

# A Review on ST-segment elevation myocardial infarction

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**Abstract-** ST-Segment Elevation Myocardial Infarction (STEMI) is a life-threatening medical emergency characterized by complete coronary artery occlusion, leading to myocardial ischemia and subsequent necrosis. Over the years, STEMI has remained a significant cause of morbidity and mortality worldwide, necessitating a comprehensive understanding of its pathophysiology, accurate diagnostic strategies, and effective treatment approaches, early diagnosis and immediate reperfusion are the most effective ways to limit myocardial ischaemia and infarct size and thereby reduce the risk of post-STEMI complications and heart failure. Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy in patients with STEMI; if PCI cannot be performed within 120minutes of STEMI diagnosis, fibrinolysis therapy should be administered to dissolve the occluding thrombus. Thrombolytic therapy is the only effective medication for myocardial infarction (MI), cardiovascular diseases are one of the biggest global killers in the present health scenario where streptokinase can a molecule with immense therapeutic values to the developing countries, streptokinase is a biological macromolecule involved in dissolution of fibrin cloth and favourably used.

**Keywords:** STEMI, History, Evaluation, Pathophysiology, acute coronary angiography, stem cell therapy.

## 1. INTRODUCTION

The motivation for this comprehensive review of ST-Segment Elevation Myocardial Infarction (STEMI) stems from the critical importance of this cardiovascular emergency in contemporary medicine. STEMI is a significant cause of worldwide morbidity and mortality, necessitating a thorough understanding of its pathophysiology, diagnosis, and management. One of the primary research gaps this review seeks to address is the need for a comprehensive and up-to-date synthesis of the existing literature and guidelines related to STEMI. While individual studies and guidelines exist, there is a need for more total reviews that bring together the latest research findings and evidence-based recommendations. Myocardial ischemia that results from a perfusion-dependent imbalance between supply and demand leads to myocyte necrosis which develops progressively depending on different factors (organ, species, cardiac work, duration of ischemia, collateral blood flow, etc.) In patients with myocardial infarction, 30-day mortality rates are between 7.8 - 11.4 percent (data reported by the American Heart Association in 2015). Of these, 18 percent men and 23 percent women (>45 years of age) succumb within a year of their initial infarction; mortality rates are worse in both sexes 5 years post-infarction and among survivors, an important cohort develop heart failure. Investing in primary prevention for CAD is of utmost importance even in the young population with an incidence of coronary events of 1% per year in men and 0.4% in women between the ages of 30 and 54 years. In Daly's distribution by age, 6% of the total was in persons younger than 45 years and 28% in those aged 45 to 65 years. It has been suggested that etiopathogenic and prognostic characteristics of acute myocardial infarction (AMI) in young patients may differ from those in older patients. However, smoking and dyslipidaemia have been reported as the most important risk factors of this population.

Some studies have highlighted that women with STEMI present worse short- and long-term outcomes than men. In addition, young women, in particular, have worse short-term and long-term outcomes than men and that women continue to receive less-aggressive invasive and pharmacological therapy than men.

In this study, we evaluated the clinical characteristics and prognosis of a cohort of patients with premature STEMI and possible differences in regard to the sexes. We aimed to compare the survival rates of men and women with premature STEMI treated with primary PCI with the rates of the general population matching in age, sex, and geographic region. Further, the cholesterol profile and pharmacological therapy in primary and secondary prevention were evaluated in this cohort.

## STEMI

STEMI is the product of prolonged total occlusion in a pericardial coronary vessel. It is mainly due broken either occlusive or non-occlusive. The main symptom of STEMI is shortness of breath, nausea, vomiting, and

unconsciousness. Similar to angina, pain is felt in the chest, throat, arm, epigastrium, or back. Nevertheless, the pain is more severe and longer. Most patients described it as oppressive pain in the chest. The result of the electrocardiogram test indicates the ST-segment element in 12-lead and cardiac marker elevation as Troponin.

### History and Physical-

Prior to performing an ECG and collecting troponins the history and physical provide the only clues that lead to a diagnosis of myocardial infarction. Initial evaluation should include a focused physical examination and a brief history. Patients should be asked about the characteristics of the pain and associated symptoms, risk factors or history of cardiovascular disease, and recent drug use. Risk factors for an ST-elevation myocardial infarction include age, gender, family history of premature coronary artery disease, tobacco use, dyslipidaemia, diabetes mellitus, hypertension, abdominal obesity, sedentary lifestyle, a diet low in fruits and vegetables, psychosocial stressors. Cocaine use can cause an ST-elevation myocardial infarction regardless of risk factors. History of known congenital abnormalities can be helpful.

### Evaluation-

Evaluation of patients with acute onset of chest pain should begin with an electrocardiogram (ECG) and troponin level. The American College of Cardiology, American Heart Association, European Society of Cardiology, and the World Heart Federation committee established the following ECG criteria for ST-elevation myocardial infarction (STEMI):

- New ST-segment elevation at the J point in 2 contiguous leads with the cut-off point as greater than 0.1 mV in all leads other than V2 or V3
- In leads V2-V3 the cut-off point is greater than 0.2 mV in men older than 40 years old and greater than 0.25 in men younger than 40 years old, or greater than 0.15 mV in women

Patients with a pre-existing left bundle branch block can be further evaluated using Sgarbossa's criteria:

- ST-segment elevation of 1 mm or more that is concordant with (in the same direction as) the QRS complex
- ST-segment depression of 1 mm or more in lead V1, V2, or V3
- ST-segment elevation of 5 mm or more that is discordant with (in the opposite direction) the QRS complex

Epidemiology.

### Epidemiology-

Cardiovascular disease remains the leading cause of morbidity and mortality in both men and women in the United States. It is estimated that this year, approximately 720,000 Americans will have a new coronary event (AMI or death secondary to coronary heart disease) and another approximately 335,000 will have a recurrent event.<sup>5</sup> Overall, the incidence of STEMI has decreased significantly over time, including over the last decade.

### Pathophysiology-

AMI occurs when profound and prolonged ischemia leads to irreversible myocardial cell damage and necrosis. In cases of STEMI, this is typically the result of a completely obstructive intracoronary thrombus. In a landmark study, de Wood et al performed early coronary angiography in 322 patients with "transmural myocardial infarction" characterized by ST-segment elevation progressing to Q waves. At 4 hours from symptom onset, total coronary occlusion was present in 87% and decreased to 65% .

### The Pivotal role of acute coronary angiography

The safety and diagnostic potential of coronary angiography during the early hours of acute myocardial infarction was reported 40 years ago. A radial procedure is generally preferred, except in case of cardiogenic shock with a need for mechanical support. In addition to being a prelude to percutaneous coronary intervention (PCI) of the infarct-related coronary artery, acute coronary angiography allows identification of patients with multi-vessel disease who may need additional revascularisation of non-infarct-related arteries. Furthermore, clinical scenarios without thrombotic coronary obstruction such as Takotsubo syndrome and spontaneous coronary artery dissections or myocardial infarctions due to dissections of the aortic root and other conditions that may require surgical intervention can be identified and treated accordingly.

### Pharmacotherapy

According to current guidelines, to prevent stent thrombosis and/or recurrent myocardial infarction all patients are treated with dual antiplatelet therapy consisting of aspirin in combination with either clopidogrel, prasugrel or ticagrelor, usually for one year. Other durations, in particular shorter, as well as how to deal with patients with atrial fibrillation necessitating anticoagulant therapy are currently being studied. A tailored approach based on the balance of bleeding versus thrombotic risks may become the best option. Intravenous heparin is essential during acute PCI to prevent

catheter thrombosis. A large number of additional pharmacological interventions have been studied to further improve clinical outcomes. New advances in antithrombotic therapy together with preventive measures after ST-segment elevation myocardial infarction (STEMI) have been studied extensively as the clinical syndrome is an acute thrombus-driven event. Oral antiplatelet agents such as aspirin and P2Y<sub>12</sub> inhibitors like prasugrel, ticagrelor and intravenous antiplatelet agents (abciximab, eptifibatid and tirofiban), and intravenous anticoagulant agents (unfractionated heparin, low-molecular-weight heparin and bivalirudin) are the focus of research. Recently it was suggested that prasugrel might be more effective than other antiplatelet agents, without an increased bleeding risk. Furthermore, cangrelor, a rapid onset and potent intravenous P2Y<sub>12</sub> inhibitor, became available but its role has yet to be determined. A personalised approach using genetic testing to adjust and guide antiplatelet therapy may further improve outcome especially in high-risk patients. Many antithrombotic regimens, gluco-metabolic interventions and a host of other pharmacological interventions have been studied, often with promising evidence in pre-clinical studies, but so far without consistent positive results in clinical settings. As preprocedural TIMI flow, before angioplasty, is a major determinant of survival, there is a need for pharmacological interventions, including thrombolytic therapy, either at home or in the ambulance, before cath-lab arrival. Optimal secondary prevention and rehabilitation are important for long-term outcome.

### Classification of Myocardial Infarction

According to the Fourth Universal Definition of Myocardial Infarction, a myocardial infarction (MI) is defined as an acute myocardial injury accompanied by symptoms of myocardial ischemia, signs of ischemia on an ECG, or evidence of a new regional wall motion abnormality. Type 1 and type 2 MIs are distinguished by pathophysiology.) A type 1 MI is “caused by atherothrombotic coronary artery disease and usually precipitated by atherosclerotic plaque disruption (rupture or erosion)”, while a type 2 MI is “caused by a mismatch between oxygen supply and demand by a pathophysiological mechanism other than coronary atherothrombosis.” Before the routine use of acute interventions, the Killip Classification was used to predict mortality during STEMI. This system focused on physical examination and the development of heart failure to predict risk, as described below.

**Class I:** No evidence of heart failure (HF): mortality 6%

**Class II:** Findings of mild to moderate HF (S3 gallop, rales < halfway up lung fields or elevated jugular venous pressure): mortality 17%

**Class III:** Pulmonary edema: mortality 38%

**Class IV:** Cardiogenic shock defined as systolic blood pressure (BP) < 90 mm Hg and signs of hypoperfusion such as oliguria, cyanosis and sweating: mortality 67%

The original data (from 1967) showed the mortality rates listed above for each class. With advances in therapy, mortality rates have declined about 30% to 50% in each

### Targeting pathophysiological pathways in myocardial infarction: new therapeutic strategies

#### Promising treatments in animal models

Reasonable therapeutic targets in the early stages of reperfusion injury may become essential for cardiac repair so that early report on potential anti-inflammatory therapy were later challenged by experimental studies on knockout mice. Also spatial activity of anti-inflammatory intervention may have a critical role, considering that distinct signals may occur within infarcted and border zone. Furthermore, translation from mouse model to human beings presents several limitations. In humans, MI is usually triggered by sudden plaque erosion/rupture in subjects characterized by middle-aged age, comorbidities (diabetes, hypertension, and dyslipidaemia), gender differences, poly-pharmacological treatments, and genetic background. All these factors contribute to final infarct size, in addition to the ischaemic preconditioning, eventually due to previous episodes of angina or prior coronary micro embolization. On the contrary, MI is experimentally induced in anesthetized, young, healthy mice subjected to sudden coronary occlusion and reperfusion. Furthermore, the high heart rate and the small size of mouse heart ensure oxygen and nutrients supply by diffusion, so that no >70% of the AAR is actually infarcted. Concerning clinical outcome, ventricular arrhythmias are a very common cause of death in humans, whereas their incidence is very low in mice. Specifically, we included pre-clinical studies testing compounds not yet translated in human beings. In this regard, CC and CXC chemokine inhibition has been largely investigated as potential strategy to reduce reperfusion-related inflammation. However, although the inhibitors of CCL5/CCR5 (Maraviroc) and CXCL12/CXCR4 (Plerixafor) have already been approved by EMEA for clinical use in HIV infection and stem cell mobilization, respectively, the evidence in MI was disappointing. The greatest concerns arose from immunological side effects, especially in prolonged treatment. On the other hand, promising results are expected by non-selective chemokine inhibitors. The activation of cannabinoid receptor 2 (CB<sub>2</sub>) showed cardio protective effect, potentially related to a down-regulation of chemokine expression, and suppression of oxidative stress and apoptosis. Reduction of infarct size has been described in mice treated with CB<sub>2</sub> agonists, which were also effective in preventing arterial restenosis after percutaneous intervention (PCI) similarly, also adipocytokines have been suggested as potential target. By suppressing the enzymatic activity of intracellular and extracellular nicotinamide

phosphoribosyl transferase (Nampt, also called 'visfatin'), acute treatment with the compound FK866 reduced infarct size. Treatment with anti-inflammatory adipocytokines chemerin and omentin prevented reperfusion injury by suppressing leukocyte recruitment and cardiomyocyte apoptosis. Finally, inhibitors of NADPH oxidase and free radical scavenger have so far provided interesting results.

### **New strategies that target inflammation**

As discussed earlier, inflammation plays an important part in atherogenesis and plaque evolution. The CANTOS trial was the first to validate the inflammatory hypothesis in a large cohort of patients with CAD: targeting the IL-1 $\beta$  innate immune pathway with canakinumab (an anti-IL-1 $\beta$  human monoclonal antibody) led to a clinically meaningful 15% relative reduction in major cardiovascular events compared with placebo, regardless of the LDL level. The CIRT trial evaluated a different approach to target inflammation, using a therapy with low-dose methotrexate; however, this therapy did not result in lower IL-1 $\beta$ , IL-6 or C-reactive protein (CRP) levels than placebo. The trial was stopped early and did not show a difference between the groups with regard to the composite end point of non-fatal MI, nonfatal stroke or cardiovascular death. Instead, methotrexate was associated with elevations in the levels of liver enzymes, reductions in leukocyte counts and haematocrit levels and an increased incidence of non-basal-cell skin cancers. One of the explanations for the conflicting results of the CANTOS and CIRT trials may be based on the fact that CANTOS included only patients with high residual inflammatory risk and limited the enrolment to those with persistently elevated high-sensitivity CRP levels, whereas CIRT did not screen for CRP levels. Both CIRT and CANTOS enrolled patients with atherosclerosis who were in stable condition, and there are few data in the acute setting. Anakinra, an IL-1 receptor inhibitor, was evaluated in two small phase II studies among patients with acute MI, reducing high-sensitivity CRP levels. In addition to the interleukin pathway, T cell activation signalling, synthetic inhibitors of the protein tyrosine phosphatase, low doses of IL-2 and infusion of autologous regulatory T cells are in development or represent future areas of research to target inflammation in ACSs.

### **Stem cell therapy**

Stem cell therapy has been presented as a promising future therapeutic option over the past decade, particularly in cardiology. Repairing damaged tissue following an MI by injecting undifferentiated cells into the myocardium is an incredibly challenging strategy that could potentially limit the development of heart failure, regardless of the treatment administered before the PCI. However, there are many uncertainties with regard to this strategy. The regulatory mechanism of stem cell differentiation into cardiomyocytes remains unclear. Thus, which cell types should be used for cell transplantation, the mode of delivery, the optimal environment to guarantee that stem cells differentiate into cardiomyocytes and the optimal timing for stem cell transplantation remain unclear. In addition, recent calls for retraction of journal articles and the pause of the related CONCERTHF trial have contributed to the uncertainty about the role of stem cell therapy in heart failure after MI. Personalized medicine and artificial intelligence. Regardless of the pathway targeted, one of the challenges will be to identify and select the right population that may derive the greatest benefit from new treatments. Whereas trials draw inferences about populations, machine learning explores large data sets and uses algorithms that can make predictions regarding outcomes in individual patients. In health care, global interest in the potential of machine learning has increased. In fact, deep learning algorithms have already demonstrated high accuracy in detecting left ventricular diastolic dysfunction on ECG. Personalized benefit–risk estimates are another possible utilization of machine learning algorithms. Further, the use of machine learning models to define the population of interest, in everyday practice or in clinical trials, may change the way patients

### **CONCLUSION**

Over the past decade, major advances in the early detection and reperfusion strategies of acute MI have led to a substantial reduction in morbidity and mortality. To further optimize the clinical outcome in these patients, many efforts have been geared towards cardioprotection against myocardial reperfusion injury with mechanical (ischaemic post-conditioning, remote ischaemic pre-conditioning, therapeutic hypothermia and hypoxemia) and pharmacologic interventions (atrial natriuretic peptide, cyclosporine A, and exenatide). Although mechanical and pharmacologic cardioprotection in acute MI in the animal models and initial observational trials hold promise, these concepts of cardioprotection need to be further firmly tested in randomized clinical trials. In addition, stem cell therapy with BMC in acute and chronic MI have yielded promising results but still needing confirmation in larger randomized trials. The SCIPIO trial with autologous C-kit-positive cardiac stem cells and the CADUCEUS trials with cardiosphere-derived autologous stem cells application in acute MI signify reduced infarct size and improved left ventricular function that may shift the pendulum in favour of stem cell trials to further improve outcome in these patients.

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