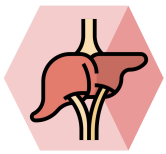
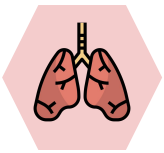
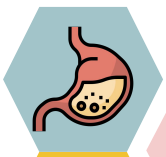
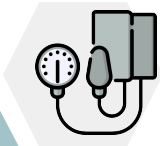
Medicine
TEAM 437

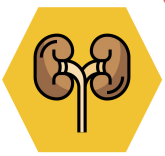
MED437
KING SAUD UNIVERSITY

Acute Coronary Syndrome






Objectives :

1. Distinguish STE and NSTE acute coronary syndromes by diagnosis, prognosis and treatment strategy.
2. Understand how ACS differs pathophysiologically from chronic coronary syndromes.
3. Devise a diagnostic approach for establishing ACS.
4. Outline treatment strategies for ACS
5. Assess the short- and long-term prognosis of different types of ACS
6. Devise a pharmacotherapy treatment plan for a patient undergoing primary PCI for STEMI.
7. Devise a pharmacotherapy treatment plan for a patient undergoing fibrinolytic for STEMI.
8. Devise a pharmacotherapy treatment plan for a patient with NSTE-ACS.
9. Design a therapeutic regimen for a patient with ACS prior to discharge from hospital.
10. Discover online, electronic and app resources to assist clinicians with implementation of practice guidelines.

Done by :

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Special thanks for Faisal AlSaif & Abdulelah AlDossari for the great summary!

Resources :

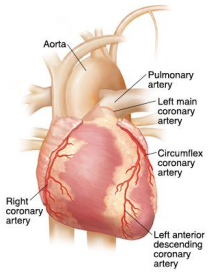
437 slides, 436 team, Davidson 22nd edition & Kumar 8th edition.

Revised by:

Yazeed Al-Dossare.

Anatomy recap

1. Left main coronary arises from the left coronary sinus of Valsalva and divides into:
   a. Left anterior descending (LAD) which supplies the **anterior wall** of the heart.
   b. Circumflex (Cx) which supplies the back of the heart.
2. The right coronary artery (RCA) arises from the right sinus of Valsalva and supplies the **inferior wall** of the left ventricle and the right ventricle



Introduction

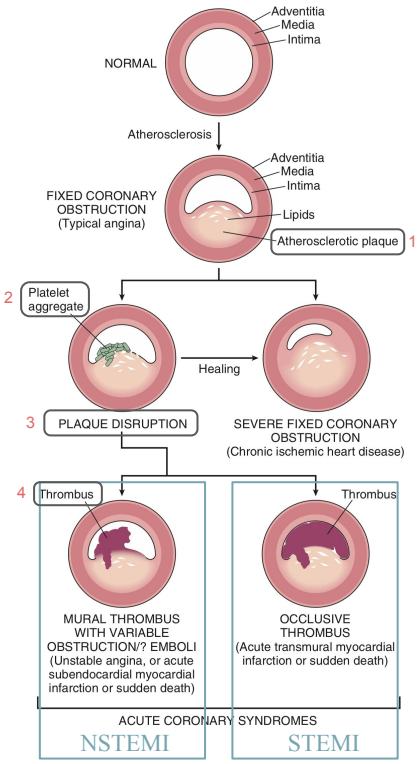
Few concepts you should remember before start:

- We have two steps to develop ACS: 1) Developing Atherosclerosis plaque —> 2) Ruptured AT plaque.
- Development of AT plaque in the coronary artery cause stable angina which called myocardial ischemia.
- Ischemia is an inadequate blood supply to the organ that results subsequently in infarction, which is localized area of necrosis.

Acute coronary syndrome is a term that encompasses both unstable angina and myocardial infarction (MI). It is characterised by new-onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest in the absence of myocardial damage. In contrast, MI occurs when symptoms occur at rest and there is evidence of myocardial necrosis, as demonstrated by an elevation in cardiac troponin or creatine kinase-MB isoenzyme.

ACS is NOT ischemic (stable coronary disease), it is infarction (damage).

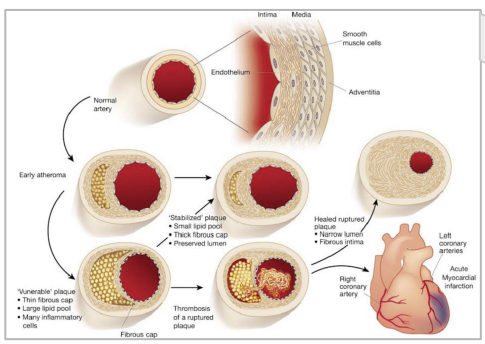
How ACS happens?



Pathophysiology:

The common mechanism to all ACS is **rupture or erosion of the fibrous cap of a coronary artery plaque.** This leads to platelet aggregation and adhesion, localized thrombosis, vasoconstriction and distal thrombus embolization. The presence of a rich lipid pool within the plaque and a thin fibrous cap are associated with an increased risk of rupture. Thrombus formation and the vasoconstriction produced by platelet was release of serotonin and thromboxane A2, results in myocardial ischaemia due to reduction of coronary blood flow.

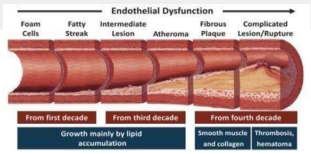
Extra

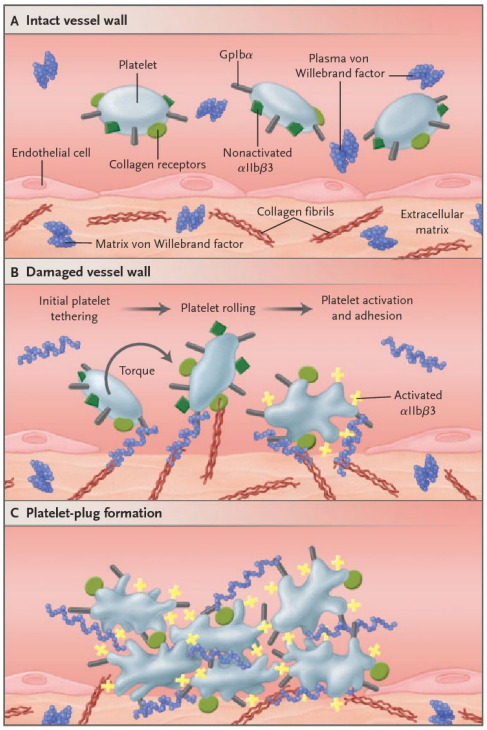


How ACS happens?

important

- Due to plaque rupture, which lead to expose of collagen and vWF.
- Platelet will bind to it and send signals like:
  a. Thromboxane A2 (aspirin works here)
  b. ADP (clopidogrel and Ticagrelor work here)
- These signals will attract more platelets which will attach to each other by fibrinogen to form thrombus which will close the vessel.
- Complete occlusion => STEMI.
- Partial occlusion => UA or NSEMI.



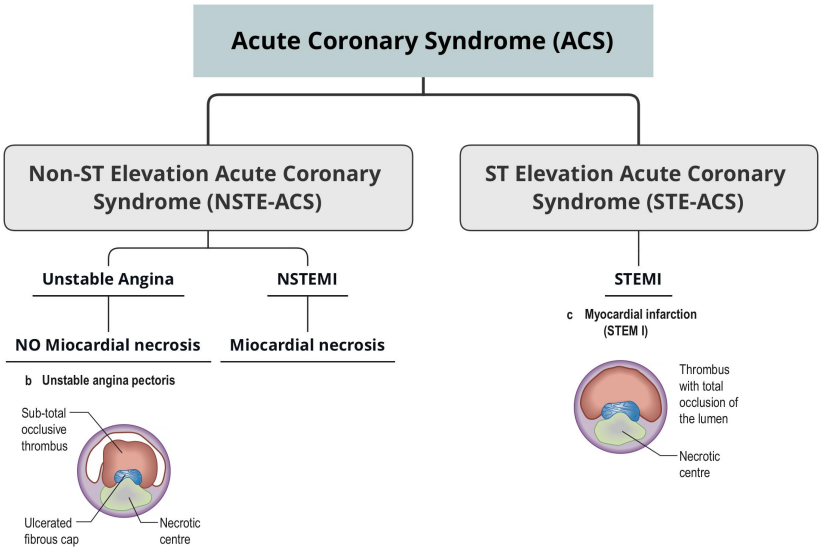


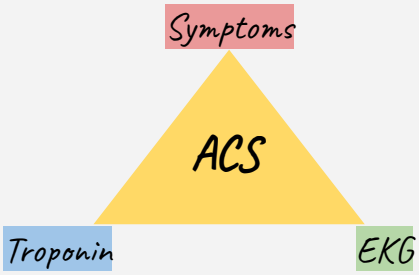
Risk factors

Obstructive Sleep Apnea Syndrome (OSA) is a risk factor to Cardiovascular diseases and premature death. The symptoms are: snoring, choking attacks during sleep, dry mouth on awakening, headache, nocturia and excessive daytime sleepiness.

Most important risk factors:		**Less reliable risk factors:**
Modifiable	**Non-modifiable**	**hard to measure or determine their role in the disease**
1. Diabetes mellitus: the **worst** risk factor. **2. Smoking.** **3. Hypertension.** the most **common** risk factor. **4. Hyperlipidemia** (**high** LDL and **low** HDL) "patients with familial hyperlipidemia can have fatty streaks when they were young" (High HDL is cardioprotective feature) **5. Obesity**	Patient's age is above 45 in **men** and above 55 in **women**. "In our population we saw some cases in patients who were late twenties or thirties" Family history of premature CAD, it should be: - In first-degree relatives. - In males under 55; females under 65. (premature).	- Physical inactivity - Poor diet - Emotional stress - Excess alcohol ingestion

What are the types of ACS?





Dr. Waleed AlHarbi notes:

1. Symptoms + EKG (STE)
   - STEMI
2. Symptoms + troponin / Normal EKG
   - NSTEMI
3. Symptoms / Normal troponin & EKG
   - Unstable angina

18.62 Clinical features of acute coronary syndromes

Symptoms

- Prolonged cardiac pain: chest, throat, arms, epigastrium or back
- Anxiety and fear of impending death
- Nausea and vomiting
- Breathlessness
- Collapse/syncope

Physical signs

- Signs of sympathetic activation: pallor, sweating, tachycardia
- Signs of vagal activation: vomiting, bradycardia
- Signs of impaired myocardial function
  - Hypotension, oliguria, cold peripheries
  - Narrow pulse pressure
  - Raised JVP
  - Third heart sound
  - Quiet first heart sound
  - Diffuse apical impulse
  - Lung crepitations
- Signs of tissue damage: fever
- Signs of complications: e.g. mitral regurgitation, pericarditis

Extra

When a patient comes with chest pain and you are suspecting ACS, the first thing you should ask for is ECG.
Based on ECG you classify the condition either ST-Elevation or Non-ST-Elevation. So, it is all based on the ECG but further investigations should be done. The next step is to investigate his enzymes.

What are the differences between USA and NSTEMI?
Unstable angina is a tissue ischemia with Highly suspicious symptoms. NSTEMI is a tissue necrosis. Also, in NSTEMI cardiac enzymes levels are elevated with associated symptoms, while in USA cardiac enzymes levels are normal. WHY? Because cells are not dead (no necrosis).

Acute coronary syndrome (ACS)	
ST-elevation myocardial infarction (STEMI)	**Severe** ACS presentation. Usually lasts for more than 20 mins. ECG shows ST elevation due to **transmural infarction,** which is an infarction that involves the whole myocardium thickness. Although it might be asymptomatic in one-third of patients, and that is typically seen in postoperative patients, elderly, diabetic, and women. **The pain does not usually respond to sublingual glyceryl trinitrate.** (ST Elevation occurs mostly when the vessel is totally occluded. But always there are exceptions !)
non-ST-elevation myocardial infarction (NSTEMI)	Usually **more** than 20 minutes. **ECG shows ST depression** due to **subendocardial infarction** (tissue necrosis). **Subendocardial infarction indicates** that only the first third of the myocardium is infarcted, if the blood doesn't return it progresses to STEMI. • In NSTEMI, the occlusion size is between USA and STEMI. • Non-ST Elevation occurs mostly when the vessel is not completely occluded (for example: 80%). • Remember : always there are exceptions !
Unstable angina (UA)	Usually **less** than 20 minutes. ECG shows ST depression due to tissue ischemia.

- We see ST-segment depression with unstable angina and NSTEMI. We can differentiate between them with the biochemical markers test.
- ST-segment elevation is an early indication of MI.

How to approach to Chest Pain?

1. Clinical presentation
2. ECG
3. Cardiac biomarkers

Patients with an ACS may complain of a new onset of chest pain, chest pain at rest, or a deterioration of pre-existing angina. However, some patients present with atypical features including indigestion, pleuritic chest pain or dyspnoea. Physical examination can detect alternative diagnoses such as aortic dissection, pulmonary embolism or peptic ulceration. In addition it can also detect adverse clinical signs such as hypotension, basal crackles, fourth heart sounds and cardiac murmurs.

Signs & symptoms: (SOCRATES)

- **Site & onset: Substernal, severe & persistent pain.**
- **Character: dull, heavy** and **pressure-like** pain.
- **Radiation:** shoulders, arms, and jaws.
- **Associated Symptoms:**
  - *Sympathetic effect:* Diaphoresis, cool and clammy skin, Palpitation and Syncope.
  - *Parasympathetic effect:* Nausea, Vomiting & weakness
  - *Inflammatory response:* Mild fever
- **Cardiac findings:**
  - S_4 (and S_3 if systolic dysfunction present) gallop.
  - Dyskinetic bulge (in anterior wall MI).
  - Systolic murmur (if mitral regurgitation or VSD).
- **Other:**
  - Pulmonary rale (id heart failure present)
  - Jugular venous distention (if heart failure or right vent. MI)
- **Remember:** you have to ask the patient about the **onset** (sudden or gradual), the **duration**, aggravators **& relievers and severity** (using scale from 1 - 10 or other methods).
- We have to differentiate between stable and unstable angina by asking about if the chest pain is even at rest or only with exertion.

What Are the Differential Diagnosis of Chest Pain in ER?

Life-Threatening Causes of CP:

CARDIAC	NON-CARDIAC
Acute coronary syndrome substernal, radiating to arm, dyspnea on exertion, diaphoresis, worse with exertion	**Acute pulmonary embolism** sudden onset, pleuritic, dyspnea, tachycardia, tachypnea, hypoxia, evidence of lower extremity deep venous thrombosis
Aortic dissection sudden onset, severe, tearing, radiating to the back (associated with neurologic deficits, AR), unequal arm BP >20 mmHg, wide mediastinum	**Tension pneumothorax** sudden onset, sharp, pleuritic, decreased breath sounds and chest excursion, hyperresonant percussion, hypoxia
Acute pericarditis & tamponade sudden onset, pleuritic, better with sitting forward, radiating to the back, pericardial rub, ± tamponade (distant heart sounds, hypotension, JVD)	**Esophageal rupture/perforation** severe, increase with swallowing, fever, abdominal pain, history of endoscopy, foreign body ingestion, trauma, vomiting

When To Call Angina Stable Vs. Unstable Symptoms?

Unstable Anginal Symptoms	Stable Anginal Symptoms (typical or atypical)
• New onset with normal activities • Crescendo, increase in severity, • Not relieved by NTG (nitroglycerin) • Duration: more than 20 min. • Comes even with Rest	• Substernal chest pain or discomfort • Provoked by exertion or emotional stress • Relieved by rest or nitroglycerine

What is the Difference Between Typical and Atypical Angina?

Chest pain in Typical Angina:

- meets all the above 3 characteristics.

Chest pain in Atypical Angina:

- Meets 2 of the above characteristics.

Non-Cardiac chest pain:

- Meet 1 or none of the above characteristics.

What Symptoms Increase or Decrease the Likelihood of ACS?

INCREASE THE LIKELIHOOD	LR (95 % CI) LR: Likelihood-ratio CI: Confidence interval	DECREASE THE LIKELIHOOD	LR (95 % CI)
Radiates to the right arm or shoulder	4.7 (1.9–12)	Pleuritic	0.2 (0.1–0.3)
Radiates to both arms or shoulders	4.1 (2.5–6.5)	Sharp	0.3 (0.2–0.5)
Precipitated by exertion	2.4 (1.5–3.8)	Positional	0.3 (0.2–0.5)
Radiates to the left arm	2.3 (1.7–3.1)	Reproducible with palpation	0.3 (0.2–0.4)
Associated with diaphoresis	2.0 (1.9–2.2)		

Box. Risk Stratification for Acute Myocardial Infarction and Acute Coronary Syndrome According to Components of the Chest Pain History

Low Risk

Pain that is pleuritic, positional, or reproducible with palpation or is described as stabbing[2,3,24,25,29]

Probable Low Risk

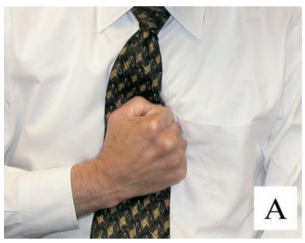
Pain not related to exertion or that occurs in a small inframammary area of the chest wall[14,31,42]

Probable High Risk

Pain described as pressure, is similar to that of prior myocardial infarction or worse than prior anginal pain, or is accompanied by nausea, vomiting, or diaphoresis[3,14,24,25,27-29]

High Risk

Pain that radiates to one or both shoulders or arms or is related to exertion[3,14,24,25,27,29]

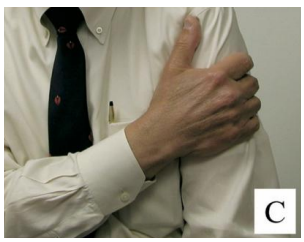


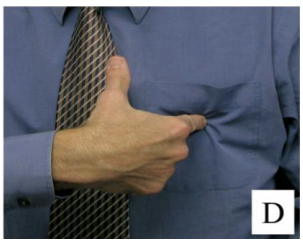
Levine sign

CLINICAL SIGNIFICANCE

- The Levine Sign has a poor sensitivity for chest pain related to myocardial ischemia or infarction.
- A patient pointing to a specific point on the chest likely does not have discomfort due to cardiac ischemia or myocardial infarction.
- Larger areas of chest discomfort correlate with a greater likelihood of cardiac ischemia or myocardial infarction.

High likelihood of ACS because it spread





Low likelihood of ACS

ACS without CP

- 33% of all ACS diff. symptoms (SOB, diaphoresis)
- Women, DM, >70 y.o., prior HF
- Worse prognosis b.c. of missed diagnosis.

How to approach to Chest Pain?

1 Clinical presentation

2 ECG

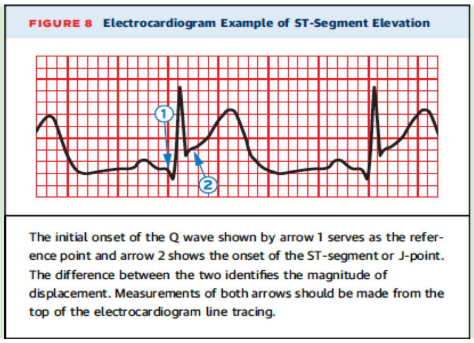
3 Cardiac biomarkers

Electrocardiogram is usually done to monitor the ST segment.

- **ST segment elevation** is seen with STEMI due to transmural ischaemia. ST segment elevation must be **higher than 1 mm** and seen in at least two leads. Otherwise, it's not considered elevation.
- **A T-wave inversion and Q wave** (not present normally) are highly suggestive for ACS. They may not appear during the first day of onset, so your diagnosis can't be based upon them.
- Note that **normal ECG does not exclude the possibility of ACS.**
- ECG must be performed as soon as the patient presents to the ER. In fact ECG must be performed upon anyone who presents with chest pain of any cause.

TABLE 2 Electrocardiographic Manifestations Suggestive of Acute Myocardial Ischaemia (in the Absence of Left Ventricular Hypertrophy and Bundle Branch Block)

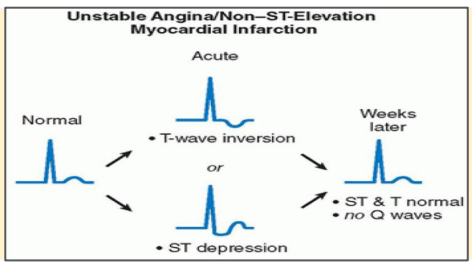
ST-elevation
New ST-elevation at the J-point in 2 contiguous leads with the cut-point: ≥1 mm in all leads other than leads V_2–V_3 where the following cut-points apply: ≥2 mm in men ≥40 years; ≥2.5 mm in men <40 years, or ≥1.5 mm in women regardless of age.[a]
ST-depression and T wave changes
New horizontal or downsloping ST-depression ≥0.5 mm in 2 contiguous leads and/or T inversion >1 mm in two contiguous leads with prominent R wave or R/S ratio >1.



50% of patients with NSTE-ACS have normal EKG

TABLE 3 Electrocardiographic Changes Associated With Prior Myocardial Infarction (in the Absence of Left Ventricular Hypertrophy and Left Bundle Branch Block)

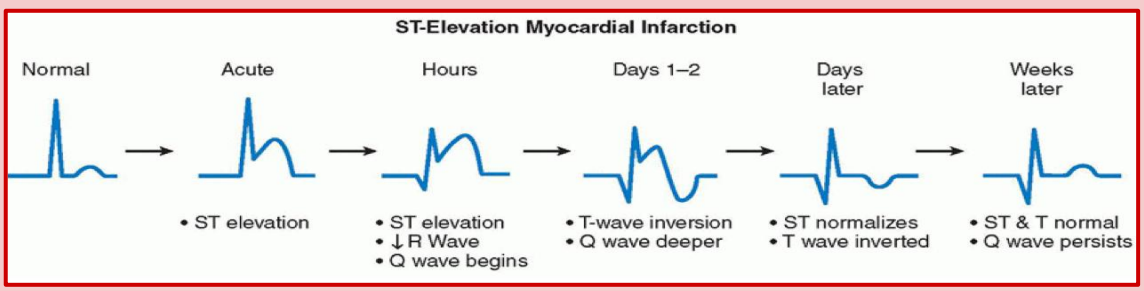
Any Q wave in leads V_2–V_3 >0.02 s or QS complex in leads V_2–V_3.
Q wave ≥0.03 s and ≥ 1 mm deep or QS complex in leads I, II, aVL, aVF or V_4–V_6 in any 2 leads of a contiguous lead grouping (I, aVL; V_1–V_6; II, III, aVF).[a]
R wave >0.04 s in V_1–V_2 and R/S >1 with a concordant positive T wave in absence of conduction defect.



They can have T-wave inversion or ST depression

Tells you how much the patient is having MI

important



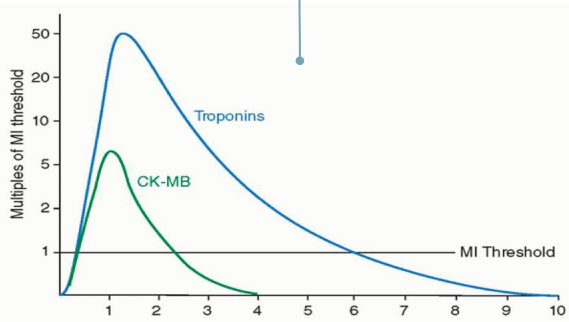
How to approach to Chest Pain?

1 Clinical presentation

2 ECG

3 Cardiac biomarkers

- Elevated **CK-MB** and **troponin-I** indicate STEMI or NSTEMI. (because there is necrosis)
- Normal CK-MB and troponin-I indicates unstable angina.
- CK-MB is used to detect reinfarction (because it returns to normal before troponins).



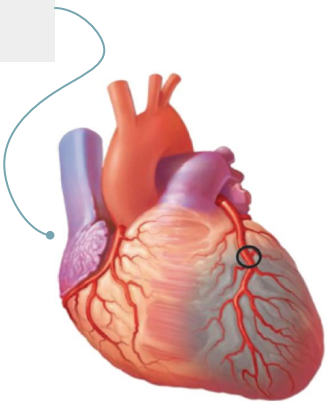
Troponin	- **Cardio-specific proteins.** - **Troponin I, and T are the most sensitive & specific markers for myonecrosis.** - **Released with 4-6hrs, but can last upto 2 week**
Creatine Kinase (CK)	- Creatine Kinase (CK) is released from multiple organs such as the myocardium, skeletal muscles, and the brain. We don't use it anymore, Only in special cases - The Iso-form **CK-MB,** is cardio-specific. (Not that much specific) - **Starts to rise 4-6 hrs after onset of ischemia, then falls within 48-72 hrs.**

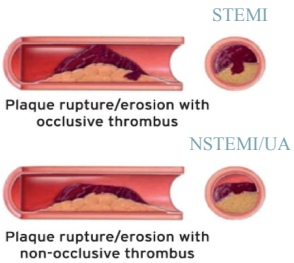
You'll find **similar ECG findings in both NSTEMI and Unstable angina**, so we need biochemical markers to differentiate between the two:

Markers	Elevated	Normal	Indication
Troponin-I & T + CK-MB	+++	-	STEMI or NSTEMI
Troponin-I & T + CK-MB	-	+++	Unstable Angina

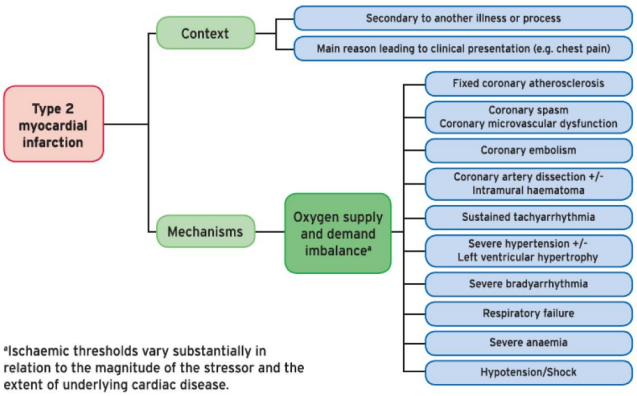
MI type 1

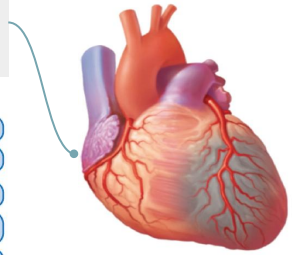
- There is occlusive thrombus

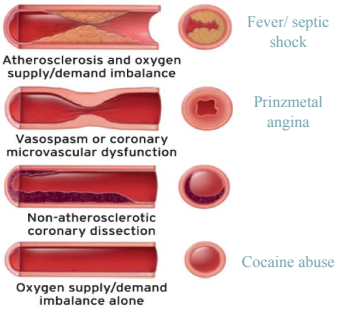




MI type 2







- No plaque rupture
- It's NOT ACS
- Treat the cause, don't give Aspirin and heparin.
- In type 2 troponin is positive due to myocardial necrosis because of stable coronary disease or increase the demand.

TABLE 1 Reasons for the Elevation of Cardiac Troponin Values Because of Myocardial Injury

Myocardial injury related to acute myocardial ischaemia

Atherosclerotic plaque disruption with thrombosis.

Myocardial injury related to acute myocardial ischaemia because of oxygen supply/demand imbalance

Reduced myocardial perfusion, e.g.,
- Coronary artery spasm, microvascular dysfunction
- Coronary embolism
- Coronary artery dissection
- Sustained bradyarrhythmia
- Hypotension or shock
- Respiratory failure
- Severe anaemia

Increased myocardial oxygen demand, e.g.,
- Sustained tachyarrhythmia
- Severe hypertension with or without left ventricular hypertrophy

Other causes of myocardial injury

Cardiac conditions, e.g.,
- Heart failure
- Myocarditis
- Cardiomyopathy (any type)
- Takotsubo syndrome
- Coronary revascularization procedure
- Cardiac procedure other than revascularization
- Catheter ablation
- Defibrillator shocks
- Cardiac contusion

Systemic conditions, e.g.,
- Sepsis, infectious disease
- Chronic kidney disease
- Stroke, subarachnoid haemorrhage
- Pulmonary embolism, pulmonary hypertension
- Infiltrative diseases, e.g., amyloidosis, sarcoidosis
- Chemotherapeutic agents
- Critically ill patients
- Strenuous exercise

Extra

ACS Facts

- ⅓ HF presentation to ER due to ACS
- ½ of all NSTE-ACS have no ischemic EKG changes
- Use TIMI score for NSTE-ACS with app

TIMI Score **important**

- **TIMI score (Predict 30d and 1yr mortality in UA/NSTEMI)**

Mnemonic: The TIMI Score was developed in **AMERICA**

1. **A**ge >= 65yo
2. **M**arkers (Elevated cardiac biomarkers)
3. **E**CG (ST segment deviation (>=0,5 mm)
4. **R**isk factors (3 or more CAD)
5. **I**schemic chest pain (at least 2 or more anginal events in <24hrs)
6. **C**oronary stenosis (prior stenosis of 50% or more)
7. **A**spirin usage in past 7 days.

- **0-1: low risk, 2-3: moderate risk, >=4:high risk.**

- TIMI 0-1: 5% all cause mortality, recurrent MI/ischemia requiring revascularization at 14d.
- 2: 8%
- 3: 13%
- 4: 20%
- 5: 26%
- 6-7: 41%

Why is important? Because according to the score the procedure might be invasive (moderate to high risk) or non invasive (low risk).

Management of ACS

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The aim of the therapy is to:

1. Open Artery and Improve oxygen supply:

a. Supplemental O_2 (ONLY if O2 Sat <95%) .
b. Coronary vasodilators (Nitroglycerine) (increase supply and dilates systemic veins (decrease preload and thus O_2 demand)
c. Antiplatelet agents
d. Reperfusion therapy by 2 ways:
   i. Fibrinolytic therapy
   ii. Primary Percutaneous coronary intervention (PCI)
e. Antithrombotic agents.

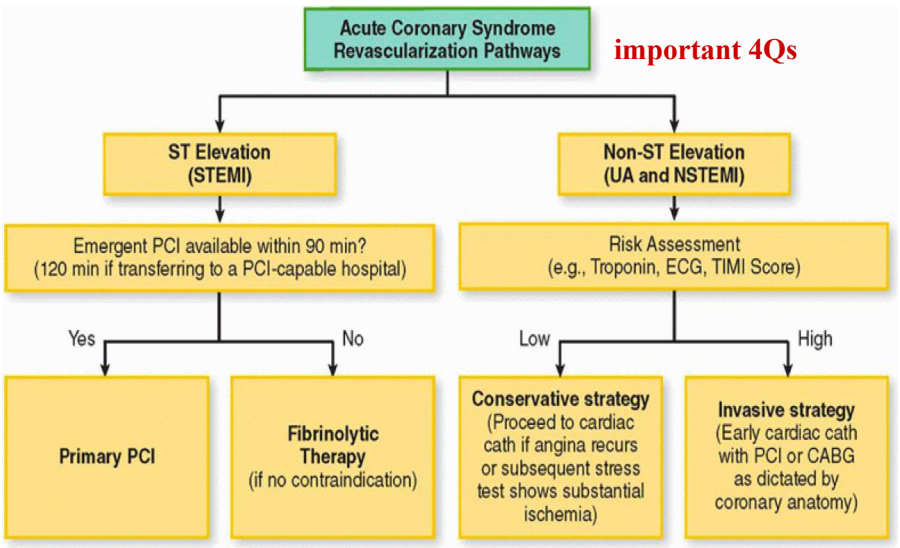
- NSTEMI and Unstable Angina are managed by all of above except fibrinolytics.
- STEMI are managed by all of the above including Fibrinolytics.
- Remember: use fibrinolytics ONLY in STEMI and within the first 12 hours after the onset of symptoms.

2. Reduce O2 demand:

a. Beta blockers (Block the stimulation of heart contractility and therefore reduce o2 demand)
b. Analgesics (Morphine) (analgesic as well as vasodilator)

3. Other medications:

a. ACE inhibitors. (acts as a vasodilator)
b. Statin therapy. (Pleiotropic effect) (reduction in the plaque lipids which will make the plaque more stable) Statin decreases LDL but this is not why we use it in the ER. we use it because of its anti-inflammatory property



If STEMI and PCI is not available you need to transfer the patient to PCI-capable hospital in 120 min if more time is needed to transfer give :

1. Aspirin
2. Clopidogrel or ticagrelor
3. Heparin before transferring

PCI vs. fibrinolytics discussion is based on how fast can you open the blood vessel and do PCI from administration to the action of stunting, not on the onset of symptoms (you have 24 hours).

- if fibrinolytic is contraindicated then do PCI as soon as possible.

ACS Treatments important

Pharmacological therapy:

- **Anti-ischemic therapies**
  - Beta blocker
  - Nitrates
  - +/- CCB
- **Antithrombotic therapies**
  - **Antiplatelet drugs**
    - Aspirin
    - $P2Y_{12}$ inhibitors
      like: clopidogrel, ticagrelor
    - +/- GP IIb/IIIa inhibitor

    We usually use aspirin and one $P2Y_{12}$ inhibitors
  - **Anticoagulants (Use one)**
    - -UFH
    - -LMWH
    - -Bivalirudin
    - -Fondaparinux
  - **Fibrinolytic agents**
- **Adjunctive therapies**
  - Statin
  - ACE inhibitor

Anti-ischemic Therapy

Don't memorize trials
Just Know there's a reason why we use these drugs

- **BB** - COMMIT-CCS trial Day 2-15 After ACS event, In elderly atenolol is Better
  - Reduced the endpoint of death/ MI/ cardiac arrest
  - 1 month up to 3 year for normal LVEF If LVRF abnormal then give BB forever
- **ACEI** - ISIS-4 6 weeks, PEACE no benefit
- **Statin** - PROVE-IT trial Start with high dose of Statin
  - LDL? Superior stabilization of vulnerable plaque
- **NTG**
- **PPI** Reduce the risk of bleeding
- **Regular activities** - 1 week if revascularized/ 1 month for sports

Discharge the patient with the following drugs
If patient have a **stent**:
1. Aspirin
2. P2Y12
3. BB
4. ACEI
5. Statin

If **no stent**, add heparin for 48h up to 8 days.

Antiplatelets

Clinical trials :

- **ISIS-2**
  - Within 24hr of STEMI reduce CV mortality by 23% at 5 weeks f/u
  - Benefit of SK & Aspirin were additive with 42% decrease mortality
- **CURE Trial**
  - Effects on Clopidogrel in addition to Aspirin in patients with ACS without ST-Elevation.

Don't memorize trials
Just Know there's a reason why we use these drugs

1. **Aspirin (ASA):**
   Aspirin will inhibit cox-1 enzyme which lead to inhibition of platelet aggregation . Chewable 160 to 325 mg at presentation, then 75 to 325 mg daily.

2. **P2Y12 inhibitors:** (can be used for patients with aspirin allergy)

   More potent than ASA and is combined with ASA and both agents are powerful adjuncts to reperfusion therapy. Examples: Clopidogrel, Ticagrelor and Prasugrel.

Only know the MOA of aspirin and P2Y12 inhibitors

- **Platelet Activation**

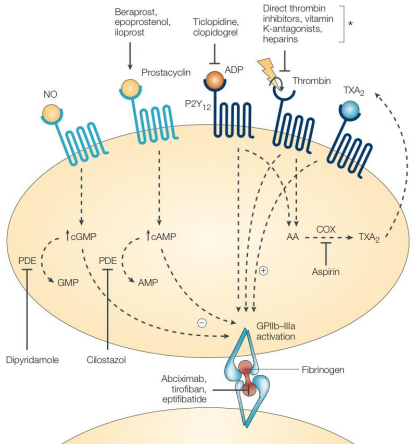
Activators:

- Collagen
- vWF
- Thrombin

Consequences of activation:

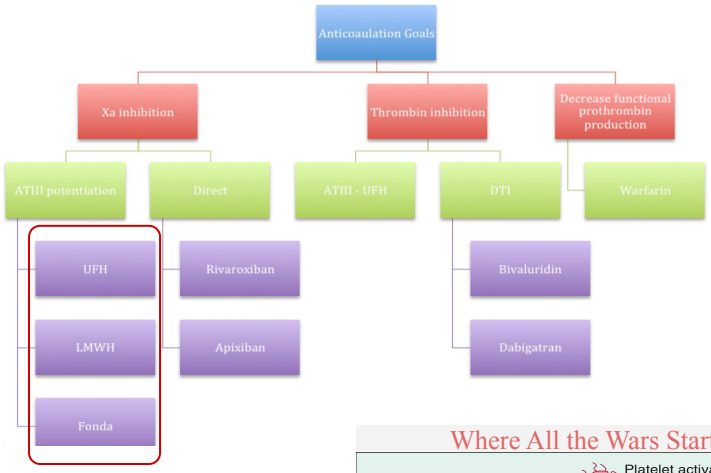
AA —> COX1 —> TXA2
—> Release of granule content:

- ADP
- Serotonin
- Fibrinogen

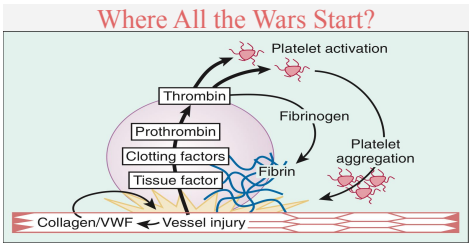


Anticoagulants

- Anticoagulants are typically stopped after the PCI
- If PCI is not performed, anticoagulants are typically administered for at least 48 hours, and preferably longer, for the duration of hospitalization (up to 8 days)



Just know what's in the red box, the rest is not important now



- **LMWH > UFH**

Low Molecular Heparin or Unfractionated Heparin

- Prevents further thrombosis and aids in insuring patency of the occluded artery.
- Greater anti-Xa activity (so greater thrombin inhibition).
- Greater release of tissue factor pathway inhibitor.
- Less thrombocytopenia.
- Higher bioavailability so s/c administration.
- Less binding to plasma protein so more consistent effect and no monitoring required.

If the patient had a HIT Before then don't give heparin or LMWH Give fondaparinux

TABLE 87-3 Comparison of the Features of Heparin, Low-Molecular-Weight Heparin, and Fondaparinux

FEATURE	HEPARIN	LMWH	FONDAPARINUX
Source	Biologic	Biologic	Synthetic
Molecular weight	15,000	5000	1728
Target	Xa and IIa	Xa and IIa	Xa
Bioavailability (%)	30	90	100
Half-life (hr)	1	4	17
Renal excretion	No	Yes	Yes
Antidote	Complete	Partial	No
HIT	<5%	<1%	Never

HIT: heparin induced thrombocytopenia

ACS Treatments

Reperfusion therapy: Reperfusion therapy is the ultimate destination,you have to open the artery either chemically (Thrombolytics = Fibrinolytics) or mechanically (PCI).

Fibrinolytic agents

1- Fibrinolytics (Thrombolytics): (door to needle time <30 min)

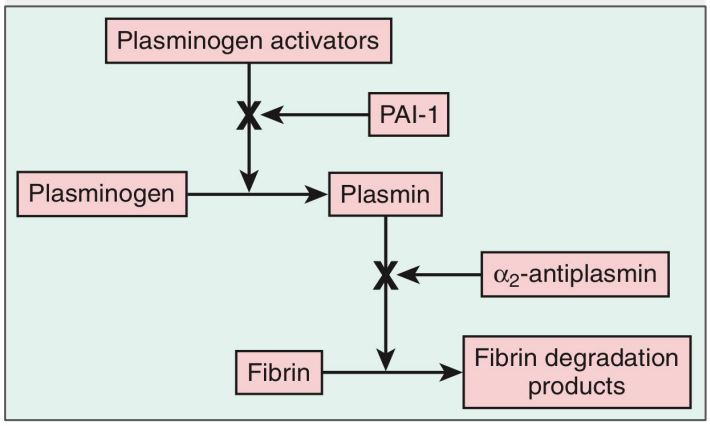
- ONLY USED FOR STEMI (NOT NSTEMI).
- Reduces short and long term mortality following MI.
- Should be given during a 12hr window, and given As soon as possible. There is no benefit if you give it after 12 hrs.

  Because after 12hrs the damage that has been done to the heart is irreversible so reperfusion by fibrinolytic won't be useful
- If Fibrinolytics fails after 30-60 minutes, refer to PCI.[1]

There are 2 types of fibrinolytics:

1. Non Fibrin specific: Streptokinase. we don't use it anymore
2. Fibrin specific: Tenecteplase (TNK) - Alteplase (first choice) - Reteplase.

MOA: no need to remember the details



Drug	Dosage	Add On
tPA Accelerated regimen 3 Doses	**15mg** IV bolus — > **0.75mg/kg (max 50)** over 30 min —>**0.5mg/kg (max35)** over 1hr	Better than SK (**GUSTO-1**) **100mg** over 90 min
rPA 2 Doses	**10U** over 2 min then **10U** at 30 min	**=tPA**
know this one! **TNK** 1 Dose	Single bolus over 10 sec **<60 kg=30mg 90≥50mg** 5mg increment/10kg	**=tPA** (**ASSENT-2**) but less non-cerebral bleeding & Tx

All pts get ASA load/UFH 60U/Kg max 4000 then infusion 12U/Kg max 1000U/hr PTT target 50-70 (UFH not beneficial with SK)

ACS Treatments

Reperfusion therapy:

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Fibrinolytic agents

Absolute Contraindications to thrombolytic therapy	Relative Contraindications to thrombolytic therapy
➔ Any prior intracranial haemorrhage. ➔ Know cerebral vascular lesion. ➔ Known intracranial neoplasm. ➔ Ischaemic stroke within past 3 months. ➔ Recent major trauma/surgery/head injury (within 3 months) ➔ Active bleeding or Known bleeding disorder (excluding menses) ➔ Suspected Aortic dissection. (Never use fibrinolytics in these conditions) **The worst bleeding ever is the intracranial bleeding, so DON'T GIVE Fibrinolytics if there is a risk of intracranial bleeding.**	➔ Oral anticoagulant therapy (example: Warfarin) ➔ Pregnancy or within 1 week postpartum. ➔ Noncompressible vascular punctures ➔ Traumatic resuscitation ➔ Poor controlled Refractory hypertension (systolic blood pressure >180 mmHg) ➔ Internal bleeding, e.g. active peptic ulcer ➔ Dementia. (Fibrinolytics here are relatively contraindicated but still the doctors have the decision to use it according to the patient condition. For example: patient with severe MI coming to a hospital without a cath lab, the doctor can use fibrinolytics to save his life even if the patient has one of the above situations.)

2- Revascularization (surgical): An angiography must be done first. It's either via CABG or PCI

CABG (Coronary Artery Bypass Graft)[2]

2 : 25 minutes

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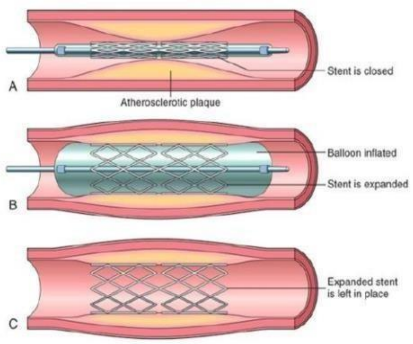
Used when the patient has:

- **Three-vessels occlusion.**
- Left main coronary artery occlusion.
- Left ventricular dysfunction.

PCI (Percutaneous coronary intervention)

1 : 42 minutes



The procedure only aims to remove the clot, but a stent [3] could be placed in the artery to improve the outcome. Preferred treatment for STEMI, as long as it's performed within 90 minutes from patient's admission. **(door to balloon time <90 minutes).**

Complication of PCI:

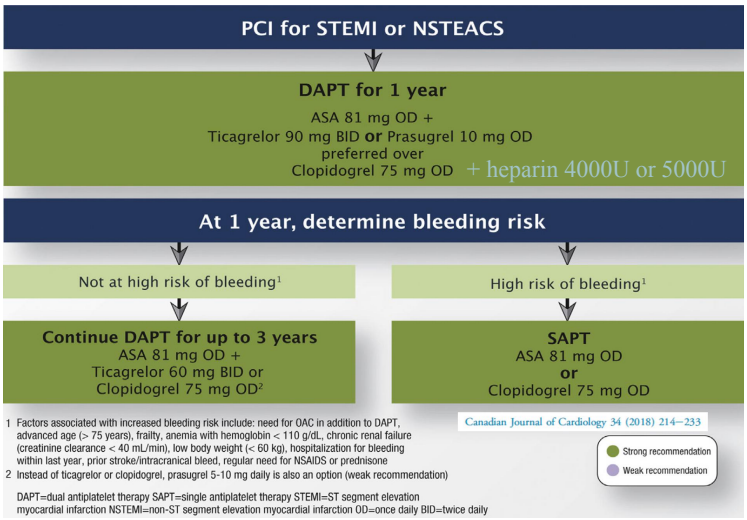
- Rupture of coronary artery on inflation.
- Restenosis.
- Hematoma at the site of entry (e.g. femoral area hematoma).

Used when the patient has:

- **One-vessel occlusion**.
- Two-vessels occlusion.
- No improvement despite maximal medical therapy of ACS.

[1] Remember Time is a muscle!
[2] Requires open heart surgery.
[3] Either a bare metal stent, or a drug-eluting stent. The latter is better.

ACS Treatments important



- Take the patient to the cath lab to assess the need for stent
- PCI? then stop heparin
- No need for PCI? then continue heparin for 48h up to 8 days.
- In ACS pts. **without PCI**: give both aspirin & clopidogrel/ticagrelor for **one year** bc. there's 10% chance increase in ACS incidence in the first year.
- If patient **with PCI** then give aspirin **for life & clopidogrel/ticagrelor for 1 year.**

At the end of the lecture the doctor said that regardless of stenting or not give aspirin for life and clopidogrel for 1 year. !

Risk factors modification:

- Try to modify the risk factors.
- Smoking cessation among other risk factors modification shows the most immediate effect.
- The goal of LDL level is below 100 mg/dL. Statins ,among other lipid lowering agents, is the only one that reduces mortality rate.

Mnemonic (discharge medications after ACS) : ABCDE
A: Aspirin and anti-anginals
B : Beta blockers and blood pressure
C : Cholesterol and cigarettes
D : Diet and diabetes
E : Education and exercise

TIME IS MUSCLE:

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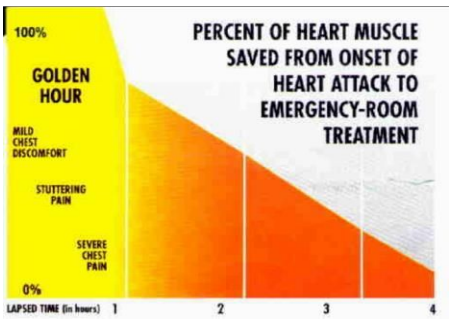
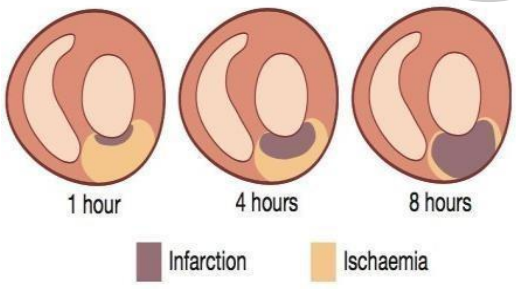




Time is important! As we move forward damage progresses and infarction size increases; it gets harder to manage the patient and more serious complications probability increases. When it's been already 12 hours since the onset of pain there would be no point in the acute management as the injury has already been irreversible.

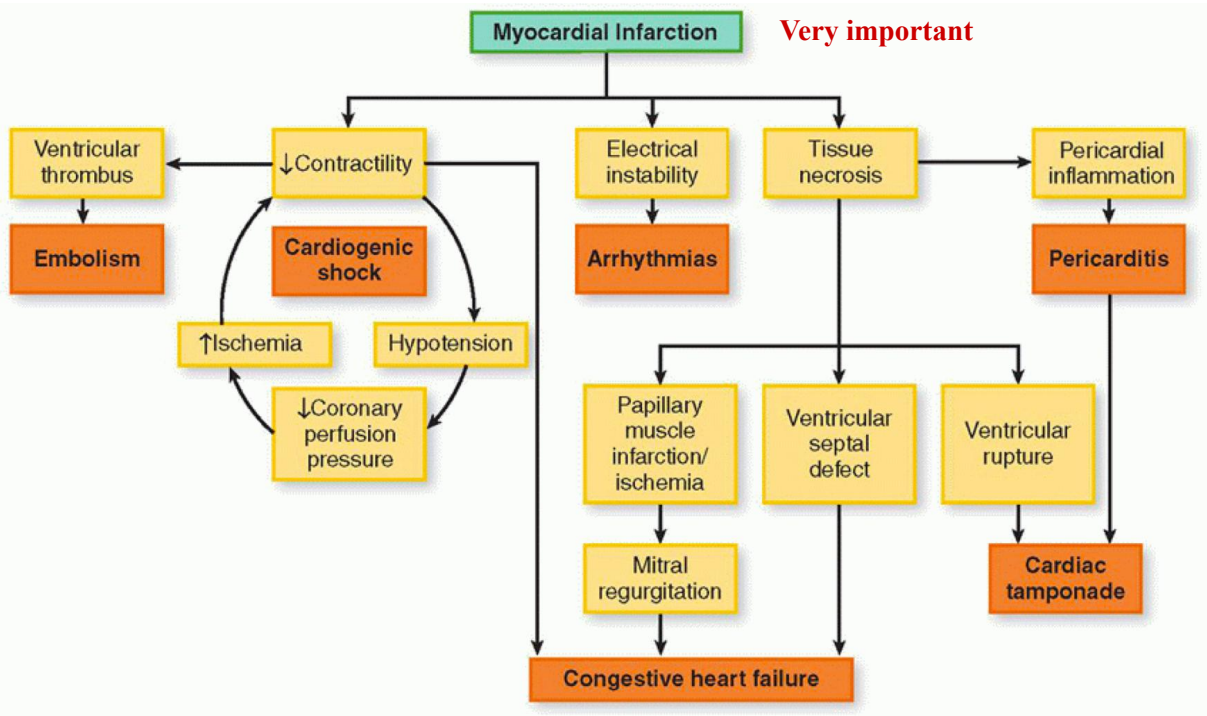
The first hour is the golden hour.

MI Complications

- **Congestive heart failure and its complication:**

  Most common cause of in-hospital mortality. If severe may lead to cardiogenic shock (insufficient cardiac output).
- **Recurrent infarction**
- **Electrical Arrhythmias [4]:**

Includes:	Notes
Atrial fibrillation **-Ventricular fibrillation**	**(immediately use defibrillator and CPR).** 436
Ventricular tachycardia	Most common cause of death in first few days after MI is ventricular arrhythmia either VT or V-Fib
Sinus tachycardia	May be caused by pain, anxiety or fever and it worsen ischemia.
Sinus bradycardia	• Commonly occurs during early stages of acute MI, especially right- sided MI. • It might be a protective mechanism [5].
Asystole and AV block	associated with ischemia involving conduction tracts). It usually appears within first 24 hours; and as time pasts it becomes less likely to happen.



*It is important to notice that some of them may lead to another.

[4] Will be discussed in an upcoming lecture

[5] By reducing Oxygen demand.

Summary 436

	Unstable angina	NSTEMI	STEMI
Troponin (I & T) CK-MB	**-ve**	**+ve**	**+ve**
Notes	• A chest pain with no pattern lasts **less** than **20 minutes** • ST depression due to ischemia	• Pain lasts **more** than **20 minutes** • ST depression due to subendocardial infarct that involves inner 1\3 of the wall Complications of MI: • Electrical (tachy / brady arrhythmias) • Heart failure (pulmonary edema) • Cardiogenic shock	• Sever ACS presentation • ST Elevation due to the infarct involving the myocardial thickness • **No response** to sublingual glyceryl trinitrate

"A **46 y/o man** known to have **DM** and **HTN** comes to the ER with **central crushing** chest pain"
this is a typical scenario for an ACS pt. and to differentiate between the types we need to do the following investigations

1- **ECG:** to monitor the ST elevation.
2- **CK-MB:** released in MI pt.(4-6 h) after the onset and then falls within (48-72h)
3-**Troponin:** released in MI pt. (4-6 h) and can last up to 2 weeks.

Pharmacological Therapy

1. Increase O2 supply

Vasodilators: Nitroglycerine	Antiplatelet: Aspirin + P2Y12 inhibitor: clopidogrel, ticagrelor and prasugrel.	Antithrombotic: Unfractionated Heparin or Low Molecular Heparin.

2. Reduce O2 demand

Beta blockers: acebutolol, atenolol, propranolol ... etc.	Analgesics for the pain

3. Other medications

ACE inhibitors: captopril, benazepril … etc.	Statin therapy

Reperfusion Therapy

1. Fibrinolytic

For STEMI only!!

Used within the first 12 hours after the onset of the symptoms

2 types: Non-fibrin specific: streptokinase
Fibrin specific: tenecteplase (TNK) – alteplase reteplase

Absolute contraindication (never use fibrinolytics):

Prior intracranial hemorrhage
cerebral vascular lesions
intracranial neoplasm
suspected aortic dissection
ischemic stroke within the past 3 months
active bleeding or known bleeding disorder
recent close-head trauma / surgery within 3 months

Relative contraindication where it depends on the doctor's decision:

Oral anticoagulant, pregnancy\ 1 week postpartum, internal bleeding (peptic ulcer)… etc.

2. Primary PCI

- Preferred treatment for STEMI
- Best time time to open the artery is within 60 minutes

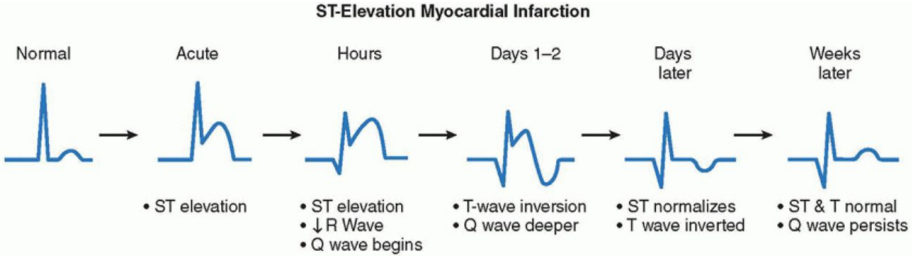
Summary 437

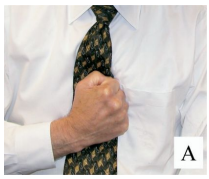
- **ACS happens due to a plaque rupture leading to plug formation and stenosis of arteries.**
- **Stable VS unstable angina symptoms**

Stable Angina*	Unstable Angina
• Substernal • Relieved by rest or NTG • Provoked by exertion or emotional stress	• New with normal activity • Increasing: frequency or severity, not relieved by NTG, usually more than 20 minutes • At rest

* Typical if all three, atypical if 2, noncardiac if only 1.

- Female, diabetic, age more then 70 or have previous HF are more likely to have Atypical (No CP) presentation and misdiagnosed .





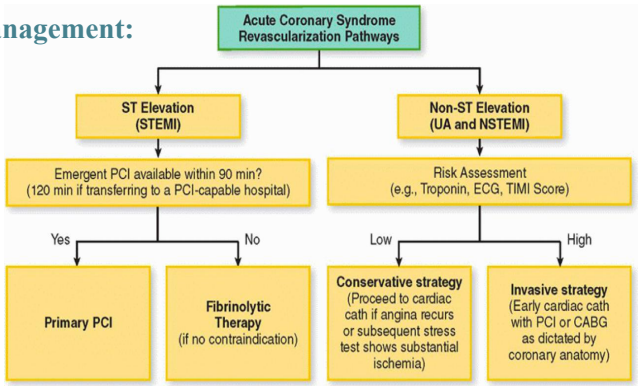
Levine sign

- TIMI score is used to classify NSTE-ACS according to severity :

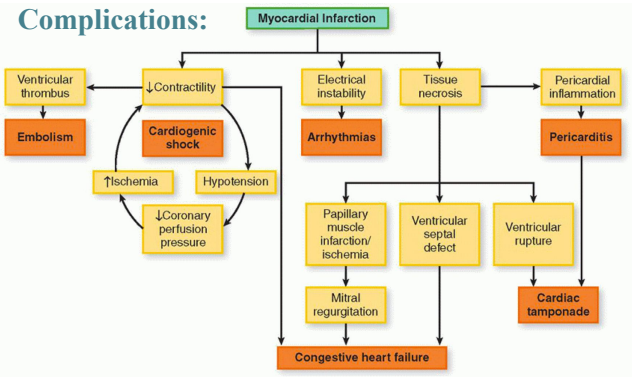
1. Age ≥ 65
2. ≥ 3 CAD risk factors*
3. Known CAD (stenosis ≥ 50%)
4. ASA use in past 7 days
5. Severe angina (≥ 2 episodes in 24 hrs)
6. EKG ST changes ≥ 0.5mm
7. Positive cardiac marker

*Hypertension, hypercholesterolemia, diabetes, family history of CAD, or current smoker

Management:



Complications:



- Aspirin is used after ACS for life time, it's the best initial thereby and decreases mortality.
- P2Y12 inhibitors (Clopidogrel or Ticagrelor) is given for one year.
- Course of management: STEMI → Aspirin, clopidogrel, heparin, activate cath lab → in the cath lab: angiogram, found the problem, put a stent → Aspirin, clopidogrel, Statin, ACEI, beta blocker, Stop heparin (if you didn't put a stent for a reason continue in heparin for 48h-8days)
- Fibrinolytic: TNK (1 dose , 5 mg/10kg, <60 kg=30mg, 90³50mg)

Side notes:

- Levine's sign (*see picture above*) is not sensitive.
- Larger areas of chest discomfort correlate with a greater likelihood of cardiac ischemia or myocardial infarction.
- Don't give sildenafil while using NTG
- Most common cause of sexual dysfunction in cardiac patients is anxiety (but if he asks about a drug it's beta blocker).

Examine Yourself !!

1. Which one of the following represent the aim of managing patient with acute coronary syndrome?
    A. Opening the occluded artery and improving oxygen supply.
    B. Reducing O2 demand.
    C. Both A and B.
    D. None of above.

2. A 55-year-old man has just arrived in accident and emergency complaining of 30 minutes of central crushing chest pain. Which feature is most indicative of myocardial infarction at this moment in time?
    A. Inverted T waves
    B. ST elevation
    C. Q waves
    D. Raised troponin

3. A 80 years old female diabetic came to the emergency 9 hours ago with central chest pain, burning, troponin was 10 mg/dl (high), vital sign is normal. ECG shows deep T wave inversion in V1-V3. Which of the following is the diagnosis?
    A. NSTEMI
    B. Pericarditis
    C. Unstable angina
    D. Pulmonary Embolism

4. Fibrinolytic are only used in which of the following conditions?
    A. NSTEMI within the first 12 hours.
    B. STEMI within the first 12 hours.
    C. Unstable angina
    D. All of above.

5. All of the following are absolute contraindication of fibrinolytic therapy except?
    A. Any prior intracranial hemorrhage.
    B. Know cerebral vascular lesion.
    C. Ischemic stroke within past 3 months.
    D. Pregnancy or within 1 week postpartum.

6. A 55-year-old man with type 2 diabetes presents with a 1-hour history of severe central chest pain. Which of the following statements is true?
    A. normal baseline troponin and elevated 6-hour troponin level is suspicious of myocardial infarction
    B. normal ECG excludes myocardial infarction
    C. normal initial troponin level excludes myocardial infarction
    D. Failure of chest pain to resolve with nitrates confirms myocardial infarction

Examine Yourself !!

7. Which of the following are the worst factor for ACS ?
    A. DM
    B. HTN
    C. Smoking
    D. Hyperlipidemia

8. A 59-year-old male smoker complains of severe substernal squeezing chest pain of 30-minute duration. The paramedics have given sublingual nitroglycerin and oxygen by nasal cannula. His blood pressure is 110/70 mmHg and heart rate 90 bpm on arrival to the emergency room. The ECG is normal. Which of the following is the best next step? (Extra Question)
    A. Echocardiography
    B. Thallium stress test
    C. Aspirin
    D. Coronary angiography
    E. Coronary artery bypass

9. A 49-year-old man is rushed to accident and emergency complaining of a 20-minute history of severe, crushing chest pain. After giving the patient glyceryl trinitrate (GTN) spray, he is able to tell you he suffers from hypertension and type 2 diabetes and is allergic to aspirin. The most appropriate management is:
    A. Aspirin
    B. Heparin.
    C. Clopidogrel.
    D. Warfarin

10. A 65-year-old female has just arrived to the emergency department complaining of 20 minutes of central crushing chest pain. Which ONE of the following features is most indicative of myocardial infarction in this patient?
    A. Peaked T wave.
    B. Presence of U wave.
    C. ST elevation.
    D. Q waves.

11. A 40 years old male presents to the ER having 1 day history of chest pain. the pain started gradually, and continued until coming to the ER. It was located in the center of the chest and did not radiate, and was somewhat worse on lying on his back. He did not notice a change of pain severity with exertion. His vital signs were normal, and ECG revealed ST elevation from V1 to V6 ,I, AVL, II, III and AVF. The most likely diagnosis of this chest pain is:
    A) Acute myocardial infarction
    B) Acute pulmonary embolism
    C) Pericarditis
    D) Gastro -esophageal reflux

1-C / 2-B / 3-A / 4-B / 5-D / 6-A / 7-A / 8-C / 9-C / 10-C / 11-C / 12-C