Asian Journal of Advances in Medical Science

4(1): 1-14, 2022

PATHOPHYSIOLOGY, INVESTIGATIONS, AND MANAGEMENT IN CASES OF MYOCARDIAL INFARCTION

OMAR ELSAKA [a*], MONEER AYMAN NOURELDEAN [a], MOHAMED ADEL GAMIL [a], MOSTAFA TAREK GHAZALI [a], ASHRAF HAMADA ABD AL-RAZIK [a] AND DALIA HISHAM [a]

[a] Department of Cardiology, Mansoura University, Faculty of Medicine, Mansoura Manchester Medical Program (MMMP), Mansoura, Egypt.

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Received: 20 October 2021
Accepted: 30 December 2021
Published: 06 January 2022

Review Article

ABSTRACT

Background: Reduced or full suspension of blood flow to a region of the myocardium causes myocardial infarction (MI), sometimes known as "heart attack." Myocardial infarction can be "silent," causing hemodynamic deterioration and abrupt death, or it can be a catastrophic event that causes hemodynamic deterioration and death. The most common cause of myocardial infarction is coronary artery disease, which is the leading cause of death in the United States. The myocardium is deprived of oxygen when a coronary artery is blocked. Myocardial cell loss and necrosis can occur when the myocardium is deprived of oxygen for an extended period. Patients may complain of chest pain or pressure that spreads to the neck, jaw, shoulder, or arm. Myocardial ischemia may be accompanied by ECG alterations and elevated biochemical markers such as cardiac troponins, in addition to the history and physical exam. This exercise covers the etiology, diagnosis, and treatment of myocardial infarction, as well as the role of the interprofessional team in enhancing patient care.
Conclusion: This review article aims to review the basic pathophysiology of myocardial infarction, explain the management protocol when a patient is diagnosed with acute myocardial infarction, including all necessary laboratory and another diagnostic testing, summarise long-term management and rehabilitation for a patient post-MI, and explain interprofessional team strategies for improving care coordination and communication to advance the prevention and management of myocardial infarction.

Keywords: Coronary artery disease; fibrinolytic therapy; myocardial infarction; primary percutaneous coronary intervention; unstable angina.

1. INTRODUCTION

Reduced or full suspension of blood flow to a region of the myocardium causes myocardial infarction (MI), sometimes known as "heart attack." Myocardial infarction can be "silent" and go unnoticed, or it can be a life-threatening occurrence that results in hemodynamic worsening and death. The most common cause of myocardial infarction is coronary artery disease, which is the leading cause of death in the United States. The myocardium is deprived of oxygen when a coronary artery is blocked. Myocardial cell loss and necrosis can occur when the myocardium is deprived of oxygen for an extended

**Corresponding author: Email: omarelsaka0808@gmail.com;*

period. Patients may complain of chest pain or pressure that spreads to the neck, jaw, shoulder, or arm. Myocardial ischemia may be accompanied by ECG alterations and elevated biochemical markers such as cardiac troponins, in addition to the history and physical exam [1].

2. ETIOLOGY

The condition that causes the majority of acute coronary syndrome (ACS) instances is atherosclerosis. An acute thrombus that obstructs an atherosclerotic coronary artery causes 90 percent of myocardial infarctions (MIs). Coronary thrombosis is thought to be caused mostly by plaque rupture and erosion. Platelet activation and aggregation, coagulation pathway activation, and endothelial vasoconstriction occur as a result of plaque erosion or rupture, leading to coronary thrombosis and occlusion. Flow dynamics and endothelial shear stress are implicated in the etiology of susceptible plaque development inside the coronary vasculature. A considerable body of evidence suggests that the culprit lesions in many cases are stenoses with a diameter of less than 70% and are located proximally within the coronary tree. Coronary atherosclerosis is most noticeable near artery branching points. Atheromas with a big lipid-rich core surrounded by a thinning fibrous crown is the culprit lesions that are more prone to rupture [2].

The following are non-modifiable risk factors for atherosclerosis: Age, sex, family history of early coronary heart disease, and male-pattern baldness are all factors to consider. The following are modifiable risk factors for atherosclerosis: Tobacco use (smoking or otherwise), Hypercholesterolemia and hypertriglyceridemia, including hereditary lipoprotein abnormalities, dyslipidemia, diabetes mellitus, hypertension, and obesity are all examples of hypercholesterolemia and hypertriglyceridemia (abdominal obesity), Psychosocial stress, sedentary lifestyle and/or lack of exercise are all factors to consider. Reduced fruit and vegetable consumption, poor oral hygiene, Type A personality, elevated homocysteine levels, and the presence of peripheral vascular disease are all factors to consider [3].

Other than atherosclerosis, MI can occur for a variety of reasons. The following are non-atherosclerotic causes of MI: Vasculitis-related coronary occlusion, Hypertrophy of the ventricles (eg, left ventricular hypertrophy, hypertrophic cardiomyopathy), Coronary artery emboli are caused by cholesterol, air, or sepsis products. Coronary artery injury, Vasospasm of the coronary arteries (primary coronary vasospasm) (variant angina), The use of drugs (eg, cocaine, amphetamines, ephedrine), Arteritis, Aneurysms of the coronary arteries, for example, are types of coronary anomaly. The heavy effort, fever, or hyperthyroidism, for example, all increase oxygen demand. Hypoxemia and severe anemia are examples of factors that reduce oxygen delivery. Aortic dissection with retrograde coronary artery involvement, as well as respiratory illnesses, including influenza [4].

Hypoxia caused by carbon monoxide poisoning or acute respiratory diseases can also cause MI. Marfan syndrome, Kawasaki illness, Takayasu arteritis, progeria, and cystic medial necrosis are all conditions that can cause pediatric coronary artery disease. Acute MI in children and adolescents is uncommon. Children with acute MI usually have either an acute inflammatory condition of the coronary arteries or an anomalous origin of the left coronary artery, whereas adults develop coronary artery disease as a result of lifelong deposition of atheroma and plaque, which causes coronary artery spasm and thrombosis. Intrauterine MI can also happen, and it's commonly linked to coronary artery stenosis [5].

3. PATHOPHYSIOLOGY

Acute myocardial infarction can occur when one or more big epicardial coronary arteries are occluded for longer than 20 to 40 minutes. The occlusion is frequently thrombotic and occurs when a plaque in the coronary arteries ruptures. Because there is a paucity of oxygen in the heart, sarcolemmal disruption and myofibril relaxation occur. These mutations are one of the initial ultrastructural changes in the MI process, followed by mitochondrial abnormalities. The liquefactive necrosis of cardiac tissue occurs as a result of prolonged ischemia. From the sub-endocardium to the sub-epicardium, the necrosis spreads. It's thought that the subepicardium has better collateral circulation, which helps it live longer. The heart function is weakened depending on whatever part of the body is damaged by the infarction. The infarcted area heals by scar formation due to the myocardium's limited regeneration ability, and the heart is frequently reshaped with dilatation, segmental hypertrophy of remaining viable tissue, and cardiac dysfunction [6].

4. HISTORY AND PHYSICAL

Myocardial ischemia is caused by a mismatch between oxygen supply and demand, which can lead to myocardial infarction. Ischemic symptoms are identified using the patient's history, electrocardiographic results, and increased serum biomarkers. Chest pain, upper extremity pain,

mandibular or epigastric discomfort might occur during exercise or at rest due to myocardial ischemia. Dyspnea and tiredness, which are ischemic equivalents, can also be symptoms of myocardial ischemia. The pain in the chest is frequently retrosternal and is described as a feeling of pressure or weight. The discomfort usually radiates to the left shoulder, neck, or arms without any evident cause, and it can be intermittent or continuous. The discomfort frequently lasts longer than 20 minutes. It is usually unaffected by changes in the region's location or active movement. Sweating, nausea, stomach pain, dyspnea, and syncope are some of the other symptoms that can occur. Atypical symptoms, such as palpitations, or more severe manifestations, such as cardiac arrest, can occur as a result of a MI. MI can sometimes manifest itself without causing any symptoms [7].

5. COMPLICATIONS

Complications are frequently linked to heart damage sustained during a heart attack, which can result in abnormal heart rhythms (arrhythmias): Electrical "short circuits" can occur, resulting in abnormal heart rhythms, some of which can be fatal. A heart attack may damage so much cardiac tissue that the remaining heart muscle is unable to pump enough blood out of the heart, resulting in heart failure. Cardiac failure can be a brief condition or a chronic condition caused by substantial and irreversible heart damage. Sudden cardiac arrest occurs when the heart suddenly stops beating due to an electrical disruption resulting in an irregular heart rhythm (arrhythmia). Heart attacks raise the risk of abrupt cardiac arrest, which can result in death if not treated quickly [8].

6. EPIDEMIOLOGY

6.1 United States Statistics

Coronary artery disease (CAD) is the largest cause of mortality in the United States, with an estimated 500,000-700,000 fatalities due to CAD each year, accounting for almost one-third of all deaths in the population over the age of 35. In the United States, about 1.5 million occurrences of myocardial infarction (MI) occur each year, with a yearly incidence rate of about 600 cases per 100,000 persons. In comparison to ST-elevation MI (STEMI), the proportion of individuals diagnosed with non–ST-elevation MI (NSTEMI) has steadily increased. Despite a significant reduction in age-adjusted death rates due to acute MI since the mid-1970s, the total number of MI-related deaths in the United States has remained stable. Men have a three-fold higher mortality rate than women when it comes to acute MI. It is more common in black patients than in white patients, with the difference disappearing by the age of 75. Coronary mortality is lower in the Hispanic population than it is in the black and white populations [9].

6.2 European Statistics

In Europe, coronary artery disease is the leading cause of death. Between the mid-1960s and the mid to late 1990s, death rates linked to coronary artery disease (CAD) decreased by over 30% throughout the European Union; nevertheless, death rates associated with acute MI increased in Eastern European countries in the early 1990s, followed by a fall. Cardiovascular mortality in the Russian Federation remained unchanged [10].

6.3 Cardiovascular Disease in other Developed Countries and Developing Nations

According to a study of death certificates from the World Health Organization (WHO) database, CAD mortality in Japan was much lower than in the United States and Europe, and by the mid-1990s, it had dropped by around 30%. A considerable increase in CAD-related mortality has been observed in China, which is most likely due to an increase in cardiovascular disease risk factors, particularly smoking and dyslipidemia. Other emerging countries, such as India, Latin America, the Middle East, and Sub-Saharan Africa, are likely to have a major increase in the prevalence of CAD and related mortality, with an estimated 80 percent increase from about 9 million in 1990 to a projected 20 million by 2020. These international trends in the incidence of CAD and subsequent acute MI are thought to be largely related to the consequences of social and economic changes in these countries, which have resulted in improved healthcare access and longer life expectancies, as well as the adoption of westernized diets, reduced physical activity, and higher rates of smoking [11].

A major Canadian-led global study (INTERHEART trial) in 52 countries across Africa, Asia, Australia, Europe, the Middle East, North and South America discovered nine easily measured risk factors (smoking, abnormal blood lipid levels, hypertension, diabetes, obesity, diet, physical activity, alcohol consumption, and psychosocial factors) that account for over 90% of the risk for acute MI. These risk factors are observed in practically every geographic region and racial/ethnic group around the world, and they are consistent in both men and women, according to the INTERHEART researchers. According to the

INTERHEART trial, smoking 1-5 cigarettes per day raised the risk of an acute MI by 40%, and the risk rose as the amount of tobacco smoked per day increased. It also found that all types of tobacco are harmful, including filtered and nonfiltered cigarettes, pipes and cigars, and chewing tobacco, and that abdominal obesity is a greater risk factor than body mass index (BMI), implying that waist-to-hip ratio measurement could replace BMI as an indicator of obesity [12].

7. PROGNOSIS

Acute myocardial infarction (MI) has a 30% fatality rate, with roughly half of the deaths occurring before the patient arrives at the hospital. Within the first year after myocardial infarction, an additional 5-10% of survivors die. Within a year of their index incident, over half of all MI patients are rehospitalized. Overall, the prognosis is highly diverse and is mostly determined by the size of the infarct, the patient's residual left ventricular function, and whether or not revascularization was performed. Successful early reperfusion (STEMI goals: patient arrival to fibrinolysis infusion within 30 minutes OR patient arrival to percutaneous coronary intervention [PCI] within 90 minutes), preserved left ventricular function, and short- and long-term treatment with beta-blockers, aspirin, and angiotensin-converting enzyme (ACE) inhibitors are all linked to a better prognosis [13].

The following factors are linked to a worse prognosis: Diabetes mellitus, previous vascular disease, advanced age (eg, cerebrovascular disease or peripheral vascular disease), The risk score for unstable angina/non–ST-elevation acute coronary syndrome (NSTE-ACS) is elevated thrombolysis in MI (TIMI) (TIMI risk score contains 7 factors: 65 years old, three risk factors for cardiac disease, previous coronary disease, ST-segment deviation 0.5 mm, two bouts of angina in the previous 24 hours, aspirin use in the previous week, and high cardiac enzyme levels), Reperfusion is delayed or ineffective. Left ventricular function is deteriorating (the strongest predictor of outcome), Congestive heart failure (Killip classification II) or frank pulmonary edema (Killip classification III) are both signs of congestive heart failure. BNP (B-type natriuretic peptide) levels that are elevated, The inflammatory marker high sensitive C-reactive protein (hs-CRP) is elevated. Electrocardiograph (ECG) lead aVR is involved. Depression. Five baseline indicators upon presentation of patients with acute MI have been shown to account for approximately 90% of prognostic predictors of 30-day death from acute MI. Age, systolic blood pressure on presentation, Killip classification, heart rate, and anatomic site of the MI are among these characteristics [14].

8. KILLIP CLASSIFICATION

For risk stratification, the Killip classification is extensively employed in patients with acute MI, as follows: Individuals in Killip class I have no clinical indications of heart failure. Individuals with rales or crackles in the lungs, and S 3 gallop, and high jugular venous pressure are classified as Killip class II. Individuals with frank acute pulmonary edema are classified as Killip class III. Individuals with cardiogenic shock or hypotension (measured as systolic blood pressure 90 mmHg) with indications of poor cardiac output are classified as Killip class IV (oliguria, cyanosis, or impaired mental status) [15].

9. INVESTIGATIONS

The following are some of the goals of laboratory testing and imaging: For diagnosis and differential diagnosis (point–of–care testing and cardiac troponin levels testing at a central laboratory), assess the presence or absence of myocardial infarction (MI). To determine the location, nature, and extent of MI (ST-elevation MI [STEMI] or non–ST-elevation MI [NSTEMI]) (ie, to estimate infarct size), To detect recurrent ischemia or myocardial infarction (MI) (extension of MI), Early and late consequences of MI should be detected, and the patient's prognosis should be estimated [16].

In the first evaluation and triage of individuals suspected of having an acute coronary syndrome (ACS), the electrocardiogram (ECG) is the most significant tool. The following laboratory tests are used to diagnose myocardial infarction (MI): Biomarkers/enzymes for the heart: Due to its superior sensitivity and accuracy, the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) guidelines recommend cardiac troponin as the only cardiac biomarker that should be measured at presentation in patients with suspected MI. Troponin is a contractile protein that isn't found in normal serum and is only released when myocardial necrosis occurs. A complete blood cell count (CBC), a comprehensive metabolic panel, and a lipid profile are among the tests that can be done [17].

10. ELECTROCARDIOGRAPHY

In the first evaluation and triage of individuals suspected of having an acute coronary syndrome (ACS), the electrocardiogram (ECG) is the most significant tool. Obtaining an ECG by emergency medical services (EMS) personnel at the point of first

medical contact in patients with symptoms consistent with ST-elevation myocardial infarction (STEMI) not only confirms the diagnosis in more than 80% of cases but also aids in the detection of life-threatening arrhythmias and allows for early and prompt defibrillation therapy, if necessary. The American College of Cardiology (ACC), the American Heart Association (AHA), and the European Society of Cardiology (ESC) have included the importance of obtaining a 12-lead ECG promptly (within 10 minutes of presentation) in their recommendations for ACS and STEMI management, with interpretation by an experienced physician [18].

Upon presentation, ECGs should be conducted serially to check progression and changes with and without pain. Because the symptoms of acute MI can be subtle, any patient over the age of 45 who is having any type of thoracoabdominal discomfort, including new epigastric pain or nausea, should have an ECG performed. When suggestive symptoms or risk factors for early coronary artery disease are present in younger patients, an ECG should be explored. Missed cases are disproportionately represented by younger patients. An ECG is a quick, low-risk, and inexpensive test [19].

11. DIFFERENT ECG ABNORMALITIES

Because not all individuals with myocardial ischemia develop MI, the ECG is an efficient tool for distinguishing between acute MI and the myocardial ischemia that commonly precedes it. The transition from ischemia to infarction is marked by a series of electrical anomalies that can be seen on an ECG. Furthermore, these changes are confined, which aids in the diagnosis of the affected myocardial region in the majority of cases. In STEMI, normal ST-segment elevation lasts for hours and is followed by T-wave inversion and the emergence of Q waves in the first few days. Initial ST depression or T-wave inversion associated with MI, on the other hand, can be difficult to distinguish from ischemia without MI or other unrelated disorders. Non–ST-elevation MI (NSTEMI) or subendocardial ischemia without MI can cause ST-segment depression followed by T-wave inversion without the formation of Q waves (Figs. 1, 2, 3) [20].

The following are high-probability ECG characteristics of MI: The existence of new Q waves and ST-segment elevation more than 1 mm in two anatomically contiguous leads. The following are intermediate-probability ECG findings of MI: Nonspecific ST-T wave abnormalities include ST-segment depression, T-wave inversion, and other nonspecific ST-T wave abnormalities. Normal ECG findings are low-probability ECG signs of MI. ECG results that are normal or nonspecific do not rule out the probability of a heart attack. If there is diffuse ST depression in the precordial and extremities leads and

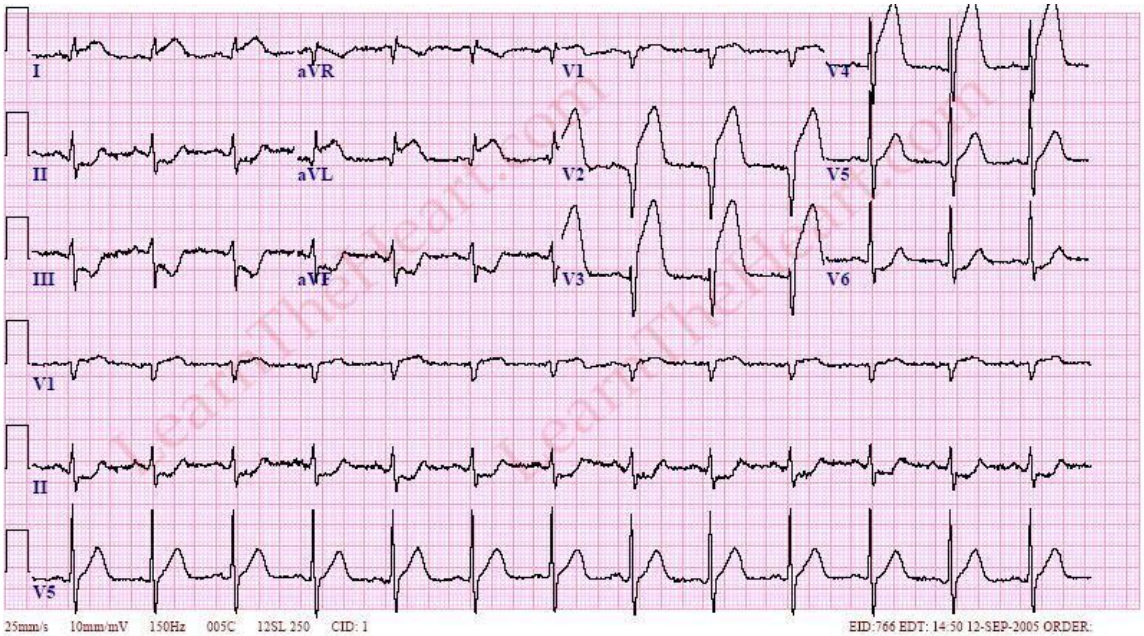

Fig. 1. Anterior Wall ST Segment Elevation Myocardial Infarction (MI) ECG [20]

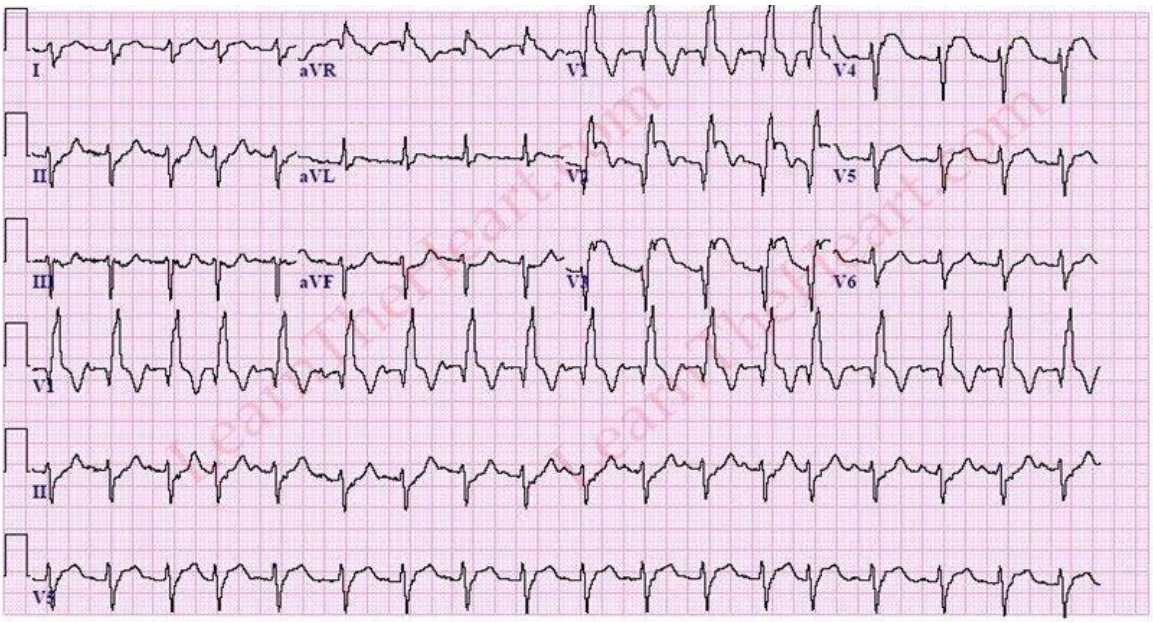

Fig. 2. Anterior Wall ST elevation MI with RBBB ECG (20)

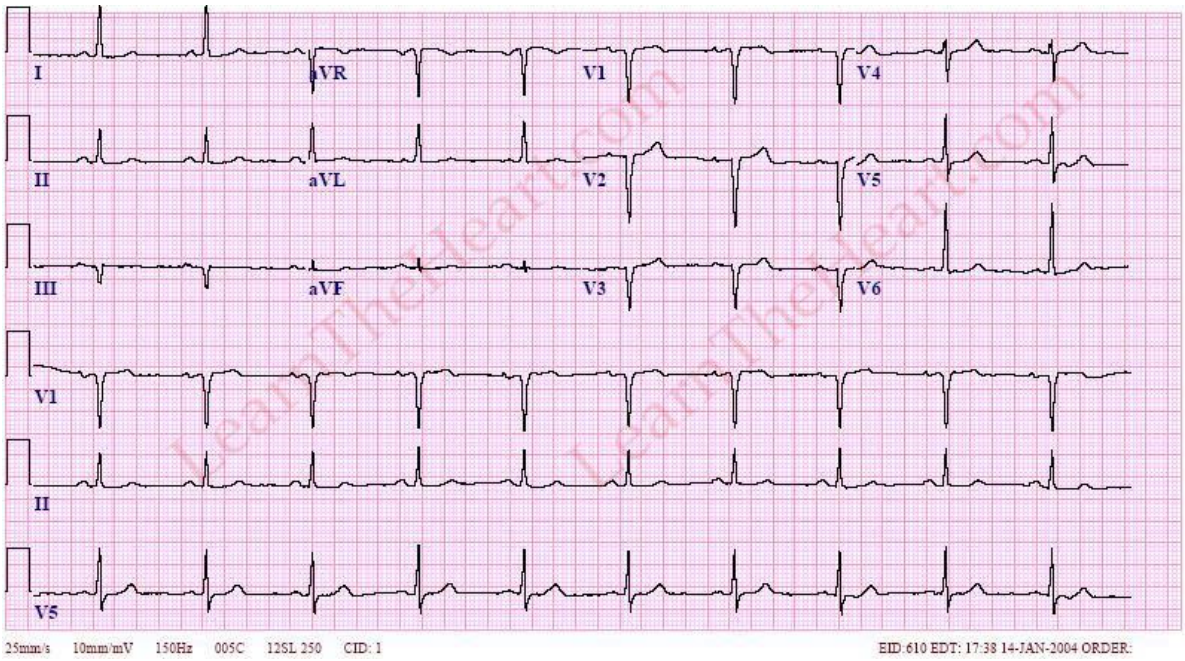

Fig. 3. Old Anterior Wall Myocardial Infarction (MI) ECG (20)

more than 1 mm ST elevation in lead aVR, this could indicate stenosis of the left main coronary artery or the proximal part of the left anterior descending coronary artery, which requires immediate care [21].

The following is a map of the affected myocardium based on the distribution of ECG anomalies in MI: Right ventricular - RV4, RV5, and posterior wall - R/S ratio greater than 1 in V1 and V2, and T-wave changes in V1, V8, and V9. Inferior wall - II, III, aVF, Lateral wall - I, aVL, V4 through V6, Anteroseptal - V1 through V3, Anterolateral - V1 through V6, Right ventricular - RV4, RV5, and posterior wall - R/S ratio [22].

Precordial ST depressions, inverted and hyperacute T waves, or both may be seen in true posterior-wall MIs. When using right-sided chest leads, ST-segment elevation and upright hyperacute T waves may be seen. T waves that are hyperacute (symmetrical and

typically, but not always, pointed) are a common early indicator of MI at any locus. The presence of anomalies in a large number of ECG leads frequently implies severe damage or pericarditis. Other than acute MI, the typical ECG alterations might be detected in other situations. Patients with a history of MI with a left ventricular aneurysm, for example, may show chronic ST elevations due to dyskinetic wall motion rather than acute myocardial damage. Misplaced precordial leads, early repolarization anomalies, hypothermia (elevated J point or Osborne waves), and hypothyroidism can all cause ST-segment alterations. In hypertrophic cardiomyopathy, false Q waves can be detected in the septal leads (HCM). They could also be caused by cardiac rotation. With secondary repolarization alterations, left ventricular hypertrophy can cause significant T-wave inversion. Ischemia or electrolyte abnormalities might cause the QT segment to be prolonged [23].

Saddleback In patients with a hereditary propensity to life-threatening arrhythmias, ST-segment elevation (Brugada epsilon waves) may be detected in leads V1-V3. This elevation could be mistaken for the one seen in acute anterior MI. Changes in T waves, which are usually extensive and global, including all leads, can be caused by diffuse brain damage and hemorrhagic stroke. In the proper clinical situation, convex ST-segment elevation with upright or inverted T waves is often symptomatic of MI. ST depression and T-wave alterations may also be signs of NSTEMI progression. Due to the presence of timed ventricular contractions, patients with a permanent pacemaker may confuse STEMI detection by 12-lead ECG. Left ventricular hypertrophy, pericarditis, ventricular-paced arrhythmias, hypothermia, hyperkalemia, and other electrolyte imbalances, and left ventricular aneurysm are among non-ischemic causes of ST-segment elevation [24].

12. CARDIAC BIOMARKERS

Various cardiac biomarkers have previously been used to assess patients with suspected acute myocardial infarction (MI) (acute coronary syndrome [ACS] and ST-elevation MI [STEMI]). Surrogates for myocardial necrosis have included cardiac-specific troponins I and T, creatine kinase (CK), the MB isoenzyme of creatine kinase (CK-MB), and myoglobin. Cardiac troponin detection and quantification have improved substantially over the years, thanks to advances in technology that enable very sensitive cardiac troponin assays to be done on automated platforms. Although the use of point-of-care testing (POCT) for cardiac biomarkers appears to improve early diagnosis and has the benefit of a faster turnaround time, it does so at the cost of significantly lower sensitivity and accuracy when compared to data acquired from central laboratory testing (Fig. 4) [25].

Serial cardiac troponin measurements are suggested after the initial level is acquired at presentation, 3 to 6 hours following symptom start. If the first readings are negative, more tests should be taken after the 6-hour mark. After the commencement of MI, the release of several cardiac biomarker peaks is shown in the graph below [26].

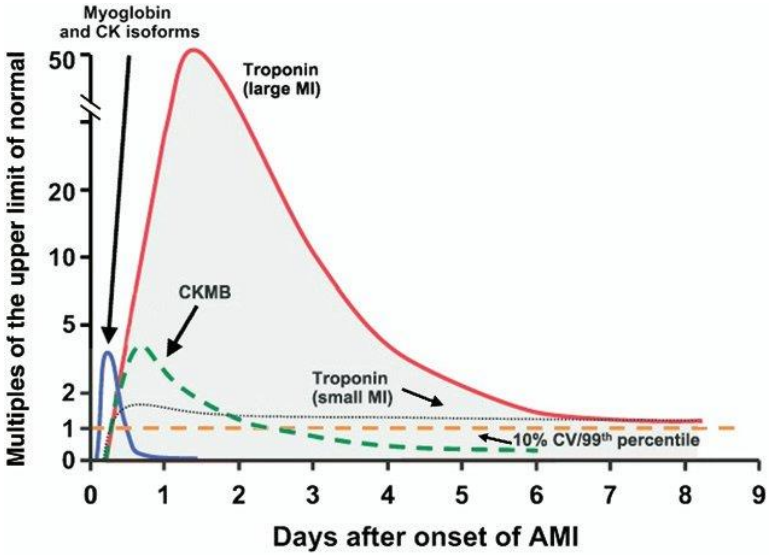

Fig. 4. Cardiac Biomarkers [25]

13. CARDIAC TROPONIN

Troponin is a contractile protein that isn't ordinarily found in the bloodstream. Only when cardiac necrosis develops is it released. Two of the three troponin subunits are formed from the heart (troponin I and troponin T). In patients with acute myocardial infarction (MI), highly sensitive assays may now identify cardiac troponin with a high degree of certainty. In patients with symptoms suggestive of acute MI, clinical practice guidelines have changed to urge relying only on the results of sensitive or high-sensitivity troponin I or troponin T assays for diagnostic and prognostic purposes [27].

Serum levels rise within 3-12 hours of the onset of chest discomfort, peak at 24-48 hours, and then gradually decline over 5-14 days to return to baseline. Troponin levels have been extensively investigated in the emergency room for individuals with chest discomfort. Baseline troponin levels should be measured, followed by repeated troponin tests 3 hours later; both the absolute value of the troponin level and the degree of change in the troponin level should be examined. This has been linked to a higher percentage of accuracy in the diagnosis of acute MI [28].

14. B-TYPE NATRIURETIC PEPTIDE

B-type natriuretic peptide (BNP) is a 32-amino-acid polypeptide released by the heart's ventricles in response to cardiomyocyte strain. Although measuring BNP or N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) for the diagnosis of acute myocardial infarction (MI) is not recommended, these biomarkers may be useful in risk stratification and prognostication of patients with acute MI who are at risk of developing congestive heart failure [29].

15. COMPLETE BLOOD CELL COUNT

If a myocardial infarction (MI) is suspected, a complete blood cell (CBC) count should be obtained before thrombolytic drugs are administered to rule out anemia as a source of decreased oxygen delivery. In the case of acute myocardial infarction, leukocytosis is also prevalent, but not universal. If an IIb/IIIa drug is being evaluated, a platelet count is required; also, the patient's white blood cell (WBC) count may be slightly raised in the event of a MI, indicating an acute inflammatory state. Because of heparin-induced thrombocytopenia, the platelet count may drop dangerously low after treatment (HIT). The leukocyte count may appear normal at first, but it usually increases within 2 hours and peaks in 2-4 days, with a shift to the left and a predominance of polymorphonuclear leukocytes. Elevations usually last for a week or two [30].

16. CHEMISTRY PROFILE (COMPREHENSIVE METABOLIC PANEL)

Keep an eye on potassium and magnesium levels if you have a heart attack. Before cardiac catheterization and treatment with an angiotensin-converting enzyme (ACE) inhibitor, the creatinine level is also required. Because many patients are diagnosed with diabetes for the first time when they report a MI, blood glucose levels are crucial to monitor. The erythrocyte sedimentation rate (ESR), which is not routinely monitored, climbs above reference range values within 3 days and can stay elevated for weeks. Within 24 hours of a MI, the serum lactate dehydrogenase (LDH) level climbs above the reference range, peaks within 3-6 days, and recovers to baseline within 8-12 days [31].

If any clinical symptoms imply hypoxemia, blood oxygenation should be evaluated and corrected periodically; hypoxemia might be caused by lung congestion, atelectasis, or ventilatory impairment due to MI complications or severe sedation or analgesia. In the absence of carbon dioxide retention, fingertip oximetry may be sufficient to evaluate arterial blood gases without the need for a puncture (ABGs). Patients on thrombolytic medicines may have bleeding as a result of such puncturing. Normal oxygen saturation, on the other hand, does not rule out the possibility of respiratory failure [32].

17. LIPID PROFILE

Because levels can fluctuate after 12-24 hours of an acute illness, a lipid profile may be useful if acquired at the time of presentation. Regardless of the lipid profile results, all patients with the acute coronary syndrome should begin on a high-intensity statin [33].

18. CARDIAC IMAGING

Imaging has a wide range of applications in the treatment of acute myocardial infarction (MI), however, it is mostly employed to confirm or rule out coronary artery disease (CAD). Furthermore, imaging can aid in determining the structure and severity of myocardial perfusion problems. Some sort of stress testing may help to confirm the diagnosis and guide therapy in lower-risk patients who are suspected of having acute coronary syndrome (ACS) but do not have serial electrocardiographic (ECG) alterations or positive serial cardiac biomarker findings. Consult a

cardiologist if you have highly suspected or proven ACS so that you can get an urgent coronary angiography; this technique can be used to definitively diagnose or rule out CAD. Following that, therapeutic suggestions can be made based on the angiographic findings and the patient's comorbidities, which may include medication therapy, percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) surgery [34].

When there is a low to intermediate risk of CAD and cardiac troponin and/or ECG readings are ambiguous, multidetector computed tomography (MDCT) coronary angiography may be explored as an alternative to invasive angiography to rule out ACS. This imaging technique can be utilized to triage patients with chest discomfort in the emergency room. In the emergency department, myocardial perfusion imaging (MPI) with single-photon emission CT (SPECT) or positron emission tomography (PET) scanning has a low yield for detecting ischemia in low-risk patients. As a result, SPECT or PET scanning is not frequently used to identify MI in patients with negative serial troponin values and nondiagnostic ECGs. To evaluate the ventricular function and wall-motion problems, echocardiography is highly recommended and essential. Pericardial effusion, ischemic mitral regurgitation, and cardiac tamponade are among conditions that might aggravate an acute MI [35].

19. MANAGEMENT

In the treatment of acute myocardial infarction (MI), the initial priority for healthcare providers is to diagnose the problem as soon as possible. In general, the goal of the first treatment for acute MI is to restore perfusion as soon as feasible to save as much of the damaged myocardium as possible. Percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery are two examples of medical or mechanical methods. Although the first treatment for the various types of an acute coronary syndrome (ACS) may appear to be identical, it is critical to determine whether the patient is suffering from an ST-elevation MI (STEMI) or a non–STEMI (NSTEMI), as definitive remedies differ. The urgency of therapy and the level of evidence for various pharmacologic choices are two important concerns and variations. Inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) has emerged as a viable approach for lowering residual cardiovascular disease risk over the last decade. PCSK9 is a protein that promotes the degradation of low-density lipoprotein (LDL) receptors (LDLR). PCSK9 is inhibited by monoclonal antibodies, which prevents LDLR degradation. This activity will raise the number of LDLRs, which will boost LDL clearance and, as a result, lower LDL-C levels [36].

The first PCSK9 inhibitor, evolocumab (Repatha), was approved by the FDA in December 2017 for the prevention of strokes, heart attacks, and coronary revascularizations. The evolocumab cardiovascular outcomes trial findings were used to support the approval (FOURIER). Evolocumab showed significant improvements for 27,564 participants with established cardiovascular disease in the FOURIER clinical study. Evolocumab lowered the risk of heart attack by 27%, the risk of stroke by 21%, and the risk of coronary revascularization by 22% when used in conjunction with optimal statin therapy, according to the study. Furthermore, evolocumab was found to reduce the risk of the primary composite outcome by 15%, which comprised hospitalization for unstable angina, coronary revascularization, heart attack, stroke, or cardiovascular mortality [37].

Patients and bystanders who notice symptoms early and activate the emergency medical service (EMS) system, thereby shortening the time to definitive treatment, have a lower risk of morbidity and mortality from MI. If the patient goes into cardiac arrest, trained prehospital staff can administer life-saving interventions. The availability of early defibrillation is critical for better survival. Approximately one out of every 300 patients with chest discomfort who are transported to the emergency department in a private vehicle die en route. Several studies in the United States have found that individuals with STEMI seldom call 911, and only around 40% of patients with a documented cardiac episode use EMS [38].

20. ACUTE MANAGEMENT

All patients with symptoms of ischemia lasting fewer than 12 hours and persistent ST-segment elevation should get reperfusion treatment. If the treatment can be completed within 120 minutes of the ECG diagnosis, primary percutaneous coronary intervention (PCI) is favored over fibrinolysis. After clearing out contraindications, fibrinolysis should be initiated within 10 minutes following STEMI if PCI is not an immediate possibility (>120 minutes). A normal PCI or a rescue PCI can be performed if transport to a PCI facility is available in 60 to 90 minutes following a bolus of the fibrinolytic agent and the patient passes reperfusion requirements. If fibrinolysis is desired, fibrin-specific drugs such as tenecteplase, alteplase, or reteplase should be used (class I) [39].

Discomfort relief, dyspnea, and anxiety: Myocardial infarction chest pain is linked to sympathetic arousal,

which produces vasoconstriction and a higher workload for the ischemic heart. The most often utilized analgesics for pain treatment are intravenous opioids (e.g., morphine) (Class IIa). According to the findings of the CRUSADE quality improvement effort, morphine consumption is linked to a higher risk of death and poor clinical outcomes. The research was based on the CIRCUS (Does Cyclosporine Improve Outcome in STEMI Patients) database, which revealed no significant side effects related to the use of morphine in a case of anterior ST-segment elevation MI. In severely nervous patients, a modest anxiolytic (typically a benzodiazepine) may be recommended (class IIa). Patients with hypoxemia (SaO2 90% or PaO2 60mm Hg) should receive additional oxygen (Class I) [40].

Nitrates: In terms of symptom alleviation and ST depression regression, intravenous nitrates are more effective than sublingual nitrates (NSTEMI). The dose is gradually increased until symptoms are reduced, blood pressure in hypertensive individuals is normalized, or adverse effects such as headache and hypotension are detected. Beta-blockers: This class of medications lowers heart rate, blood pressure, and myocardial contractility, decreasing myocardial oxygen consumption. They diminish the effects of circulating catecholamines by blocking beta receptors throughout the body, including the heart. Beta-blockers should not be administered if coronary vasospasm is suspected. In both STEMI and NSTEMI, an oral loading dose of 150 to 300 mg (non-enteric coated formulation) and a long-term maintenance dose of 75 to 100 mg per day is indicated, regardless of treatment method (class I). Thromboxane A2 synthesis is inhibited by aspirin throughout the platelet's lifecycle [41].

The majority of P2Y12 inhibitors are inert prodrugs that must be oxidized by the hepatic cytochrome P450 system to produce an active metabolite that irreversibly blocks P2Y12 receptors. The exception is ticagrelor, which is an orally active medication that does not require activation. ATP-induced platelet aggregation is inhibited when P2Y12 receptors are inhibited. Clopidogrel, prasugrel, and ticagrelor are the most regularly used P2Y12 inhibitors. Clopidogrel is taken as a loading dose of 300 to 600 mg, followed by 75 mg per day. When compared to clopidogrel, prasugrel, 60 mg loading dosage, and 10 mg per day maintenance dose have a quicker onset. Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor, as well as a parenteral anticoagulant, should be used in patients undergoing PCI. Prasugrel or ticagrelor are reported to be superior to clopidogrel in PCI. In NSTEMI and UA, aspirin and clopidogrel have also been demonstrated to reduce the number of ischemic events. Unfractionated heparin, enoxaparin, and bivalirudin are the anticoagulants utilized during PCI. If the patient has heparin-induced thrombocytopenia, bivalirudin is suggested during initial PCI [42].

21. LONG-TERM MANAGEMENT

Treatment with high-intensity statins to reduce low-density lipoproteins (LDLs) and stabilize atherosclerotic plaques is advised. It has been discovered that high-density lipoproteins are protective. Antithrombotic therapy: Aspirin should be taken for the rest of one's life, and whether or not another drug should be added depending on the treatment performed, such as PCI with stent implantation. Patients with systolic left ventricular dysfunction, heart failure, hypertension, or diabetes should take ACE inhibitors. If no additional contraindications exist, beta-blockers are suggested for patients with an LVEF of less than 40%. Blood pressure goals of less than 140/90 mm Hg can be achieved with antihypertensive medication. In a patient with left ventricular dysfunction, mineralocorticoid receptor antagonist treatment is suggested (LVEF less than 40 percent). Glucose-lowering medication for diabetics to meet their current blood sugar targets [43].

22. LIFESTYLE MODIFICATIONS

The most cost-effective secondary measure for preventing MI is quitting smoking. Smoking has a pro-thrombotic effect, which has a strong link to atherosclerosis and heart attacks. Weight loss, alcohol, and diet: A low-saturated-fat diet that emphasizes whole grains, vegetables, fruits, and seafood is thought to be cardioprotective. Bodyweight should be maintained at a BMI of 20 to 25 kg/m2 and a waist circumference of 94 cm for males and 80 cm for women [44].

23. GUIDELINES

The American College of Cardiology Foundation and the American Heart Association (ACCF/AHA), as well as the European Society of Cardiology (ESC), have developed guidelines for the treatment of patients with ST-segment elevation myocardial infarction (STEMI). The 2013 ACCF/AHA guidelines, as well as the 2012 and 2017 ESC guidelines, emphasize the significance of getting a 12-lead electrocardiogram (ECG) within 10 minutes of presentation (class I, level of evidence: B, for all three guidelines). In all patients with suspected STEMI (class I, level of evidence: B), the 2017 ESC guidelines recommend ECG monitoring with defibrillator capacity as soon as possible, but do not

recommend prehospital cooling with a rapid infusion of large volumes of cold intravenous fluid immediately after the return of spontaneous circulation (class IIa, level of evidence: C). The following are some of the other ACCF/AHA recommendations for STEMI patients [45].

I am in class one. Level of evidence: A: All eligible STEMI patients with symptomatic onset within the last 12 hours should get reperfusion treatment. When primary PCI can be performed quickly by competent doctors, it is the preferred route of reperfusion. Direct EMS transport of STEMI patients to a PCI-capable hospital for primary PCI is advised, with an optimum first medical contact (FMC)-to-device time system objective of 90 minutes or less. Patients who arrive at a non-PCI-capable hospital should be transferred immediately to a PCI-capable hospital, with an FMC-to-device time system objective of 120 minutes or less. In the absence of contraindications, fibrinolytic therapy should be given to STEMI patients at non-PCI-capable facilities when the expected FMC-to-device time exceeds 120 minutes due to unavoidable delays. If fibrinolytic therapy is recommended or chosen as the primary reperfusion method, it should be started within 30 minutes of arriving at the hospital. In comatose STEMI patients with out-of-hospital cardiac arrest caused by ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), including those who receive primary PCI, start therapeutic hypothermia as soon as possible. If an out-of-hospital cardiac arrest patient's initial ECG shows STEMI, angiography and PCI should be performed as soon as possible. In the context of clinical and/or ECG evidence of persistent ischemia, primary PCI is the optimal reperfusion technique for patients with STEMI and symptom onset within the previous 12 to 24 hours (Evidence level: B) [46].

The ESC guidelines from 2012 and 2017 agree with the ACCF/AHA recommendations and also encourage routine blood samples for serum indicators during the acute phase. However, don't wait for the results before starting reperfusion therapy. (Level of evidence: C, Class I) In addition, according to the 2017 ESC guidelines, the following should be taken into account for the first diagnosis (class IIa, level of evidence B for both): When a posterior MI (circumflex occlusion) is highly suspected, extra posterior chest wall leads (V 7-V 9) are used, as are additional right precordial leads (V 3R and V 4R) in the case of an inferior MI to diagnose concurrent right ventricular infarction [47].

24. DISCUSSION

An imbalance in oxygen supply and demand causes myocardial infarction (MI), which is most commonly triggered by plaque rupture with thrombus formation in an epicardial coronary artery, resulting in an abrupt reduction in blood supply to a section of the myocardium. Many episodes are either "silent" or are not clinically recognized by patients, families, and health care professionals, although the clinical presentation of a patient is a significant component in the total evaluation of a patient with MI. The presence of cardiac biomarkers in the bloodstream usually implies myocardial necrosis and is a helpful diagnostic aid [48].

MI is part of a group of conditions known as an acute coronary syndrome (ACS). Unstable angina, non–ST-segment elevation MI (NSTEMI)—collectively known as non–ST-segment acute coronary syndrome (NSTE ACS)—and ST-segment elevation MI make up the ACS continuum that represents continuing myocardial ischemia or damage (STEMI). The electrocardiogram may or may not show ST-segment or T-wave changes in patients with ischemia pain (ECG). On the ECG, ST elevations indicate active and ongoing transmural myocardial damage. Most STEMI patients have Q waves in the absence of prompt reperfusion therapy, indicating a dead zone of myocardium that has suffered irreparable damage and death [49].

Without ST elevations, patients are diagnosed with unstable angina or NSTEMI, which is distinguished by the presence of cardiac enzymes. Alterations in the surface ECG, such as ST-segment depressions or T-wave morphological changes, may or may not occur in both of these situations. MI can cause systolic or diastolic dysfunction, as well as an elevated risk of arrhythmias and other long-term consequences. Coronary thrombolysis and mechanical revascularization have changed the primary therapy of acute MI, owing to their ability to save the myocardium when used early after ischemia begins [49].

Even when recanalization is induced just 6 hours or more after the start of symptoms, the moderate prognostic benefit of an opened infarct-related artery may be realized; that is when the rescue of considerable portions of compromised ischemic myocardium is no longer likely. The opening of an infarct-related artery can enhance ventricular function and collateral blood flow, as well as diminish infarct growth, ventricular aneurysm formation, and left ventricular dilatation. It can also reduce late arrhythmia and mortality associated with ventricular aneurysms [50].

Beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and statins

have all been shown to be beneficial. The Observations From the TRITON-TIMI 38 Trial (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel–Thrombolysis in Myocardial Infarction 38) was published by the American College of Cardiology (ACC), the American Heart Association (AHA), the European Society of Cardiology, and the World Heart Federation, and it better defines a universal definition of MI, as well as a classification system and risk factors for cardiovascular death (50).

25. CONCLUSION

The best way to diagnose and treat individuals with ischemic heart disease is to work with a multidisciplinary team. Cardiology teams specialized in the care of these individuals can be found at most hospitals. Time to therapy is crucial in the management of MI in patients who report chest pain. As a result, healthcare personnel, particularly emergency room nurses, must be conversant with the signs of MI and the need for prompt triage. A cardiology consultation should be scheduled right away to ensure that the patient is treated within the recommended time range. Because MI is linked to several significant consequences, these patients should be treated in an ICU setting.

Ischemic heart disease has no cure, and all therapies are symptom-based. Preventing coronary artery disease is the key to bettering outcomes. The patient should be educated on the benefits of a balanced diet, the necessity of controlling blood pressure and diabetes, exercising frequently, quitting smoking, keeping a healthy body weight, and being compliant with medications by their primary care provider and nurse practitioner. The pharmacist should inform the patient of the different types of medications used to treat ischemic heart disease, as well as their benefits and side effects. Only by collaborating in this way can the morbidity and mortality of myocardial infarction be reduced.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ibanez B, James S, Agewall S, et al, for the ESC Scientific Document Group . 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018 Jan 7. 39 (2):119-77.
2. 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: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. J Am Coll Cardiol. 2017 Oct 17. 70 (16):2048-90.
3. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 Dec 23. 130 (25):e344-426.
4. Andersen HR, Nielsen TT, Rasmussen K, et al, for the DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003 Aug 21. 349 (8):733-42.
5. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA. 2000 Aug 16. 284(7):835-42.
6. Apple FS. A new season for cardiac troponin assays: it's time to keep a scorecard. Clin Chem. 2009 Jul. 55 (7):1303-6.
7. Armstrong PW, Westerhout CM, Welsh RC. Duration of symptoms is the key modulator of the choice of reperfusion for ST-elevation myocardial infarction. Circulation. 2009 Mar 10. 119 (9):1293-303.
8. Bates ER, Nallamothu BK. Commentary: the role of percutaneous coronary intervention in ST-segment-elevation myocardial infarction. Circulation. 2008 Jul 29. 118 (5):567-73.
9. Becker L, Larsen MP, Eisenberg MS. Incidence of cardiac arrest during self-transport for chest pain. Ann Emerg Med. 1996 Dec. 28 (6):612-6.
10. Burchfield JS, Xie M, Hill JA. Pathological ventricular remodeling: mechanisms: part 1 of 2. Circulation. 2013 Jul 23. 128 (4):388-400.
11. Chatzizisis YS, Coskun AU, Jonas M, Edelman ER, Feldman CL, Stone PH. Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: molecular, cellular, and vascular behavior. J Am Coll Cardiol. 2007 Jun 26. 49(25):2379-93.

12. Concheiro-Guisan A, Sousa-Rouco C, Fernandez-Santamarina I, Gonzalez-Carrero J. Intrauterine myocardial infarction: unsuspected diagnosis in the delivery room. Fetal Pediatr Pathol. 2006 Jul-Aug. 25(4):179-84.
13. Costa e Silva R, Pellanda L, Portal V, Maciel P, Furquim A, Schaan B. Transdisciplinary approach to the follow-up of patients after myocardial infarction. Clinics (Sao Paulo). 2008 Aug. 63 (4):489-96.
14. Cremer PC, Khalaf S, Agarwal S, et al. Myocardial perfusion imaging in emergency department patients with negative cardiac biomarkers: yield for detecting ischemia, short-term events, and impact of downstream revascularization on mortality. Circ Cardiovasc Imaging. 2014 Nov. 7 (6):912-9.
15. Critchley J, Liu J, Zhao D, Wei W, Capewell S. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. Circulation. 2004 Sep 7. 110 (10):1236-44.
16. Cullen L, Parsonage WA, Greenslade J, et al. Delta troponin for the early diagnosis of AMI in emergency patients with chest pain. Int J Cardiol. 2013 Oct 3. 168 (3):2602-8.
17. de Lemos JA, Morrow DA, Bentley JH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. N Engl J Med. 2001 Oct 4. 345 (14):1014-21.
18. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation. 2004 Mar 16. 109 (10):1223-5.
19. Diercks DB, Peacock WF 4th, Hollander JE, et al. Diagnostic accuracy of a point-of-care troponin I assay for acute myocardial infarction within 3 hours after presentation in early presenters to the emergency department with chest pain. Am Heart J. 2012 Jan. 163 (1):74-80.
20. Ellis SG, Armstrong P, Betriu A, et al, for the Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events Investigators. Facilitated percutaneous coronary intervention versus primary percutaneous coronary intervention: design and rationale of the Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial. Am Heart J. 2004 Apr. 147 (4):E16.
21. Fujita M, Nakae I, Kihara Y, et al. Determinants of collateral development in patients with acute myocardial infarction. Clin Cardiol. 1999 Sep. 22 (9):595-9.
22. Gislason GH, Jacobsen S, Rasmussen JN, et al. Risk of death or reinfarction associated with the use of selective cyclooxygenase-2 inhibitors and nonselective nonsteroidal antiinflammatory drugs after acute myocardial infarction. Circulation. 2006 Jun 27. 113 (25):2906-13.
23. Goldstein JA, Chinnaiyan KM, Abidov A, et al, for the CT-STAT Investigators. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. 2011 Sep 27. 58 (14):1414-22.
24. Haaf P, Reichlin T, Corson N, et al. B-type natriuretic peptide in the early diagnosis and risk stratification of acute chest pain. Am J Med. 2011 May. 124 (5):444-52.
25. Holmes MV, Millwood IY, Kartsonaki C, et al, for the China Kadoorie Biobank Collaborative Group. Lipids, lipoproteins, and metabolites and risk of myocardial infarction and stroke. J Am Coll Cardiol. 2018 Feb 13. 71 (6):620-32.
26. Jaffe AS. Third universal definition of myocardial infarction. Clin Biochem. 2013 Jan. 46 (1-2):1-4.
27. James SK, Lindahl B, Siegbahn A, et al. N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open occluded arteries (GUSTO)-IV substudy. Circulation. 2003 Jul 22. 108 (3):275-81.
28. Kacprzak M, Kidawa M, Zielińska M. Fever in myocardial infarction: is it still common, is it still predictive?. Cardiol J. 2012. 19 (4):369-73.
29. Killip T 3rd, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol. 1967 Oct. 20(4):457-64.
30. Kolodgie FD, Virmani R, Burke AP, et al. Pathologic assessment of the vulnerable human coronary plaque. Heart. 2004 Dec. 90 (12):1385-91.
31. Kundi H, Kiziltunc E, Korkmaz A, Cicek G, Ornek E, Ileri M. A novel risk scoring system to predict cardiovascular death in patients with acute myocardial infarction: CHA2DS2-VASc-CF score. Clin Appl Thromb Hemost. 2018 Mar. 24 (2):273-8.
32. Kwong JC, Schwartz KL, Campitelli MA, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. N Engl J Med. 2018 Jan 25. 378 (4):345-53.

33. Lee KL, Woodlief LH, Topol EJ, et al, for the GUSTO-I investigators. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. Circulation. 1995 Mar 15. 91 (6):1659-68.
34. Lee-Lewandrowski E, Januzzi JL Jr, Grisson R, Mohammed AA, Lewandrowski G, Lewandrowski K. Evaluation of first-draw whole blood, point-of-care cardiac markers in the context of the universal definition of myocardial infarction: a comparison of a multimarker panel to troponin alone and to testing in the central laboratory. Arch Pathol Lab Med. 2011 Apr. 135 (4):459-63.
35. Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart. 2002 Aug. 88 (2):119-24.
36. Lloyd-Jones D, Adams RJ, Brown TM, et al, for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010 Feb 23. 121 (7):948-54.
37. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. JAMA. 2000 Jul 5. 284 (1):60-7.
38. Macintyre CR, Heywood AE, Kovoor P, et al. Ischaemic heart disease, influenza and influenza vaccination: a prospective case control study. Heart. 2013 Dec. 99 (24):1843-8.
39. Marban E. Myocardial stunning and hibernation. The physiology behind the colloquialisms. Circulation. 1991 Feb. 83 (2):681-8.
40. Mathews R, Peterson ED, Li S, et al. Use of emergency medical service transport among patients with ST-segment-elevation myocardial infarction: findings from the National Cardiovascular Data Registry Acute Coronary Treatment Intervention Outcomes Network Registry-Get With The Guidelines. Circulation. 2011 Jul 12. 124 (2):154-63.
41. McGill HC Jr, McMahan CA, Zieske AW, et al. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler Thromb Vasc Biol. 2000 Aug. 20 (8):1998-2004.
42. Morrow DA, Rifai N, Antman EM, et al. C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes: a TIMI 11A substudy. Thrombolysis in Myocardial Infarction. J Am Coll Cardiol. 1998 Jun. 31 (7):1460-5.
43. Mueller C. Biomarkers and acute coronary syndromes: an update. Eur Heart J. 2014 Mar. 35 (9):552-6.
44. O'Gara PT, Kushner FG, Ascheim DD, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013 Jan 29. 127 (4):e362-425.
45. Okrainec K, Banerjee DK, Eisenberg MJ. Coronary artery disease in the developing world. Am Heart J. 2004 Jul. 148 (1):7-15.
46. Patel MR, Mahaffey KW, Armstrong PW, Weaver WD, Tasissa G, Hochman JS, et al. Prognostic usefulness of white blood cell count and temperature in acute myocardial infarction (from the CARDINAL Trial). Am J Cardiol. 2005 Mar 1. 95 (5):614-8.
47. Rathore SS, Gersh BJ, Weinfurt KP, Oetgen WJ, Schulman KA, Solomon AJ. The role of reperfusion therapy in paced patients with acute myocardial infarction. Am Heart J. 2001 Sep. 142(3):516-9.
48. Reddy KS. Cardiovascular disease in non-Western countries. N Engl J Med. 2004 Jun 10. 350 (24):2438-40.
49. Reichlin T, Irfan A, Twerenbold R, et al. Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction. Circulation. 2011 Jul 12. 124(2):136-45.
50. Risøe C, Kirkeby OJ, Grøttum P, Sederholm M, Kjekshus JK. Fever after acute myocardial infarction in patients treated with intravenous timolol or placebo. Br Heart J. 1987 Jan. 57 (1):28-31.