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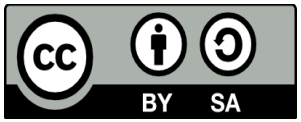

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Cardiovascular Sequence

Acute Coronary Syndromes (ACS)

Kim A. Eagle, M.D.

University of Michigan Cardiovascular Center

Fall 2012

University of Michigan Medical School

Kim A. Eagle, MD

Director

University of Michigan

Cardiovascular Center

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Consultant: NIH NHLBI

Acute Coronary Syndromes

Key Words: ST elevation MI, non-STE, ACS, cardiac biomarkers, treatment of ACS, mechanical complications of MI

Objectives:

1. To learn how the admission ECG dictates early therapy for ACS.
2. To learn how to use cardiac biomarkers to diagnose ACS.
3. To become familiar with strategies for treatment in ACS.
4. To become familiar with mechanical complications of ACS.

Lecture Outline

- Pathogenesis of ACS
- Clinical features of ACS
- Treatment of ACS
- Complications
- Post ACS risk stratification

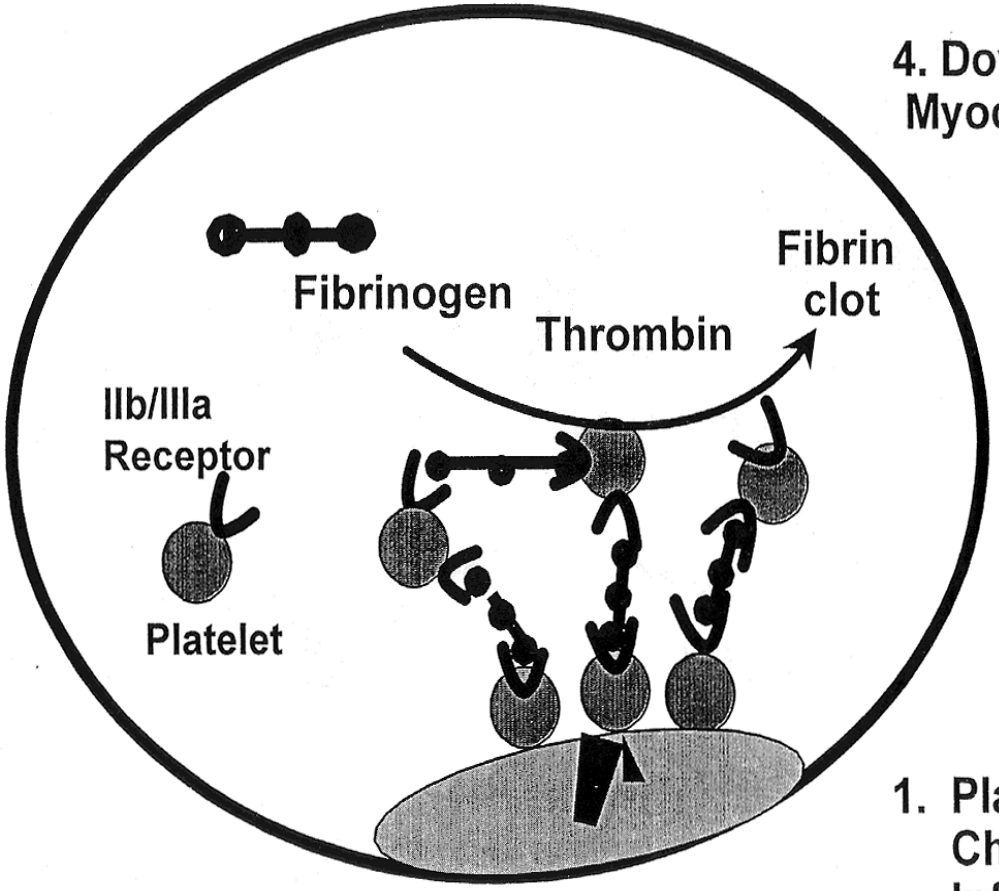
Pathogenesis of ACS

- Normal hemostasis
- Endogenous antithrombotic mechanisms
- Pathogenesis of coronary thrombosis
- Nonatherosclerotic causes of ACS

Pathogenesis: ACS

- > 90% - plaque disruption with platelet aggregation ⟶ intracoronary thrombus
- Concepts of clot formation
- Continuum of ACS from unstable angina to STE MI

Pathophysiology of Acute Coronary Syndromes



4. Downstream from thrombus
Myocardial ischemia/necrosis

3. Activation of Clotting Cascade - Thrombin

2. Platelet Adhesion
Activation
Aggregation

1. Plaque Rupture
Cholesterol content
Inflammation (CRP, Mphage)

Stable CAD

Acute Coronary Syndromes

Unstable angina

Non-ST Elevation MI
(Non-Q-wave MI)

ST-Elevation MI
(Q-wave MI)

The continuum of acute coronary syndromes ranges from unstable angina, through non-ST-elevation myocardial infarction (also referred to as “non-Q-wave” myocardial infarction [MI]), to ST-elevation MI (also referred to as “Q-wave” MI).

Normal Hemostasis

Vessel wall injury

- 1st defense ⟶ Platelets
  - "Primary hemostasis" ⟶ Platelet plug

- 2nd defense ⟶ Subendothelial
  - Tissue factor activates plasma
  - Coagulates proteins
    - "Secondary hemostasis" ⟶ Fibrin clot

Endogenous Antithrombotic Mechanisms

Inactivation of clotting factors

- Antithrombin III
- Protein C / Protein S / thrombomodulin
- Tissue factor pathway inhibitor

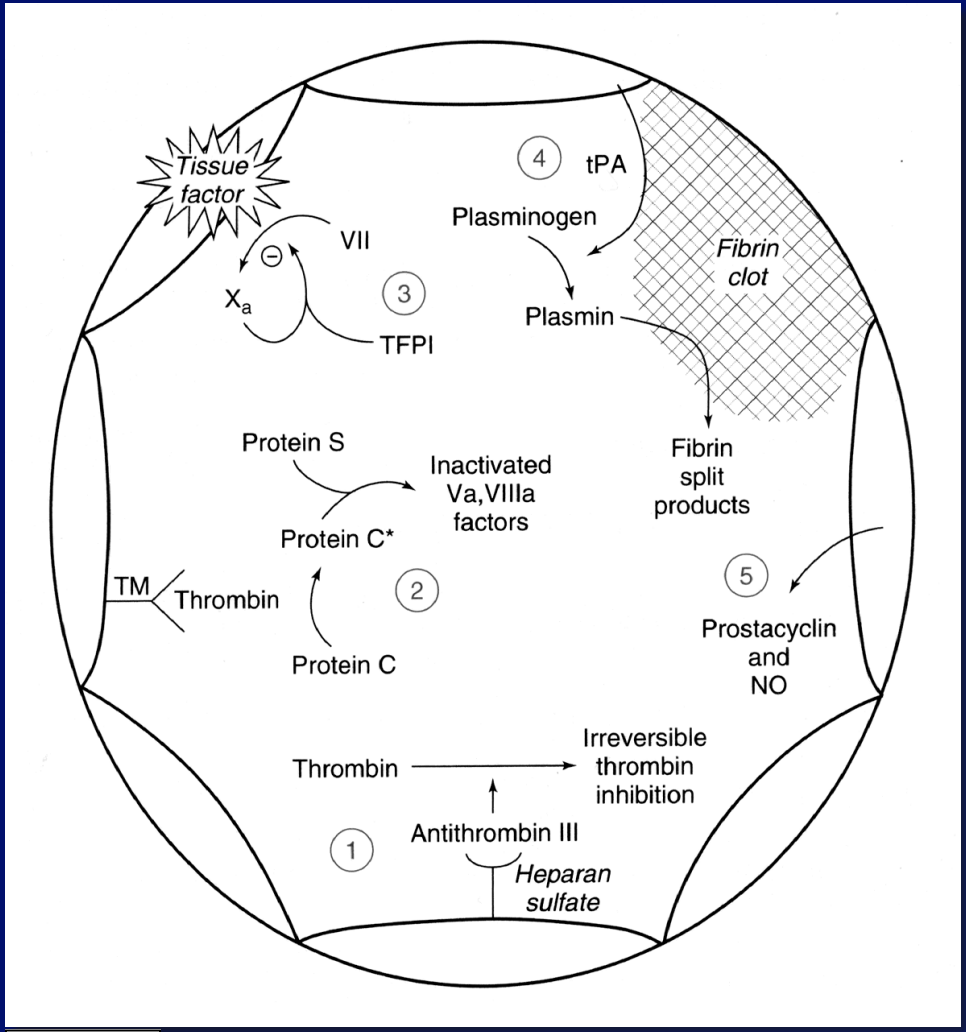
Lysis of fibrin clots

- Tissue plasminogen activator

Endogenous platelet inhibition & vasodilation

- Prostacyclin
- Nitrous oxide

Endogenous Protective Mechanisms



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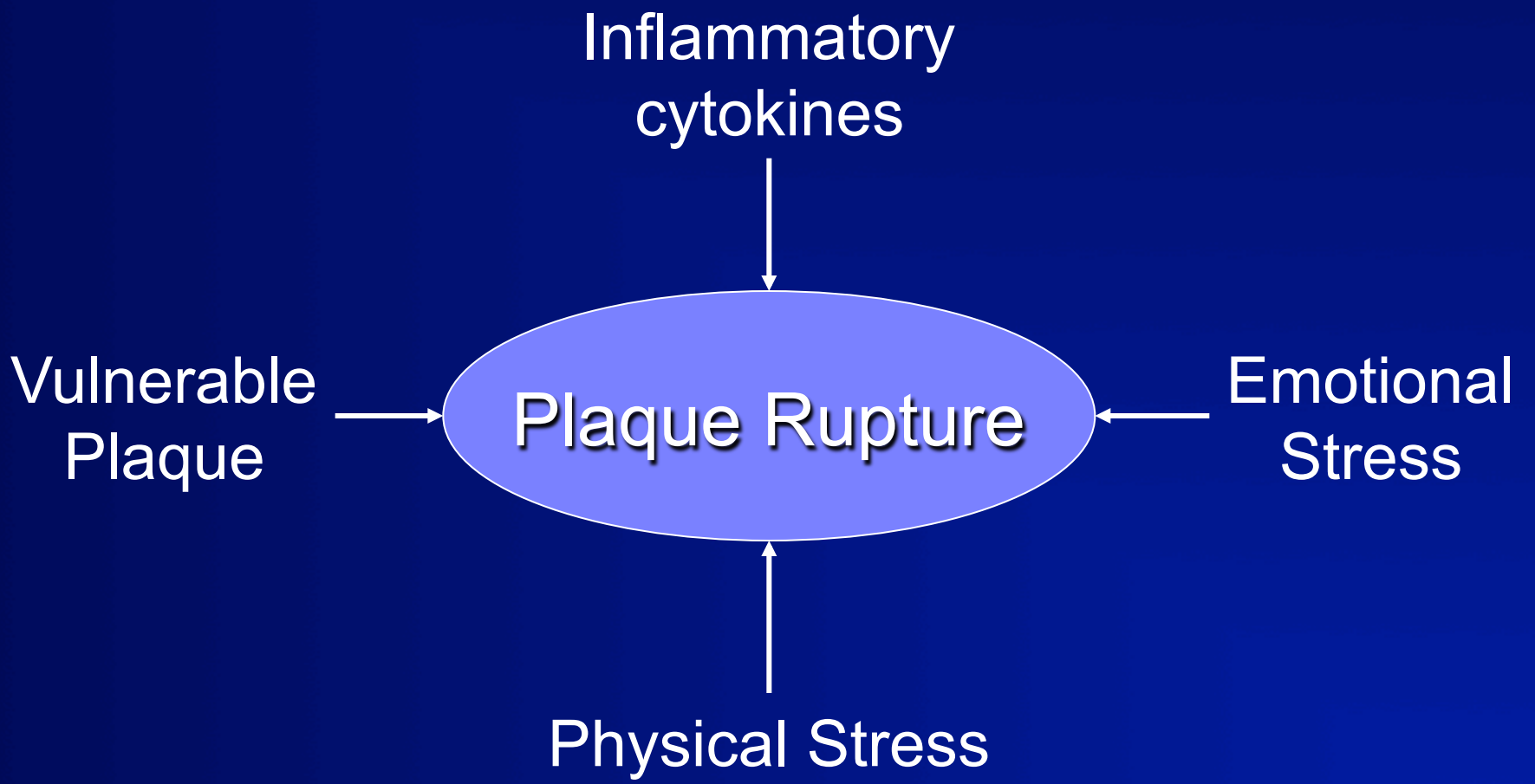
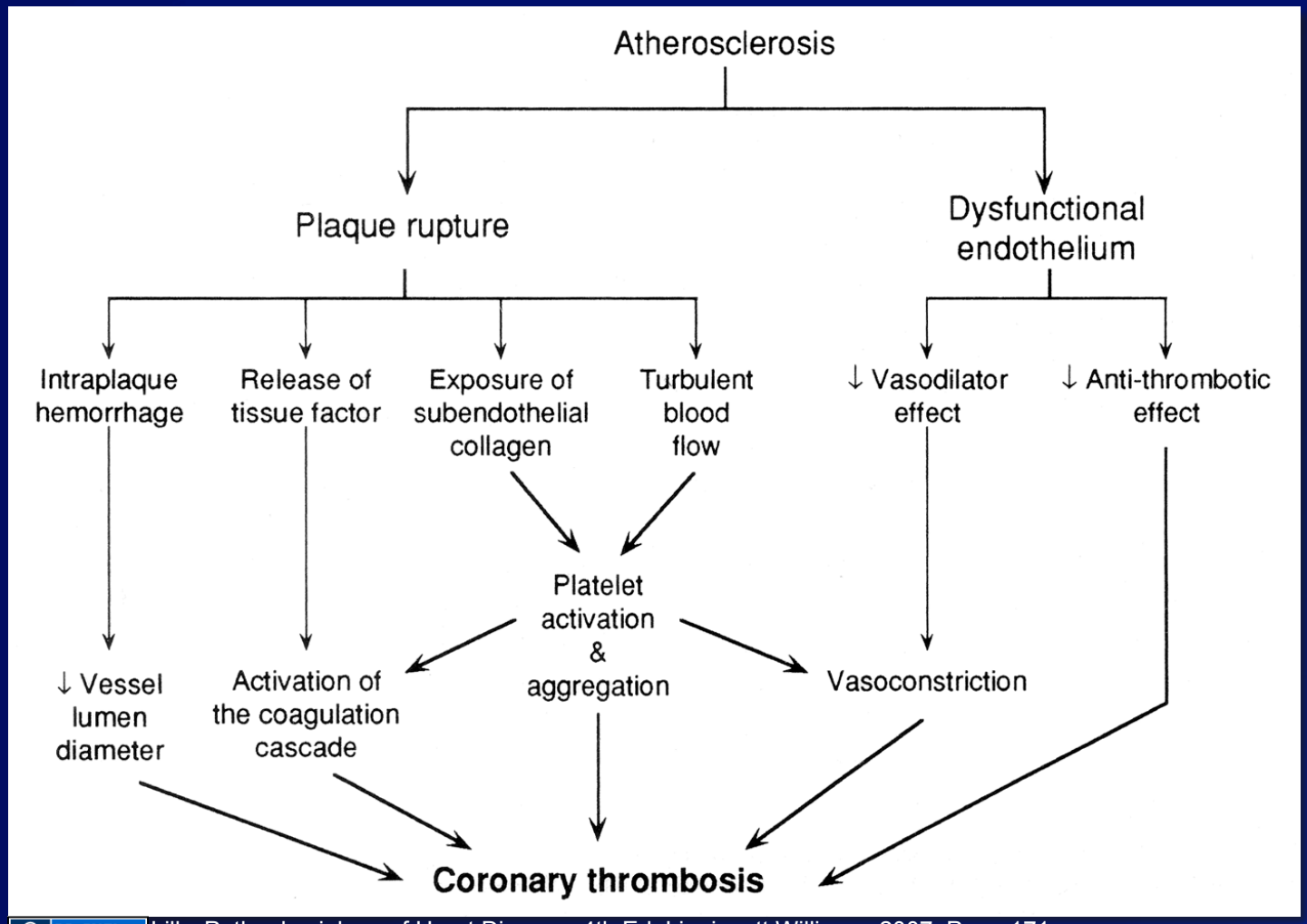
Triggers to Plaque Rupture



Mechanisms of Coronary Thrombosis



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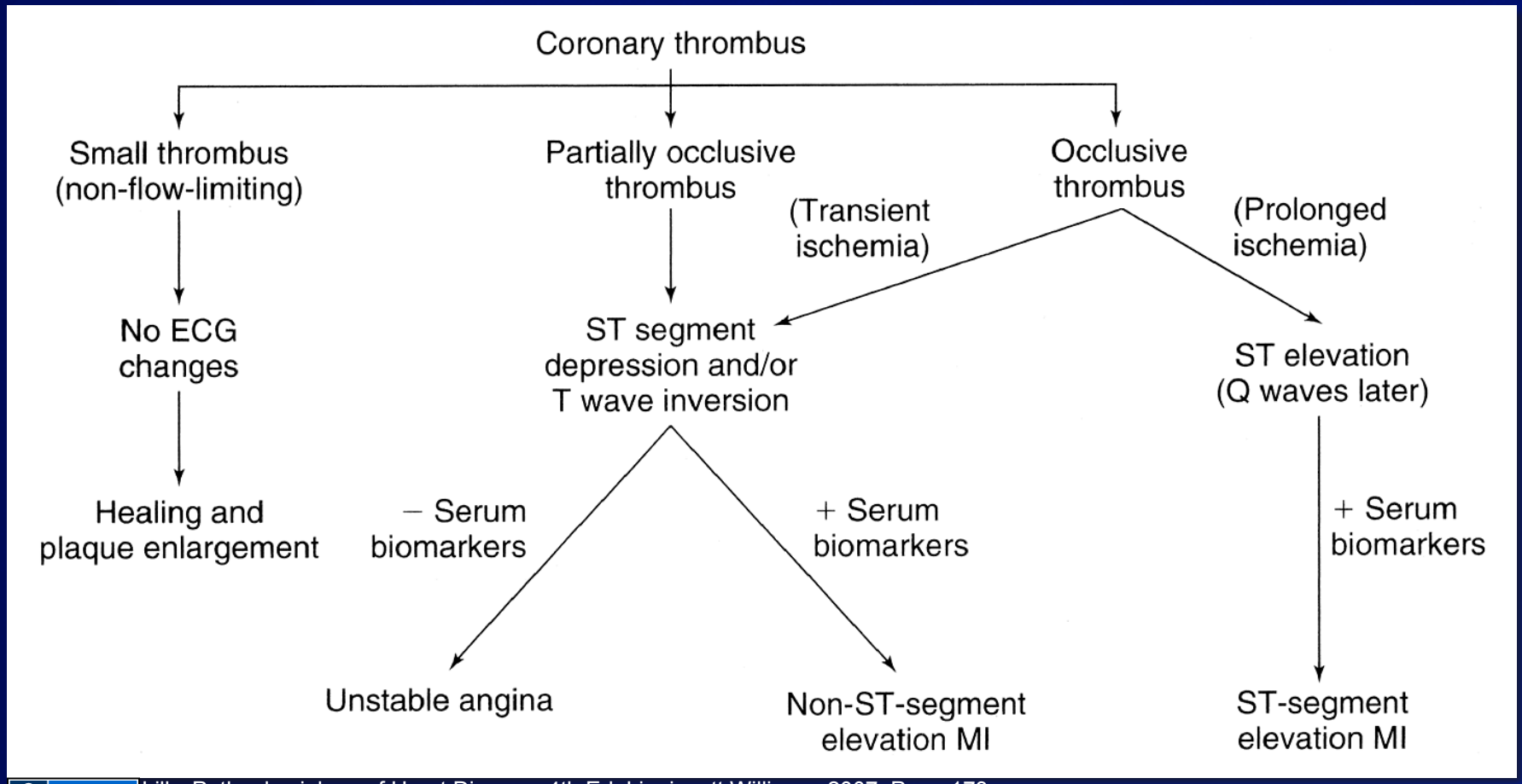
Consequences of Coronary Thrombosis



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Causes of Acute Coronary Syndromes

- Atherosclerosis with superimposed thrombus
- Vasculitic syndromes
- Coronary emboli (e.g., from endocarditis, artificial valves)
- Congenital anomalies of the coronary arteries
- Coronary trauma or aneurysm
- Severe coronary artery spasm (primary or cocaine-induced)
- Increased blood viscosity (e.g., polycythemia vera, thrombocytosis)
- Significantly increased myocardial oxygen demand (e.g., aortic stenosis)

Extent of Myocardial Injury

Determined by:

- LV mass perfused by vessel
- Magnitude/Duration of flow ↓
- Oxygen demand of affected tissue
- Adequacy of collaterals
- Tissue response to ischemia

Clinical Features: ACS

Stable CAD

Acute Coronary Syndromes

Unstable angina

Non-ST Elevation MI
(Non-Q-wave MI)

ST-Elevation MI
(Q-wave MI)

The continuum of acute coronary syndromes ranges from unstable angina, through non-ST-elevation myocardial infarction (also referred to as “non-Q-wave” myocardial infarction [MI]), to ST-elevation MI (also referred to as “Q-wave” MI).

Unstable Angina

- Prior stable angina → ↑ in:
  - Frequency
  - Duration
  - Intensity
- Angina at rest… previously only on provocation
- New onset angina

Acute Myocardial Infarction

- History and exam
- EKG changes
- Serum markers

Symptoms

Pain	– Pressure – Burning (hot) – Chest/arms/jaw/back
Sympathetic response	– Sweats – Tachycardia – Cool, clammy skin
Parasympathetic response	– Nausea – Vomiting – Weak
Inflammatory response	– Mild fever
Other	– Dyspnea – Asymptomatic

Physical Findings

- Inspection

BP - often increase anterior MI

- often decrease inferior MI

HR - often increase anterior MI

- often decrease inferior MI

RA p^{o} - increase in RV MI

Physical Findings

- Palpation

  LV Bulge - dyskinetic anterior wall

- Auscultation

  Gallop - S4-LV stiff

  Sounds - S3-LV fatigue

  Murmurs - Mitral regurgitation

  - VSD

Differential Diagnosis

- Cardiac

  Pericarditis
  - Sharp, pleuritic pain
  - PT prefers to sit
  - Friction rub
  - EKG diffuse STE

  Aortic Dissection
  - Instantaneous onset of severe pain
  - Pulse deficits or AI
  - Wide mediastinum (CXR)

Differential Diagnosis

- Pulmonary

  Pulmonary Embolus
  - Pleuritic pain
  - Dyspnea
  - Reason for clotting

  Pneumonia
  - Cough, sputum, fever
    - Consolidaton changes

- Gastrointestinal

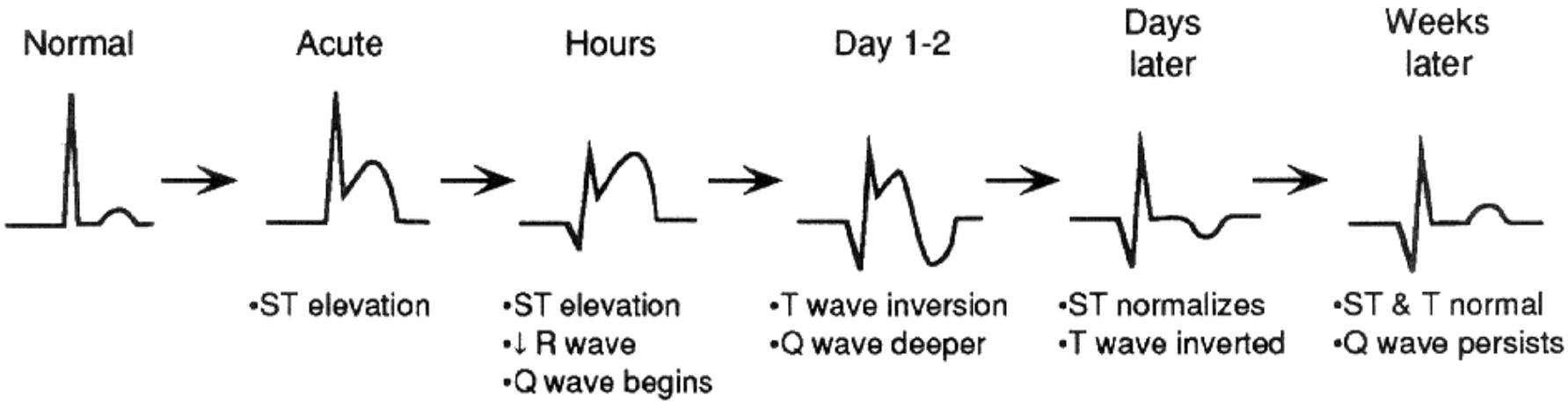
  Esophageal Spasm
  - Retrosternal burning (acid)
  - After meals or at night

Diagnosis of ACS

	Unstable Angina	Myocardial Infarction	
		NSTEMI	STEMI
Typical symptoms	Crescendo, rest, or new onset severe angina	Prolonged "crushing" chest pain, more severe and wider radiation than usual angina	
Serum biomarkers	No	Yes	Yes
ECG initial findings	ST depression and/or T wave inversion	ST depression and/ or T wave inversion	ST elevation (and Q waves later)

NSTEMI, non-ST-elevation myocardial infarction (MI); *STEMI*, ST-elevation MI

Q-wave Myocardial Infarction



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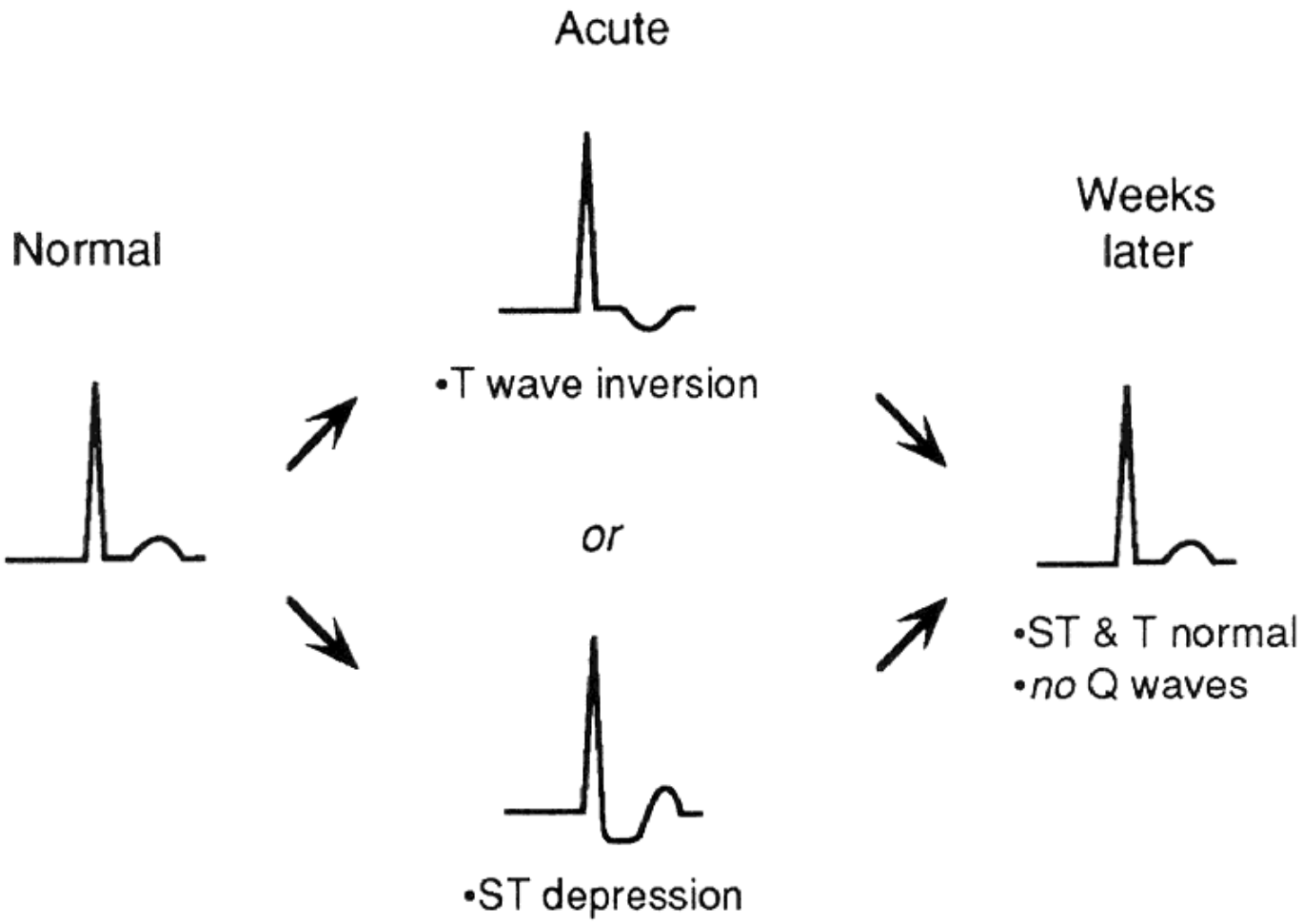
Non-Q-wave Myocardial Infarction



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Serum Markers of Myocardial Infarction

- Myocardial necrosis causes sarcolemma disruption
- Intracellular macromolecules are released
- Can be measured by serial blood testing
- Pattern and level of rise correlates with timing and size of MI

Cardiac-Specific Troponins

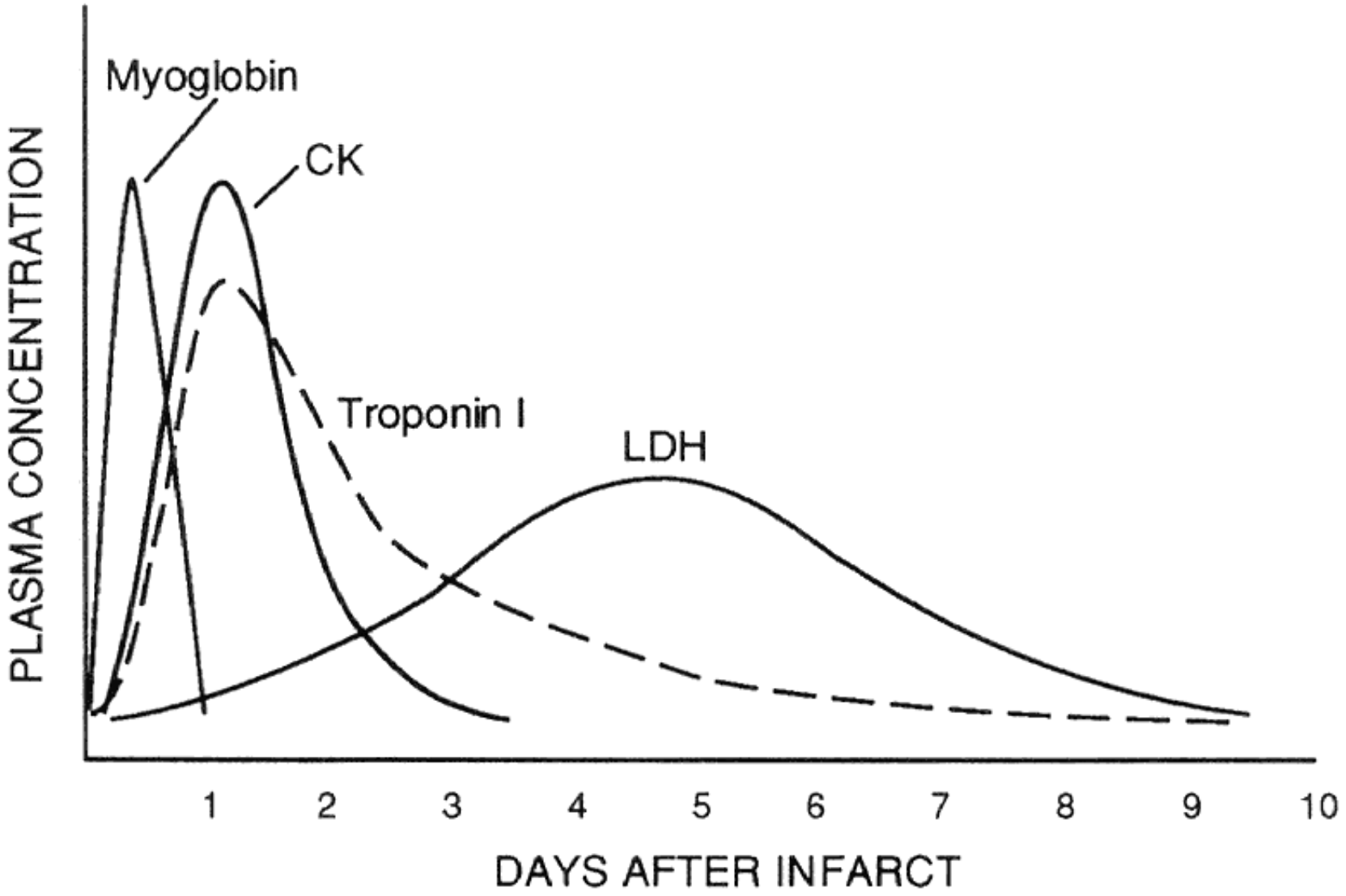
- Regulatory protein that controls interaction between actin & myosin
- 3 subunits: TnC, I, T } Skeletal & cardiac muscle
- Unique cardiac troponins I and T exist - absent in serum of healthy people
- Powerful marker of myocyte damage
- Rise at 3-4 hours post-MI, peak 18-36 hrs, decline slowly 10-14 days

Creatinine Kinase

- Enzyme that converts ADP to ATP
- Found in many tissues: heart, brain, skeletal muscle, kidney, etc.
- Can be elevated after injury to any of these tissues
- 3 isoenzymes:
  - CK-MM
  - CK-MB
  - CK-BB

CPK-MB

- Makes up 1-3% of skeletal CK
- Makes up much higher % of cardiac CK
- Rises 4-8 hours after MI, peaks by 24 hours
- Returns to normal in 48-72 hours


Myoglobin
CK
Troponin I
LDH
PLASMA CONCENTRATION
1
2
3
4
5
6
7
8
9
10
DAYS AFTER INFARCT

Treatment of Acute Coronary Syndromes:

STE vs. Non STE

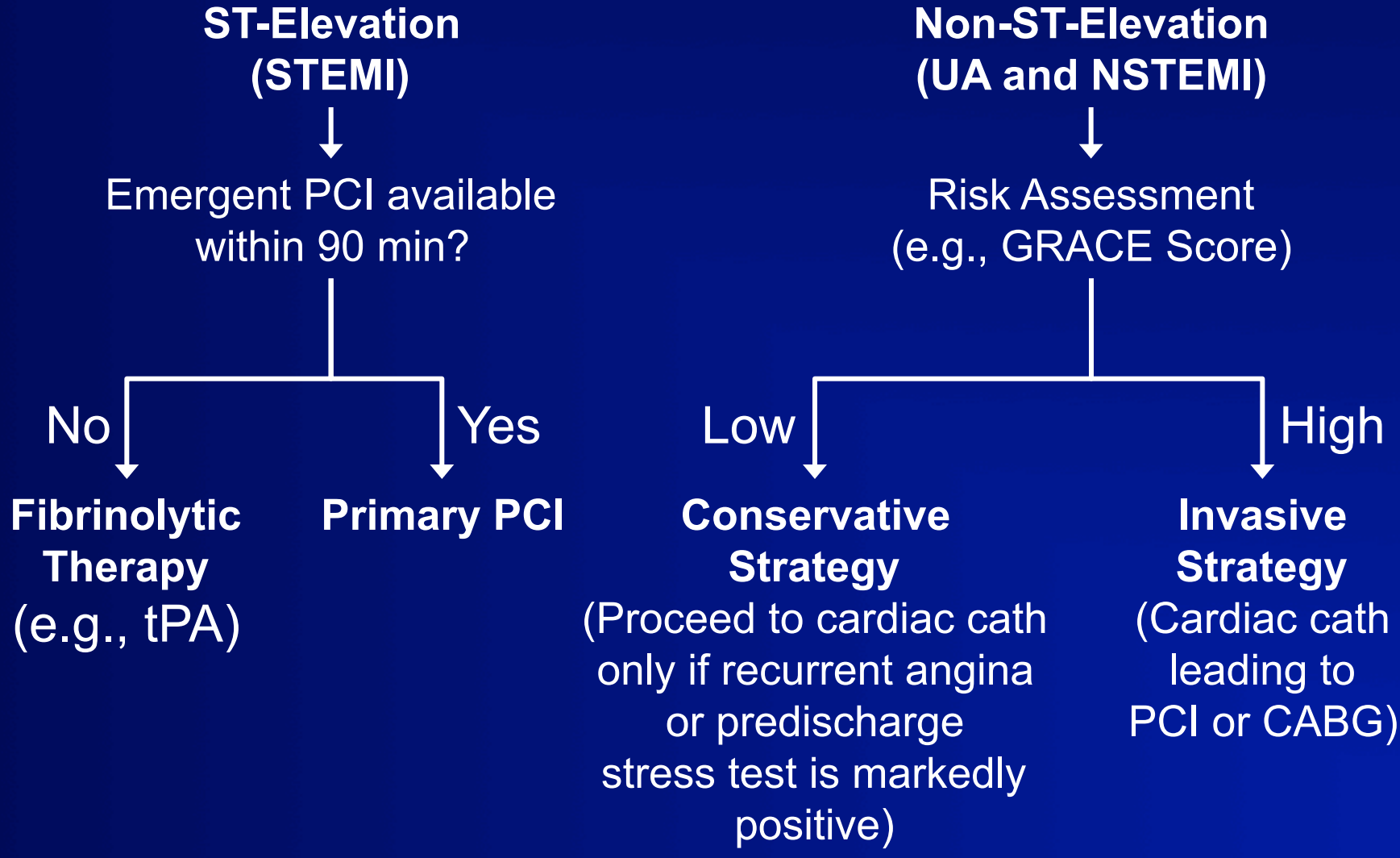
Treatment of Acute Coronary Syndromes

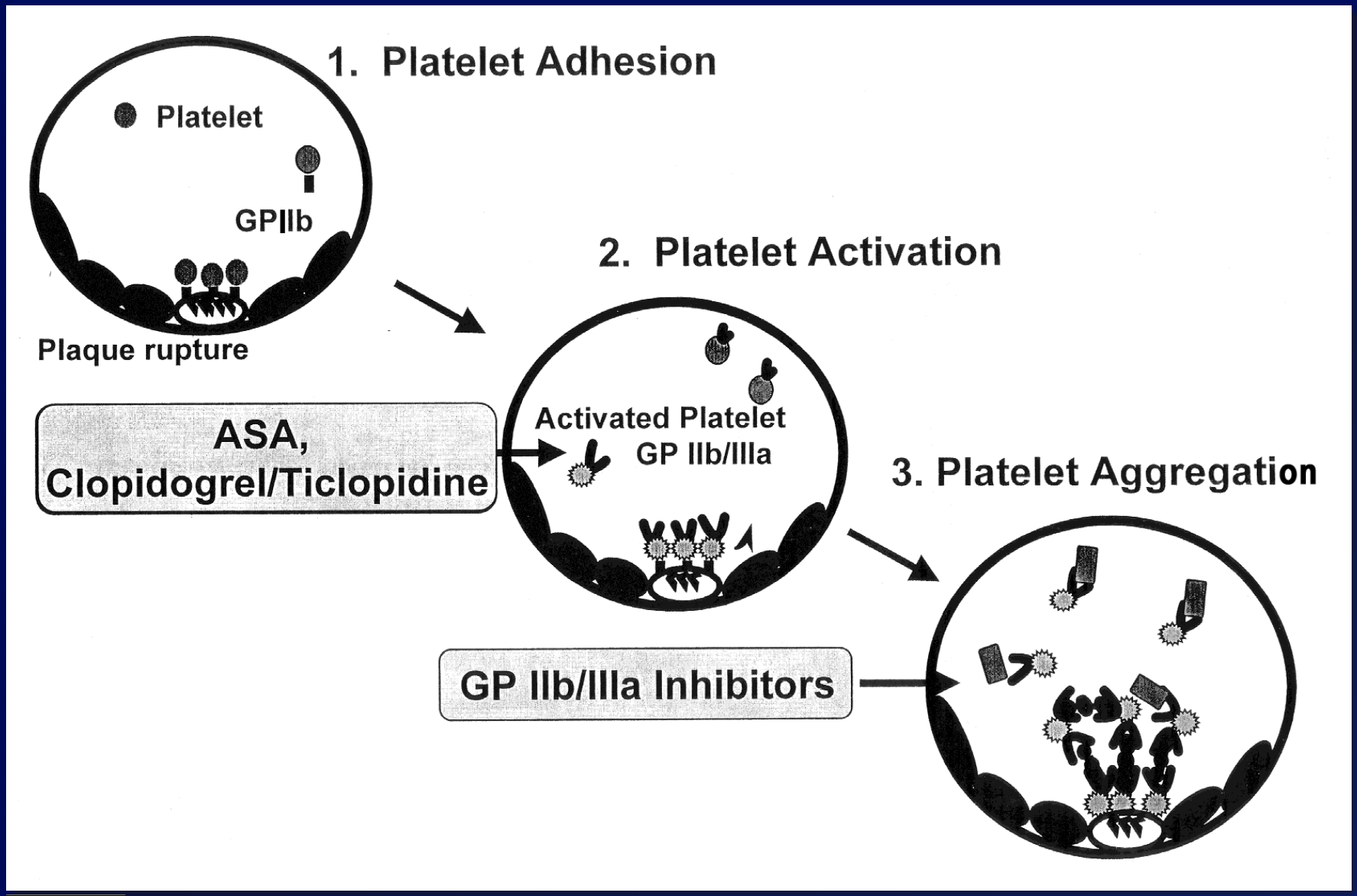
- **Anti-ischemic therapies**
  - B-blocker
  - Nitrates
  - +/- Calcium channel blocker
- **General measures:**
  - Pain control (morphine)
  - Supplemental O_2 if needed
- **Antithrombotic therapies**

  Antiplatelet agents:
  - Aspirin
  - Clopidogrel (or prasugrel)
  - GP IIb/IIIa inhibitor (for selected high risk patients; may be deferred until PCI)

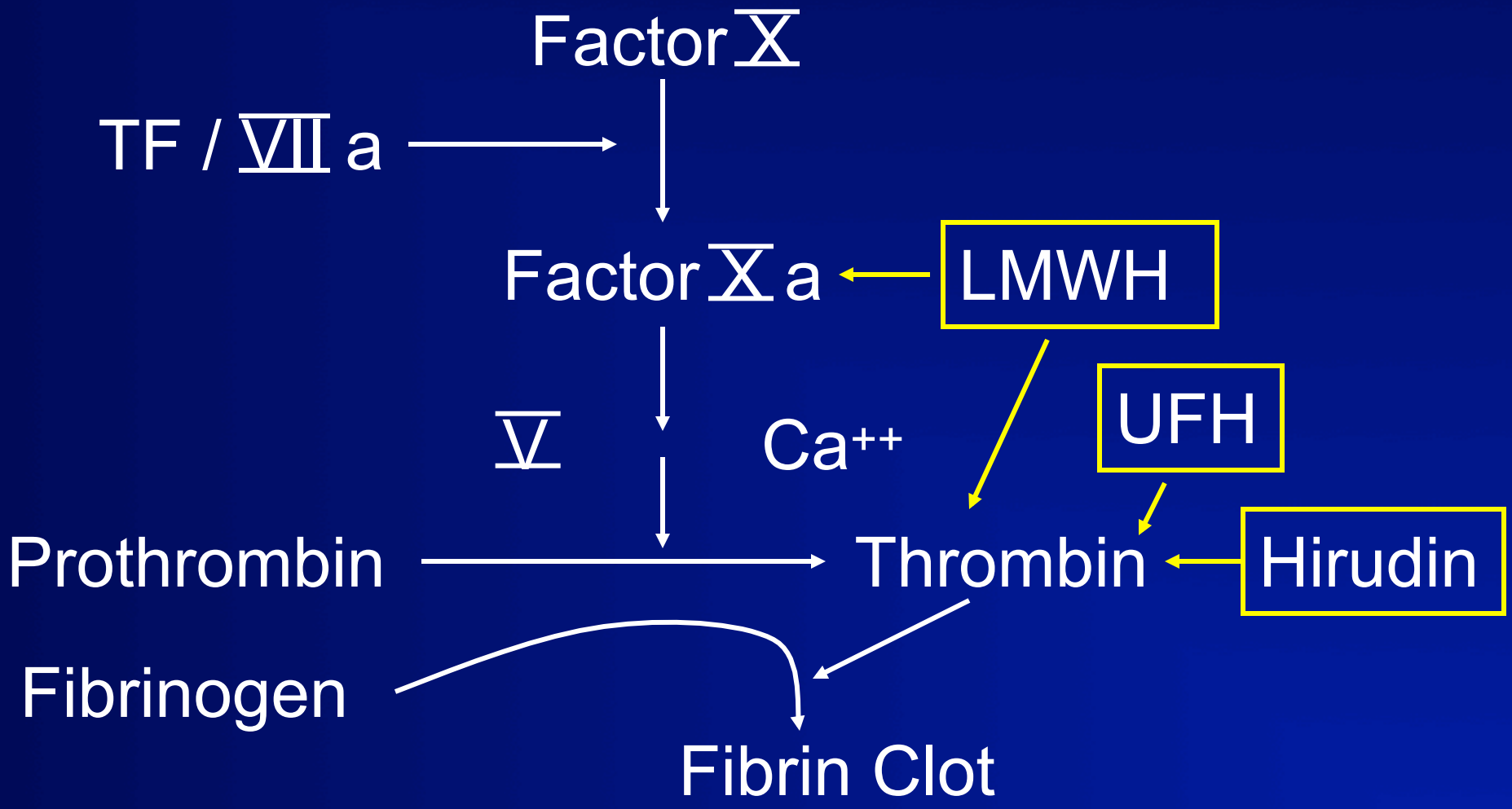
  Anticoagulants (use one):
  - LMWH (enoxaparin)
  - Unfractionated intravenous heparin
  - Fondaparinux
  - Bivalirudin (should be used in ACS patient only if undergoing PCI)
- **Adjunctive therapies:**
  - Statin
  - Angiotensin converting-enzyme inhibitor

Treatment of Acute Coronary Syndromes

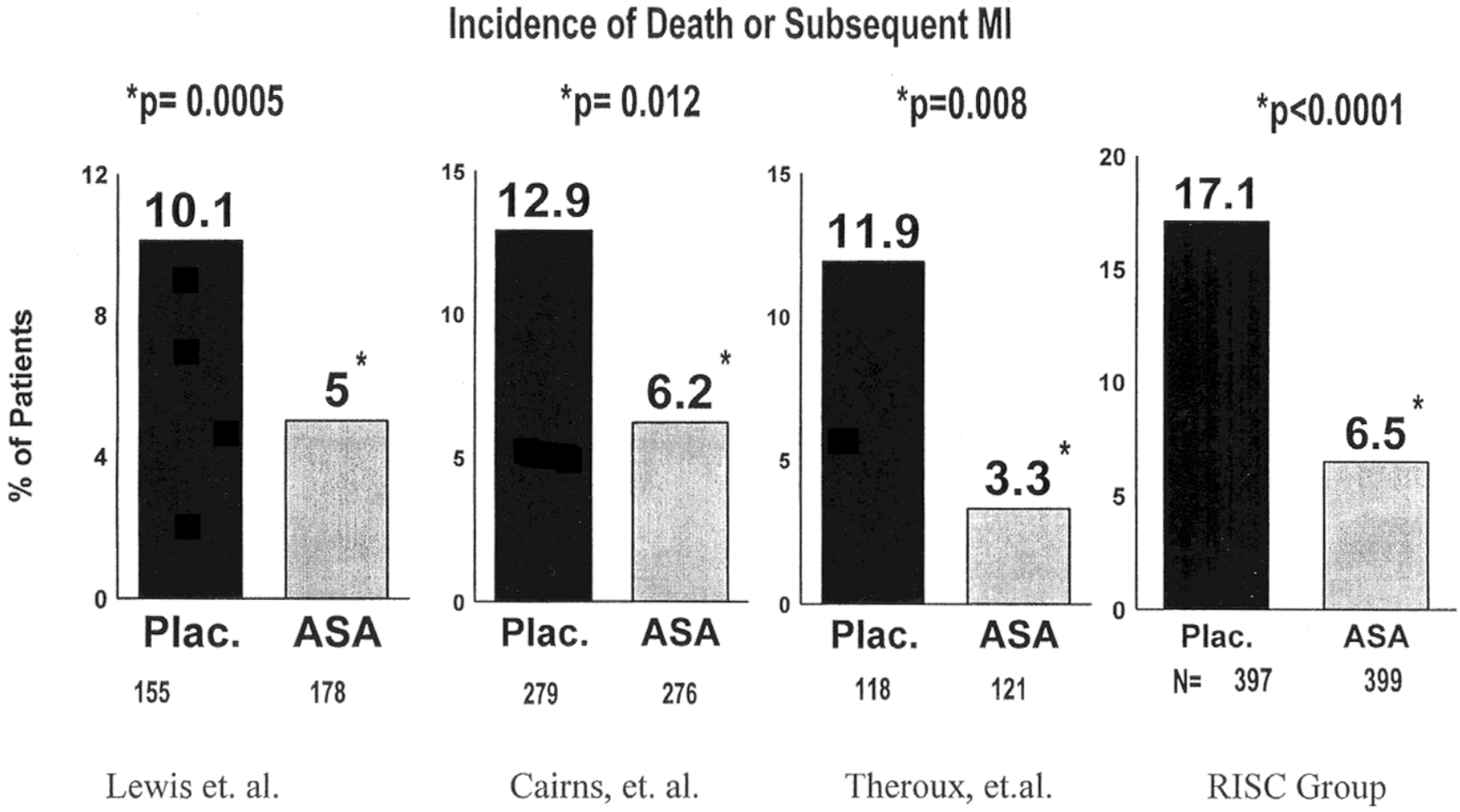



1. Platelet Adhesion
Platelet
GPIIb
Plaque rupture
2. Platelet Activation
ASA,
Clopidogrel/Ticlopidine
Activated Platelet
GP IIb/IIIa
3. Platelet Aggregation
GP IIb/IIIa Inhibitors

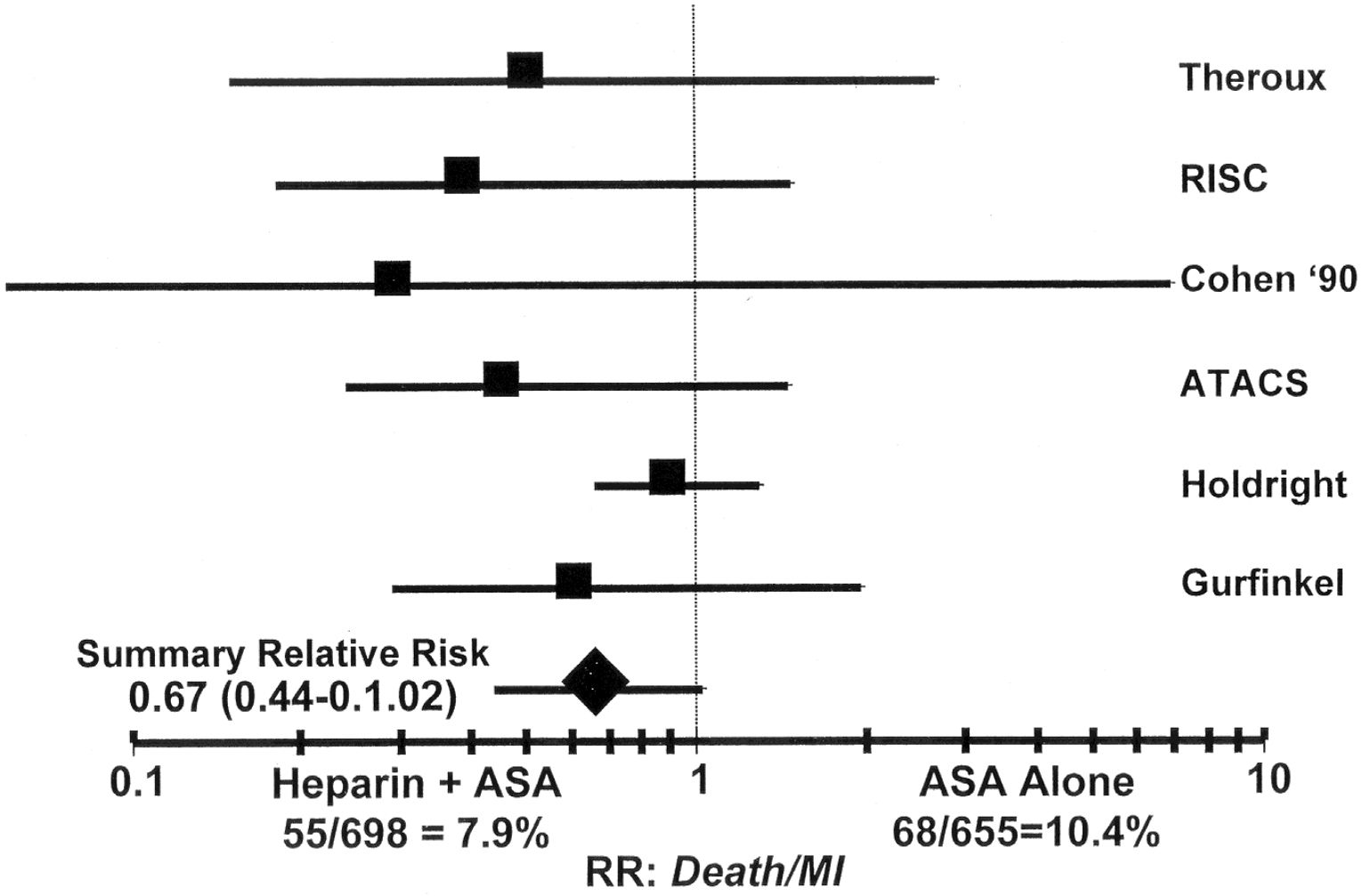
Antithrombin Rx



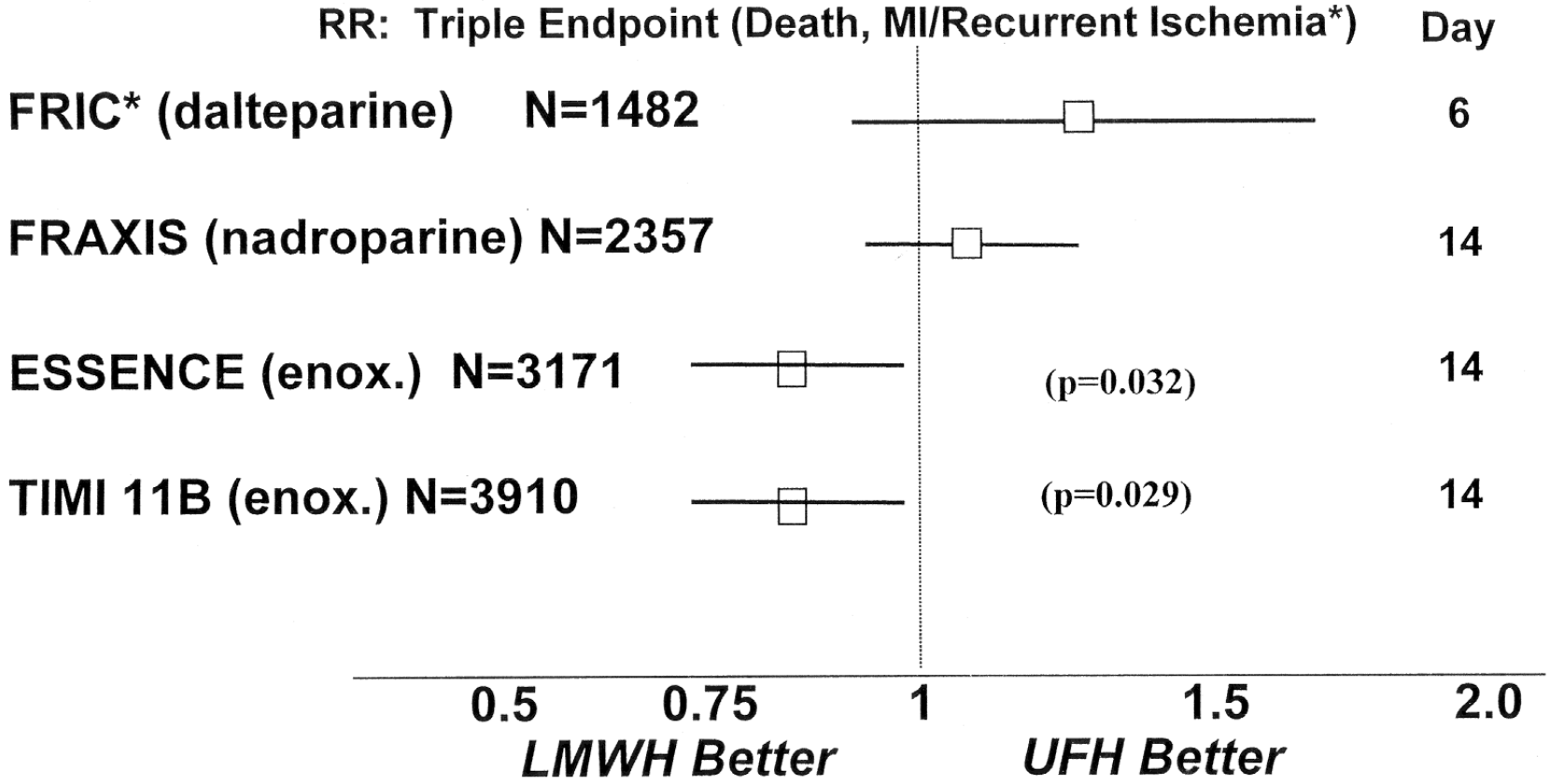
Effect of ASA in Non-ST Elevation MI and Unstable Angina



Meta-analysis
Heparin + ASA vs. ASA alone



LMWH in Unstable Angina



*Definition of recurrent angina/urgent revasc differs between trials

Nitrates

- Reduce ischemia (not mortality)
- Venodilation: ↓ R heart return
- Coronary vasodilation
- Usually given SL then IV

Beta Blockers

- ↓ Sympathetic drive; HR & BP
- ↓ O_2 demand
- ↓ Shear stress
- ↓ Sudden death, death, recurrent MI

Non Dihydropyridine Calcium Channel Blockers

- ↓ Heart rate
- Vasodilate
- Relieve ischemia, not mortality
- Don't give in patients with sx/ signs of heart failure

Non - STE ACS:

Conservative vs. Early Invasive Approach

Early Invasive

- Urgent catheterization performed after initial medical Rx
- Allows rapid identification & Rx of critical CAD
- More PCI/CABG

Conservative

- Cath patients with recurrent ischemia in hospital
- Cath patients with inducible ischemia on pre-discharge stress test

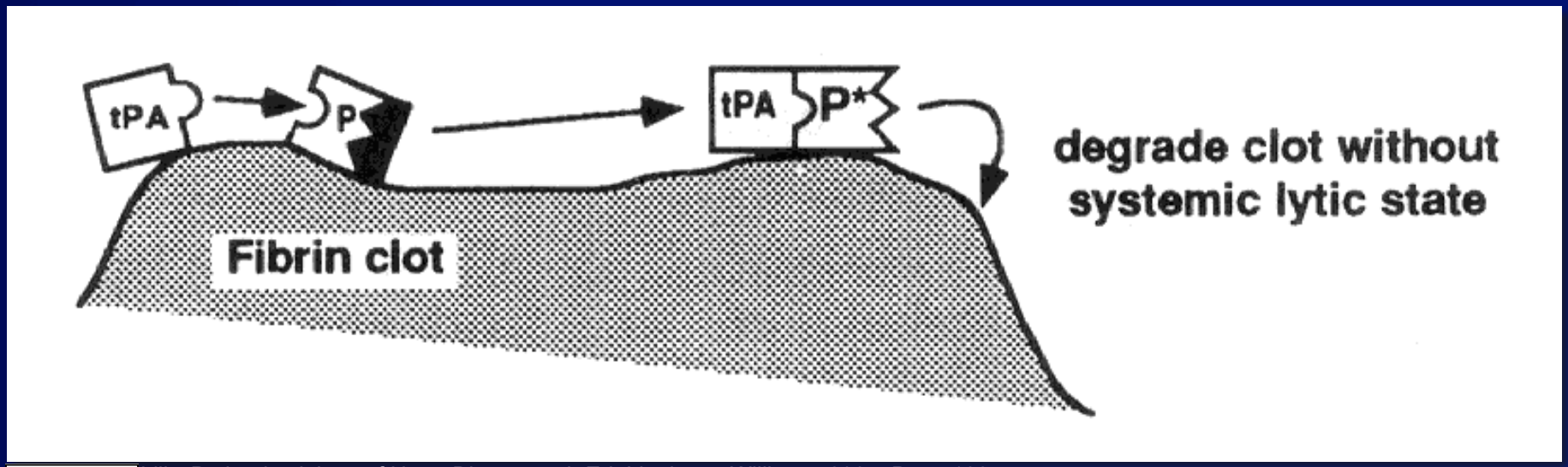
Invasive vs. Conservative

- Recent clinical trials show less infarction/ reinfarction & possibly death with invasive strategy
- Especially in higher risk patients:
  - ST segment deviation
  - Elevated biomarkers
  - Multiple risk factors… esp. DM

Acute Treatment: STE MI

- Reperfusion: Thrombolysis vs. PTCA
- ASA
- O_2
- Beta blockers
- Nitrates
- ACE inhibitors
- Morphine
- Anticoagulants

A



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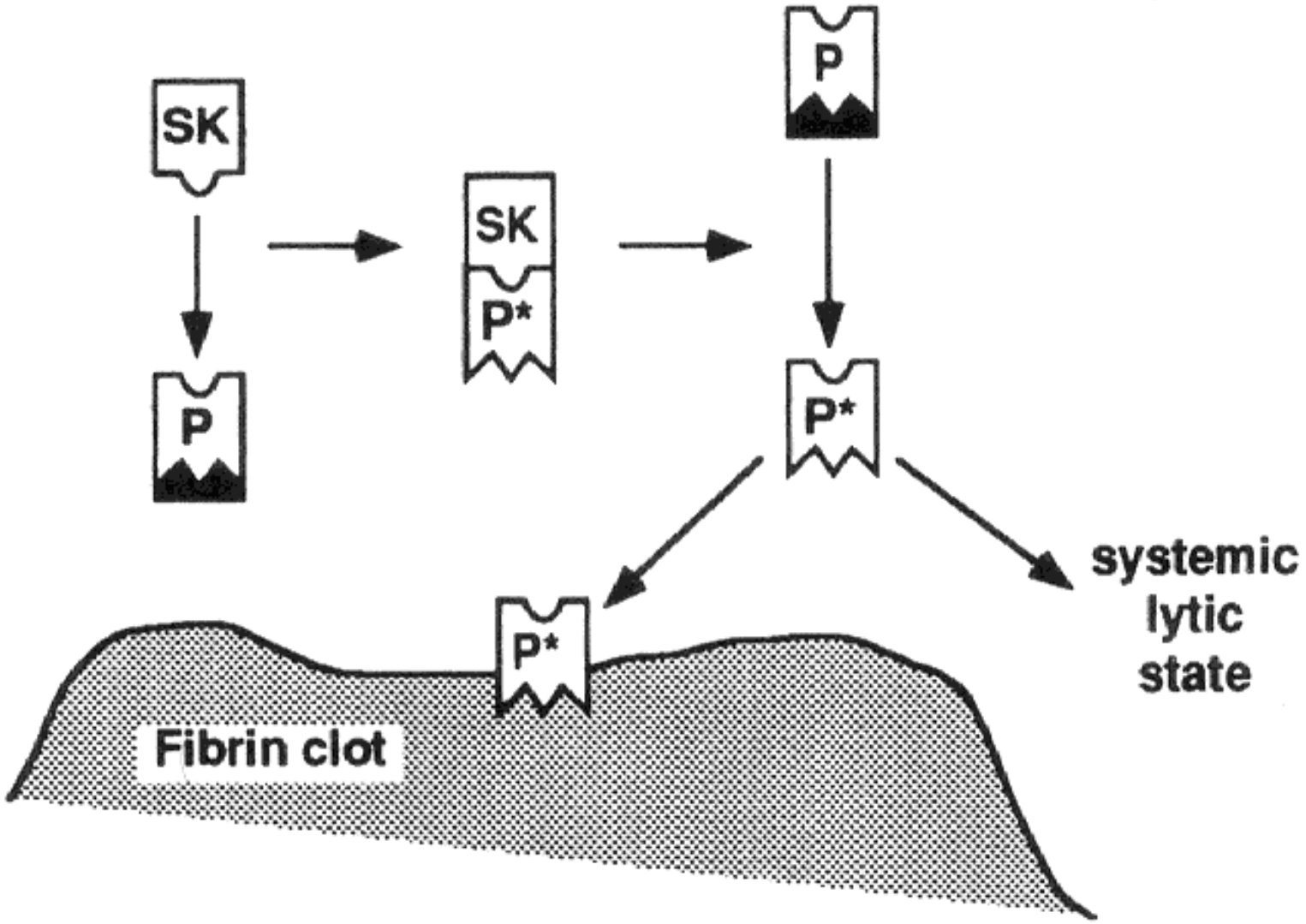

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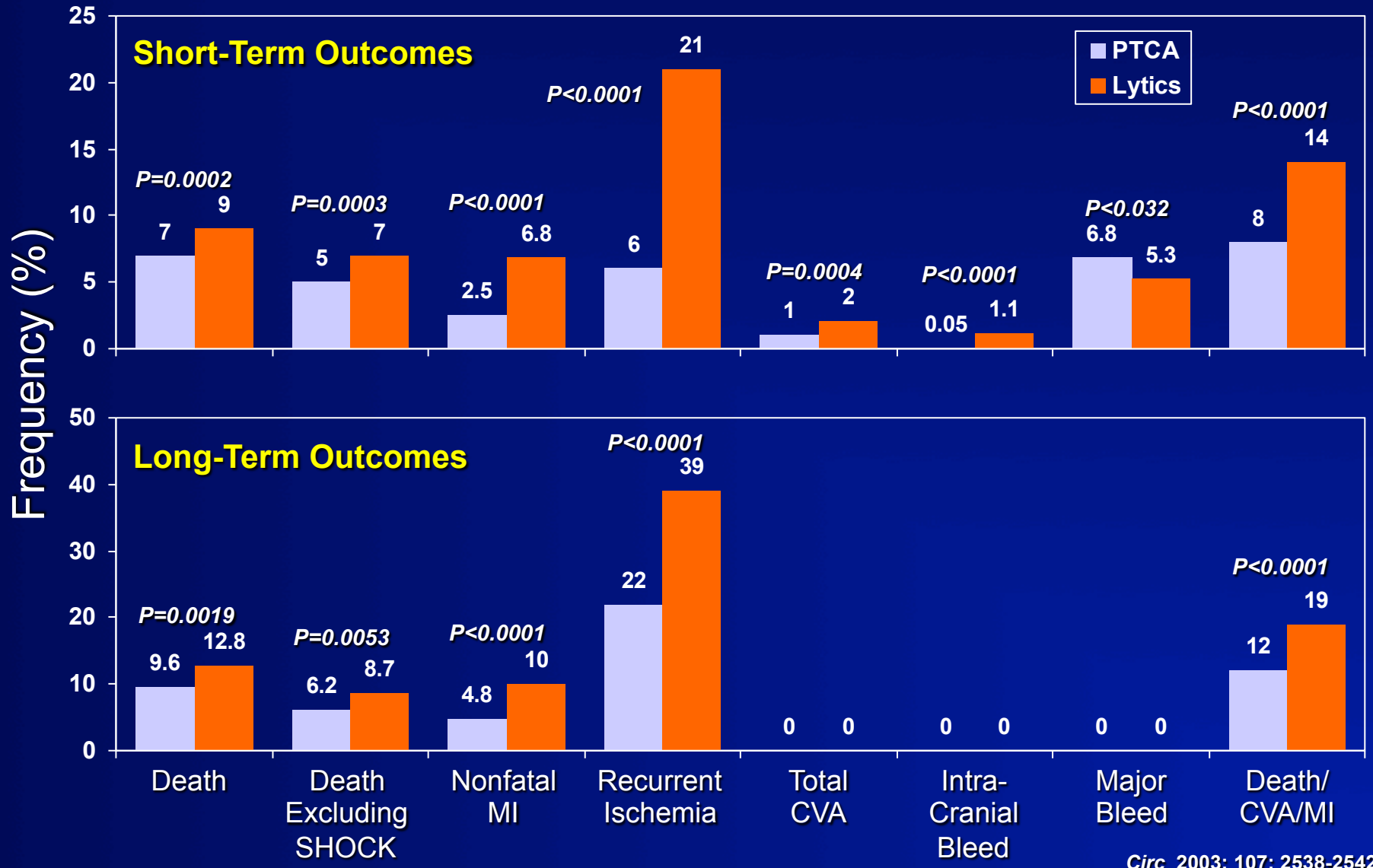
PCI vs. Lytic



Circ 2003; 107: 2538-2542

Additional Rx: STE MI

- Maintain vessel patency
- Restore balance between 0_2 supply and demand
- Relieve chest pain
- Prevent complications

Aspirin

- Reduces mortality & reinfarction
- Give immediately on presentation and daily thereafter
- If aspirin allergy, use clopidogrel

Heparin

- Give 1-2 days IV after PCI or lysis with tPA, rPA, or TNK-tPA… NOT SK
- Also if:
  - Atrial fibrillation
  - LV thrombus
  - New anterior MI with large wall motion change
- All others: SQ heparin while at bed rest to prevent DVT

ß- Blockers

- ↓ Risk arrhythmia, reinfarction, rupture, death
- Give IV, then orally unless contraindication exists (asthma, hypotension, significant bradycardia)

Nitrates

- Reduce pain/ischemia
- Relieve pain
- Reduce pulmonary congestion in heart failure

ACE - Inhibitors

- Limit adverse LV remodeling
- ↓ Heart failure/death
- ↓ MI
- Benefit additive ASA, BB
- Esp. benefit anterior MI and/or LV dysfunction

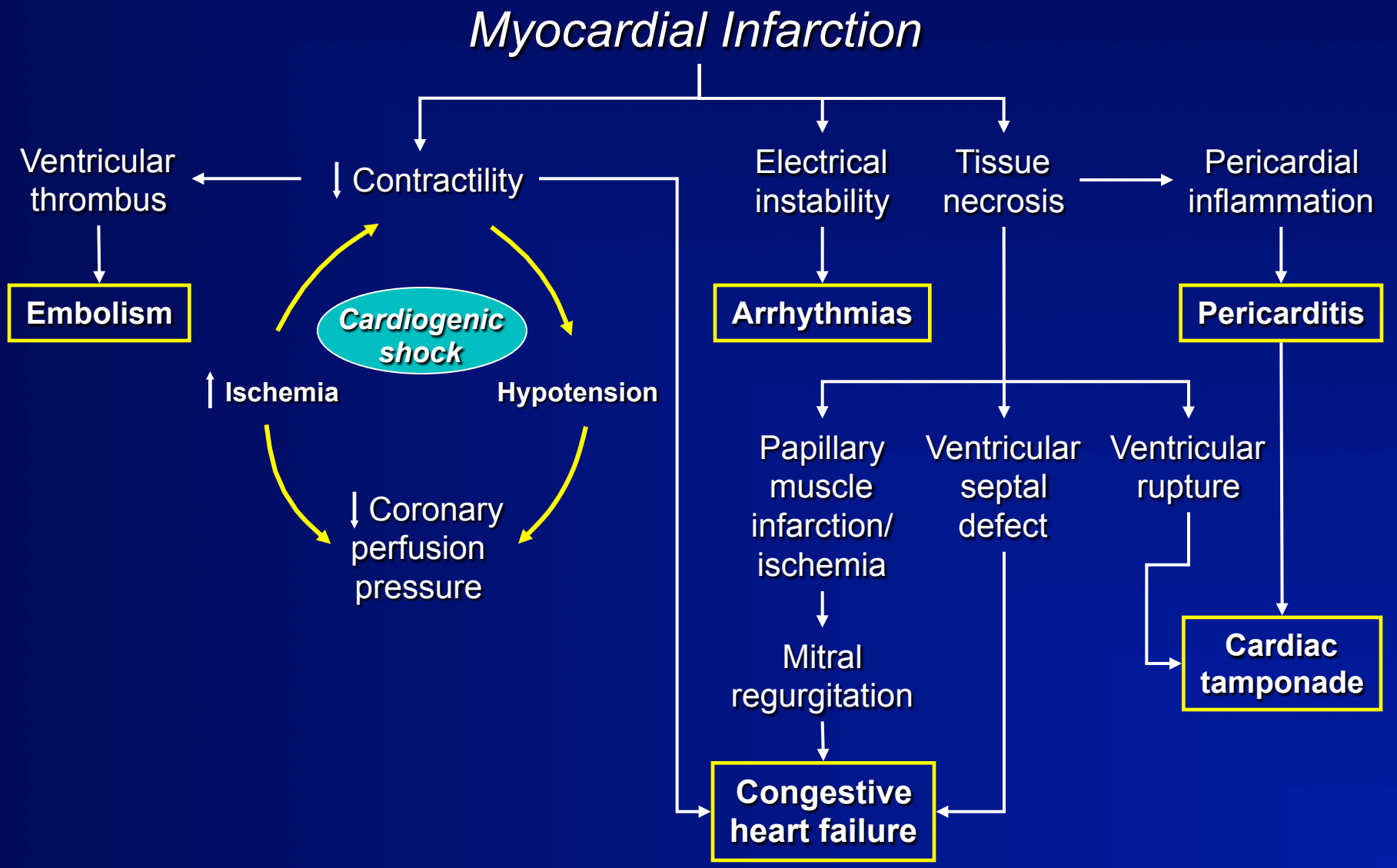
Statins

- Reduce reinfarction, death
- More benefit when started early
- Give if LDL cholesterol is > 100

Acute MI: Complications

- Recurrent ischemic/reinfarction
- Arrhythmias
- Myocardial dysfunction
- Mechanical complications
- Pericarditis
- Thromboembolism

Complications of MI



Recurrent Ischemia

- Angina or ischemia confers increase risk for reinfarction
- Should lead to angiography and revascularization for most pts.

Arrhythmias in Acute MI

Rhythm	Cause
• Sinus Bradycardia	- ↑Vagal tone - ↓SA nodal artery perfusion
• Sinus Tachycardia	- CHF - Volume depletion - Pericarditis - Chronotrophic drugs (e.g. Dopamine)
• APB's, atrial fib, VPB's, VT, VF	- CHF - Atrial Ischemia - Ventricular ischemia - CHF
• AV block (1º, 2º, 3º)	- IMI: ↑ Vagal tone and ↓AV nodal artery flow - AMI: Extensive destruction of conduction tissue

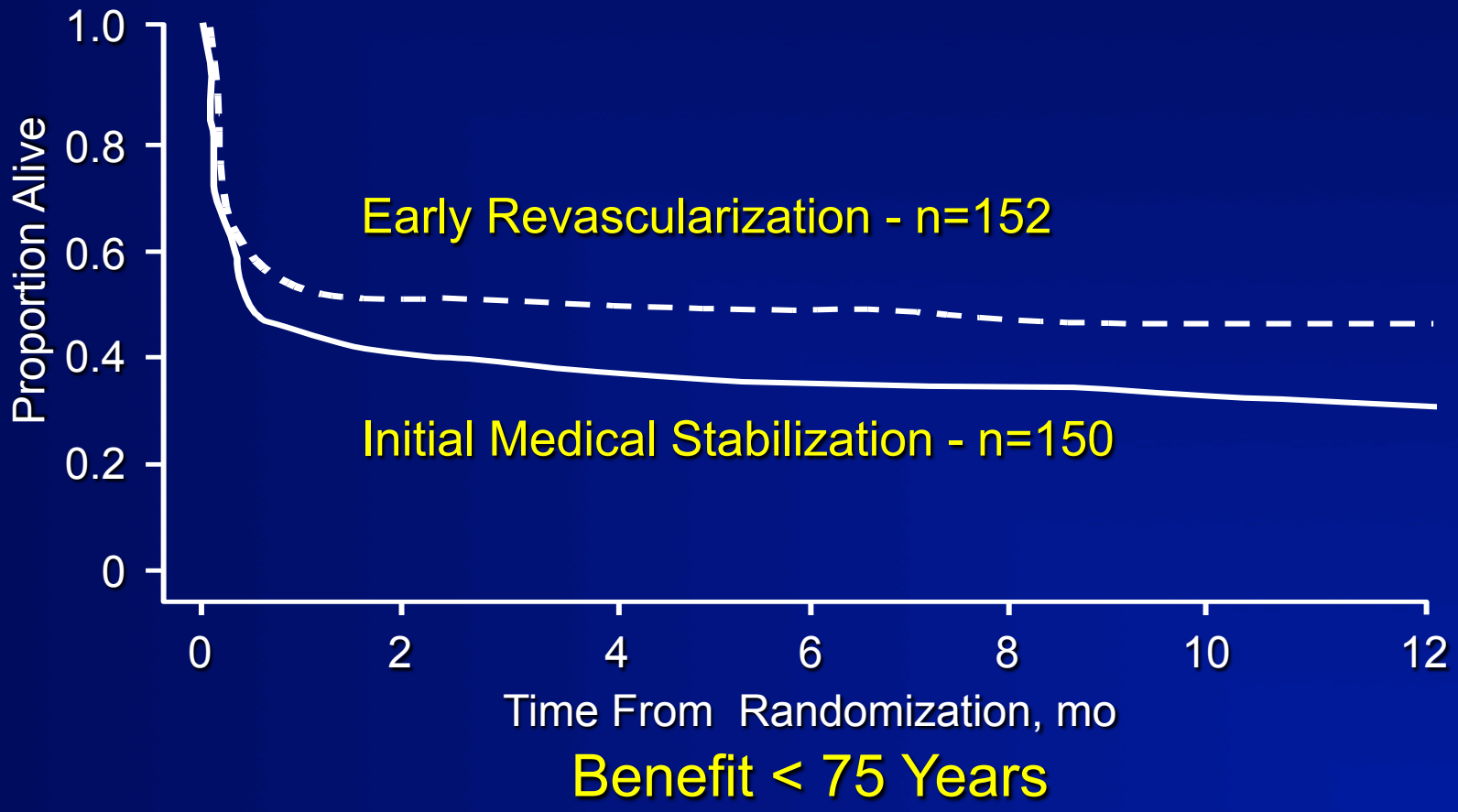
Blood Supply in the Conduction System

Conduction Pathway	Primary Arterial Supply
• SA node	- RCA (70% of patients)
• AV node	- RCA (85% of patients)
• Bundle of His	- LAD (septal branches)
• RBB	- Proximal portion by LAD
	- Distal portion by RCA
• LBB	
Left anterior fascicle	- LAD
Left posterior fascicle	- LAD and PDA

Myocardial Dysfunction

- Congestive Heart Failure
  - Systolic or diastolic
  - Treated with vasodilators, diuretics, and Rx to reverse ischemia
- Cardiogenic Shock
  - Depressed CO
  - Hypotension
  - Poor perfusion of vital organs
  - Treatment: Look/Treat reversible cause
  - Inotropes/vasodilators/IABP

Cardiogenic Shock - MI - 1Y



Benefit < 75 Years

Shock (JS Hochman et al.) *JAMA* 2001; 285:190

RV Infarction

- Common in IMI's
- Sx/signs:
  - Hypotension
  - Increase RA Pressure
- Rx:
  - Volume, hemodynamic monitoring…PA line

Papillary Muscle Infarction

- “Common” in inferoposterior MI
- Leads to acute mitral valve regurgitation
- Left heart failure/pulmonary edema
- Rx: Coronary revascularization; IABP; valve repair

Free Wall Rupture

- More likely in elderly, HTN, women
- Usually rapidly fatal
- Occasional walls off to form pseudoaneurysm
- Urgent surgery is best chance

Ventricular Septal Defect

- Heralded by left to right shunting at ventricular level
- RV volume overload
- Loud systolic murmur over sternum
- Usually requires surgical repair

True Ventricular Aneurysm

- Occurs late
- More often in non-reperfused STE MI's
- Complications: Clot, CHF, arrhythmias

Pericarditis

- More common in non-reperfused STE MI
- Fever, sharp pain with pleuritic tendency, friction rub
- Treatment: nonsteroidal anti-inflammatory agent; heparin relatively contraindicated

Thromboembolism

- Clot forms on infarcted akinetic myocardium
- Most common in large anterior MI
- Can cause embolic stroke
- Rx: 3-6 months anticoagulants
- If clot seen on echo or LVEF < 30% or if large anterior MI

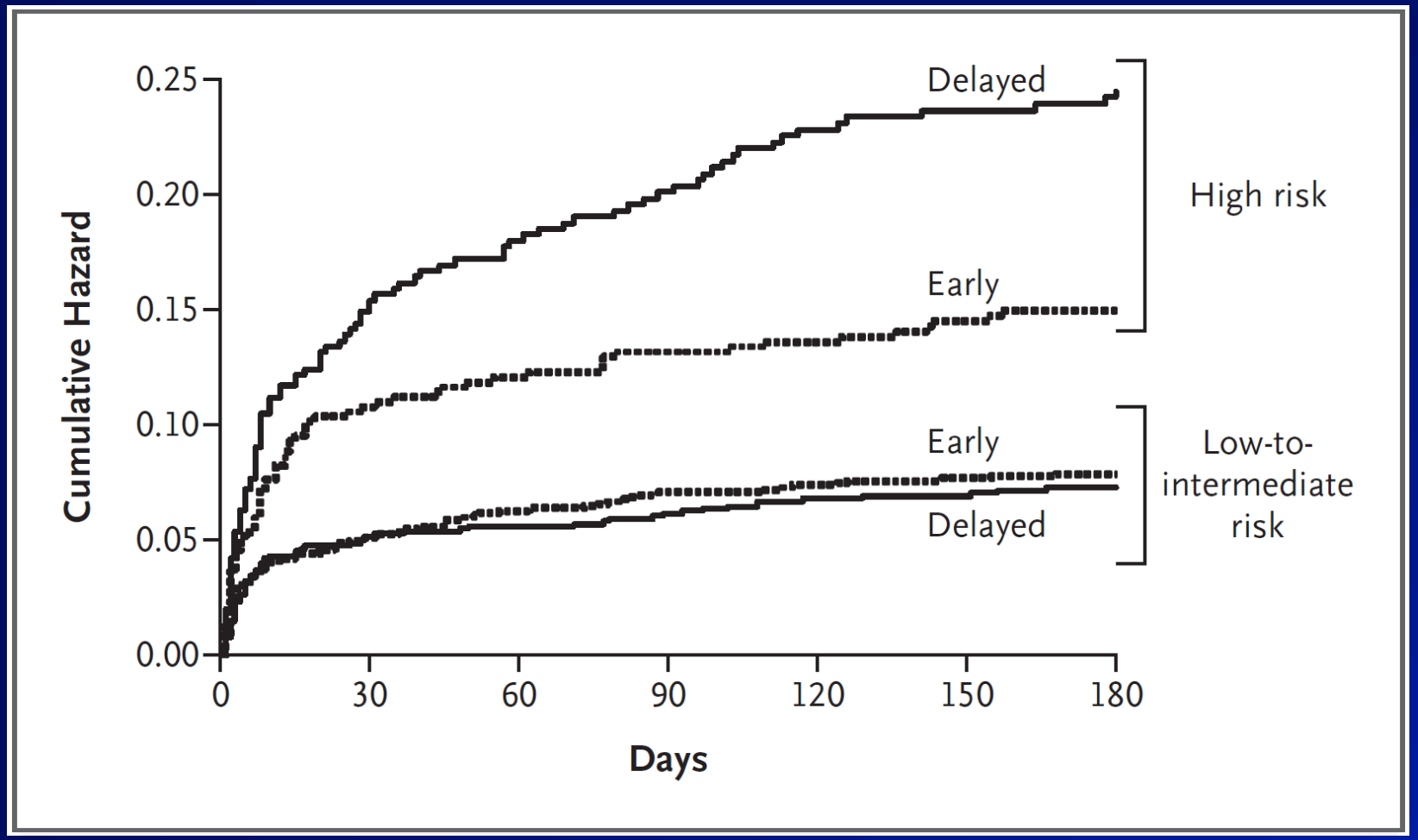
Post MI Risk Stratification and Management

Predictor of Poor Outcome	Method to Detect	Treatment
Poor LVEF	Echocardiogram	ACE, BB
Residual Ischemia	Pre D/C ETT Max ETT later	Cath; ASA,BB
Arrhythmias	Monitoring/ Observation	Directed

Standard Discharge Rx

- 3 to 5 day length of stay
- ASA; clopidogrel
- Beta blocker
- ACE for CHF; LVEF $\leq$ 40%, perhaps all
- Warfarin as noted
- Cardiac Rehab
- PRN Nitrates
- Exercise prescription
- Low fat diet
- Smoking Cessation
- Statin if LDL cholesterol $\geq$ 100 mg/dl

Kaplan–Meier Cumulative Risk of the Primary Outcome, Stratified According to GRACE Risk Score at Baseline



PD-INEL Mehta SR et al. *NEJM* 2009;360:2172.