four cell types, through the factors they secrete, contribute to atherogenesis. Therefore, in the early stages, intimal plaques consist of aggregates of smooth muscle cells, macrophages, and foam cells. The death of these cells releases lipids and necrotic debris. As atherosclerosis progresses, the atheroma is modified by ECM synthesized by smooth muscle cells; collagen is particularly prominent in the fibrous cap. The lesion typically retains a necrotic core composed of lipid-laden cells, cholesterol crystals, foam cells, fibrin, thrombus, and other plasma proteins. These plaques often exhibit calcification.

As atherosclerotic plaques mature, they become more prone to clinical complications. Plaque rupture, ulceration, or erosion exposes highly thrombogenic substances to the bloodstream, leading to partial or complete vascular occlusion and thrombosis. If the patient survives, the thrombus may organize and incorporate into the growing plaque. Other complications include:

- Hemorrhage within the plaque

  Rupture of the fibrous cap or thin-walled vessels in neovascularization regions can cause intraplaque hemorrhage, potentially expanding the plaque or triggering rupture.

- Atheroembolism

  Plaque rupture may release atherosclerotic debris into the circulation, generating microemboli.

- Aneurysm formation

  Loss of elastic tissue and ischemic atrophy may weaken the underlying arterial wall, leading to aneurysm formation and potential rupture.

2.2 Acute plaque complications

When examining the plaques responsible for myocardial infarction and acute coronary syndromes, it is often found that these plaques are asymptomatic and cause sudden, unexpected changes that lead to these conditions. Therefore, pathological and clinical studies show that most plaques that undergo sudden deterioration and result in coronary occlusion previously only exhibited mild to moderate lumen narrowing that was not critically severe. This suggests that many asymptomatic adults may be at risk for catastrophic coronary events. While imaging methods that could detect these types of lesions in a preventive manner are being developed, it is clear that standard angiographic studies are inadequate for visualizing such lesions until after the event has occurred.

Plaques rupture when they are unable to withstand the mechanical stresses exerted by vascular shear forces. The events that trigger sudden changes in plaques and subsequent thrombosis are complex, involving both intrinsic factors (such as plaque structure and composition) and external elements (such as blood pressure, platelet reactivity, and vasospasm). The fibrous cap undergoes continuous remodeling, which can either stabilize the plaque or make it more susceptible to rupture. Collagen, the main structural component of the fibrous cap, explains its mechanical strength and stability. The balance of collagen synthesis and degradation affects the integrity of the cap. Consequently, plaques with thin fibrous caps and active inflammatory cells within a necrotic core are more likely to rupture and are referred to as "vulnerable plaques" [3, 5, 6].

Collagen in atherosclerotic plaques is primarily produced by smooth muscle cells (SMCs), and thus the loss of these cells reduces the cap's resistance. Collagen turnover is regulated by metalloproteinases (MMPs), and their activity is modulated by tissue inhibitors of metalloproteinases (TIMPs). Inflammatory processes within the plaque contribute to collagen degradation and a reduction in collagen synthesis, which impacts the mechanical properties of the fibrous cap.

External factors also contribute to acute plaque changes. Adrenergic stimulation can increase systemic blood pressure or induce local vasoconstriction, thus increasing the physical stresses on a particular plaque.

Partial or complete thrombosis associated with an unstable plaque is a central factor in acute coronary syndromes. In its most severe form, the thrombus completely occludes the affected vessel. In contrast, in other coronary syndromes, thrombus-related lumen obstruction may be incomplete and can be resolved or reduced over time.

Coronary artery wall thrombi can also embolize. Small embolic thrombus fragments are often found in the distal intramyocardial circulation, sometimes accompanied by microinfarcts in patients who suddenly die from atherosclerosis. Thrombin and other thrombus-related factors are potent activators of smooth muscle cells and therefore contribute to the growth of atherosclerotic lesions.

Vasoconstriction poses a threat to lumen size and can increase local mechanical forces, thereby accelerating plaque deterioration. In atheromatous regions, vasoconstriction can be triggered by:

- Circulating adrenergic agonists
- Platelet contents released locally
- Contraction factors (such as endothelin)
- Impaired endothelial cell (EC) function leading to reduced release of endothelial-derived relaxing factors (such as nitric oxide)
- Mediators released by perivascular inflammatory cells

These complex interactions highlight the multifactorial nature of plaque destabilization and the potential for acute cardiovascular events [5, 6].

3. Pathophysiology of acute coronary syndromes

3.1 Left ventricular function

When a significant portion of the myocardium experiences sudden ischemia due to the interruption of antegrade flow in the epicardial coronary arteries, myocardial contraction and shortening are immediately affected. Four abnormal contraction patterns typically develop in sequence. Initially, dyssynchrony occurs, causing dissociation in the timing of contraction between adjacent segments. This is followed by a reduction in hypokinesis or shortening. Eventually, akinesis, or the cessation of shortening, develops, and finally, dyskinesis, characterized by paradoxical expansion and systolic bulging, becomes evident.

In areas of the myocardium not affected by the infarct, early hyperkinesis may occur as a compensatory mechanism to offset the functional losses in other regions. During this phase, the sympathetic nervous system and the Frank-Starling mechanism are activated to further compensate for the acute functional deficits. However, this compensatory mechanism is not effective enough to prevent the development of dyskinesis in other infarcted regions.

This hyperkinesis continues during the first 2 weeks following acute coronary syndromes. During this period, following reperfusion of infarcted areas, recovery and a decrease in myocardial stunning can be observed. STEMI patients may also exhibit a reduction in myocardial contractile function in non-infarcted regions. This finding may stem from a previous occlusion of the coronary artery supplying the non-infarcted myocardium or from a loss of collateral circulation due to the recent infarction. On the other hand, the development of collateral vessels before the occurrence of STEMI may help preserve regional systolic function and allow for improvements in early left ventricular ejection fraction (EF) following infarction.

When a significant portion of the myocardium is ischemically injured, left ventricle (LV) pump function deteriorates, leading to a reduction in cardiac output, stroke volume, blood pressure (BP), and peak dP/dt, while end-systolic volume increases. The extent of this increase in end-systolic volume is a powerful predictor of mortality following STEMI. Paradoxical systolic expansion of a damaged region of the ventricle further diminishes LV stroke volume. As necrotic myocytes lose their structural cohesion, the infarcted region stretches and thins, particularly in the case of large anterior infarctions, contributing to infarct expansion. This maladaptive remodeling can initiate a cycle of progressive ventricular dilation. Medications that inhibit the renin-angiotensin-aldosterone system (RAAS) can help mitigate ventricular dilation, which is influenced by infarct size, artery patency, and RAAS activation, even in the absence of overt LV dysfunction symptoms.

Over time, edema and subsequent fibrosis increase the stiffness of the infarcted myocardium beyond pre-infarct levels. This increased stiffness can paradoxically improve LV function by preventing abnormal systolic wall motion or dyskinesia. Clinical symptoms correlate with specific diastolic LV stiffness parameters, even in cases of small infarctions. If more than 15% of the myocardial segment exhibits abnormal contraction, ejection fraction (EF) may decline, and LV end-diastolic pressure and volume may rise. When more than 25% of the LV demonstrates abnormal contraction, the likelihood of heart failure (HF) increases, and damage exceeding 40% of the LV often leads to cardiogenic shock, which is frequently fatal.

During the healing phase, some recovery in wall motion may occur as stunned but viable myocardium regains function. However, persistent wall motion abnormalities affecting 20–25% of the LV are associated with hemodynamic signs of LV failure, significantly worsening long-term survival outcomes. The diastolic properties of the left ventricle also undergo significant changes following ischemic injury or infarction, including a reduction in the peak rate of LV pressure decline (peak −dP/dt), an increase in the time constant of LV pressure relaxation, and an initial elevation in LV end-diastolic pressure.

Over the course of several weeks, LV end-diastolic volume gradually increases, and diastolic pressure trends back toward normal levels. Similar to systolic dysfunction, the extent of diastolic abnormalities correlates directly with the size of the infarct. Larger infarctions typically lead to more pronounced alterations, contributing to the progression of LV dysfunction and an increased risk of clinical heart failure.

3.2 Ventricular remodeling

Following an ACS, changes in the size, shape, and thickness of the left ventricle (LV) occur, affecting both infarcted and non-infarcted myocardial segments. These alterations are collectively termed ventricular remodeling and have significant implications for ventricular dimensions, function, and prognosis. Remodeling is driven by LV dilation in conjunction with hypertrophy of the remaining non-infarcted myocardium.

In addition to infarct size, key factors influencing LV dilation include ventricular volume, loading conditions, and the patency of the infarct-related artery. Elevated ventricular pressures increase wall stress and contribute to the risk of infarct expansion. However, maintaining patency of the infarct artery promotes myocardial scar formation and increases tissue turgor in the infarct zone, thereby reducing the likelihood of ventricular dilation and infarct expansion.

Inflammation plays a crucial role in the healing process and influences whether myocardial remodeling is adverse or adaptive. Early post-MI, ejection fraction (EF) correlates only modestly with long-term LV volumes. Surprisingly, large infarctions do not always result in severe remodeling, while smaller infarcts can sometimes lead to substantial adverse ventricular changes.

This variability in outcomes may partly be attributed to genetic or epigenetic differences in the regulation of the healing process, driven by variable inflammatory responses. Excessive ventricular dilation may occur when the inflammatory response triggers excessive matrix degradation. Conversely, a more balanced inflammatory process that promotes fibrotic healing can result in greater scar deposition and less ventricular dilation, contributing to better structural outcomes.

3.3 Biomarkers of ACS

Proteins released into the bloodstream from damaged myocardial cells serve as markers of myocardial injury. Ischemia leading to necrosis compromises the sarcolemmal membrane, allowing intracellular macromolecules, including serum and plasma cardiac markers, to diffuse into the cardiac interstitium and subsequently enter the microvasculature and lymphatic system near the infarct zone.

The appearance of these macromolecules in the peripheral circulation is influenced by factors such as the extent of myocardial injury, the intracellular location of the marker, molecular weight, regional blood and lymphatic flow, and the clearance rate from the bloodstream.

Although the development of highly sensitive serum and plasma markers has enabled clinicians to detect much lower levels of myocardial injury, these tests do not provide direct information about the cause of damage. Non-ischemic conditions, such as myocarditis or exposure to myocardial toxins, can also cause myocardial injury without meeting the criteria for myocardial infarction (MI).

The increased sensitivity of cardiac markers has led to the recognition of myocardial injury in cases unrelated to plaque rupture, necessitating criteria that place myocardial injury in a clinical context.

In patients presenting with STEMI, treatment should not be delayed while awaiting biomarker assay results. Immediate clinical evaluation and a 12-lead ECG are essential for initiating urgent reperfusion strategies.

3.3.1 Measurement of cardiac-specific troponins in myocardial infarction (MI)

All patients with suspected MI should undergo cardiac-specific troponin testing at the earliest possible time during their initial evaluation. In cases of STEMI, waiting for biomarker results should never delay urgent interventions. From a cost-effectiveness standpoint, measuring both cardiac-specific troponin (cTn) and CK-MB is generally unnecessary.

Due to its continuous release from necrotic myocytes, cardiac troponin I (cTnI) levels may remain elevated for 7–10 days following MI, while cardiac troponin T (cTnT) levels can persist for up to 10–14 days. This prolonged elevation makes cTn measurements useful for diagnosing MI after the acute phase.

In STEMI patients who undergo successful reperfusion of the infarct-related artery, a rapid release of cardiac troponins often indicates successful recanalization. Routine serial measurements to track the peak and decline of cTn levels are typically unnecessary since cTn levels, particularly when assessed using high-sensitivity assays, may peak late and remain elevated for several days, especially in cases of large infarctions.

Detecting reinfarction should rely on clinical presentation, ECG findings, and at least two serial biomarker tests. If cTn levels are elevated but stable or decreasing at the time of recurrent symptoms, an additional increase of more than 20% is indicative of reinfarction. If initial cTn levels are within normal limits, standard assay-specific criteria and testing intervals should be applied.

In some cases, concurrent measurement of CK-MB may be beneficial for detecting early reinfarction, as CK-MB levels decline more rapidly than cTn.

3.4 Electrocardiography

The electrocardiogram (ECG) remains the cornerstone diagnostic tool for evaluating patients with suspected ischemic symptoms. Immediate reperfusion should be strongly considered for patients presenting with chest pain and ECG changes indicative of or concerning STEMI. While typical ECG patterns of STEMI are well-documented, atypical presentations are also possible.

One specific but insensitive sign of an anteroseptal MI is the presence of a new right bundle branch block (RBBB) accompanied by a Q wave in lead V1, as the right bundle is supplied by the septal perforators branching off the left anterior descending artery (LAD).

The distribution of ST-segment elevations across ECG leads can help localize the site of the occlusion in the infarct-related artery. The extent of ST deviation, infarction location, and QRS duration are important indicators of adverse outcomes. Additionally, the degree of ST-segment resolution provides valuable non-invasive feedback on the effectiveness of reperfusion, whether achieved through fibrinolysis or primary percutaneous coronary intervention (PCI).

Although there is broad consensus on criteria for recognizing anterior and inferior infarctions, disagreement persists regarding criteria for lateral and posterior infarctions. The term "inferobasal" may better describe the anatomical position of what is traditionally labeled as a posterior infarction. These infarcts are often better identified by placing leads in the V7 and V8 positions.

Patients presenting with an abnormal R wave in lead V1 ($\geq$0.04 seconds in duration and/or an R/S ratio $\geq$ 1 without preexcitation or right ventricular hypertrophy) along with inferior or lateral Q waves are more likely to have an isolated occlusion of the dominant left circumflex artery without collateral circulation. This group tends to experience lower ejection fractions (EF), increased end-systolic volumes, and higher complication rates compared to those with inferior infarctions due to isolated right coronary artery (RCA) occlusion.

ST-segment elevations in lead aVR, which reflect the basal intraventricular septum, are observed in up to 30% of STEMI cases. These findings often point to the left main coronary artery or multivessel disease and are associated with worse clinical outcomes.

Many patients exhibit permanent ECG changes following a STEMI, particularly when Q waves develop, marking infarction. However, in a significant number of cases, the classic ECG changes may resolve over time, with Q wave regression and even complete normalization of the ECG.

Several conditions can mimic the electrocardiographic features of MI by producing patterns that resemble infarction, known as "pseudoinfarction." These include:

- Structural cardiac abnormalities: Ventricular hypertrophy, primary myocardial diseases, and cardiac tumors (both primary and metastatic).

- Electrical disturbances: Conduction abnormalities, preexcitation syndromes, and early repolarization.

- Systemic or metabolic conditions: Hyperkalemia, intracranial hemorrhage, and pulmonary embolism.

- Infiltrative and muscular diseases: Cardiac amyloidosis, sarcoidosis, hypertrophic cardiomyopathy, and forms of muscular dystrophy.

- Other cardiac conditions: Pericarditis, traumatic heart disease, and pneumothorax.

Accurate clinical assessment is essential to differentiate true infarction from these pseudoinfarction patterns to avoid misdiagnosis and ensure appropriate management.

3.5 Echocardiography

Echocardiography is an essential and practical diagnostic tool for patients with suspected myocardial infarction (MI) due to its portability and availability at the point of care. In cases where chest pain is suggestive of ischemia but the ECG is non-diagnostic, the identification of regional wall motion abnormalities strongly supports the presence of myocardial ischemia.

Beyond its role in diagnosing ischemia, echocardiography is valuable for evaluating chest pain when an aortic dissection is suspected. The detection of an intimal flap characteristic of aortic dissection can significantly influence treatment decisions. However, transthoracic echocardiography (TTE) has limited sensitivity compared to other imaging modalities, such as computed tomography (CT) angiography, for identifying aortic dissections.

Echocardiographic assessment of left ventricle (LV) function correlates well with angiographic findings and is a critical prognostic tool following MI. Early echocardiography can help detect:

- Stunned myocardium: Identifying contractile reserve in potentially viable tissue.

- Residual ischemia: Highlighting areas still at risk.

- Heart failure risk: Stratifying patients for future heart failure development.

- Mechanical complications: Identifying issues such as ventricular thrombus, acute mitral or tricuspid regurgitation, and ventricular septal defects.

Although TTE is effective for most patients, it may yield suboptimal results in individuals with poor echocardiographic windows, particularly those on mechanical ventilation. In such cases, transesophageal echocardiography (TEE) or cardiac magnetic resonance (CMR) imaging may be superior for evaluating infarct size, infarct location, ventricular septal defects, and papillary muscle dysfunction.

4. Conclusions

Acute coronary syndrome (ACS) encompasses a spectrum of conditions caused by the sudden, reduced blood flow to the myocardium, leading to myocardial ischemia and, in severe cases, infarction. The primary pathophysiological mechanism involves the rupture of an atherosclerotic plaque within a coronary artery, resulting in thrombus formation. Plaque rupture exposes subendothelial elements, activating platelets and initiating a coagulation cascade that leads to clot development. The extent and stability of the thrombus determine the severity of coronary obstruction, with partial blockage causing unstable angina and complete occlusion leading to myocardial infarction. Other contributory factors include coronary vasospasm, endothelial dysfunction, and inflammation. The ischemic damage caused by ACS disrupts myocardial cell membranes, releasing cardiac biomarkers such as troponin into the bloodstream. Early recognition and intervention are critical in ACS management to restore perfusion and minimize myocardial injury (**Table 2**).

Time	Features	Light microscope	Electron microscope
Reversible injury			
0–half hour	None	None	Relaxation of myofibrils, glycogen loss, mitochondrial swelling
Irreversible injury			
0.5–4 hours	None	Usually none, waviness of fibers at the border	Sarcolemmal disruption; mitochondrial amorphous densities
4–12 hours	Dark mottling	Early coagulable necrosis, edema, hemorrhage	
12–24 hours	Dark mottling	Coagulative necrosis, pyknosis of nuclei, hypereosinophilia, marginal contraction band necrosis, early neutrophilic infiltrate	
1–3 days	Mottling with yellow-tan infarct center	Coagulative necrosis, with loss of nuclei and striations, brisk interstitial infiltrate of neutrophils	
3–7 days	Hyperemic border, central yet low-tan softening	Beginning disintegration of dead myofibers, with dying neutrophils, early phagocytosis of dead cells by macrophages at the infarct border	
7–10 days	Maximally yet low-tan and soft, with depressed red-tan margins	Well-developed phagocytosis of dead cells, granulation tissue at margins	
10–14 days	Red-gray depressed infarct borders	Well-established granulation tissue with new blood vessels and collagen deposition	
2–8 weeks	Gray-white scar, from the border toward the core of the infarct	Increased collagen deposition, with decreased cellularity	
>2 months	Scarring complex	Dense collagenous scar	

Table 2.
Pathologic changes in myocardial infarction [7].

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References

[1] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Circulation. 2018;**138**(20):e618-e651. Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000617

[2] Libby P, Pasterkamp G, Crea F, Jang IK. Reassessing the mechanisms of acute coronary syndromes. Circulation Research. 2019;**124**(1):150-160. Available from: https://pubmed.ncbi.nlm.nih.gov/30605419/

[3] Tomaniak M, Katagiri Y, Modolo R, de Silva R, Khamis RY, Bourantas CV, et al. Vulnerable plaques and patients: State-of-the-art. European Heart Journal. 2020;**41**(31):2997-3004. Available from: https://pubmed.ncbi.nlm.nih.gov/32402086/

[4] Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). European Heart Journal. 2023;**44**(38):3720-3826. DOI: 10.1093/eurheartj/ehad191

[5] Costopoulos C, Maehara A, Huang Y, Brown AJ, Gillard JH, Teng Z, et al. Heterogeneity of plaque structural stress is increased in plaques leading to MACE: Insights from the PROSPECT study. JACC: Cardiovascular Imaging. 2020;**13**(5):1206-1218. Available from: https://pubmed.ncbi.nlm.nih.gov/31326476/

[6] Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, et al. Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. Journal of the American College of Cardiology. 2015;**66**(4):337-346. Available from: https://pubmed.ncbi.nlm.nih.gov/26205589/

[7] Vinay K, Abbas AK, Aster JC, Perkins JA. Robbins & Cotran Pathologic Basis of Disease. 10th ed. Philadelphia, PA: Elsevier; 2021. pp. 485-500

Chapter 3

The Role of Cardiac Magnetic Resonance in Acute Coronary Syndrome

Marija Zdravkovic, Maja Popovic and Viseslav Popadic

Abstract

Cardiac magnetic resonance is a non-invasive, non-radiating imaging modality that can provide substantial information in patients with and after acute coronary syndrome. It is important in diagnosis, prognosis, and treatment decisions, as well as stratification of patients after acute coronary syndrome. Its usefulness in the estimation of infarction area, the presence of microvascular obstruction, and the morphology and function of the left ventricle is crucial in identifying patients with an increased risk of heart failure after myocardial infarction. Also, it is important in the evaluation of residual ischemia, where novel techniques in myocardial perfusion estimation are highly sensitive and specific. On the other hand, Cardiac magnetic resonance (CMR) can provide answers in patients with myocardial infarction without obstructive coronary artery disease, differentiating between various potential pathophysiological mechanisms. It can identify and stratify patients with ischemic cardiomyopathy after acute myocardial infarction and provide timely treatment decisions.

Keywords: acute coronary syndrome, myocardial infarction, cardiac magnetic resonance, ischemic heart disease, cardiac imaging, myocardial fibrosis

1. Introduction

Cardiac magnetic resonance (CMR) in patients with acute myocardial infarction, especially in those with ST-elevation myocardial infarction (STEMI), allows the detection and detailed assessment of myocardial edema, microvascular obstruction, and intramyocardial hemorrhage while providing significant information about the size of the infarct area and myocardial area at risk. Despite the progress in the treatment of ST-elevation myocardial infarction, which resulted in a decreased mortality rate in previous decades, the incidence of post-infarction heart failure and associated serious adverse events is still high. Therefore, cardiac magnetic resonance is an indispensable method in stratifying the risk of left ventricular remodeling to assess arrhythmia risk and, consequently, the risk of sudden cardiac death [1].

Considering the changes in the size of the infarct area and the expression of edema during the first few days after STEMI, there is still no clear consensus on when to perform CMR during the acute phase. However, it is recommended to perform CMR in the period between the 3rd and 5th day or from the 4th to the 7th day, and at the latest until the 10th day after primary percutaneous coronary intervention (pPCI) [2].

2. Cardiac magnetic resonance in the estimation of the infarct size

The size of the infarct zone is generally estimated based on the quantification of the late gadolinium enhancement (LGE) in the myocardium (**Figure 1**). The gadolinium contrast agent cannot penetrate the intact cell membrane of cardiomyocytes but accumulates in the necrosis area, i.e., ruptured cell membranes, as is the case with acute myocardial infarction. Gadolinium can also accumulate in the interstitium due to the expansion of the interstitium in the case of collagen deposition and redistribution of the contrast agent from the vascular compartment to the interstitial space (chronic phase of myocardial infarction) [3]. Accumulation of gadolinium in the infarct zone is with transmural distribution in patients with ST-elevation myocardial infarction, while in patients with acute myocardial infarction without ST-segment elevation it is mostly with subendocardial distribution. In patients with ST-elevation myocardial infarction, several zones of interest are distinguished within the infarct territory [4].

The size of the infarct zone assessed by cardiac magnetic resonance is strongly associated with the incidence of heart failure hospitalization and overall mortality at 1-year follow-up. With the increase in the size of the infarct zone by 5%, there is an increase in the relative risk for hospitalization due to heart failure and mortality in the one-year follow-up of 20% [5].

3. Assessment of microvascular obstruction and intramyocardial hemorrhage

Microvascular obstruction (MVO) refers to the impossibility of coronary microvasculature reperfusion in the previously ischemic area despite the establishment of optimal flow through the infarcted artery. Microvascular obstruction is registered as a dark zone, i.e., as a zone of reduced signal intensity, within the zone of increased signal intensity on early gadolinium enhancement sequences (early microvascular obstruction) or conventional late gadolinium enhancement sequences (late microvascular obstruction) (**Figure 2**) [6]. It is shown that for every 1% absolute increase in the zone of microvascular

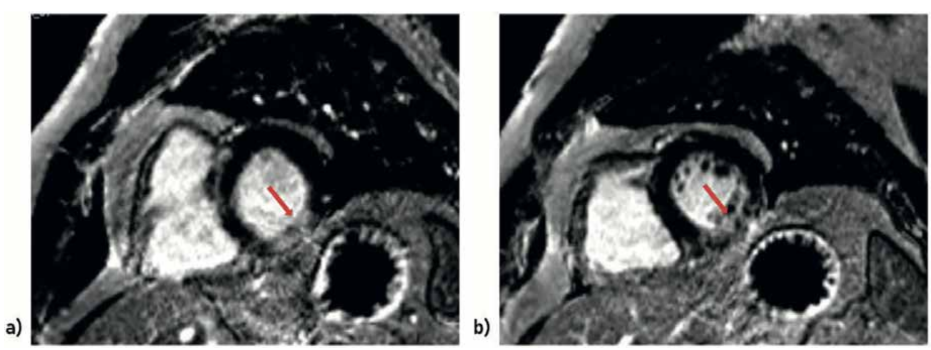

Figure 1.
LGE in acute ST-elevation myocardial infarction: LGE PSIR sequence, short axis; transmural LGE (transmural myocardial infarction) in (a) basal, and (b) medial inferior segment of the left ventricle.

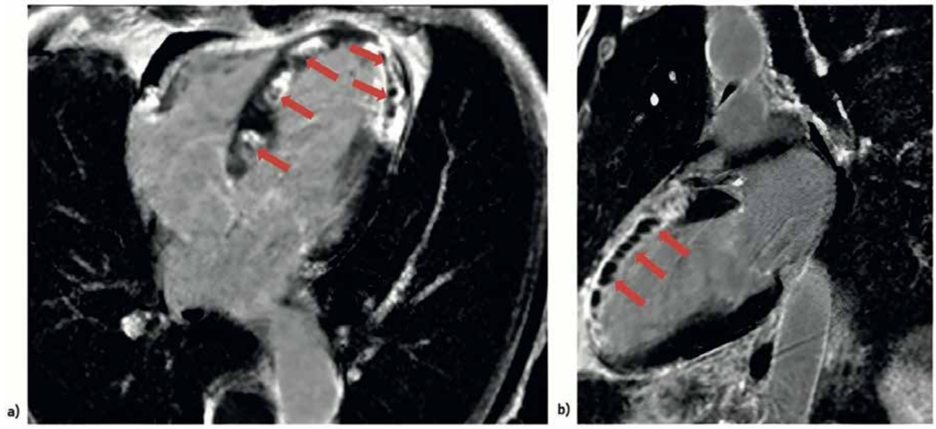

Figure 2.
Microvascular obstruction in a patient with acute ST-elevation myocardial infarction: (a) LGE PSIR sequence, four chambers view; transmural LGE (transmural myocardial infarction), within which there are zones of reduced myocardial signal intensity – microvascular obstruction (MVO) (red arrow) in the basal, mid, and apical septal segments and in the apical lateral segment of the left ventricle; (b) LGE PSIR sequence, two chambers view; transmural zones LGE (transmural myocardial infarction), within which there are zones of reduced myocardial signal intensity - MVO (arrow) in the mid and apical anterior segment of the left ventricle.

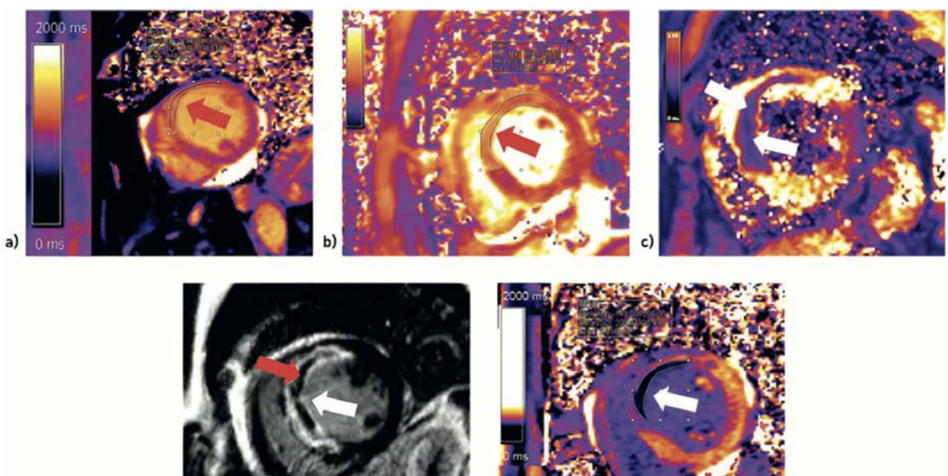

Figure 3.
Intramyocardial hemorrhage finding on T2 myocardial map after acute myocardial infarction of anteroseptal localization and correlation with native T1 myocardial map, T2 myocardial map, LGE, and post-contrast T1 myocardial map: (a) Native T1 myocardial map, mid-short axis view; transmural prolonged native T1 time (transmural myocardial edema) in the anterior and anteroseptal segments; (b) T2 myocardial map, mid-short axis view; transmural prolonged T2 time (transmural myocardial edema) in the anterior and anteroseptal segments; (c) T2* myocardial map, mid-short axis view; transmural shortened T2 time in the anterior and anteroseptal segments (intramyocardial hemorrhage); (d) LGE PSIR, mid-short axis view; transmural LGE (transmural myocardial infarction) in the anterior and anteroseptal segments (white arrow) with MVO (red arrow); (e) Post-contrast T1 myocardial map, mid-short axis view; transmural shortened post-contrast T1 time in the anterior and anteroseptal segments (transmural myocardial infarction).*

obstruction, there is a relative increase in the risk of overall one-year mortality by 14%, as well as an increase in the one-year risk of heart failure hospitalization by 8% [7].

If microvascular obstruction after STEMI is pronounced, extravasation of erythrocytes into the surrounding myocardium may occur, which is marked as intramyocardial hemorrhage. Hemoglobin breakdown products, as well as residual iron accumulation in the myocardium, can be detected as a zone of the hypointense core within the infarct territory on a T2* sequence or T2* map. Compared with the standard T2* sequence, the T2* map showed a better sensitivity for the detection of intramyocardial hemorrhage (**Figure 3**). The presence of microvascular obstruction and intramyocardial hemorrhage is associated with worse clinical outcomes in patients after STEMI, especially the presence of intramyocardial hemorrhage. A value of T2* time shorter than 20 ms indicates the existence of microvascular obstruction and intramyocardial hemorrhage and is associated with an increased risk of developing systolic dysfunction and ventricular arrhythmia. A T2* time shorter than 10 ms is associated with an increased risk of developing heart failure after acute myocardial infarction [8, 9]. The assessment of circumferential strain can also be important via the feature-tracking technique, which has been shown to have prognostic significance regarding the recovery of left ventricular function in these patients [10].

4. The importance of assessing the myocardial area at risk

The myocardial area at risk refers to the territory of the infarcted artery in which a myocardial infarction would have occurred if timely reperfusion of the still viable

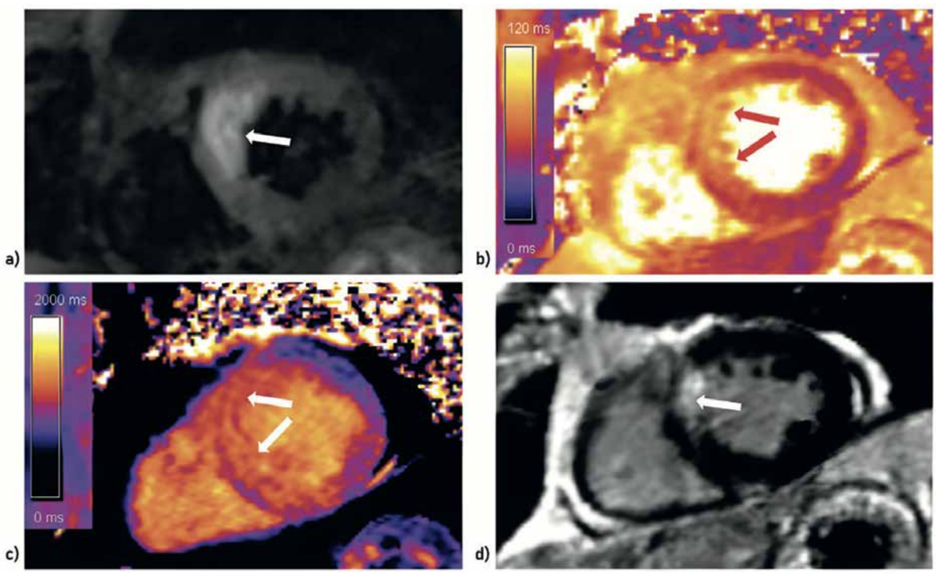

Figure 4.
STIR sequence, T2 myocardial map, native T1 myocardial map, and LGE sequence in the evaluation of the myocardial area at risk in a patient with acute ST-elevation myocardial infarction: (a) Short tau inversion recovery (STIR) sequence, mid-short axis view; transmurally increased myocardial signal intensity (transmural myocardial edema) in the mid-anteroseptal segment; (b) T2 myocardial map, mid-short axis view; transmurally prolonged T2 time (transmural myocardial edema) in the mid-anteroseptal and inferoseptal segments; (c) Native T1 myocardial map, mid-short axis view; transmurally prolonged native T1 time (transmural myocardial edema) in the mid-anteroseptal and inferoseptal segments; (d) LGE PSIR sequence, mid-short axis view; transmural LGE phenomenon (transmural myocardial infarction) in the mid-anteroseptal segment - the LGE (necrosis zone) is smaller in volume compared to the myocardial edema zone (the difference is the zone of salvaged myocardium).

myocardium had not occurred. The myocardial zone at risk includes the myocardial zone under infarction (infarct core - cardiomyocyte necrosis) and the zone with reversible myocardial injury.

The myocardial area at risk refers to the entire territory in the zone of the infarcted artery that is under myocardial edema, while the infarcted zone is limited to the territory under the late gadolinium enhancement. The difference between these two territories is the so-called zone of "salvaged myocardium." The estimation of this area is extremely important for risk stratification and monitoring of the effects of new cardioprotective therapeutic modalities on reducing the infarct zone size [11]. Myocardial maps can be of large importance in the evaluation of the zone of myocardium under edema, bearing in mind their high sensitivity. A post-contrast T1 myocardial map can be used to evaluate the size of the infarcted zone in the acute phase instead of assessment based on LGE sequences, while a native T1 myocardial map can be used to evaluate the zone of chronic myocardial infarction (focal field of interstitial fibrosis as a consequence of ischemia).

The myocardial T2 map is predominantly used to quantify the territory of the myocardium under edema (area of prolonged T2 time), which indicates the size of the area at risk (**Figure 4**). The importance of extracellular volume (ECV) assessment in the infarcted zone has not yet been fully investigated, although the current conclusions indicate a good predictive power of ECV for distinguishing the acute from the chronic phase of myocardial infarction (**Figure 5**) [12].

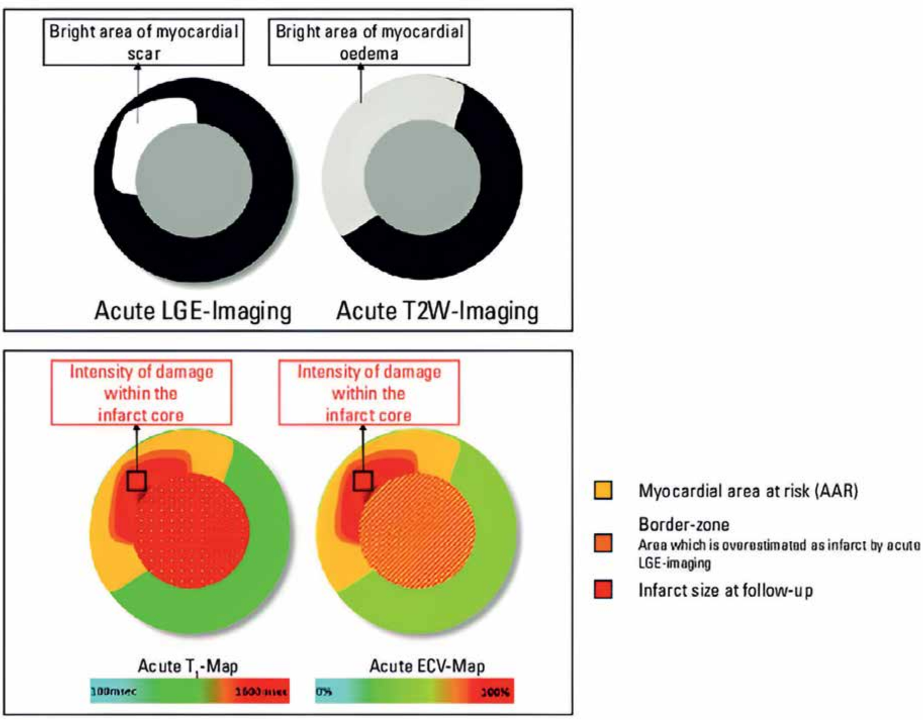

Figure 5.
Schematic presentation of the significance of myocardial maps and extracellular volume (ECV) assessment in patients with acute myocardial infarction [11].

5. The importance of the infarct zone size on subsequent left ventricular remodeling and clinical outcomes

It has been shown that the size of the infarct zone assessed by cardiac magnetic resonance is strongly associated with subsequent negative left ventricular remodeling. Infarct zone that covers less than 18.5% of the total mass of the myocardium in 15% of cases consequently leads to negative remodeling of the left ventricle, while in patients in whom the infarct zone covers more than 18.5% of the total myocardial mass, pronounced remodeling occurs in as many as 40% of patients after STEMI (**Figure 6**) [13]. The criteria for evaluating pronounced negative remodeling of the left ventricle after STEMI include an increase of over 12% in the indexed value of the end-diastolic left ventricular volume.

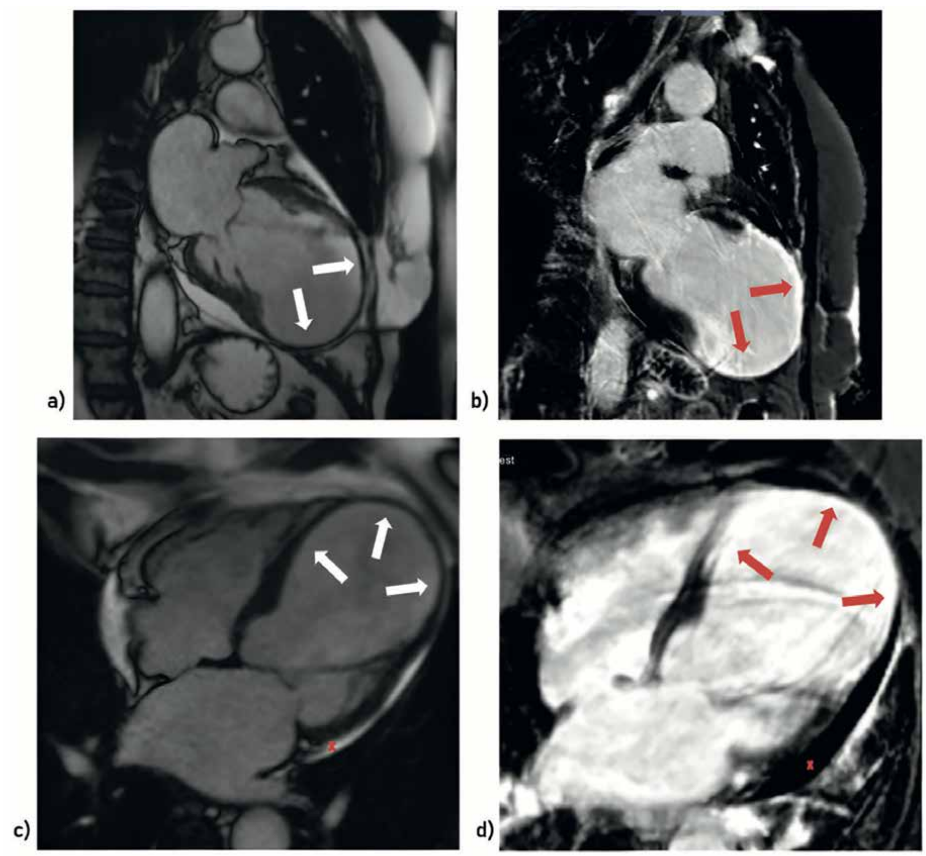

Figure 6.
Influence of the infarct zone size on the process of subsequent negative left ventricle remodeling after acute transmural myocardial infarction: (a) Cine sequence, two chambers view; dilated, remodeled left ventricle, with thinned mid and apical anterior segments, apical inferior segment and apex (aneurysmically dilated); (b) LGE PSIR sequence, two chambers view; transmural LGE (transmural myocardial infarction) in thinned segments – mid and apical anterior segments, apical inferior segment, apex; (c) Cine sequence, four chambers view; dilated, remodeled left ventricle, with mid and apical septal thinning segments, mid and apical lateral segment and apex (aneurysmally expanded); (d) LGE PSIR sequence, four chambers view; transmural LGE (transmural myocardial infarction) in thinned segments - mid and apical septal segments, mid and apical lateral segments and apex (aneurysmically dilated).

Cardiac magnetic resonance has a role in the evaluation of the right ventricle function, especially after the myocardial infarction of inferior localization, where the LGE can also be registered in the myocardium of the right ventricle, which is a significant prognostic factor in these patients [14].

In addition to a significant increase in end-diastolic volume due to dilatation of the left ventricle, there is also an increased risk of arrhythmia in these patients due to the large myocardial scar burden. Therefore, stratification in terms of the sudden cardiac death risk, and timely prevention, is extremely important [15, 16].

6. Significance of myocardial deformation assessment by cardiac magnetic resonance after acute myocardial infarction

Assessment of myocardial deformation (strain) by means of cardiac magnetic resonance has great prognostic significance after acute myocardial infarction. Sophisticated techniques and methods of data processing, primarily feature-tracking techniques, enabled the precise determination of all three main patterns of myocardial movement that are conditioned by the orientation of myocardial layers (longitudinal and circumferential shortening and radial increase in wall thickness) (**Figure 7**).

In patients with acute myocardial infarction, it was shown that the estimation of the global circumferential strain has the greatest importance for further prognosis. Based on this parameter, the extensiveness or transmurality of myocardial infarction can be estimated, both in the acute and chronic phases, as well as the presence of microvascular obstruction, and also the functional recovery of the left ventricle after reperfusion therapy.

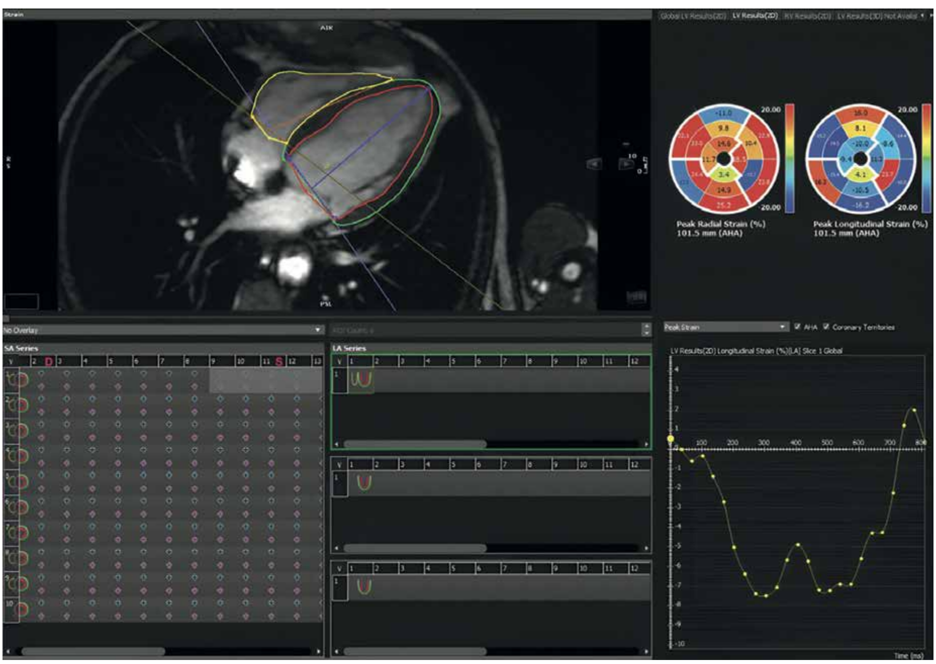

Figure 7.
Analysis of myocardial deformation and evaluation of segmental contractility by CMR feature-tracking techniques within a specialized post-processing program (radial and longitudinal strain values are presented on a 16-segment American Heart Association (AHA) left ventricular myocardium model).

Assessment of myocardial deformation outside the infarct zone (remote myocardium) can enable additional stratification of patients who are at increased risk of negative left ventricular remodeling, development of heart failure, and ventricular arrhythmia. It has been shown that risk stratification in patients after acute myocardial infarction by assessing myocardial deformation is non-inferior to assessment through LGE sequences, which is of particular importance considering that this technique does not require the application of a gadolinium-based contrast agent [17].

7. Detection of residual iron accumulation in the myocardium and impact on left ventricular remodeling

Intramyocardial hemorrhage and accumulation of residual iron in the myocardium as a result of extravasation of erythrocytes and their disintegration is an important predictor of subsequent negative remodeling of the left ventricle and can be detected by cardiac magnetic resonance in about 40% of patients after STEMI [18]. It is believed that the mechanism is actually inflammatory and that the accumulation of iron in the myocardium promotes the inflammatory process in the chronic phase. It is shown that over 50% of patients in whom intramyocardial hemorrhage was registered in the acute phase have signs of residual iron accumulation after 6 months, which is associated with more pronounced negative remodeling of the left ventricle and worse clinical outcomes in further follow-up [19].

8. Importance of remote myocardium evaluation on clinical outcomes of patients after stemi

Compensatory changes in the extracellular matrix of the myocardium outside the infarct zone (remote myocardium), expressed through the value of the extracellular volume (ECV), can be important in the prediction of negative remodeling of the left ventricle. It has been shown that elevated ECV in this zone can be maintained even 6 months after the acute phase of myocardial infarction and that it is associated with an increase in end-diastolic volume and worse clinical outcomes. Similar results were obtained in the case of monitoring the value of the native T1 time [20, 21].

9. Left ventricular remodeling and arrhythmic risk assessment

Based on cardiac magnetic resonance studies in the acute phase of myocardial infarction, it was concluded that patients with initially reduced global systolic function, increased end-diastolic volume, a large infarct zone, and signs of the presence of microvascular obstruction and intramyocardial hemorrhage have an increased arrhythmia risk in further follow-up [22]. Estimated infarct zone in the acute phase greater than 23.5 g/m^2 of the indexed mass of the left ventricular myocardium or 31% of the total left ventricular (LV) mass, with an ejection fraction lower than 36%, proved to be an important prognostic factor of increased arrhythmic risk in a two-year follow-up [23]. Cardiac magnetic resonance is, therefore, an irreplaceable diagnostic method for the stratification of patients with an increased risk of sudden cardiac death, both in the acute and chronic phases.

10. Cardiomagnetic resonance in the evaluation of acute myocardial infarction complications

Cardiac magnetic resonance represents an important diagnostic method in cases of acute myocardial infarction complications, primarily due to its high temporal and spatial resolution and the possibility of recording pre- and post-contrast sequences. It is important for the visualization of aneurysmal formations, thrombus masses, valvular complications (papillary muscle rupture, mitral insufficiency), post-infarct ventricular septal defect (VSD), and post-infarct pericardial damage [24, 25]. Bearing in mind that the mechanical complications of acute myocardial infarction are an emergency condition and early recognition and care have immeasurable importance, the echocardiographic examination is still the gold standard in diagnostics. Visualization and differentiation of thrombus masses in the lumen of the left ventricle, aneurysms/pseudoaneurysms of the left ventricle, as well as post-infarction pericardial damage, are the most common indications for a CMR exam.

10.1 Thrombus in the left ventricle

Formation of left ventricular thrombus after acute myocardial infarction is registered in about 6–8% of patients in whom cardiac magnetic resonance is performed in the first 7 days after the acute event [26]. The risk of thrombus formation is highest in those patients with acute myocardial infarction of anterior localization, reduced global systolic function, and formed aneurysm of the left ventricle apex (**Figure 8**). In patients with STEMI of anterior localization and reduced EF, a thrombus in the lumen of the left ventricle is registered in one-fifth of patients [27]. It is important to emphasize that cardiac magnetic resonance has significantly higher sensitivity in detecting left ventricular thrombus compared to echocardiography. It has been shown that the presence of left ventricular thrombus in patients after STEMI is associated with an increased risk of complications during hospitalization but also of serious adverse cardiovascular events during one-year follow-up. The patients with a large infarct zone and signs of microvascular obstructions are in a very high-risk group. The thrombus is visualized in the lumen of the left ventricle as a clearly limited, avascular hypointense mass, with the absence of signal intensity enhancement at LGE sequences. On the myocardial maps, bearing in mind that it is an avascular structure, moderately prolonged values of the native T1 time (mainly 1100–1200 ms) are registered, with extended T2 time values. In the case of a recently formed thrombus, slightly shorter values of the native T1 time are registered compared to older thrombi due to the increased presence of methemoglobin [28]. For easier differentiation of cardiac masses, masses rich in adipose tissue, melanomas, and calcifications of the mitral annulus have a shortened native T1 time, while pericardial cysts have the longest native T1 time values [29].

10.2 Post-infarction pericardial damage

Cardiac magnetic resonance, in addition to a detailed assessment of myocardial pathology, also provides useful information on early post-infarction pericardial damage. In some CMR studies, signs of pericardial damage were registered in almost half of the patients after STEMI. The most frequently registered signs included pericardial effusion and/or pericardial enhancement on LGE sequences (**Figure 9**). Patients with post-infarction pericardial damage had higher values of troponin and C-reactive protein, a more extensive infarction zone, and a more pronounced

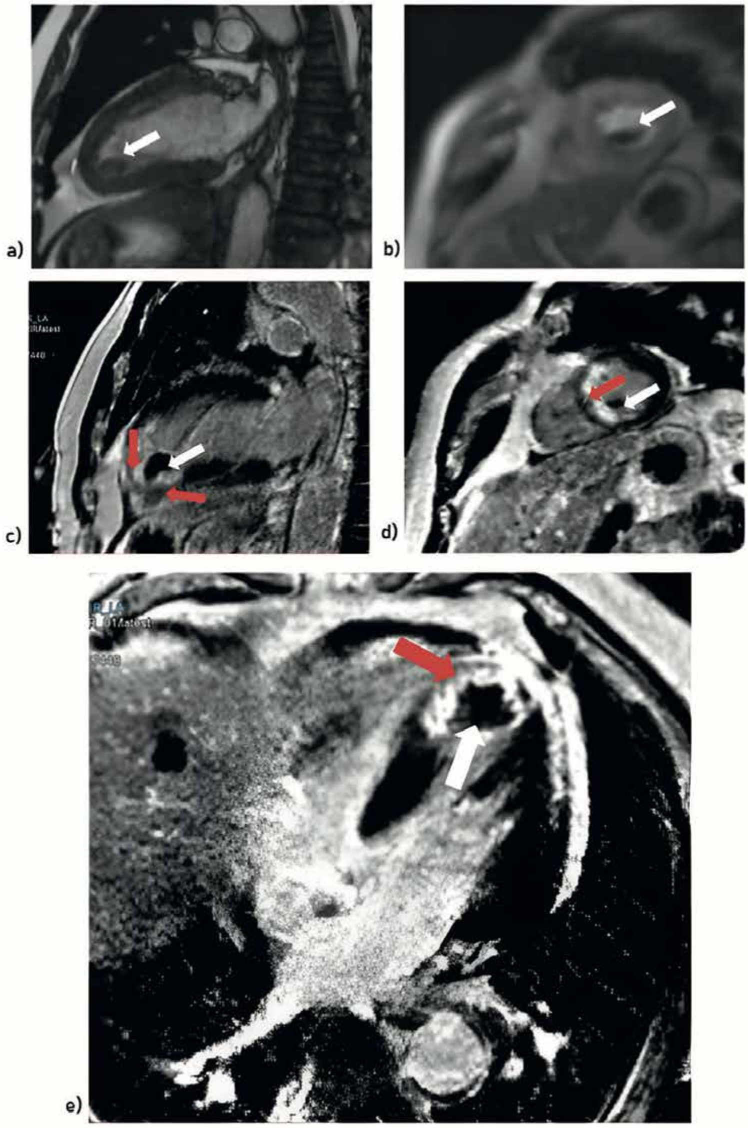

Figure 8.
Thrombus in the apex of the left ventricle in a patient with ST-elevation myocardial infarction of anteroseptal localization: (a) Cine sequence, two chambers view; thrombus mass in the apex of the left ventricle; (b) Rest perfusion study, apical short axis view; avascular mass - thrombus mass in the apex of the left ventricle; (c) LGE PSIR sequence, two chambers view; transmural LGE in the apical anterior and inferior segments - transmural myocardial infarction (red arrow), avascular mass - thrombus mass in the apex of the left ventricle (white arrow); (d) LGE PSIR sequence, apical short axis view; transmural LGE in the apical septal and partially inferior segments - transmural myocardial infarction (red arrow), avascular mass - thrombus mass in apex of the left ventricle (white arrow); (e) LGE PSIR sequence, four chambers view; transmural LGE in the apical septal segment - transmural myocardial infarction (red arrow), avascular mass - thrombus mass in the apex of the left ventricle (white arrow).

degree of microvascular obstruction. The presence of a more pronounced pericardial effusion is associated with worse clinical outcomes during a one-year follow-up in terms of overall mortality, myocardial reinfarction, and heart failure hospitalizations (**Figure 10** and **Table 1**) [30].

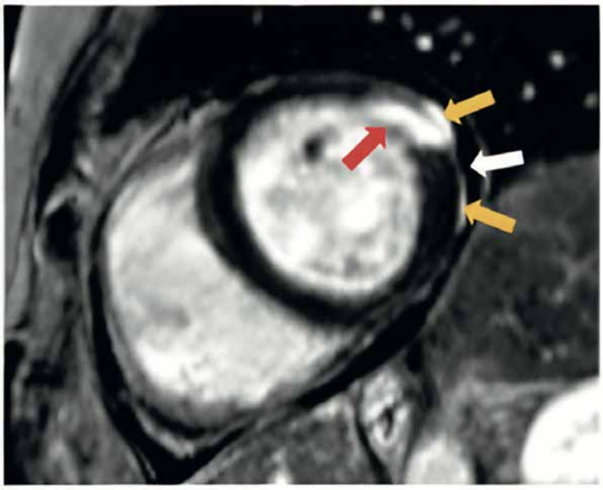

Figure 9.
Post-infarction pericardial damage after ST-elevation myocardial infarction: LGE PSIR sequence, mid-short axis view; transmural LGE (transmural myocardial infarction) in the mid-anterolateral segment (red arrow); late pericardial enhancement along with the mid-inferolateral and anterolateral segments (yellow arrow); circular pericardial effusion (white arrow).

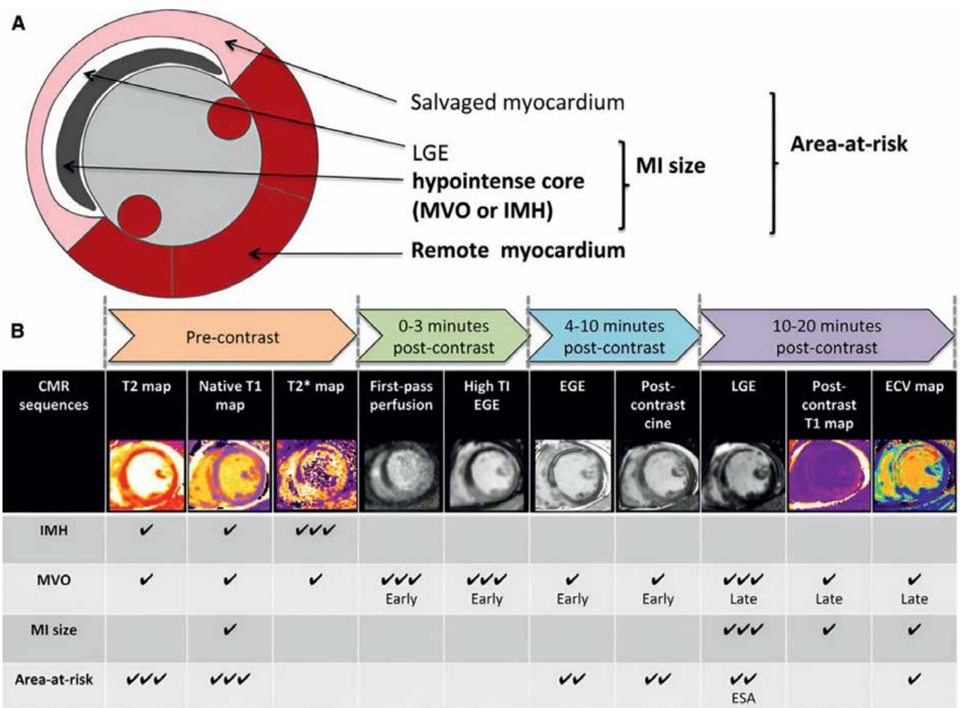

Figure 10.
Schematic representation of different zones within the territory of myocardial infarction and methods for the detection and assessment of the infarct area size, area at risk, microvascular obstructions and intramyocardial hemorrhages on cardiac magnetic resonance [1]. Note: ECV: extracellular volume; EGE: early gadolinium enhancement with gadolinium; MI: myocardial infarction; LGE: late gadolinium enhancement; IMH: intramyocardial hemorrhage; MVO: microvascular obstruction; FPP: first-pass perfusion; TI: inversion time.

Terminology	Definition
Myocardial infarction size	This refers to the mass or volume of infarcted myocardium and is conventionally quantified by late gadolinium enhancement.
Early microvascular obstruction	This can be identified as areas of dark core within the Myocardial Infarction (MI) zone with first-pass perfusion or Early Gadolinium Enhancement (EGE) imaging performed with a fixed, high TI (e.g., 440 to 500 ms at 1.5 T) acquired at 1–4 min after contrast injection.
Late microvascular obstruction	This can be identified as a dark core within the areas of hyperenhancement on conventional late gadolinium enhancement (LGE) sequences acquired >10 min after contrast injection.
Intramyocardial hemorrhage	This can be identified with T2* -weighted imaging or T2* mapping. Breakdown of the erythrocyte membrane eventually leads to ferritin and hemosiderin deposits within the macrophages, and the iron-degradation products can be detected with T2* imaging. Most studies have used a cutoff value for T2*of <20 ms to detect intramyocardial hemorrhage, but a threshold-based method of 2 SDs below the mean remote myocardial T2* can also be used. In centers where T2* imaging is not available, many studies have also used T2-weighted imaging, but its diagnostic performance is less robust than T2*-weighted imaging.
Area at risk	This refers to the territory supplied by the infarct-related artery and includes both the reversibly injured myocardial (the salvaged myocardium) and the infarcted myocardium. The area at risk can be indirectly assessed by CMR with late gadolinium enhancement imaging (to derive the endocardial surface area), T2-weighted imaging, T2 mapping, native T1 mapping, EGE imaging, precontrast Steady-state free precession (SSFP) cine, and postcontrast SSFP cine imaging.
Myocardial salvage and myocardial salvage index	Myocardial salvage can be calculated by subtracting the MI size from the area at risk. The myocardial salvage index refers to the ratio of the myocardial salvage to the area at risk.
Remote myocardium	This is usually defined as a myocardial segment 180° from the infarcted territory.

CMR: cardiac magnetic resonance; LGE: late gadolinium enhancement; EGE: early gadolinium enhancement; SSFP: steady-state free precession.

Table 1.
Cardiac magnetic resonance in acute myocardial infarction (definitions and terminology).

11. Cardiac magnetic resonance in myocardial infarction without coronary artery obstruction (minoca)

In large observational studies, the proportion of patients who present with clinical and laboratory signs of acute myocardial infarction but without findings of obstructive coronary disease ranges between 4 and 13% [31]. The pathophysiological basis of myocardial injury in these patients includes various mechanisms, including atherosclerotic plaque rupture, coronary artery dissection, coronary artery spasm, type 2 myocardial infarction, clinically unrecognized myocarditis, Takotsubo cardiomyopathy, and others [32]. Patients presenting as Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA) are mostly younger and female, although the predictors of future serious adverse cardiovascular events are similar to those of acute myocardial infarction and obstructive coronary disease [33]. It should be underlined that MINOCA is a working diagnosis and that timely detection of the cause of myocardial injury and initiation of therapy is extremely important. Cardiac magnetic resonance presents the gold standard of non-invasive diagnostics in patients with myocardial infarction without coronary artery obstruction.

Based on a meta-analysis of CMR studies in patients with MINOCA, it was concluded that in 33% of cases, the cause was myocarditis, in 24%, a typical picture of acute myocardial infarction, while in 26% of cases, no significant abnormalities were registered [34]. Other causes included the existence of Takotsubo cardiomyopathy, dilated cardiomyopathy, apical hypertrophy, as well as disorders associated with thrombophilia. It is recommended that a CMR examination should be done in the first 7 days after the initial presentation, bearing in mind that delaying the examination can sometimes result in the lack of clear signs of the cause and the inability to make the correct diagnosis [35].

11.1 Acute myocardial infarction

As already stated, the possible pathophysiological basis of MINOCA can be rupture or erosion of the atherosclerotic plaque or plaque ulceration with spontaneous autolysis of the resulting intracoronary thrombus when the presence of obstructive coronary artery disease is not observed on coronary angiography during the index procedure [33]. The mentioned mechanisms result in a typical picture of acute myocardial infarction on CMR examination (the existence of a zone of myocardial edema and LGE with subendocardial or transmural distribution that corresponds to the vascularization zone of one of the coronary arteries) (**Figure 11**).

Based on LGE sequences, the sensitivity and specificity of cardiac magnetic resonance for detecting acute myocardial infarction are 99% [36]. It is important to note that patients with acute myocardial infarction as a presentation

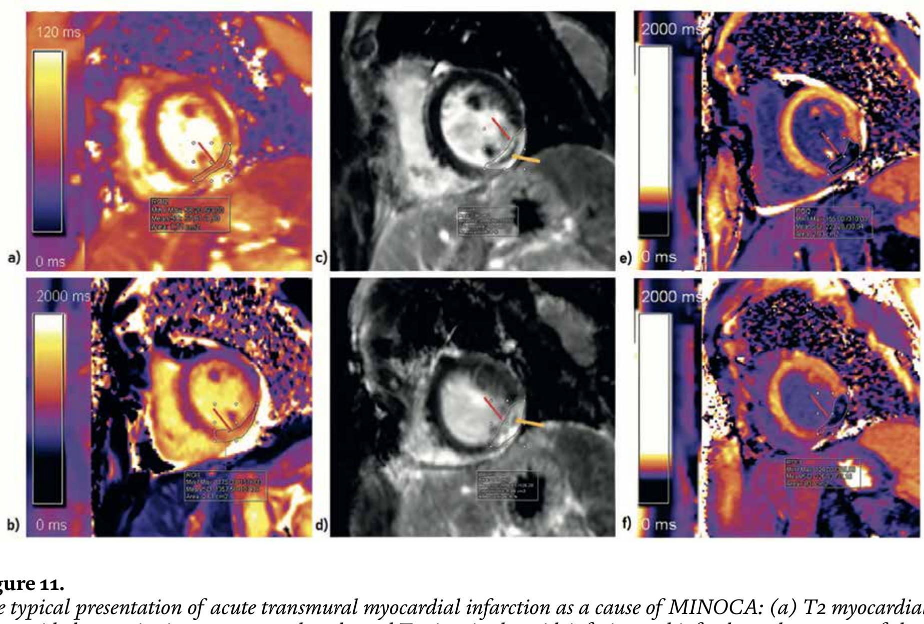

Figure 11.
The typical presentation of acute transmural myocardial infarction as a cause of MINOCA: (a) T2 myocardial map, mid-short axis view; transmural prolonged T2 time in the mid-inferior and inferolateral segments of the left ventricle - myocardial edema; (b) Native T1 myocardial map, mid-short axis view; transmural prolonged T1 time in the mid-inferior and inferolateral segments of the left ventricle – myocardial edema; (c) and (d) LGE PSIR sequence with quantification of LGE, mid-short axis view; transmural LGE (red arrow - involves 6% of the mass of the left ventricular myocardium) with central zones of reduced signal intensity (microvascular obstruction - MVO; yellow arrow) in the mid-inferior and inferolateral segments - transmural myocardial infarction with MVO zone; (e) and (f) Post-contrast T1 myocardial map, mid-short axis view; transmural shortened T1 time in the mid-inferior and inferolateral segments – transmural myocardial necrosis (transmural myocardial infarction).

of MINOCA have a smaller infarct zone, a smaller percentage of transmural extension of the changes, but also a smaller number of affected segments, which in most cases correspond to the territory of the left anterior descending artery (LAD) [37].

11.2 Myocarditis

Cardiac magnetic resonance represents the gold standard of non-invasive diagnosis of myocarditis, which is based on the existence of the so-called Lake Louise criteria or modified Lake Louise criteria that also implemented the finding of myocardial maps [38]. These criteria include the presence of signs of myocardial edema and necrosis or fibrosis, with a typical distribution for myocarditis. The most important sequences that can detect typical signs of acute myocarditis are the T2W sequence and LGE sequence, as well as parametric myocardial T2 and native T1 maps, with the presence of regional or global left ventricular dysfunction [39]. Unlike acute myocardial infarction, the typical distribution of myocardial edema/necrosis/fibrosis is subepicardial and/or mid-wall, while in a certain number of cases, it can also be transmural (**Figure 12**). A certain degree of sparing of the subendocardial layer is characteristic [40]. Also, in cases of multifocal or diffuse myocarditis, the presence

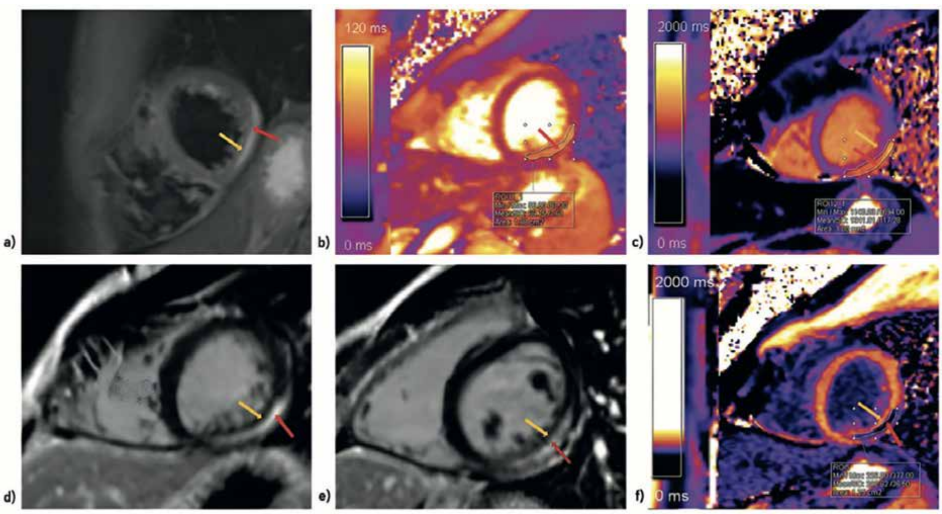

Figure 12.
Findings of acute focal myocarditis as a cause of MINOCA: (a) STIR sequence, mid-short axis view; subepicardial and mid-wall increased signal intensity of the myocardium in the mid-inferior and inferolateral segments of the left ventricle - myocardial edema (red arrow), with a preserved subendocardial layer of the myocardium (yellow arrow); (b) T2 myocardial map, mid-short axis view; transmural zone prolonged T2 time in the mid-inferior and inferolateral segments of the left ventricle - myocardial edema; (c) Native T1 myocardial map, mid-short axis view; subepicardial and mid-wall prolonged T1 time in the mid-inferior and inferolateral segments of the left ventricle - myocardial edema (red arrow), with preserved subendocardial layer of the myocardium (yellow arrow); (d) and (e) LGE PSIR sequence, mid-short axis view; subepicardial and mid-wall LGE, in the mid-inferior and inferolateral segments of the left ventricle - myocardial necrosis (red arrow), with preserved subendocardial layer of the myocardium (yellow arrow); (f) Post-contrast T1 myocardial map, mid-short axis view; subepicardial and mid-wall, shortened T1 time in the mid-inferior and inferolateral segments of the left ventricle (red arrow) - speaks in favor of myocardial necrosis, with a preserved subendocardial layer of the myocardium (yellow arrow). On the sequences shown, an acute myocardial lesion is present in the subepicardial and mid-wall layers, sparing the subendocardial layer, which excludes a lesion of a vascular origin – finding corresponds to acute focal myocarditis.

of myocardial edema/necrosis or fibrosis does not correspond to the vascularization territory of any of the coronary arteries. In a significant percentage of cases, there is pericardial involvement, as well as the existence of pericardial edema, pericardial adhesions, or pericardial effusion [41].

11.3 Takotsubo cardiomyopathy

Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy, is a type of non-ischemic cardiomyopathy based on a sudden, reversible injury to the myocardium in the absence of occlusive coronary artery disease. The pathophysiological substrate is the phenomenon of the so-called "stunned myocardium" as a reaction to a stressogenic agent. Cine sequences on cardiac magnetic resonance provide significant information about left ventricular contractility and function. A characteristic contractile dysfunction pattern is observed, which equally affects the anterior, inferior, and lateral segments and does not correspond to the territory of one of the coronary arteries. Although, in most cases, typical ballooning of the apical segments is observed, it is important to point out that about 40% of patients with Takotsubo cardiomyopathy have an atypical presentation [42]. The feature-tracking sequence, which obtains the parameters of longitudinal, circumferential, and radial strain, which is most often disturbed in the medioapical segments of the left ventricle, can be of help in assessing the segmental contractility of the myocardium, but as already stated, it does not correspond to the distribution of a certain coronary artery. Sequences for the detection of myocardial edema and necrosis/fibrosis are also of exceptional importance. Myocardial edema can be detected using a T2W sequence or T2 myocardial maps in dysfunctional segments, but without the presence of LGE with a typical distribution corresponding to a vascular lesion in the territory of one of the coronary arteries (indicating a reversible lesion) (**Figure 13**). On perfusion studies, a diffuse defect in myocardial perfusion can be observed, especially pronounced in the medioapical segments [43]. Therefore, based on the characteristic apical ballooning, the presence of myocardial edema without a clear vascular distribution, and the absence of the LGE, this type of cardiomyopathy can be diagnosed with great certainty. Timely prevention of possible complications, which include obstruction of the left ventricular outflow tract, acute heart failure, the occurrence of arrhythmias, and others, is extremely significant.

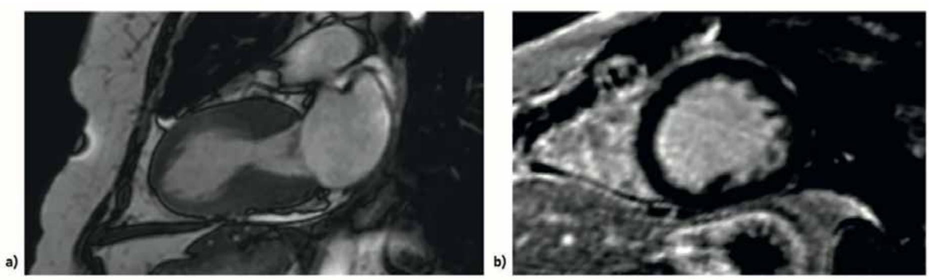

Figure 13.
The finding of Takotsubo cardiomyopathy as the cause of MINOCA: (a) Cine sequence, two chambers view; a characteristic finding of "ballooning" due to dysfunctional mid and apical segments of the left ventricle; (b) LGE PSIR sequence, apical short axis view; absence of LGE in dysfunctional segments.

In the process of examining the potential causes of MINOCA, one should take into account coronary artery embolism as part of thrombophilia, as well as coronary artery spasm, which is proven by intracoronary provocation tests.

11.4 Prognostic significance of cardiac magnetic resonance in patients with MINOCA

Patients with MINOCA have been reported to have similar prognoses and outcomes to patients presenting with single- or double-vessel coronary artery disease [44]. Four-year mortality in patients in whom cardiac magnetic resonance registers signs of acute myocardial infarction, myocarditis, or Takotsubo cardiomyopathy ranges from 1.6% to 27.3% depending on the cause, while 24% of patients have a serious adverse cardiovascular event (MACE) in the seven-year follow-up [45]. The strongest predictor of serious adverse cardiovascular events is represented by the presence of the LGE, especially if it affects more than two segments with transmural distribution [46].

Based on the results of a meta-analysis of 26 CMR studies in patients with MINOCA, 8–26% of patients had a completely normal finding, with no noted areas of edema, LGE, or perfusion defects. Therefore, the time of the examination in relation to the initial presentation, as well as the search for other potential causes, is extremely important for further treatment and prognosis [47].

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References

[1] Bulluck H, Dharmakumar R, Arai AE, Berry C, Hausenloy DJ. Cardiovascular magnetic resonance in acute ST-segment-elevation myocardial infarction: Recent advances, controversies, and future directions. Circulation. 2018;**137**(18):1949-1964

[2] Perazzolo Marra M, Lima JA, Iliceto S. MRI in acute myocardial infarction. European Heart Journal. 2011;**32**(3):284-293

[3] Emrich T, Halfmann M, Schoepf UJ, Kreitner KF. CMR for myocardial characterization in ischemic heart disease: State-of-the-art and future developments. European Radiology Experimental. 2021;**5**(1):14

[4] Bello D, Einhorn A, Kaushal R, Kenchaiah S, Raney A, Fieno D, et al. Cardiac magnetic reso- nance imaging: Infarct size is an independent predictor of mortality in patients with Coro- nary artery disease. Magnetic Resonance Imaging. 2011;**29**(1):50-56

[5] Lønborg J, Vejlstrup N, Kelbæk H, Holmvang L, Jørgensen E, Helqvist S, et al. Final infarct size measured by cardiovascular magnetic resonance in patients with ST elevation myo- cardial infarction predicts long-term clinical outcome: An observational study. European Heart Journal Cardiovascular Imaging. 2013;**14**(4):387-395

[6] Bulluck H, Rosmini S, Abdel-Gadir A, White SK, Bhuva AN, Treibel TA, et al. Residual myocardial iron following Intramyocardial Hemorrhage during the convalescent phase of Reperfused ST-segment-elevation myocardial infarction and adverse left ventricular Remodeling. Circulation. Cardiovascular Imaging. 2016;**9**(10):e004940

[7] Ghobrial M, Bawamia B, Cartlidge T, Spyridopoulos I, Kunadian V, Zaman A, et al. Microvascular obstruction in acute myocardial infarction, a potential therapeutic target. Journal of Clinical Medicine. 2023;**12**(18):5934

[8] Wu KC. CMR of microvascular obstruction and hemorrhage in myocardial infarction. Journal of Cardiovascular Magnetic Resonance. 2012;**14**(1):68

[9] Stiermaier T, Thiele H, Eitel I. Coronary microvascular obstruction: Key factor in the prognosis of ST-segment-elevation myocardial infarction. Circulation. Cardiovascular Imaging. 2017;**10**(6):e006568

[10] Mangion K, McComb C, Auger DA, Epstein FH, Berry C. Magnetic resonance imaging of myocardial strain after acute ST-segment-elevation myocardial infarction: A systematic review. Circulation. Cardiovascular Imaging. 2017;**10**(8):e006498

[11] Garg P, Saunders LC, Swift AJ, Wild JM, Plein S. Role of cardiac T1 mapping and extracellular volume in the assessment of myocardial infarction. Anatolian Journal of Cardiology. 2018;**19**(6):404-411

[12] Alkhalil M, Borlotti A, De Maria GL, Wolfrum M, Dawkins S, Fahrni G, et al. Hyper-acute cardiovascular magnetic resonance T1 mapping predicts infarct characteristics in patients with ST elevation myocardial infarction. Journal of Cardiovascular Magnetic Resonance. 2020;**22**(1):3

[13] Podlesnikar T, Pizarro G, Fernández-Jiménez R, Montero-Cabezas JM, Greif N, Sánchez-González J, et al.

Left ventricular functional recovery of infarcted and remote myocardium after ST-segment elevation myocardial infarction (METOCARD-CNIC randomized clinical trial substudy). Journal of Cardiovascular Magnetic Resonance. 2020;**22**(1):44

[14] Pezel T, des Besseyre Horts T, Schaaf M, Croisille P, Bière L, Garcia-Dorado D, et al. Predictive value of early cardiac magnetic resonance imaging functional and geometric indexes for adverse left ventricular remodelling in patients with anterior ST-segment elevation myocardial infarction: A report from the CIRCUS study. Archives of Cardiovascular Diseases. 2020;**113**(11):710-720

[15] Das A, Plein S, Dall'Armellina E. Role of CMR in prognostic stratification in myocardial infarction. Revista Española de Cardiología. 2019;**72**(2):115-119

[16] Kidambi A, Motwani M, Uddin A, Ripley DP, McDiarmid AK, Swoboda PP, et al. Myocardial extracellular volume estimation by CMR predicts functional recovery following acute MI. JACC: Cardiovascular Imaging. 2017;**10**(9):989-999

[17] Nucifora G, Muser D, Tioni C, Shah R, Selvanayagam JB. Prognostic value of myocardial deformation imaging by cardiac magnetic resonance feature-tracking in patients with a first ST-segment elevation myocardial infarction. International Journal of Cardiology. 2018;**271**:387-391

[18] Moon BF, Iyer SK, Hwuang E, Solomon MP, Hall AT, Kumar R, et al. Iron imaging in myocardial infarction reperfusion injury. Nature Communications. 2020;**11**(1):3273

[19] Carberry J, Carrick D, Haig C, Ahmed N, Mordi I, McEntegart M, et al. Persistent iron within the infarct Core after ST-segment elevation myocardial infarction: Implications for left ventricular Remodeling and health outcomes. JACC: Cardiovascular Imaging. 2018;**11**(9):1248-1256

[20] Fan ZY, Wu CW, Wesemann LD, Ouchi E, Bautista M, Qiu J, et al. Predictive value of major adverse cardiac events by T2-mapping texture analysis of the myocardial remote zone in patients with acute myocardial infarction. Clinical Radiology. 2022;**77**(3):241-249

[21] Reinstadler SJ, Stiermaier T, Liebetrau J, Fuernau G, Eitel C, de Waha S, et al. Prognostic significance of remote myocardium alterations assessed by quantitative noncontrast T1 mapping in ST-segment elevation myocardial infarction. JACC: Cardiovascular Imaging. 2018;**11**(3):411-449

[22] Reindl M, Eitel I, Reinstadler SJ. Role of cardiac magnetic resonance to improve risk prediction following acute ST-elevation myocardial infarction. Journal of Clinical Medicine. 2020;**9**(4):1041

[23] Marcos-Garcés V, Perez N, Gavara J, Lopez-Lereu MP, Monmeneu JV, Rios-Navarro C, et al. Cardiac magnetic resonance outperforms echocardiography to predict subsequent implantable cardioverter defibrillator therapies in ST-segment elevation myocardial infarction patients. Frontiers in Cardiovascular Medicine. 2023;**10**:991307

[24] Flavian A, Carta F, Thuny F, Bernard M, Kober F, Moulin G, et al. Cardiac MRI in the diagnosis of complications of myocardial infarction. Diagnostic and Interventional Imaging. 2012;**93**(7-8):578-585

[25] Florian A, Jurcut R, Ginghina C, Bogaert J. Cardiac magnetic resonance

imaging in ischemic heart disease: A clinical review. Journal of Medicine and Life. 2011;**4**(4):330-345

[26] Alhassan DA, Waheed KB, Sharif MN, Ul Hassan MZ, Ghaffar F, Salem KS, et al. Detection of left ventricular thrombi on cardiac magnetic resonance viability studies. Journal of the Saudi Heart Association. 2020;**32**(3):368-376

[27] Chaosuwannakit N, Makarawate P. Left ventricular thrombi: Insights from cardiac magnetic resonance imaging. Tomography. 2021;**7**(2):180-188

[28] Camaj A, Fuster V, Giustino G, Bienstock SW, Sternheim D, Mehran R, et al. Left ventricular thrombus following acute myocardial infarction: JACC state-of-the-art review. Journal of the American College of Cardiology. 2022;**79**(10):1010-1022

[29] Caspar T, El Ghannudi S, Ohana M, Labani A, Lawson A, Ohlmann P, et al. Magnetic resonance evaluation of cardiac thrombi and masses by T1 and T2 mapping: An observational study. The International Journal of Cardiovascular Imaging. 2017;**33**(4):551-559

[30] Massalha E, Brodov Y, Oren D, Fardman A, Natanzon SS, Mazin I, et al. Pericardial involvement in ST-segment elevation myocardial infarction as detected by cardiac MRI. Frontiers in Cardiovascular Medicine. 2022;**9**:752626

[31] Agewall S, Beltrame JF, Reynolds HR, et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. European Heart Journal. 2017;**38**:143-153

[32] Abdu FA, Mohammed AQ, Liu L, Xu Y, Che W. Myocardial infarction with nonobstructive coronary arteries (MINOCA): A review of the current position. Cardiology. 2020;**145**(9):543-552

[33] Singh T, Chapman AR, Dweck MR, Mills NL, Newby DE. MINOCA: A heterogenous group of conditions associated with myocardial damage. Heart. 2021;**107**(18):1458-1464

[34] Daneshrad JA, Ordovas K, Sierra-Galan LM, Hays AG, Mamas MA, Bucciarelli-Ducci C, et al. Role of cardiac magnetic resonance imaging in the evaluation of MINOCA. Journal of Clinical Medicine. 2023;**12**(5):2017

[35] Liang K, Nakou E, Del Buono MG, Montone RA, D'Amario D, Bucciarelli-Ducci C. The role of cardiac magnetic resonance in myocardial infarction and non-obstructive coronary arteries. Frontiers in Cardiovascular Medicine. 2022;**8**:821067

[36] Gatti M, Carisio A, D'Angelo T, Darvizeh F, Dell'Aversana S, Tore D, et al. Cardiovascular magnetic resonance in myocardial infarction with non-obstructive coronary arteries patients: A review. World Journal of Cardiology. 2020;**12**(6):248-261

[37] Mileva N, Paolisso P, Gallinoro E, Fabbricatore D, Munhoz D, Bergamaschi L, et al. Diagnostic and prognostic role of cardiac magnetic resonance in MINOCA: Systematic review and meta-analysis. JACC: Cardiovascular Imaging. 2023;**16**(3):376-389

[38] Puntmann VO, Zeiher AM, Nagel E. T1 and T2 mapping in myocarditis: Seeing beyond the horizon of Lake Louise criteria and histopathology. Expert Review of Cardiovascular Therapy. 2018;**16**(5):319-330

[39] Pasupathy S, Beltrame JF. Refining the role of CMR imaging in MINOCA.

JACC: Cardiovascular Imaging. 2021;**14**(9):1784-1786

[40] Heidecker B, Ruedi G, Baltensperger N, Gresser E, Kottwitz J, Berg J, et al. Systematic use of cardiac magnetic resonance imaging in MINOCA led to a five-fold increase in the detection rate of myocarditis: A retrospective study. Swiss Medical Weekly. 2019;**149**:w20098

[41] Tornvall P, Gerbaud E, Behaghel A, Chopard R, Collste O, Laraudogoitia E, et al. Myocarditis or "true" infarction by cardiac magnetic resonance in patients with a clinical diagnosis of myocardial infarction without obstructive coronary disease: A meta-analysis of individual patient data. Atherosclerosis. 2015;**241**(1):87-91

[42] Bratis K. Cardiac magnetic resonance in Takotsubo syndrome. European Cardiology. 2017;**12**(1):58-62

[43] Ojha V, Khurana R, Ganga KP, Kumar S. Advanced cardiac magnetic resonance imaging in takotsubo cardiomyopathy. The British Journal of Radiology. 2020;**93**(1115):20200514

[44] Lu X, Zhu S, Lu Y, Li Y. Long term all-cause mortality after myocardial infarction with non-obstructed vs obstructed coronary artery disease: A meta-analysis of adjusted data. BMC Cardiovascular Disorders. 2024;**24**(1):9

[45] Pasupathy S, Air T, Dreyer RP, Tavella R, Beltrame JF. Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries. Circulation. 2015;**131**(10):861-870

[46] Bucciarelli V, Bianco F, Francesco AD, Vitulli P, Biasi A, Primavera M, et al. Characteristics and prognosis of a contemporary cohort with myocardial infarction with non-obstructed coronary arteries (MINOCA) presenting different patterns of late gadolinium enhancements in cardiac magnetic resonance imaging. Journal of Clinical Medicine. 2023;**12**(6):2266

[47] Collste O, Sörensson P, Frick M, Agewall S, Daniel M, Henareh L, et al. Myocardial infarction with normal coronary arteries is common and associated with normal findings on cardiovascular magnetic resonance imaging: Results from the Stockholm myocardial infarction with Normal coronaries study. Journal of Internal Medicine. 2013;**273**:189-196

Chapter 4

Understanding Acute Coronary Syndrome from the Perspective of Traditional Chinese Medicine

Xinjue Shan and Yuanhui Hu

Abstract

This chapter delves into the understanding of acute coronary syndrome (ACS) from the perspective of traditional Chinese medicine (TCM). It starts with the different thinking frameworks of Chinese and Western medicine and emphasizes the holistic concepts of "balance," "harmony," and "regulation" in TCM. This chapter explores the multiple causes of ACS, including internal and external factors such as dysfunction of the internal organs, wrong emotions, and disharmony of daily life. The four diagnostic methods of TCM provide a comprehensive assessment that goes beyond symptoms and captures underlying imbalances and pathogenic factors. The principles of treatment in TCM prioritize maintaining the balance of Yin and Yang. It focuses on restoring balance and enhancing the body's ability to heal itself through health cultivation, such as regular diet, daily life, emotions, and exercise. This chapter acknowledges the limitations of TCM in emergency situations and argues for a holistic, individualized approach to managing ACS by combining TCM with Western medicine. This fusion of modern science and TCM holds great promise for creating a more holistic and effective healthcare system in the future. It also makes people think on a scientific level about the shift in thinking behind it.

Keywords: traditional Chinese medicine (TCM), acute coronary syndrome (ACS), Yin-Yang theory, holism, modern science

1. Introduction

Nowadays, there is a "traditional Chinese medicine (TCM) fever" in the world. Many doctors from Western countries have come to China from far and wide to study TCM seriously. As a matter of fact, not only TCM, but also many ancient medical systems, such as Ayurveda in India, traditional herbalism in Germany, and traditional therapies in England, are experiencing a revival movement. Obviously, this is a competition and a challenge to the traditional Western medical market, as well as a challenge to modern science.

In today's era of rapidly changing medical technology, many patients have had the experience of going to the hospital due to various discomforts, undergoing a series of comprehensive examinations with advanced instruments, only to be told that "everything is normal, you are very healthy." This seemingly reassuring conclusion often leaves patients feeling confused and helpless, as if their suffering has been ignored. In such cases, patients naturally seek other possible solutions, and traditional therapies such as acupuncture and massage, herbal medicine, Qigong, homeopathy, and so on, have been "resurrected." These once-marginalized ancient medicines are gradually gaining a foothold in the Western medical market under the banner of "alternative medicine" or "complementary medicine." Data show that the use of alternative medicine has been growing at a considerable rate [1, 2]. More and more patients are turning to TCM in search of a more holistic and natural approach to health.

With the development of society and the improvement of living standards, the health problems faced by people have also changed. The threat of acute infectious diseases and traumatic accidents has gradually decreased, while chronic diseases, functional disorders, and sub-health states have become new challenges. Modern Western medicine has significant advantages in the treatment of acute diseases, but it does have some shortcomings in dealing with the chronic phase and functional disorders.

Taking acute coronary syndrome (ACS) as an example, acute attacks of ACS are more urgent and dangerous, requiring immediate treatment, while chronic symptoms and functional disorders require long-term management and a high degree of patient cooperation. Both have their own challenges in terms of the difficulty of treatment, but the urgency and potential mortality of an acute episode make it somewhat less treatable. However, the aim of medical treatment should be to avoid this as much as possible, which requires long-term management of chronic symptoms and dysfunction, with a high-level of attention and sustained effort from both the patient and the healthcare team. Therefore, holism, treatment based on disease differentiation, and treating pre-disease concepts advocated by ancient medicine, such as TCM, are gradually gaining importance.

It is worth noting that many ancient medicines are "holistic." The most typical of these is TCM. The gradual popularity of TCM is not only due to its effectiveness in the treatment of certain diseases but also because of the concepts of health care and attitude toward life that it advocates. The theory of TCM, it is full of the ideas of "balance of Yin and Yang," "harmony," "harmony between man and nature," "treatment based on disease differentiation," and other integrated concepts. It emphasizes the harmonious coexistence of man and nature and focuses on prevention as the mainstay and treatment as a supplement, which coincides with modern people's pursuit of quality of life. Therefore, the revival and popularity of TCM is not only an inevitable trend of medical development but also an embodiment of social progress and a change in people's health concepts.

This trend is also a challenge and a revelation to modern science. Modern science emphasizes empirical evidence, analysis, and reduction, while ancient medicine such as TCM focuses more on experience, synthesis, and wholeness. There are significant differences in methodology between the two, but both are committed to the improvement of human health. This challenge has prompted modern science to begin reflecting on its limitations and to seek dialog and integration with ancient medicine. Further, the revival of ancient medicine also reflects the respect and preservation of global cultural diversity. Each system of medicine is an important part of its national culture and carries unique wisdom and experience. In the context of globalization, the exchange and mutual learning of these medical systems not only help to enrich global medical resources but also help to promote understanding and respect among different cultures.

To summarize, the global "TCM fever" and the revival of ancient medicine is not only a competition and challenge in the medical market but also a revelation and impetus to modern science. It prompts us to re-examine the nature and purpose of medicine and explore a more comprehensive, effective, and humanized medical model.

2. Different ways of thinking in Chinese and Western medicine

In the wave of "TCM fever," there is naturally a lot of modern scientific research on TCM within the scientific circles, which is basic researches. On the surface, it seems that the purpose of "modern scientific research on TCM" is to require the understanding and knowledge of the mechanism of TCM, including herbs, acupuncture, and Qigong, from the perspective of modern science. In fact, this is a process of collision, conflict, exchange, and integration of two cultures. Modern science originated in the West and is based on the Western way of thinking. Therefore, in a deeper sense, the proposition of the so-called "modern scientific research" is to try to understand the ancient medicine, with its strong oriental mystical color from the Western culture and ways of thinking. So, what is the difference between Eastern and Western cultures? There are so many, even in the field of medicine alone, that many books could not be written on the subject.

2.1 Tai Chi and Nehushtan

In order to understand the difference between Chinese and Western medicine, we can start with two symbols that are commonly used in medicine (**Figures 1** and **2**). **Figure 1** is the Tai Chi diagram, a symbol of TCM thought, which is used to express the balance and interaction between "Yin" and "Yang." **Figure 2** is Nehushtan, a "copper snake," a symbol of Western medicine, derived from the *Bible*. It can be seen in front of many pharmacies in Europe and the United States.

From these two different medical symbols, we can easily see the difference in their structure and meaning. Understanding the Tai Chi diagram from the perspective of TCM, can be regarded as a figurative expression of the Yin-Yang theory.

1. Yin and Yang depending on each other: The Tai Chi diagram consists of two "fish," Yin and Yang, with the Yin fish and the Yang fish encircling each other,

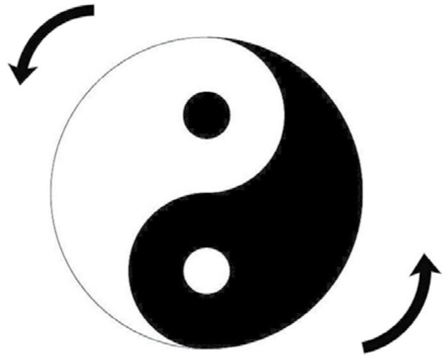

Figure 1.
Tai Chi, symbol of TCM.

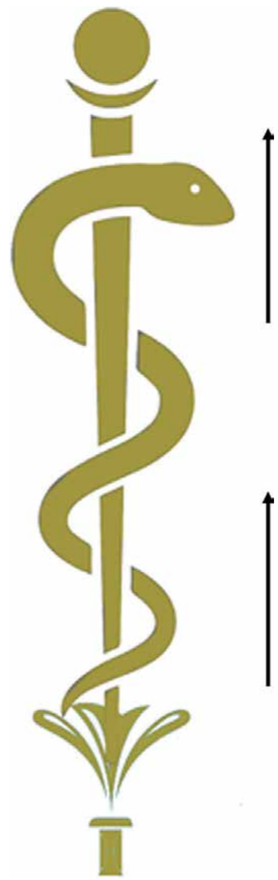

Figure 2.
Nehushtan, a symbol of Western medicine.

which embodies the relationship of Yin and Yang as interdependent and inseparable. In TCM theory, Yin and Yang are the basic elements of the human body and the natural world, which depend on each other and work together to maintain life activities.

2. Mutual conversion between Yin and Yang: The Yin and Yang fish in the Tai Chi diagram are connected at the head and tail, forming a dynamic cycle, which embodies the characteristics of the mutual transformation of Yin and Yang. In TCM theory, Yin and Yang are not static but are transformed into each other with the changes of time and environment, such as the alternation of day and night, and the change of seasons, etc.

3. Dynamic balance of Yin and Yang: Tai Chi as a whole presents a balanced and harmonious state, reflecting the idea of the dynamic balance of Yin and Yang. In TCM theory, health is the state of balance between Yin and Yang, while disease is the manifestation of imbalance between Yin and Yang. The purpose of TCM treatment is to adjust Yin and Yang and restore the balance.

4. Yin and Yang being rooted mutually: Yin and Yang are used and rooted for each other. Yang depends on Yin for its existence, and Yin also depends on Yang for its existence.

5. Wan and wax of Yin and Yang: The Tai Chi diagram is constantly rotating. As the Yang (white) grows, the Yin (black) seed arises in the center of the Yang. Then, the Yin grows again, and then, in the center of the Yin, the seed of the Yang appears again. And so on, and so on. In the theory of TCM, Yin and Yang are not fixed but wax and wane with the changes of time and environment. For example, the body's Yang Qi is relatively strong during the day and relatively weak at night.

However, in the medical thought symbolized by the Nehushtan, there is no idea of balance, compromise or Doctrine of the Mean. On the contrary, in this symbol, we can see an image of death and survival. Therefore, some people call modern Western medicine "allopathic medicine" or "conquering medicine." Obviously, this is totally different from the Yin-Yang thoughts of TCM. From the structural point of view, the Nehushtan is a linear structure with a head and a tail, while the Tai Chi diagram is a non-linear structure without a head or a tail.

By the way, ancient German medicine is called "homeopathic medicine," which means opposite or even opposite to "allopathic medicine." After World War II, "homeopathic medicine" was once banned in Germany, and it was not until the 1970s that the ban was lifted. Now, like "TCM fever," "homeopathic medicine" has become a very popular medicine in Europe, America, and India.

2.2 Five elements

We can also see the difference in the thinking structure between the East and the West from the Chinese "five elements" and the Greek "five elements" (**Figures 3** and **4**).

Obviously, the ancient Greek "Five Elements" is a linear structure with a beginning and an end (**Figure 3**), while the ancient Chinese "theory of five-element" (**Figure 4**) is a non-linear structure without a beginning or an end. In ancient Greek, there is only "earth generating water, water generating air, air generating fire, fire generating ether." There is no cycle and is a "linear relationship" in modern mathematical terms. In the ancient Chinese "theory of five-element," there is "earth (spleen) generating metal (lung), metal generating water (kidney), water generating wood (liver), wood generating fire (heart), fire generating earth" of the generating relationship. It is a cyclic relationship and a kind of "non-linear relationship" in mathematical terms. At the same time, there is "earth restraining water, water restraining fire, fire restraining metal, metal restraining wood, wood restraining earth" of the restraining relationship. There is another non-linear cyclic relation. When modern science develops from "linear" to "non-linear," the difference between these two structures becomes more meaningful, and can even be regarded as the conversion of one culture to another.

2.3 Reductionism and holism

Modern Western medicine, modern biology, physiology, psychology, etc. are basically based on a "reductionism" way of thinking. It can be understood as breaking down a system into smaller and smaller parts, so as to find out which one of the parts

Figure 3.
The five elements in Greek.

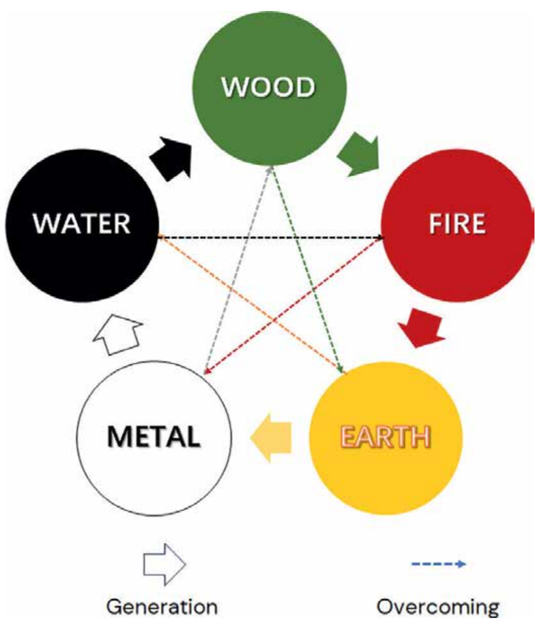

Figure 4.
The five elements in TCM.

is wrong, and then solve the problem in a clear way. We should first recognize that this "reductionism" way of thinking has been extremely successful in many medical studies. Suppose a patient is admitted to the hospital with sudden onset chest pain for 3 hours. Electrocardiogram showed ST-segment elevation, diagnosed as ST-segment elevation myocardial infarction (STEMI). Treatment measures: immediately intervene to target the mechanism of action of each component of blood clots and platelets in the blood vessel, give thrombolytic drugs (such as urokinase) with antiplatelet drugs (aspirin and clopidogrel) and anticoagulant therapy, and so on. As a result, the patient's chest pain was relieved, ST-segment regression, and cardiac enzymes decreased. Successful reperfusion prevented massive myocardial infarction.

In fact, almost the entire success of modern Western medicine has been based on a mindset of successful "divide," "fight" and "conquer." This is why modern Western medicine is also known as "allopathic medicine." Nowadays, this "divide," "fight" and "conquer" way of thinking is still used quite successfully in the study of hereditary diseases and genes, because they are still black or white, and the enemy is clearly distinguishable from us.

It is not as if there are no such thoughts in TCM. For example, when the evil Qi of ACS patients, such as blood stasis, turbid phlegm, are exuberance, and the patient's physique is strong or the illness is serious, expelling stasis by aggressive purgation, clearing away phlegm to open vital orifices will be used to address the evil Qi. However, this is not a core idea throughout. The key is to emphasize how to balance, harmonize, and condition the body in order to drive out evil Qi (pathological factors) and prevent recurrence by restoring one's balance, rather than mere removal and conquer. The concepts of "balance," "harmony," "regulation," and so on run through the whole theory of TCM.

The success of ACS therapy lies in its ability to target specific types of myocardial infarction quickly and effectively; however, their limitations are also apparent, mainly in terms of limited therapeutic options, large individual differences, neglect of the patient's overall condition, and a high risk of recurrence. Therefore, modern treatments are gradually shifting toward a "holistic" approach in order to manage the patient's condition in a more comprehensive manner and to improve treatment outcomes and quality of life.

A recent study pointed out that it is more appropriate to classify myocardial infarction into occlusive myocardial infarction and non-occlusive myocardial infarction, rather than STEMI and non-STEMI, which reflects the shift from detailed classification to holistic consideration [3, 4]. Several studies have also demonstrated the efficacy of combining Chinese and Western medicine in the treatment of ACS, which supported the application of holistic thinking in the treatment of complex diseases [5, 6]. The treatment of ACS is also undergoing a shift from "reductionism" to "holism," which can help to manage the patient's condition in a more comprehensive way and improve the therapeutic efficacy.

From the above discussion, we can see that the Eastern and Western modes of thinking are different. There are the concepts of "separating" and "divide" in order to simplify the problem so that science can develop step by step from simple to complex. And the development of science to today, the simple issues are more or less. Slowly, the human body is being studied as a whole system. Instead of focusing only on the regulation of one organ or signaling pathway, more attention is being paid to the interactions between organs, tissues, and signaling pathways. How to make the human body as a whole maintain coordination and harmony, is the beginning of the face of the complexity of the problem, but also the beginning of using "holistic" thinking. In fact, this is the reason for the emergence of "TCM fever." In today's globalization, can we integrate the advantages of the Eastern and Western modes of thinking, so as to find a new path in the medical field? This is an important question in science today.

3. Understanding of causes of ACS

In fact, in both the East and the West there has always been the idea of "holism" in medicine. TCM, which is fully consistent with the philosophical thinking of the *I Ching*, has developed this integrated concept into a complete and self-consistent theoretical system. In terms of understanding of etiology, it is believed that there are two main causes of disease in TCM: internal and external disorders, and disturbance of seven emotions (wrong emotions). That is to say, the "disharmony" between the internal and external worlds and the "disharmony" of the internal world.

3.1 "Disharmony" of the internal world

From the perspective of TCM, the human body is regarded as an organic whole, and the internal organs are interconnected and interact with each other. Dysfunctions of the heart, liver, spleen, kidney, and other internal organs, such as syndrome of liver depression and Qi stagnation, spleen deficiency with the damp encumbrance, failure of kidney Yang, etc., not only affect the normal function of their respective internal organs but also through the meridians and collaterals, Qi and blood affecting the normal functioning of the heart, thus increasing the risk of cardiovascular diseases. Therefore, not only should we pay attention to the pathology of the heart itself, but also consider the impact of dysfunction of the liver, spleen, lung, and kidneys on the heart from a holistic point of view. The pathological factors of ACS can be analyzed from the following aspects:

1. Qi stagnation and blood stasis: In the theory of TCM, the heart is the master of the blood vessels, and Qi stagnation and blood stasis is an important pathogenesis of cardiovascular diseases. Any factor that leads to poor circulation of Qi and blood will result in blood stasis and blockage of the heart veins. Thrombosis in modern medicine has similarities with blood stasis in TCM and it can be seen as a manifestation of Qi stagnation and blood stasis at the microscopic level [7, 8].

2. Internal blocking of turbid phlegm: Poor diet and damage to the spleen and stomach can lead to internal generation of turbid phlegm. Turbid phlegm upturns to the heart and chest, blocking the vascular of the heart, which is also one of the important pathologies of ACS. Phlegm internalization can be understood as the process of plaque formation, while plaque rupture can be seen as a manifestation of turbid phlegm uploading into the heart and chest [9].

3. Deficiency of healthy Qi: Deficiency of healthy Qi, including deficiency of Qi, blood, Yin, and Yang. It leads to a decline in the body's resistance and makes it susceptible to external evils, thus inducing ACS. For example, the syndrome of kidney Yang deficiency leads to a deficiency of heart Yang, the heart failing to

be warmed and poor blood circulation, which can easily lead to the formation of blood stasis. At the same time, Yang deficiency cannot transform water, which may lead to the internalization of turbid phlegm, further aggravating the obstruction of the vessel of the heart. Endothelial dysfunction in modern medicine and deficiency of healthy Qi in TCM both involve the body's defense and repair capabilities [10].

4. Affected by six excesses: Wind, cold, summer-heat, dampness, dryness, fire and other external influences attack the body, especially cold, which can directly attack the vessel of the heart, resulting in a contracture of the vessel and trigger ACS. Although these are six external evil Qi, in TCM theory, these cannot cause disease alone and there must be a foundation of deficiency of healthy Qi to cause disease. So, they are listed here. Inflammatory reactions in modern medicine and six excesses in TCM can affect the normal function of the heart [11].

These intrinsic pathologic factors interact with each other and work together to promote the development and progression of ACS. Understanding these factors can help to better prevent and treat ACS.

3.2 "Disharmony" between the internal and external worlds

The holistic concept of TCM not only embodies the belief that the human body is a whole but also emphasizes the "harmony between man and nature." The occurrence of human diseases is closely related to the external environment. Therefore, when considering the risk of ACS, we should not only focus on the patients themselves but also take into account the patient's physiques, emotions, diet, lifestyle, social environment and other factors.

3.2.1 Disharmony of emotions

In the theory of TCM, it has been always believed that emotions are a very critical factor in causing disease. The heart stores spirit and serves as the organ like a monarch. Excessive "seven emotions" (joy, anger, anxiety, thinking, sorrow, fear, fright) can lead to dysfunction of internal organs, especially, the heart, emotional changes first affect the heart. Prolonged mental tension, excessive stress, or emotional fluctuations can lead to the mental spirit floating astray, and the heart losses its nutrition, thus increasing the symptoms such as palpitations and chest pain. Emotions such as anger, worry and contemplation can easily affect the function of the liver and spleen, which in turn leads to Qi stagnation and blood stasis, and heart vessel obstruction. And to a certain extent, the emotions are not only affected by external influences but also have a certain relationship with the physique, for example, some patients are prone to feel anxious and angry.

With the development of "psychosomatic medicine," Western medicine has become more and more aware of the importance of "emotions" and "disharmony" in medicine. An individual's psychological state and mood management play an important role in the pathogenesis of ACS. Emotional stress can act as a pathogenic trigger. Stress can lead to elevated levels of hormones such as adrenaline and cortisol, which can promote the progression of atherosclerosis [12]. Depression and anxiety can affect prognosis and treatment adherence [13]. Therefore, for patients with ACS, in addition to traditional pharmacologic and interventional treatments, emotional management and psychological support are also crucial to help improve treatment outcomes and patients' quality of life. Besides, many bad emotions come from social and family disharmony. Therefore, the social environment is also closely related to morbidity. "Disharmony" between the internal and external worlds is a more fundamental source of disease. It also reflects the philosophical idea of "holism."

3.2.2 Disharmony of daily life

The individual's daily routine and external factors, such as diet and living also play a crucial role, especially in the theory of TCM health care. (1) Irregularity in daily life: Irregular work and rest, such as staying up late, insomnia, can lead to an imbalance of Yin and Yang, consuming and damage Qi and blood, which contributes to the heart failing to be nourished. (2) Overstrain and idleness: Overstrain and idleness can lead to poor circulation of the Qi and blood, heart vessel are blocked. Especially overwork, easy to overconsumption of heart nutrient, increase the risk of cardiovascular disease. (3) Dietary intemperance: Overeating or preference for flavors, such as preference for sweet and fatty food, can lead to phlegm and dampness, blocking the heart vessel. At the same time, the spleen and stomach serve as the organ in charge of the granary. Dietary intemperance can also affect the function of the spleen and stomach, which may lead to nutritional imbalance, affecting the function of other organs.

From the point of view of modern medicine, although ACS has a clear pathological basis, that is, rupture or erosion of atherosclerotic plaques in the coronary arteries, leading to thrombosis and coronary artery blockage, ACS does not occur in every individual under the same pathological basis. This is because, in addition to the pathological changes in the coronary arteries, the individual's overall health status and lifestyle also play an important role. Unhealthy lifestyles, such as high-fat diets, physical inactivity, smoking, and excessive alcohol consumption, increase the risk of coronary atherosclerosis, thereby increasing the likelihood of ACS. Conversely, healthy lifestyles, such as a balanced diet, moderate exercise, and smoking cessation, reduce this risk. Second, an individual's cardiovascular health is an important factor in the development of ACS. This includes the degree of stenosis in the coronary arteries, the stability of the plaque, and the presence of other cardiovascular diseases such as hypertension and diabetes. Together, these factors determine an individual's risk for ACS.

Thus, the causes of ACS are not only the pathological changes in the coronary arteries, but also the individual's overall health, lifestyle, and psychological state. Collectively, these elements influence a person's likelihood of acquiring ACS. Therefore, the prevention and treatment of ACS require a comprehensive intervention that takes these factors into account. Through such a holistic analysis, we can gain a more comprehensive understanding of the causes of ACS, thus providing a more comprehensive strategy for prevention and treatment.

4. Understanding of symptoms of ACS

In today's rapidly changing medical technology, many patients may have had the experience of going to the hospital because of chest tightness, chest pain, and other discomforts. Doctors use a variety of advanced instruments, such as electrocardiograms, coronary angiograms, etc., to conduct a comprehensive and detailed examination, and eventually present a large number of laboratory reports. However, sometimes after scrutinizing these reports, the doctors may say with a smile, "All the indicators are within the normal range, you are not in any serious trouble, you can go home without worry." Such a conclusion is inevitably confusing and even a bit helpless for patients who are experiencing significant discomfort, as if their symptoms are being ignored. Put yourself in the patient's shoes and you may be wondering: am I really okay? And where did my symptoms come from?

Of course, this is usually only present in the early stages of the disease. ACS can have some atypical symptoms in the early stages of the disease. Some patients, especially the elderly, women, and diabetics, may present with atypical symptoms such as nausea, vomiting, and abdominal or back pain rather than typical chest pain. These atypical symptoms may lead to misdiagnosis of other conditions, such as gastrointestinal disorders. In the early stages of the disease, electrocardiograph may not yet show significant changes or the changes may be mild and easily overlooked or misdiagnosed. Elevation of cardiac enzymes usually becomes apparent only a few hours after the onset of the disease, and may not be elevated at an early stage, making diagnosis difficult. Therefore, the reasons why ACS is easy to be misdiagnosed by Western medicine in the early stage of the disease are manifold.

From the perspective of TCM, it is not only need to focus on visual manifestations such as chest pain and chest tightness but also emphasize the dysfunction of the internal organs and disharmony of Yin and Yang behind these symptoms. For example, chest pain may be recognized as "static blocking of heart blood," and shortness of breath may be related to "insufficiency of heart Qi." For these hidden symptoms, TCM doctors use a comprehensive analysis of four diagnostic methods to determine the patient's overall condition.

1. Inspection: TCM practitioners will carefully observe the patients from the outside, including inspection tongue, vitality, complexion, vitality and behavior, and discharge. For example, a pale or dark face may indicate a deficiency of Qi and blood or internal obstruction of blood stasis. A dark tongue with petechiae or thick and greasy tongue coating may indicate phlegm and stasis.

2. Listening and smelling: This examination includes listening to sounds and smelling the odors. A weak voice may indicate a deficiency of Qi. Shortness of breath or accompanied by rales may indicate phlegm obstruction of the airway.

3. Inquiry: The contents included in the inquiry examination are very abundant, and a Ten-inquiry Poem was circulated in ancient times, which mainly includes asking about cold and heat, sweating, head and body, defecation and urination, diet and taste, sleep, previous diseases, and the onset of disease. TCM practitioners will ask patients in detail about their symptoms, medical history, and lifestyle habits. For example, the nature, duration, and triggering factors of chest pain, and whether there are other accompanying symptoms such as palpitations, insomnia, and night sweats.

4. Palpation: This examination means taking the pulse. There are 28 types of pulses summarized in TCM. The following are common in ACS. A string-like and tight pulse means that the pulse beats with both strength and tension as if the strings of a zither were being pulled tightly. This type of pulse is usually associated with liver depression and stagnation of Qi, implying emotional upset. A sunken and unsmooth pulse, that is, the pulse beats deeply and not smoothly, as if the blood

encounters obstruction as it flows through the vessel. This type of pulse is usually associated with blood stasis and internal obstruction, implying that there is stagnant blood and poor circulation in the body.

Combined with the knowledge of Western medicine, we know that ACS is usually associated with pathophysiological processes such as coronary atherosclerosis, plaque rupture, and thrombosis. In TCM theory, these pathological changes may be related to internal factors such as "phlegm" and "blood stasis." Pathologic factors such as blood stasis and Qi deficiency quietly form the basis for the development of ACS, which puts patients in a susceptible state. They are like hidden undercurrents that begin to surge at a level not yet touched by Western diagnostic criteria. These TCM pathological factors do not always wait until Western medicine's instruments and laboratory reports sound the alarm, but leave their traces as early as the first signs of the disease. It is for this reason that Chinese medicine demonstrates a unique advantage in the prevention and treatment of ACS: through four diagnostic methods, it is able to capture the traces of these pathological factors at an early stage, and then take targeted measures to prevent the development of the disease, realizing the goal of preventing disease before it occurs, and preventing changes in the event of an existing disease.

The forward-looking concept of prevention and treatment makes TCM play an irreplaceable role in caring for health. As *The Yellow Emperor's Inner Classic* says: Therefore, the sage does not wait until a disease has occurred to treat it, but treats it before it occurs, just as he does not wait until a disorder has occurred to govern it, but governs it before it occurs. If a disease has already occurred and then is treated, and a disorder has already formed and then is governed, it would be like digging a well when one is thirsty, and making weapons when war has occurred. It would all be too late. This paragraph emphasizes the importance of preventing disease, that is, intervening before it occurs and taking precautions. This idea not only applies to medicine but also extends to daily life, reminding people to against a rainy day and to take precautions.

5. Understanding of treatment of ACS

Looking back at the entire history of human medicine, which is full of explorations and challenges, human beings have always been confronted with the threat of diseases, the limitations of treatment means, and the lack of health resources. Therefore, for a long time, the pursuit of effective treatment, prolonged life, and alleviation of disease pain and suffering, or the so-called improvement of medical standards, has become the main goal pursued by the medical profession. With the rapid development of biotechnology and medicine, many countries have made remarkable progress in the medical field. In these countries, "improving the standard of medical care" is no longer the only mission, and perhaps the integration of the advantages of different medical systems to improve the effectiveness of treatment and the quality of life of patients has become a new challenge.

5.1 Principles of treatment

Man is the most intelligent life form in the world, not a "dead man," not a "machine." Therefore, human beings are always moving and changing. In fact, from the point of view of health care, it is also necessary to be able to "move" and "static," which is the real "harmony." More specifically, driving, going to work, study is to be able to tension, to be able concentrate, which is a kind of ability. After work, rest and sleep, is to be able to fully relax, which is a kind of opposite ability. You can not have one without the other. The former is an "ordered state"; the latter is a "disordered state." That is to say, true harmony is to keep swinging back and forth between "order" and "disorder." That is, the balance of Yin and Yang is emphasized in TCM. The core treatment principle of TCM is to restore the balance of Yin and Yang in the human body.

5.1.1 Emphasizing the self-healing ability: Health cultivation

The human body system is not only "alive," but also has a strong self-healing ability. TCM emphasizes that there is a self-regulating system within the human body that can automatically regulate the imbalance of Yin and Yang and restore it to a harmonious state. This ability, in TCM theory, is graphically referred to as "healthy Qi" or "self-healing ability." As long as there is sufficient healthy Qi in the body, external evils (like the six excesses mentioned earlier) will not be able to easily invade the body. Healthy Qi is like a natural barrier for the human body, protecting us from diseases. However, if the disease is too intense or the healthy Qi is too weak, it can also lead to illness.

Therefore, TCM advocates "treating pre-disease." By intervening in advance, we can strengthen the healthy Qi and prevent the occurrence of diseases. Early intervention can detect potential problems in the body in a timely manner, blocking the development of diseases and preventing minor illnesses from becoming major ones. Early intervention can also effectively reduce the incidence of disease, thereby saving medical resources and reducing the economic burden on society and individuals.

The concept of treating the future, highlights the need for health cultivation. Health cultivation is the enhancement of the body's healthy Qi and self-repairing ability through various methods (such as light food, regular daily life, regular emotions and exercise, etc.). It also emphasizes conformity to the laws of nature, and coordination with the natural rhythms such as the change of seasons and the alternation of day and night, so as to maintain the health of the body. The man and nature are one.

Health cultivation is a long-term way of life. Through continuous practice of health cultivation, the body's self-repairing ability can be continuously enhanced to achieve a long and healthy life. In the modern fast-paced, high-stress living environment, people's bodies are often susceptible to imbalances caused by the interference of various factors. Individuals with ACS need to be particularly vigilant about managing their lifestyle and emotional well-being. Engaging in stress-reducing activities, maintaining a balanced diet, exercising regularly and adhering to medical advice are all essential components of a comprehensive approach to managing ACS and preventing its recurrence. As a matter of fact, this is one of the major reasons why Qigong has become so popular in recent years in both the East and the West. Therefore, it is all the more necessary to pay attention to early intervention and health cultivation in order to maintain and enhance the body's self-healing ability.

5.1.2 Deficiencies of TCM in the treatment of ACS

Despite the unique advantages of TCM, the TCM approach does have some shortcomings in the treatment of ACS. First, the efficiency of first aid is limited. TCM treatments such as herbal decoctions and acupuncture usually take a certain amount of time to work, and during an acute attack of ACS, patients need rapid and effective first aid to open the occluded coronary arteries and restore blood flow to the myocardium. In contrast, thrombolytic therapy and interventional procedures in Western medicine can achieve this goal more quickly. Western medicine's nitrates and antiplatelet drugs have obvious advantages in this regard.

Secondly, diagnostic means are insufficient. For diseases such as ACS, which require precise judgment of the degree of coronary artery lesions, the diagnostic means of TCM appear to be insufficiently precise and objective. Modern medical tests such as electrocardiogram and coronary angiography can diagnose ACS more directly and accurately.

Finally, the problems of standardization of TCM have not been solved so far. TCM treatment is highly individualized and lacks uniform standards and norms. In an emergency situation such as an acute attack of ACS, what is needed is a standardized and regulated treatment plan to ensure the therapeutic effect and patient safety. Compared with Western medicine, TCM is relatively under-supported by modern scientific research and lacks large-sample, randomized controlled clinical trials to verify its efficacy and safety.

Therefore, in the treatment of acute attacks of ACS, it is usually recommended to use Western medicine as the primary emergency treatment and Chinese medicine as the secondary treatment, taking advantage of their respective strengths and working together to maintain the health of patients.

5.2 TCM for ACS: A comprehensive strategy integrating health cultivation, treating pre-disease and integration of Chinese and Western medicine

5.2.1 Approaches of health cultivation: Laying the cornerstone of health

1. Dietary regulation: (1) Light diet: Reduce the intake of high-fat and high-cholesterol foods, and eat more vegetables, fruits and whole grains. (2) Dietary therapy: Use medicinal food that has the effect of activating blood circulation and removing blood stasis, benefiting Qi and nourishing Yin, such as *Salvia miltiorrhiza*, Hawthorn, Milk vetch root, *Ophiopogon japonicus* and so on, or as a substitute for tea. (3) In a moderate manner: Avoid overeating and eat at regular intervals to regulate the spleen and stomach, and to nourish the heart.

2. Be careful in daily life: (1) Follow the laws of nature and avoid alternating hot and cold to maintain the balance of Yin and Yang in the body. (2) Regular work and rest: Ensure adequate sleep, avoid staying up late, and maintain the stability of the biological clock. (3) Exercise in moderation: Engage in moderate aerobic exercise, such as walking, Tai Chi, eight trigrams boxing, etc., in order to promote the circulation of Qi and blood. It does not advocate too intense and extreme exercise in TCM. Rather, it emphasizes finding peace and harmony in one's own mind through moderate exercise.

3. Emotional regulation: (1) Peace of mind: keep a relaxed mood, avoid excessive anxiety, depression, and other adverse emotions. (2) Relaxation training: Meditation, deep breathing, and other relaxation training can be carried out to relieve psychological pressure. (3) Social interaction: Maintain good social relationships and actively participate in social activities.

5.2.2 Treating pre-disease: Prevention first, guarding heart health

1. Early screening: Combines four diagnostic methods of TCM and modern medicine's testing methods to detect potential risks of heart disease at an early stage. Regular medical checkups: Regular cardiovascular health checkups to detect and deal with potential problems in a timely manner.

2. For those who have symptoms and have not yet been diagnosed, treatment based on syndrome differentiation: According to the individual's physiques and symptoms, suitable TCM will be used to regulate the condition.
   If there is a deficiency of Qi and blood stasis, then benefiting Qi and activating blood: commonly used herbs such as Astragalus, Salvia miltiorrhiza and Radix Panax ginseng. When syndrome of internal heat due to Yin deficiency, then nourishing Yin to clear heat: Chinese herbs such as Ophiopogonis and Asparagus can be used.
   Chinese herbal foot soak: Use Chinese herbs that have the effect of activating blood circulation and removing blood stasis, warming meridians to dissipate cold to soak the feet to improve blood circulation in the lower limbs and the whole body.
   Acupuncture and moxibustion: By stimulating specific acupoints, it can harmonize Qi and blood and dredge the meridians. Cupping: Used to remove dampness from the body and dredge the meridians. Massage: Promote blood circulation and relieve muscle tension through massage techniques.

3. Emotional relief: Through psychological counseling, music therapy, etc., to channel bad emotions, maintain mental health and prevent heart disease.

4. Smoking cessation and alcohol restriction: Smoking and excessive alcohol consumption are both risk factors for ACS, and smoking should be firmly cessation, and alcohol intake should be restricted.

5. Weight control: Maintain a healthy weight and avoid obesity.

5.2.3 Specific treatment method: The combination of Chinese and Western medicine, classification and staged treatment

1. ACS categorized treatment:

   STEMI: Thrombolytic and interventional treatments of Western medicine are used in the acute stage to rapidly open the occluded blood vessels. TCM is used to activate blood and resolve stasis, benefit Qi, and nourish Yin in the recovery stage to promote myocardial repair.

   Non-ST-segment elevation acute coronary syndrome (NSTE-ACS): Likewise, Western medicine is used for drug treatment, such as antiplatelet, anticoagulation, and plaque stabilization. At the same time, it is combined with TCM conditioning to improve blood circulation and relieve angina pectoris.

2. ACS staged treatment:

Acute period: Western medicine is the mainstay, rapidly controlling the condition, such as interventional therapy and medication. Chinese medicine is supplemented by the use of herbal injections and acupuncture to alleviate symptoms.

Recovery period: Western medicine continues medication to control risk factors. Using herbs, acupuncture, etc. to promote recovery and prevent recurrence.

Stabilization period: TCM is the mainstay, using TCM therapies and health cultivation methods to regulate the body, and strengthen resistance. Regular follow-ups to monitor the condition are also needed.

It should be noted that health cultivation and treatment methods should be carried out under the guidance of professional Chinese medicine practitioners, especially specialty therapies, in order to ensure safety and effectiveness. Meanwhile, for patients who have been diagnosed with ACS, treatment should be carried out in strict accordance with the doctor's prescription, and the TCM regimen can be used as an adjunctive treatment under the doctor's advice.

In the concept of "quality of care," the integration of Chinese and Western medicine in the treatment of ACS is particularly important. Because ACS is a complex and variable disease, it requires a combination of various treatments for long-term management and recuperation. It is like a long-lasting "battle," which requires the combination of Chinese and Western medicine, and careful treatment of one course of treatment after another, in order to achieve better results.

6. Mingling of ancient wisdom and modern technology

In today's medical world, the combination of TCM and Western medicine has become a trend, and in the treatment of ACS, this combination has shown unique advantages.

Acupuncture, as a treasure of Chinese medicine, plays a unique role in the treatment of ACS. By stimulating specific acupoints, such as Neiguan and Shenmen, acupuncture can regulate heart function, relieve angina, and improve myocardial blood supply. Some studies have shown that acupuncture can significantly reduce the frequency of angina attacks and improve the quality of life of patients with ACS [14].

Chinese herbs have also shown great strength in the treatment of ACS. Drugs that activate blood circulation and remove blood stasis such as *Salvia miltiorrhiza*, *Panax ginseng*, and safflower can improve blood circulation, reduce blood viscosity, and prevent thrombosis [8]. *Astragalus*, maitake and other drugs that benefit Qi and nourish Yin can enhance myocardial contractility and improve myocardial metabolism [15]. Danshen dripping pills, as a Chinese medicinal preparation, have been widely used in the adjuvant treatment of ACS and achieved good clinical results [16].

Qigong, as a method of physical and mental conditioning, plays an important role in the recovery period of ACS. Through the practice of pranayama and guiding, Qigong can regulate the nervous system, lower blood pressure, and relieve psychological pressure, thus favoring the recovery of the heart. However, there is a lack of clinical evidence.

Specific modalities of integration:

Diagnostic combination: The advanced testing methods of Western medicine (e.g., electrocardiogram, coronary angiogram) are combined with a comprehensive analysis of four diagnostic methods of TCM to realize a more accurate diagnosis.

Therapeutic combination: Acute stage Western interventional therapy (such as stent implantation) together with TCM (acupuncture, Chinese herbs, etc.) to realize the acute treatment of the symptoms and the slow treatment of the root cause.

Combination of rehabilitation: Western medicine's rehabilitation training (e.g., cardiac rehabilitation exercises) is combined with Chinese medicine's acupuncture, massage, and Qigong to promote the patient's overall recovery.

Combination of prevention: Western medicine's preventive measures (e.g., medication, lifestyle interventions) are combined with Chinese medicine's concepts of health cultivation (e.g., dietary regimen, emotional, and emotional conditioning) to achieve prevention before disease.

In conclusion, the combination of TCM and Western medicine shows a broad prospect in the treatment of ACS. The organic combination of TCM specialty therapies, such as acupuncture, herbal medicine, Qigong, and modern Western medical technology, is not only the inheritance and development of traditional medicine but also a supplement and challenge to modern science. With the deepening of research and the accumulation of clinical practice, the combination of Chinese and Western medicine in the treatment of ACS will become more mature and perfect, and make greater contributions to the cause of human health.

7. Traditional Chinese medicine challenges modern science

From a scientific point of view, the combination of Chinese medicine and Western medicine is not only a fusion of treatment methods but also a profound scientific change. Some medical experts from the East and the West have really seen the core of the combination of these ancient wisdoms with modern medicine, and the concepts of TCM such as the balance of Yin and Yang and the harmonization of Qi and blood have gradually been accepted by Western medicine. For example, from the perspectives of "systems biology" and "personalized medicine," some modern medical concepts coincide with holism and treatment based on syndrome differentiation.

We can regard the treatment of ACS by combining Chinese and Western medicine as a dynamic balance between "whole" and "local," between "prevention" and "treatment." Through this balance, we can not only better cope with the disease, but also improve the overall health and quality of life of patients. For example, in the treatment of ACS, Western medicine's interventional therapy can rapidly open up occluded coronary arteries, while Chinese medicine's activation of blood circulation and elimination of blood stasis and benefiting Qi can improve myocardial microcirculation and promote myocardial repair. This dynamic balance between "whole" and "local," "prevention" and "treatment" not only improves the therapeutic effect but also enhances the overall health and quality of life of patients.

However, although these ancient medicines are full of the wisdom of the ancients, today in the twenty-first century, we hope to have new developments, a deeper understanding of these ancient medicines, as well as better, more objective, and quantitative means of monitoring. There is still no better research methodology to study these ancient medicines which include holism. Especially, in the study of Chinese herbal medicine and acupuncture, modern research methods are still dominated by reductionism. Although the application of reductionism theory helps to deeply understand some specific components or mechanisms, it also has obvious limitations.

In herbal medicine research, the application of reductionism would neglect the importance of compounding. Herbal therapy emphasizes the holistic concept and treatment based on syndrome differentiation, and compounding between drugs is the key to therapeutic efficacy. The splitting theory tends to focus on the effect of a single component, ignoring the synergistic or antagonistic effect produced when multiple drugs work together. Too much focus on a single ingredient may lead to drug development that deviates from the holistic therapeutic concepts of TCM, and the drugs developed may not fully reflect the original therapeutic efficacy of the herbs. In acupuncture research, it can be said that Western medicine is still in the early stages of exploring the meridians and acupoints. It also ignores the diversity of acupuncture techniques and psychological factors. All of these studies also ignored individual differences.

"Cooperation" and "coordination" are the key to the thoughts of "holism," which is also a high-level requirement. However, how to scientifically and quantitatively study the organism from the perspective of "holism," that is, how to scientifically and quantitatively study, measure and calculate the degree of "cooperation" and "coordination"? It is not yet clear. If modern science, especially biology, physiology, pathology, and so on, cannot get out of this kind of thinking mode of "separating," "confronting" and "conquering," which has great limitations, how can we study the theories like TCM? How can we study "holistic medicine" which is rich in "harmonious" thinking like TCM?

8. Profound changes at the scientific level

The huge change in the medical market, which combines Chinese and Western medicine, is not only seen by doctors, but also by medical equipment and drug companies, medical insurance companies, the general public, and the government. In fact, in addition to the superficial changes in the medical market, science, especially biology and physics, is also facing a huge change. And this, which is very intrinsic but very profound, is a challenge to science. These two great transformations echo with each other and will have a huge and profound impact on the entire human mind in the twenty-first century.

This challenge is, in fact, a process of cultural integration. In the short term, the process of cultural integration is a painful one, but in the long-term, the integration of different cultures produces a new and better culture. Medicine and science, as part of culture, will of course benefit greatly from this fusion of cultures. There is an old Chinese saying, "Learn from the past to understand the new." As a human being, it is beneficial for the future of one's life if one can often summarize the experiences of the past. This applies not only to individuals but also to society. By constantly summarizing our historical experience, we can better guide our future development.

Changes in science have even slightly preceded changes in the medical marketplace. Cutting-edge research in modern physics has provided quantitative research tools for holistic medical concepts such as "balance," "harmony" and "conditioning." Physics is based on the idea that "the whole is greater than the parts," the development of "synergistics," "dissipative structure" and "uncertainty principle" and other theories have been developed. Unfortunately, however, only a few biologists, physiologists and psychologists have paid attention to these recent achievements and important changes. Therefore, only if more doctors, biologists, physiologists, and psychologists are aware of these important changes in the world of physics, and if these new ideas and progress are introduced into the study of medical science, will it be possible to face the holistic ideas of classical medicine, such as TCM, and carry out real scientific research.

Like the "Renaissance," this "retro movement" in the medical field, which is called "TCM fever," seems on the surface to be a conservative backward-looking movement. In fact, it is also a forward-looking and very positive innovation. So, we are very fortunate to be living in a time when we are witnessing this great change. As we said in the title of this section: we are facing two great transformations: external medicine and internal science, and these two great transformations echo each other. These two changes will in turn lead to a great change in human thought.

Therefore, this great change in science will not only provide a harmonious and unified theoretical framework, thus putting many classical and modern Western medicines together harmoniously into a unified medicine that will better benefit mankind. More importantly, this great change in physics, medicine, biology, physiology, and psychology will lead to a great change in the thinking of the entire human race, from the thinking of "separating," "confronting" and "conquering" to the thinking of "balancing," "harmonizing" and "regulating." This change of mindset will be more important, more essential, and more beneficial to humanity than the establishment of "unified medicine."

9. Conclusions

The chapter focuses on understanding ACS from the perspective of TCM. The holistic approach of TCM complements the strengths of Western medicine to provide a comprehensive strategy for the prevention and treatment of ACS and improving quality of life. It also makes people think on a scientific level about the shift in thinking behind it.

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References

[1] Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997: Results of a follow-up national survey. Journal of the American Medical Association. 1998;**280**(18):1569-1575. DOI: 10.1001/jama.280.18.1569

[2] Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular diseases. Journal of the American College of Cardiology. 2010;**55**(6):515-525. DOI: 10.1016/j.jacc.2009.07.074

[3] McLaren JdA JN, Aslanger EK, Pendell Meyers H, et al. From ST segment elevation MI to occlusion MI: The new paradigm shift in acute myocardial infarction. JACC: Advances. 2024;**3**(11):101314. DOI: 10.1016/j.jacadv.2024.101314

[4] Zoni CR, Mukherjee D, Gulati M. Classification of acute coronary syndrome from a therapeutic perspective. JACC: Advances. 2025;**4**(2):101552. DOI: 10.1016/j.jacadv.2024.101552

[5] Guo SQ, Han SB, Zhang JP, et al. Effect of Shexiang Baoxin Pill on clopidogrel resistance in patients with acute coronary syndrome. Pharmacology and Clinic of Traditional Chinese Medicine. 2015;**31**(1):242-244. DOI: 10.13412/j.cnki.zyyl.2015.01.079

[6] Cheng B, Chen P, Deng Y. Efficacy and safety of integrated traditional Chinese medicine and standard Western medicine for patients with acute coronary syndrome: Protocol for a systematic review and meta-analysis. Annals of Palliative Medicine. 2021, 2021;**10**(5):5763-5766. DOI: 10.21037/apm-21-681

[7] Wolberg AS, Rosendaal FR, Weitz JI, et al. Venous thrombosis. Nature Reviews. Disease Primers. 2015;**1**:15006. DOI: 10.1038/nrdp.2015.6

[8] Li D, Li Y, Yang S, et al. Mechanism and potential target of blood-activating Chinese botanical drugs combined with anti-platelet drugs: Prevention and treatment of atherosclerotic cardiovascular diseases. Frontiers in Pharmacology. 2022;**13**:811422. DOI: 10.3389/fphar.2022.811422

[9] Li J, Du Y, Cai C, et al. Effectiveness and safety of treating carotid atherosclerotic plaques with the method of nourishing qi, promoting blood circulation and expelling phlegm: A systematic review and meta-analysis. Frontiers in Pharmacology. 2022;**13**:1059737. DOI: 10.3389/fphar.2022.1059737

[10] Cui L, Liu Y, Hu Y, et al. Shexiang Tongxin Dropping Pill alleviates M1 macrophage polarization-induced inflammation and endothelial dysfunction to reduce coronary microvascular dysfunction via the Dectin-1/Syk/IRF5 pathway. Journal of Ethnopharmacology. 2023;**316**:116742. DOI: 10.1016/j.jep.2023.116742

[11] Chen J, Wei X, Zhang Q, et al. The traditional Chinese medicines treat chronic heart failure and their main bioactive constituents and mechanisms. Acta Pharmaceutica Sinica B. 2023;**13**(5):1919-1955. DOI: 10.1016/j.apsb.2023.02.005

[12] Libby P. The changing landscape of atherosclerosis. Nature. 2021;**592**(7855):524-533. DOI: 10.1038/s41586-021-03392-8

[13] Tokgozoglu L, Canpolat U. Does depression and anxiety increase

subclinical atherosclerosis more in dyslipidemic women than men? European Journal of Preventive Cardiology. 2020;**27**(8):797-799. DOI: 10.1177/2047487319883722

[14] Zhang N, Xie B, Du J, et al. Effect of acupuncture and exercise rehabilitation on quality of life in acute coronary syndrome patients after percutaneous coronary intervention. American Journal of Translational Research. 2024;**16**(6):2662-2669. DOI: 10.62347/KIFR7353

[15] Chen M, Zhong G, Liu M, et al. Integrating network analysis and experimental validation to reveal the mitophagy-associated mechanism of Yiqi Huoxue (YQHX) prescription in the treatment of myocardial ischemia/reperfusion injury. Pharmacological Research. 2023;**189**:106682. DOI: 10.1016/j.phrs.2023.106682

[16] Bai R, Yang Q, Xi R, et al. The effectiveness and safety of Chinese Patent Medicines based on syndrome differentiation in patients following percutaneous coronary intervention due to acute coronary syndrome (CPM trial): A nationwide cohort study. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023;**109**:154554. DOI: 10.1016/j.phymed.2022.154554

Section 2

Management of Acute Coronary Syndrome

Chapter 5

Arrhythmic Complications in Acute Coronary Syndrome: Mechanisms, Manifestations, and Management

Karnika Senthilkumar, Umashankar Lakshmanadoss and Paul Chacko

Abstract

Acute Coronary Syndrome (ACS) is frequently complicated by cardiac arrhythmias, which significantly contribute to morbidity and mortality. The pathophysiological basis of these arrhythmias includes ischemia-induced electrophysiological disturbances, electrolyte imbalances, autonomic dysfunction, and reperfusion injury. This review examines the spectrum of arrhythmias in ACS, including ventricular tachyarrhythmias (ventricular tachycardia and ventricular fibrillation), bradyarrhythmias (sinus bradycardia, atrioventricular blocks), and atrial arrhythmias (atrial fibrillation). We discuss risk stratification, mechanisms, ECG characteristics, and evidence-based management strategies. Early recognition and treatment of arrhythmias in ACS are crucial to prevent sudden cardiac death and improve patient outcomes.

Keywords: arrhythmias, acute coronary syndrome, Torsades de pointes, ventricular tachycardia, heart block

1. Introduction

Acute Coronary Syndrome (ACS) encompasses a spectrum of conditions, including unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI). This group of disorders is caused by the rupture or erosion of atherosclerotic plaques, resulting in partial or complete occlusion of a coronary artery, leading to myocardial ischemia, injury, and necrosis. While the primary focus in ACS management is to restore coronary blood flow and minimize myocardial damage, an often underestimated and potentially fatal complication of ACS is the development of arrhythmias.

Arrhythmic complications in ACS commonly occur due to disturbances in the electrical activity of the heart. They range from benign, self-limiting rhythms to life-threatening ventricular fibrillation, causing severe outcomes such as sudden cardiac death (SCD). Early detection and appropriate management of arrhythmias in ACS are crucial to improving patient outcomes. This review article aims to provide a comprehensive overview of the mechanisms, clinical manifestations, and management strategies for arrhythmic complications in ACS.

2. Pathophysiology of arrhythmias in ACS

The occurrence of arrhythmias in ACS is primarily due to myocardial ischemia, injury, and infarction. These changes disrupt the normal electrical conduction of the heart, leading to various types of arrhythmias. The specific mechanisms behind arrhythmias in ACS depend on the type of ACS (NSTEMI, STEMI, or unstable angina), the extent of myocardial damage, and the degree of ischemia. Key factors contributing to arrhythmogenesis in ACS include:

1. *Ischemia*: In the early stages of ACS, myocardial ischemia is the primary cause of arrhythmias. Ischemic tissues change ion channel function, leading to altered action potential duration and membrane potential, creating a substrate for arrhythmias. Additionally, ischemic myocardial regions have reduced oxygen supply, causing cellular damage and electromechanical instability. Monomorphic VT is most commonly due to reentry mechanisms, especially in the setting of structural heart disease (like scar tissue from prior MI). But ACS leading on to automaticity can also cause monomorphic VT, in the setting of preexisting scar due to prior myocardial infarction, though it is much less common.

2. *Injury*: The injury caused by myocardial infarction (MI) further destabilizes the electrical system of the heart. Infarcted tissues no longer participate in normal conduction and can serve as reentry circuits for arrhythmias. In STEMI, this injury is usually transmural (involving the full thickness of the myocardial wall), while in NSTEMI, the injury is typically subendocardial (involving the inner part of the myocardial wall).

3. *Reentry mechanism*: One of the most common mechanisms for arrhythmias in coronary artery disease is reentry, where the electrical impulse travels in a circular path around a nonconducting area, such as an infarcted tissue. Reentry can cause both atrial and ventricular arrhythmias, including atrial fibrillation and ventricular tachycardia.

4. *Autonomic nervous system (ANS) imbalance*: In the acute phase of ACS, an imbalance between the sympathetic and parasympathetic branches of the ANS can contribute to arrhythmogenesis. Sympathetic overactivity increases the risk of tachyarrhythmias, while parasympathetic overactivity can lead to bradyarrhythmias.

5. *Electrolyte disturbances*: Myocardial ischemia and injury can alter the concentration of key electrolytes such as potassium, calcium, and magnesium. These disturbances further exacerbate electrical instability and increase the susceptibility to arrhythmias.

6. *Left ventricular dysfunction*: In the context of large infarctions or extensive myocardial damage, left ventricular dysfunction can develop, further increasing the risk of arrhythmias, particularly life-threatening ones like ventricular fibrillation (VF).

3. Risk factors for arrhythmias in ACS

Several factors increase the risk of arrhythmias in patients with ACS:

1. *Extent of myocardial damage*: Larger infarctions and those involving the anterior wall of the left ventricle are more likely to result in arrhythmias.

2. *Electrolyte imbalances*: Hypokalemia, hyperkalemia, hypomagnesemia, and hypercalcemia can all predispose to arrhythmias in ACS.

3. *Impaired left ventricular function*: Reduced ejection fraction and heart failure increase the risk of developing life-threatening arrhythmias.

4. *Previous history of arrhythmias*: Patients with a history of atrial fibrillation, ventricular arrhythmias, or other heart rhythm disorders are at increased risk in the setting of ACS.

5. *Autonomic dysfunction*: An imbalance between the sympathetic and parasympathetic nervous systems can increase susceptibility to arrhythmias.

4. Types of arrhythmias in ACS

Arrhythmias in ACS can be broadly classified into *supraventricular* and *ventricular* arrhythmias, with the latter being more likely to result in life-threatening conditions such as sudden cardiac death.

4.1 Supraventricular arrhythmias

Supraventricular arrhythmias are commonly observed during the acute and subacute phases of ACS and originate above the bundle of His—typically in the atria or atrioventricular node. They can worsen myocardial ischemia, precipitate heart failure, and increase the risk of thromboembolic complications. Supraventricular arrhythmias include conditions such as atrial fibrillation and flutter.

4.1.1 Atrial fibrillation (AF)

Atrial fibrillation is one of the most common arrhythmias seen in ACS, especially in patients with STEMI and its prevalence increases with age [1]. Studies indicate that AF occurs in approximately 5–23% of patients hospitalized with ACS, with variability depending on the population studied and diagnostic criteria used [2]. Several factors increase the likelihood of developing AF, including older age, more extensive myocardial injury, the presence of heart failure symptoms, reduced left ventricular function, and involvement of multiple coronary arteries [3, 4]. The presence of AF in the setting of ACS is associated with increased morbidity and mortality, including higher risks of heart failure and stroke [5].

4.1.2 Pathophysiology

The development of AF is driven by a wide range of contributing factors, making its underlying mechanisms both intricate and multifaceted. These include mechanical influences such as atrial dilation or stretch, functional triggers like myocardial ischemia, inflammation, and disturbances in autonomic tone, as well as metabolic contributors such as elevated catecholamine levels and atrial natriuretic peptide [6]. The relationship between AF and acute coronary syndrome (ACS) is bidirectional, typically falling into two clinical scenarios: one where AF serves as a predisposing factor for ACS, and another where ACS precipitates the onset of AF [7].

AF may facilitate the progression or worsening of coronary artery disease (CAD) by fostering a pro-inflammatory and pro-thrombotic environment. The disorganized atrial contractions characteristic of AF can impair endothelial function and enhance systemic inflammation, both of which are key elements in atherogenesis. Furthermore, AF increases myocardial oxygen consumption and can reduce effective cardiac output, which may predispose patients to Type 2 myocardial infarction, where a mismatch exists between oxygen demand and supply. In less common cases, AF may even cause ACS through embolization of atrial thrombi into the coronary circulation [7].

Conversely, existing CAD can predispose the myocardium to arrhythmogenic conditions that favor AF development. Ischemia can disrupt the electrophysiological integrity of cardiomyocytes, promoting reentry circuits or creating fibrotic areas due to atrial infarction. These structural changes provide a substrate for sustained arrhythmias. Additionally, ischemic injury may stimulate abnormal automaticity and focal ectopic activity, triggering episodes of AF. Following ACS, increased sympathetic nervous system activity, oxidative stress, and inflammation contribute to autonomic remodeling. This neurohormonal imbalance is a significant driver in initiating and maintaining AF during or after an ischemic event. Notably, new-onset AF is more likely when coronary lesions affect the proximal segments of the right coronary or circumflex arteries—areas responsible for supplying the atrial myocardium [7].

4.1.3 Clinical features

AF may be asymptomatic or cause symptoms such as palpitations, chest pain, shortness of breath, dizziness, or fatigue. It can also exacerbate heart failure symptoms and increase the risk of thromboembolic events such as ischemic stroke.

4.1.4 Diagnosis

The standard 12-lead electrocardiogram (ECG) is the gold standard investigation to confirm a diagnosis of AF [8]. The atrial electrical impulses are unsynchronized with the ventricles in AF, resulting in an abnormal waveform on ECG. A normal waveform includes a P wave, a QRS complex, and a T wave. In contrast, AF is characterized by the absence of distinct P waves, which are instead replaced by multiple erratic fibrillatory (F) waves, along with an irregular rhythm marked by inconsistent intervals between successive R waves [9].

In the context of ACS, the classical interpretation of ST elevation or depression maybe less accurate with coexisting AF, particularly with a rapid ventricular response. Rapid heart rates can lead to ST depression even in the absence of coronary artery disease, especially when the depression is less than 2 mm, reducing its specificity for ischemia [10, 11]. Conversely, high rates may also obscure true ST-segment deviations, lowering the sensitivity of a standard 12-lead ECG in detecting acute myocardial infarction during episodes of rapid AF. In such cases, when ST-elevation is not clearly visible, cardiac biomarkers often become essential for confirming the diagnosis [12].

4.1.5 Management

Management of AF in ACS must be individualized and include the following elements:

4.1.5.1 Rate vs. rhythm control

- *Rate control* is typically first-line unless AF is causing instability. It reduces myocardial oxygen demand and improves diastolic filling.
    - *Beta-blockers* (e.g., metoprolol): Preferred unless contraindicated by hypotension or severe bradycardia.
    - *Calcium channel blockers* (e.g., diltiazem): Alternative in patients without heart failure with reduced ejection fraction.
    - *Amiodarone*: Useful for both rate and rhythm control in hemodynamically compromised patients.
- *Rhythm control* may be preferred in:
    - Hemodynamic instability
    - Symptomatic patients despite rate control
    - Persistent AF after stabilization
    - Reversible causes (e.g., pericarditis, electrolyte abnormalities)
    - *Electrical cardioversion* is more effective and often used in unstable settings.
    - *Pharmacological cardioversion* (e.g., amiodarone) is slower but useful when sedation or anesthesia is high-risk.

4.1.5.2 Anticoagulation

- Stroke risk must be balanced against bleeding, particularly in patients receiving dual antiplatelet therapy (DAPT).
- Use CHA_2DS_2-*VASc* score to assess need for anticoagulation. Patients with a score of 2 or more require anticoagulation.
    - Anticoagulation options:
    - *Low molecular weight heparin (LMWH)* or *unfractionated heparin* acutely

- *Warfarin* or *DOACs* for long-term therapy
- *Triple therapy* (DAPT + anticoagulant) increases bleeding risk and should be minimized in duration, usually to 1–4 weeks, followed by dual therapy (anticoagulant + one antiplatelet) [13, 14].

4.1.6 Atrial flutter

Atrial flutter (AFL) is encountered less frequently than AF in ACS, but it shares several pathophysiological features and clinical implications. Though less common, AFL in ACS is clinically significant due to its association with hemodynamic instability, thromboembolic risk, and resistance to pharmacological rate control.

4.1.7 Pathophysiology

The most typical form of AFL is classified as "typical" flutter, characterized by a macro-reentrant circuit encircling the tricuspid annulus in the right atrium [15]. Acute coronary events can precipitate this arrhythmia by inducing atrial ischemia and mechanical strain—particularly when right atrial pressure is elevated. These changes can create a substrate for reentry by slowing conduction and altering refractory periods.

Unlike AF, which results in chaotic atrial activity, AFL generally produces a more organized atrial rhythm. The ventricular response is often regular and rapid, commonly around 150 beats per minute due to 2:1 atrioventricular (AV) conduction. However, this rhythm can fluctuate based on AV nodal properties and external factors such as medications or autonomic tone [16].

4.1.8 Clinical features

The symptoms of AFL often resemble those of AF, with patients reporting palpitations, lightheadedness, shortness of breath, or fatigue. However, due to the regularity of the rhythm, physical examination may reveal a consistent tachycardia, distinguishing it from the irregularly irregular pulse characteristic of AF. Notably, AFL may be more resistant to pharmacological rate control, particularly because the organized atrial activity drives a consistently rapid ventricular rate, often refractory to standard AV nodal blockers.

4.1.9 Diagnosis

ECG is the primary diagnostic tool. Typical AFL presents with classic "sawtooth" flutter waves, best appreciated in the inferior leads (II, III, aVF) and V1. These flutter waves usually occur at a rate of 300 bpm, with variable ventricular responses depending on AV nodal conduction.

In cases of recurrent or refractory AFL, an electrophysiology study (EPS) may be indicated to define the reentrant circuit and assess suitability for ablation.

4.1.10 Management

4.1.10.1 Rate control

Similar to AF, rate control in AFL typically involves beta-blockers or non-dihydropyridine calcium channel blockers. However, these agents may be less effective in

AFL due to the often rapid and regular ventricular rate, particularly in the setting of 2:1 conduction [17].

4.1.10.2 Rhythm control

Electrical cardioversion is highly effective and often the first-line intervention in hemodynamically unstable patients or those with ongoing symptoms. Pharmacological options such as amiodarone may be considered when immediate cardioversion is not feasible.

4.1.10.3 Catheter ablation

For patients with recurrent or persistent typical AFL, catheter ablation offers a curative option. It involves targeting the cavotricuspid isthmus to interrupt the reentrant circuit. Ablation is particularly recommended in symptomatic patients who are either refractory to or intolerant of medical therapy [16].

4.1.10.4 Anticoagulation

As with AF, the risk of stroke in AFL necessitates thorough thromboembolic risk assessment. The CHA_2DS_2-VASc scoring system is applied similarly, and anticoagulation should be initiated accordingly, especially in patients with persistent or recurrent AFL. The risk of thrombus formation in the left atrial appendage, although less studied in AFL than AF, is still present and warrants equivalent preventive strategies.

5. Ventricular arrhythmias

Ventricular arrhythmias (VA) arise from the ventricles and include a range of disorders, from benign premature beats to life-threatening conditions like ventricular tachycardia and ventricular fibrillation. Ventricular arrhythmias may occur at any stage of MI, ranging from acute infarction to the post-MI period. Although the incidence of ventricular arrhythmias has decreased in the hospital phase of ACS due to prompt interventions and medical therapy, adverse outcomes such as cardiac arrest and SCD remained increased, particularly in the first 30 days [18].

5.1 Premature ventricular contractions (PVCs)

Premature ventricular contractions (**Figure 1**) occur when the heartbeat is initiated by the Purkinje fibers instead of the sinoatrial node and there is a pause before the next regular heartbeat [19]. They are typically triggered by acute ischemia, reperfusion injury, or heightened sympathetic activity and may serve as an early marker of myocardial electrical instability.

5.2 Pathophysiology

PVCs in the setting of ACS may indicate localized areas of increased automaticity or reentry circuits in ischemic myocardium. While isolated or infrequent PVCs are common and often transient, their occurrence—especially when frequent, multifocal, or occurring in short-coupled pairs—may signal an increased risk of progression

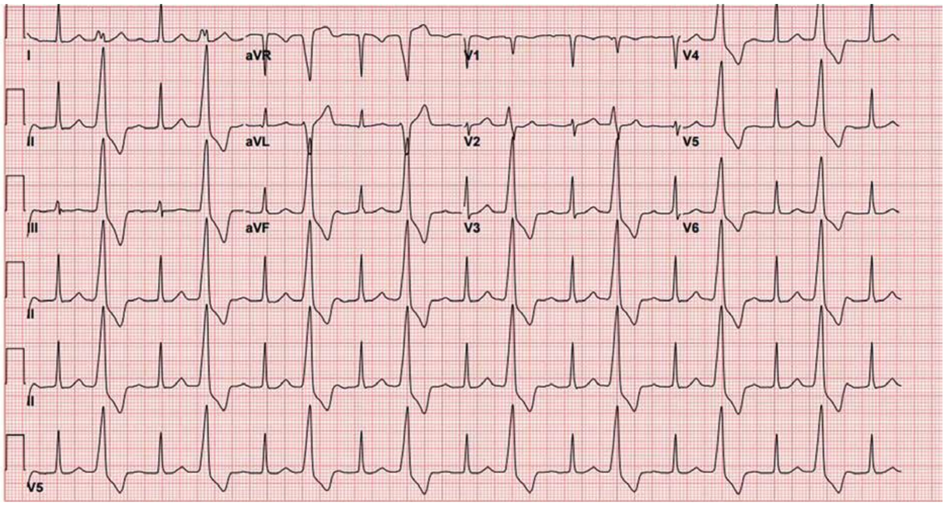

Figure 1.
ECG showing PVCs in bigeminy. Note that there are alternating normal sinus beats and PVCs that are characterized by wide QRS complexes and the absence of a P wave.

to sustained ventricular arrhythmias, such as ventricular tachycardia (VT) or ventricular fibrillation (VF), which can be life-threatening [20]. PVCs have historically been recognized as a risk factor for SCD after a MI [21].

5.3 Clinical features

In ACS patients, PVCs may be asymptomatic and detected only during ECG monitoring. However, they can also be associated with palpitations, a sense of skipped or irregular heartbeats, dizziness, or anxiety. In some cases, frequent PVCs during ACS can contribute to hemodynamic compromise by reducing stroke volume, especially in patients with impaired ventricular function. Though rare, PVCs may lead to syncope or act as triggers for sustained VT or VF, particularly during the vulnerable peri-infarct period [16].

The clinical impact of PVCs in ACS is often determined by their frequency, morphology, coupling interval, and presence of underlying myocardial dysfunction. Studies have shown that PVCs occurring within the first 24–48 hours of myocardial infarction are associated with increased mortality, especially when they degenerate into more serious arrhythmias [22].

5.4 Diagnosis

The initial diagnostic approach typically involves a 12-lead ECG to detect ectopic ventricular beats. **Figure 2** depicts PVCs during a STEMI. However, since PVCs often occur sporadically, a standard ECG may not capture them during the brief recording period. This test also helps distinguish PVCs from premature atrial contractions (PACs), which originate from the atria rather than the ventricles. In patients with PVCs, the ECG may also reveal additional abnormalities, such as:

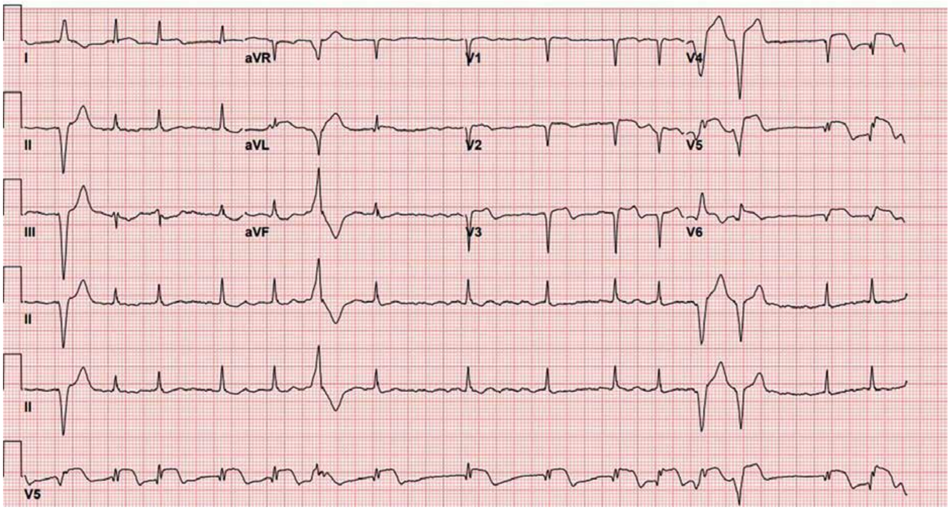

Figure 2.
ECG demonstrating STEMI with PVCs. ST segment elevation can be prominently seen in leads V2-V5 and the wide QRS complexes without preceding P waves represent PVCs.

- Electrolyte imbalances (e.g., peaked T waves or prolonged QT interval)
- Signs of left ventricular hypertrophy
- Indicators of acute ischemia, including ST-segment elevation or depression, and/or T wave inversion

To further evaluate palpitations and identify the presence of PVCs or differentiate them from other arrhythmias, continuous ambulatory monitoring using a 24- or 48-hour Holter monitor may be necessary [16].

5.5 Management

In the acute phase of ACS, the primary goal is to stabilize the patient and restore coronary perfusion. Isolated PVCs without hemodynamic instability or progression to sustained arrhythmias generally do not require specific treatment. Their frequency often diminishes as myocardial perfusion is restored through reperfusion therapy (e.g., percutaneous coronary intervention or thrombolysis).

However, in patients with frequent or symptomatic PVCs, or those associated with hypotension or signs of ventricular arrhythmia, treatment may be necessary. First-line management includes:

- *Correction of reversible causes*, such as hypokalemia, hypomagnesemia, or hypoxia.
- *Beta-blockers*, which are commonly used in ACS and help suppress ventricular ectopy by reducing sympathetic drive.

- *Avoidance of pro-arrhythmic medications*, such as class Ic antiarrhythmics, in the setting of ischemia or infarction.

Prophylactic antiarrhythmic therapy solely for PVC suppression is not recommended due to lack of survival benefit and potential harm, as shown in studies such as the Cardiac Arrhythmia Suppression Trial [23]. If PVCs are frequent and contributing to ventricular dysfunction (PVC-induced cardiomyopathy), further assessment and possibly catheter ablation may be considered later in the course of care, after stabilization.

5.6 Ventricular tachycardia (VT)

Ventricular tachycardia (VT) is a frequently encountered and potentially life-threatening arrhythmia in ACS, particularly in patients presenting with a STEMI. The incidence of VT in ACS has decreased with the advent of timely reperfusion therapies such as percutaneous coronary intervention (PCI), but it remains a critical clinical concern, especially in those with large infarct areas or reduced left ventricular ejection fraction (LVEF).

VT is observed in approximately 6–10% of patients with acute MI, most commonly within the first 48 hours of symptom onset. Early VT is generally associated with acute ischemia or reperfusion injury, whereas late VT—occurring days to weeks after MI, is often due to structural remodeling and scar formation, which may necessitate long-term preventive strategies [14, 20].

5.7 Pathophysiology

VT in ACS typically arises from *reentrant circuits* within areas of ischemic or infarcted myocardium. During an infarction, injured cardiac tissue exhibits altered conduction properties, creating regions of unidirectional block and slow conduction. These changes facilitate the development of macro-reentry pathways, especially around areas of myocardial scar or border zones of infarction, which are the primary substrate for sustained monomorphic VT.

In addition, *triggered activity* due to early after-depolarizations (EADs) or delayed after-depolarizations (DADs), and *abnormal automaticity*, may contribute to the initiation of VT, particularly in the setting of electrolyte disturbances or sympathetic overactivity [24].

5.8 Clinical features

VT may present with a range of symptoms, depending on its duration, rate, and impact on cardiac output. Common manifestations include:

- Palpitations
- Dizziness or lightheadedness
- *Syncope* or near-syncope, especially in sustained VT
- Chest discomfort or shortness of breath
- *Hemodynamic instability*, including hypotension, shock, or cardiac arrest.

VT that results in loss of cardiac output—such as pulseless VT—requires immediate recognition and intervention, as it may rapidly progress to ventricular fibrillation (VF) and SCD.

5.9 Diagnosis

Diagnosis of VT in the ACS setting is based on continuous ECG monitoring and 12-lead ECG. VT is defined by:

- A regular wide QRS complex rhythm (QRS ≥120 ms)
- Rate > 100 bpm
- AV dissociation (P waves independent of QRS)
- Capture or fusion beats (diagnostic in wide-complex tachycardia)

In ACS, telemetry is essential for early detection of ventricular arrhythmias. Ambulatory Holter monitoring or implantable loop recorders may be considered later for risk stratification in post-MI patients with unexplained syncope or suspected arrhythmias [25].

5.10 Management

Management of VT in ACS is dictated by the patient's hemodynamic status and the timing of arrhythmia onset.

5.10.1 Acute management

- *Hemodynamically unstable VT* requires *immediate synchronized electrical cardioversion.*
- *Stable sustained VT* may be initially managed with *antiarrhythmic drugs*:
  - *Amiodarone* is the first-line agent due to its efficacy in both ischemic and nonischemic cardiomyopathy.
  - *Lidocaine* can be useful in ischemia-driven VT, particularly when amiodarone is contraindicated or unavailable. Its use has declined due to concerns over efficacy and neurotoxicity, but it remains a valid option in specific ACS-related VT cases [23].
- *Beta-blockers* should be administered early in ACS to reduce sympathetic stimulation and lower the risk of recurrent VT [25].

5.10.2 Long-term risk reduction

- *Implantable cardioverter-defibrillator (ICD)*: In patients who survive VT/VF during ACS but have persistently reduced LVEF (<35%) after optimal medical therapy, an ICD may be indicated for secondary prevention after a 40-day waiting period post-MI.

- *Catheter ablation*: Considered in cases of recurrent monomorphic VT or electrical storm unresponsive to medical therapy, especially in the presence of defined arrhythmic substrates [25].

5.11 Sustained monomorphic VT

Sustained monomorphic ventricular tachycardia (SMVT) is a life-threatening arrhythmia that occurs in a small but significant subset of patients with ACS. While ventricular fibrillation and polymorphic VT are more commonly recognized in the acute ischemic phase, SMVT typically occurs later, particularly in the setting of myocardial scarring. Its presence signals a high risk of morbidity and mortality, requiring prompt recognition and management.

5.12 Pathophysiology

The primary mechanism of SMVT in ACS patients is *macro-reentry*, often facilitated by areas of heterogeneous conduction and fibrosis within infarcted myocardium. Scar tissue provides the substrate for reentrant loops, particularly in the border zones of infarcted areas [26]. The arrhythmia is typically *monomorphic*, indicating a single consistent reentrant pathway and QRS morphology on ECG.

5.13 Clinical features

Patients may present with palpitations, syncope, or hemodynamic collapse depending on ventricular function and rate of the tachycardia. Those with preexisting left ventricular dysfunction are particularly prone to hemodynamic instability. SMVT in the context of ACS is associated with an increased risk of SCD and adverse long-term outcomes.

5.14 Diagnosis

On ECG, SMVT presents as:

- Regular broad-complex tachycardia (QRS > 120 ms)
- Monomorphic QRS complexes, reflecting a stable and repetitive reentry circuit
- Atrioventricular (AV) dissociation: Independent atrial and ventricular activity may be observed (P and QRS complexes at different rates).
- Capture or fusion beats: These may help distinguish VT from supraventricular tachycardias with aberrancy.

Figure 3 shows an ECG trace of a patient with monomorphic VT.

5.15 Management

5.15.1 Hemodynamically unstable VT

Immediate intervention is required in patients presenting with hypotension, chest pain, altered mental status, or signs of shock. The first-line treatment is *synchronized electrical cardioversion* and advanced cardiovascular life support (ACLS).

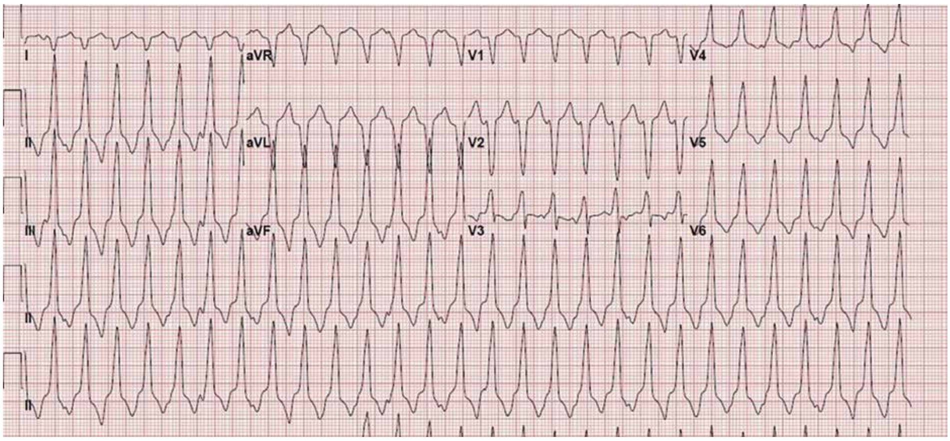

Figure 3.
ECG portraying monomorphic VT. Regular, wide-complex tachycardia is observed with uniform QRS morphology and no discernible P waves.

5.15.2 Hemodynamically stable VT

In patients who are conscious and maintaining adequate perfusion, pharmacologic therapy may be attempted:

- IV Amiodarone
- IV Procainamide
- Verapamil can be given if there is no structural heart disease and there is a known history of verapamil-sensitive VT [20].

5.15.3 Long-term management

Patients who survive an episode of SMVT, especially in the context of structural heart disease or reduced ejection fraction, should be evaluated for:

- *Implantable Cardioverter-Defibrillator (ICD)* therapy
- *Catheter ablation*: Considered in recurrent or drug-refractory VT
- *Optimization of heart failure therapy* if present

Early electrophysiology consultation and secondary prevention strategies are essential in improving outcomes [20].

6. Accelerated Idioventricular rhythm (AIVR)

Accelerated Idioventricular Rhythm (AIVR) is a ventricular arrhythmia characterized by a regular, wide-complex rhythm with a rate typically between 50 and 110 beats per minute. It is commonly observed during the reperfusion phase of an acute MI and is generally considered a benign and self-limiting arrhythmia [27].

6.1 Pathophysiology

The primary mechanism underlying AIVR is enhanced automaticity of ventricular pacemaker cells. This enhancement may result from increased vagal tone and decreased sympathetic tone, particularly during the reperfusion phase of an AMI. The ectopic ventricular focus assumes control when its intrinsic rate surpasses that of the sinoatrial node [27, 28].

On ECG, AIVR is characterized by:

- Regular rhythm with a rate typically between 50 and 120 bpm.
- Wide QRS complexes (≥120 ms) due to ventricular origin.
- Fusion and capture beats may be present, indicating simultaneous activation of the ventricles by both sinus and ventricular impulses.

6.2 Management

In most cases, AIVR is self-limiting and does not require specific treatment. Management focuses on addressing the underlying cause, such as optimizing reperfusion strategies in AMI. Antiarrhythmic therapy is generally avoided, as it may suppress the ventricular rhythm and lead to bradycardia or asystole [29].

7. Ventricular fibrillation (VF)/pulseless VT

Ventricular Fibrillation (VF) and Pulseless Ventricular Tachycardia (VT) are life-threatening arrhythmias that can occur during the acute phase of ACS. VF is characterized by rapid, disorganized electrical activity in the ventricles, leading to ineffective myocardial contractions and cessation of cardiac output. Pulseless VT, a rapid ventricular rhythm without effective circulation, can deteriorate into VF if not promptly treated. Both arrhythmias are major causes of SCD in ACS patients.

The incidence of VF and sustained VT in the context of ACS varies. Studies have reported that among patients hospitalized with acute myocardial infarction (MI), 5–10% experience VF or VT, with an additional 5% developing these arrhythmias within 48 hours of admission [20]. Notably, VF is the most common arrhythmia leading to SCD in patients with coronary artery disease, accounting for approximately 450,000 deaths annually in the United States [30].

7.1 Pathophysiology

VF typically arises from multiple reentrant circuits within the ventricular myocardium, leading to chaotic electrical activity that prevents effective ventricular contraction and blood ejection. Ischemia-induced alterations in ion channel function and myocardial conduction contribute to the development of these reentrant circuits. The increased automaticity in the Purkinje fibers adjacent to ischemic myocardial tissue during an acute MI serves as a focal trigger for VT. Additionally, triggered activity, caused by early or late afterdepolarizations, may surpass the myocardial refractory threshold, producing ectopic beats that initiate arrhythmias. Pulseless VT, often a precursor to VF, involves a rapid and organized ventricular rhythm that fails to produce adequate cardiac output, leading to hemodynamic collapse.

Both VF and pulseless VT present with sudden loss of consciousness and absence of palpable pulses due to the abrupt cessation of effective cardiac output. Without immediate intervention, these arrhythmias are invariably fatal.

7.1.1 Management

7.1.1.1 Immediate intervention

The cornerstone of management for VF and pulseless VT is prompt defibrillation. Early defibrillation, combined with high-quality cardiopulmonary resuscitation, significantly improves survival outcomes.

Advanced Cardiovascular Life Support (ACLS) guidelines recommend [31]:

- *Immediate defibrillation*: Deliver a biphasic shock as soon as possible.
- *CPR*: Resume high-quality chest compressions immediately after defibrillation, minimizing interruptions.
- Medications:
    - *Epinephrine*: Administer 1 mg intravenously every 3–5 minutes during resuscitation efforts.
    - *Amiodarone*: Consider 300 mg IV bolus for refractory VF or pulseless VT, followed by a possible additional 150 mg IV bolus.

Following successful resuscitation, comprehensive post-cardiac arrest care is crucial [31]:

- *Coronary reperfusion*: Urgent coronary angiography with percutaneous coronary intervention (PCI) is indicated, especially if there is evidence of ongoing ischemia or STEMI.
- *Hemodynamic support*: Maintain adequate blood pressure and organ perfusion using fluids and vasopressors as needed.
- *Targeted Temperature Management (TTM)*: Consider cooling to 32–36°C for patients who remain comatose after return of spontaneous circulation (ROSC) to improve neurological outcomes.
- *Implantable Cardioverter-Defibrillator (ICD)*: Evaluate for ICD placement for secondary prevention of SCD in patients with significant left ventricular dysfunction or other high-risk features.

The prognosis after VF or pulseless VT in the setting of ACS depends on several factors, including the timeliness of defibrillation, underlying cardiac function, and the presence of comorbidities. Rapid defibrillation and advanced post-resuscitation care are associated with improved survival and neurological outcomes. However, the overall mortality rate remains high, underscoring the importance of preventive strategies and early intervention.

7.2 Torsades de pointes

Torsades de Pointes (TdP) is a specific form of polymorphic ventricular tachycardia characterized by a distinctive twisting of the QRS complexes around the isoelectric baseline on ECG. While TdP is more commonly associated with congenital or acquired long QT syndrome, it can also occur in ACS, particularly when accompanied by factors that prolong the QT interval. **Figure 4** portrays polymorphic ventricular tachycardia (PMVT) with a normal QT interval, and **Figure 5** shows PMVT in the presence of long QT syndrome. Although less frequent than other arrhythmias in ACS, TdP is significant due to its potential to degenerate into ventricular fibrillation, necessitating prompt recognition and management.

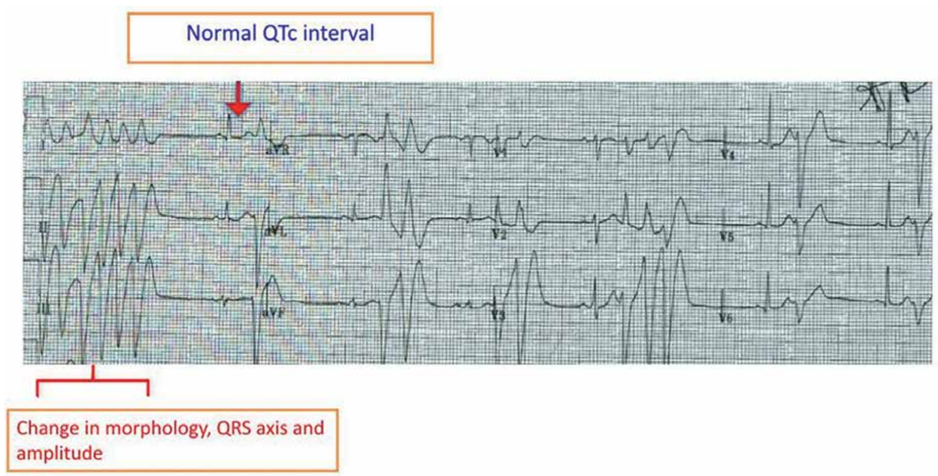

Figure 4.
ECG showing PMVT with a normal QTc interval, indicative of ischemia induced arrhythmia.

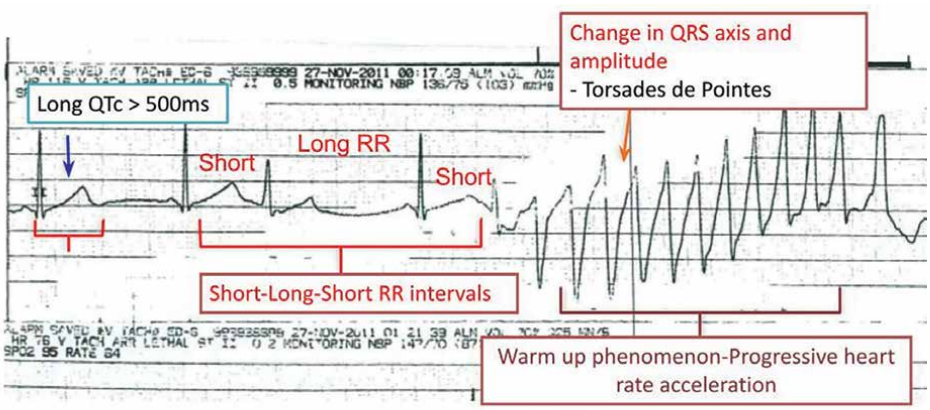

Figure 5.
ECG illustrating PMVT with long QT syndrome. There is a markedly prolonged QT interval, short-long-short RR intervals, and torsades des pointes. The warm-up phenomenon can be seen (progressive acceleration of the heart rate).

The incidence of TdP in ACS patients is relatively low but increases in the presence of certain risk factors:

- *Electrolyte imbalances*: Hypokalemia and hypomagnesemia are common in ACS and can predispose patients to TdP by prolonging the QT interval.

- *QT-prolonging medications*: Drugs such as certain antiarrhythmics, antibiotics (e.g., clarithromycin), and antipsychotics can exacerbate QT prolongation, increasing the risk of TdP [32, 33].

- *Bradycardia*: Slow heart rates can lead to QT prolongation, creating a substrate for TdP.

- *Genetic polymorphisms*: Certain genetic variants, such as the KCNH2-K897T polymorphism, have been associated with an increased risk of TdP following myocardial infarction [34].

7.3 Pathophysiology

TdP arises from abnormalities in ventricular repolarization, leading to a prolonged QT interval. This prolongation can result in early afterdepolarizations (EADs), which may trigger the arrhythmia. In the context of ACS, ischemia can exacerbate repolarization abnormalities, further increasing the risk.

7.4 Clinical features

Patients with TdP may experience:

- *Palpitations*: A sensation of rapid or irregular heartbeats.

- *Dizziness or syncope*: Due to transient decreases in cardiac output during episodes.

- *Sudden cardiac arrest*: If TdP degenerates into ventricular fibrillation.

It is noteworthy that some patients may remain asymptomatic, with TdP detected incidentally on ECG.

7.5 Diagnosis

TdP (as shown in **Figure 6**) is identified on ECG by:

- *Polymorphic QRS Complexes*: QRS complexes that appear to twist around the isoelectric line.

- *Prolonged QT interval*: A corrected QT (QTc) interval exceeding 500 ms is considered high risk.

- *Pause-dependent initiation*: Episodes often follow a long-short RR interval sequence.

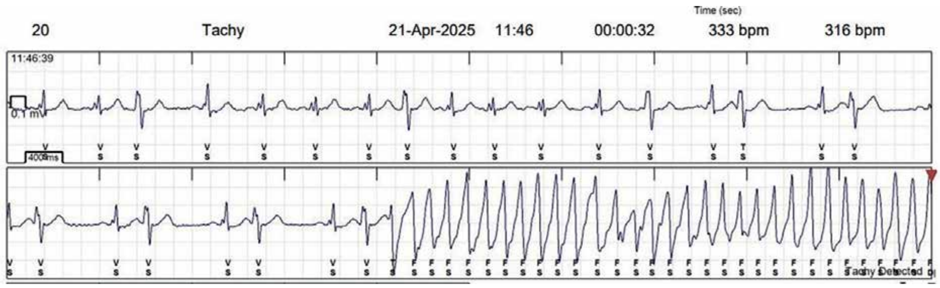

Figure 6.
ECG showing Torsades de Pointes. The lower tracing shows irregular QRS complexes that twist around the isoelectric line, consistent with TdP, at a heart rate of 316 beats per minute.

7.6 Management

7.6.1 Acute management

1. *Magnesium sulfate*: Administer 2 grams intravenously over 1–2 minutes, regardless of serum magnesium levels, as it stabilizes the myocardial membrane and suppresses EADs [35].

2. *Electrolyte correction*: Maintain potassium levels above 4.5 mmol/L and correct any hypomagnesemia or hypocalcemia to reduce TdP risk [35].

3. *Discontinue QT-prolonging drugs*: Identify and stop any medications that may contribute to QT prolongation.

4. *Overdrive pacing or isoproterenol*: In cases associated with bradycardia, increasing the heart rate can shorten the QT interval and prevent recurrent episodes [35].

5. *Defibrillation*: If TdP progresses to ventricular fibrillation or the patient becomes hemodynamically unstable, immediate defibrillation is warranted.

7.6.2 Long-term management

- *Risk factor modification*: Address and correct modifiable risk factors, including electrolyte imbalances and medication use.

- *Beta-blockers*: May be considered in patients with congenital long QT syndrome but are generally avoided in acquired cases unless specifically indicated.

- *Implantable Cardioverter-Defibrillator (ICD)*: In patients with recurrent TdP episodes or those at high risk for sudden cardiac death, ICD placement may be considered.

8. Bradyarrhythmias in ACS

Sinus bradycardia is defined as a heart rate less than 60 beats per minute, with a normal P-QRS-T morphology. It is frequently observed in patients with *inferior wall*

MI, primarily due to *ischemia of the sinoatrial (SA) node* as a result of the right coronary artery being blocked.

8.1 Diagnosis

- HR < 60 bpm.
- Normal sinus rhythm with intact P wave before every QRS complex.
- Normal axis and morphology of QRS and T waves.

8.2 Clinical features

Although often benign, sinus bradycardia can cause symptoms such as:

- Hypotension
- Dizziness or syncope
- Heart failure exacerbation

8.3 Management

- *Asymptomatic*: Observation and supportive care.
- Symptomatic (e.g., hypotension, syncope):
    - *First-line*: Intravenous *Atropine* 0.5 mg IV push, repeat every 3–5 minutes to a maximum of 3 mg.
    - *If unresponsive*: Consider *temporary transcutaneous pacing*, *dopamine*, or *epinephrine infusion*.
    - In rare cases, *transvenous pacing* may be needed [36].

9. Atrioventricular (AV) blocks

AV blocks refer to delayed or interrupted conduction from the atria to the ventricles. They are stratified into *first-degree, second-degree* (Mobitz I and II), and *third-degree (complete)* blocks.

9.1 First-degree AV block

9.1.1 Pathophysiology

First-degree AV block is due to delayed conduction at the AV node without any missed beats. It is a common finding in athletes, younger patients with an increased vagal tone, and MI, particularly an inferior MI. It is typically asymptomatic and benign; therefore, it does not require treatment unless symptomatic or progressive.

9.1.2 ECG findings

- PR interval > 200 ms
- Every P wave followed by a QRS complex.

9.1.3 Second-degree AV block

Mobitz Type I (Wenckebach).

9.1.4 Pathophysiology

There is a progressive delay in AV conduction until an atrial impulse is completely blocked, resulting in a P wave that is not followed by a QRS complex. Mobitz type 1 can be a normal variant and is seen in individuals with an increased vagal tone. However, inferior myocardial ischemia may cause this rhythm.

9.1.5 ECG findings

- Progressive PR interval prolongation followed by a non-conducted P wave.
- Grouped beating pattern.

9.1.6 Management

- *Asymptomatic*: Monitor.
- *Symptomatic* (e.g., hypotension, syncope):
  - *Atropine* may be effective.
  - Pacing (transcutaneous or transvenous) rarely required due to transient nature.

9.2 Mobitz type II

9.2.1 Pathophysiology

Mobitz Type II is due to a sudden failure of conduction below the AV node (His-Purkinje system) without preceding PR prolongation. Conduction failure may be due to a variety of reasons such as infarction, necrosis, or fibrosis. There is an increased risk of progression to complete heart block, which is associated with a poor prognosis.

9.2.2 ECG findings

- Constant PR intervals with intermittent dropped QRS complexes.

9.2.3 Management

- Immediate *temporary pacing* is indicated.
- Atropine is often ineffective.
- Consider a *permanent pacemaker* if persistent or symptomatic.

9.3 Third-degree AV block

9.3.1 Pathophysiology

In complete AV block, no atrial impulses are conducted to the ventricles; as a result, atrial and ventricular activities are independent (AV dissociation).

- Can occur in both *anterior* and *inferior MIs*:
  - Inferior MI: often transient and due to AV nodal ischemia.
  - Anterior MI: indicates extensive damage and poor prognosis.

9.3.2 ECG findings

- P waves and QRS complexes are present but unrelated.
- QRS may be narrow (nodal escape) or wide (ventricular escape).

9.3.3 Management

- *Immediate temporary pacing* (transcutaneous or transvenous).
- *Permanent pacemaker* if the block persists beyond 2 weeks or is not reversible.

10. Summary of management of arrhythmic complications in ACS

The management of arrhythmias in ACS involves both immediate and long-term strategies aimed at preventing life-threatening arrhythmias, controlling symptoms, and improving prognosis.

10.1 Immediate management

- *Defibrillation*: In patients with VF or pulseless VT, immediate defibrillation is essential for survival. For patients with sustained VT or VF, resuscitation efforts should be initiated as soon as possible.
- *Antiarrhythmic medications*: Drugs such as amiodarone or lidocaine may be used for the management of sustained VT or other arrhythmias.

- *Rate control*: In cases of supraventricular arrhythmias like AF or atrial flutter, beta-blockers, calcium channel blockers, or digoxin may be used for rate control.

10.2 Long-term management

- *Implantable Cardioverter-Defibrillator (ICD)*: For patients with a history of VT or VF and low left ventricular ejection fraction (usually <35%), an ICD may be implanted for secondary prevention of sudden cardiac death.

- *Electrolyte management*: Correction of electrolyte imbalances (e.g., potassium, magnesium) is essential in preventing arrhythmias.

- *Antiarrhythmic therapy*: Long-term use of beta-blockers, ACE inhibitors, and antiarrhythmic agents may be considered for patients with ongoing arrhythmic risk.

10.3 Preventive measures

- *Coronary reperfusion*: Early coronary reperfusion *via* percutaneous coronary intervention (PCI) or fibrinolysis can prevent further ischemic injury, reducing the risk of arrhythmias.

- *Risk stratification*: Identifying patients at high risk for arrhythmias allows for early intervention, including continuous monitoring and appropriate use of medications.

11. Conclusion

Arrhythmic complications in ACS are common and can have serious consequences, including SCD. Understanding the mechanisms and risk factors for arrhythmias in ACS allows for better risk stratification and tailored management. Early recognition and treatment of arrhythmias, especially life-threatening conditions like ventricular fibrillation, are critical for improving patient outcomes. In addition to acute management, long-term strategies such as implantable cardioverter-defibrillators and appropriate use of antiarrhythmic medications can help prevent recurrence and reduce mortality in patients with ACS.

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References

[1] Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: Incidence, risk factors, and prognosis in the Manitoba follow-up study. The American Journal of Medicine. 1995;**98**(5):476-484

[2] Poçi D, Hartford M, Karlsson T, Edvardsson N, Caidahl K. Effect of new versus known versus no atrial fibrillation on 30-day and 10-year mortality in patients with acute coronary syndrome. The American Journal of Cardiology. 2012;**110**(2):217-221

[3] Schmitt J, Duray G, Gersh BJ, Hohnloser SH. Atrial fibrillation in acute myocardial infarction: A systematic review of the incidence, clinical features and prognostic implications. European Heart Journal. 2009;**30**(9):1038-1045

[4] Crenshaw BS, Ward SR, Granger CB, Stebbins AL, Topol EJ, Califf RM. Atrial fibrillation in the setting of acute myocardial infarction: The GUSTO-I experience. Global utilization of streptokinase and TPA for occluded coronary arteries. Journal of the American College of Cardiology. 1997;**30**(2):406-413

[5] Kea B, Alligood T, Manning V, Raitt M. A review of the relationship of atrial fibrillation and acute coronary syndrome. Current Emergency and Hospital Medicine Reports. 2016;**4**(3):107-118

[6] Greco A, Capodanno D. Therapeutic uncertainties: First finding of atrial fibrillation in acute coronary syndrome. European Heart Journal Supplements: Journal of the European Society of Cardiology. 2022;**24**(Suppl. I):I43-II6

[7] Liang F, Wang Y. Coronary heart disease and atrial fibrillation: A vicious cycle. American Journal of Physiology. Heart and Circulatory Physiology. 2021;**320**(1):H1-H12

[8] Freedman B, Camm J, Calkins H, Healey JS, Rosenqvist M, Wang J, et al. Screening for atrial fibrillation: A report of the AF-SCREEN international collaboration. Circulation. 2017;**135**(19):1851-1867

[9] Asgari S, Mehrnia A, Moussavi M. Automatic detection of atrial fibrillation using stationary wavelet transform and support vector machine. Computers in Biology and Medicine. 2015;**60**:132-142

[10] Androulakis A, Aznaouridis KA, Aggeli CJ, Roussakis GN, Michaelides AP, Kartalis AN, et al. Transient ST-segment depression during paroxysms of atrial fibrillation in otherwise normal individuals: Relation with underlying coronary artery disease. Journal of the American College of Cardiology. 2007;**50**(19):1909-1911

[11] Pradhan R, Chaudhary A, Donato AA. Predictive accuracy of ST depression during rapid atrial fibrillation on the presence of obstructive coronary artery disease. The American Journal of Emergency Medicine. 2012;**30**(7):1042-1047

[12] Friedman HZ, Weber-Bornstein N, Deboe SF, Mancini GB. Cardiac care unit admission criteria for suspected acute myocardial infarction in new-onset atrial fibrillation. The American Journal of Cardiology. 1987;**59**(8):866-869

[13] Vranckx P, Valgimigli M, Jüni P, Hamm C, Steg PG, Heg D, et al. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel

or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: A multicentre, open-label, randomised superiority trial. Lancet. 2018;**392**(10151):940-949

[14] Frampton J, Ortengren AR, Zeitler EP. Arrhythmias after acute myocardial infarction. The Yale Journal of Biology and Medicine. 2023;**96**(1):83-94

[15] Johner N, Namdar M, Shah DC. Typical atrial flutter: A practical review. Journal of Cardiovascular Electrophysiology. Published online January 7, 2025. DOI: 10.1111/jce.16542

[16] Rodriguez Ziccardi M, Goyal A, Maani CV. Atrial flutter. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540985/ [Updated 2022 Dec 8]

[17] January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. Heart Rhythm. 2019;**16**(8):e66-e93

[18] Solomon SD, Zelenkofske S, McMurray JJ, Finn PV, Velazquez E, Ertl G, et al. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. The New England Journal of Medicine. 2005;**352**(25):2581-2588

[19] Gianni C, Burkhardt JD, Trivedi C, Mohanty S, Natale A. The role of the Purkinje network in premature ventricular complex-triggered ventricular fibrillation. Journal of Interventional Cardiac Electrophysiology. 2018;**52**(3):375-383

[20] Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. Heart Rhythm. 2018;**15**(10):e190-e252

[21] Ruberman W, Weinblatt E, Goldberg JD, Frank CW, Shapiro S. Ventricular premature beats and mortality after myocardial infarction. The New England Journal of Medicine. 1977;**297**(14):750-757

[22] Rautaharju PM, Surawicz B, Gettes LS, Bailey JJ, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part IV: The ST segment, T and U waves, and the QT interval: A scientific statement from the American Heart Association electrocardiography and arrhythmias committee, council on clinical cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. Journal of the American College of Cardiology. 2009;**53**(11):982-991

[23] Echt DS, Liebson PR, Mitchell LB, Peters RW, Obias-Manno D, Barker AH, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The cardiac arrhythmia suppression trial. The New England Journal of Medicine. 1991;**324**(12):781-788

[24] Thomas DE, Jex N, Thornley AR. Ventricular arrhythmias in acute coronary syndromes—Mechanisms and management. Continuing Cardiology Education. 2017;**3**(1):22-29

[25] Whitaker J, Wright MJ, Tedrow U. Diagnosis and management of ventricular tachycardia. Clinical Medicine (London, England). 2023;**23**(5):442-448

[26] de Bakker JM, van Capelle FJ, Janse MJ, Tasseron S, Vermeulen JT, de Jonge N, et al. Slow conduction in the infarcted human heart. 'Zigzag' course of activation. Circulation. 1993;**88**(3):915-926

[27] Gildea TH, Levis JT. ECG diagnosis: Accelerated Idioventricular rhythm. The Permanente Journal. 2018;**22**:17-173

[28] Perron AD, Sweeney T. Arrhythmic complications of acute coronary syndromes. Emergency Medicine Clinics of North America. 2005;**23**(4):1065-1082

[29] Riera AR, Barros RB, de Sousa FD, Baranchuk A. Accelerated idioventricular rhythm: History and chronology of the main discoveries. Indian Pacing and Electrophysiology Journal. 2010;**10**(1):40-48

[30] Kong MH, Fonarow GC, Peterson ED, Curtis AB, Hernandez AF, Sanders GD, et al. Systematic review of the incidence of sudden cardiac death in the United States. Journal of the American College of Cardiology. 2011;**57**(7):794-801

[31] Perman SM, Elmer J, Maciel CB, Uzendu A, May T, Mumma BE, et al. 2023 American Heart Association focused update on adult advanced cardiovascular life support: An update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2024;**149**(5):e254-ee73

[32] Nachimuthu S, Assar MD, Schussler JM. Drug-induced QT interval prolongation: Mechanisms and clinical management. Therapeutic Advances in Drug Safety. 2012;**3**(5):241-253

[33] Vieweg WV, Hancox JC, Hasnain M, Koneru JN, Gysel M, Baranchuk A. Clarithromycin, QTc interval prolongation and torsades de pointes: The need to study case reports. Therapeutic Advances in Infectious Disease. 2013;**1**(4):121-138

[34] Crotti L, Hu D, Barajas-Martinez H, De Ferrari GM, Oliva A, Insolia R, et al. Torsades de pointes following acute myocardial infarction: Evidence for a deadly link with a common genetic variant. Heart Rhythm. 2012;**9**(7):1104-1112

[35] Thomas SH, Behr ER. Pharmacological treatment of acquired QT prolongation and torsades de pointes. British Journal of Clinical Pharmacology. 2016;**81**(3):420-427

[36] Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, et al. 2018 ACC/AHA/HRS guideline on the evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. Circulation. 2019;**140**(8):e382-e482

Chapter 6

Protocol-Driven Triage and Management of Acute Coronary Syndrome in Non-tertiary Cardiac Centers

Ibrahim Abdullah Mohammed Abdulhabeeb

Abstract

Acute coronary syndrome (ACS) encompasses a spectrum of ischemic cardiac events, including unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). It results from coronary artery occlusion due to plaque rupture, thrombosis, or endothelial dysfunction, leading to myocardial ischemia or infarction. Early recognition and classification of ACS are crucial for timely intervention and improved prognosis. Electrocardiography (ECG) and high-sensitivity troponins (hs-Tn) form the cornerstone of ACS diagnosis, guiding urgent risk stratification and management decisions. Primary percutaneous coronary intervention (PCI) remains the gold standard for STEMI, while NSTEMI treatment is risk-stratified based on clinical stability and biomarker dynamics. Advances in dual antiplatelet therapy, anticoagulation, statins, and lifestyle modifications have significantly reduced mortality and recurrent events. This chapter explores pathophysiology, diagnosis, and contemporary evidence-based management strategies to optimize outcomes.

Keywords: acute coronary syndrome, myocardial infarction, STEMI, NSTEMI, unstable angina, coronary artery disease, electrocardiography, troponin, primary PCI, risk stratification, dual antiplatelet therapy, anticoagulation, statins, secondary prevention

1. Introduction

Acute coronary syndrome (ACS) is a life-threatening condition resulting from an acute reduction in coronary blood flow, leading to myocardial ischemia and potential infarction. It remains a major cause of morbidity and mortality worldwide [1]. ACS is classified into ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA), each requiring a different approach to management [2].

Over the past decade, advances in ACS management—including early reperfusion strategies, more effective antithrombotic therapies, and aggressive lipid-lowering interventions—have significantly improved patient survival and long-term outcomes [3]. However, challenges remain in early recognition, risk stratification, and timely therapeutic decision-making.

This chapter provides a structured approach to understanding ACS symptoms, causes, diagnostic methods, and treatment options, with a focus on recent guideline updates and their impact on prognosis [4].

2. Pathophysiology of acute coronary syndrome

Acute coronary syndrome (ACS) results from a sudden disruption in coronary blood flow, typically caused by atherosclerotic plaque rupture, erosion, or thrombosis, leading to varying degrees of myocardial ischemia and infarction [5]. The severity of ischemia and the extent of myocardial damage determine whether the presentation is unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), or ST-elevation myocardial infarction (STEMI) [6].

2.1 Mechanism of ACS

The progression of ACS follows a pathophysiologic continuum, beginning with coronary plaque instability and thrombus formation:

2.1.1 Plaque disruption

- Atherosclerotic plaques develop over time due to lipid accumulation, inflammation, and endothelial dysfunction [7].

- Plaque rupture or erosion exposes thrombogenic material, triggering platelet adhesion and activation [8].

2.1.2 Thrombus formation

- Platelets aggregate and release prothrombotic mediators (e.g., thromboxane A2, ADP, and serotonin), leading to fibrin clot formation [9].

- The degree of thrombus formation determines the severity of coronary obstruction and whether it results in UA, NSTEMI, or STEMI [10].

2.1.3 Myocardial ischemia and infarction

- *Partial or transient occlusion* → Ischemia without infarction (UA) or subendocardial infarction (NSTEMI) [11].

- *Complete occlusion* → Transmural infarction (STEMI) [12].

2.2 Differentiation between UA, NSTEMI, and STEMI

See **Table 1**.

Feature	Unstable angina (UA)	NSTEMI	STEMI
Coronary occlusion	Partial, non-occlusive thrombus	Partial, transient occlusion	Complete occlusion
Myocardial necrosis	No necrosis	Subendocardial necrosis	Transmural necrosis
ECG changes	ST depression, T-wave inversion, or normal	ST depression, T-wave inversion	ST-elevation in contiguous leads
Troponins	Normal	Elevated	Significantly elevated
Management Aaproach	Risk stratification and medical therapy	Early invasive strategy (within 24 h if high-risk)	Immediate reperfusion (PCI/thrombolysis)

Table 1.
Key differences between unstable angina (UA), NSTEMI, and STEMI in terms of coronary occlusion, myocardial damage, and clinical severity.

3. Clinical presentation of acute coronary syndrome

Acute coronary syndrome (ACS) presents with a wide spectrum of symptoms, ranging from mild, transient ischemia to severe, prolonged chest pain with hemodynamic compromise [13]. The key determinant of symptom severity is the extent and persistence of myocardial ischemia, which varies between unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) [14].

Although chest pain (angina) is the most common symptom, its pattern, duration, and associated features help differentiate between these conditions. Furthermore, atypical symptoms can complicate early diagnosis, particularly in elderly, diabetic, and female patients [15].

3.1 Common symptoms of ACS

The classic symptom of ACS is retrosternal chest pain or discomfort, described as:

- Pressure, tightness, heaviness, or squeezing.
- Gradual in onset, not sudden sharp pain.
- Radiation to the left arm, neck, jaw, or epigastrium.
- Accompanied by autonomic symptoms, such as diaphoresis, nausea, vomiting, dizziness, or a sense of impending doom [16].

However, not all patients experience typical chest pain. In some cases, ACS may present atypically with:

- Dyspnea (shortness of breath) is the primary complaint.
- Epigastric discomfort, nausea, or belching, mimicking gastrointestinal symptoms.
- Palpitations, dizziness, or syncope in cases with arrhythmic complications.

- Fatigue, weakness, or confusion, especially in elderly or diabetic patients [17].
- Recognizing these variations in symptom presentation is crucial for early diagnosis and management.

3.2 Differentiating symptoms in UA, NSTEMI, and STEMI

While all ACS subtypes share the underlying cause of myocardial ischemia, their clinical manifestations differ based on the severity and duration of coronary artery occlusion [18].

3.2.1 Unstable angina (UA)

Unstable angina is characterized by transient ischemia without myocardial necrosis. It is a high-risk condition, often preceding NSTEMI or STEMI [19].

Patients with UA typically report one of the following:

1. *New-onset angina:* Chest discomfort developing within the last few weeks, occurring with mild exertion.
2. *Crescendo angina:* Previously stable angina that has become more frequent, prolonged, or intense.
3. *Rest angina:* Chest discomfort occurring at rest, lasting less than 20 minutes, but resolving spontaneously or with nitroglycerin.

Unlike myocardial infarction, pain in UA does not persist for long durations and typically improves with medical therapy. However, its unpredictability and progression risk make urgent evaluation necessary.

3.2.2 Non-ST-elevation myocardial infarction (NSTEMI)

NSTEMI represents more severe ischemia, leading to myocardial injury, but without complete coronary occlusion [20]. The clinical presentation of NSTEMI is often similar to UA, but the key distinguishing feature is that pain is more persistent and severe [21].

Patients with NSTEMI typically report:

- Prolonged chest discomfort, lasting more than 20 minutes, often occurring at rest.
- Pain that is more intense or persistent than in UA.
- Episodes of angina that no longer respond well to nitroglycerin.
- Associated symptoms such as shortness of breath, nausea, diaphoresis, and dizziness, which may indicate a higher risk of complications.

In some patients, NSTEMI may present atypically, especially in elderly, diabetic, and female patients. Instead of chest pain, these patients may experience unexplained

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dyspnea, profound fatigue, or vague discomfort in the epigastrium or back [22]. Such silent ischemia increases the risk of missed diagnosis and delayed treatment.

3.2.3 ST-elevation myocardial infarction (STEMI)

STEMI is the most severe form of ACS, caused by complete coronary occlusion, leading to transmural infarction. The clinical presentation is often dramatic, requiring immediate medical attention [23].

Patients with STEMI typically experience:

- Severe, crushing chest pain, often described as "the worst pain of my life."
- Pain lasting more than 30 minutes, with no relief from nitroglycerin or rest.
- Intense autonomic symptoms, including profuse sweating, nausea, vomiting, and a sense of impending doom.
- Severe dyspnea, especially in patients with left ventricular dysfunction or pulmonary congestion.

In some cases, STEMI does not present with classic symptoms, leading to potential misdiagnosis [24].

3.3 Clinical implications of symptom recognition

Recognizing the pattern and evolution of symptoms in ACS is crucial for:

- Distinguishing between stable and unstable ischemic conditions.
- Identifying high-risk patients who require urgent intervention.
- Reducing delays in diagnosis, particularly in atypical presentations [25].

A systematic approach to pain assessment, risk factor evaluation, and early diagnostic testing is essential for distinguishing ACS subtypes and guiding appropriate management strategies [26].

3.4 Summary

The clinical presentation of ACS varies widely, with chest pain being the most common symptom but atypical presentations frequently occurring in vulnerable populations. While unstable angina presents as transient ischemia without myocardial necrosis, NSTEMI and STEMI involve prolonged ischemia with increasing severity. Recognizing these differences and understanding when symptoms suggest high-risk ischemia is crucial for prompt and effective treatment.

4. Diagnostic approach in acute coronary syndrome

Early and accurate diagnosis of acute coronary syndrome (ACS) is critical for timely risk stratification and appropriate management. Diagnosis is based on three essential pillars:

1. Clinical presentation (previously discussed in Chapter 3)

2. Electrocardiogram (ECG) findings

3. Cardiac biomarkers, primarily troponins

The combination of these factors determines whether the patient has unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), or ST-elevation myocardial infarction (STEMI) and guides the urgency of treatment.

4.1 Electrocardiogram (ECG): The first and Most critical test

The *12-lead ECG* is the first-line diagnostic tool in ACS and should be performed within *10 minutes* of patient arrival. Its primary role is to identify *STEMI*, as early recognition enables immediate reperfusion therapy [27].

4.1.1 ECG criteria for STEMI

- ST-segment elevation ≥1 mm in at least two contiguous leads, except in:

- V2-V3, where ≥2 mm (men <40 years) or ≥ 1.5 mm (women) is required [28].

- New or presumed new left bundle branch block (LBBB) with ACS symptoms [18].

- ST-elevation patterns suggestive of specific infarct locations: STEMI Location and ECG Changes (**Table 2**)

4.1.2 ECG in NSTEMI and UA

- NSTEMI presents with ST-segment depression, T-wave inversions, or dynamic changes but no ST-elevation.

- Unstable Angina (UA) may have a normal ECG or transient ischemic changes that resolve with symptom relief [29].

- *Serial ECGs* are essential, especially in *NSTEMI/UA*, to detect evolving changes.

STEMI location	Affected coronary artery	ECG leads with ST-elevation
Anterior STEMI	Left anterior descending (LAD)	V1-V4
Inferior STEMI	Right coronary artery (RCA)	II, III, aVF
Lateral STEMI	Left circumflex (LCx)	I, aVL, V5, V6
Posterior STEMI	Left circumflex (LCx) or RCA	ST depression in V1-V3 (requires posterior leads)
Right Ventricular STEMI	Right coronary artery (RCA)	V4R (right-sided lead placement)

Table 2.
STEMI location, affected coronary artery, and ECG leads with ST-elevation.

Key Clinical Point: In *STEMI*, ECG alone is diagnostic and mandates *immediate reperfusion*. In *NSTEMI/UA*, ECG findings are supportive but *not definitive*, requiring biomarker confirmation.

4.2 Cardiac biomarkers: The key to detecting myocardial necrosis

4.2.1 High-sensitivity troponin (hs-Tn): The gold standard

Troponins (*TnI, TnT*) are highly specific for myocardial injury and remain the *biomarker of choice* for diagnosing myocardial infarction. *High-sensitivity Troponin (hs-Tn)* enables *earlier detection* compared to *conventional troponin (cTn)* [30].

hs-Tn Testing Interpretation

- Positive hs-Tn: Confirms myocardial necrosis, distinguishing NSTEMI from UA.
- *Negative hs-Tn (at 3 hours):* Strongly rules out myocardial infarction in *low-risk patients*.
- *Significant rise or fall (>20–50%)* over time confirms an acute event, differentiating *ACS from chronic myocardial injury* (e.g., heart failure and chronic kidney disease).

hs-Tn Rapid Rule-In and Rule-Out Strategies

- Single hs-Tn > 52 ng/L at admission → Strongly suggests NSTEMI or STEMI.
- hs-Tn < 5 ng/L with no ECG changes at 2 hours → Excludes myocardial infarction in low-risk patients.
- Delta Change (2-hour difference):
    - Increase >10 ng/L → Likely acute myocardial infarction.
    - Stable levels → Likely *non-ACS causes* of troponin elevation [31].

Clinical Relevance: hs-Tn enables rapid risk stratification, reducing unnecessary admissions and expediting early intervention in high-risk patients.

4.2.2 Conventional troponin I (cTnI) and troponin T (cTnT)

In settings where *hs-Tn is unavailable*, conventional troponins remain the standard. However, they require *serial measurements (0, 3, and 6 hours)* due to lower sensitivity in early detection [32].

- *cTnI/T* rises within *3–6 hours*, peaks at *12–24 hours*, and normalizes within *7–14 days*.
- A positive result (>99th percentile) confirms myocardial necrosis but does not differentiate ACS from non-ACS causes.

4.2.3 Alternative biomarkers when troponins are unavailable

If troponin testing is unavailable, creatine kinase (CK) and CK-MB may be used, but their specificity is lower (**Table 3**) [25].

Key Takeaway: Troponins (hs-Tn or cTn) should always be the first choice. CK-MB may help if troponins are unavailable, they should not be replaced.

4.3 Additional diagnostic tests

Beyond *ECG and biomarkers*, additional tests help refine diagnosis and *risk stratification*.

4.3.1 Echocardiography

- Assesses wall motion abnormalities, supporting ACS diagnosis.
- Useful in differentiating STEMI from pericarditis and NSTEMI from non-cardiac chest pain.

4.3.2 Stress testing (exercise ECG, stress Echo, or myocardial perfusion imaging)

- Used only in stable, low-risk patients to evaluate ischemia.
- Contraindicated in *acute ACS* due to the risk of *provoking infarction*.

4.3.3 Coronary angiography (definitive test)

- Urgent in STEMI for immediate PCI.
- Early invasive strategy in high-risk NSTEMI/UA.
- Identifies culprit lesions and the extent of coronary artery disease.

Biomarker	Rise time	Peak time	Normalization	Clinical utility
hs-Troponin (hs-TnI/hs-TnT)	1–3 hours	12–24 hours	7–14 days	Gold standard, highest sensitivity for myocardial necrosis
Conventional troponin I (cTnI)/troponin T (cTnT)	3–6 hours	12–24 hours	7–14 days	Less sensitive than hs-Tn but still highly specific
CK-MB	3–6 hours	12–24 hours	2–3 days	Moderate specificity, used if troponin unavailable
Total CK	4–6 hours	24–36 hours	3–4 days	Less specific, may rise with skeletal muscle injury
Myoglobin	1–3 hours	6–9 hours	1 day	Earliest marker, but lacks cardiac specificity

Table 3.
Comparison of cardiac biomarkers in ACS.

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Key Takeaway: Troponins (hs-Tn or cTn) should always be the first choice. CK-MB may help if troponins are unavailable but should not replace them.

4.4 Summary

The diagnostic approach in ACS relies on a systematic assessment combining ECG, cardiac biomarkers, and additional imaging to determine the urgency of intervention. STEMI is primarily ECG-diagnosed and requires immediate reperfusion, while NSTEMI relies on troponins for confirmation. High-sensitivity troponin (hs-Tn) has revolutionized ACS diagnosis, enabling early rule-in and rule-out strategies, improving patient triage, and reducing unnecessary admissions.

5. Management strategies in acute coronary syndrome

The management of acute coronary syndrome (ACS) aims to:

- Relieve ischemia
- Prevent infarct progression
- Reduce complications
- Improve long-term survival

The approach varies depending on the ACS subtype (*STEMI, NSTEMI, or UA*), but all patients require *immediate evaluation and stabilization* before definitive treatment.

5.1 General management for all ACS patients

Regardless of whether a patient has *STEMI, NSTEMI, or Unstable Angina (UA),* the *initial emergency management* follows the same principles.

5.1.1 Early hospital measures (first 10 minutes)

1. *Oxygen:* Only if *SpO_2 < 90%* or in respiratory distress.
2. Cardiac Monitoring: Continuous ECG monitoring for arrhythmias.
3. IV Access: Establish at least two large-bore IV lines.
4. Analgesia:
    - *Sublingual nitroglycerin* for symptom relief, unless hypotensive.
    - *Morphine (2–4 mg IV)* for persistent pain despite nitrates.

5. Antiplatelet Therapy (Dual Antiplatelet Therapy – DAPT):

   - Aspirin (Loading dose: 162–325 mg, then 81 mg daily) [6].
   - *P2Y12 inhibitor:* Ticagrelor 180 mg, Prasugrel 60 mg, or Clopidogrel 300 mg if others are contraindicated [28].

6. Anticoagulation:

   - *Unfractionated Heparin (UFH)* or *Enoxaparin*, depending on patient risk and renal function [33].

7. β-Blockers (Metoprolol, Bisoprolol) if no signs of cardiogenic shock [34].

Mnemonic for Initial ACS Management:
MONA-B (*Morphine, Oxygen, Nitrates, Aspirin, Beta-blockers*).
Once the patient is stabilized, definitive treatment is guided by the specific ACS subtype.

5.2 Specific Management for each ACS type

5.2.1 ST-elevation myocardial infarction (STEMI): Immediate reperfusion strategy

STEMI is an emergency requiring *urgent reperfusion* to restore coronary blood flow. The treatment goal is to initiate *reperfusion within*:

- 90 minutes for PCI (Percutaneous Coronary Intervention)
- 30 minutes for fibrinolysis if PCI is unavailable within 120 minutes [35]

Primary PCI – First-Line Therapy

- Preferred over fibrinolysis whenever available
- Coronary angiography followed by stenting of the culprit artery
- *Glycoprotein IIb/IIIa inhibitors* (e.g., abciximab and eptifibatide) may be used in high-risk cases [25].

Fibrinolysis – When PCI is Unavailable

- Administer Alteplase, Tenecteplase, or Reteplase within 30 minutes if PCI is not accessible within 120 minutes.
- Contraindications to fibrinolysis include:
- Active bleeding, recent major surgery, prior *hemorrhagic stroke*, or severe hypertension *(>180/110 mmHg)* unresponsive to treatment.
- If fibrinolysis is unsuccessful (indicated by persistent pain and/or less than 50% resolution of ST elevation).

Post-Reperfusion Care

- Continue DAPT for at least 12 months.
- *High-intensity statins* (Atorvastatin 80 mg or Rosuvastatin 40 mg).
- *ACE inhibitors/ARBs* for patients with *EF < 40%* or heart failure symptoms.
- Echocardiography within 24–48 hours to assess left ventricular function.

5.2.2 Non-ST-elevation myocardial infarction (NSTEMI): Risk-based strategy

NSTEMI does *not always* require immediate PCI. Management is based on *risk stratification* using the *GRACE score*:

- Very high-risk NSTEMI
  - Refractory angina, hemodynamic instability, ventricular arrhythmias, or acute heart failure → Urgent angiography within 2 hours.
- High-risk NSTEMI (GRACE score > 140, dynamic ECG changes, troponin rise, diabetes, prior MI) → Early angiography within 24 hours.
- *Low-risk NSTEMI* → Initial *medical management* with angiography within *24–72 hours* if symptoms persist [36].

Pharmacologic Treatment for NSTEMI

- *Dual antiplatelet therapy (DAPT):* Aspirin + ticagrelor/prasugrel/clopidogrel.
- Anticoagulation: UFH, enoxaparin, or fondaparinux.
- *Nitrates and β-blockers* for symptom relief.
- *PCI if ischemia persists* despite medical therapy.

Key difference from STEMI:
NSTEMI patients do not require immediate reperfusion, but urgent intervention is needed in very high-risk cases.

5.2.3 Unstable angina (UA): Conservative vs. invasive strategy

Unstable angina is clinically similar to NSTEMI but *without myocardial necrosis (normal troponins).*
Management Strategy

- High-risk UA (frequent/prolonged rest angina, ECG changes, or prior CAD) → Early invasive strategy (angiography within 24–72 hours).

- Low-risk UA (no dynamic ECG changes, resolved symptoms) → Conservative strategy with medical management.

Pharmacologic Therapy for UA

- Antiplatelet therapy (DAPT)
- Anticoagulation (UFH or enoxaparin)
- Nitrates, β-blockers, and statins for symptom control
- Stress testing after symptom stabilization to evaluate ischemia

5.3 Long-term secondary prevention for all ACS patients

After acute management, secondary prevention is critical to reduce recurrent events.

1. Dual Antiplatelet Therapy (DAPT):
    - Aspirin (81 mg daily) for life
    - *P2Y12 inhibitor* (ticagrelor, prasugrel, or clopidogrel) *for 12 months*
2. Lipid Management:
    - *High-intensity statins* (atorvastatin 80 mg or rosuvastatin 40 mg).
    - Consider PCSK9 inhibitors if LDL-C remains >55 mg/dL.
3. Blood pressure and heart failure control:
    - ACE inhibitors or ARBs for hypertension, diabetes, or EF <40%.
    - *β-Blockers* for post-MI patients with *EF < 40%*.
4. Lifestyle modifications:
    - Smoking cessation
    - Exercise and weight control
    - Diabetes control (HbA1c <7%) [37]

5.4 Summary

The management of ACS depends on early recognition, rapid stabilization, and appropriate treatment selection based on the ACS subtype.

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- STEMI requires immediate reperfusion *via* PCI or fibrinolysis.
- NSTEMI management is guided by risk stratification, with early invasive therapy in high-risk cases.
- Unstable Angina follows a similar approach to NSTEMI but does not cause myocardial necrosis.

Post-ACS care is crucial, with DAPT, statins, and lifestyle modifications playing key roles in preventing recurrent events.

6. Conclusion

Acute coronary syndrome (ACS) remains a major cause of morbidity and mortality worldwide, requiring early recognition, rapid diagnosis, and appropriate intervention to improve patient outcomes. The pathophysiology of ACS is driven by plaque instability, thrombosis, and coronary artery occlusion, with clinical manifestations ranging from unstable angina (UA) to non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI). The diagnostic approach is based on clinical symptoms, ECG findings, and cardiac biomarkers, particularly high-sensitivity troponin (hs-Tn), which has revolutionized early detection and risk stratification. ECG remains the cornerstone of STEMI diagnosis, guiding immediate reperfusion strategies, whereas biomarkers are crucial for differentiating NSTEMI from unstable angina. When hs-Tn is unavailable, conventional troponin, CK-MB, or total CK may be used, but they lack the sensitivity of hs-Tn assays.

The management strategy for ACS varies depending on the subtype:

- STEMI requires urgent reperfusion, preferably *via* primary PCI within 90 minutes, or fibrinolysis if PCI is unavailable within 120 minutes.
- NSTEMI treatment is risk-based, with early invasive management in high-risk patients and medical stabilization in lower-risk cases.
- Unstable Angina shares similarities with NSTEMI but requires tailored risk assessment, with an emphasis on conservative vs. early invasive strategies.

Beyond acute management, long-term secondary prevention is crucial to reduce recurrent events. Dual antiplatelet therapy (DAPT), high-intensity statins, β-blockers, and lifestyle modifications form the foundation of post-ACS care, along with aggressive blood pressure and glucose control.

Recent advancements in early diagnostic strategies, optimized reperfusion techniques, and enhanced pharmacological therapies have significantly improved survival rates and reduced long-term complications in ACS patients. However, ongoing challenges remain in early recognition of atypical presentations, timely intervention in high-risk NSTEMI, and ensuring adherence to secondary prevention strategies.

A systematic, evidence-based approach to ACS, integrating rapid risk stratification, individualized treatment plans, and guideline-directed therapies, remains the key to optimizing patient outcomes and reducing cardiovascular mortality.

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References

[1] Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. Journal of the American College of Cardiology. 2018;**72**(18):2231-2264

[2] Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction. European Heart Journal. 2018;**39**(2):119-177

[3] Roffi M, Patrono C, Collet J-P, et al. 2015 ESC guidelines for the management of acute coronary syndromes. European Heart Journal. 2016;**37**(3):267-315

[4] Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation. 2005;**111**(25):3481-3488

[5] White HD, Chew DP. Acute myocardial infarction. Lancet. 2008;**372**(9638):570-584

[6] Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. Circulation. 2014;**130**(25):e344-e426

[7] Falk E, Nakano M, Bentzon JF, Finn AV, Virmani R. Update on acute coronary syndromes: The pathologists' view. European Heart Journal. 2013;**34**(10):719-728

[8] Davies MJ. The pathophysiology of acute coronary syndromes. Heart. 2000;**83**(3):361-366

[9] Libby P. Mechanisms of acute coronary syndromes and their implications for therapy. The New England Journal of Medicine. 2013;**368**(21):2004-2013

[10] Ross R. Atherosclerosis—An inflammatory disease. The New England Journal of Medicine. 1999;**340**(2):115-126

[11] Ruggeri ZM. Platelets in atherothrombosis. Nature Medicine. 2002;**8**(11):1227-1234

[12] Fuster V, Badimon L, Badimon JJ. The pathogenesis of coronary artery disease and the acute coronary syndromes. The New England Journal of Medicine. 1992;**326**(5):310-318

[13] Cannon CP, Braunwald E. Unstable angina and non-ST elevation myocardial infarction. Journal of the American College of Cardiology. 2009;**54**(9):981-991

[14] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Circulation. 2013;**127**(4):e362-e425

[15] Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease. Journal of the American College of Cardiology. 2016;**68**(10):1082-1115

[16] Ibanez B, James S, Agewall S, et al. 2018 ESC guidelines for myocardial infarction management. European Heart Journal. 2018;**39**(2):119-177

[17] Jneid H, Addison D, Bhatt DL, et al. 2017 AHA/ACC clinical performance and quality measures for adults with ST-elevation and non-ST-elevation myocardial infarction. Circulation. 2017;**135**(9):e105-e141

[18] Collet JP, Thiele H, Barbato E, et al. 2020 ESC guidelines for the management

of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021;**42**(14):1289-1367

[19] Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndromes. European Heart Journal. 2011;**32**(23):2999-3054

[20] Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction. Journal of the American College of Cardiology. 2007;**50**(7):e1-e157

[21] Patel MR, Peterson ED, Dai D, et al. Low diagnostic yield of elective coronary angiography. The New England Journal of Medicine. 2010;**362**(10):886-895

[22] Canto JG, Shlipak MG, Rogers WJ, et al. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. Journal of the American Medical Association. 2000;**283**(24):3223-3229

[23] DeFilippis AP, Trainor PJ, Blaha MJ, et al. The role of chest pain characteristics in suspected acute coronary syndromes. The American Journal of Medicine. 2015;**128**(10):1129-1138

[24] McSweeney JC, Cody M, Crane PB, et al. Women's early warning symptoms of acute myocardial infarction. Circulation. 2003;**108**(21):2619-2623

[25] Gibson CM, de Lemos JA, Antman EM. Time is muscle: Translation into practice. Journal of the American College of Cardiology. 2004;**44**(5):879-882

[26] Bhatt DL, Steg PG, Mehta SR, et al. Ticagrelor compared with clopidogrel in patients with acute coronary syndromes. The New England Journal of Medicine. 2009;**361**(11):1045-1057

[27] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. Journal of the American College of Cardiology. 2013;**61**(4):e78-e140

[28] Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal. 2018;**39**(2):119-177

[29] Jaffe AS, Ravkilde J, Roberts R, et al. It's time for a change to a troponin standard. Circulation. 2000;**102**(11):1216-1220

[30] McCarthy CP, Raber I, Chapman AR, et al. Myocardial injury in the era of high-sensitivity troponin assays. JAMA Cardiology. 2019;**4**(10):1034-1042

[31] Braunwald E. Unstable angina: An etiologic approach to management. Circulation. 1998;**98**(21):2219-2222

[32] Apple FS, Sandoval Y, Jaffe AS, Ordonez-Llanos J. Cardiac troponin assays: Guide to understanding analytical characteristics and their impact on clinical care. Clinical Chemistry. 2017;**63**(1):73-81

[33] Roffi M, Patrono C, Collet J-P, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2016;**37**(3):267-315

[34] Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline on dual antiplatelet therapy. Journal of the American College of Cardiology. 2016;**68**(10):1082-1115

[35] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA STEMI management guidelines. Circulation. 2013;**127**(4):e362-e425

[36] Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for ACS management. European Heart Journal. 2011;**32**(23):2999-3054

[37] Jneid H, Addison D, Bhatt DL, et al. 2017 AHA/ACC clinical performance measures for MI. Circulation. 2017;**135**(9):e105-e141

Chapter 7

Role of Mechanical Circulatory Support in Management of Acute Coronary Syndromes

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Abstract

Selecting the optimal mechanical circulatory support (MCS) device and the timing of initiation for cardiogenic shock (CS) due to acute coronary syndromes (ACS) are nuanced decisions that depend on shock severity, the affected cardiac structures, patient comorbidities, and available expertise. We present three patients who presented with ACS complicated by CS due to different mechanisms and required different MCS devices. The first patient presented with acute inferior ST-segment elevation myocardial infarction (STEMI) complicated by right ventricular failure and an intracardiac right-to-left shunt, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was crucial in emergency management. The second patient presented with acute anterior STEMI complicated by CS, with a poor angiographic outcome, and a temporary left ventricular assist device (LVAD) was crucial for resuscitation after the failure of the intra-aortic balloon pump (IABP). The third patient was an elderly man with multiple comorbidities and chronic ischemic heart disease (IHD), who presented with non-STEMI (NSTEMI) complicated by cardiac arrest. Impella insertion was appropriate for short-term resuscitation and for supporting the percutaneous coronary intervention (PCI) procedure. A careful approach with early selective MCS use in the course of patients with ACS who are not responding to initial therapy is advisable, preferably under the guidance of a multidisciplinary shock team.

Keywords: acute coronary syndromes, mechanical circulatory support, extracorporeal membrane oxygenation, Impella, intra-aortic balloon pump, cardiogenic shock

1. Introduction

Cardiogenic shock (CS) is a life-threatening condition that complicates about 10% of patients with acute coronary syndrome (ACS), with critical hemodynamic, metabolic, and cellular dysfunctions resulting in multi-organ system failure and increased mortality [1, 2]. Clinically, CS is defined as a persistent systolic blood pressure (SBP) <90 mmHg for 30 min or the need to use catecholamines to maintain

SBP > 90 mmHg, with evidence of organ hypoperfusion and adequate intravascular volume [1]. The CS complicating ACS can be caused by left or right ventricular dysfunction, arrhythmias, acute valve dysfunction, or ventricular septum or wall rupture [1]. Management includes hemodynamic stabilization, ensuring tissue perfusion, and restoring myocardial reperfusion. Revascularization of the culprit coronary artery in patients with ACS-CS is the most effective intervention to improve outcomes and has been given as a class I recommendation by the American and European guidelines [3, 4].

Hemodynamic stabilization usually starts with vasoactive and inotropic drugs to maintain adequate cardiac output, but these drugs should be used at the least required doses and for a short duration due to their side effects, including increased myocardial oxygen requirements and arrhythmias, which will aggravate the myocardial injury and delay recovery [2, 5, 6]. Assessment of cardiac filling pressures is crucial to manage the fluid status, especially in the case of right ventricular infarction. Close invasive hemodynamic monitoring, including mean arterial blood pressure (MAP), central venous pressure (CVP), urine output, central venous oxygen saturation, and pulmonary artery catheterization in selected cases, should be done to detect the patients who deteriorate and who will need mechanical circulatory support (MCS). Blood lactate is a marker of impaired tissue perfusion, and lactate clearance was used in CS and MCS to differentiate hospital outcomes [7, 8].

Several devices have been used for MCS to achieve hemodynamic support in patients with CS due to ACS, with variable reports about efficacy and complications [3, 4, 9–11]. The conflicting results may be related to study designs, timing of MCS, revascularization, LV unloading, and the centers' experience. The routine use of IABP or VA-ECMO was not recommended by the American College of Cardiology (ACC) 2025 guidelines due to the absence of survival benefits [3]. We present three patients with ACS complicated by cardiogenic shock due to different mechanisms. They received different MCS devices after multidisciplinary discussions, and they had different clinical outcomes. We reviewed the current literature about MCS devices in patients with CS complicating ACS.

2. Patients with acute myocardial infarction (AMI) who received MCS

a. *Case 1*: A 61-year-old man with a body mass index (BMI) of 26.8 kg/m^2, systemic hypertension (HTN), diabetes mellitus (DM), ischemic heart disease (IHD), and previous percutaneous coronary interventions (PCIs) to the left anterior descending artery (LAD) and right coronary artery (RCA). He presented at the emergency room (ER) with acute inferior STEMI complicated by ventricular fibrillation (VF), for which he received three defibrillation shocks and cardiopulmonary resuscitation (CPR) for 16 minutes. After invasive ventilation and stabilization of the hemodynamics with inotropic support, the patient was shifted to the catheterization laboratory. Coronary angiography revealed RCA proximal total occlusion and free left coronary angiography. Thrombus aspiration was done, and intracoronary tirofiban was injected to achieve TIMI flow III, then stenting was done. During PCI, the patient required two defibrillation shocks and amiodarone and lidocaine injections. Temporary pacemaker was inserted because of bradycardia. Peripheral VA-ECMO was inserted *via* femoral approach for cardiorespiratory support before shifting the patient to coronary care unit (CCU) (**Figure 1**).

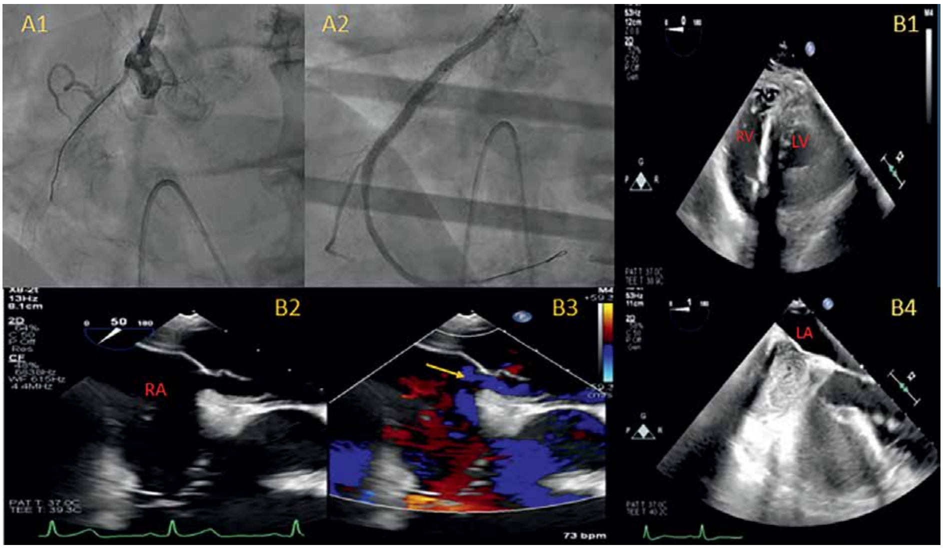

Figure 1.
Right coronary angiograms show RCA proximal total occlusion (A1) and TIMI III after PCI (A2). TEE shows good LV contractility (B1) and distended right-side chambers with patent PFO (yellow arrow, B2&3). TEE after VA-ECMO support with bubble test shows closure of the shunt (B4).

Transesophageal echocardiography (TEE) was done and revealed a normal-sized left ventricle with an ejection fraction (EF) of 45% and a dilated right ventricle with severe dysfunction. TEE showed patent foramen ovale (PFO) with right-to-left shunt due to elevated right-sided pressures. PFO explained the hypoxemia with the absence of pulmonary edema during the PCI. The TEE did not reveal significant valve dysfunction. The patient gradually regained consciousness, and brain computed tomography (CT) excluded acute brain vascular insult. The CCU course included acute kidney injury and ischemic hepatitis that gradually recovered without a need for dialysis. The patient had significant thrombocytopenia with a nadir of 41 (10^9/L) without significant bleeding. After 5 days of extracorporeal membrane oxygenation (ECMO) support, decannulation was done, and TEE revealed mild RV dilatation and mid dysfunction without any shunt. Gradual weaning of milrinone was done, and the patient required synchronized cardioversion for atrial flutter that did not recur. The patient was discharged alive without neurological deficit after a 14-day CCU stay and a 23-day hospital stay (**Figure 1**).

b. *Case 2*: A 46-year-old man with a BMI of 22.9 kg/m^2, current smoking, type II DM, systemic HTN, IHD, and previous PCI to RCA. He presented to a local hospital with acute anterior STEMI and received thrombolysis with TPA. He was referred to our tertiary care center with cardiogenic shock. Invasive mechanical ventilation was done, and inotropic support was used. Chest X-ray (CXR) revealed bilateral pulmonary congestion. The patient had acute kidney injury (AKI) and ischemic hepatitis. Continuous renal replacement therapy (CRRT) was done due to volume overload and metabolic acidosis. TTE was done and revealed mildly dilated LV with EF 35%, anterolateral akinesia, grade II diastolic dysfunction, E/e´ 13, normal RV, no valve dysfunction, and no LV thrombus. Coronary angiography was done and showed diffusely diseased LAD with mid-segment thrombus and codominant circumflex artery (CX) with a mid-segment significant lesion and occluded posterior descending artery (PDA). The RCA was codominant without significant lesions. Thrombectomy was done from the LAD and CX vessels, and intracoronary adenosine was injected. Balloon dilatation was done to the CX but showed no reflow. Intra-aortic balloon counterpulsation was used for cardiac support. Echocardiography was repeated and revealed LV end-diastolic volume (EDV) 136 ml, end-systolic volume (ESV) 101 ml, end-diastolic diameter (EDD) 5.3 cm, end-systolic diameter (ESD) 4.7 cm, EF of 25%, E/e′ 27, TAPSE 19 mm, normal RV size and function, extensive akinesia of anterior, inferior, and lateral walls, and moderate mitral regurgitation (MR) with a peak E velocity of 1.13 m/sec (**Figure 2**).

Gradual weaning off the ventilator was done after 12 days of admission, and gradual weaning off inotropes was tried many times, but the patient was inotropes-dependent due to the very poor performance of the left ventricle. A multidisciplinary discussion was done for the possibility of MCS in the form of a ventricular assist device. The decision was to postpone MCS as the patient developed bouts of fever and leukocytosis due to urinary tract infection. Hemodynamic deterioration occurred again due to combined sepsis and CS, as confirmed by the pulmonary artery catheter. Invasive mechanical ventilation was done after 7 days of extubation, and a gradual increase of inotropic support was done. After antibiotic therapy was delivered and a drop of inflammatory markers and peripheral vascular resistance occurred, the decision was made to go for temporary LVAD (CentriMag) implantation. Under general anesthesia and cardiopulmonary bypass time of 56 minutes, the LVAD was inserted. Weaning off inotropes and the ventilator was quickly achieved, and discontinuation of CRRT was done. Anticoagulation was achieved using unfractionated heparin infusion. Ambulation and physiotherapy were applied to help recovery, and the plan was to go for a durable LVAD when appropriate. After 16 days of LVAD support,

Figure 2.
Coronary angiograms show patent RCA with TIMI III (A1), CX, and OM significant lesions with no flow after PCI (red arrows, A2-4). TTE shows distended LV and normal RV size and function with TAPSE 19 mm (B1-3).

the patient had acute left-sided weakness, and brain CT imaging showed multiple hypodensities mainly at the right middle cerebral artery (MCA) and left posterior cerebral artery (PCA) territories, suggesting an embolic nature. The echocardiography was repeated, and the aortic valve was not opening, but without thrombi. MDM was done, including the neurology team for the anticoagulation, and the decision was to resume heparin but with a lower PTT target. After 5 days, the patient developed seizures with loss of consciousness; invasive mechanical ventilation was done, antiepileptic therapy was delivered, and a brain CT scan showed hemorrhagic transformation without hydrocephalus. The neurosurgery team denied any surgical intervention. Gradual deterioration of consciousness occurred, and brain death occurred. The patient was declared dead after an ICU stay of 3 months.

c. *Case 3:* An 80-year-old man with a BMI of 21.6 kg/m^2, systemic HTN, DM, chronic kidney disease (CKD), and IHD without previous revascularization. He presented at the ER with shortness of breath and orthopnea. Blood pressure (BP) was 106/66 mmHg, heart rate (HR) was 75 bpm, respiratory rate (RR) was 29 bpm, temperature was 36.6°C, and SPO2 was 86% on ambient air. Chest examination revealed bilateral wheezes and bi-basal crackles. ECG showed sinus rhythm with incomplete left bundle branch block (LBBB) and diffuse anterolateral T wave inversion. CXR revealed an increased cardiothoracic ratio, bilateral hilar congestion and accentuated broncho-vascular markings. Initial laboratory workup revealed hemoglobin of 104 g/L, a platelet count of 253 (10^9/L), a white blood cell count of 7.6 (10^9/L), serum creatinine of 193 umol/L, serum Na of 141 mmol/L, pro-BNP of 7372 ng/L, alanine transaminase of 23 unit/L, procalcitonin of 0.3 mcg/L, and Troponin-T of 0.335 mic/L. Transthoracic echocardiography (TTE) revealed a normal-sized LV with an EF of 35–40%, restrictive diastolic dysfunction, and hypokinesia of the infero-posterior and lateral walls. The RV was normal in size and function. There was mild mitral regurgitation (MR), moderate tricuspid regurgitation (TR), and PASP 55 mmHg. Anti-failure treatment started with intravenous nitrates, vasodilators, diuresis, dual antiplatelets, and therapeutic anticoagulation. Simple nasal oxygen was applied, and the patient did not require mechanical ventilation. The diagnosis was made as a non-STE myocardial infarction (NSTEMI), for which coronary angiography was done and revealed a normal left main (LM) artery bifurcating into LAD and CX. The LAD showed a proximal focal stenotic lesion of around 80% with TIMI III. The CX showed proximal subtotal occlusion with TIMI I flow and diffusely diseased obtuse marginal (OM) branches with TIMI II flow. The RCA showed proximal total occlusion with retrograde filling from the left system. Many trials of PCI to CX were done but were unsuccessful. Because of renal impairment, the procedure was aborted and planned for a new trial later on. The patient started to have deterioration of renal function, and serum creatinine reached 273 umol/L, but he did not require renal replacement therapy. After 5 days of initial catheterization, cardiac arrest in ventricular fibrillation happened, defibrillation shock was delivered, and CPR was done for 9 minutes. Invasive mechanical ventilation was done, and inotropic support was used. The decision was made to go for Impella insertion and trial of PCI. Stenting of the LAD proximal segment was done. Removal of the Impella was done, and gradual weaning off inotropes and the ventilator happened. The patient was discharged alive without the need for dialysis (**Figure 3**).

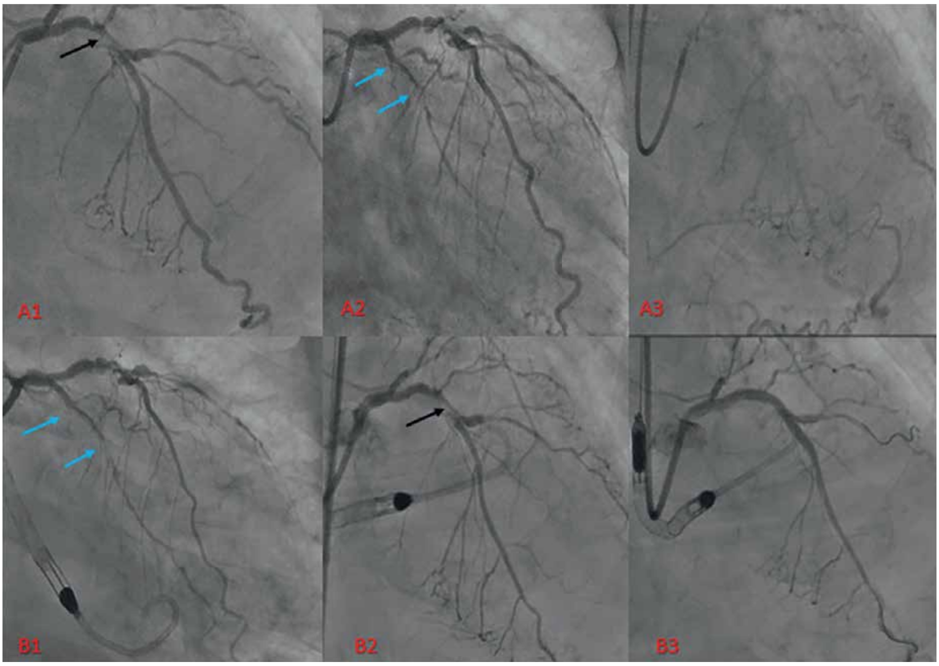

Figure 3.
Coronary angiogram showed LAD proximal significant lesion (A1, black arrow), CX and OM subtotal lesions with TIMI I-II (A2, blue arrows), and retrograde filling of RCA (A3). Impella-supported PCI (B1-3) showed successful stenting of the LAD proximal segment with TIMI III.

3. Discussion

3.1 Pathophysiology of cardiogenic shock in ACS

Cardiogenic shock (CS) complicating acute coronary syndromes (ACS) is a state of critical end-organ hypoperfusion caused by primary pump failure. Following a large acute myocardial infarction (AMI), extensive loss of myocardium leads to a sharp decline in contractility and cardiac output, precipitating hypotension and tissue hypoperfusion [6, 12]. Compensatory neurohormonal mechanisms activate immediately—catecholamine surge and renin-angiotensin-aldosterone system (RAAS) upregulation—which initially attempt to maintain perfusion but ultimately worsen the hemodynamics. These mechanisms induce peripheral vasoconstriction and fluid retention, raising afterload and preload on an already failing left ventricle [13]. The result is often a vicious cycle: reduced cardiac output leads to ischemia of the remaining myocardium, further impairing contractility and propagating shock. At the cellular level, prolonged ischemia and oxidative stress trigger an intense inflammatory response. In CS, there is evidence of a systemic inflammatory state analogous to sepsis, with cytokine release and nitric oxide overproduction causing maldistribution of blood flow and loss of vascular tone with microcirculatory dysfunction [14]. Inflammation and oxidative damage also induce myocardial stunning and cell death beyond the initial infarct. Hence, CS after AMI is not purely a consequence of pump failure but a complex multisystem syndrome involving systemic inflammatory activation, vasodilatory shock features, and microvascular collapse [14].

The clinical consequences are multi-organ in scope. Impaired forward output and hypotension lead to inadequate coronary perfusion (worsening myocardial ischemia) and reduced renal and hepatic blood flow, causing acute kidney injury and ischemic hepatitis [14]. Anaerobic metabolism ensues, evidenced by lactic acidosis. Hyperlactatemia and rising filling pressures indicate the shock spiral: as cardiac output drops, elevated left ventricular end-diastolic pressure (LVEDP) and pulmonary capillary wedge pressure cause pulmonary edema, hypoxemia, and further strain on the heart. Systemically, patients exhibit cool, clammy skin, poor urine output, and altered mental status from hypoperfusion. If unbroken, this cascade rapidly progresses to irreversible shock and death. Despite modern reperfusion therapies, in-hospital mortality of AMI with CS remains around 40–50% [12]. This stark figure underscores that, beyond opening the infarct artery, adjunctive strategies are needed to interrupt the downward spiral of CS in ACS.

3.2 Potential benefits of mechanical circulatory support

Mechanical circulatory support (MCS) devices are designed to stabilize hemodynamics in CS by increasing organ perfusion and unloading the failing heart. A range of devices is available—from intra-aortic balloon pumps (IABPs) to percutaneous ventricular assist devices (VADs) and extracorporeal membrane oxygenation (ECMO)—each with distinct mechanisms to augment circulation.

- *Intra-aortic balloon pump (IABP):* The IABP is the simplest form of MCS and has been used for decades. It consists of a balloon catheter placed in the descending aorta that inflates in diastole and deflates just before systole. This counterpulsation increases diastolic pressure to improve coronary blood flow and decreases afterload during systole [15]. The net hemodynamic effect is a mild increase in cardiac output (up to ~0.5–1.0 L/min support) and reduced left ventricular wall stress, thereby lowering myocardial oxygen demand [15, 16]. By improving coronary perfusion and unloading the LV, IABP can help interrupt the ischemia-inflammation cycle in shock, though its support level is the lowest among MCS options.

- *Impella (percutaneous left ventricular assist device):* Impella devices are catheter-mounted microaxial flow pumps that actively pull blood from the left ventricle and expel it into the aorta. The Impella CP, for example, can provide ~3.5 L/min of forward flow, substantially augmenting cardiac output [17, 18]. The primary benefit of Impella is direct ventricular unloading: by continuously removing blood from the LV, it lowers LV end-diastolic volume and pressure and reduces LV wall tension [18]. This drop in wall stress and pressure translates into decreased myocardial oxygen consumption while maintaining systemic perfusion. Impella support also increases mean arterial pressure and cardiac power output, thus improving end-organ perfusion [18]. In essence, Impella serves as an "internal bypass" of the left ventricle, allowing it to rest and recover while demand is reduced. This mechanism can limit ongoing ischemia and infarct extension in AMI by reducing LV workload.

- *TandemHeart:* The TandemHeart is another percutaneous ventricular assist device that bypasses the left ventricle. It uses a transeptal cannula in the left atrium to divert oxygenated blood to an extracorporeal centrifugal pump, which then delivers blood to the femoral artery (or axillary artery) *via* an outflow cannula. The TandemHeart can provide flows of approximately 3–5 L/min [19]. Hemodynamically, it significantly increases systemic flow and cardiac power, like Impella. By shunting blood directly from the left atrium, TandemHeart reduces left atrial pressure and LV preload, indirectly unloading the left ventricle. This results in decreased pulmonary congestion and myocardial oxygen demand, comparable to the unloading achieved by Impella [19]. Unlike VA-ECMO, TandemHeart does not oxygenate blood (no membrane oxygenator in circuit) since it utilizes already oxygenated blood from the pulmonary circulation [20]. TandemHeart is typically used in severe LV failure when greater flow than an IABP can provide is needed, but it requires expertise in transseptal puncture and large-bore access.

- *Venoarterial ECMO:* VA-ECMO is the most comprehensive support, providing both cardiac and respiratory support. It drains blood from the venous system (e.g., *via* a large cannula in the femoral vein) and pumps it through an oxygenator, then returns it to the arterial circulation (*via* a cannula in a femoral or axillary artery). Modern VA-ECMO circuits can deliver 4–7 L/min of flow, effectively taking over full circulatory support [4, 21]. This ensures perfusion of vital organs even if native cardiac output is minimal. Importantly, ECMO is the only device that provides *respiratory* support, oxygenating blood and removing CO_2, which is lifesaving in patients with concurrent respiratory failure or profound hypoxemia. By maintaining systemic pressure and flow, ECMO can stabilize a patient in extremis (e.g., during cardiac arrest or refractory shock) when used as part of extracorporeal CPR. However, a key limitation is that VA-ECMO *does not unload* the left ventricle; in fact, by increasing aortic perfusion pressure, it can raise LV afterload and lead to ventricular distension if the native heart is too weak to eject. This can worsen pulmonary edema and myocardial oxygen demand unless the LV is vented. Therefore, ECMO is often used in combination with an unloading strategy (such as adding an IABP or Impella or creating an atrial septostomy) to decompress the LV [4, 21]. Despite this caveat, ECMO's ability to provide immediate full circulatory support and oxygenation makes it a crucial rescue therapy in the sickest shock patients.

In summary, MCS devices improve hemodynamics by raising cardiac output and mean arterial pressure to restore tissue perfusion, while many also directly reduce the workload on the injured myocardium. This dual approach—"pump more and work less"—can break the downward spiral of CS, giving time for definitive therapies (revascularization, pharmacologic therapy) to take effect and for stunned myocardium to recover [15, 18]. Clinical evidence supports that these devices can acutely improve hemodynamic parameters and metabolic indices in shock. For instance, early deployment of Impella in AMI shock has been shown to significantly increase cardiac power output and blood pressure while lowering filling pressures and lactate levels [16]. By sustaining organ perfusion and unloading the heart, MCS offers a *bridge to recovery or to further interventions* in a condition that otherwise carries a grave prognosis.

3.3 Timing of MCS insertion

The timing of MCS initiation in CS is a critical determinant of outcomes and has been the subject of intense investigation. An ongoing debate is whether "early" insertion of MCS (proactively, at the first signs of shock or even before shock fully manifests) is superior to "late" or rescue insertion (after medical therapy fails or shock progresses). Early MCS could theoretically stabilize hemodynamics and prevent the cascade of cellular injury, whereas late MCS might be futile once multi-organ failure has set in.

Early vs. late insertion: Observational data and pilot studies suggest that earlier initiation of MCS in CS is associated with better reversal of shock and possibly improved survival, likely because it prevents prolonged hypoperfusion. By contrast, initiating support only in refractory shock or after cardiac arrest might be "too little, too late" for many patients. The National Cardiogenic Shock Initiative (NCSI), for example, adopted a protocol of early Impella insertion (before or immediately after PCI) in AMI-CS and reported remarkably high survival to discharge (~71%) in a pilot cohort [22]. Although non-randomized, these results bolster the concept of rapid hemodynamic support—encapsulated in the phrase "door-to-support time," analogous to door-to-balloon time. Early MCS may mitigate ongoing myocardial injury by unloading during an infarct and maintaining end-organ perfusion, thereby avoiding the spiraling organ dysfunction [22, 23].

The IABP-SHOCK II trial [13] provides insight into one end of the spectrum: it tested routine early use of IABP versus no planned IABP in AMI shock. In that German multicenter trial, IABPs were inserted soon after shock diagnosis and prior to or during PCI in the intervention arm. The result was neutral—30-day mortality was ~40% in both groups (39.7% with IABP vs. 41.3% controls) with no significant difference. Longer-term follow-up likewise showed no mortality benefit. The trial also found no significant differences in time to hemodynamic stabilization or organ perfusion markers. Thus, early use of an IABP did not improve outcomes in a broad shock population, leading guidelines to withdraw routine IABP recommendations. Some interpret this to mean that timing is not important, but an alternate view is that the *level* of support provided by IABP is too low to impact outcomes (as later trials with more powerful devices suggest).

The DanGer Shock trial (Danish-German Cardiogenic Shock trial) investigated early active support with an Impella CP microaxial pump versus standard care in AMI with shock [18]. Patients were randomized *at presentation* to routine Impella insertion on top of usual care (including prompt PCI) or to usual care alone. Notably, randomization often occurred prior to revascularization (57% were randomized before PCI), and the Impella was placed immediately after randomization, with a median insertion time of ~15 minutes. DanGer Shock found a significant reduction in 6-month mortality with early Impella support: 45.8% mortality in the Impella group vs. 58.5% in standard care (HR 0.74, $p = 0.04$) ~13% at 6 months in favor of early LV unloading. However, this benefit came at the cost of more frequent complications. The implications are that aggressive early unloading might improve survival in AMI-CS, supporting the paradigm of "early MCS"—at least with a device capable of substantial hemodynamic support. DanGer Shock's positive outcome contrasts with IABP-SHOCK II and raises the hypothesis that timing plus device selection both matter: a higher level of support instituted early can favorably alter the trajectory of shock [13, 18].

Another facet of timing is the concept of unloading the myocardium *even before* reperfusion in AMI to reduce infarct injury. The Door-to-Unloading approach was tested in a pilot Door-To-Unload (DTU) trial in anterior STEMI patients without shock [16]. Patients were randomized to immediate PCI vs. 30 minutes of Impella CP unloading prior to PCI. Importantly, all patients were hemodynamically stable (no shock); the goal was to see if delaying reperfusion slightly to unload the ventricle could limit reperfusion injury. The DTU pilot demonstrated that a 30-minute delay for LV unloading is feasible and safe: adherence to the unloading protocol was 100%, and there was no increase in 30-day MACE (major adverse events) or infarct size compared to immediate PCI [16]. In fact, unloading-first showed a trend toward smaller infarct size in high-risk patients (those with large anterior ST elevations). While not directly a shock trial, this study suggests that *preemptive* support does not harm and may confer myocardial protection. Translating this to shock, one could infer that initiating support as early as possible—perhaps even prior to or during revascularization—could improve cardiac recovery and outcomes.

On the other hand, the very late initiation of MCS, after prolonged shock or cardiac arrest, has poor outcomes. In *IMPRESS* [15], a small trial of patients in CS (nearly 90% had cardiac arrest before device insertion), Impella 2.5 was compared to IABP as a late rescue strategy. The population was extremely sick (median lactate ~8 mmol/L, many with anoxic brain injury). The trial found no difference in 30-day mortality: ~46% for Impella vs. 50% for IABP ($p = 0.92$), and by 6 months, both groups had 50% mortality. Notably, the Impella conferred higher complication rates (33% major bleeding vs. 8% with IABP) without a survival advantage. The authors noted that the late timing (post-cardiac arrest in many) likely negated potential benefits—many deaths were due to neurological injury, meaning hemodynamic support came too late to change the outcome. This underscores that once shock is very advanced, even the most powerful MCS may not rescue the patient. The *ECLS-SHOCK trial* [17] similarly tested the routine early ECMO vs. no ECMO in AMI shock and found no 30-day mortality difference (47.8 vs. 49.0%), with most patients in both arms receiving some form of late rescue support as needed. Thus, if MCS is initiated only after deterioration or used indiscriminately without patient selection, the benefits may not materialize.

In aggregate, the evidence suggests that *timing is crucial*. Early initiation of MCS (particularly with effective LV unloading) appears beneficial in improving hemodynamics and possibly survival. The best scenario is likely early recognition of shock (or impending shock) and rapid deployment of support *before* irreversible end-organ damage or cardiac arrest occurs. This must be balanced against the risks of devices and the reality that not all patients will benefit (e.g., those with overwhelming neurological injury or multi-organ failure on presentation). A reasonable approach is to consider MCS at the first signs of persistent instability despite initial therapy, rather than waiting until fulminant shock ensues.

3.4 Complications associated with MCS

The decision to use MCS in ACS must carefully weigh the potential benefits against device-related complications. All forms of MCS carry a nontrivial risk of adverse events, owing to the need for large-bore vascular access, continuous blood-contacting pumps, and the critical condition of patients. Major complications include bleeding, thrombosis (and embolism), limb ischemia, infection, and device malfunctions.

- *Bleeding:* Bleeding is among the most common complications, exacerbated by the combination of large cannulas and necessary systemic anticoagulation. Gastrointestinal bleeding, access site bleeding, and surgical-site bleeding (if surgical MCS) are frequently observed. In ECLS-SHOCK, for example, moderate or severe bleeding occurred in 23% of ECMO-supported patients versus 10% in those managed medically [17]. Similarly, Impella devices have been associated with higher rates of major bleeding; the IMPRESS trial noted 33% of Impella patients had a major bleed vs. 8% with IABP [15]. Bleeding may require transfusions and can worsen outcomes by inducing anemic hypoxia or hypotension. Meticulous anticoagulation management and frequent monitoring are required to minimize hemorrhagic risk.

- *Thrombosis and embolism:* All MCS circuits predispose to thrombus formation due to contact between blood and artificial surfaces and altered flow patterns. Thrombi can form on device surfaces (oxygenator, pump components, or cannulas) and embolize, causing strokes or systemic emboli. The IABP has a lower thrombosis risk but still requires anticoagulation to prevent catheter thrombus. Impella pumps can cause thrombus if flow is suboptimal or during positioning; device-related stroke is an infrequent but devastating risk. VA-ECMO circuits are particularly thrombogenic—clots can form in the oxygenator or cannulas and embolize systemically or to the brain. Systemic thromboembolism rates on ECMO vary, but stroke rates of 5–15% have been reported in some series [24, 25]. Meticulous anticoagulation is mandatory, though it increases bleeding risk, creating a challenging balance.

- *Limb ischemia and vascular injury:* Arterial access for MCS can compromise limb perfusion. Large-bore cannulas (15–19 Fr for ECMO, 14 Fr for Impella CP, etc.) placed in the femoral artery can occlude flow to the leg. Without prophylactic measures (such as placement of a distal perfusion catheter), critical limb ischemia can develop. In the ECMO arm of ECLS-SHOCK, 11% of patients suffered a peripheral vascular complication requiring surgical intervention, compared to ~4% in controls [17]. IABP, with a smaller 7.5 Fr sheath, has a lower incidence (~2–4% limb ischemia). Proper cannula size selection relative to artery diameter and use of reperfusion catheters can reduce this risk. Beyond ischemia, vascular complications also include arterial dissection or perforation, which can occur during large sheath insertion [26, 27]. These can be catastrophic, requiring emergent surgical repair. Careful ultrasound-guided access and prompt surgical consultation for any signs of vascular compromise are essential when using large devices.

- *Infection:* The invasive nature of MCS and the critical illness of the host predispose to infections. Common infection sites include the catheter insertion sites (leading to local infection or bacteremia), the urinary tract (from indwelling catheters), and the lungs (especially if mechanical ventilation is also used). Each additional day on MCS is a risk factor for infection, so strict aseptic technique during insertion and maintenance and early weaning of unnecessary lines are important [28]. If a patient stabilizes, shifting from femoral cannulation to an axillary approach for IABP or surgical placement of an LVAD can allow ambulation and may lower infection risk at groin sites. Empiric antibiotics are not routinely recommended, but a low threshold for surveillance cultures and prompt treatment of suspected infection are warranted in these immunocompromised patients.

- *Device malfunction:* Mechanical failures can occur, including pump stoppage, oxygenator failure, tubing rupture or kinking, and console issues. IABPs can migrate or rupture, which may cause acute loss of support or embolization of balloon debris. Impella devices may reposition or suction against the ventricle, causing abrupt hemodynamic deterioration until repositioned. ECMO circuits can crack, or pump motors can overheat or fail. Regular equipment checks and having backup components ready (e.g., a spare oxygenator or pump) are part of the protocol in advanced centers.

- *Hemolysis:* This is a specific complication of rotary pumps like Impella or TandemHeart—high shear forces can lyse red blood cells, leading to hemoglobinuria and renal injury. Markers of hemolysis (plasma-free Hb, LDH) should be monitored. If severe hemolysis occurs, it may necessitate device speed adjustments or exchange.

In summary, MCS should be deployed with an appreciation of these risks. Multidisciplinary shock teams must employ strategies to mitigate complications: meticulous access technique and limb perfusion monitoring to prevent ischemia, protocolized anticoagulation and monitoring to balance bleeding vs. clotting risks, and vigilant sterile technique and surveillance for infection. It is this delicate risk-benefit balance that partly explains why randomized trials of MCS in shock have sometimes failed to show outcome improvements—any potential survival benefit may be offset by device-related morbidity if devices are used without careful management. Thus, patient selection and complication management are as important as the decision to initiate support.

3.5 Choosing the appropriate MCS modality for each patient

Selecting the optimal MCS device for a given patient with CS is a nuanced decision that depends on shock severity, the affected cardiac structures (left, right, or biventricular failure), patient comorbidities, and available expertise. A useful framework is the SCAI shock stage classification, which stratifies shock severity from Stage A ("at risk") to Stage E ("extremis") and can guide escalation of support [29]. In general, as shock severity (SCAI stage) increases, the need for more robust support and possibly combination devices rises. Clinical parameters such as blood pressure, lactate, use of catecholamines, and end-organ function also inform the choice.

- *Beginning shock (SCAI Stage B):* For patients with hypotension responsive to fluids or low-dose inotropes and no signs of organ hypoperfusion, invasive MCS may not be immediately required. Careful monitoring in an ICU with possible IABP support can be considered if the patient has ongoing ischemia or mild pump failure. An IABP is the least invasive device and can be inserted rapidly. While routine use is not indicated for all, in patients with borderline hemodynamics or ischemia (e.g., large anterior MI with hypotension but not fulminant shock), an IABP might be a reasonable choice to improve coronary perfusion and reduce afterload as a temporizing measure. Current European guidelines suggest IABP *may* be considered (Class IIa) in the special scenario of cardiogenic shock due to mechanical complications of MI (e.g., acute VSD or severe MR), where it can stabilize the patient as a bridge to surgical repair. Otherwise, routine IABP use in AMI shock is not recommended (Class III), given the lack of benefit in trials [4].

- *Classic cardiogenic shock (Stage C):* In cases of hypotension with hypoperfusion, more active support is typically indicated. If predominantly left ventricular failure (e.g., large LV infarct) is present, a percutaneous LV assist device like the Impella CP is often a logical choice. Impella can be deployed in the cath lab at the time of PCI in an unstable STEMI patient. It provides significant hemodynamic augmentation and unloads the LV, which can be crucial in halting the shock spiral. Clinical guidelines and studies increasingly support the early use of Impella in appropriate patients [3, 30]. Patient factors guiding Impella choice include adequate aortic valve anatomy (no mechanical valve or severe calcification), no aortic regurgitation, and peripheral access large enough for the 14 Fr sheath. If the patient has these, Impella CP can be rapidly placed. In right ventricular shock (acute RV failure, e.g., RV infarct or pulmonary embolism), an Impella RP or a venoarterial ECMO might be more appropriate, as left-sided devices will not directly support the RV. Impella RP is a percutaneous RVAD inserted *via* venous access to pump blood from the RA to the pulmonary artery, indicated if isolated RV shock with preserved LV [3, 30].

- *Deteriorating shock (Stages D and E):* For patients worsening despite initial support (e.g., on high-dose vasopressors and an Impella but still hypotensive or developing multi-organ failure), escalation to VA-ECMO or combination support is often necessary. VA-ECMO is suitable in this scenario because it can provide full biventricular support and oxygenation, essentially stabilizing the circulation when the heart cannot maintain any output. It is particularly indicated if the patient is in profound shock or cardiac arrest, where ECMO can serve as salvage (eCPR). For example, a patient in refractory ventricular fibrillation arrest from MI might be placed on ECMO emergently to restore circulation. However, because ECMO increases afterload, in a patient with some LV function remaining, one might combine ECMO with an Impella or IABP to vent the LV (the so-called ECPella approach) [31]. The need for combination therapy can be decided by monitoring pulmonary pressures and LV size on echo after ECMO initiation—if the LV is distending, adding an unloading device is indicated.

TandemHeart may be chosen in centers experienced with it, particularly if very high flows are needed and the team is skilled in transseptal access. In practice, TandemHeart has similar indications to Impella for LV shock, but its use has been somewhat supplanted by Impella due to ease of insertion. It might be considered if an Impella is insufficient or contraindicated (e.g., LV thrombus might favor TandemHeart since its inflow is in LA).

Patient-specific factors are crucial in modality selection. For instance, peripheral arterial disease might preclude femoral ECMO or large Impella placement—in such cases, an axillary IABP or surgically placed axillary Impella 5.5 (which provides ~5 L/min of support) could be used to avoid limb ischemia. If the shock is due to an acute mechanical defect (like papillary muscle rupture causing acute mitral regurgitation), IABP is often the first choice to stabilize hemodynamics by reducing afterload and improving coronary perfusion until surgical repair, as reflected in guidelines (Class IIa for IABP in mechanical complications) [4]. In patients who are candidates for transplant or durable LVAD, the use of surgical LVAD (like CentriMag as a temporary surgical LVAD) or ECMO as a bridge may be considered, with early involvement of heart failure teams.

Clinical guidelines emphasize individualized selection and the importance of expertise. The ESC guidelines on ACS reiterate that routine use of short-term MCS in CS has not yet shown outcome improvement in randomized trials, and they call for reserving MCS for patients who do not stabilize with medical therapy and for use in experienced centers (generally a Class IIb recommendation for considering MCS in refractory shock). They specifically recommend against routine IABP in MI shock (Class III) except in mechanical complications, as noted above [4].

The American Heart Association (AHA) consensus documents advocate a shock team approach: a multidisciplinary team rapidly assesses the patient's SCAI shock stage and etiology of shock and then determines the best device or combination for that scenario [3, 30]. This approach ensures that factors like the patient's size, peripheral access, cardiac anatomy, and comorbid conditions (e.g., bleeding risk) are considered alongside hemodynamic needs. It also facilitates timely implantation—ideally, a protocol is in place such that if a patient is, say, SCAI Stage C and on high-dose vasopressors, an Impella is placed within an hour, but if they progress to Stage D/E, escalation to ECMO is triggerable without delay [3, 30].

In summary, choosing the right MCS involves matching the device's capabilities to the patient's needs: smaller support (IABP) for mild shock or specific indications, percutaneous LV or RV assist (Impella, TandemHeart, Impella RP) for predominant ventricle failure in moderate shock, and VA-ECMO for severe biventricular or cardiac arrest situations. Institutional experience is key—centers with a high volume of shock cases tend to have better outcomes, presumably due to proficiency in device insertion and complication management. Guidelines increasingly stress that MCS should be used in centers of excellence or *via* hub-and-spoke models where patients can be transferred to specialized centers if needed. Ultimately, the goal is to provide sufficient support to maintain perfusion and myocardial rest, but not to overuse devices in patients unlikely to benefit. Careful patient selection—considering factors like neurologic status (no benefit to escalate support if severe anoxic brain injury is already present), reversible vs. irreversible cause of shock, and contraindications—is essential in deciding not only which device to use, but whether to use MCS at all.

4. Conclusions

Recent studies provide more nuanced support for MCS in ACS-related shock: *targeted, early LV unloading (Impella/TandemHeart) in appropriate patients may improve outcomes*, whereas indiscriminate use of ECMO or IABP in all shock patients does not confer benefit. Current guidelines incorporate these findings by advocating a tailored approach: The use of MCS should be selected early in the course for patients who are not responding to initial therapy, preferably under the guidance of a multidisciplinary shock team and in centers with expertise. Ongoing and future trials (such as the Door-to-Unload pivotal trial and large registries) will further refine these recommendations. The goal is to improve the still-unacceptably high mortality of CS by deploying MCS in a way that maximizes benefit and minimizes harm—an objective that demands both sound evidence and sound clinical judgment.

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References

[1] Zeymer U, Bueno H, Granger CB, Hochman J, Huber K, Lettino M, et al. Acute Cardiovascular Care Association position statement for the diagnosis and treatment of patients with acute myocardial infarction complicated by cardiogenic shock: A document of the Acute Cardiovascular Care Association of the European Society of cardiology. European Heart Journal Acute Cardiovascular Care. 2020;**9**(2):183-197. DOI: 10.1177/2048872619894254. Epub 2020 Mar 2

[2] Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, et al. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. Journal of the American Heart Association. 2014;**3**(1):e000590. DOI: 10.1161/JAHA.113.000590

[3] Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the Management of Patients with Acute Coronary Syndromes: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2025;**151**(13):e771-e862. DOI: 10.1161/CIR.0000000000001309. Epub 2025 Feb 27. Erratum in: Circulation. 2025 Apr;151(13):e865. DOI: 10.1161/CIR.0000000000001328

[4] Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC guidelines for the management of acute coronary syndromes. European Heart Journal Acute Cardiovascular Care. 2024;**13**(1):55-161. DOI: 10.1093/ehjacc/zuad107. Erratum in: Eur Heart J Acute Cardiovasc Care. 2024;13(5):455. DOI: 10.1093/ehjacc/zuad156

[5] Thiele H, Ohman EM, de Waha-Thiele S, Zeymer U, Desch S. Management of cardiogenic shock complicating myocardial infarction: An update 2019. European Heart Journal. 2019;**40**(32):2671-2683. DOI: 10.1093/eurheartj/ehz363

[6] van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, et al. Council on quality of care and outcomes research; and mission: Lifeline. Contemporary Management of Cardiogenic Shock: A scientific statement from the American Heart Association. Circulation. 2017;**136**(16):e232-e268. DOI: 10.1161/CIR.0000000000000525. Epub 2017 Sep 18

[7] Marbach JA, Stone S, Schwartz B, Pahuja M, Thayer KL, Faugno AJ, et al. Lactate clearance is associated with improved survival in cardiogenic shock: A systematic review and meta-analysis of prognostic factor studies. Journal of Cardiac Failure. 2021;**27**(10):1082-1089. DOI: 10.1016/j.cardfail.2021.08.012

[8] Laimoud M, Machado P, Lo MG, Maghirang MJ, Hakami E, Qureshi R. The absolute lactate levels versus clearance for prognostication of post-cardiotomy patients on veno-arterial ECMO. ESC Heart Failure. 2024;**11**(6):3511-3522. DOI: 10.1002/ehf2.14910. Epub 2024 Jul 9

[9] Paddock S, Meng J, Johnson N, Chattopadhyay R, Tsampasian V, Vassiliou V. The impact of extracorporeal membrane oxygenation on mortality in patients with cardiogenic shock post-acute myocardial infarction: A systematic review and meta-analysis. European Heart Journal Open. 2024;**4**(1):oeae003. DOI: 10.1093/ehjopen/oeae003

[10] Dhruva SS, Ross JS, Mortazavi BJ, Hurley NC, Krumholz HM, Curtis JP, et al. Use of mechanical circulatory support devices among patients with acute myocardial infarction complicated by cardiogenic shock. JAMA Network Open. 2021;**4**(2):e2037748. DOI: 10.1001/jamanetworkopen.2020.37748

[11] Kieserman JM, Kuznetsov IA, Park J, Schurr JW, Toubat O, Olia S, et al. Left ventricular unloading via percutaneous assist device during extracorporeal membrane oxygenation in acute myocardial infarction and cardiac arrest. The International Journal of Artificial Organs. 2024;**47**(6):401-410. DOI: 10.1177/03913988241254978. Epub 2024 Jun 10

[12] Laghlam D, Benghanem S, Ortuno S, Bouabdallaoui N, Manzo-Silberman S, Hamzaoui O, et al. Management of cardiogenic shock: A narrative review. Annals of Intensive Care. 2024;**14**(1):45. DOI: 10.1186/s13613-024-01260-y

[13] Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. The New England Journal of Medicine. 2012;**367**(14):1287-1296. DOI: 10.1056/NEJMoa1208410. Epub 2012 Aug 26

[14] Kologrivova I, Kercheva M, Panteleev O, Ryabov V. The role of inflammation in the pathogenesis of cardiogenic shock secondary to acute myocardial infarction: A narrative review. Biomedicine. 2024;**12**(9):2073. DOI: 10.3390/biomedicines12092073

[15] Ouweneel DM, Eriksen E, Sjauw KD, van Dongen IM, Hirsch A, Packer EJ, et al. Percutaneous mechanical circulatory support versus intra-aortic balloon pump in cardiogenic shock after acute myocardial infarction. Journal of the American College of Cardiology. 2017;**69**(3):278-287. DOI: 10.1016/j.jacc.2016.10.022. Epub 2016 Oct 31

[16] Kapur NK, Alkhouli MA, DeMartini TJ, Faraz H, George ZH, Goodwin MJ, et al. Unloading the left ventricle before reperfusion in patients with anterior ST-segment-elevation myocardial infarction. Circulation. 2019;**139**(3):337-346. DOI: 10.1161/CIRCULATIONAHA.118.038269

[17] Thiele H, Zeymer U, Akin I, Behnes M, Rassaf T, Mahabadi AA, et al. Extracorporeal life support in infarct-related cardiogenic shock. The New England Journal of Medicine. 2023;**389**(14):1286-1297. DOI: 10.1056/NEJMoa2307227. Epub 2023 Aug 26

[18] Møller JE, Engstrøm T, Jensen LO, Eiskjær H, Mangner N, Polzin A, et al. Microaxial flow pump or standard care in infarct-related cardiogenic shock. The New England Journal of Medicine. 2024;**390**(15):1382-1393. DOI: 10.1056/NEJMoa2312572. Epub 2024 Apr 7

[19] Schrage B, Ibrahim K, Loehn T, Werner N, Sinning JM, Pappalardo F, et al. Impella support for acute myocardial infarction complicated by cardiogenic shock. Circulation. 2019;**139**(10):1249-1258. DOI: 10.1161/CIRCULATIONAHA.118.036614

[20] Baran DA, Grines CL, Bailey S, Burkhoff D, Hall SA, Henry TD, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheterization and Cardiovascular Interventions. 2019;**94**(1):29-37. DOI: 10.1002/ccd.28329. Epub 2019 May 19

[21] Bilchenko AO, Gritsenko OV, Kolisnyk VO, Rafalyuk OI, Pyzhevskii AV, Myzak YV, et al. Acute myocardial infarction complicated by cardiogenic shock in Ukraine: Multicentre registry analysis 2021-2022. Frontiers in Cardiovascular Medicine. 2024;**11**:1377969. DOI: 10.3389/fcvm.2024.1377969

[22] Basir MB, Lemor A, Gorgis S, Patel KC, Kolski BC, Bharadwaj AS, et al. Early utilization of mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: The National Cardiogenic Shock Initiative. Journal of the American Heart Association. 2023;**12**(23):e031401. DOI: 10.1161/JAHA.123.031401. Epub 2023 Nov 28

[23] Rao SV. Mechanical circulatory support in cardiogenic shock - Persistence and Progress. The New England Journal of Medicine. 2024;**390**(15):1436-1438. DOI: 10.1056/NEJMe2402310. Epub 2024 Apr 7

[24] Laimoud M, Ahmed W. Acute neurological complications in adult patients with cardiogenic shock on veno-arterial extracorporeal membrane oxygenation support. The Egyptian Heart Journal. 2020;**72**(1):26. DOI: 10.1186/s43044-020-00053-5

[25] Lorusso R, Barili F, Mauro MD, Gelsomino S, Parise O, Rycus PT, et al. In-hospital neurologic complications in adult patients undergoing venoarterial extracorporeal membrane oxygenation: Results from the extracorporeal life support organization registry. Critical Care Medicine. 2016;**44**(10):e964-e972. DOI: 10.1097/CCM.0000000000001865

[26] Laimoud M, Saad E, Koussayer S. Acute vascular complications of femoral veno-arterial ECMO: A single-Centre retrospective study. The Egyptian Heart Journal. 2021;**73**(1):15. DOI: 10.1186/s43044-021-00143-y

[27] Gulkarov I, Khusid E, Worku B, Demissie S, Guerges M, Salemi A, et al. Meta-analysis of the effect of vascular complications on mortality in patients undergoing femoral venoarterial extracorporeal membrane oxygenation. Annals of Vascular Surgery. 2021;**71**:488-495. DOI: 10.1016/j.avsg.2020.09.042. Epub 2020 Nov 5

[28] Aslam S, Cowger J, Shah P, Stosor V, Copeland H, Reed A, et al. The International Society for Heart and Lung Transplantation (ISHLT): 2024 infection definitions for durable and acute mechanical circulatory support devices. The Journal of Heart and Lung Transplantation. 2024;**43**(7):1039-1050. DOI: 10.1016/j.healun.2024.03.004. Epub 2024 May 1

[29] Naidu SS, Baran DA, Jentzer JC, Hollenberg SM, van Diepen S, Basir MB, et al. SCAI SHOCK stage classification expert consensus update: A review and incorporation of validation studies: This statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. Journal of the American College of Cardiology. 2022;**79**(9):933-946. DOI: 10.1016/j.jacc.2022.01.018. Epub 2022 Jan 31

[30] Henry TD, Tomey MI, Tamis-Holland JE, Thiele H, Rao SV, Menon V, et al. Invasive Management of Acute Myocardial Infarction Complicated by cardiogenic shock: A scientific statement

from the American Heart Association. Circulation. 2021;**143**(15):e815-e829. DOI: 10.1161/CIR.0000000000000959. Epub 2021 Mar 4

[31] D'Ettore N, Cardinale A, Maj G, Bertolin S, Audo A, Montisci A, et al. ECPella 5+ in patients with cardiogenic shock: Potential for improved outcomes. Journal of Cardiothoracic and Vascular Anesthesia. 2025;**39**(6):1526-1533. DOI: 10.1053/j.jvca.2025.02.017. Epub 2025 Feb 12

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