Diagnosis of Acute Myocardial Infarction

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Abstract

Diagnosis of acute myocardial infarction (AMI) has to be made early in the emergency triage since maximal mortality occurs within first hour and the benefits of all interventions are greater once these are instituted early. Diagnosis is easy and based on simple principals of good history, physical examination, early and complete 12 lead electrocardiogram and use of echocardiography which should be available in the emergency triage area. Subsequently biomarkers are also available for documentation and risk stratification. The other causes of acute severe chest pain should be kept in mind and ruled out. The role of myocardial perfusion imaging for diagnosis of AMI is limited. The diagnosis also involves an estimation of the size of infarct, duration since onset of the process, any acute complications of AMI and the likely vessel involved since these have significant therapeutic implications.

Diagnosis of acute myocardial infarction (AMI) has to be made early in the emergency triage since maximal mortality occurs within first hour and the benefits of all interventions are greater once these are instituted early. Conventionally, AMI is diagnosed in the emergency based on ST segment elevation of more than 1.5 mm in 2 or more leads. Chest pain, electrocardiogram and cardiac enzymes have conventionally been used for diagnosis of AMI.[1] Echocardiography in the emergency room is being used more and more frequently with greater accuracy for the same. The role of myocardial perfusion imaging for diagnosis of AMI is limited in this acute setting due to lack of 24 hrs availability and the time taken in conducting this evaluation.[2] The diagnosis also involves an estimation of the size of infarct, duration since onset of the process, any acute complications and the likely vessel involved, since these have significant therapeutic implications. Diagnostic evaluation process should also include a fast assessment of patients risk factors (hypertension, diabetes and renal functions) and medications patient is already taking since this effects the subsequent management approach.

Clinical Presentation

Chest pain is the usual symptom which brings these patients to medical attention. Pain is severe, diffuse, retrosternal and radiates to arms or from jaws to umbilicus. Pain does not get relieved with sublingual nitrates or usual pain killers. It is often associated with eructations and retrosternal burning. Commonly patients mistake it for acid peptic symptoms and waste precious time with antacids. It is accompanied with vomiting, sweating and breathlessness. About 15-20% of infarcts can be painless specially in elderly and diabetics. Equal number may have less characteristic pain than described above. The pain needs to be distinguished from other causes of acute severe chest pain which can bring patients to emergency room.[3-5]

Pericarditis

Pericarditis causes a steady substernal pain relatively rapid in onset, relieved by sitting forward and increases on recumbence. Radiation to the trapezius ridge is characteristic and highly specific for pericarditis. Presence of pericardial rub and pain characteristics usually help to distinguish pericarditis from myocardial infarction.[6]

Aortic Dissection

The abrupt onset severe chest pain (tearing or stabbing) with

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changing location with maximum intensity at the onset, unlike crescendo pattern of infarct pain is suggestive of aortic dissection. Ascending aortic dissection produces pain in the anterior chest whereas interscapular or abdominal pain suggests involvement of descending aorta. Physical characteristics suggesting a connective tissue disorder (eg. Marfan's syndrome, Ehler Danlos syndrome) pulse deficits, aortic regurgitation (AR) murmur should arouse the suspicion of aortic dissection. ECG changes when present indicate coronary ischemia but in 1-2% of cases, aortic dissection is accompanied by changes suggesting acute inferior wall MI. Most type A dissections arise just above right sinus of Valsalva with retrograde extension producing occlusion of right coronary ostia and thus complicates the clinical picture.[7-8]

Pulmonary Embolism

Chest pain in pulmonary embolism is attributed to either sudden distention of pulmonary artery and right ventricular ischemia mimicking angina or formation of pulmonary infarct with pleuritic pain. Patients often have ECG changes of acute cor-pulmonale such as $S_1Q_{III}T_{III}$ with T wave inversion in leads V_1-V_4. Other pulmonary cause hyperventilation is often seen in young individuals with dyspnoea more than pain. In pneumothorax patients have sudden onset dyspnoea and pain which is often one-sided and decreased respiratory movements are seen on that side.[9]

Gastrointestinal causes

Gastrointestinal reflux disease presents as burning pain associated with supine/prone positions. It is not associated with any ECG changes. Esophageal spasm can produce chest pain similar to angina but without changes in ECG/biomarkers. Patients with peptic ulcer disease can have epigastric/retrosternal severe pain and diaphoresis occurring 60-90 minute after food without ECG changes. The continuous pain after bout of vomiting and retching with subsequent hematemesis is suggestive of Mallory-Wiess Syndrome. Right hypochondrium and/or epigastric pain radiating to shoulder and back generally associated with fever and abdominal tenderness is a presenting feature of acute cholecystitis or pancreatitis. Palpation of abdomen and chest is important for making such diagnosis.

Musculoskeletal causes

Costochondritis (Teitz syndrome) may produce localized pain which is reproducible on movement and palpation.

Thus, although pain of myocardial infarction is quite distinctive it may be mimicked by other conditions. A good short history of type of pain, duration, accompanying symptoms, risk factors and preceding activities before the pain can be useful.
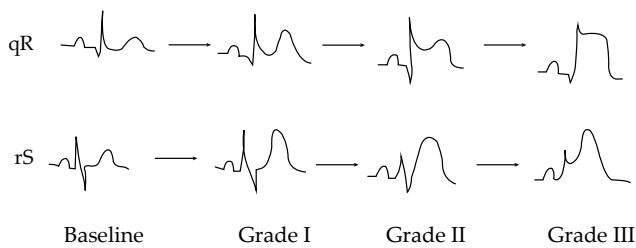
Fig. 1 : Serial ECG changes in early acute myocardial infarction

Examination of pulse and blood pressure and respiratory rate help greatly in risk stratification of these patients. Palpation and auscultation are also helpful in these acutely distressed individuals. In the hurry to do an early ECG these things should not be missed.

Electrocardiogram

ECG is generally the first investigation available for making a diagnosis in a patient presenting with acute severe chest pain.[10-11] Tall T waves and ST elevation are the hallmarks of early presentation within minutes of onset of pain. The third change – appearance of Q waves, is delayed and seen after 6 hours of onset. Q waves denote significant myocardial necrosis. The initial changes of upright and tall T wave with concave upward ST segment elevation subsequently, gives way to T wave inversion and ST coving with convexity upwards over one day to one week. Q waves once they appear generally persist through out life. T wave change is in larger area and it denotes ischemia, ST segment change is in lesser number of leads and denotes myocardial injury and Q waves overlie and denote central area of myocardial necrosis. Arrhythmias are common during early ECG specially frequent and complex VPC's and ventricular tachycardia in some. Inferior wall infarct patients often have sinus bradycardia early.

Shortly after occlusion of a coronary artery, serial ECG changes are detected by leads facing the ischemic zone, as shown in Figure 1. First, the T waves become tall, symmetrical, and peaked (grade 1 ischemia). Second, there is ST elevation (grade 2 ischemia) without distortion of the terminal portion of the QRS. Third, changes in the terminal portion of the QRS complex may appear (grade 3 ischemia).[12] The changes in the terminal portion of the QRS are explained by prolongation of the electrical conduction in the Purkinje fibers in the ischemic region.

The changes of infarction are generally seen in the leads overlying the infarct area. Thus, in inferior wall infarct changes are seen in leads II, III, aVF; in anterior infarct in lead V_1-V_4 and in anterolateral infarct in lead I, aVL and V_5-V_6. RV infarct is diagnosed by ST elevation in V_3R and V_4R.[13] In presence of RBBB the changes of infarction are not effected and so are diagnosed by usual principals. Pseudoinfarct pattern (false positive) may be seen in early repolarization pattern, hypertrophic cardiomyopathy, Brugada syndrome, peri/myocarditis and in metabolic disturbances such as hyperkalemia.

Diagnosing infarction in presence of LBBB

ST-segment elevation with tall, positive T waves is frequently seen in the right precordial leads with uncomplicated LBBB. Secondary T wave inversions are present in the lateral precordial leads. However, the appearance of ST-segment elevations in the lateral leads with concordant T waves suggests IHD (sensitivity 73%, specificity 92%). ST-segment depressions and/or deep T wave inversions in leads V1 to V3 also suggests underlying

Table 1 : Heart blocks (Complete heart block) in patients with acute myocardial infarction

	Inferior MI	Anterior MI
Frequency	More common	Less common
Level	Suprahisian	Infrahisian
Escape rate	40-60	30-40
QRS Complex	Narrow	Wide
Responds to	Atropine	Isoprenaline
Mortality	10-15%	65-75%

ischemia (sensitivity 25%, specificity 96%). More marked ST-segment elevations (>0.5 mV) in leads with QS or rS waves may also be caused by acute ischemia (sensitivity 31%, specificity 92%).[14]

The presence of QR complexes in leads I, V5, or V6 or in II, III, and aVF with LBBB strongly suggests underlying infarction.

Chronic infarction is also suggested by notching of the ascending part of a wide S wave in the mid precordial leads (Cabrera sign) or the ascending limb of a wide R wave in lead I, aVL, V5, or V6 (Chapman sign).

Anterior wall MI : localization

In acute anterior wall infarction - ST elevation is usually present in V2 to V4. ST elevation in V2 to V6 may represent LAD occlusion proximal to the first diagonal branch.

- ST elevation in V4 to V6 without ST elevation in V1 to V3 usually is caused by LCX or distal diagonal occlusion.
- ST elevation in lead I and aVL signifies occlusion of first diagonal branch (if associated with ST elevation in V2) and occlusion of the first marginal branch of the LCX (if there is ST depression in V2)
- ST depression in aVL signifies LAD artery occlusion distal to the first diagonal branch.[12,15-16]
- ST elevation in the inferior leads signifies occlusion of a long LAD artery (that wraps the cardiac apex) distal to the first diagonal branch.
- ST elevation in aVR signifies LAD artery occlusion proximal to the first septal branch.
- Right bundle-branch block signifies LAD artery occlusion proximal to the first septal branch.

Inferior wall MI : localization

- ST segment elevation in lead III more than in II denotes RCA occlusion with a sensitivity of 99% and a specificity of 100%. When it is combined with ST elevation in V_1 it denotes occlusion proximal to acute marginal branch.
- ST segment elevation in lead II more than in III denotes LCx occlusion with a sensitivity of 93% and a specificity of 100%. ST elevation in V_5 and V_6 or I and aVL are also a sensitive and specific marker for LCx lesion. Abnormal R in V_1 consistent with posterior infarction is also highly specific for LCx occlusion.[17-19]

Heart blocks in MI

AV conduction blocks are commonly seen with inferior and anterior infarcts. Patients with anterior infarct commonly have fascicular blocks. Early diagnosis of bifascicular block (RBBB with left axis deviation) and trifascicular block (RBBB, left axis deviation with prolonged PR) can help in predicting subsequent complete heart block. The pattern of heart blocks and their significance in anterior and inferior infarcts is as shown in Table 1.

Table 2 : Parameters evaluated on echocardiographic examination in acute MI

Hemodynamic state	Hypovolemia
	Right ventricular infarction
	Globally reduced left ventricular contractility
Mechanical complications	Papillary muscle rupture and severe mitral regurgitation
	Ventricular septal rupture
	Free wall rupture and tamponade
Others	Left ventricular aneurysm
	Mural thrombus
	Pericardial effusion

Echocardiography

Echocardiography is helpful in the evaluation of chest pain, especially during active chest pain. The absence of LV wall motion abnormalities during chest pain usually but not always excludes myocardial ischemia or infarction, and the presence of regional wall motion abnormalities helps in confirming the diagnosis.

It helps in diagnosis and exclusion of acute MI in patients with prolonged chest pain and nondiagnostic electrocardiographic findings; estimation of the amount of myocardium at risk and final infarct size after reperfusion therapy; evaluation of patients with unstable hemodynamic findings and detecting mechanical complications; evaluation of myocardial viability; estimation of ejection fraction; and any associated abnormality (Table 2). Echo also helps in ruling out other causes of chest pain like aortic dissection, pericarditis and acute cor pulmonale associated with pulmonary embolism. Patients with hypertrophic cardiomyopathy and aortic stenosis can also present with chest pain and similar ECG changes and can be diagnosed with an echo in the emergency room itself.

For purposes of regional wall motion analysis, the ASE has recommended a 16-segment model or, optionally, a 17-segment model with an addition of the apical cap. A scoring system for grading wall motion has been developed depending upon the appearance on echocardiography and is shown in Table 3. On the basis of this wall motion analysis scheme, a wall motion score index (WMSI) is calculated to semiquantitate the extent of regional wall motion abnormalities: WMSI=Sum of wall motion scores/Number of segments visualized. A normal left ventricle has a WMSI of 1, and the index increases as wall motion abnormalities become more severe.[20]

The prognostic indicators after MI are the degree of LV systolic dysfunction, LV volume, LV sphericity, extent of coronary artery disease, MR, diastolic function, and presence of heart failure. Therefore, it is reasonable to predict that patients with a high WMSI have a greater chance for subsequent development of cardiac events. Most patients in Killip class II-IV have a WMSI of 1.7 or higher. In addition to the WMSI, restrictive Doppler filling variables derived from mitral inflow velocities correlate well with the incidence of post infarction heart failure and LV filling pressures. LA volume, a surrogate for chronic diastolic dysfunction and chronic elevation of LA pressure is also a predictor of outcome.

The presence of normal systolic function in a critically ill or hemodynamically unstable patient should lead immediately to the suspicion of a mechanical complication like 1) ventricular septal rupture, 2) papillary muscle rupture, 3) acute outflow obstruction. This may be suspected on clinical examination by appearance of a systolic murmur on precordial auscultation.

Table 3 : Scoring system for grading wall motion[42]

Score	Wall motion	Echocardial motion	Wall thickening
1	Normal	Normal	Normal(>30%)
2	Hypokinesis	Reduced	Reduced(>30%)
3	Akinesis	Absent	Absent
4	Dyskinesis	Outward	Thinning
5	Aneurysmal	Diastolic deformity	Absent or thinning

Ventricular Septal Defect (VSD)

Infarct-related VSD is diagnosed by demonstration of a disrupted ventricular septum with a left-to-right shunt. The defect is always located in the region of the thinned myocardium with dyskinetic motion. Anterior wall MI is associated with apical VSD and inferior wall MI is associated with basal VSD. The diagnosis usually can be established with a two-dimensional TTE examination.

Mitral Regurgitation (MR)

Acute MR is another important cause of systolic murmur, related to LV global or regional remodeling, papillary muscle dysfunction, papillary muscle rupture (partial or complete),[21] and acute systolic anterior motion (SAM) of the mitral valve. Papillary muscle rupture mandates urgent mitral valve replacement or repair, but MR caused by papillary muscle dysfunction or annulus dilation may improve with afterload reduction or coronary revascularization or both.

Hemodynamically, papillary muscle rupture is the most serious complication involving the mitral valve. The patients usually have a small infarct in the distribution of the right coronary or circumflex coronary artery. Because the posteromedial papillary muscle is supplied by a single coronary artery (compared with the dual supply of the anterolateral papillary muscle), rupture of the posteromedial papillary muscle is more frequent.

Acute Dynamic LVOT obstruction

It is related to the compensatory hyperdynamic motion of the posterior and inferolateral walls, resulting in systolic anterior motion (SAM) of the mitral leaflet, which causes MR, as well as the obstruction. It is more common after anterior wall MI in elderly women who have basal septal hypertrophy caused by hypertension. Patients with acute LVOT obstruction can develop severely unstable hemodynamics, including shock and pulmonary edema. The most appropriate therapies are fluids, beta blockers, alpha agonists, avoidance of vasodilators, and inotropes. This condition is not uncommon during the postoperative period in patients who receive inotropic support.

Free Wall Rupture and Pseudoaneurysm

Free Wall Rupture is a fatal complication. It occur in 1% of patient of acute myocardial infarction and it accounts for up to 7% of all infarct –related deaths. Typically, the rupture is associated with a sudden haemodynamic collapse due to cardiac tamponade (from hemopericadium) and electromechanical dissociation. Mostly it occurs within the first week and is more common in elderly females.[22] 2D-TTE may not be able to show the site of rupture but may only demonstrate a pericardial effusion with or without pericardial tamponade. The presence of pericardial effusion alone is not sufficient for diagnosis of a free wall rupture because pericardial effusion is common after acute MI. Contrast echocardiography or color flow imaging may help in identifying the rupture site.

In some cases a pseudoaneurysm forms after a free wall rupture is contained within a limited portion of the pericardial

Table 4 : Echocardiography findings in RV infarction[43-44]

| Primary	Secondary
Right ventricular dilatation	Paradoxical septal motion
Segmental wall motion abnormality of the right ventricular free wall	Tricuspid regurgitation
	Tricuspid papillary muscle rupture
Decreased descent of the right ventricular base	Pulmonary regurgitant jet pressure half-time ≤150 msec
Tricuspid valve annulus peaks systolic velocity <12 cm had a sensitivity specificity and negative predictive values of 81%,82 % and 92 %	Dilated inferior vena cava
	Right to left interatrial septal bowing
	Right to left shunting across patent foramen ovale
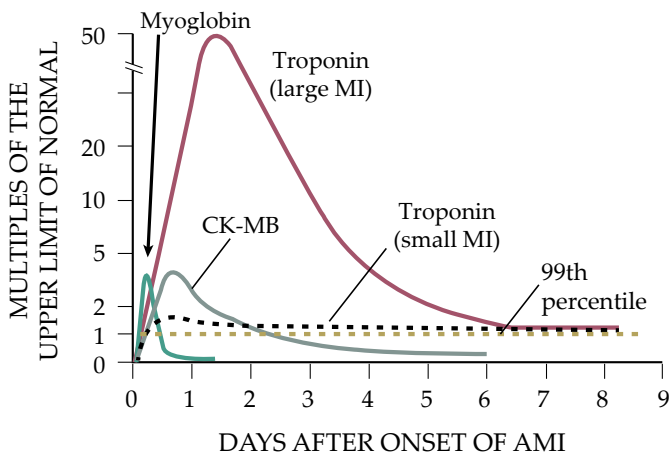
Fig. 2 : Time profile and limit of rise of cardiac biomarkers after acute myocardial infarction.

space (most frequently in the posterior wall, followed by the lateral and apical walls). A pseudoaneurysm is traditionally characterized by a small (neck) communication between the left ventricle and aneurysmal cavity (the ratio of the diameter of entry and the maximal diameter of the pseudoaneurysm is <0.5). There is always to-and-fro blood flow through the rupture site that can be documented with doppler and color flow imaging.

Right ventricular infarction (RV)

RV infraction occurs in up to 50% of patients with inferior MI, but hemodynamic compromise develops in fewer than one half of such cases. The right ventricle is predominantly supplied by acute marginal branches of the RCA and occlusion of the RCA proximal to the origin of these branches results in ischemic dysfunction of the right ventricular. The findings of RV infarction on echo are shown in Table 4.

Biomarkers

Cardiac biomarkers have conventionally being used for diagnosis of acute myocardial infarction. These have also been used in patients with NSTEMI and unstable angina for finding high risk individuals. Elevation of CPK, CPK-MB and Troponins I and T occurs in all patients with myocardial necrosis that is seen in myocardial infarction. Serial CK-MB estimations were done earlier for estimation of infarct size before echocardiography. Biomarkers are useful in patients with equivocal ECG changes although their clinical relevance in acute myocardial infarction is receding.[23,24] They are still extremely useful in NSTEMI for risk stratification. In periprocedural myocardial infarction, rise of CK-MB is important for diagnosing the infarction[25]. In routine myocardial infarction elevation of CK-MB and troponins though

Table 5 : Time window for elevation of biomarkers in acute myocardial infarction (in hours)

Biomarker	Initial elevation	Peak elevations	Return to normal
Myoglobin	1-4	6-7 hr	24 hr
MB-CK	3-12	24 Hr	48-72 hr
cTnI	3-12	24 hr	5-10 days
CTnT	3-12	12 hr-2days	5-14 days

done routinely only serves in documentation. In present day era when all reperfusion strategies have to be instituted within minutes of patients arrival in emergency with ST elevation the role of biomarkers is reducing since they begin to rise after 3-6 hrs and the lab report can also take time. The rate of appearance of these macromolecules in the peripheral circulation depends on several factors, including; intracellular location, molecular weight, local blood and lymphatic flow, and rate of elimination from the blood.[26-27] The common biomarkers used are :

Myoglobin

Highly sensitive for cardiac necrosis. It is the first biomarker to rise with myocardial necrosis but since the specificity is less so now it is rarely used in clinical practice.

Creatine Kinase

Serum CK activity exceeds the normal range within 4 to 8 hours after the onset of STEMI and declines to normal within 2 to 3 days. Although the peak CK level occurs on average at about 24 hours, peak levels occur earlier in patients who have had reperfusion as a result of the administration of fibrinolytic therapy or mechanical recanalization, as well as in patients with early spontaneous fibrinolysis.[28] False-positive results are seen in patients with muscle disease, alcohol intoxication, diabetes mellitus, skeletal muscle trauma, after vigorous exercise, convulsions, intramuscular injections, thoracic outlet syndrome, and pulmonary embolism.[29] For this reason CK isoenzymes are considered more specific.

Creatine Kinase Isoenzymes

Three isoenzymes of CK exist (MM, BB, and MB). Extracts of brain and kidney contain predominantly the BB isoenzyme; skeletal muscle contains principally MM, but also contains some MB (1% to 3%), and cardiac muscle contains both MM and MB isoenzymes. The CPK-MB estimation is used for diagnosis of myocardial necrosis in acute coronary syndrome. The MB isoenzymes of CK can also be present in small quantities in the small intestine, tongue and diaphragm. Strenuous exercise, particularly in trained long- distance runners or professional athletes, can cause elevation of both total CK and CK-MB.[30]

Cardiac specific Troponins

Cardiac-specific troponins I and T accurately distinguish skeletal from cardiac muscle damage. The troponins are now considered the preferred biomarker for diagnosing MI.[31] Other causes of raised troponins are injury to cardiac muscle, such as those resulting from myocarditis, trauma, cardiac catheterization, shock, and cardiac surgery. The cTnT assays are produced by a single manufacturer, leading to relative uniformity of cutoffs, whereas several manufacturers produce cTnI assays.[32]

While, CK-MB increases 10- to 20-fold above the upper limit of the reference range, cTnT and cTnI typically increase more than 20 times above the reference range. Thus, now Troponins are sensitive and specific markers for acute MI. CKMB is useful now for diagnosing re-infarction as troponins remains elevated for a longer time as shown in Figure 2 and Table 5.[33-35]

BNP and NT-ProBNP: Although originally BNP and NT-ProBNP were considered biomarkers for heart failure only, now they are also considered biomarkers of myocardial ischemia. Although BB/NP and NT ProBNP are not the markers for diagnosis of ACS but they have emerged as prognostic indicators of long term mortality early after an acute coronary event.[36,37]

WBC count : The elevation of the white blood cell count usually develops within 2 hours after the onset of chest pain, reaches a peak 2 to 4 days after infarction, and returns to normal in 1 week. The peak white blood cell count usually ranges from 12 to 15 × 103 /mL but occasionally rises to as high as 20 × 103 / mL in patients with large STEMI.[38]

Thus diagnosis of myocardial infarction is easy and based on simple principals of good history and physical examination, early and complete 14 lead electrocardiogram, early use of echocardiography which should be available in the emergency triage area and subsequently biomarkers are also available for documentation. The other causes of acute severe chest pain should be kept in mind and ruled out or otherwise on basis of ECG, echo and biomarkers. On the other side we should keep in mind that some patients have less prominent chest pain. The presentation may be confounding and patients often misinterpret these symptoms as acid peptic symptoms and useful time is wasted before therapies are instituted.

The definition of acute MI, itself has evolved and has been changed in the last 30 years with availability of newer markers. The recent revised definition of acute myocardial infarction was given in 2007 and has been accepted by ACC/AHA.[39-41] Is as follows :

Criteria for Acute, Evolving, or Recent MI

Either of the following criteria satisfies the diagnosis for acute, evolving, or recent MI:

1. Typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of the following:
   a. Ischemic symptoms
   b. Development of pathologic Q waves in the ECG
   c. Electrocardiographic changes indicative of ischemia (ST-segment elevation or depression)
   d. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
2. Pathologic findings of an acute myocardial infarction

Criteria for Healing or Healed Myocardial Infarction

Any one of the following criteria satisfies the diagnosis for healing or healed myocardial infarction:

1. Development of new pathologic Q waves in serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarction developed.
2. Pathologic findings of a healed or healing infarction.

Classification of myocardial infarction[39]

Myocardial infarction has been classified into five types depending upon the circumstances in which it happens. The types are as follows:

Type 1

Spontaneous myocardial infarction related to ischemia caused by a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection

Type 2

Myocardial infarction secondary to ischemia caused by increased oxygen demand or decreased supply (e.g. coronary artery spasm, coronary embolism, anemia, arrhythmias, hypertension, hypotension)

Type 3

Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, but death occurring before blood samples could be obtained.

Type 4

Myocardial infarction associated with PCI (a) during PCI, (b) Stent thrombosis.

Type 5

Myocardial infarction associated with CABG.

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