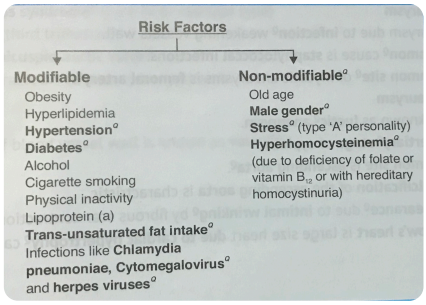
*] Risk Factors for atherosclerosis :-

1] Smoking :- i) Most crucial yet preventable risk factor for CAD [significant smoking → 2-3 packs for 10yrs]

ii) Also risk factor for Renal artery Stenosis & Peripheral vascular disease



2] Hypertension :- ≥ 140/90

3] Hypercholestrolemia :- i) do hs-CRP $\xrightarrow{\text{if }\oplus}$ do Lp(a) & Homocysteine

ii) Apo B100 / HDL ratio

iii) Low HDL-2

iv) High LDL

v) Total chol./HDL ratio

*] High LDL > Low HDL as a risk factor

⇒ Start statins only if :- a) Clinical atherosclerosis

[40 mg Atorvastatin] b) DM (40-75yrs of age)

c) LDL > 190 mg/dl

4) DM⊕ ⇒ Insulin resistance (Abdominal obesity)

5) Family h/o premature CHD

6) Males (45yrs) > Females (55yrs)

present ∈ Chest pain → No chest pain (Atypical symp)

In India age ⇒ 45-55yrs & F>M & atypical presentation

7) Obesity & Metabolic syndrome

8) Malnutrition - Inflammation related - Atherosclerosis

*) Hibernating myocardium :- Areas of myocardium which are persistantly underperfused but still viable

*) Stunned myocardium :- Segmental dysfunction which persists for variable period of time after reperfusion

*] Myocardial Ischemia → Infarction
→ Chronic Ischemia → Persistent ischemic dysfunction → Hibernating myocardium
→ Salvaged → Transient post-Ischemic dysfunction → Stunned myocardium

*] HOPE trial demonstrates that 'Ramipril' reduces fatal & nonfatal vascular events in High risk patients

*] Although ACE⊖ & ARB's are equally effective, its better to start ACE⊖ as ARB's tend to ↑ AT-2 receptor which prones for malignancy like esophageal carcinoma

⇒ ACE⊖ are C/I in :- Pregnancy, Hereditary angioedema, B/L Renal artery stenosis

⇒ Stop ACE⊖ if serum creatinine > 30% from Baseline ∈ in 1wk of starting ACE⊖ or if Hyperkalemia develops

*] Perfusion Scintigraphy/MRI :- Can Distinguish bet" stunned myocardium from scarred tissue

*] Electron Beam CT :- Quantity Cardiac Calcification

*] Agatston score :- To measure degree of Coronary artery Calcification using Hounsfield Units (↑ unit ∝ ↑ density of calcification)

*] Intravenous Ultrasound :- IOC for ostial left main lesion & Coronary dissection

Chronic Stable Angina → 1) Chest pain :- Constricting / squeezing / tightening → radiating to left arm, Neck (throat) & jaw
lasting <20 min ± Levine's sign ⊕ (clenched fist held over chest) may be seen
2) On physical exertion & relieved ± in min. by rest / sublingual GTN / continued exertion aka walking through the pain

↓ Fixed occlusion (plaque)

Plaque rupture

↓

Thrombus formation

↓

Complete Occlusion → [Transmural Infarct] → STEMI

Incomplete occlusion → [Subendocardial Infarct] → Enzymes

Enzymes → Elevated → NSTEMI

Enzymes → Normal → Unstable angina → 1) Rest angina :- Angina occurring at rest & prolonged usually > 20 min.
2) New onset Angina :- of atleast class III severity
3) Crescendo angina :- Previously diagnosed angina that has become distinctly more frequent / longer induration or ↑ by > 1 CCS class to atleast Class III severity
*) Wellens syn = Stenosis in LAD, chest pain, Deep T wave inversions or biphasic T waves in V_2 & V_3 suggestive of unstable Angina

NSTEMI + Unstable angina → Now called → Non-ST elevation - ACS [NSTE-ACS]

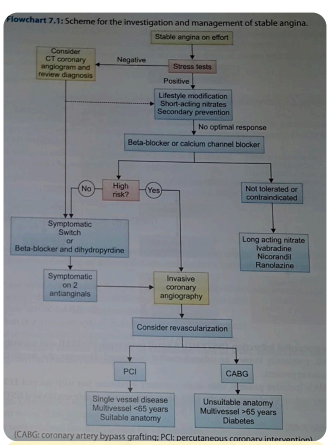
*) WHO Rose questionnaire ⇒ used for assessment of Angina

Characteristic features of stable angina	Features not suggestive of angina
Squeezing, central, substernal discomfort	
Crescendo-decrescendo in nature	
Typically lasts 2 to 5 min	Angina localized below the umbilicus or above the mandible
Can radiate to either shoulder & to both arms (especially the ulnar surfaces of the forearm & hand)	Radiation to the trapezius muscles (that radiation pattern is more typical of pericarditis)
It also can arise in or radiate to the back, interscapular region, the root of the neck, jaw, teeth, and epigastrium.	

*] Prinzmetal angina / Vasospastic angina :-

i) Chest pain at Rest for 5-15 mins (relieved by sublingual NTG)
ii) Recurrent episodes (↑ in Midnight - early morning)
iii) During the episode → Tachycardia, HTN, sweating (Diaphoresis)
iv) Patient is usually a Smoker
v) Transient ST segment elevation (+) during the episode, Angiography is (N) ← Gold std. for diagnosis
vi) Ca^{2+} ⊖ [Diltiazem] is DOC, but not β⊖ cor of vasospasm
vii) Provocation tests can be used to confirm diagnosis (Hyperventilation, Cold pressor test, Intracoronary acetylcholine challenge test, ergometrine)

*] Chronic Stable Angina :-



Flowchart 7.1: Scheme for the investigation and management of stable angina.
(CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention)

i) ∵ These patients have angina on exertion ∴ Look for Inducible Ischemia via :-

a) Treadmill stress test or Exercise ECG or Bruce protocol treadmill test :-

1) Significant :- If Downsloping ST segment depression of > 2 mm ± in 6 min before achieving max Heart Rate [HR_{max} = 220 - Age]

2) C/I :-

Absolute Contraindications to exercise testing:

- Acute myocardial infarction (within 6 days)
- High-risk unstable angina
- Uncontrolled cardiac arrhythmia with hemodynamic compromise
- Active endocarditis
- Symptomatic severe aortic stenosis
- Decompensated heart failure
- Acute pulmonary embolism or pulmonary infarction
- Acute myocarditis or pericarditis
- Severe pulmonary hypertension
- Aortic dissection

b) Myocardial perfusion scanning :-

i) Done if :- Can't perform excercise test / Can't interpret results

2) Done in 2 phases → at rest & during stress (controlled infusion of dipyridamol or dobutamine or adenosine) ± radioactive Isotopes (thallium^{201})

3) Result → If perfusion defect during stress but not at rest = Reversible Myocardial Ischemia
→ Persistent perfusion defect during both phases = Previous MI

*) To check myocardial viability :-
i) PET scan (IOC), ii) Thallium 201, iii) MRI (IOC for Ventricular func"), iv) Dobutamine echocardiography

℞ :- Sublingual NTG → 0.3 to 0.6 mg, 3 tabs ē in 20 mins → (Not responding) STEMI, NSTEMI, Unstable Angina } Limitation to Nitrates ⇒ TOLERANCE ⊖ Nitrate free 8-12 hrs daily

[other long acting oral Nitrates → Isosorbide dinitrate & mononitrate]

MOA of Nitrates :- i) Vasodilation → ↓ BP → ↓ Afterload; ↓ Venous return → ↓ Preload } ↓ O_2 consumption by Heart ; ii) ↑ O_2 supply to Heart by Coronary vasodilation

C/I :- i) ē Phosphodiesterase 5 ⊖ [Sildenafil, Tadafil, Vardenafil] → Severe Hypotension

ii) In HOCM, severe AS, Constrictive pericarditis, Closed angle glaucoma & Mitral stenosis

Pharmacologic Classes for Treatment of Angina

Medication Class	Impact on HR	Impact on BP	Physiologic Mechanism
Beta Blockers	↓	↓	Decrease pump function
Calc Channel Blockers	↓	↓	Decrease Pump function + Vaso-dilitation
Nitrates	↑	↓	Vaso-dilitation
Ranolazine	O	O	Reduced Cardi...

2nd line → i) Bβ ⊖ :- ↓ O_2 demand by Heart by ↓ Heart rate & contractility, ↓ BP, ↓ apoptosis by Inhibiting β adrenoceptors ∴ Prolong life post-MI

ii) CCB's :- Produce coronary & peripheral arterial dilation + -ve Inotropy & ↓ Conductivity ⇒ coz of -ve inotropy not to be used in Heart failure (uncompensated) & don't combine ē β ⊖ coz too much ↓ HR & ↓ contractility ; Prefer Non DHP > DHP coz No reflex tachycardia in Non-DHP (Verapamil / Diltiazem)

iii) Nicorandil :- K⁺ channel opener → Vascular smooth muscle relaxation ⇒ Dilatation & prevent Intracellular Ca^{2+} toxicity

iv) Ivabradin :- "funny (I_f) channel ⊖ → Slows diastolic depolarisation & causes Bradycardia ⇒ No effect on Contractility & Can be combined ē other drugs

v) Ranolazine :- It ⊖ late Na^+ channels → Reduces Cardiac stiffness, Does not affect HR, BP but prolongs exercise dura^n, metabolized by CYP3A4 & causes QT ↑↑

[M.Ischemia → ⊖ ↑ late Na^+ current → Na^+ overload → Ca^{2+} overload → ↑ Diastolic wall stiffness → Intramural small vessel compression → ↓ O_2 supply & ↑ O_2 demand] [CYP3A4 ⊖ shouldn't be given ē it eg. Ketoconazole, Grapefruit juice, Diltiazem, Verapamil, Macrolides & HIV protease ⊖]

3rd line → i) Trimetazidine :- pFox ⊖ [O_2 req. of Glucose pathway is ↓ than FFA pathway but During Ischemia FFA pathway used ∴ pFox ⊖ inhibits it & Resumes Glucose pathway]

ii) "Fasudil (RhoKinase ⊖) → causes Vasodilation

*] Pt ē Risk factor → Chronic stable angina; "fixed occlusion (<70% coz if more than") ; Diastolic dysfunction ; Prior MI → Systolic dysfunction → ACS

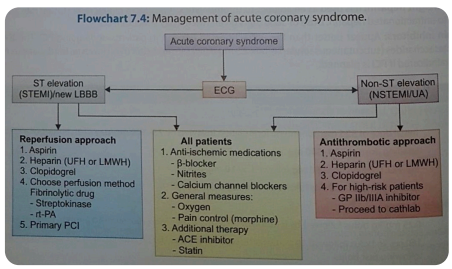


Table. Universal Definition of MI

Type	Classification	Clinical and Diagnostic Criteria
1	Spontaneous MI	Plaque rupture, ulceration, fissuring, erosion, or dissection resulting in coronary thrombosis
2	Supply/demand mismatch	Mismatch between myocardial oxygen supply and demand driven by a secondary process other than coronary artery disease
3	Suspected MI-related death	Cardiac death in a setting suggestive of ischemic process without definitive cardiac biomarker evidence of MI
4a	PCI-related MI	Rise in cardiac biomarkers accompanied by symptoms, electrocardiographic, angiographic, or imaging evidence of ischemia after PCI
4b	Stent thrombosis	Confirmed stent thrombosis in context of ischemia and dynamic cardiac biomarker changes
5	CABG-related MI	Rise in cardiac biomarkers accompanied by electrocardiographic, angiographic, or imaging evidence of ischemia after CABG

Abbreviations: CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention.

*] Acute MI :- Evidence of Myocardial Necrosis [↑ Biomarkers] in the clinical setting of Ischemia + any one of the following changes :-

i) New ST-T changes (Tall peaking Twaves followed by Twave inversions, STseg. elevation)

ii) Symptoms of Ischemia

iii) Pathological q wave

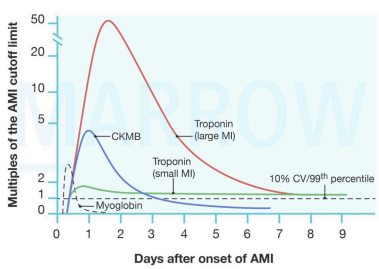
iv) Evidence of Thrombus by angiography

v) Impaired perfusion on Scintigraphy

A transient **midsystolic or late systolic apical murmur** due to **mitral regurgitation** secondary to dysfunction of the mitral valve apparatus (papillary muscle dysfunction, LV dilation) may be present in STEMI.

*] Cardiac Biomarkers :-

	Time to initial elevation	Mean time to peak elevation	Time to return to normal range
Myoglobin [1st to rise]	1-4 h	12 h	24 h
CK-MB	4-8 h	24 h	48-72 h
cTnI (Most sensitive & specific [re-infarction])	3-12 h	24 h	7-10 d
cTnT	3-12 h	12h-2d	7-10 d
LDH [Last to rise]	24 hours [Flipped LDH, $t_{1/2}$ >1]	3-6 days	2 weeks
SGOT [Non-specific]	12 hours	48 hours	4-5 days



*] AST → liver, Skeletal muscle & Cardiac muscle while ALT → liver specific ⇒ ∴ ↑ AST + N ALT :- Non Hepatological dis. like Rhabdomyolysis & MI [except Alcoholic hepatitis & Cirrhosis]

*] Do Troponin I in case of Renal failure & not T

*] Reinfarction :- >20% Increase in cTn / Absolute ↑ in cTn (>7ng/L over 2hrs) value in 2nd sample obtained 3-6 hrs later

*] Serum Myoglobin & Heart type fatty acid Binding protein [H-FABP] are smaller molecules that diffuse through Interstitial fluids after cell death ⇒ ↑ 30min after MI but are non-specific to myocardial tissue

*] General Management → Confirm Diagnosis by :- → Specific ℞ :-

M :- Morphine
O :- O_2 if ACS ē satur^n <90%.
N :- Nitroglycerine
A :- Aspirin
C :- Clopidogrel / Ticagrelor [pref]

a) ECG
b) Cardiac Biomarkers
c) Killip classification / Forester & Diamond to look for LV failure

i) Thrombolysis / PCI
ii) Bβ ⊖ unless C/I
iii) ℞ complications

Cardiac troponins

- Most specific cardiac biomarker for myocardial injury/acute MI
- Troponin elevations are useful for short & long-term prognosis in MI
- Cardiac troponin elevations **correlate** with estimation of **infarct size and risk of death**
- Newer highly sensitive assays for troponins become positive even within first 3hours after onset of chest pain in MI

*] STEMI :-

Management :- CAB [Circulation, Airway & Breathing] + ECG

℞ :- i) Aspirin (325mg stat ; India → Dispirin (Dispersible) in Water) + Ticagrelor (180mg) / Clopidogrel (300mg oral) + Atorvastatin (80mg) ⇒ Together

(Statin used to stabilise plaque, Not for its HMG-CoA reductase ⊖ Activity).

ii) ↓ Pain ⇒ Morphine (Not available in hospital) → Nitrate (0.5mg Sublingual) shift to IV NTG infusion watch out for Hypotension

Then add β⊖ (IV → Metoprolol 5mg repeat every 15-30 min) ⇒ β⊖ are C/I in :- AV Block, Left ventricular failure & Bradycardia

TOC → Revascularisation Therapy (C/I → NSAID's & Steroids coz interfere ∈ Healing of Infarcted wall)

↳ 1° Percutaneous Coronary Intervention (PCI) → Angiography + Angioplasty + Stent (1° coz done ∈ ongoing MI) can only be done in CATH lab if pt comes to a centre ∈ No PCI then do Thrombolysis / Fibrinolysis (Strepto, Uro, Tenect, Reteplase ← DOC whichever is available) → Strepto (1.5mill. Units in 100ml NS IV infusion over 1hr)

Bolus given as single infusion

*) The door to balloon time is the time interval between the first Medical contact & PCI. It is <90min if patient is arriving in a Hospital equipped ∈ PCI & is <120min for a pt. arriving in a hospital Not equipped ∈ PCI & is transported to where it can be done, if can't receive PCI ∈ in 120min do Thrombo / Fibrinolysis but rule out :- C/I → Past h/o haemorrhagic stroke, h/o non-haemorrhagic stroke in last 1yr, HTN at presentation of >180/110 mm of Hg, Suspected Aortic dissection, Any Active internal bleeding (varices, bleeding peptic ulcer etc); There is 0.5-0.9% chance of Intracranial haemorrhage & allergic reaction (2%) ⇒

∴ Take informed & written consent before giving Streptokinase. if he refuses then don't convince don't give the drug.

*] Thrombolysis ∈ in 30min is as good as PCI

—" — " — " ∈ in 1hr is 90% as good as PCI

—" — " — " has good result ∈ in 2hrs [Golden Hour]

} 3-24 hrs after which PCI can be performed — Pharmacoinvasive Approach

*] Thrombolysis has no role >12hrs except if there are signs of ongoing Ischemia on ECG

*] M/C Arrhythmia after reperfusion of an occluded coronary artery by Fibrinolytic ℞ :- Accelerated Idioventricular Rhythm

*) Tenecteplase > StreptoKinase ⇒ ↑ Fibrin specificity & affinity, No allergic reaction, single bolus dose (0.5mg/kg) administration, Patency after 1hr → >75% & ↓ Bleeding only S/E is ↑ chances of Intracranial Hemorrhage

*) GpIIb/IIIa antagonist given just before the procedure of PCI

*) β⊖ & ACE⊖ to be given ∈ in 24hrs ⇒ ↓ mortality

⇒ Types of PCI :-

*) Facilitated PCI = Thrombolysis followed by PCI ⇒ No longer Practised.

*) Rescue PCI = Thrombolysed pt look for clinical improv (no pain) + More than 50% improvement in ST elevation bet^n 30-60min if not then its failed now do PCI (90min)

*) Urgent PCI = Thrombolysis worked but pt suffers another MI (MI ∈ in 1st 5 days) now don't thrombolyse again (C/I till 6m-1yr) now do PCI.

Characteristics of Fibrinolytic Therapy in MI

Pearl #1217 • Medicine

© Marrow Q Bank E4 - Dec 2019 - pratik3kadam@gmail.com

Most fibrin specific	Tenecteplase
Least fibrin specific	Streptokinase
Shortest half-life	Alteplase
Lowest incidence of intracranial hemorrhage	Streptokinase
Fibrinolytic agent is given as a single bolus dose	Tenecteplase

*) Routine Angiography → Elective (can do anytime) after thrombolysis & do ∈ in 1st 5 days coz pt remains hospitalised for ≈ 5 days + Insurance. If not possible financially then can be done after weeks or month.

*) Follow up drugs → i) Aspirin (150mg) life long, Clopidogrel (75mg/day) / Ticagrelor (90mg/BD) for 1yr ⇒ Dual Anti-platelet therapy (DAPT)

ii) Atorvastatin (40mg/OD) for 1-3 months then taper the dose to 10-20mg/day life long irrespective of the lipid profile

iii) GP IIb/IIIa ⊖ (infusion before & during PCI) for max 2 days

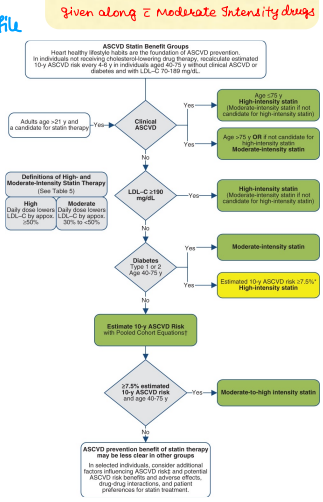
iv) Anticoagulant of Choice is LMW Heparin > UFH (monitor aPTT in UFH) (LMW → Anoxaparin available as pre-filled syrine 0.6ml BD S/C) given

*] High Intensity → Atorva [40-80mg]
→ Rosuva [20-40mg]

*] Moderate int. → Atorva [20-40mg]
→ Rosuva [5-10mg]

*] Fenofibrate only when TG > 500 & can be given along ∈ Moderate Intensity drugs

Contraindications for the use of fibrinolytic agents	
Absolute contraindications	**Relative contraindications**
History of cerebrovascular hemorrhage at any time	Current use of anticoagulants (INR ≥2)
Nonhemorrhagic stroke or other cerebrovascular events within the past year	Recent (<2 weeks) invasive or surgical procedure
Marked hypertension (systolic pressure >180mmHg and/or a diastolic pressure >110 mmHg) at any time during the acute presentation	Prolonged (>10 min) cardiopulmonary resuscitation
Suspicion of aortic dissection	Known bleeding diathesis
Active internal bleeding (excluding menses)	Pregnancy
	Hemorrhagic ophthalmic condition (e.g., hemorrhagic diabetic retinopathy)
	Active peptic ulcer disease
	History of severe hypertension that is currently adequately controlled



Category 1

Use high-intensity statins irrespective of cholesterol levels in Atherosclerotic Cardiovascular diseases (ASCVD) like MI/CAD/Angina/Stroke/TIA/PVD.

Category 2

Based on cholesterol levels in patients without ASCVD

A) LDL more than 190 - high-intensity statins (moderate intensity if age more than 75 years)

B) LDL more than 70+DM+ Age more than 40 years

C) LDL more than 70 + Age more than 40 years

D) 10 years CV risk more than 7.5%

Treatment

A – high-intensity statins

B(or)C + D - moderate-intensity statins

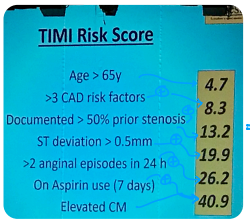
B + C(or)D - High-intensity statins

High-intensity statins : Atorvastatin 40–80 mg, Rosuvastatin 20–40 mg

Moderate-intensity statins : Atorvastatin 20–40 mg, Rosuvastatin 5–10 mg

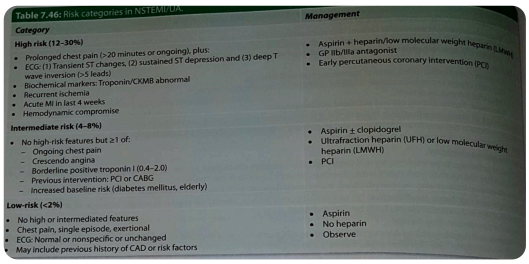
* Fenofibrate not advocated unless TG more than 500. It can be administered along with a moderate-intensity statin.

*] NSTEMI / UA :-



i) Thrombolysis is C/I & No role of 1° PCI ⇒ Rx is same as the Follow up Rx of STEMI

⇒ Tells u that pt has 2 or more Risk factors [High risk category] consider NSTEMI pt for Elective PCI



*] Complications of ACS :-

1] Arrhythmias :- i) VF
ii) AF
iii) Bradycardia → Atropine may be given CO·6 - 1·2mg IV)
} Transient & usually no hemodynamic disturbance

2] Cardiogenic Shock :- i) Cor of Arrhythmia, Hypovolemia (Excessive diuretics, vomiting or extensive MI)

3] LV failure :- i) Killip classification used to asses LV dysfunction & Predicting mortality risk in MI

*) Ventricular remodelling can be prevented by ACE ⊖ & β⊖

Class I :- No signs of LV failure
Class II :- S_3 + Basal Crepitations
Class III :- Pulmonary Edema
Class IV :- Cardiogenic Shock
} LV failure is seen in Ant wall MI → Rx :- Revascularization ± PCI

*) Cardiogenic shock occurs when Infarction ≥40% & pt. has systolic BP < 90 mm & pulm. cap. wedge pressure > 18mm

ii) RV failure = ↑ JVP + Clear lung fields + Hypotension ⇒ Suspected in a patient ± Inferior wall MI ⇒ Rx :- Fluids (if JVP/CVP not Elevated)

iii) Forrester & Diamond classification ⇒ alternative to Killip classification

Simplified Forrester & Diamond hemodynamic classification in STEMI		
Class 1	No hypotension	No pulmonary congestion
Class 2	No hypotension	Pulmonary congestion
Class 3*	Hypotension	No pulmonary congestion
Class 4 *	Hypotension	Pulmonary congestion

* Include RV and Bi-Ventricular MI. ** Cardiogenic shock . www.drsvenkatesan.co.in

4] Mechanical complications
→ Myocardial rupture :- M/C ± in first 7 days of STEMI, Common in Older women & M/C involves Anterior Wall → Early surgical Rx needed
→ Rupture of Ventricular free wall :- It is M/C of all leading to Hemopericardium & Cardiac tamponade
→ Rupture of Ventricular Septum :- Lead to Acute VSD / Lt → Rt. shunt → Pansystolic murmur radiating to Rt sternal border & Hemodyn ⊗
→ Rupture of Papillary muscle :- Lead to Severe Mitral Regurgitation → Pansystolic murmur ± S_3 ⊕

5] Embolism :- Infarct → ↓ local contractility → Stasis → Thrombus on Endocardial surface → Systemic thromboembolism

6] Ventricular Aneurysm :- Acute Anterior Transmural Infarcts → Ventricular wall may bulge outward during Systole

7] Pericarditis
→ Early :- Developing on 2nd / 3rd day
→ Late (Dressler syn.) :- Develops 2-10 wks after infarct coz of Immune mediated Rx against Necrotic muscle ⇒ Fever, Pericarditis & Pleurisy
On ECG :- PR segment depression / ST-segment elevation
Rx :- Aspirin [Note :- NSAIDs or Corticosteroids impair the infarct healing process & predispose to Myocardial rupture ∴ These are C/I in Early Postinfarction period]

*] PCI related MI :- Elevation of cTn > 5 times normal in presence of MI & ECG changes, angiographic or imaging abnormality [even cTn rise of > 20% counts]

*] CABG related MI :- Elevation of cTn > 10 times the ⓝ baseline values in presence of new pathological Q waves, angiographic / imaging abnormality

An antiproliferative agent is attached to the stent by use of a thin polymer coating. This antiproliferative drug elutes from the stent over a 1 to 3 month period after implantation**.**

- The **first-generation** devices were coated with either **sirolimus or paclitaxel.**
- **Second-generation** drug-eluting stents use newer agents such as **everolimus, biolimus, and zotarolimus**. These second-generation drug-eluting stents are more effective with fewer complications like stent thrombosis than the first generation stents.

Revascularization with PCI (percutaneous coronary intervention) is indicated in high-risk patients who have one or more of the following:

- New ST-segment depression
- Diabetes mellitus
- Renal dysfunction - eGFR <60mL/min per $1.73m^2$
- Ejection fraction <40%
- Early postinfarction angina
- PCI within the past 6 months
- Prior CABG
- Refractory angina
- Symptoms of congestive heart failure
- Hemodynamic instability
- Recurrent angina at rest/low-level activity despite treatment
- Elevated troponin T or troponin I
- Sustained VT or VF