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Pathophysiology and Stages of Myocardial Infarction– A Known Scenario Yet To Be Focused.

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ABSTRACT: Myocardial Infarction commonly known as Heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. Principle causes of MI are1. Atherosclerosis 2. Non-atherosclerotic. There are 5 stages of MI: i. Spontaneous ii. MI secondary to ischemia iii. MI resulting in death iv. MI related to stent thrombosis v. MI related to CABG. Cardi-ac Biomarkers (Trop T or I) evaluation is the primary step for detection of Myocardial Infarction. ECG changes including ST segment deviation, T wave inversion, new Q wave suggest acute Myocardial Infarction. Angiogram/ Cardiac catheterization shows the progression of clot in the corresponding coronary arteries which helps in providing accurate treatment. ECHO cardiogram results also helps in detecting regional wall motion abnormalities. Immediate treatment for a patient with acuteMIincludes:Oxygensupport,sublingualnitroglycerin,adequateanalgesia,Tab.Aspirinoral.
Fibrinolysis therapy (with streptokinase or Reteplase) should be given if the ischemic chest pain lasts at least 30 minutes duration, unrelieved by nitroglycerin and is associated with ST segment elevation of at least 0.1 mv. Medical management with dual anti platelet therapy (DAPT) and anti-hypertesives, anticoagulants, statins is given in those patients with mild occlusion (10-50%) and moderate occlusion (50-70%). PTCA/stenting is indicated in patients with coronary artery lesions (70- 90%) in single vessel or double vessel occlusion, acute or threatened artery closure, focal de-novo native vessel lesions. CABG is indicated in patients with triple vessel disease, severe left main stem artery stenosis, poor left ventricular function, left main equivalent disease, disabling angina.

KEY WORDS: DAPT Therapy, Cardiomyopathies, Disabling angina, Silent infarct, ST2 Cardiac biomarker.

I. INTRODUCTION:

The term Myocardial Infarction is used when there is a necrosis of myocardial tissue in a clinical setting consistent with Myocardial Ischemia[1]. Myocardial infarction is the major cause of death in the cardiovascular diseases.

In myocardial infarction we mostly see acute chest discomfort which occurs when the supply of oxygen is inadequate and don't reach the demand of the myocardium, then the myocardial tissue becomes ischemic and results in death of the myocardial tissue. Myocardial infarction usually occurs mainly in setting of coronary atherosclerosis, but it may also reflect dynamic components of vascular resistance. When the attack begins the person experiences a sudden pain in the chest region at the center of the chest and the pain becomes often severe when it is prolonged to some duration oftime[2].

It seems to be like mild pressure with certain discomfort which is accompanied by mild difficulty in breathing known as shortness of breath, profuse sweating and strange frightened feeling[2]. This discomfort may occasionally feel like Heart burn[2].The myocardial infarction is mainly caused due to blockage of coronary artery that feeds the heart muscle with blood containing oxygen, glucose, sodium, potassium, calcium and other nutrients. This occlusion virtually always presents on the surface of a partially obstructing plaque of atheroma that shows fissuring the blocked artery, cuts off blood supply and oxygen

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supply capacity to the segment of myocardium thus it leads to the death of myocardial tissue resulting in necrosis and death of the heart muscle cells which is termed as Myocardial infarction. Myocardial infarction common occurrence in young men aged from 30- 60yrs[3].

Coronary atherosclerosis is a chronic diseased state of the myocardial infarction which is considered as CAD in which two periods like stable and unstable periods are seen. During the un-stable periods we seen activated inflammation of the vascular wall due to which the patients develop Myocardial infarction[4].

Myocardial infarction may be a minor event which passed through the chronic lifelong disease which goes off undetected in some cases and it may also be a catastrophic event in which it may even causes sudden death or severe hemodynamic detoriation[1].

CLASSIFICATION OF MYOCARDIAL INFARCTION:

Patients with myocardial necrosis but without myocardial infarction[5]:

Patients with cTnI values greater than 0.003mcg/L but without overt myocardial ischemia were classified into the following groups:

- TnI elevation related to secondary ischemia (hyper-trophic cardiac myopathy, coronary vasculitis).
- TnI elevation not related to ischemia (radiofrequency ablation, cardiac incision with surgery, chemotherapy).
- CTnI elevation due to extra cardiac conditions (infection, stroke, renal failure). CTnI elevation of indeterminate origin.

Patients with cTnI less than or equal to 0.003mcg/L were classified as having unstable angina pectoris, prior ischemic heart disease. Unstable angina pectoris was defined as instable chest dis- comfort or dynamic ECG changes indicative of ischemia prior ischemic heart disease was defined as a documented medical history of such a diagnosis or current medical treatment for ischemic heart disease.

Electrocardiographic classification of MIs:

1. **Waveform morphology:** In patients with Myocardial Ischemia caused by decreased blood supply, the initial 12-lead ECG typically shows ;1. predominant ST- segment (STE) as part of STE acute coronary syndrome (STE-ACS), or 2. no predominant STE, i.e. non-STEACS(NSTE-ACS).

- Patients with predominant STE are classified as having either aborted Myocardial Infarction (MI) or ST- elevation MI (STEMI) based on the absence or presence of biomarkers of Myocardial necrosis.
- NSTE-ACS patients are classified as having either unstable angina or NSTEMI, based also on the absence or presence of biomarkers of myocardial necrosis.
- NSTE-ACS may indicate high risk, and a more aggressive approach should be considered.
- patients with typical symptoms and ST elevation should be referred for emergent reperfusion therapy (by percutaneous coronary intervention).
- In a minority of patients with acute total coronary occlusion, no ST-elevations are pre-sent in the 12 -lead ECG.[6]

Patients without Myocardial Necrosis[5]:

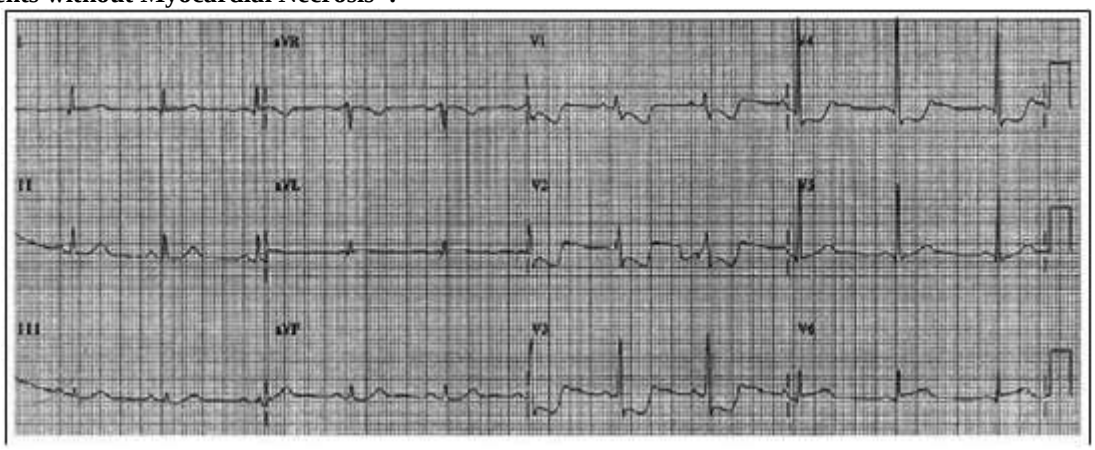

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Figure:1 12-Lead ECG recorded during chest pain in a patient with acute occlusion of the left circumflex coronary artery. No lesions were present in the other coronary arteries. The ECG shows ST depression in leads V1 to V4 and only minor ST elevation, not fulfilling ST elevation myocardial infarction criteria, in leads I, aVL, and V6.[7]

2. Age:

- Acute vs subacute vs "old".

3. Localization:

- Affectedwall.
- Culpritvessel.

Classification of MIs by morphology [8]:

Acute Coronary Syndrome

STElevationMI(STEMI)

- ST elevations in≥2anatomically depressions contiguousleads
- +/- ST depression and/orTwave inversions inotherleads

Non- ST elevation MI(NSTEMI) andUnstableAngina (UA)

→ may or may not have ST and/or T waveinvesions

→ EKG may be completelynormal

→ NSTEMI and UA differentiated only by elevation of biomarkers(e.g. troponin).

Other common EKG findings during or following MIs: Pathologic Q waves
New QRS axis deviation Poor R wave progression
Conduction block (e.g., AV block, Bundle branch block)

Stages of Myocardial Infarction [1,9]:

Type-1: (Spontaneous MI)

It is related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with intraluminal thrombus in one or more of the coronary arteries, leading to decreased myocardial blood flow or distal platelet emboli and thereby resulting in myocyte necrosis. The patient may or may not have underlying Obstructive Coronary Artery Disease (CAD).

Type-2[5]: (MI secondary to an ischemic balance) Myocardial Infarction secondary to ischemia due to either increased oxygen demand or decreased supply.

Conditions with decreased oxygen supply were [5]:

i. Anemia defined as a hemoglobin concentration<5.5 mmol/L (men) and <5.0 mmol/L (women).
ii. Shock defined as systolic blood pressure <90mm hg along with signs of organ dysfunction (i.e., metabolic acidosis, arterial oxygen tension<8kpa, oliguria or

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encephalopathy)

iii. Bradyarrhythmia that requires medical management or cardiacpacing.

iv. Coronary embolus in the presence of an increased risk of embolism 9 left heart endo-carditis, intracardiac mural thrombus, documented venous thrombus, and a patent foramen ovale or atrial septumdefect)

v. Respiratory failure with an arterial oxygen tension <8kpa and clinical presentations of acute respiratory failure lasting ≥ 20minutes.

Conditions with increased oxygen demand were 5:

i. Ventricular tachyarrhythmia which lasts for about ≥20minutes.

ii. Supraventricular tachyarrhythmia which lasts for about ≥20 minutes with a ventricular rate>150beats/min.

iii. Hypertensive pulmonary edema defined as the presence of a systolic blood pressure> 160mmhg, sings of pulmonary edema, and need for treatment with nitrates ordiuretics.

iv. Arterial hypertension with a systolic blood pressure>160mm hg and associated left ventricular hypertrophy identified by echocardiography orelectrocardiogram.

Type 3: (MI resulting in death when biomarker values are unavailable)

Sudden, unexpected cardiac death before the blood samples for biomarkers could be drawn/ before their appearance in the circulation.

Type 4a (MI related to percutaneous coronary intervention [PCI]):

Elevation of biomarker values (CTn is preferred) to more than times the 99th percentile of the URL in patients with normal baseline valves) or a rise of values over 20 if the baseline values are evaluated but stable or falling.

In addition, any of the following are required:

- Symptoms suggestive of myocardialischemia.
- New ischemic ECG changes or newBBB.
- Angiographic loss of patency of a major coronary artery or a side branch or persistent slow flow or no flow orembolization.
- Demonstration of the new loss of viable myocardium or new regional wall motion abnormality by cardiacimaging.

Type 4b (MI related to stent thrombosis):

MI associated with stent thrombosis as detected by coronary angiography or autopsy in the setting of myocardial ischemia in combination with a risk and/ or fall of cardiac bio- markers with at least one value above the 99th percentile URL.

Type 5 (MI related to Coronary Artery Bypass Grafting [CABG]):

- Elevation of cardiac biomarkers values more than 0 times the 99th percentile URL in patients with normal baseline CTn values in addition, either
- New pathologic Q waves or new BBB
- Angiographic- documented new graft or native coronary artery occlusion, or Evidence of new loss of viable myocardium or new regional wall motion ab- normality by cardiac imaging is required.

Gross morphological appearance of a MI can vary patterns include[10]:

Transmural infract: Involving the entire thickness of the left ventricular wall from endocardium, to epicardium, usually the anterior free wall and septum with extension into the right ventricular wall in wall in 15-30 isolated infarcts of right ventricular and right atrium are extremely rare.

Sub endocardial infarct: Multifocal areas of necrosis confined to the inner 1/3 -1/2 of the left ventricular wall. These don't show the same evolution of changes seen in transmural myocardial infarction.

Gross morphological changes evolve over time as follows [angiography][10]:

Time from onset – finding:

- 18 – 24 hours: pallor of myocardium.
- 24 – 72 hours: pallor with some hyperemia (blood flow increases). 3 – 7 days: hyperemic border with central yellowing.
- 10 – 21 days: maximally yellow and soft.
- 7 weeks: white vascular margins with fibrosis Macroscopic changes over time [10] :-
- – 3 hours: wavy myocardial fibers but no inflammatorycells.
- – 3 hours: staining defect in myocardial fiber cytoplasm with tetrazole / basic fuschsin dye.
- 4 – 12 hours: coagulation necrosis with loss of constrains contraction, bands, edema, hemorrhage and early neutrophilic infiltrate.
- 18 – 24 hours: continuing coagulation necrosis, pykosis of nuclei, and marginal contraction bands.
- 24 – 72 hours: total loss of nuclei and cross striations along with heavy neutrophilic infiltrate.

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- 3 – 7 days: macrophage and mono nuclear infiltrate beings fibro vascular response begins.
- 10 – 2 days: fibro vascular response with prominent granulation tissue containing capillaries and fibroblasts.
- 7 weeks: fibrosis with dense collagenous connective tissue and no inflammation

AETIOLOGY:

For Type – I Myocardial infarction:

Atherosclerotic plaque rupture on an artery supplying the heart muscle is the major cause of acute MI[11]. Ulcerative, fissuring erosion/ dissection with intraluminal thrombus in one or more of the coronary arteries, leads to decreased myocardial blood flow / distal plate- let emboli and thereby resulting in myocyte necrosis[12].Damage or failure of procedures such as PTCA/CABG may cause a Myocardial infarction. Spasm of coronary arteries, such as Prinz mentals angina (variant angina) may cause blockage[13].

Tissue death: If impaired blood flow to the heart lasts longer, it triggers a process called ischemic cascade; the heart cells in the territory of the blocked coronary artery die(infarction), mainly through necrosis and don' t grows back. As the artery is blocked, ultimately cells lack oxygen, needed to produce ATP in mitochondria. This leads to an ischemic cascade of intracellular changes, necrosis and apoptosis of affectedcells[14].

For Type – II Myocardial infarction:

Type 2 MI is mostly caused due to nonatherosclerotic causes. The most common triggering factors associated with type 2 MI was operative stress (20%), followed by sepsis (19%), arrhythmias (18.63%), heart failure (15%), and anemia (12%)[15]. Hyperthyroidism, Low b. p, fewer RBCS, Respiratory infections, particularly influenza, ventricular hypertrophy (left ventricular hypertrophy, cardiomyopathy), Arteritis, aortic dissection, with retrograde involvement of coronary arteries, coronary occlusion secondary to vasculitis, coronary trauma, hypoxia due to carbon monoxide poisoning or acute pulmonary disorders[16].drugs use (cocaine, amphetamines, ephedrine) also cause type -2 MI. The most common associated arrhythmia was tachyarrhythmia, especially atrial fibrillation. In the majority of patients, more than one trigger wasidentified.

PATHOPHYSIOLOGY:

- Occlusive intra coronary thrombus: A thrombus overlying a plaque causes 75% of MI, Plaque erosion in the remaining 25%.
- Vasospasm: With/ without coronary atherosclerosis and possible association with platelet aggregation.
- Emboli: From left sided mural thrombosis, vegetative endocarditis or paradoxic emboli from the right side of the heart through a patent foramen ovale.
- Molecular Events during MI related to initial ischemic event, reperfusion and subsequent inflammatory response up to 6hours following the initial ischemic event, most cell loss occurs via apoptosis, after that necrosis predominates. Ischemic epithelial cells express adhesion molecules that attract neutrophils that subsequently migrate into damaged myocardium[17].
- ST segment elevation Myocardial infarction reflects the rupture or erosion of an atherosclerotic plaque with thrombotic occlusion of an epicardial coronary artery and transmural ischemia. The size of resulting infarct depends upon the following they are;
- Ischemic area at risk according to its size,
- The duration and periodic changes of coronary occlusion, Extent of coronary micro vascular dysfunction[18].

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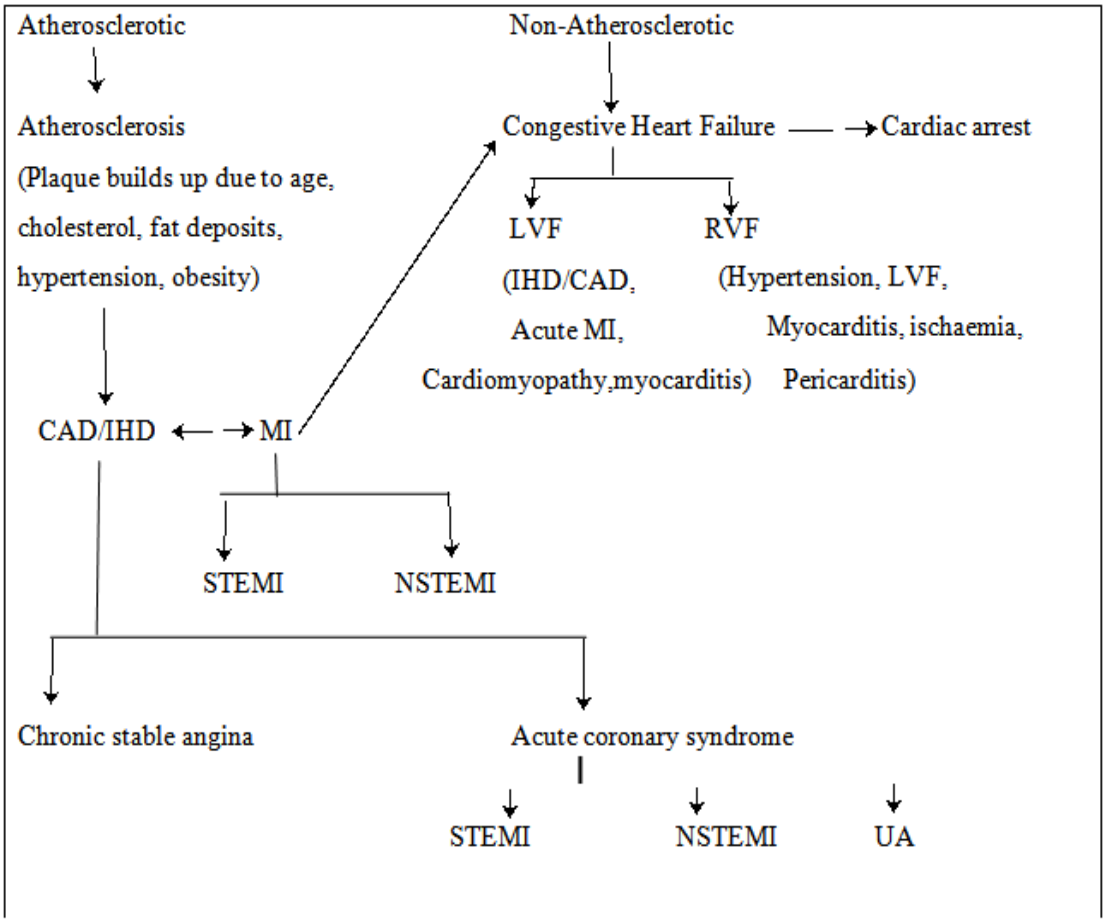

Figure:2 Pathophysiology of Myocardial Infarction

CLINICAL SIGNS:

The term myocardial infarction reflects cell death of cardiac myocytes caused by ischemia, which is the result of a perfusion imbalance between supply and demand. Ischemia in a clinical setting most often can be identified from the patient's history and from the ECG. Possible ischemic symptoms include various combinations of chest, upper extremity, jaw, or epigastric discomfort with exertion or at rest. The discomfort associated with acute myocardial infarction usually lasts at least 20 minutes which is often diffuse, not localized, not positional, not affected by movement of the region, and it may be accompanied by dyspnea, diaphoresis, nausea, or syncope[19].pain might be felt as an unexplained anxiety, or even pain might be absent atall.[20]

TYPICAL SIGNS THAT INDICATE MYOCARDIAL INFARCTION:

1. Levine's sign, in which a person localizes the chest pain by clenching one or both fists over their sternum, Is classically a predictive of cardiac chest pain, although a prospective observational study revealed it had a poor positive predictivevalue.[21]
2. Chest pain, pressure, squeezing, chesttightness.
3. shortness ofbreath, nausea, lightheadedness.
4. breaking out in a cold sweat.

Key features to diagnosis Type –II MI:[22]

An elevated but changing troponin value.

- Clinical features inconsistent with Type –I acute myocardial infarction
- Clinical conditions known to increase the oxygen demand / decrease the oxygen supply like tachycardia
- Potentially confounding clinical conditions clinical conditions / comorbidities that are potentially associated / known to be associated with myocardial injury
- Absence of symptoms / signs indicating other non-ischemic causes of troponin elevations lie

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Myocarditis.

CLINICAL MANIFESTATIONS:

In myocardial infarction the symptoms include various combinations of chest, upper extremity, mandibular, or epigastric discomfort during exertion or at rest, or an ischemic equivalent such as dyspnea or fatigue[23]. Often, the discomfort is diffuse, not localized, nor positional, nor affected by movement of the region. However, these symptoms are not specific for myocardial ischemia and can be observed in other conditions such as gastro intestinal, neurological, pulmonary, Musculo skeletal complaints. Myocardial infarction may occur in atypical symptoms such as palpitations, sweating, nausea, vomiting, fatigue, even without symptoms very brief episodes of ischemia too short to causenecrosiscanalsocause CT nrelease and elevations, massivesurgeofcatecholamines causing pain, low B.P loss of consciousness due to inadequate blood flow to brain, cardiogenic shock and sudden death due to ventricular fibrillation.[24]

Silent infarction:

It can have happened without any symptoms at all. These cases can be later discovered on ECG using blood enzyme test or at autopsy after a person has died. Such silent myocardial infarction represents 20 to 64 of all infarctions and is common in elderly, and in those with diabetes mellitus, and after hearttransplantation.[25]

DIAGNOSIS:

Criteria for prior myocardial infarction:

- Development of Q waves pathologically with or without symptoms
- Imaging evidence of a region of myocardium which is loss of viable tissue that is thinned and fails to contract, in the absence of non – ischemiccause.
- Pathological findings of a myocardium which is healed or yet to be healed from myocardial infarction[1].
- **Biomarker Evaluation**: A MI, according to current conscious is defined by elevated cardiac Biomarkers with a rising/ falling trend and at least one of the following:
- Symptoms related to ischemia.
- Changes on ECG (ST segment, new LBB/ pathogenic Q wave). Change in motion of the heart wall on imaging.
- Demonstration of a thrombus on angiogram (or) at autopsy.

Cardiac Biomarkers:

These are substances that are released in to the blood when the heart is damaged (or) stressed. These are used to detect the presence of ACS and Cardiac ischemia and to evaluate their severity as soon as possible, so that appropriate therapy can be initiated. Current bio- marker test of choice for detecting heart- damage is troponin, which is considered to be best.[26]Other cardiac bio markers are less specific for heart. Measured level of markers is in direct proportional relationship to extent of myocardial injury. Measurement of these markers is used to help diagnose, evaluate, and monitor patients with suspected acute Coronary Syndrome.

Cardiac Biomarkers are:

→ CK-MB/ myoglobin (5-25 IU/L).
→Trop-T (<0.2ng/ml).
→ Trop-I (<1.5ng/ml).
→ Trop-C.
→ CPK (creatinine kinase).

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→ LDH (100-210 IU/L).
→ BNP (<100 pg/ml).

- Troponin I and Troponin T are cardiac specific and sensitive biomarkers of myocardial damage.[27,19.] A rise in troponin occurs within 1-3 hrs of injury to the heart muscle and peaks with- in 1-2 days.
- Trop-T > 0.40ng/ml→ Indicate Acute MI.
- Troponin I is a useful cardiac Biomarker for post operation cardiac surgery patient. Elevated Troponin I indicates mental stress induced ischemia; patient recently have had a heart attack.
- Decreased troponin I indicates that the patient may not experience heart attack.
- Elevated Lactate Dehydrogenase enzyme used in differential diagnosis of acute myocardial infarction. It has 2 advantages 1) increased elevation is present for as long as 6-8 days after attack,2) technical procedure is far often less complicated than other enzyme tests.[28]
- **BNP** (B-type natriuretic peptide): BNP and NT-Pro BNP, the two most commonly used natriuretic peptides, play a major role in diagnosis, assessment of heart failure[29], and is shown to be a strong predictor of short term and long-term mortality with acute coronary syndrome. BNP greater than 100 pg/ml indicates heart failure. NT-PRO BNP (N-terminal-pro BNP), a more stable form of BNP greater than 125 Pg/ml is cut off level for heart failure in elderlypatients.

CK-MB:

- Increased in CK-MB indicates myocardial necrosis i.e.., Myocarditis, PE, CHF, aortic dis-section[1].
- Used to detect re-infarction.
  - / 5-25 IU/L (normalrange)
- CK-MB is elevated with past cardiac surgery, inflammation/ electrical cardio version. It rises within 4-8 hours and returns to normal within 2-3 days.[30]
- Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by new ST elevation or new LBBB, or evidence of fresh thrombus by coronary angiography, but death occurring blood samples could be obtained, or at a time before the appearance of cardiac markers in the blood. For percutaneous coronary intervention patients, the normal baseline indicative of peri –procedural myocardial necrosis. By convention, increases in the biomarkers for greater than 3x 99th percentile URL are indicative to the percutaneous coronary intervention related myocardial infarction[1,9].

For coronary artery bypass grafting patients the normal baseline troponin values, elevations of biomarkers are indicative to the peri – procedural myocardial necrosis. By conventional increase in the biomarkers for greater than x 99th percentile of URL and all the above cases including leads to the indication of coronary artery bypass grafting related myocardial infarction. Copeptin may be useful to rule out MI rapidly when used along with troponin.[31]

ST2 Cardiac biomarker:

ST2 provides prognostic information that is independent of other cardiac biomarkers such as BNP, NT-Pro BNP, highly sensitive troponin, GDF-15, and galectin-3.ST2 is a strong predictor of cardiovascular death and risk of developing new heart failure in STEMI, NSTEMI and Acute coronary syndrome patients with a quartile (>35ng/ml)[32].

ECG:

Series of leads placed on persons chest that measure electrical activity associated with contraction of heart muscle.[33]

ECG Findings in Myocardial infarction:

- Increased in ST- segment.
- Changes in shape/ flippingof tissue Indicate Acute MI[1,19] New Qwave
- New LBBB.
- Inverted T wave acute ischemia. ST seg depression acute ischemia. Q wave elevation acute ischemia.
- ST - T changes (ST depression, T wave inversion) - indicates acute NSTEMI.
- ST elevation in V1 when V2 has either less significant ST elevation or has ST depression indicates right ventricular infarct[8].
- ST depression and T wave inversion in leads with broad R waves (I, aVL, V5 - V6) and ST elevation in leads with prominent QS

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complexes (V1 - V3 +/, II, III and a VF) and ST - T changes in the same direction as the QRS complex in Left Bundle Branch Block (LBBB) indicates ischemia orinfarction[8].

- ST elevation ≥ 1mm in a lead with a positive QRS complex or ST depression ≥ 1mm in V1, V2 OR V3 indicates myocardial infarction in the presence of LBBB[8].
- ST elevation**,** new rise in V2 and V3 >2mm for males/ >1mm for females in two other adjacent chest/ limb leads. →STEMI.[26,19]
- Early STEMI/ST elevation is associated with infarction and may be preceded by changes: Peak T-Waves

ST depression Inversion of T waves[26].

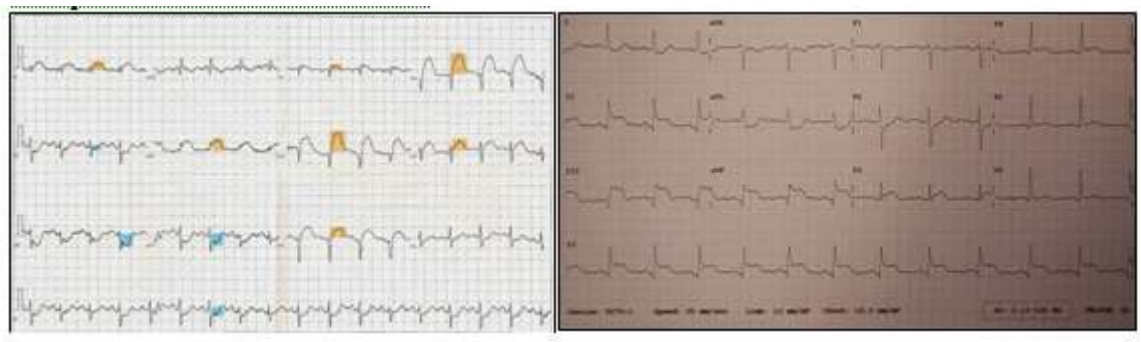

Figure:3 A 12 lead ECGshowingAWMI
Figure:4 A 12-lead ECG showing a STEMI. Elevation of the ST segment can be seen in some leads.

Conditions that cofound the ECG Diagnosis of MI [1]:

- QS complex in lead V1-normal.
- Q wave <0.038 and <1/4 of R-wave in lead-III – normal
- Q waves < 0.03 seconds and <1/4 of the R-wave amplitude in leads I, AVL, AVF and V4-V6.
- Qwavemay benormal in AVL. If thefrontal QRSaxisisbetween 60 and 90∘
- Pre-excitation, obstructive/ dilated cardio myopathy, LBBB, RBBB, left anterior hemi block, left and right ventricular hypertrophy, Myocarditis, acute/ pulmonale/ hyperkalemia may be associated with Q/QS complexes in the absence ofMI.

- **ECG indications for re – infarctions [1]:**
- ST segment elevation greater than equal to 0.1mv reoccurring in patient having a lesser degree of ST elevation.
- New pathogenomic Q waves in at least 2 continuous leads, when associated with ischemic symptoms
- **NOTE**: Re – elevations of ST segment can, also be seen in threatening myocardial rupture and should lead to additional diagnostic work up.
- **ECG indications for coronary re – vascularization [1]:**
- New ST – T segment abnormalities common in patients who have underwent CABG.
- New pathological Q – waves appear in territories other than those identified before surgery. New wall motion abnormalities.
- Elevated biomarkers.

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Hemodynamic instability.

Figure:5 Blue = lateral wall = circumflex artery

– Yellow = inferior wall = right coronary artery
– Red = anterior wall = left anterior descending artery

Common injury patterns and likely culprit vessels [8] :

Affected walls(s)	primary ischemic changes (e.g., - ST elevation, Q waves)	Reciprocal changes (e.g., - ST depression)	Most likely culprit vessel
Septal	V1-V2	-	LAD
Anterior	V3-V4, V2, +/-V5	II, III, aVF	LAD
Lateral	V5-V6, +/-I, +/-aVL	II, III, aVF	Cx
High lateral	I and aVL only	II, III, aVF	LAD
Inferior	II, III, and aVF	V2-V3 and/ or I, aVL	RCA AND Cx
Anterioseptal (usually apical anterior)	V1-V4	II, III, aVF	LAD
Anteriolateral	V3-V6, I, aVL	II, III, aVF	LAD
Inferolateral	II, III, aVF, V5- V6, +/-I, +/- aVL	V2 - V3	Cx

ECHO CARDIOGRAPHY:

It is an ultrasound of the heart echocardiography. It was standard 2 dimensional, 3 dimensional and Doppler ultra sound to create images of heart[34]. It is routinely used for the diagnosis, management and follow up of patients with any suspected/ known heart disease.

2D-Echocardiography is an important tool in assessing wall motion abnormality in patients with suspected cardiac disease. It is a tool which helps in reaching an early diagnosis of Myocardial Infarction showing regional wall motion abnormality of the heart. Also, it is important in treatment and follow up in patients with heart failure, by assessing ejection fractionally.

3D-Echocardiography can help detect Valvular defects[35], Cardiomyopathies, such as hyper- trophic Cardiomyopathy, dilated Cardiomyopathy, and many others[36].

Stress echocardiography may also help determine whether any chest pain or associated symptoms are related to heart disease. The biggest advantage to echocardiography is that it is not invasive (does not involve breaking the skin or entering body cavities) and has no known risks or side effects.

Not only can an echocardiogram create ultrasound images of heart structures, but it can also produce accurate assessment of the blood flowing through the heart by Doppler echocardiography, using pulsed- or continuous-wave Doppler ultrasound. This allows assessment of both normal and abnormal blood flow through the heart.

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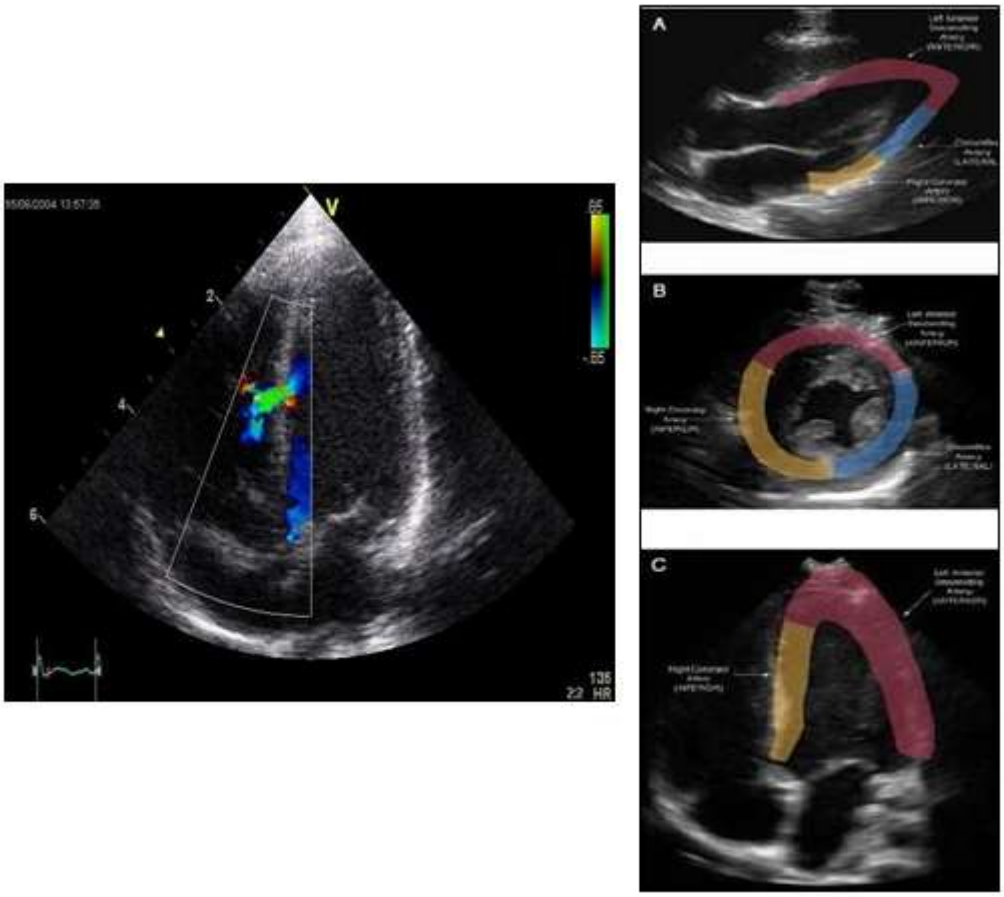

Figure:6 2D ECHO showing ventricularseptaldefect.
Figure:7 Echocardiogram images with outlinedregional wall motion abnormality territories of A) PSLAX B) PSAX, and C) abnormality territories of A) PSLAX B) PSAX.

Coronary Angiography[37]:

It is most commonly used to visualize the blood in the coronary arteries. A catheter is inserted to visualize the desired area. The catheter is inserted through the artery in the forearm, and is advanced through the arterial system into the main coronary artery. X-ray images allows visualization of the size of the artery openings. However, the presence or absence of atherosclerosis or atheroma within the walls of the arteries cannot be clearly determined.

It can visualize coronary artery stenosis, or narrowing of the blood vessel. The degree of the stenosis can be determined by comparing the width of the lumen of narrowed segments of blood vessel with wider segments of adjacent vessel.

It allows the recognition of occlusion, stenosis, restenosis, thrombosis or aneurismal enlargement of the coronary artery lumens; heart chamber size; heart muscle contraction performance; and some aspects of heart valve function. Coronary artery luminal narrowing reduces the flow reserve for oxygenated blood to the heart, which produces intermittent angina. Very advanced luminal occlusion usually produces a hearttack.

Indications:

- Heart attack (STEMI, NSTEMI, Unstable angina) abnormal stress Test.
- New onset of unexpected heart failure.
- survival of sudden cardiac death or dangerous cardiac arrythmias. persistent chest pain despite optimal medical therapy.
- Workup of suspected Prinz mental angina (coronary vasospasm)[38].

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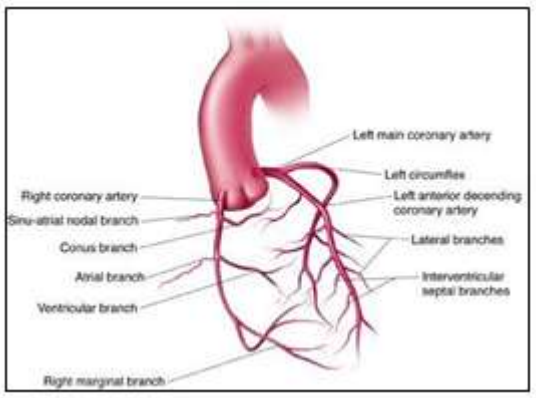

Figure:8 Heart and It associate arteries.

Magnetic resonance angiography and venography:

Magnetic resonance angiography MRA generates pictures of the arteries to evaluate them for stenosis or aneurysms, occlusions, vessel wall dilations, at risk of rupture,

MRA is used to evaluate arteries of neck and brain, the thoracic and abdominal aorta, the renal arteries, and the legs called a run - off. Contrast enhanced magnetic resonance angiography uses injection of MRI contrast agents and is currently the most common method performing MRA[39].

MRV used to image veins and used to detect the venous blood.

Cardiac stress test or thread mill test:

It is a cardiological test that measures the heart ability to response to external in a control- led clinical environment. It shows how well your heart work during physical activity because excerise makes heart pump harder and faster. An exercise stress test can reveal the problems with blood flow within the heart. Doctor recommends stress test u have signs and symptoms of CAD and Arrythmia.

This test as guide treatment decisions and measure the effectiveness of the treatment or deter- mine the severity if you have already been diagnosed with cardiac disease. An exercise stress test provides more information about exercise tolerance than a pharmacologic stress test[40].

Diagnostic value: Thread mill test sensitivity 73 - 90%, specificity 50 - 74%.

Nuclear stress test:

The best-known example of nuclear stress test is Myocardial Perfusion Imaging(MPI). MPI is a nuclear medicine test which is performed in conjugation with exercise of pharmacological stress testing. The radioactive tracer (myoview) is administered during stress and rest followed by images of cardiac perfusion obtained with a gamma camera[41]. MPI shows how well blood flows through heart muscle and how well the heart muscle is pumping. It can show areas of heart muscle that are not getting enough blood flow. It is also used for the assessment of thrombolytic therapy effectiveness and early risk stratification of patients with acute myocardial infarction, hypertrophic cardio myopathy and heart wall motion abnormalities. It can also detect regions of myocardial infarction by showing decreased resting perfusion. The functions myocardium is also evaluated by calculating left ventricular ejection fraction (LVEF of heart) which is done in conjugation with cardiac stress test.

Magnetic Resonance Imaging:

Cardiovascular MRI has high spatial resolution and moderate temporal resolution. It is a standard for the assessment of myocardial function and has similar capability to echocardiography in suspected acute infarction. It is also used in the assessment of Myocardial ischemia, Cardiomyopathy, Myocarditis, Iron over load, vascular diseases and Congenital heart diseases. However, it is not commonlyused.

TREATMENT:

ACC/AMA Guidelines for AMI

On arrival in the ED patient with suspected acute MI should receive O2 by nasal prongs

↓

Sublingual nitroglycerin

(unless systolic arterial pressure is less than 90mm hg/H.R is less than 50bpm (or) > 100bpm)

↓

Adequate analgesia with morphine sulphate/

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meperidine
↓
Aspirin 160-325mg orally.
↓
A 12 lead ECG should be performed.
↓
ST segment elevations =/>1mV in contagious leads provides strong evidence of Thrombotic coronary artery occlusion and makes the patient for immediate reperfusion therapy either by fibrinolysis/ primary percutaneous transluminal coronary angioplasty (PTCA).
↓
Symptoms consist with acute Mi and LBB should be managed like ST segment elevation. In contrast patient without STEMI should not receive thrombolytic therapy. The benefit of primary PTCA in these patients remains uncertain.
↓
Age > 65 years, between < 70 kgs, systemic arterial hypertension and Tissue Plasminogen activator (TPA) administration are variables increase the risk of Intracranial Hemorrhage that usually occurs within the 1st day of thrombolytictherapy.

Hospital Management- In 1st 24 hours:
Once hospitalized patient with Acute MI should be monitored by ECG continuously and diagnosis of Acute MI confirmed by serial ECGs and managements of serum cardiac markers of myocyte necrosis, such as Creatinine kinase Isoenzyme/ Cardiac specific Troponin T/I.
↓
Patient should be monitored closely for adverse Electrical/ Mechanical events because reinfarction and death occur not frequently within 1st 24 hours.
↓
Patient physical activity must be limited for at least 12 hours and pain/ anxiety should be minimized with analgesics.
↓
Epinephrine, Defibrillator, Transvenous Pacemaker, Atropine, Lidocaine, Transcutaneous pacing patches should be immediately available.
↓
Patient survived from large AWMI/having a LV mural thrombus are at a high risk of embolic stroke, which can be reduced by administering IV heparin.
↓
When TPA (Reteplase) is administered IV heparin increases the likelihood of patency in infarct related artery (assessed angiographically) but this may not necessarily lead to improved out- come.
↓
Hence considering the benefit of TPA + Heparin therapy all the patients undergo primary PTCA large doses of IV heparin is recommended, Aspirin 160-325 mg daily initially given in the ED, should be continued.
↓
IV heparin should be given at least 48 hours after Reteplaseis given.
↓
IV Nitroglycerin used as substitute for narcotic analgesic in AMI without bradycardia/ Tachy-cardia/hypotension.
↓
Inpatients without LBBB/ ST segment elevation in whom primary congestion is absent, Diltiazem decrease the incidence of recurrent ischemia.
↓
In patients with evolving acute MI with ST segment elevation/ LBBB an ACE inhibitor should be used within hours of admission, provided that should not have hypotension.
↓
ACE inhibitors should be continued if patients has impaired LV systolic function (Ejection fraction < 40+) or clinical CHF .in patients with no symptoms of LV dysfunction by 6weeks ACEI can be stopped.

Hospital Management after 24 hours:
After 1st day in hospital, patient with acute MI should receive Aspirin 160-325mg/day, a β blocker and an ACEI should be used for at least 6weeks. Nitroglycerin infusion for 24-48 hours and Mgso4(magnesium sulfate) should be given as needed IV heparin for an additional 48 hours in patients receiving Reteplase.
↓
Patient with myocardial ischemia that is spontaneous or provoked in days to weeks after acute MI irrespective of whether they receive thrombolytic therapy should undergo angiographic evaluation with subsequent PTCA/ surgical revascularization.
↓
Coronary angiography and subsequent revascularization should be reserved for survivors of Acute MI who have preserved LV systolic dysfunction and spontaneous/ provoked ischemia.
↓
Patient with recurrent chest pain believed due to Pericarditis should receive high dose- Aspirin 650 mg every 4-6hours.

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↓

Recurrent chest discomfort caused by myocardial ischemia should be treated with
IV nitroglycerin, aspirin, Heparin. Coronary angiography with subsequent revascularization should be considered.

↓

For a patient in Cardiogenic shock, consideration should be given to insert an intra- aortic balloon pump and emergency coronary angiography followed by PTCA/CABG.

↓

The patient with right ventricular infarct/dysfunction should be treated with Normal saline, Ionotrophic Agents if hypotension persists.

↓

In patient with Acute MI, appearance of AF is after a symptom of extensive LV systolic dysfunction. They cardio version should be performed.

↓

Patient with acute MI and symptomatic sinus bradycardia/ AV block receive Atropine. Temporary pacing should be performed if patient is unresponsive to drug therapy.

STEMI → Thrombolysis therapy (or) PTCA/CABG within90-20
minutes of contact with medical provider.

NSTEMI → Anti thrombotic (aspirin) decrease the clot sizeand
further clotting in affected artery. P2Y12 inhibitors (clopidogrel and ticagrelor) are used in both STEMI, NSTEMI including inPCI.

For very high-risk scenario → inhibitor of glycoprotein α11bβ3a receptors (Eptifibatide and trofiban) are used.

Fibrinolysis:

- If PCI can't be performed with 90-20 minutes in STEMI then fibrinolysis preferable within 30 minutes of arrival to hospital is recommended[43].
- If a person has symptoms for 12-24 hours, evidence of effectiveness of Thrombolysis is less, and if they have had more than 24 hours it isn't recommended[44].
- Thrombolysis involves use of drugs that activates the enzymes that normally dissolve blood clots. These drugs include → TPA (Reteplase, Streptokinase, Tenecteplase)[30].

Contraindications[26]:

- High risk of bleeding/ active bleeding. Past stoke of bleeds in the brain.
- Severe hypertension.
- Recent Surgery/ use of anti coagulants. Pregnancy.
- Proctivity to bleeding.
- prior intracranial hemorrhage (ICH). Known malignant intracranial neoplasm. Ischemic stroke within 3 months.
- Suspected aortic dissection.
- Active bleeding or bleeding diathesis (excluding menses) Significant closed head trauma or facial trauma within 3months. Intracranial or intraspinal surgery within 2 months.
- Severe uncontrolled hypertension.
- For streptokinase, prior treatment within the previous 6months.
- **Immediate Surgical Intervention is often required for patientwith:**
- Failed PTCA with persistent chest pain/ hemodynamic instability.
- Persistent/ recurrent ischemia refractory to medical therapy who isn't a candidate for catheter intervention.
- Cardiogenic shock and Coronary anatomy aren't amerable to PTCA.
- Medical abnormality leading to pulmonary congestial/ hypotension such as papillary muscle rupture/ ventricular septal defect.

PTCA:

- Percutaneous Transaminal Coronary Angioplasty. It is a minimally invasive procedure used to open up a blocked coronary artery, allowing blood to circulate unobstructed to the heart muscle.
- A long narrow tube called a diagnostic catheter is advanced through the introducer over the guide wire, into the blood vessel. It involves small probes inserted through peripheral blood vessels. Such as femoral artery/ radial artery into blood vessel of heart.
- Probes used to identify and clear blockages using small balloons, which are dragged through the blocked segment dragging away the clot/insertion of stent.
- Primary PTCA is treatment of choice for STEMI if it can perform in timely manner. With- in 90-120 minutes. It is also done in NSTEMI in 1-3 days particularly when considered high risk[11,43].
- In addition to clinical judgment risk stratification may be used to guide treatment such as with the TIMI and Grace scoring system[11,45].

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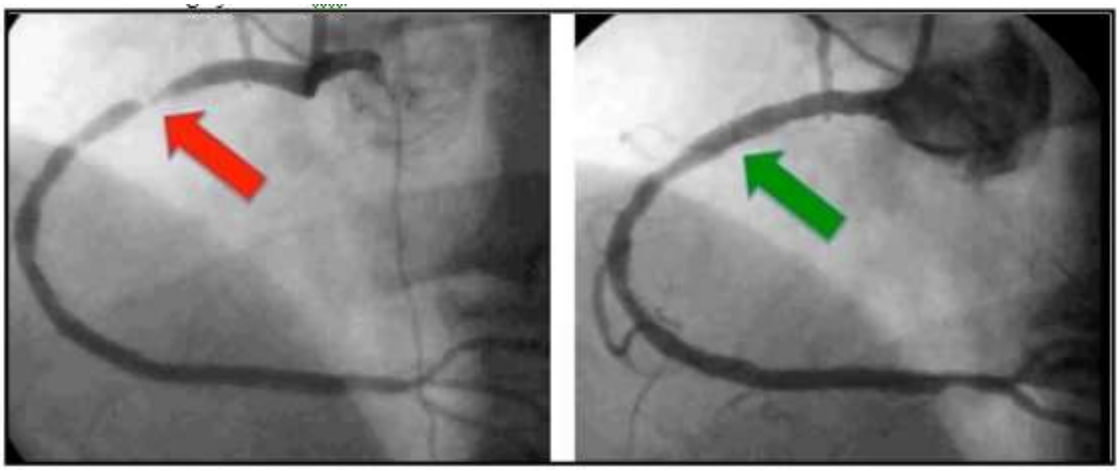

Figure9: Angiogram showing severe **Figure10:** Angiogram after PTCAstenting narrowing of right coronary artery (RCA) .

Indications for stenting[46]:

- Treatment of acute/threatened artery closure following balloon angioplasty.
- Focal denovo native vessel lesions.
- Lesions with late recoil after balloon angioplasty.
- Acute closure after balloon angioplasty, proximal left anterior descending.
- Coronary artery lesions.
- Aorta -ostial lesions.
- Stents prevent risk of restenosis.
- unstable angina
- stable angina
- high risk stress findings.
- STEMI, NSTEMI.

Contraindications[46]:

- **L**ack of cardiac surgical support.
- Coagulopathy.
- **H**yper coaguagulable states.
- Diffusely diseased vessels without focal stenoses**.** Stenosis less than 50%.
- A single diseased vessel providing all perfusion to the myocardium. Total occlusion of a coronary artery.
- Arteries<15mm in diameter.
- Critical left main coronary stenosis without collateral flow from a native vessel or previous bypass graft to the left anterior descending artery.

CABG[47]:

- Coronary Artery Bypass Surgery. It is a surgical procedure to restore normal blood flow to all destructed coronary artery. There are 2 main approaches**:**
  - The left internal thoracic artery LITA/ left internal mammary artery LIMA is diverted, to the left anterior descending branch of the left coronary artery (LAD). In this method the artery is predicted which means it is not detached from the origin.
  - In the other, a great saphenais, vein is removed from leg one end is attached to the aorta is removed from leg, one end is attached to the aorta (or) one of its major branches, and the other end is attached to the destructed artery immediately after the obstruction to restore blood flow.

Indications for CABG:

- Triple vessel disease.
- Severe left main stem artery stenosis.
- Left main equivalent disease (70 greater stenosis of left anterior descending and proximal left circumflex artery)- Particularly if left ventricular function is impaired.
- Disabling angina (class-1). Ongoing ischemia in setting of a non-ST segment elevation myocardial infarction (NSTEMI) that is unresponsive to medical therapy (class-1).
- Poor left Ventricular function but with viable, nonfunctioning myocardium above the anatomic defect that can be revascularized.
- Clinically significant CAD of 70 stenosis/ greater, in 1/more vessels in survivors of sudden cardiac arrest presumed to be related to ischemic ventricular arrhythmia.
- Clinically significant CAD of 50 stenosis/ greater, in 1or more vessels in patients undergo- ing cardiac Surgery for the other indications (eg: Valve replacement/Aortic

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Surgery).

Contraindications for CABG:

It is not appropriate in asymptomatic patients who are at aloe risk of MI/ death.

- Older patients of age > 85 years are most likely to experience perioperative complications after CABG, hence they should be carefully considered.
- Patient who will benefit from coronary revascularization. Coronary arteries incompatible with grafting.
- Absence of viable myocardium to graft. Aneurysms.
- Valvular diseases. Congenital diseases. Diseases of blood. Calcified targeted vessels.
- Intramyocardial target vessel. Diffusely diseased target vessels.

Cardiac Rehabilitation:

Benefits who have experienced MI even if there has been substantial heart damage and resultant left Ventricular failure, it should start soon after discharge from hospital. This progression includes life style advice, exercise, social support, as well as recommendations about stress management.

Long Term Management[42]:

- After Acute MI patient should continue to receive: Aspirin.
- β blocker.
- ACE inhibitors.
- Patient with LDL >130mg/dl (statin). Smoking, and alcohol cessations.
- Physical Exercise.

Discharge preparation:

Patient with recent acute MI should undergo standard THT (sub maximal at 4-7 days/ symptom limited to 10-14 days). It is done to assess:

→ Patient functional capacity and ability to do tests.

→ Efficacy of patient.

→ Stratify risk of subsequent cardiac event.

II. CONCLUSION:

They are very few studies done on pathogenesis and stages of myocardial infarction. More studies with accurate results must be needed. In this review we focused the Pathophysiology of myocardial infarction, various classification systems and the morphological features of infarct. And standard diagnostic methods for early detection of Myocardial Infarction.

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CONFLICTS OF INTEREST STATEMENT:

None of the authors have conflicts of interest with respect to this work.

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