ISCHEMIC HEART DISEASE
ACUTE CORONARY SYNDROME

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Case presentation

A50 year old male presented to emergency room complaining of sudden sever chest pain of 1 hour duration. It is retrosternal, compressive, and radited to left shoulder and arm.

Associated with sweating, nausea and vomiting

typical scinario of MI

On examination: patient is anxious, in pain, sweaty.

BP: 100/60. PULSE: 120 BPM, RR: 26/min

Chest: basal crepitations

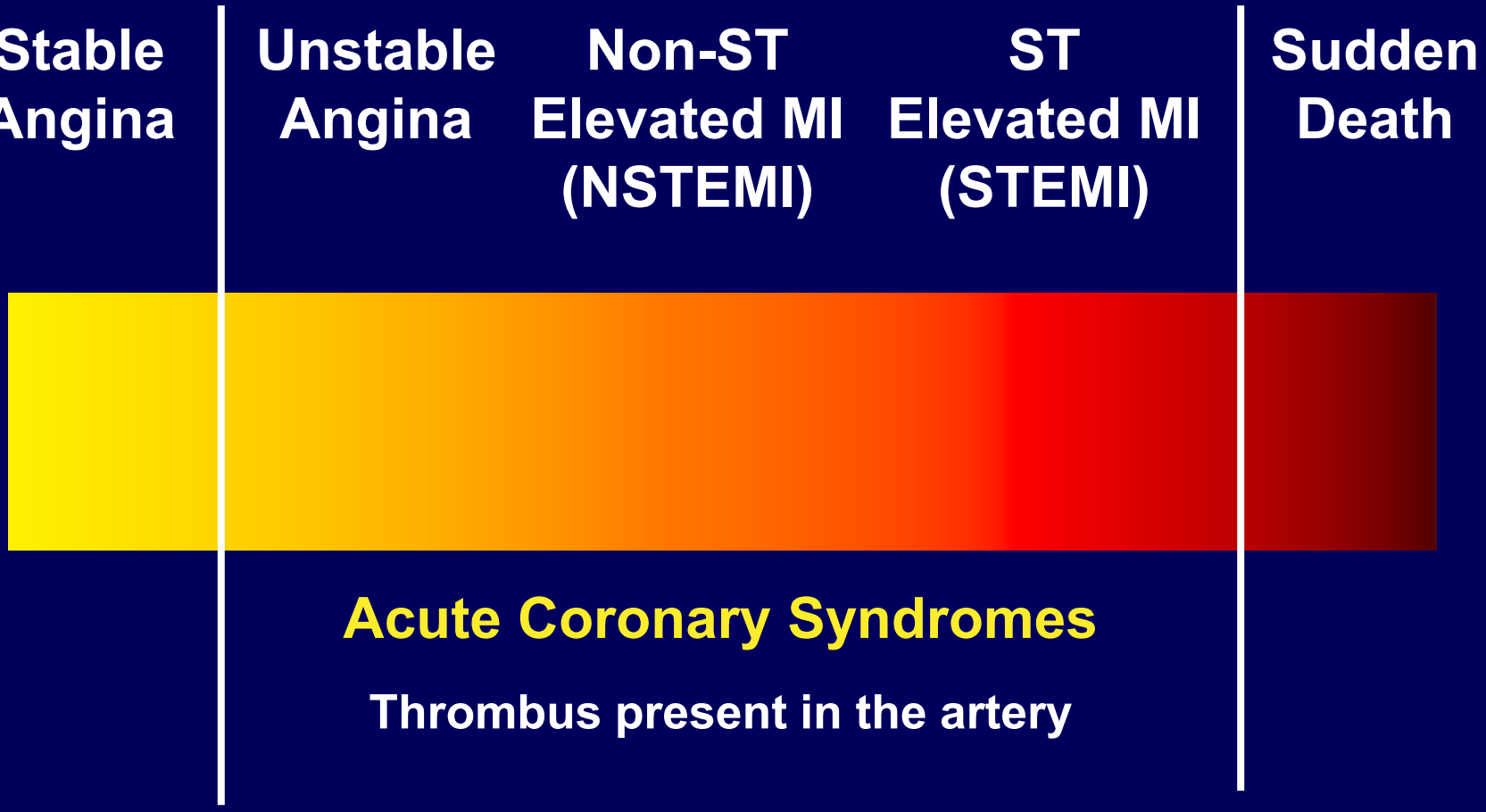
tachypnic

What is the most likely diagnosis

MI complicated with hypoxia

pathophysiology

The Spectrum of Myocardial Ischemia



Acute Coronary Syndrome

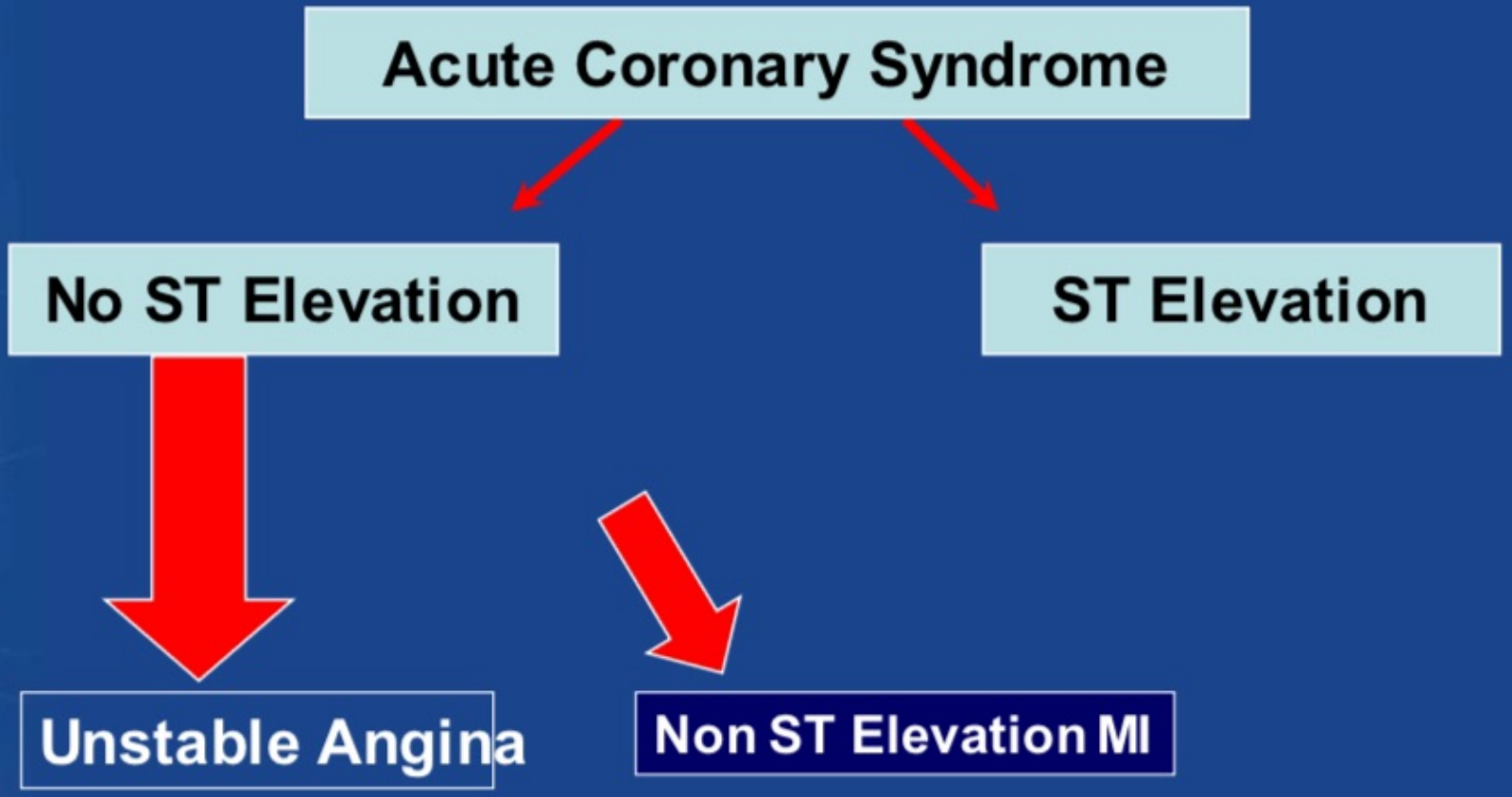
The spectrum of clinical conditions ranging from:

- STEMI (Q-wave MI): Total occlusion
- NSTEMI (non-Q wave MI): Subtotal occlusion
- unstable angina: Subtotal occlusion

Characterized by the common pathophysiology of a disrupted atherosclerotic plaque (rupture, erosion, or fissure)

unstable

Acute Coronary Syndromes



Case presentation

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Associated with sweating, nausea and vomiting

On examination: patient is anxious, in pain, sweaty.

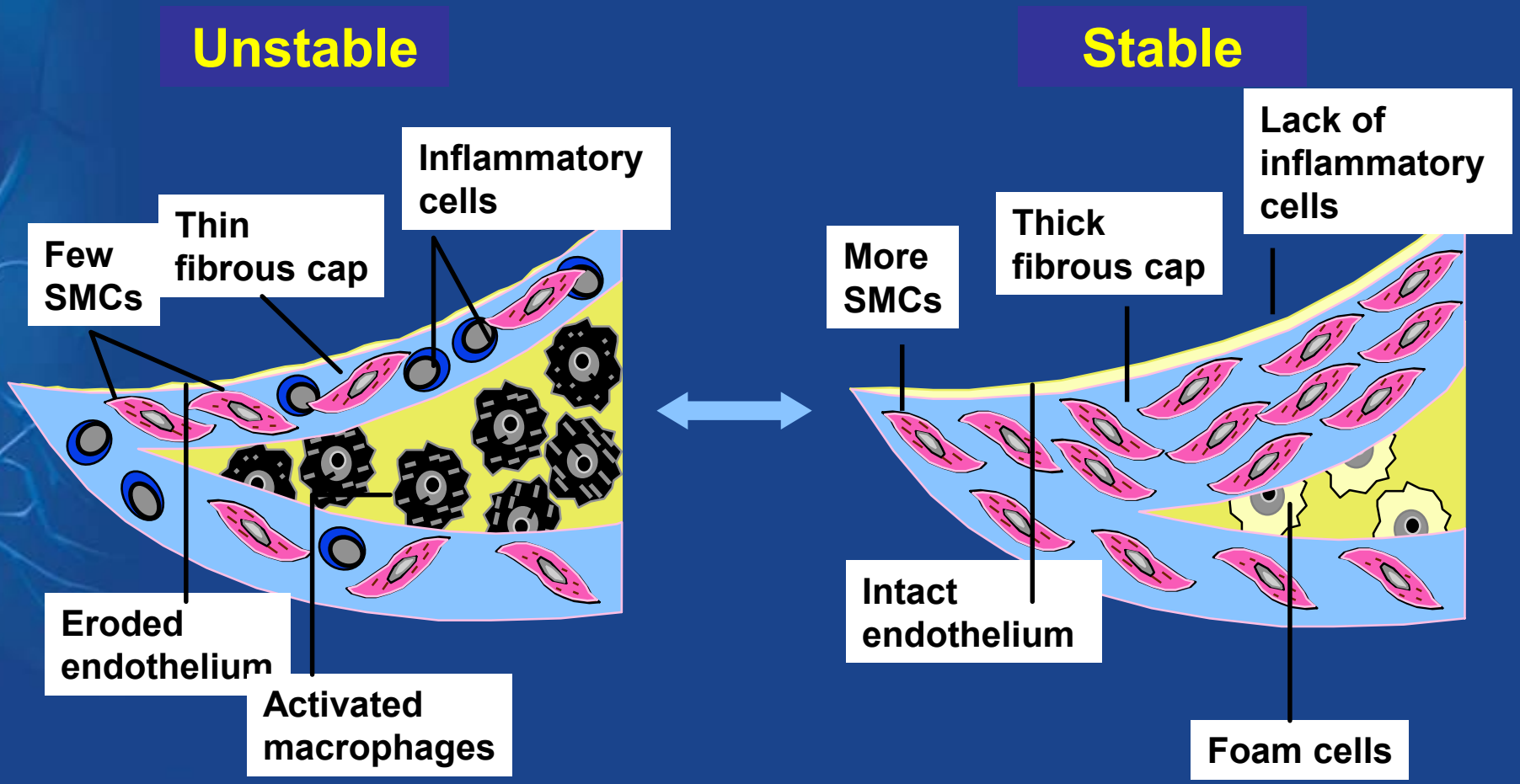
BP: 100/60. PULSE: 120 BPM, RR: 26/min

Chest: basal crepitations

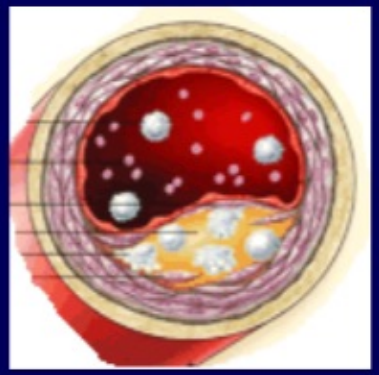
The most likely diagnosis is Myocardial infarction

Pathophysiology??

Characteristics of Unstable(RUPTURE-PRONE PLAQUE) and Stable Plaque



Pathogenesis of ACS

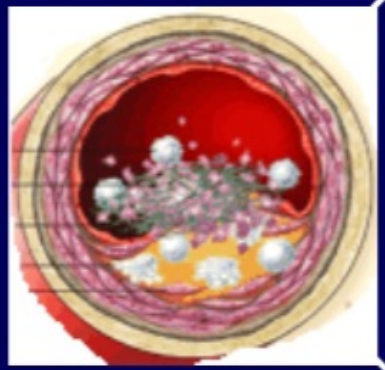


Vulnerable Plaque

Plaque rupture
(55-80%)

Exertion
BP, HR
Vasoconstriction

✓Platelet aggregation
✓Thrombus formation
✓Vasospasm



Incomplete occlusion
Distal embolization

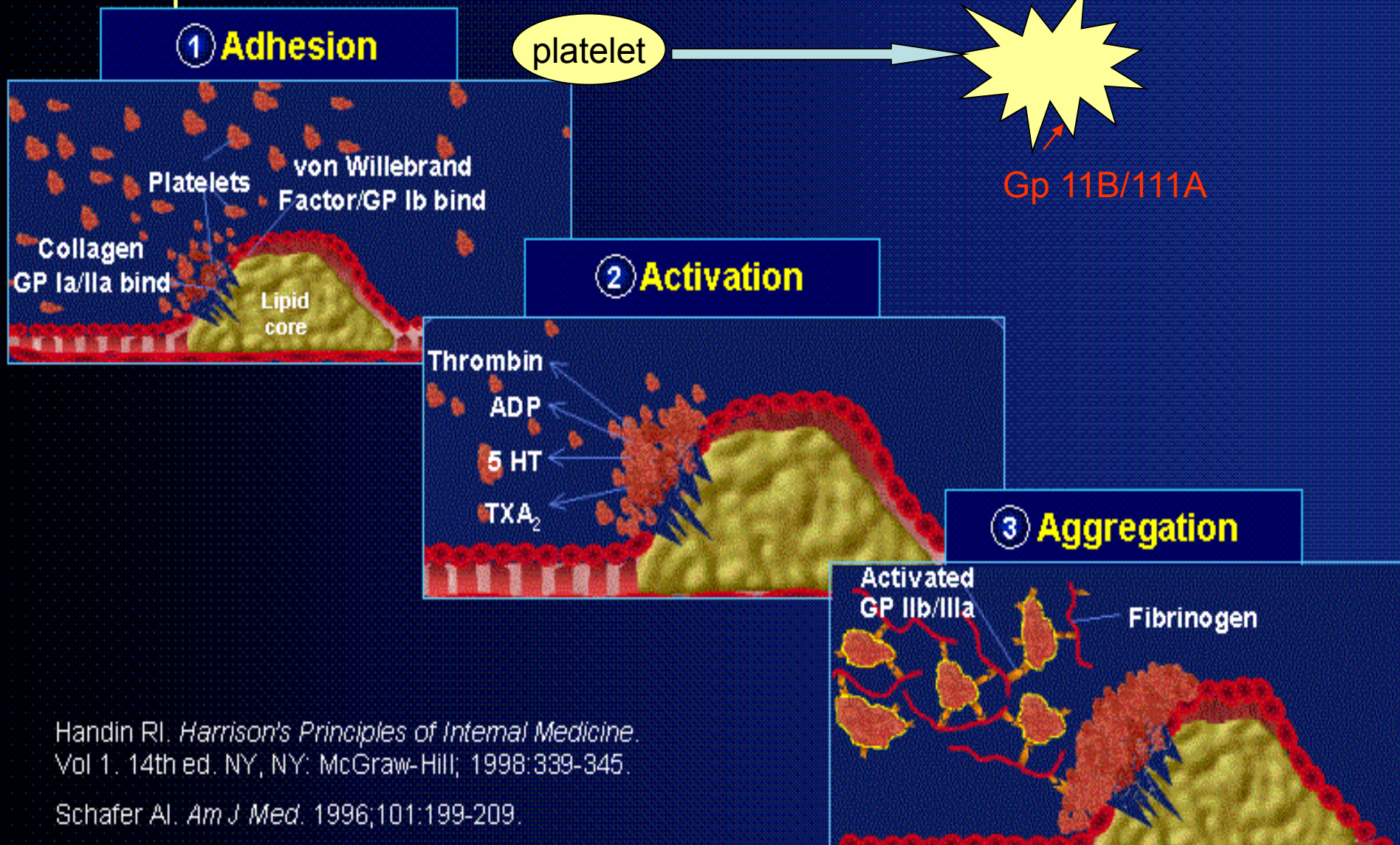
Unstable angina
NSTEMI

Complete occlusion

STEMI

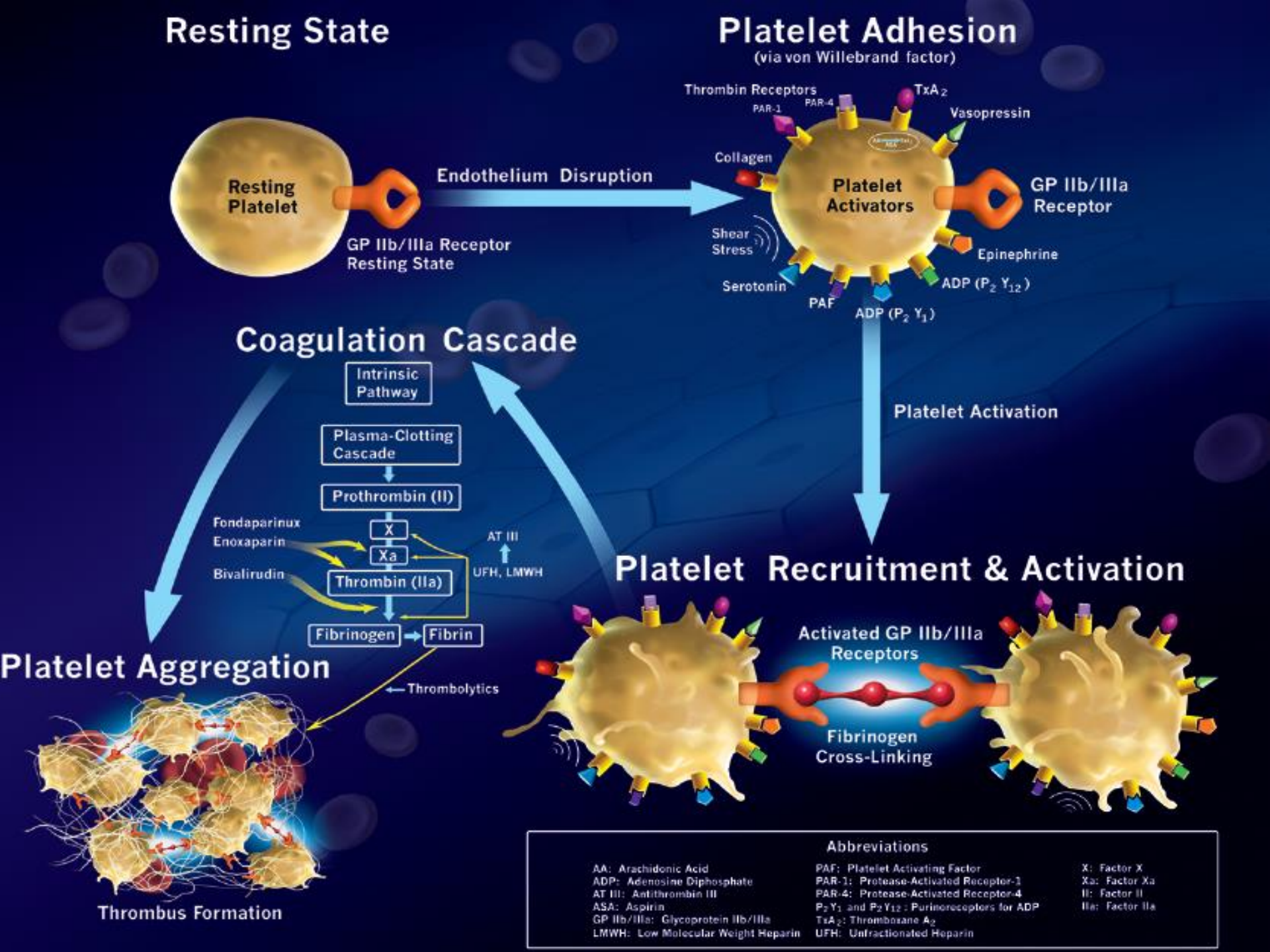
Platelet Cascade in Thrombus Formation

1. plaque rupture and then:

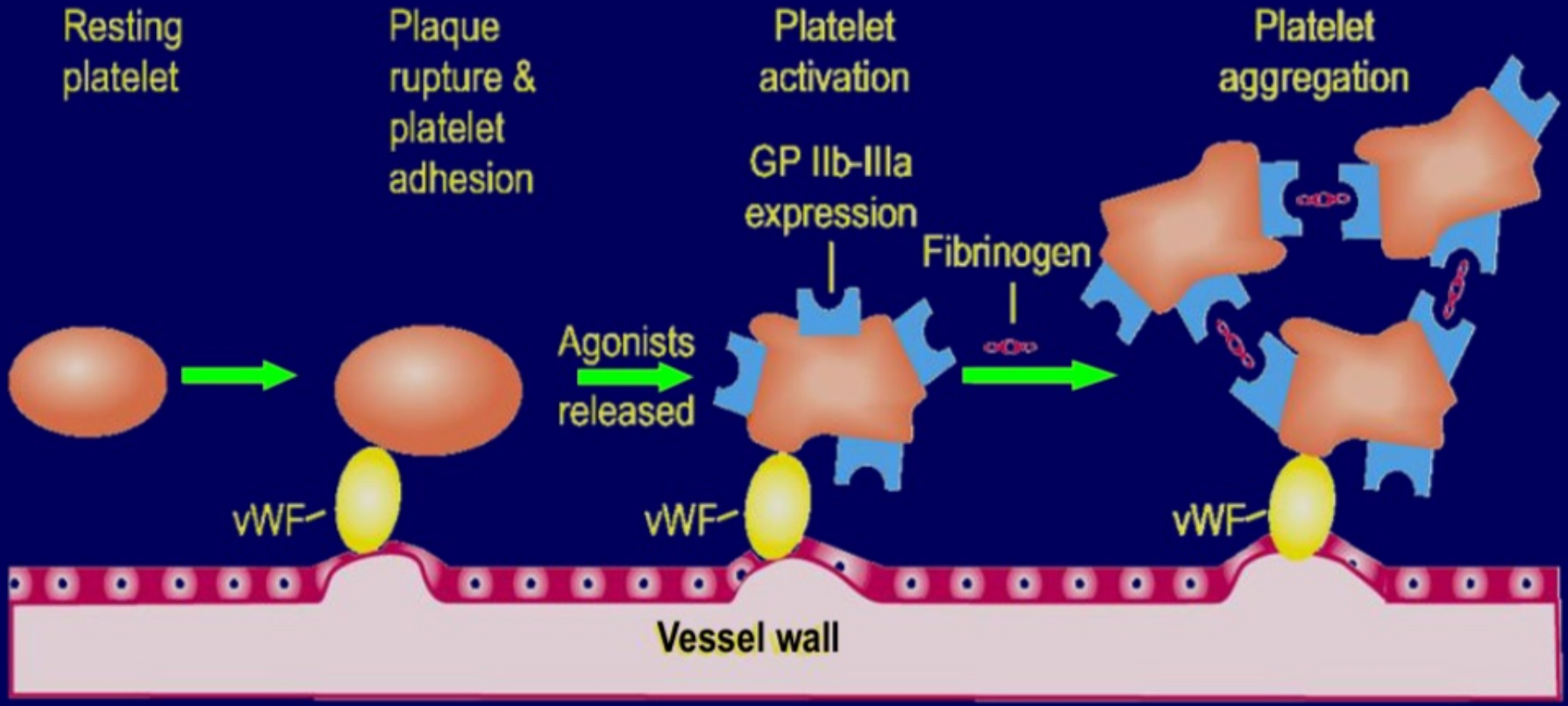


Handin RI. *Harrison's Principles of Internal Medicine*. Vol 1. 14th ed. NY, NY: McGraw-Hill; 1998:339-345.

Schafer AI. *Am J Med*. 1996;101:199-209.

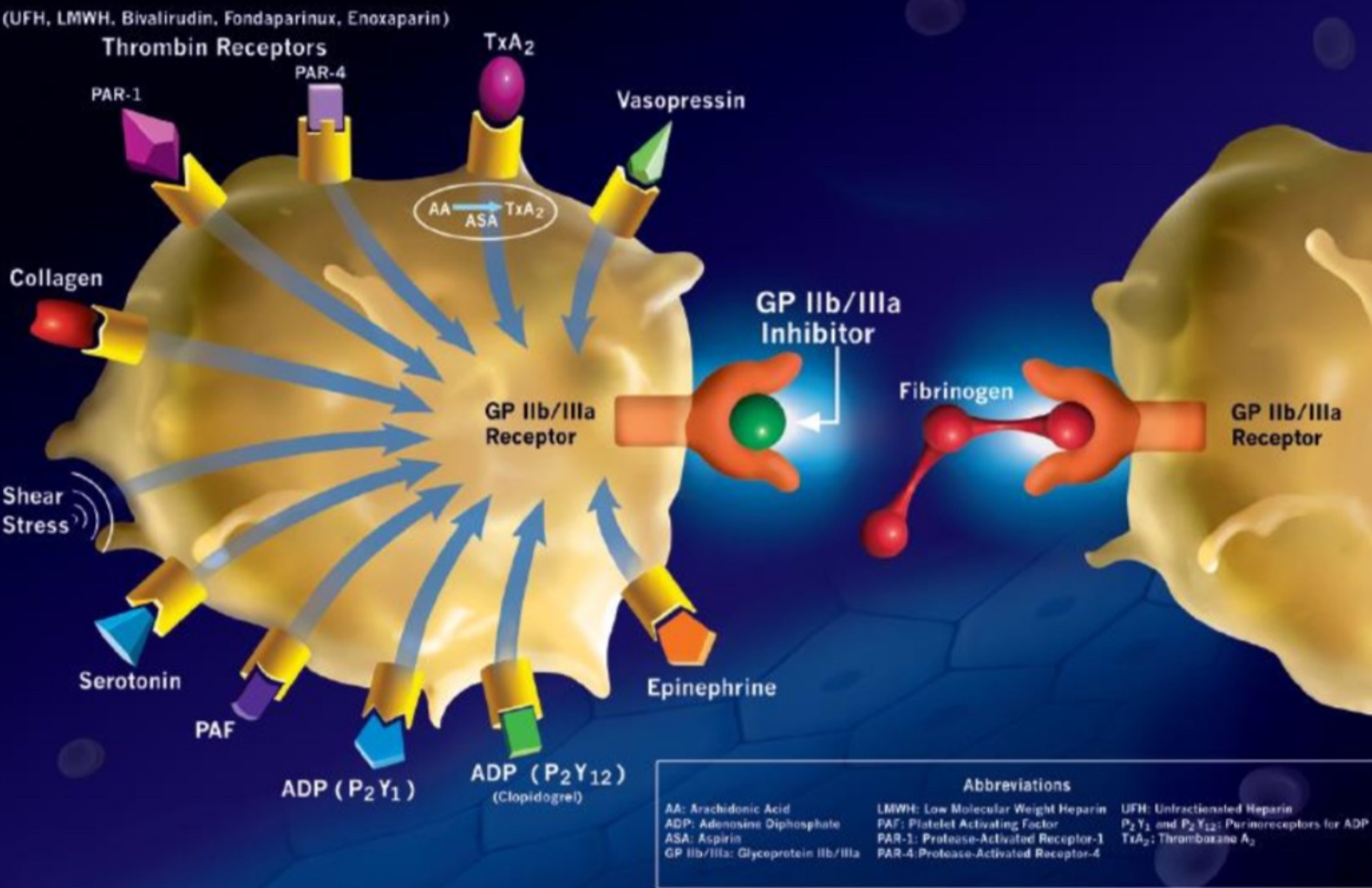

Resting State
Platelet Adhesion
(via von Willebrand factor)
Thrombin Receptors
PAR-1
PAR-4
TxA2
Vasopressin
Collagen
Resting Platelet
Endothelium Disruption
Platelet Activators
GP IIb/IIIa Receptor
GP IIb/IIIa Receptor Resting State
Shear Stress
Epinephrine
Serotonin
PAF
ADP (P2 Y12)
ADP (P2 Y1)
Coagulation Cascade
Intrinsic Pathway
Plasma-Clotting Cascade
Prothrombin (II)
Fondaparinux
Enoxaparin
Bivalirudin
X
Xa
Thrombin (IIa)
AT III
UFH, LMWH
Fibrinogen
Fibrin
Platelet Activation
Platelet Recruitment & Activation
Activated GP IIb/IIIa Receptors
Fibrinogen Cross-Linking
Platelet Aggregation
Thrombolytics
Thrombus Formation
Abbreviations
AA: Arachidonic Acid
ADP: Adenosine Diphosphate
AT III: Antithrombin III
ASA: Aspirin
GP IIb/IIIa: Glycoprotein IIb/IIIa
LMWH: Low Molecular Weight Heparin
PAF: Platelet Activating Factor
PAR-1: Protease-Activated Receptor-1
PAR-4: Protease-Activated Receptor-4
P2Y1 and P2Y12 : Purinoreceptors for ADP
TxA2: Thromboxane A2
UFH: Unfractionated Heparin
X: Factor X
Xa: Factor Xa
II: Factor II
IIa: Factor IIa

Platelet Adhesion, Activation, and Aggregation



White HD. *Am J Cardiol.* 1997; 80 (4A): 2B-10B.

IT IS IMPORTANT TO INHIBIT BOTH ACTIVATION & AGGREGATION



PATHOGENESIS OF ACS acute coronary syndrome

Plaque rupture

THROMBOSIS

1- Primary hemostasis: Initiated by platelet

platelets adhesion, activation, and aggregation---platelet plug

2- Secondary hemostasis:

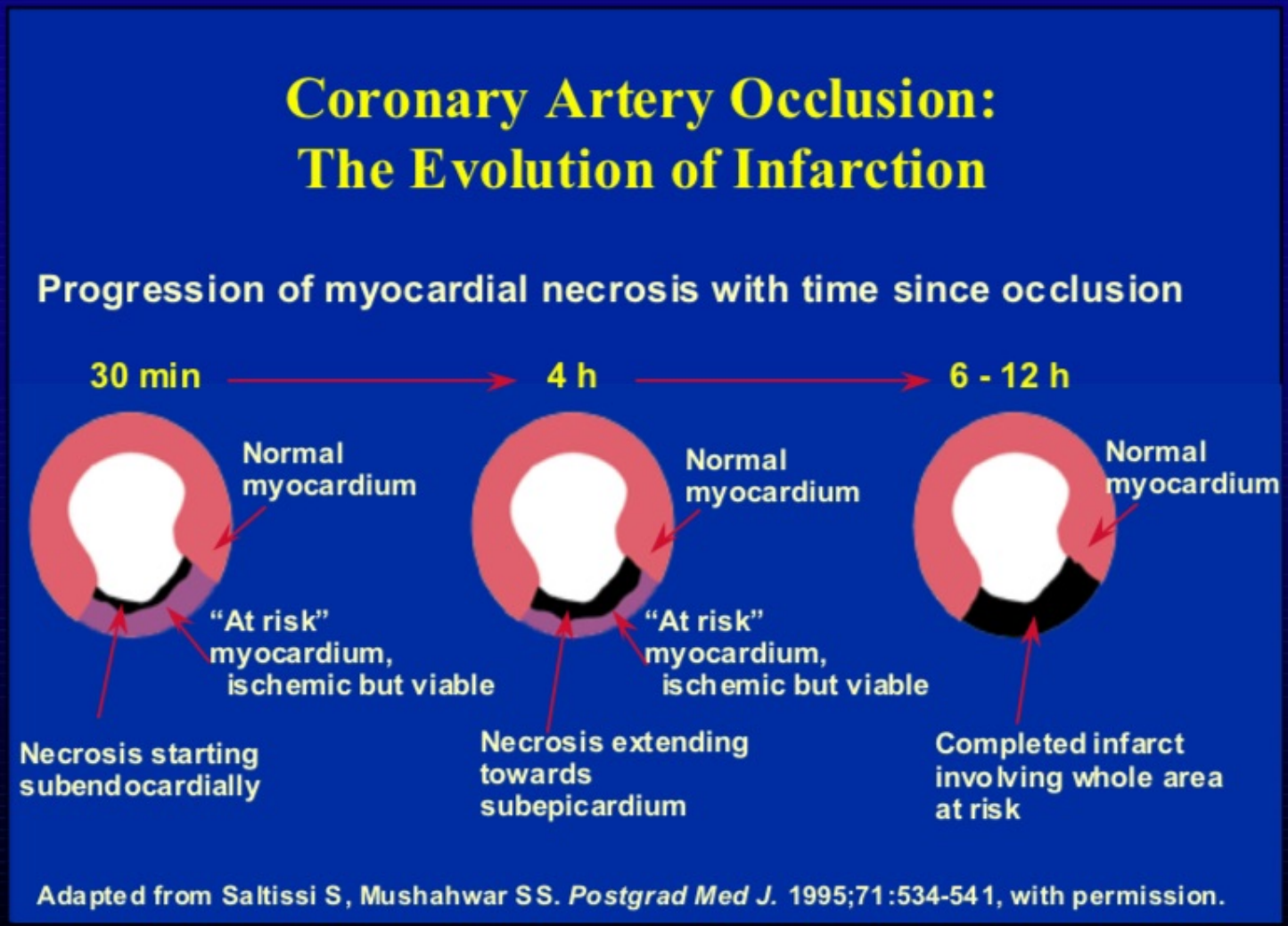
activation of the coagulation system---fibrin clot.

These two phases are dynamically interactive:

Platelet can provide a surface for coagulation enzymes

Thrombin is a potent platelet activator

Evolution of Infarction/Necrosis



ACUTE MYOCARDIAL INFARCTION

THE MOST COMMON CAUSE OF DEATH
RUPTURE ATHEROMATOUS PLAQUE---CORONARY OCCLUSION

***Clinical Manifestation*:**

Chest pain: usually at rest, early morning

> 30 minutes (site, radiation, severity, character, radiation, associated phenomena..)

painless MI (10-15%): DM, elderly present with complications

Present as: Hypotension, Heart failure, Arrhythmia

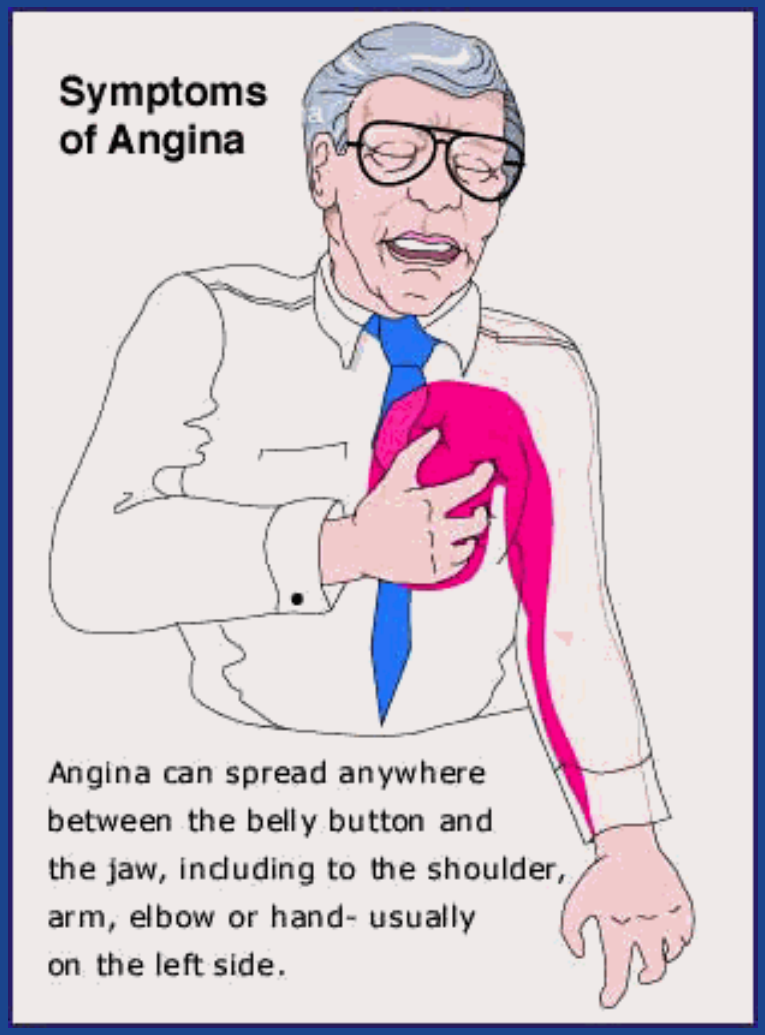
***Physical Examination*:**

anxious, stressed, sweaty , moving around trying to find rest position

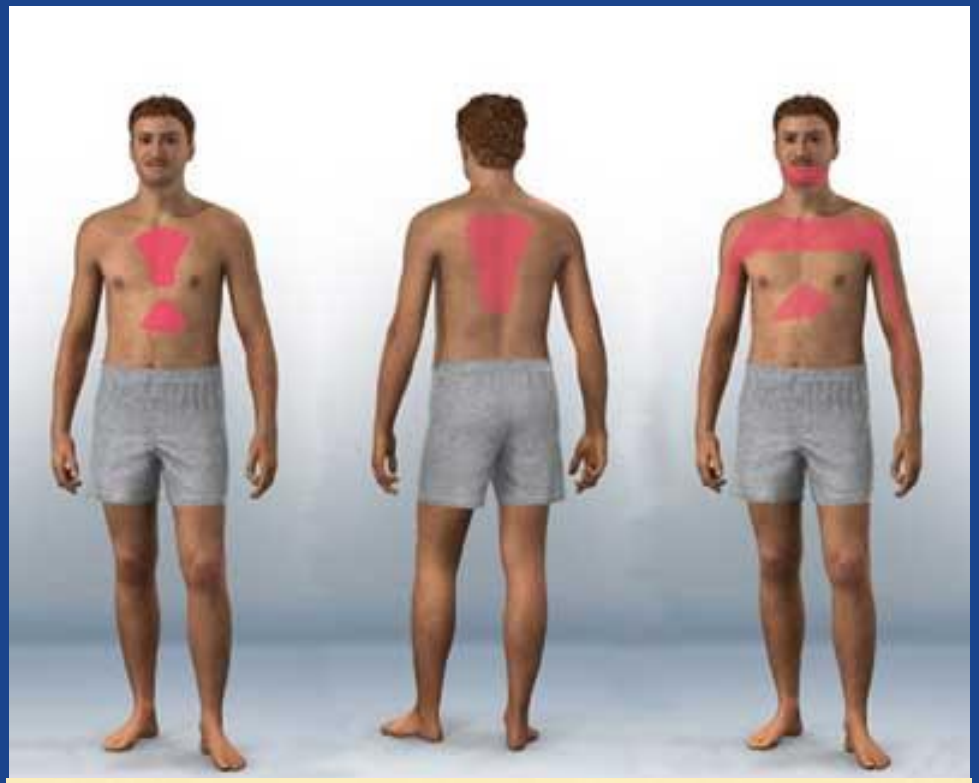
vital sign: BP, Pulse, Temp

auscultation: S4,S3, Murmure, Rub → after 24-48 hrs

↳ anything make the ventricle stiff: Ischemia



same site of angina



tooth / jaw pain
epigastric pain

Diagnosis of Myocardial Infarction

1-History

2-ECG (Electrocardiogram): STMI and NSTMI

- Hyperacute T wave
- ST-segment elevation
- Q- wave
- T- inversion
- ST-segment depresion

normal ECG will not exclude MI repeat ECG every 20-30 mins

3-Cardiac Marker: Troponin,CPK, myoglobulin,..

use Troponin T,I: 4-6 Hr (HsT 2-4 hr) 3 types: T, I, C ← skeletal muscle

*last 10-14 days

CPK:4-6 Hr, peak 17-24hr, normal 72 hr

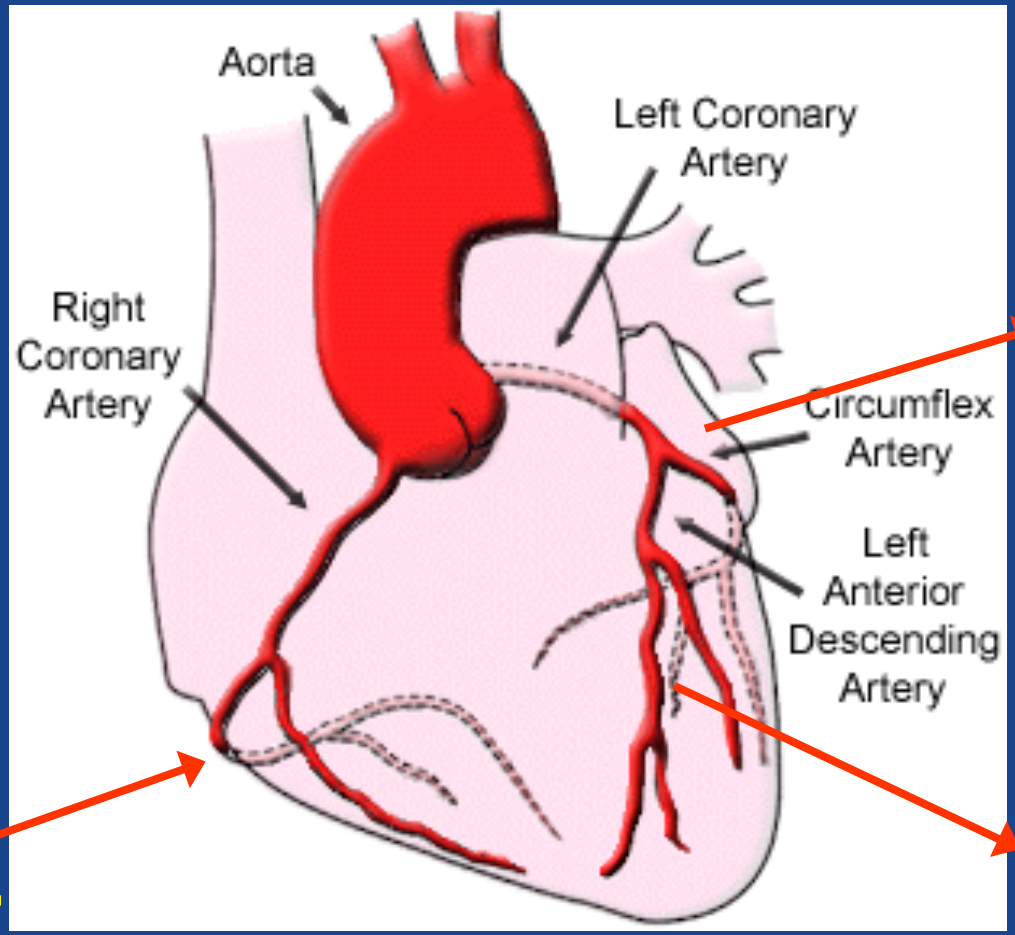
MB(MM,BB)

MB2/MB1 >1.5

① 2 positive > 3 days

② T +ve, CPK -ve < 3 days

Regions of the Myocardium



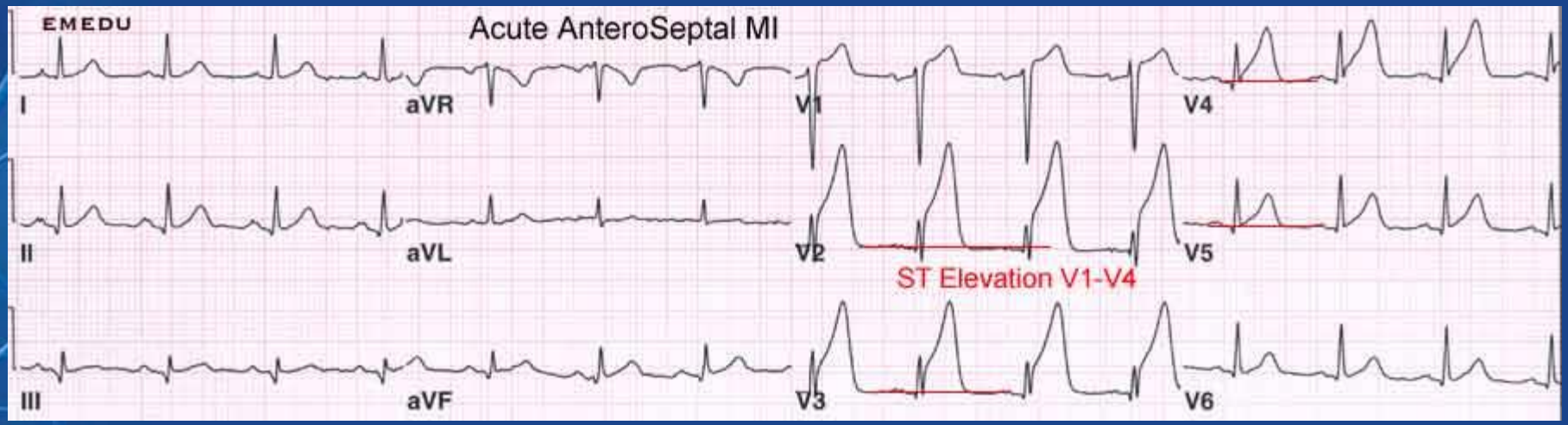
Lateral
I, AVL, V5-V6

Anterior / Septal
V1-V4

Inferior
II, III, aVF

56 YEAR MALE, C/O: CHEST PAIN OF 2 HRS. WHAT IS THE DIAGNOSIS?

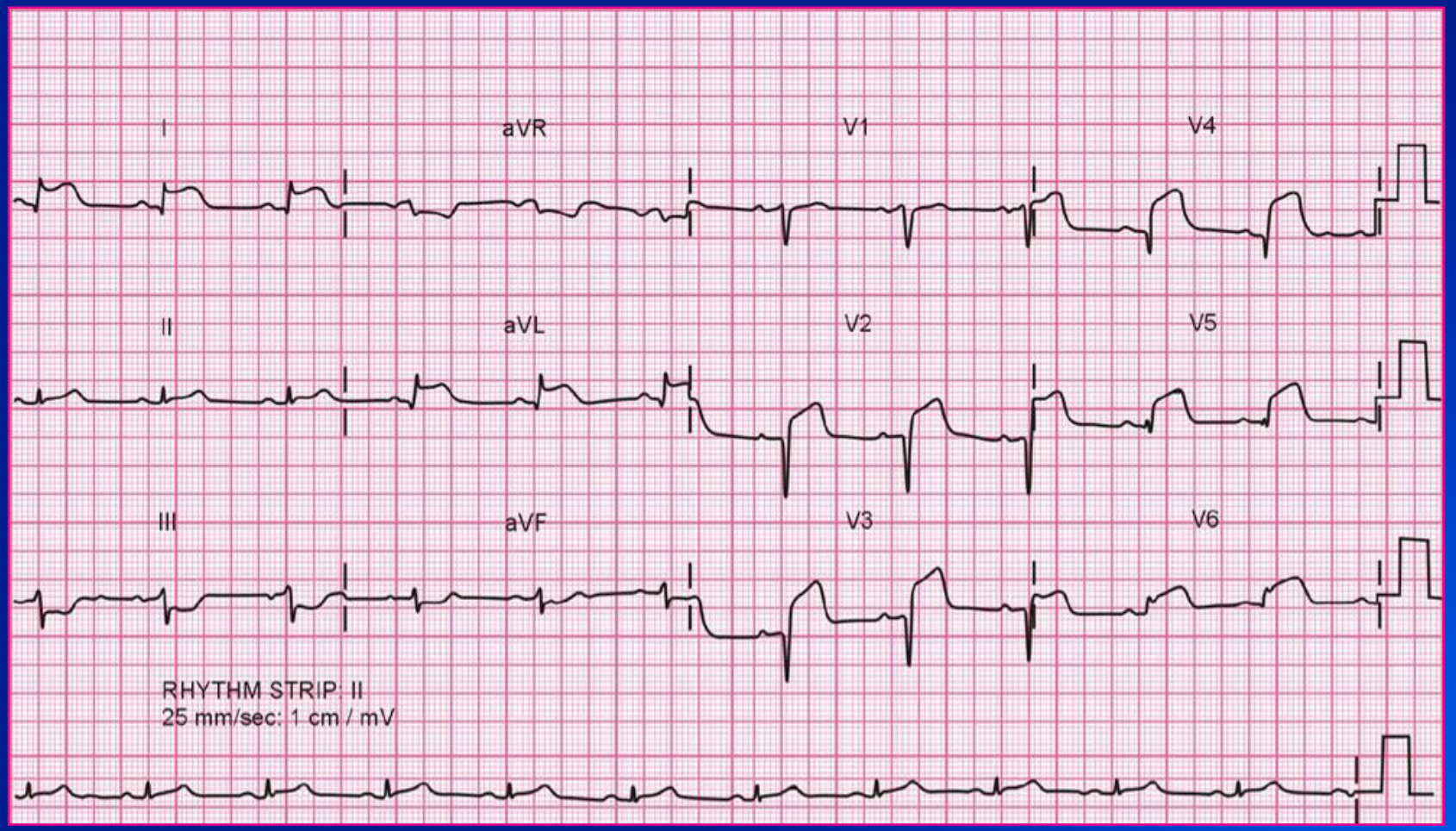
anterio septal MI



LAD / left main stem occluded

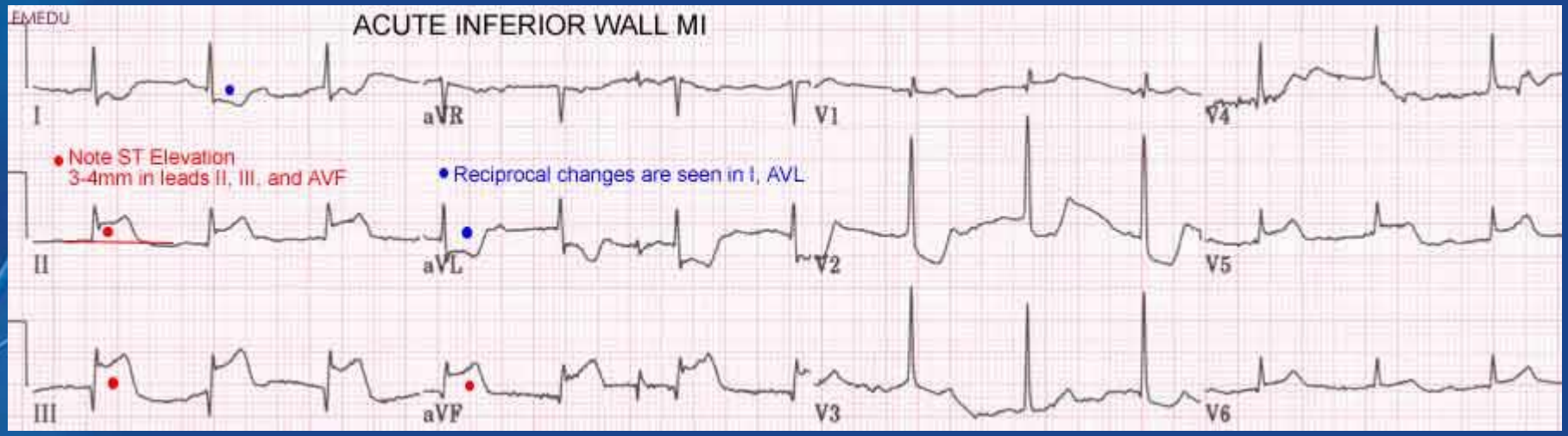
acute

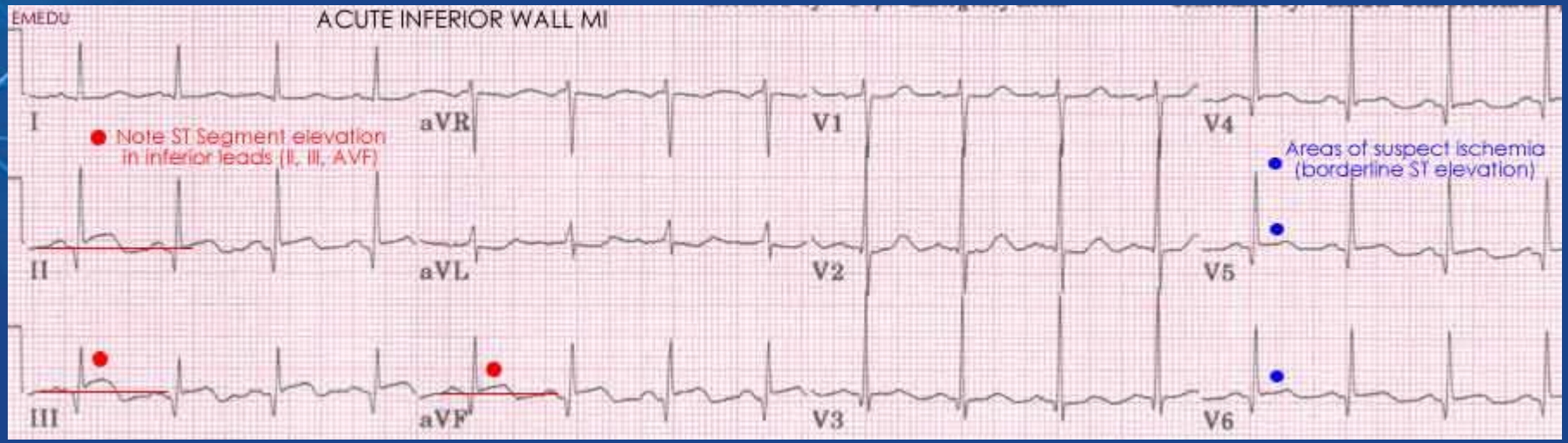
WHAT IS THE DIAGNOSIS?



56 YEAR MALE, C/O: CHEST PAIN OF 2 HRS. WHAT IS THE DIAGNOSIS?

right coronary artery occluded





LVH / hyperkalemia / acute pericarditis

ECG Criteria for Significant ST-segment elevation

↳ to be significant should be in 2 adjacent leads

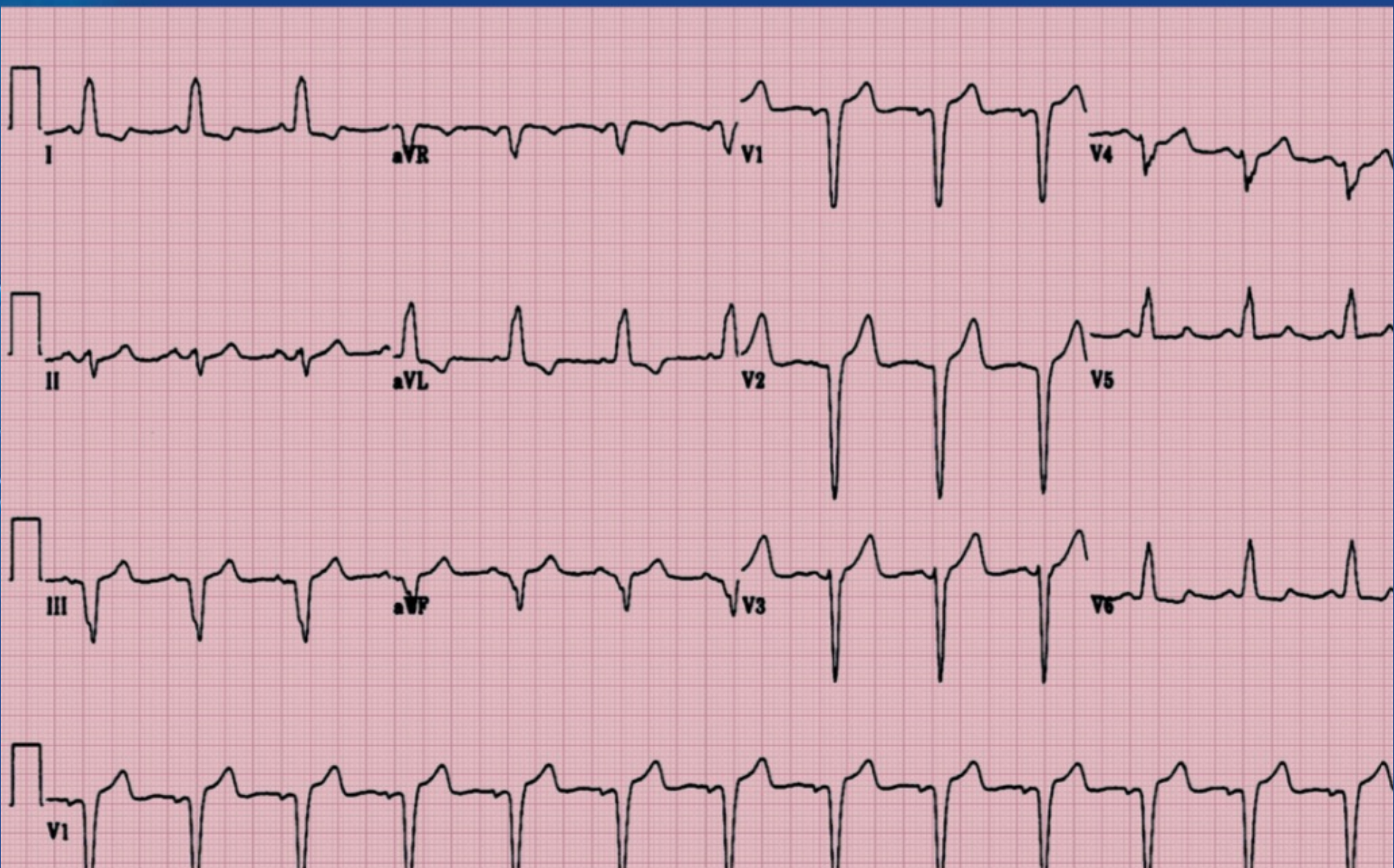
ST segment elevation

V2-V3 Leads:

Men ≥ 40 years	≥ 2 mm
≤ 40 years	≥ 2.5 mm
Women	≥ 1.5 mm

≥ leads1mm IN at least two other adjacent chest or limb leads

LBBB



ECG Criteria for Diagnosis 0f STEMI in LBBB Sgarbossa Criteria

Criterion	Location	Points
Concordant ST-segment elevation≥ 1 mm	Any lead with positive QRS deflection	5
Concordant ST-segment Depression≥ 1 mm	V1, V2, or V3	3
Disconcordant ST-segment elevation≥ 5 mm	Any lead with negative QRS deflection	2

≥ 3 had specificity of 98%
Score of 0 did not excludes STEMI

Cardiac Marker: Troponin,CPK, myoglobulin

Troponin T,I:

CPK:

Myoglobulin not used anymore

Troponin:

- Very specific and more sensitive than CK
- Rises 4-6 hours after injury (HsT 2-4 hr)
- Remains elevated for 10-14 days
- Can provide prognostic information
- Unable to detect re-infarction < 2 weeks

Non MI Causes of Troponin Elevation

+ve Troponin in:

- Tachycardia
- PE
- Cardiac failure w/ myonecrosis
- Cardiac surgery
- Myocarditis
- Renal failure: troponin I
- Shock
- Sepsis

CK/MB

used if no troponin

Rises 4-6 hours after injury and peaks at 17- 24 hours

- Remains elevated 36-48 hours
- Back to normal 72 hr
- CPK iso-enzymes: MM, BB, MB
- MB2/MB1 >1.5

- Positive if CK-MB > 5% of total CK or 2 times normal
- Elevation can be predictive of mortality
- False positives with exercise, trauma, muscle disease, DM, PE

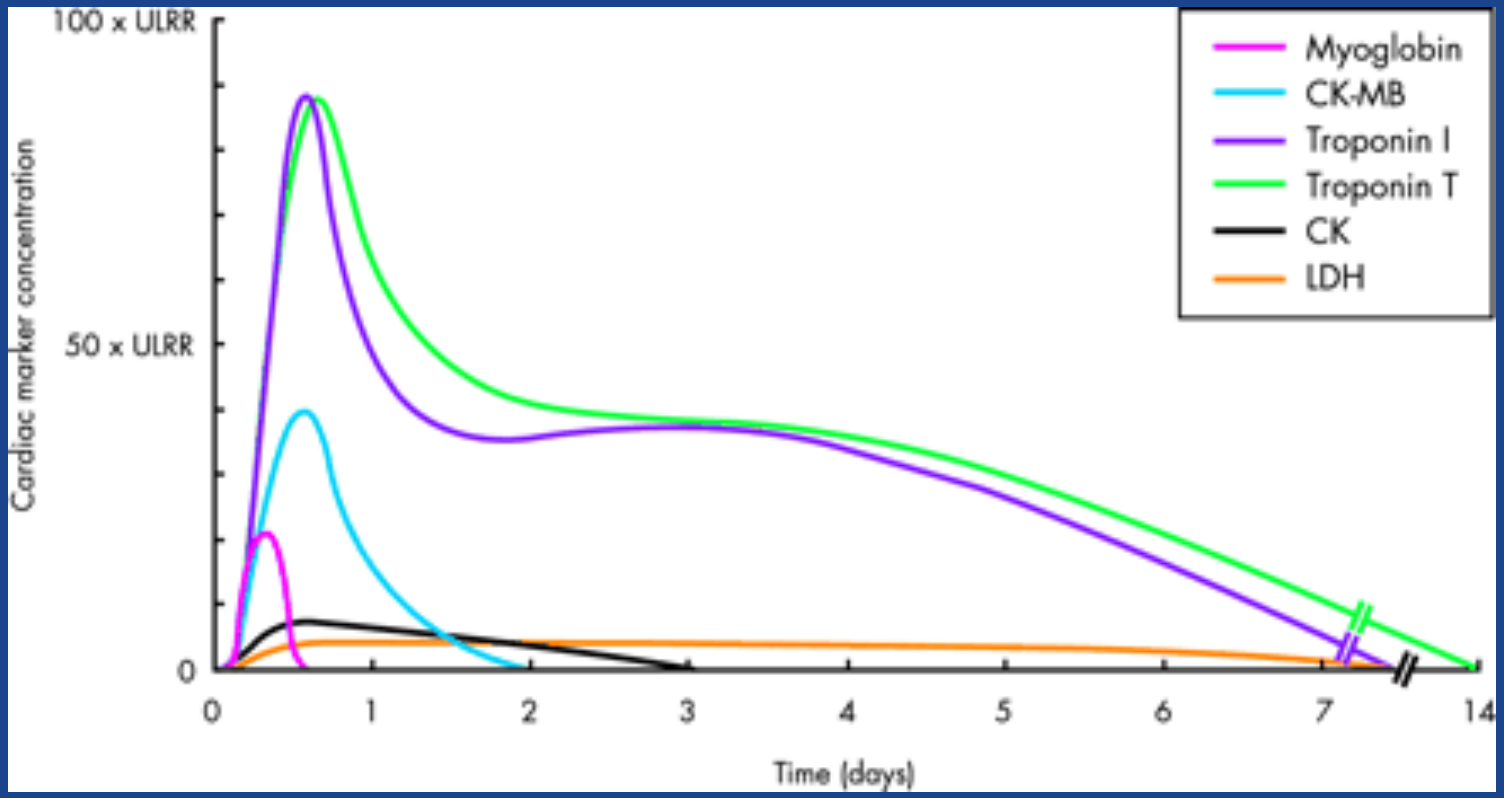
Myoglobin not used

- Rises 2-4 hours after injury and peaks at 6-12 hours
- Remains elevated 24-36 hours
- Not cardiac specific
- Rise of 25-40% over 2 hours strongly predictive of MI

Biochemical Markers III

Protein	Molecular mass (kD)	First detection	Duration of detection	Sensitivity	Specificity
Myoglobin	16	1.5–2 hours	8–12 hours	+++	+
CK-MB	83	2–3 hours	1–2 days	+++	+++
Troponin I	33	3–4 hours	7–10 days	++++	++++
Troponin T	38	3–4 hours	7–14 days	++++	++++
CK	96	4–6 hours	2–3 days	++	++

Biochemical Markers II



DIAGNOSIS OF MI-CONT

1-CBC: Increase WBC, ESR

2- Increase plasma glucose

3-Serum lipid (< 24 hr)

4-Echocardiogram:nonspecific changes(hypo, akinesia, dyskinesia

↓ bcs many causes can cause →

Management of ACS

Primary goals: Open the blocked artery

- Decrease amount of myocardial necrosis
- Preserve LV function
- Prevent major adverse cardiac events
- Treat life threatening complications

Management of ACS

Immediate general treatment (**MONA**)

- **Morphine**
  - Analgesia
  - Reduce pain/anxiety—decrease sympathetic tone, systemic vascular resistance and oxygen demand
  - Careful with hypotension, hypovolemia, respiratory depression

- **Oxygen 2-4 liters/minute**
  - Up to 70% of ACS patient demonstrate hypoxemia
  - May limit ischemic myocardial damage by increasing oxygen delivery/reduce ST elevation

Management

Immediate general treatment(MONA)

- **Nitroglycerin sublingual or spray** → in assumption he might have spasm / if the cause is MI it will not be beneficial
  - Dilates coronary vessels—increase blood flow
  - Reduces systemic vascular resistance and preload
  - Contraindications:
  - hypotension, RV infarction ,recent ED meds

  - **Aspirin 160-325mg** chewed and swallowed
  - Irreversible inhibition of platelet activation
  - Stabilize plaque and arrest thrombus
  - Reduce mortality in patients with STEMI
  - Careful with active PUD, hypersensitivity, bleeding disorders

H → heparin

TREATMENT OF MYOCARDIAL INFARCTION

IN EMERGENCY ROOM:

1-Rapid assessment

2-Establish IV access

3-12 ECG

4- Aspirin 150-300 mg Orally, Clopidogrel or ticagrelor

5-Oxygen

6-Analgesia: IV morphine, diamorphine 3-5 mg

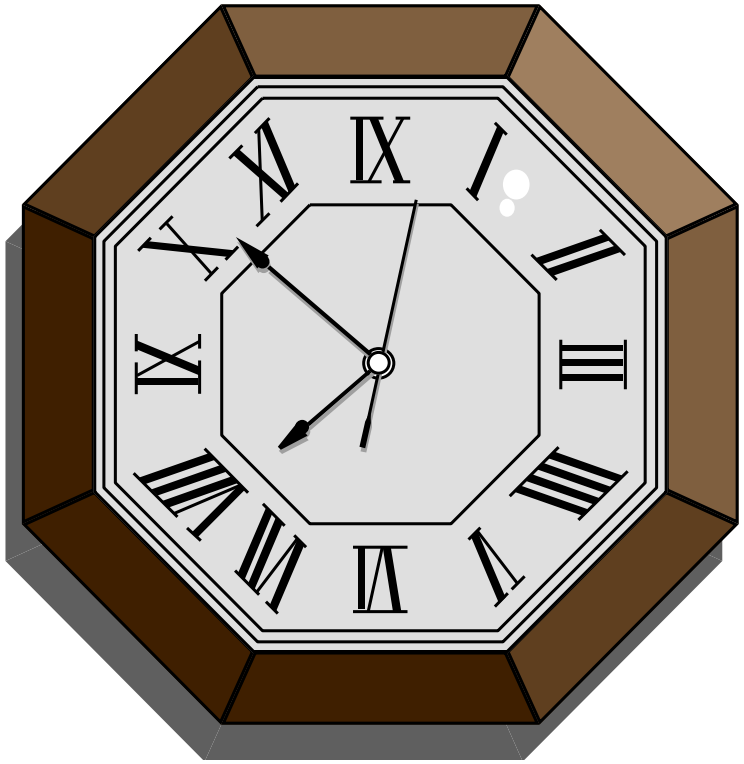
7-Antiemetic: metoclopromide 10 mg IV

8-Sublingual nitrate: if NO hypotension, RV MI

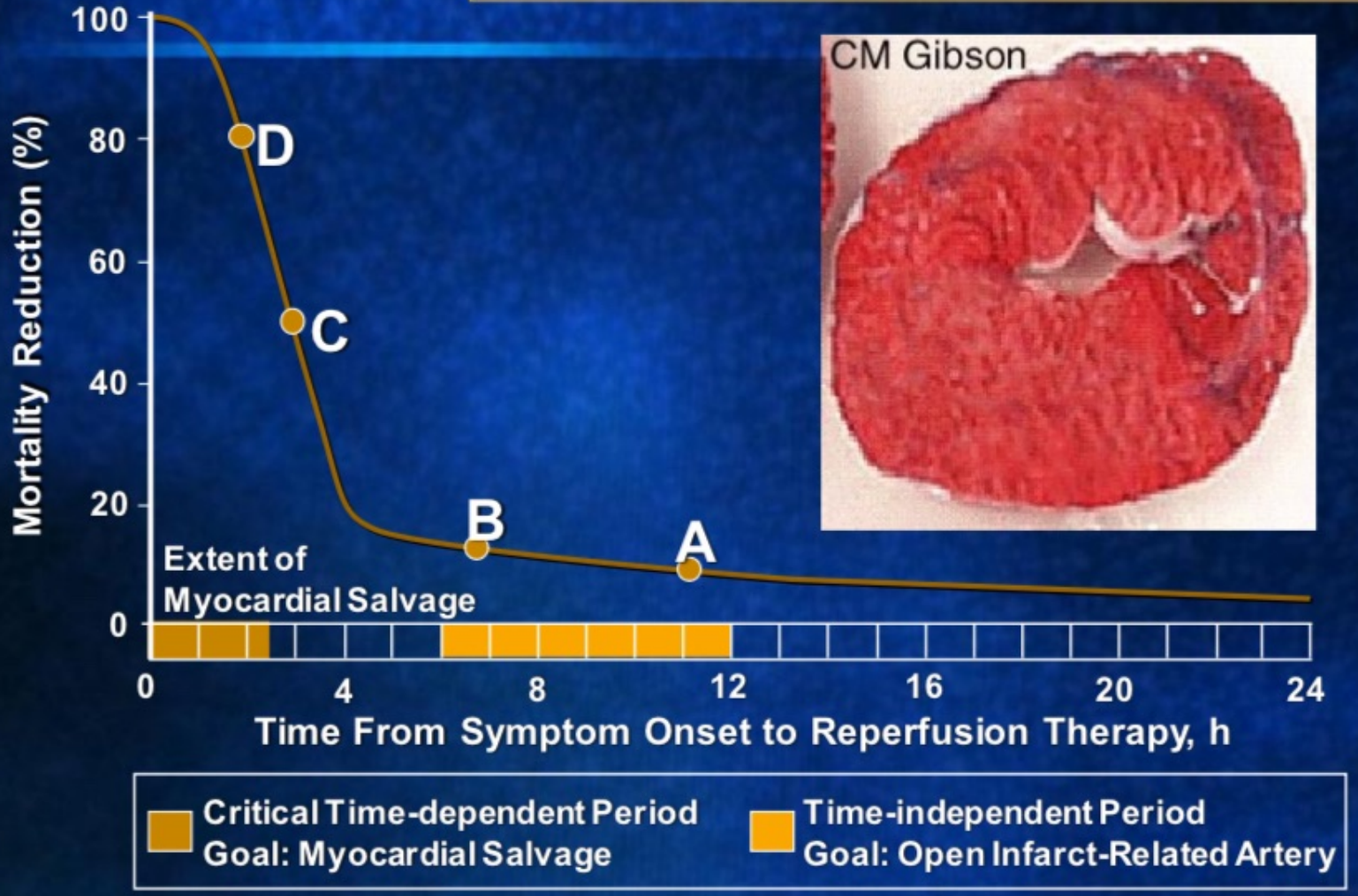
9-ECG monitor

10-Reperfusion: PCI or Thrombolytics, (CABG)

Time is Muscle!!!

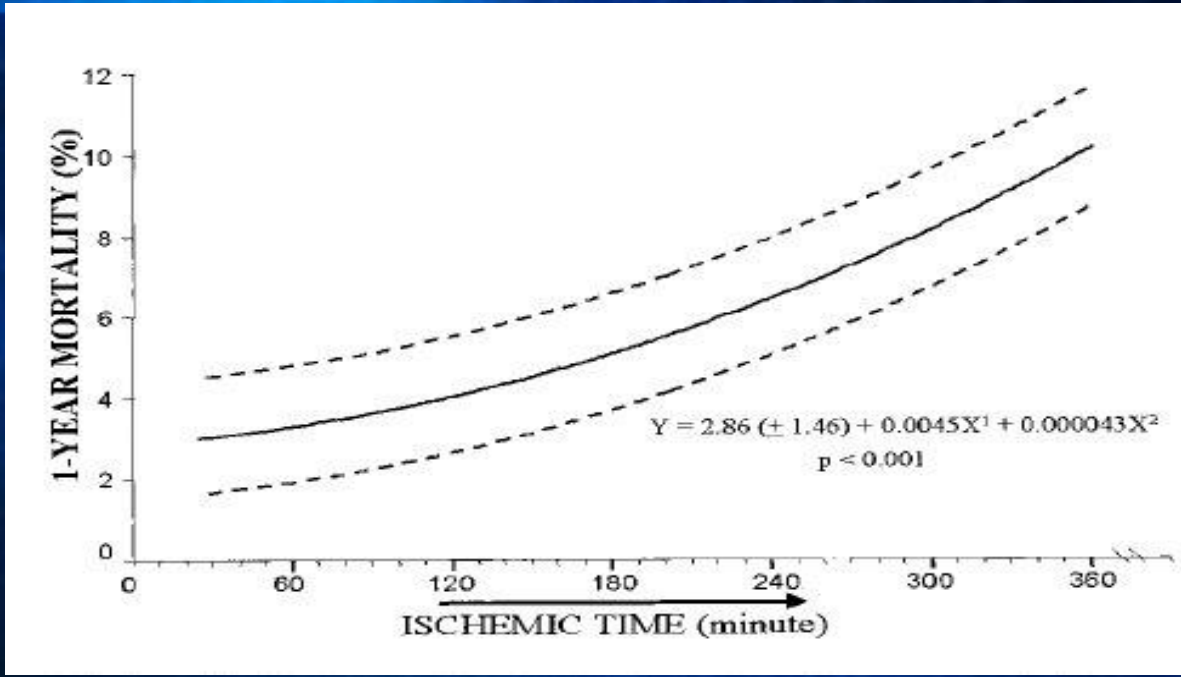


1. Time is Myocardium
2. Infarct Size is Outcome



Gersh BJ, et al. JAMA. 2005;293:979.

Reduction in Long Term Mortality



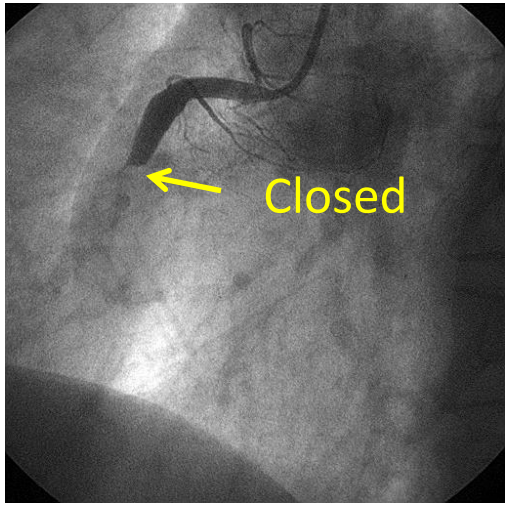
Every 30-minute delay from onset of symptoms to reperfusion. 1 year mortality is increased by 8%

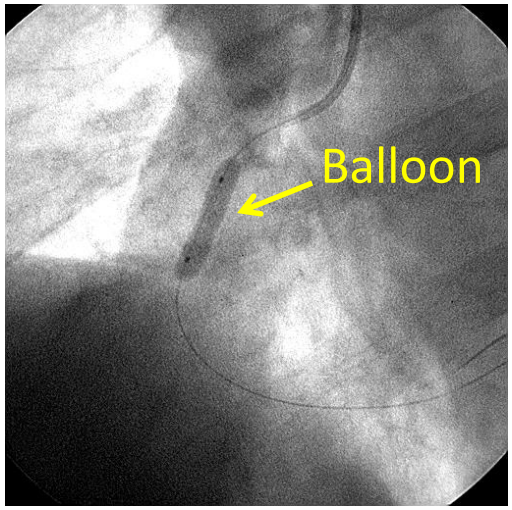
De Luca et al, Circulation 2004

Primary angioplasty

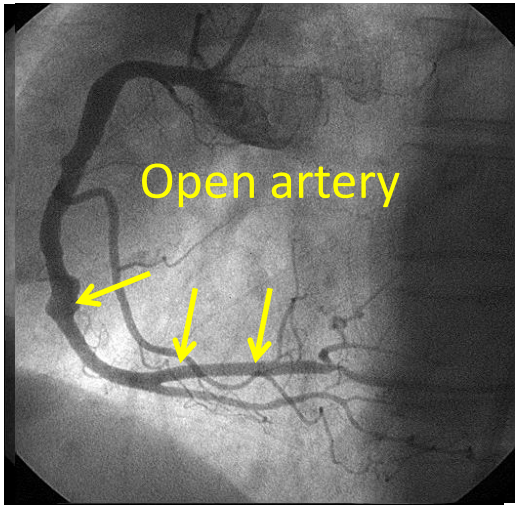
- Coronary arteries: balloon angioplasty

Arrival





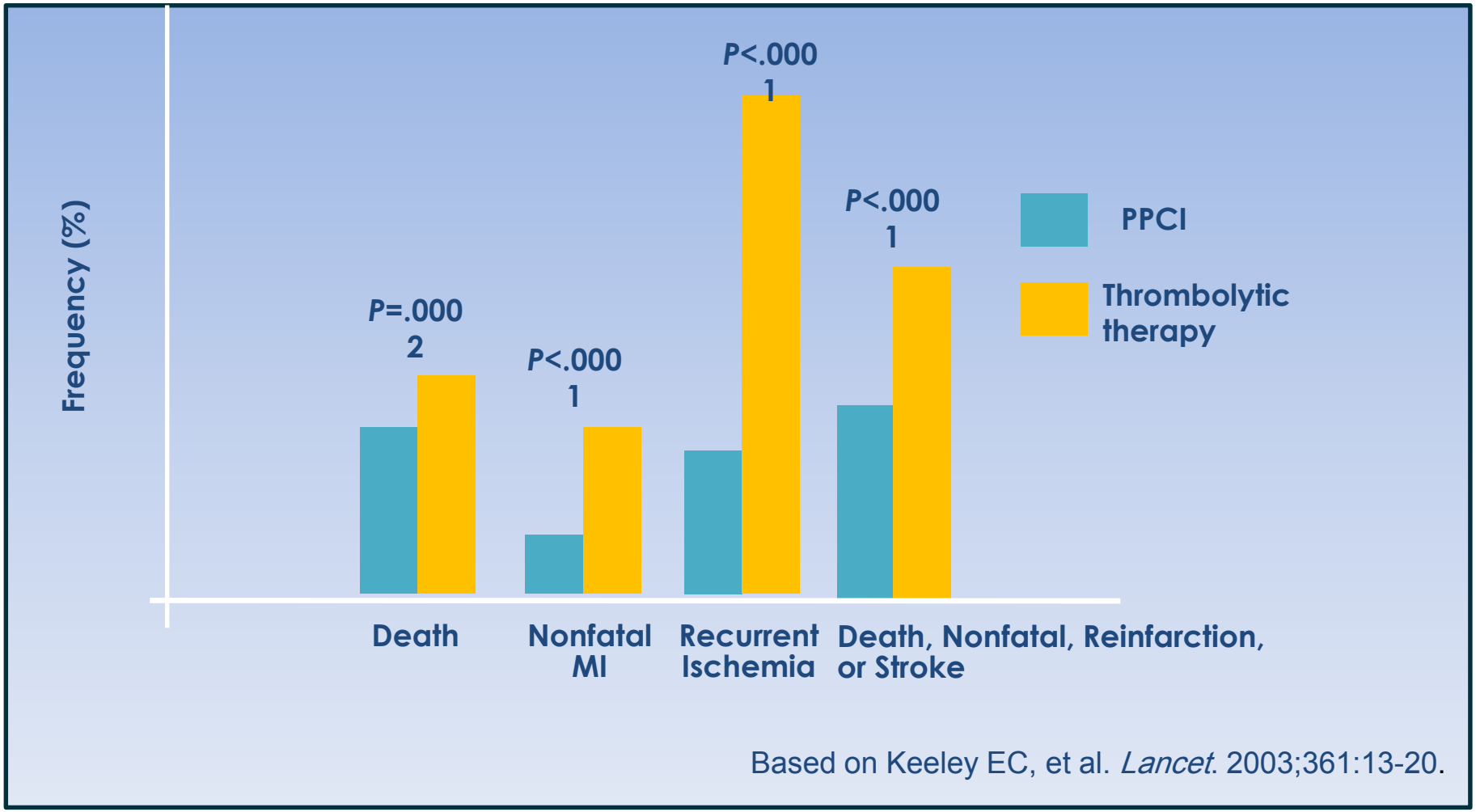
After balloon



- The European Society of Cardiology (ESC) guidelines recommend primary PCI as the preferred treatment whenever it is available within 90-120 minutes of the first medical contact

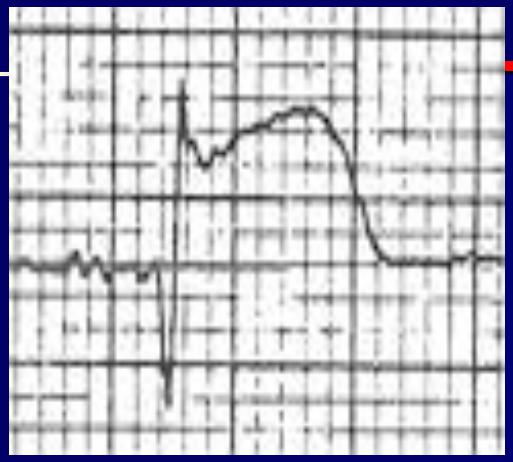
Angioplasty reduces mortality and morbidity

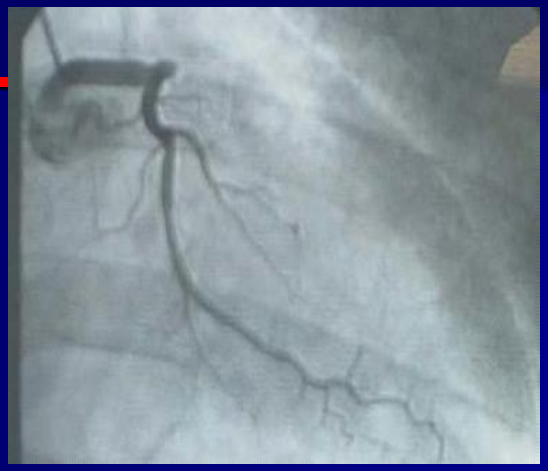
Primary PCI vs. Thrombolysis in ST-Elevation Myocardial Infarction: Meta-analysis (23 Randomised controlled trials, N=7,739)

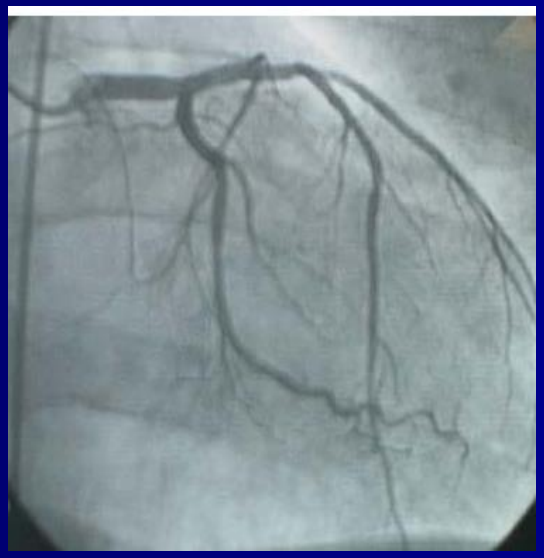


Based on Keeley EC, et al. *Lancet*. 2003;361:13-20.

Reperfusion in STEMI

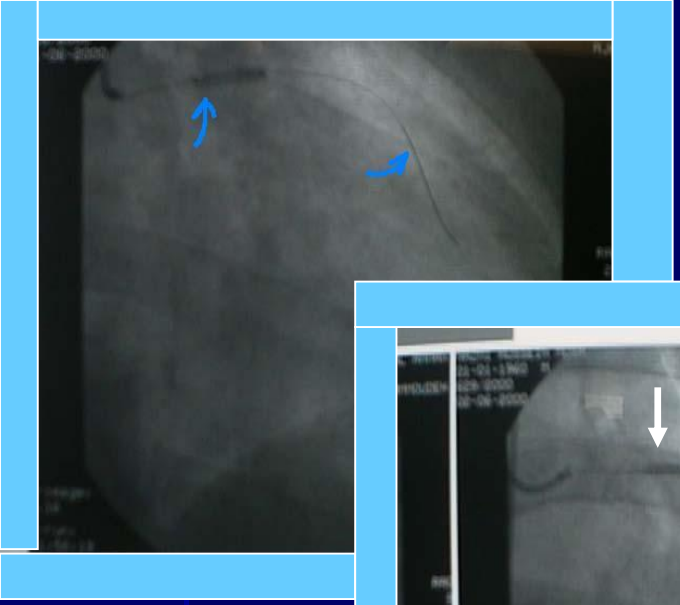


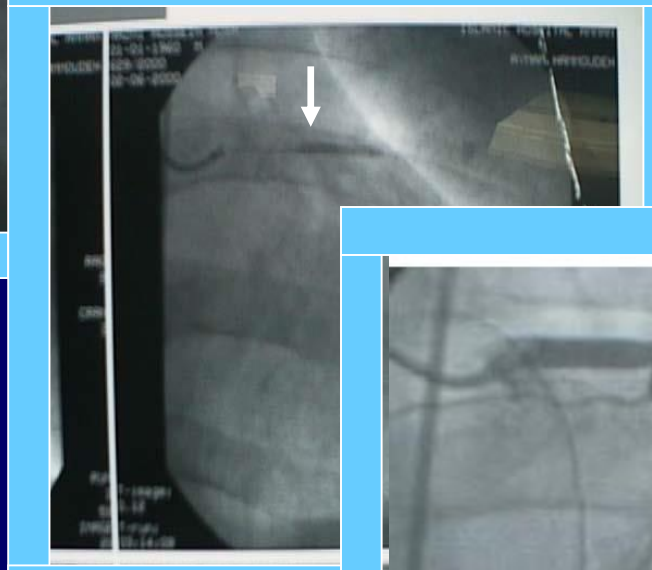


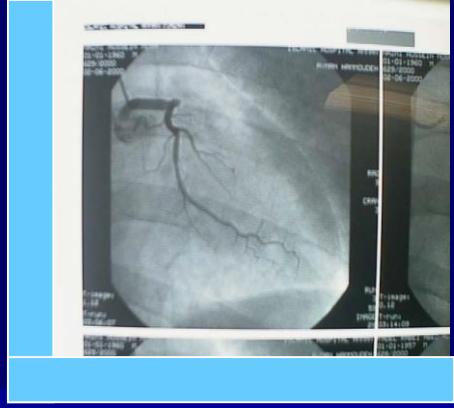


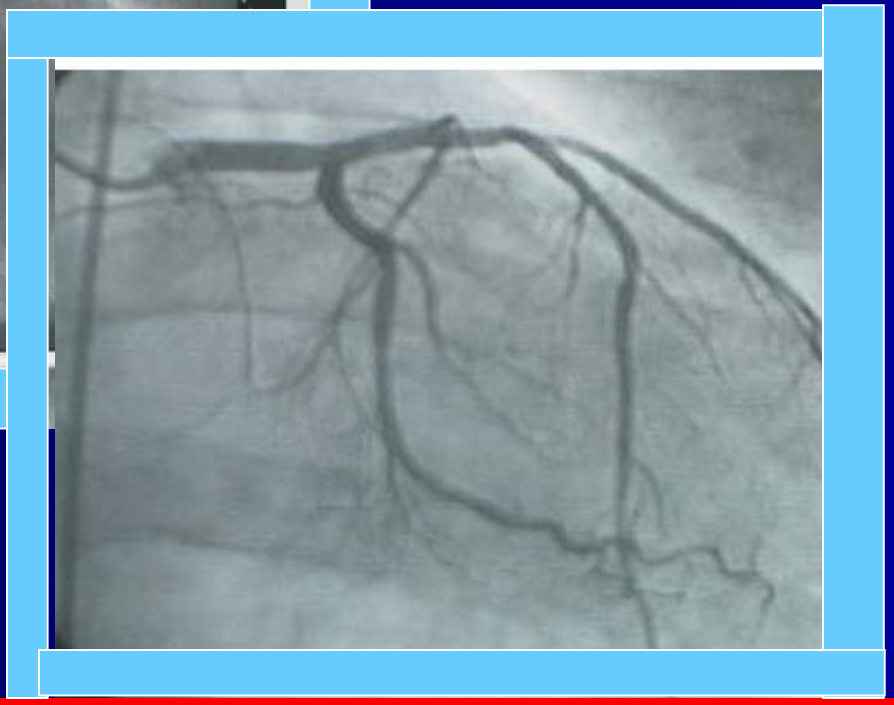
We repeat the ECG

to know if PCI is working









Reperfusion: PCI

ST-Segment elevation MI: Reperfusion
THROMBOLYSIS/ PCI
Time= Muscle

Early reperfusion: **time dependent**

- -improve survival
- -LV function preservation

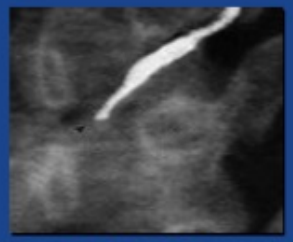
TIMI 3 flow

- -PCI: 95%, TPA:54%, STREPTO:32%

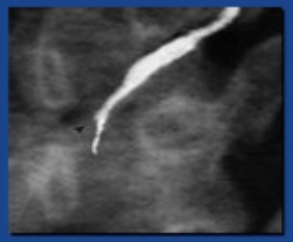
PCI: Reduce re-occlusion and recurrent thrombosis

TIMI Flow Grade Definitions[1]

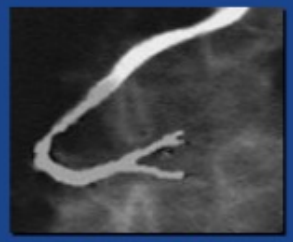
- TIMI flow grade describes epicardial blood flow:
  - Grade 0: complete occlusion
  - Grade 1: penetration of obstruction with no distal perfusion
  - Grade 2: perfusion of artery with delayed flow
  - Grade 3: full perfusion with normal flow



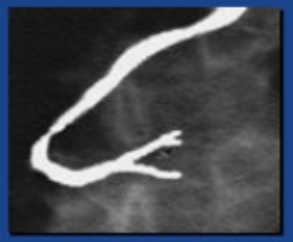
TFG 0
Occlusion



TFG 1
Penetration



TFG 2
Slow flow



TFG 3
Normal flow

1. Reproduced with permission from Gibson CM et al. *Circulation* 2004: 109: 3096–3105.

ST Elevation or New LBBB

Step 2: Select Reperfusion Strategy

Fibrinolysis generally preferred if:

- ≤3 hours from onset
- PCI not available/delayed
  - Door to balloon >90min
  - Door to balloon minus door to needle > 1hr
- Door to needle goal <30min
- No contraindications

Invasive strategy preferred if:

- >3hours from onset
- PCI available
- Door to balloon < 90min
- Door to balloon minus door to needle < 1hr
- Fibrinolysis contraindications
- High risk
- STEMI dx in doubt
- Age >75

*INDICATIONS TO THROMBOLYTIC THERAPY are ECG Changes

1-ST-elevation:

- 2 adjacent leads
- > 1mm in limb leads (L1, L11, L111, AVF,AVL)
- > 2mm in precordial leads (V1-V4)

OR

2- New Left Bundle Branch Block (LBBB)

Common Thrombolytic Regimens for STEMI[1]

	Initial treatment	Co-therapy	Contraindications
Streptokinase (SK)	1.5 million U in 100 mL 5% dextrose or 0.9% saline over 30–60 min	None or iv heparin x 24–48 hours	Prior SK or anistreplase
Alteplase (tPA)	15 mg iv bolus, then 0.75 mg/kg over 30 min, then 0.5 mg/kg iv over 60 min Total dose not over 100 mg	iv heparin x 24–48 hours	
Reteplase (rPA)	10 U + 10 U iv bolus given 30 min apart	iv heparin x 24–48 hours	
Tenecteplase**** (TNK-tPA) best	Single iv bolus 30 mg if <60 kg 35 mg if 60 kg to <70 kg 40 mg if 70 kg to <80 kg 45 mg if 80 kg to <90 kg 50 mg if ≥90 kg	iv heparin x 24–48 hours	

Note: acetylsalicylic acid (ASA) should be given to all patients without contraindications; iv=intravenous

1. Van de Werf F et al. *Eur Heart J* 2003; 24: 28–66.

Current Limitations of Pharmacologic Reperfusion

- Lack of initial reperfusion in 20-30% of patients[1]
  - Associated with a 2 X increase in mortality
- Reocclusion in 5–8% of patients[1]
  - Associated with 3 X increase in mortality
- Despite current therapy, 10% of STEMI patients die within one month after hospital discharge[2]
- Within 6 years 18% of men and 35% of women will suffer another heart attack[3]

1. Sabatine M et al. *New Eng J Med* 2005; 352: 1179–1189.
2. Goldberg RJ et al. *Am J Cardiol* 2004; 93: 288–293.
3. Antman EM et al. 2004 ACC/AHA STEMI Guidelines. Available at: www.accp.org/clinical/guidelines/stemi/index.pdf. Accessed February 2005.

Contraindications to Thrombolytic Therapy

Absolute contraindication

1-Active internal bleeding

2-Suspected aortic dissection

3-Trauma or surgery < 2 weeks

4-History of hemorrhagic CVA

5-BP> 200/120 mmHg

6-Prolonged CPR

7-Recent head trauma or known intracranial neoplasm

8-Diabetic proliferative retinopathy

9-Pregnency

10-Prvious allergy to the thrombolytic agent

Relative contraindication

1-Trauma or surgery > 2 weeks

2-Active peptic ulcer disease

3-History CVA

4-Bleedind diathesis or current use of anticoagulant

5-Uncontrolled hypertension

6-Previous exposure to streptokinase

7-Pericardial friction rub

8-Significant liver dysfunction

should be referred to PCI

COMPLICATION OF THROMBOLYTIC THERAPY

1-Hemorrhage <5% most important

2- Systemic embolization

3-CNS bleeding

4-Allergic Reaction 1-3%, anaphylaxis 0.1%

Other Routine Therapies in Acute STEMI[1]

- ASA 150–325 mg (non-enteric coated), Clopidogrel
- Beta-blockers
- Angiotensin-converting enzyme (ACE) inhibitors
- Oxygen
- statines
- Nitrates
- Heparin if indicated
- CCU: 24-48 hr
- Word: 3-5 days
- Home medication: aspirin, B-blocker, statines, ACE I, ? nitrate

1. Van de Werf F et al. *Eur Heart J* 2003; 24: 28–66.

Complications of Myocardial Infarction

electrical → benign / malignant
mechanical

1- Arrhythmias: Any type

Ventricular: PVC, VT, Accelerated Idioventricular rhythm, VF

Atrial: AF 15% in ist 24 hr, sinus brady or tachycardia, PAC

Heart Blocks: 1st, 2nd, 3rd block, BBB

2- Heart failure (pump failure). Killip Classification I-IV

if he lost 25% of his myocardium 24% heart shock

3-Myocardial rupture: 1st 10 days

free wall, septum, papillary muscle, ventricular pseudoaneurysm

4- Recurrent or extension of MI, Thromboembolism

5-Early pericarditis: ASA(NSAID and Steroids are contraindicated)

6-Dresslers syndrome 2-12 weeks: ASA, Ibuprofen

7- Left ventricular aneurysm

8-Sudden death

Differential Diagnosis of MI

sudden severe chest pain

1- Aortic Dissection

2-Massive Pulmonary Embolism retrosternal

small PE → pleuretic chest pain

3- Acute pericarditis

PROGNOSIS of MI

pre-hospital mortality:20%
hospital mortality:10-12%
1st year mortality 10%

Poor prognostic featues:

1-Heart Failure
2-EF< 40%
3- Large infarction size
4-Anerior MI
5-New BBB
6- Mobitz type 2 , and 3rd AV Block
7-Reinfarction or extension of MI
8-Frequent PVC
9-VF or VT
10-Atrial fibrillation
11-Post infarction angina
12-DM
13-Age> 70
14-female

TIMI Risk Score in STEMI

Risk factor	Score
1- Age>65	2
2- Age>75	3
3- Hist of angina	1
4- Hist of hypertension	1
5- Hist of DM	1
6- Syst BP< 100	3
7- Heart rate> 100	2
8- Killip II-IV	2
9- Ant M or LBBB	1
10- Delay treat > 4 hr	1

TIMI Risk Score in STEMI

Total Score	Risk of death at 30 days(%)
0	0.8
1	1.6
2	2.2
3	4.4
4	7.3
5	12.4
6	16.1
7	23.4
8	26.8
9-16	35.9

Post-MI Management

1- Risk factors modification (Stop smoking, BP< 140/90, HbA1c<7, Exercise, ..)

2-Aspirin, Clopidogrel or ticagrelor

Life long

3- B-blockers

4-Statines Life long

5-ACE-inhibitors

6- Aldosterone antagonist(in presence of heart failure)

if EF < 40%

UNSTABLE ANGINA

Unstable Angina

Definition:

1-New onset angina < 8 weeks

2- Angina at rest or minimal exersion

3-Crescendo angina: patient with chronic angina with increasing frequency, duration, or intensity of chest pain

4-Post MI or Revascularization angina: 2 weeks

Types:

Pathophysiology: plaque erosion or rupture, vasoconstriction, distal embolisation

Diagnosis: Clinical, ECG , *Negative cardiac markers*

Unstable Angina Classification

1- Acute: rest pain within the last 48 hr

2- Subacute: no pain within the last 48 hr

1- primary: no secondary causes

2-Secondary: sever anemia, thyrotoxicosis, hypertension, arrhythmias

1-High Risk

2-Low risk

HIGH RISK UNSTABLE ANGINA

1-Rest pain > 20 minutes but < 30 mins

2-Accelerating tempo of ischemic symptoms in preceding 48 hr

3-Clinical finding of: pulmonary edema, new S3, new MR, Hypotension, Brady or Tachycardia

3-ECG changes: transient ST segment changes, BBB, VT

4- DM

Risk Stratification

TIMI Risk Score

Predicts risk of death, new/recurrent MI, need for urgent revascularization within 14 days

1- Age > 65

2- 3 or more cardiac risk factors

3- Prior angiographic coronary obstruction (stenosis ≥ 50%)

4- ST segment deviation

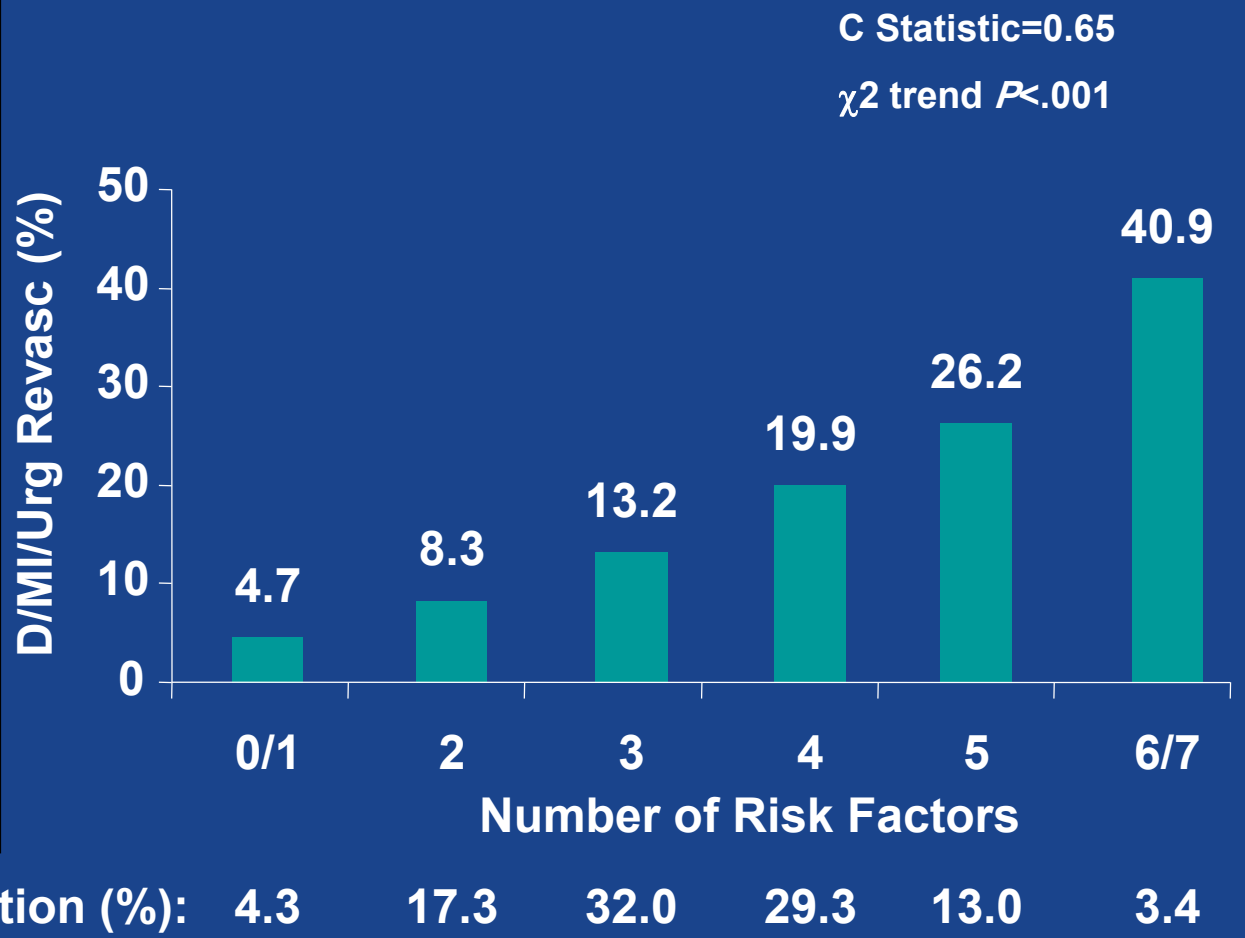
5-More than 2 angina events within the previous 24 hours

6-Use of aspirin within previous 7 days

7-Elevated cardiac markers

TIMI Risk Score For UA/NSTEMI

- Age ≥65 years
- ≥3CAD Risk Factors
- Prior Stenosis >50 %
- ST deviation
- ≥2 Anginal events ≤24 hours
- ASA in last 7 days
- Elevated Cardiac Markers (CK-MB or troponin)



Population (%):	4.3	17.3	32.0	29.3	13.0	3.4

Antman EM, et al. *JAMA.* 2000;284:835-442.

Treatment of HIGH RISK *UNSTABLE ANGINA* AND *NSTMI*

same treatment

1-CCU admission : Treat as MI except for thrombolytics

NO THROMBOLYTICS

2-Aspirin***, Clopidogrel ≥ anti platlet

3-Anticoagulant: heparin (LMWH is superior to unfractionated heparin)***

4- Nitrate (S/L, oral, IV)

5-B-blocker

6-clopidogrel, GP 11b,111a--------Cath PCI(angio)

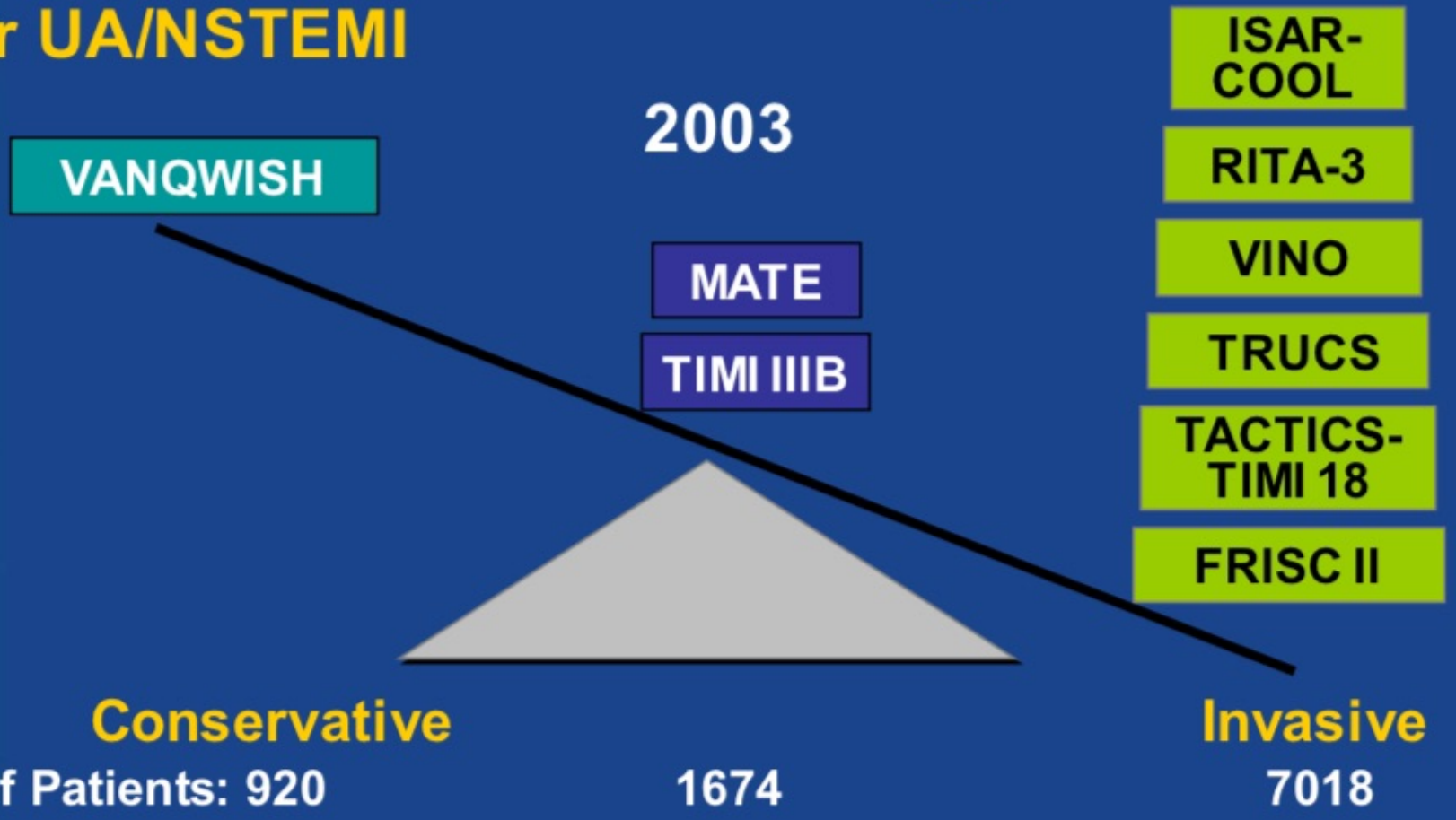
7-Statines

8- Invasive (better) or conservative management

cath medical

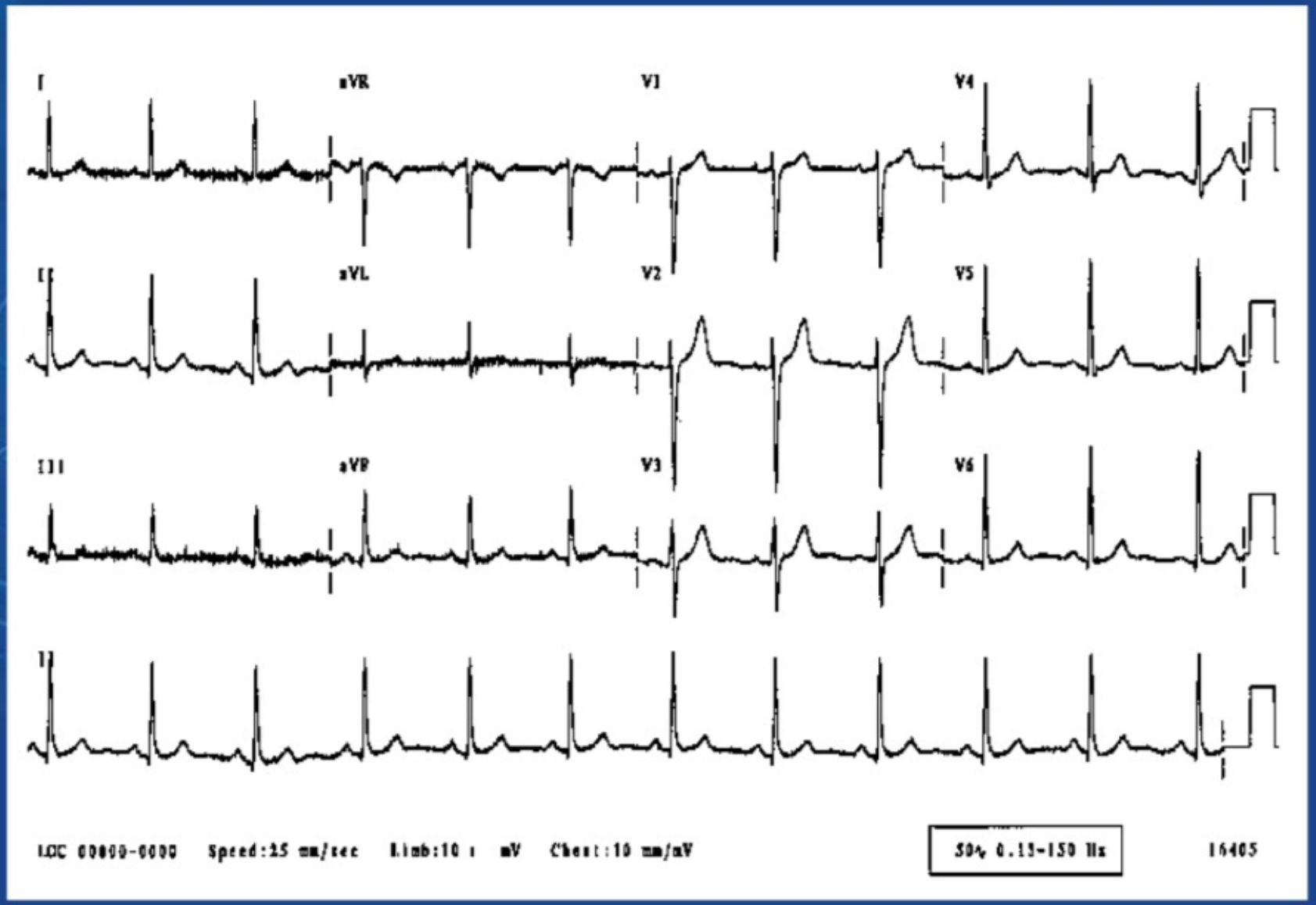
*** *improve prognosis*

Invasive vs Conservative Strategy for UA/NSTEMI

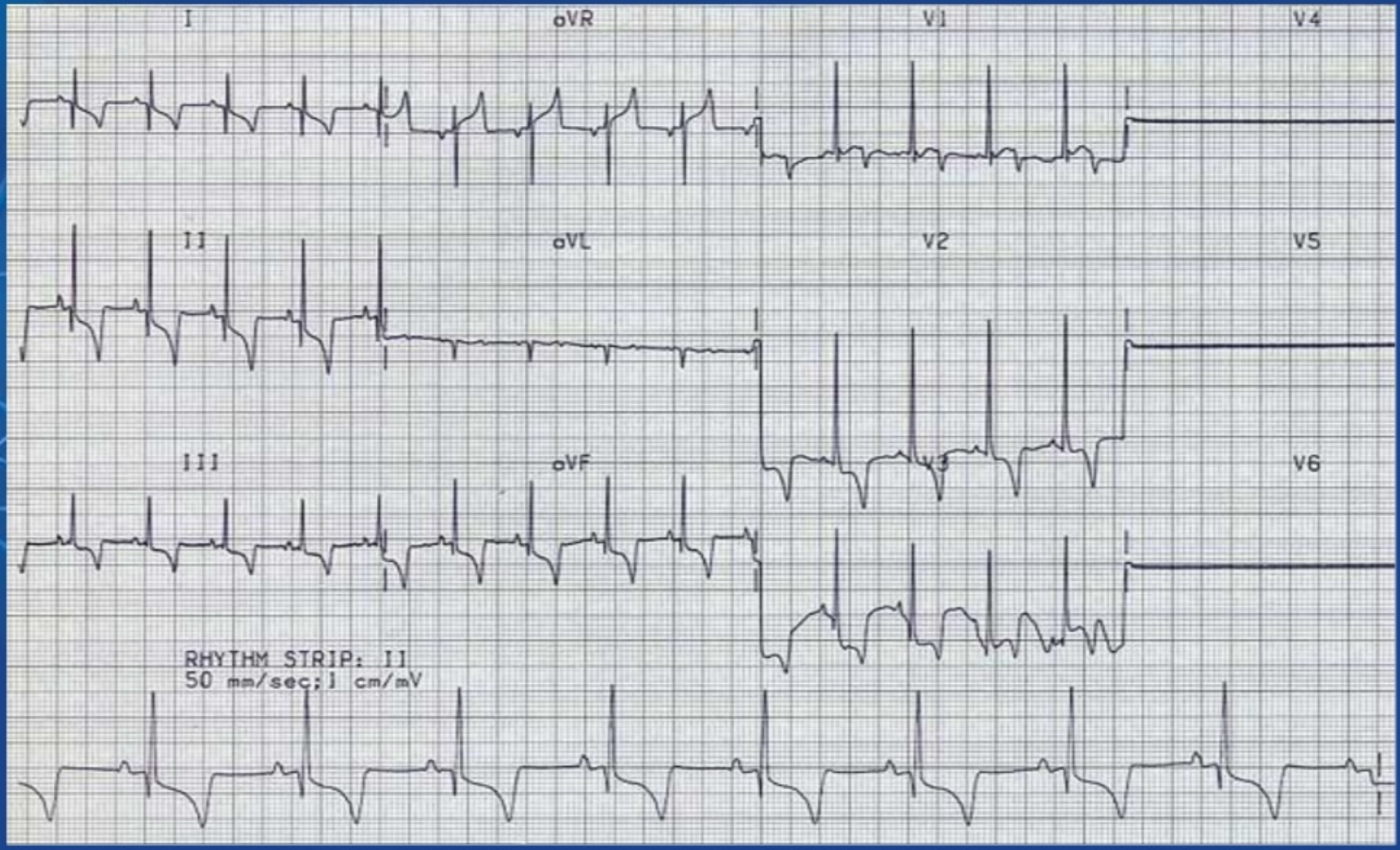


UA, unstable angina, NSTEMI, non–ST-segment myocardial infarction; ISAR, Intracoronary Stenting and Antithrombic Regimen Trial; RITA, Randomized Intervention Treatment of Angina; VANQWISH, Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital study; MATE, Medicine vs Angioplasty for Thrombolytic Exclusions trial; TACTICS-TIMI18, Treat Angina with Aggrestat® and Determine Cost of Therpay with Invasive or Conservative Strategy; FRISC, Fragmin during InStability in Coronary artery disease.

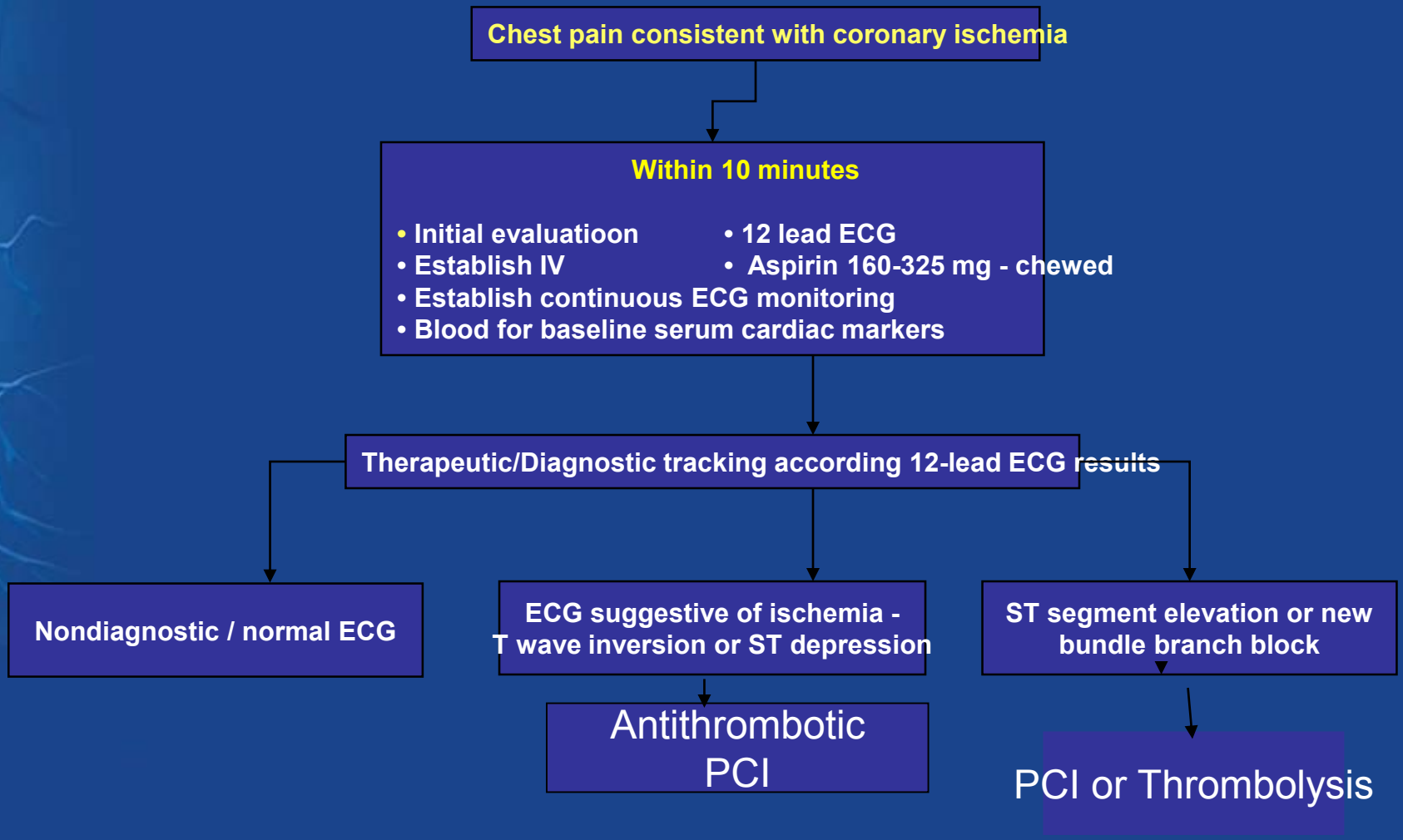
Normal or non-diagnostic EKG



ST Depression or Dynamic T wave Inversions



Algorithm for Initial Assessment and Evaluation of the Patient with Acute Chest Pain



Thank you