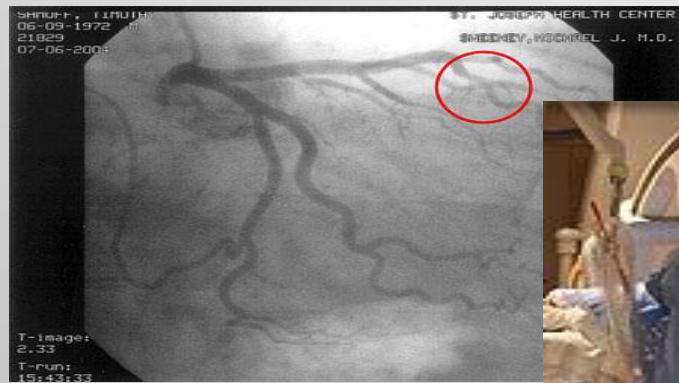


Acute Coronary Syndrome: Practical Considerations



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Disclosures

- Consultant/Speaker
 - Zoll
 - Astra Zeneca
 - Amgen
 - BI

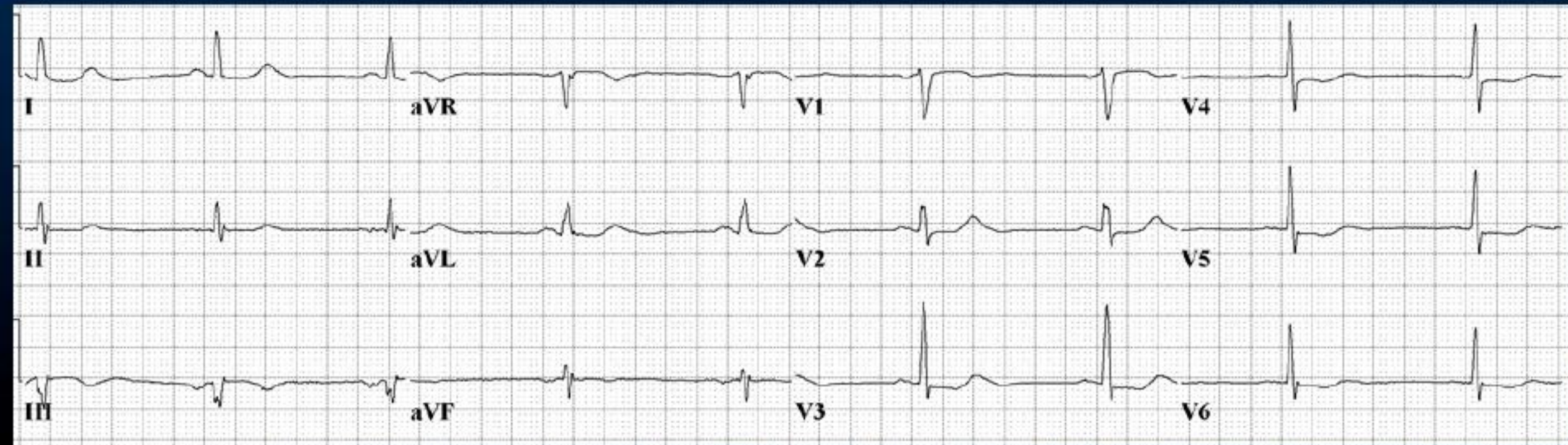
Acknowledgements:

Mayo Clinic Cardiology, Duke, Mount Sinai NY

Question 1

A 70yo male presents with intermittent central chest pressure beginning at rest last evening and is now pain free. He takes aspirin for “arthritis” and treatment for diabetes and hypertension.

HR is 90 and BP 112/80. Exam is unremarkable except for expiratory wheeze. ECG shown below. His initial cardiac troponin T is 0.5 ng/mL (normal <0.01) and creatinine 1.8 mg/dL.



Question 4

You work in a community hospital 60 minutes away from the nearest referral center with sub-specialists.

A 60 year old man with paroxysmal atrial fibrillation is awoken at 11 PM with left arm discomfort, chest fullness and mild dyspnea. When the discomfort persisted for 30 minutes, he presented to your emergency room 45 minutes after the onset of symptoms. He denies other complaints. He just flew to Hawaii for 2 days of business meetings and returned 3 days ago.

He is on Metoprolol, Apixaban, Atorvastatin, and Digoxin. He has no medical or food allergies. His exam in the ED is normal.

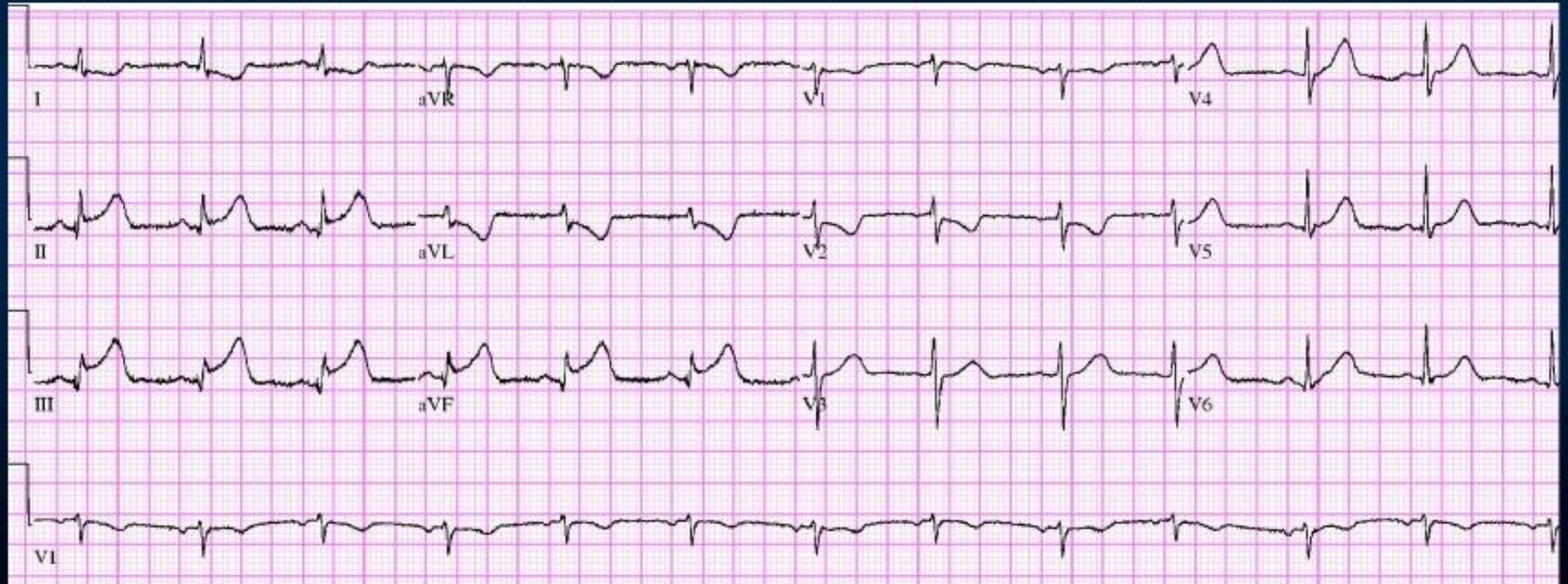
Question 4 continued...

He was started on 2 liters oxygen and given 324 mg aspirin, and 4 mg morphine IV by the nurse practitioner staffing the ED. The patient is now pain free.

Lab results are: Hemoglobin 13.8, WBC 11.3*(nl 3.5-10.5), D-Dimer 275*(nl <250), Sodium 141, Potassium 4.6, Creatinine 0.9, Glucose 155*(nl<100), pulse oximetry sat 97%, and CXR normal. Troponin is pending.

You are called to the ED to see the patient.

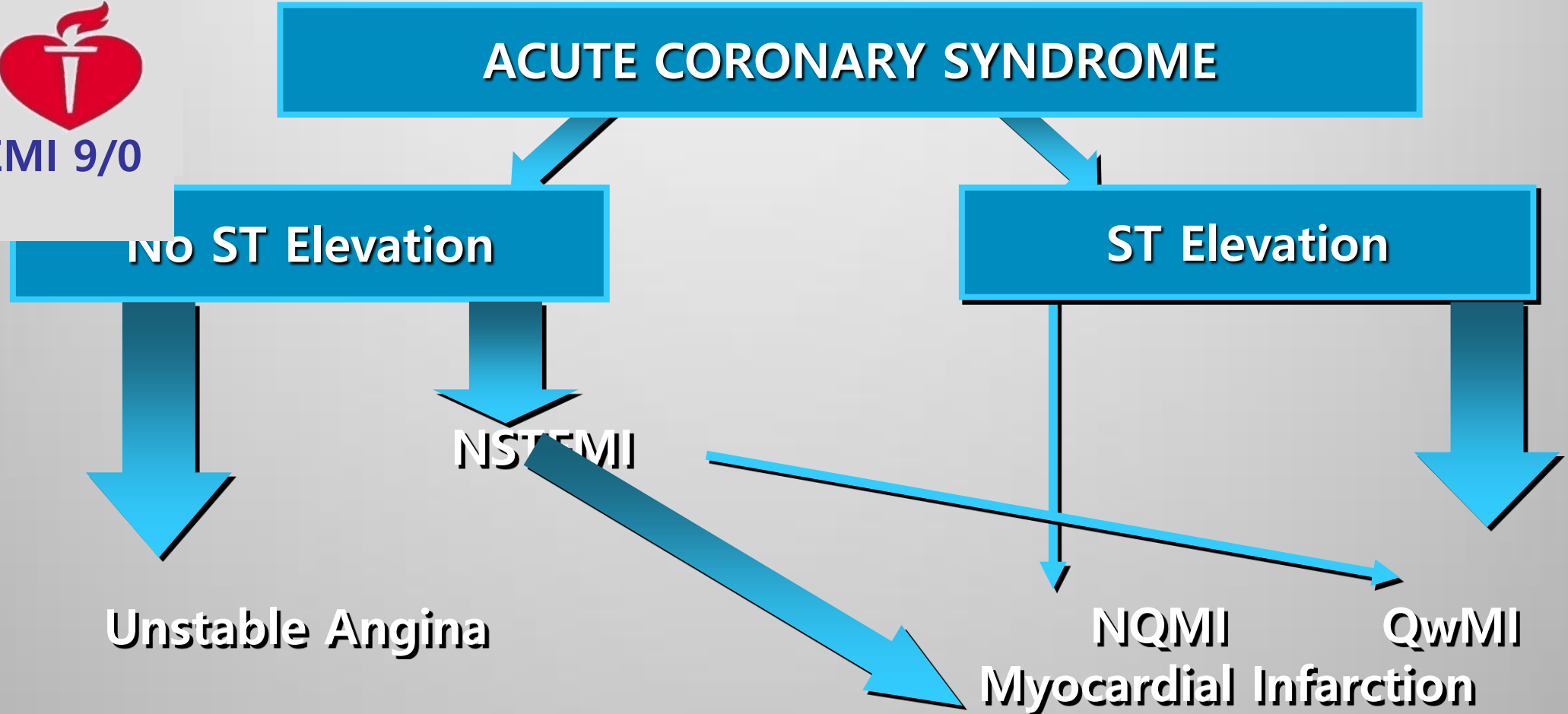
Question 4 Continued



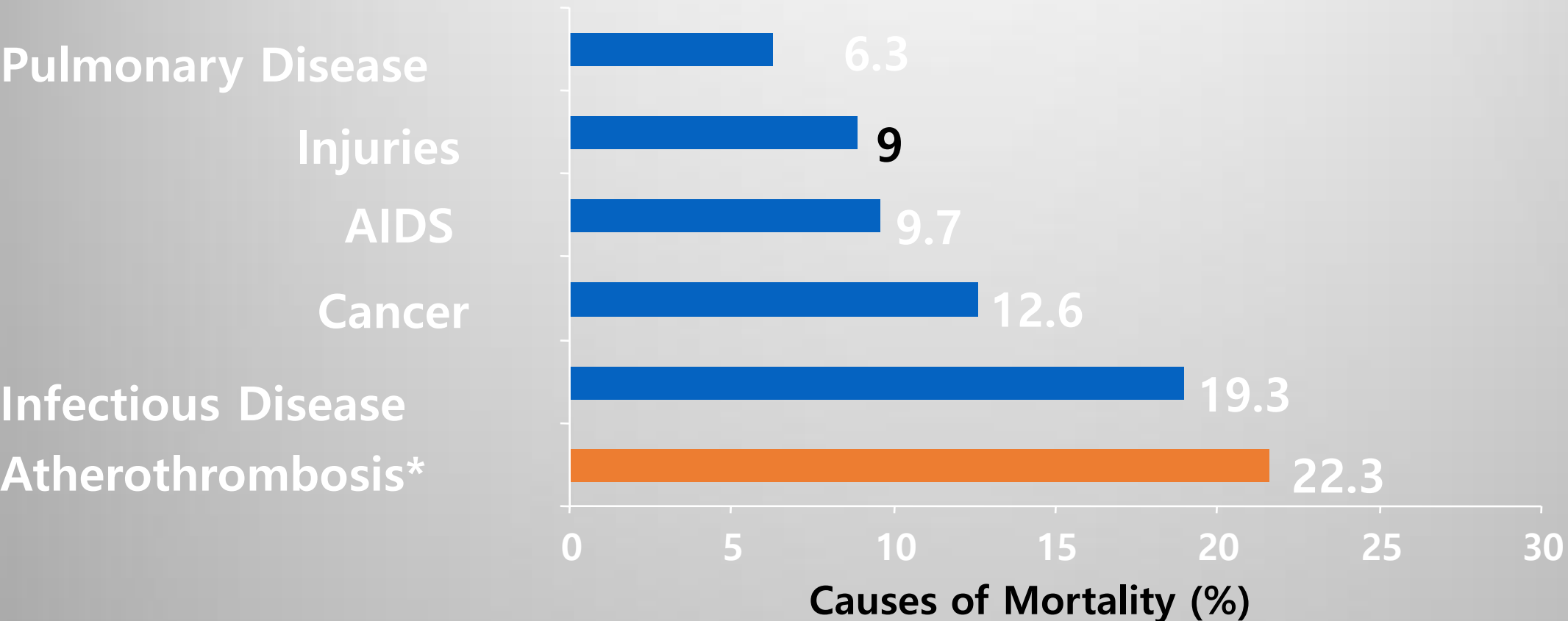
Pathogenesis



UA/NSTEMI 9/0
0



Atherothrombosis* is the Leading Cause of Death Worldwide¹



*Atherothrombosis defined as ischemic heart disease and cerebrovascular disease.

¹ *The World Health Report 2001*. Geneva: WHO; 2001.

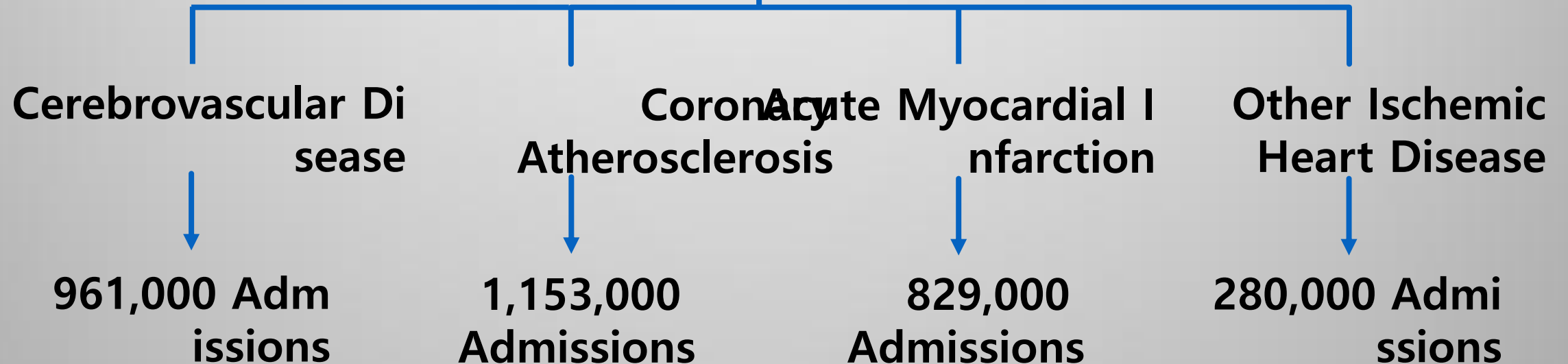
Reprod.with permission from Cannon CP. Atherothrombosis slide compendium. Available at: www.theheart.org

Hospitalizations in the US Due to Atherosclerotic Disease

Vascular Disease



3.2 Million Hospital Admissions



From Popovic JR, Hall MJ. *Advance Data*. 2001;319:1-20. Slide reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: www.theheart.org.

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology Foundation/
American Heart Association Task Force on Practice Guidelines

*Developed in Collaboration With the American College of Emergency Physicians and
Society for Cardiovascular Angiography and Interventions*

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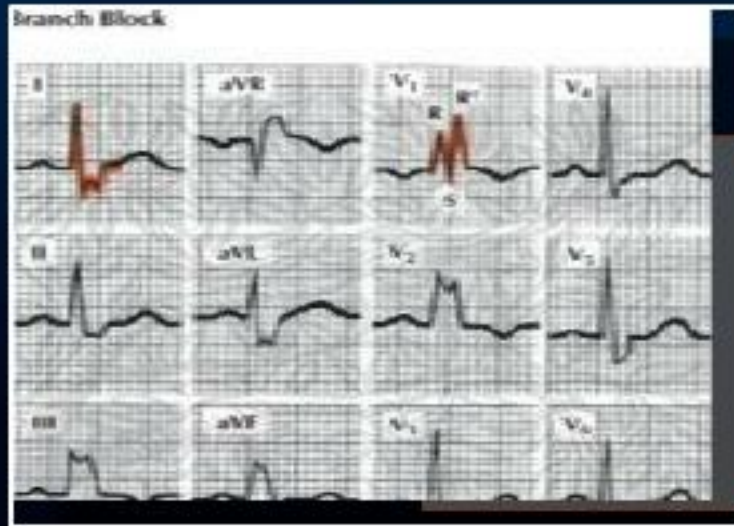
STEMI

Universal Definition & Diagnostic Criteria



ST elevation of ≥ 0.1 mV in ≥ 2 contiguous leads

men: ≥ 0.2 ; women: ≥ 0.15 mV in V₂₋₃



“New” (L)BBB

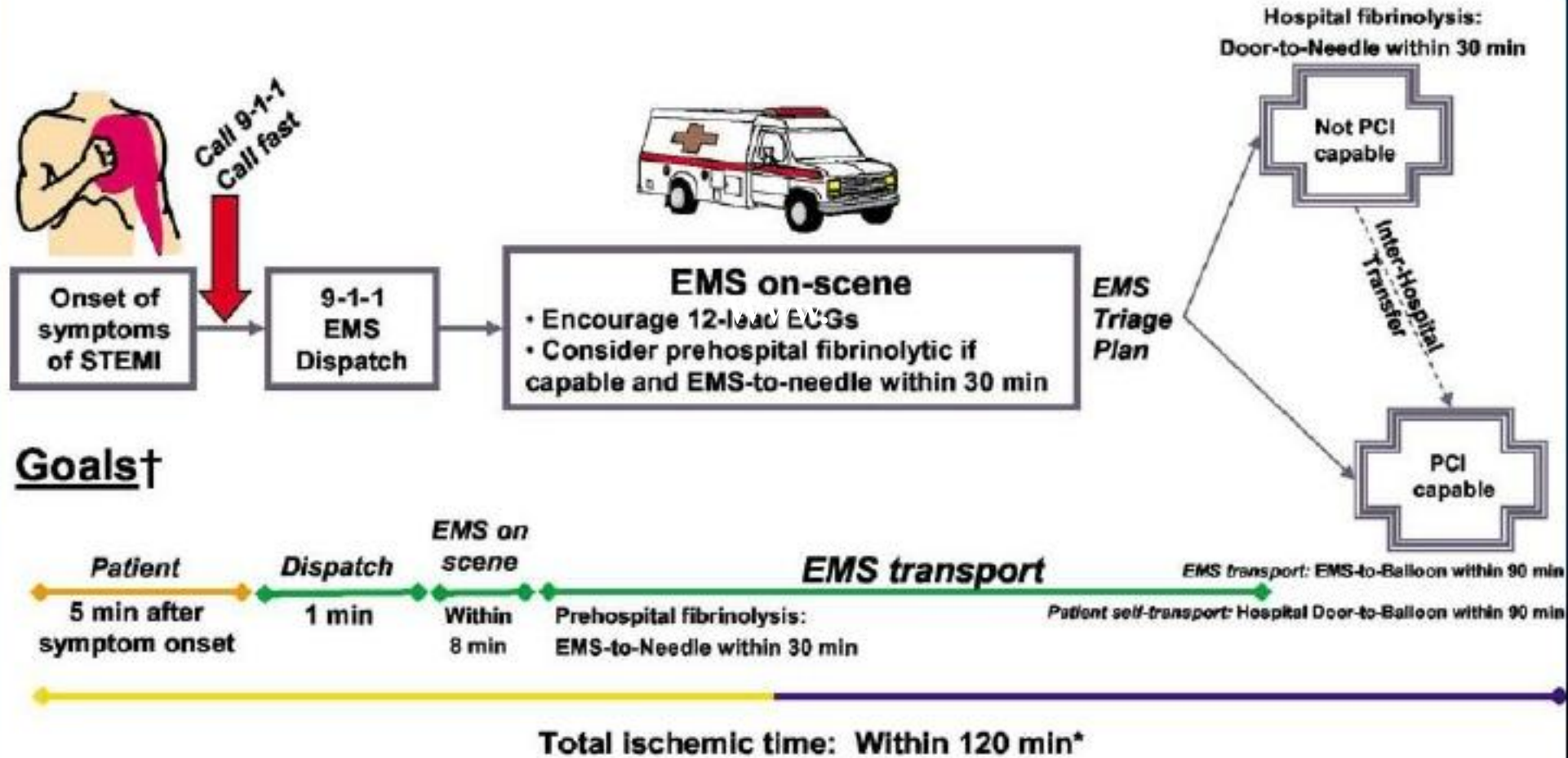
N.B. Repeat ECG q5-10 min if Non-diagnostic

STEMI

Early Management

- All acute STEMI warrant reperfusion unless contraindicated
 - patient refuses
 - limited life expectancy from other non-reversible diseases
- Resolution of symptoms is not a reason to delay/cancel reperfusion

STEMI Management Algorithm



Door-In-Door-Out

DIDO Performance Measure

- Accountability for hospitals transferring to PCI facility
 - Impacts “First contact to balloon time”

ACTION Registry Transfers (n=14821)

DIDO and In-Hospital Mortality

DIDO \leq 30 min
2.7% Mortality



DIDO $>$ 30 min
5.9% Mortality

Some Definitions

Importance of *Strategy*

Fibrinolysis

- Thrombolytic therapy given as stand-alone reperfusion therapy

Primary PCI

- No thrombolytic therapy given

Rescue PCI

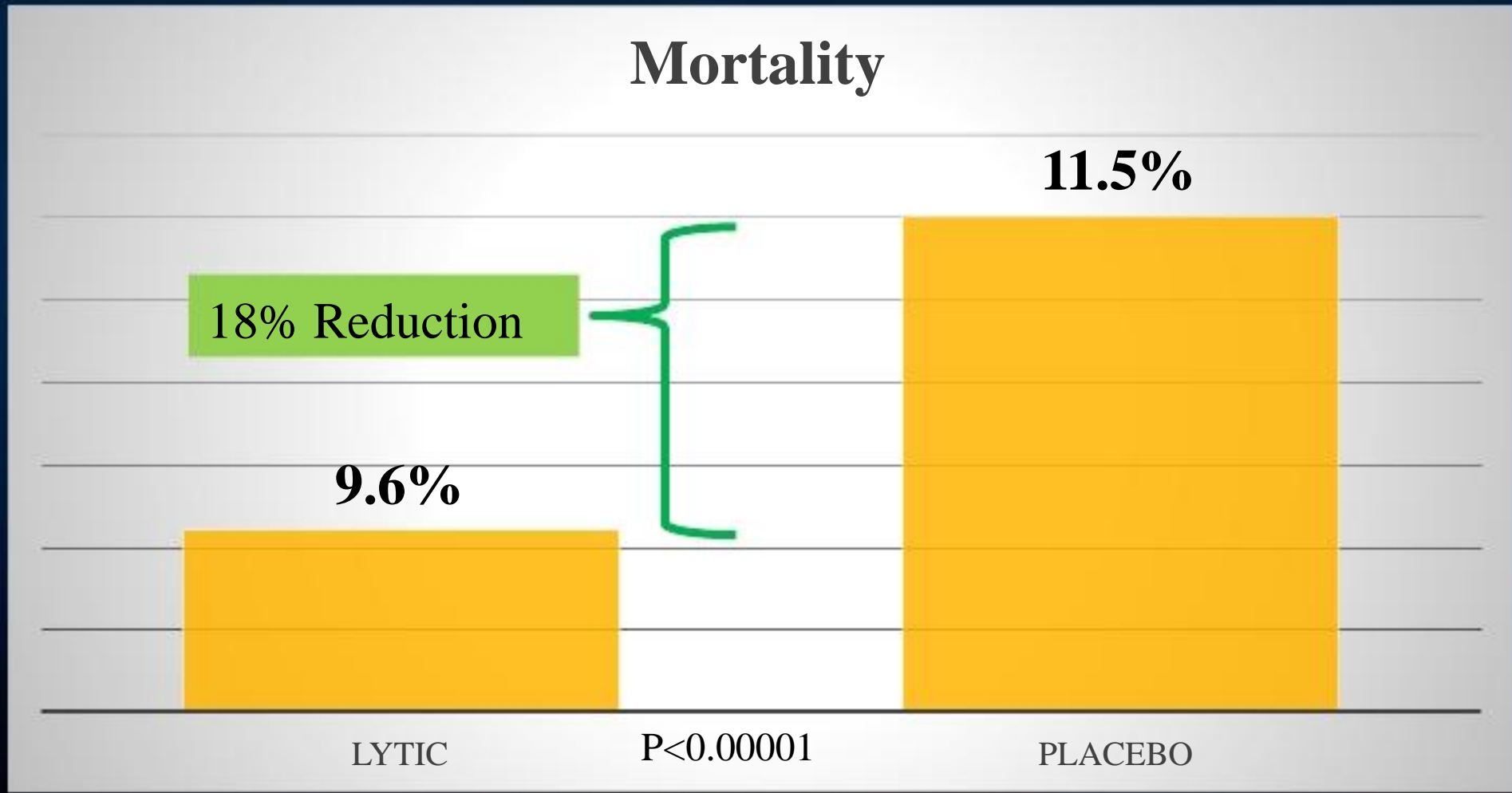
- PCI after failed thrombolytic therapy

Pharmaco-Invasive Strategy

- Thrombolytic therapy followed by elective routine angiography \pm PCI

35-Day Mortality Reduction with Thrombolysis

58,600 Patients – 9 Trials



True for:
BBB
Anterior MI
Inferior MI

Mortality
higher in ST
depression

Why Consider Primary PCI?

Shortcomings of Fibrinolysis

Thrombolytic “Ceiling”

- Normal TIMI 3 flow in only 50%

Hemorrhagic Complications

- 1% IC bleeding (frequently fatal)
- Vascular, GI, GU

Elderly

- Most to gain from reperfusion
- Up to 40% have contraindications

Contraindications to Fibrinolysis

Absolute

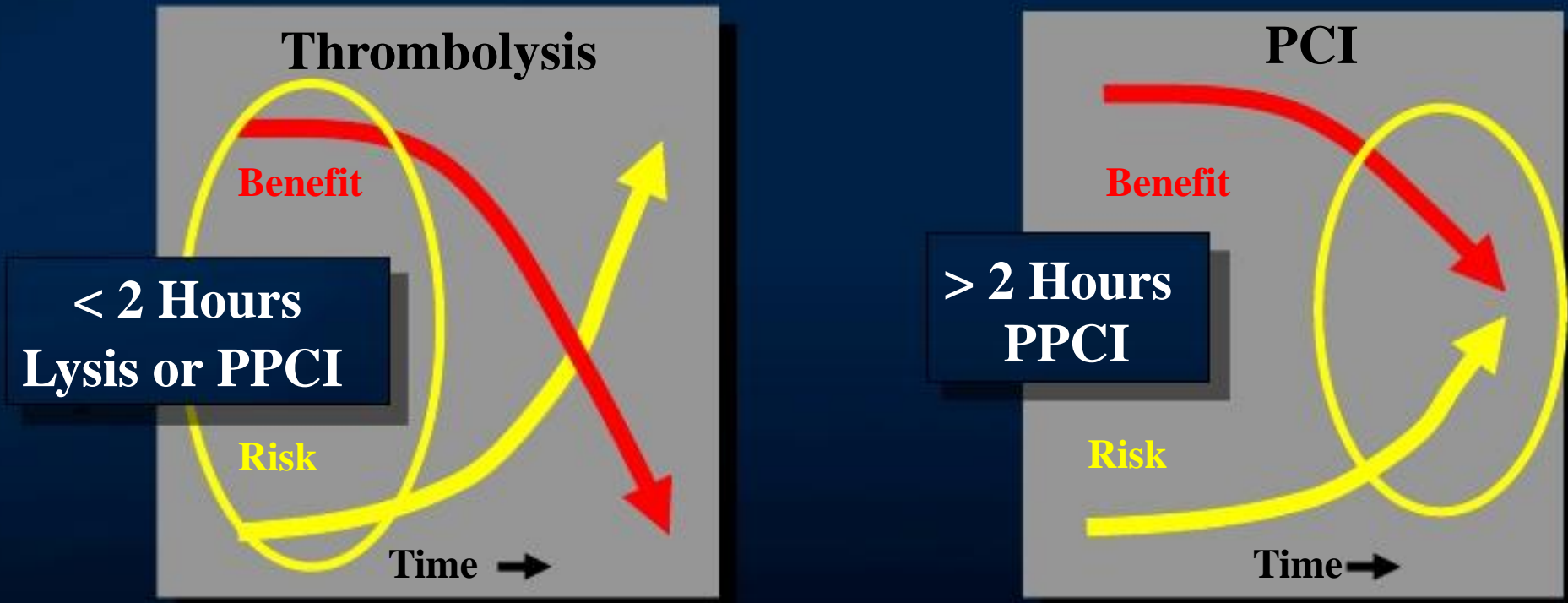
- Any prior IC hemorrhage
- Known structural cerebral vascular disease (e.g. AVM, aneurysm)
- Known malignant IC neoplasm
- Ischemic CVA <3 months (*except w/in 3 hrs*)
- Significant closed head/facial trauma <3 mo
- Suspected aortic dissection
- Active bleeding (excluding menses)

Relative

- Oral Anticoagulant therapy
- Severe HTN (SBP >180, BPD >110)
- Traumatic or prolonged CPR (>10min)
- Internal bleeding w/in 2-4 wks
- Non-compressible vascular puncture
- Pregnancy
- Prior ischemic stroke >3 mo
- Active Peptic Ulcer

Consider Primary PCI

Time to Reperfusion



Consider Pharmaco-Invasive Approach

PTCA in Acute MI

Historical Era

- Thrombolytics
- PTCA

Randomized trials
Stents

Randomized trials of stents
Stents + abciximab

Stents + tirofiban or eptifibatide

- ↓ Lytics
- GP IIb/IIIa
- Stents

PAMI

Stent-PAMI

STOPAMI

CADILLAC

PTCA

PTCA +
abciximab

Stents +
GP IIb/III

Gusto V

1990

1992

1994

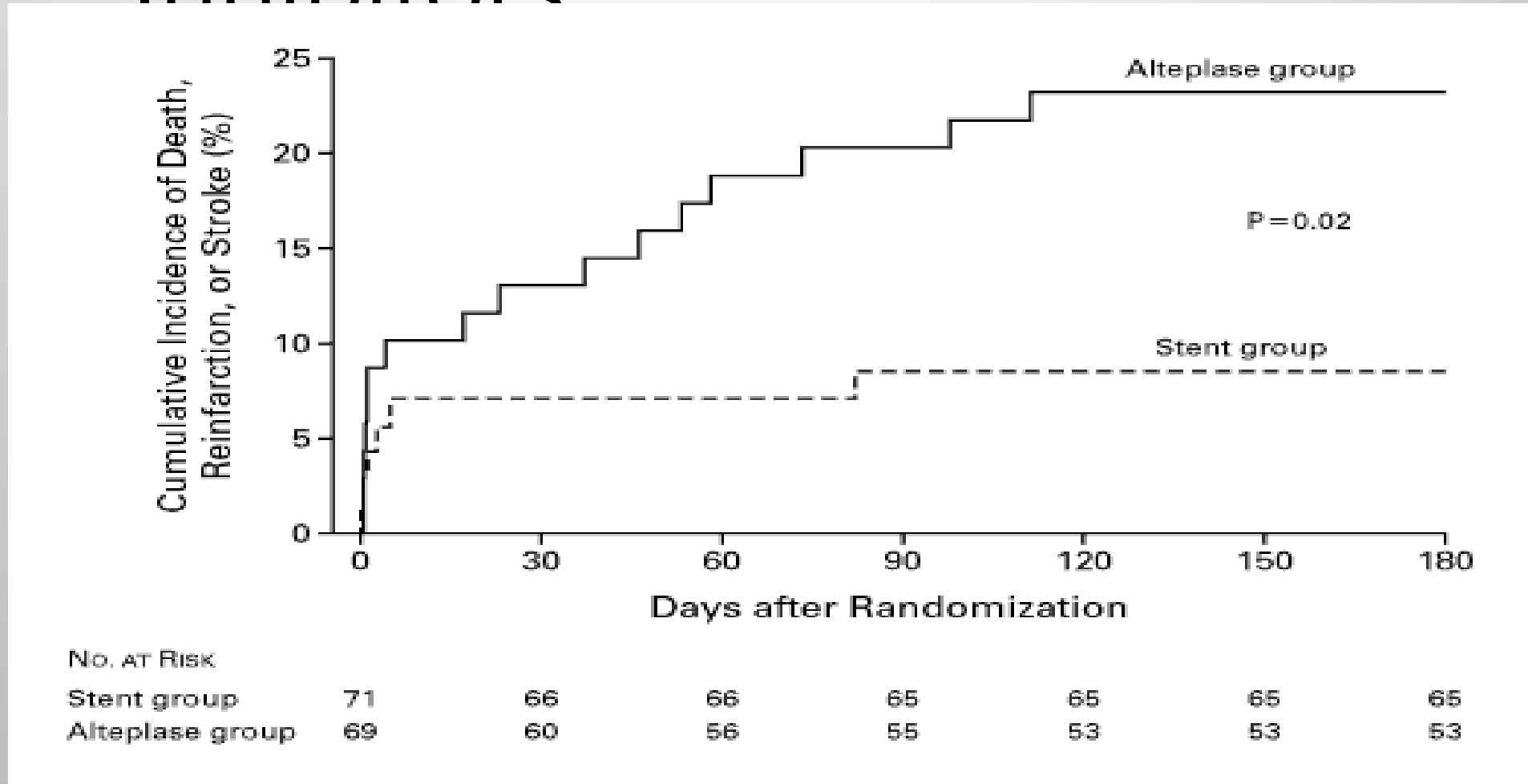
1996

1998

1999

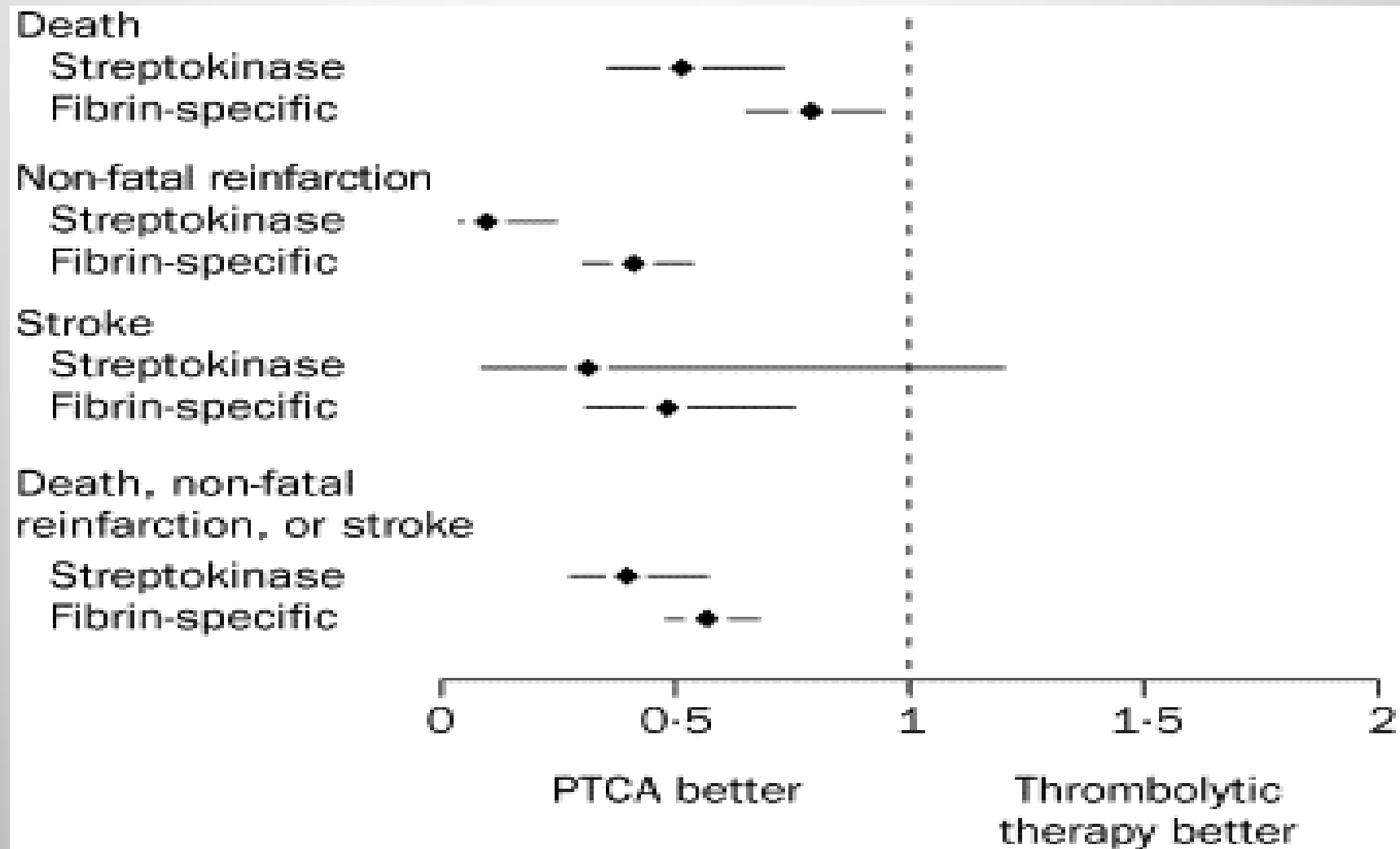
2000

Thrombolysis vs. Stent+GPIIb/IIIa Inhibitors



Schomig et al. *NEJM*, Aug 10, 2000

Revascularization: Lytics vs. PCI



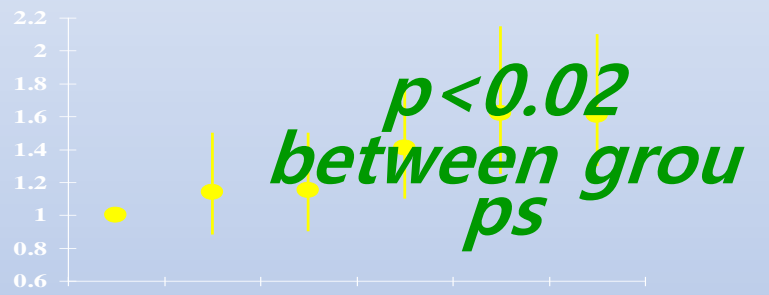
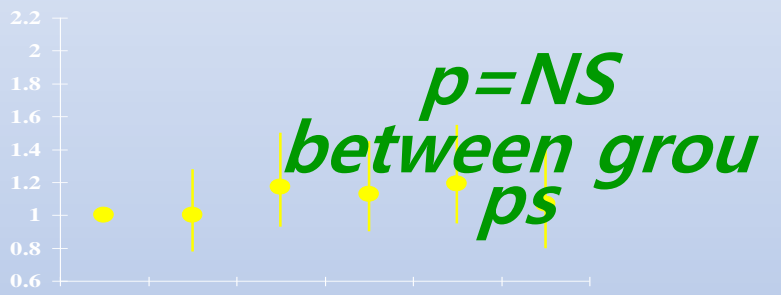
Second National Registry of Myocardial Infarction

Relationship Between Mortality & Time to PTCA

Multivariate-adjusted odds of in-hospital mortality

Symptom-onset-to-balloon time

Door-to-balloon time



0-2 >2-3 >3-4 >4-6 >6
-12 >12

0-60 61-90 91-120 121-150 15
1-180 >180

Time (hours)

Time (hours)

N: 2176 6353 5718 5852 4680
6616 4461 2627 5412

2301 2230 5734

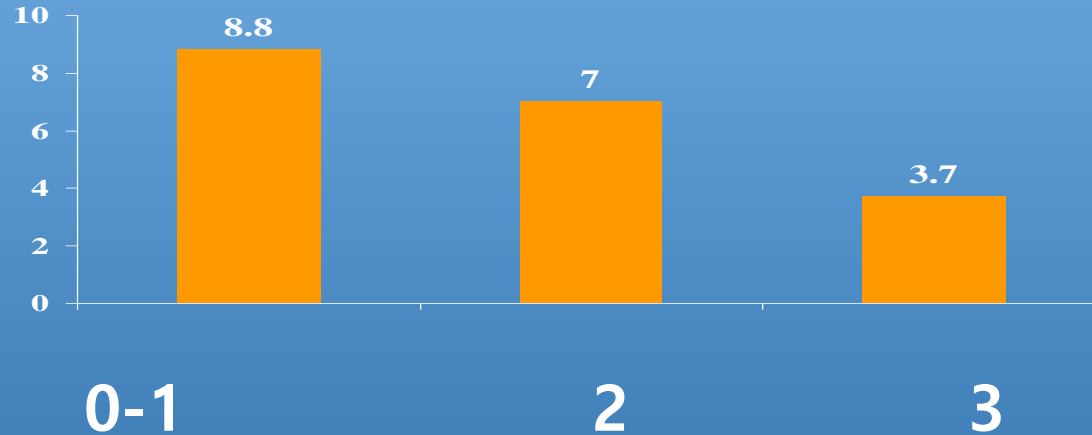
Cannon et al. JAMA 2000;283:2941

Early TIMI Flow Influences Mortality

- Meta-analysis of 8 trials in 3969 patients

p < 0.01

**Mortality
(%)**



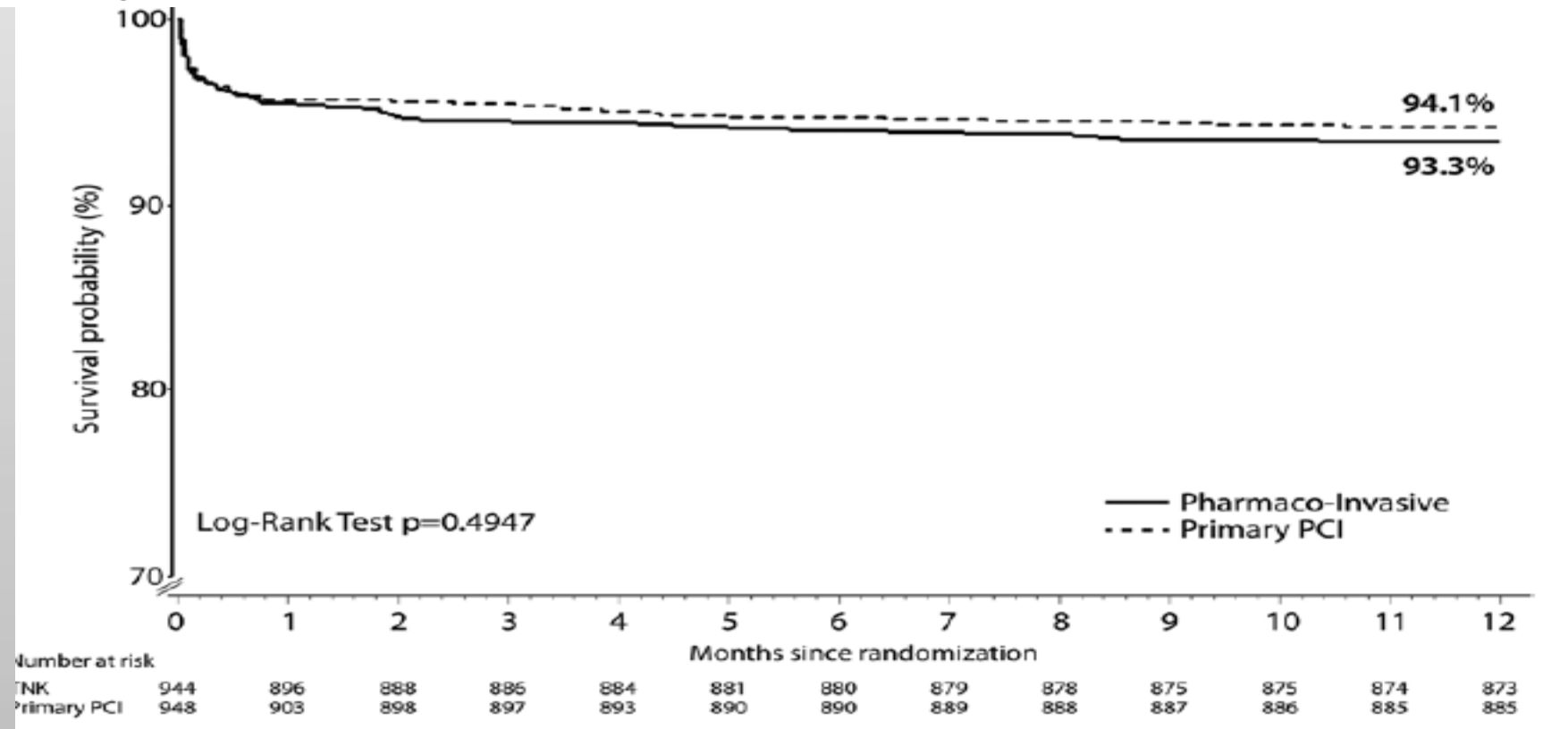
TIMI flow grade

Anderson et al. Am J Cardiol 1996;78:1-

PHARMACOINVASIVE : STREAM

ST-Segment-Elevation Myocardial Infarction Patients Randomized to a Pharmaco-Invasive Strategy or Primary Percutaneous Coronary Intervention Strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-Year Mortality Follow-Up

Peter R. Sinnaeve, MD, PhD; Paul W. Armstrong, MD; Anthony H. Gershlick, MD;
Patrick Goldstein, MD; Robert Wilcox, MD; Yves Lambert, MD; Thierry Danays, MD;
Louis Soulat, MD; Sigrun Halvorsen, MD, PhD; Fernando Rosell Ortiz, MD, PhD;
Kathleen Vandenberghe, PhD; Anne Regelin, PhD; Erich Bluhmki, PhD; Kris Bogaerts, PhD;
Frans Van de Werf, MD, PhD; for the STREAM investigators*



ST-segment elevation myocardial infarction, systems of care. An urgent need for policies to co-ordinate care in order to decrease in-hospital mortality



Ali Osama Malik ^a, Oliver Abela ^b, Gayle Allenback ^c, Subodh Devabhaktuni ^b, Calvin Lui ^b, Aditi Singh ^a, Jimmy Diep ^b, Takashi Yamashita ^d, Ji Won Yoo ^a, Sanjay Malhotra ^b, Chowdhury Ahsan ^{b,*}

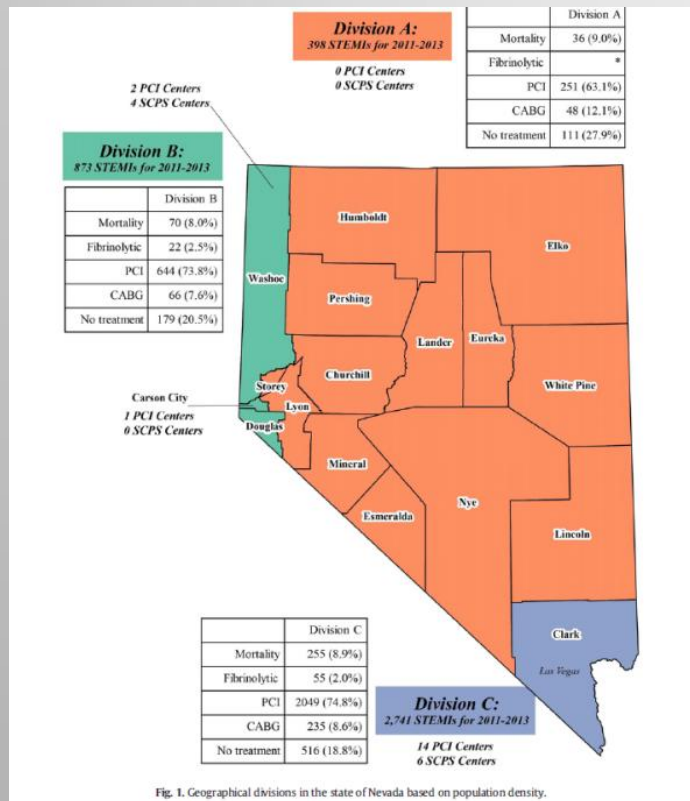
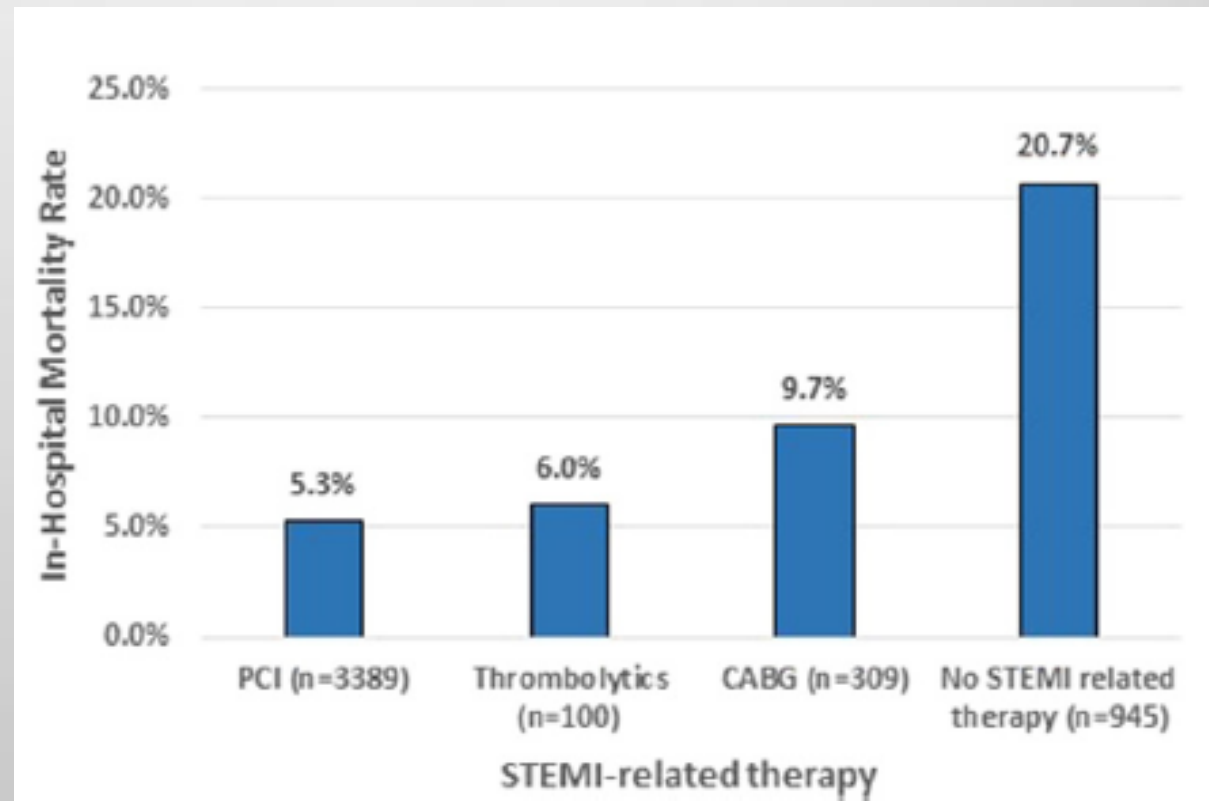
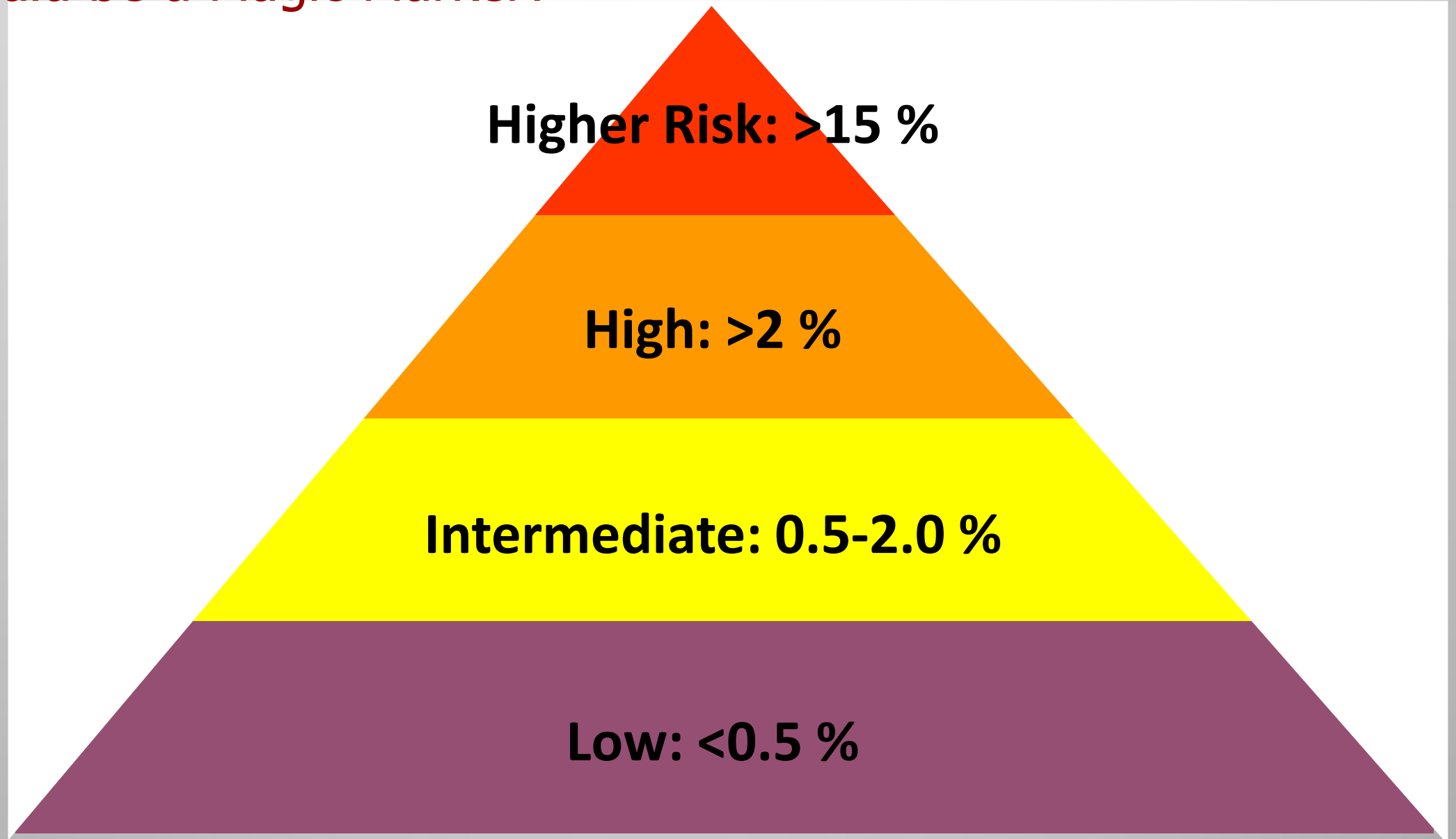


Fig. 1. Geographical divisions in the state of Nevada based on population density.



Should We Expect a Magic Marker? What Would be a Magic Marker?



On Clinton, Cholesterol & Coronary Concepts...

<http://story.news.yahoo.com/news?g=events/pl/080601billclinton&a=&tmpl=sl&ns=&l=o&e=69>



1996 = o&printer=

1992

Weight 226 #

Height 6-2

BMI 29.1

BP 130/70

HR 75

Glucose 104

Bruce V 91%

No EKG Δ

1999

TC 196

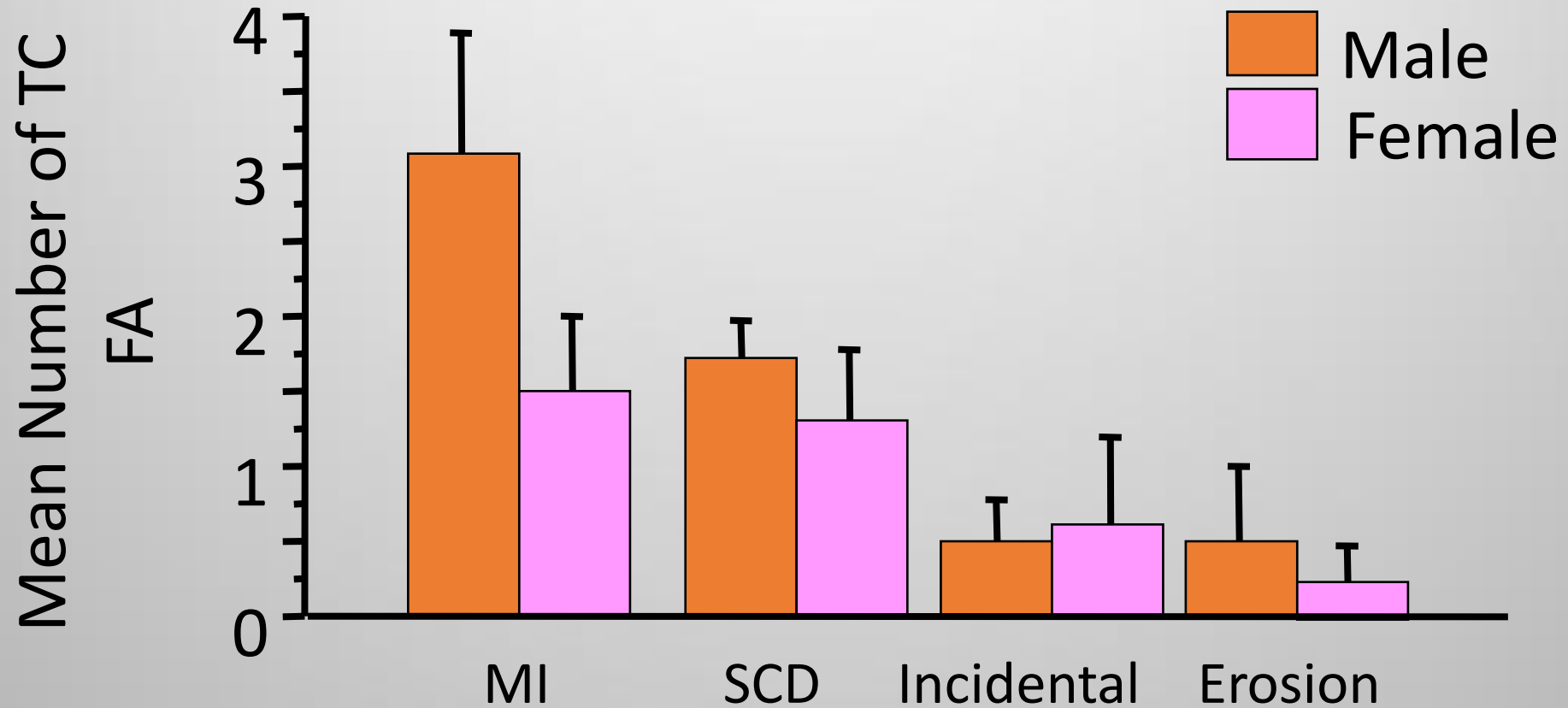
TG 80

HDL 46

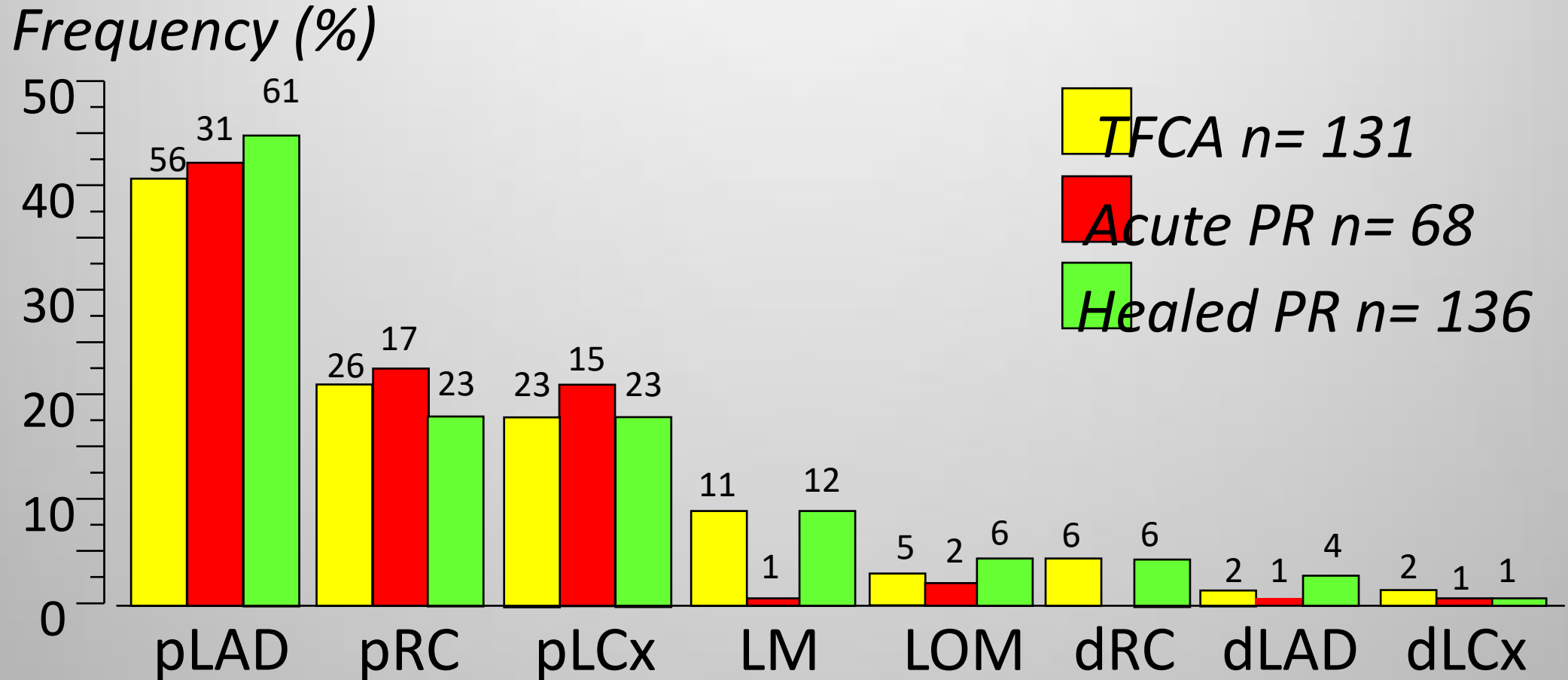
LDL 134

2001

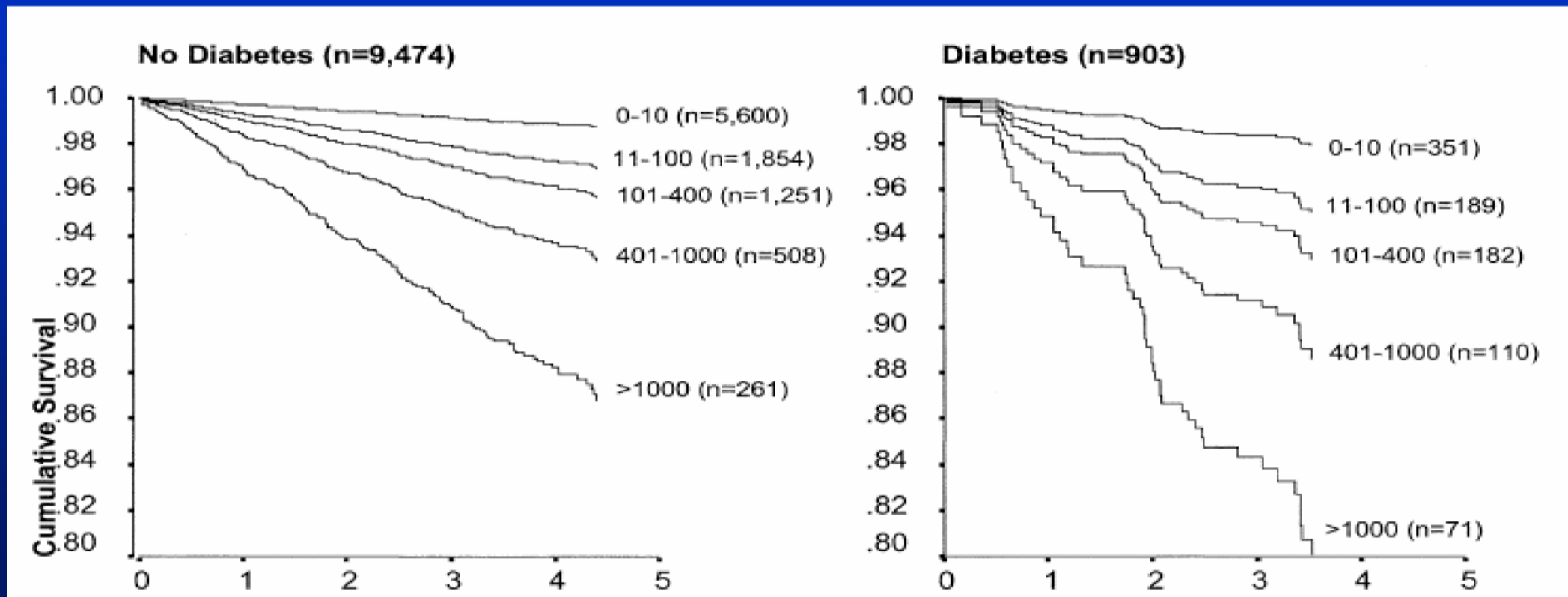
TCFA in ACS are Usually Not Many



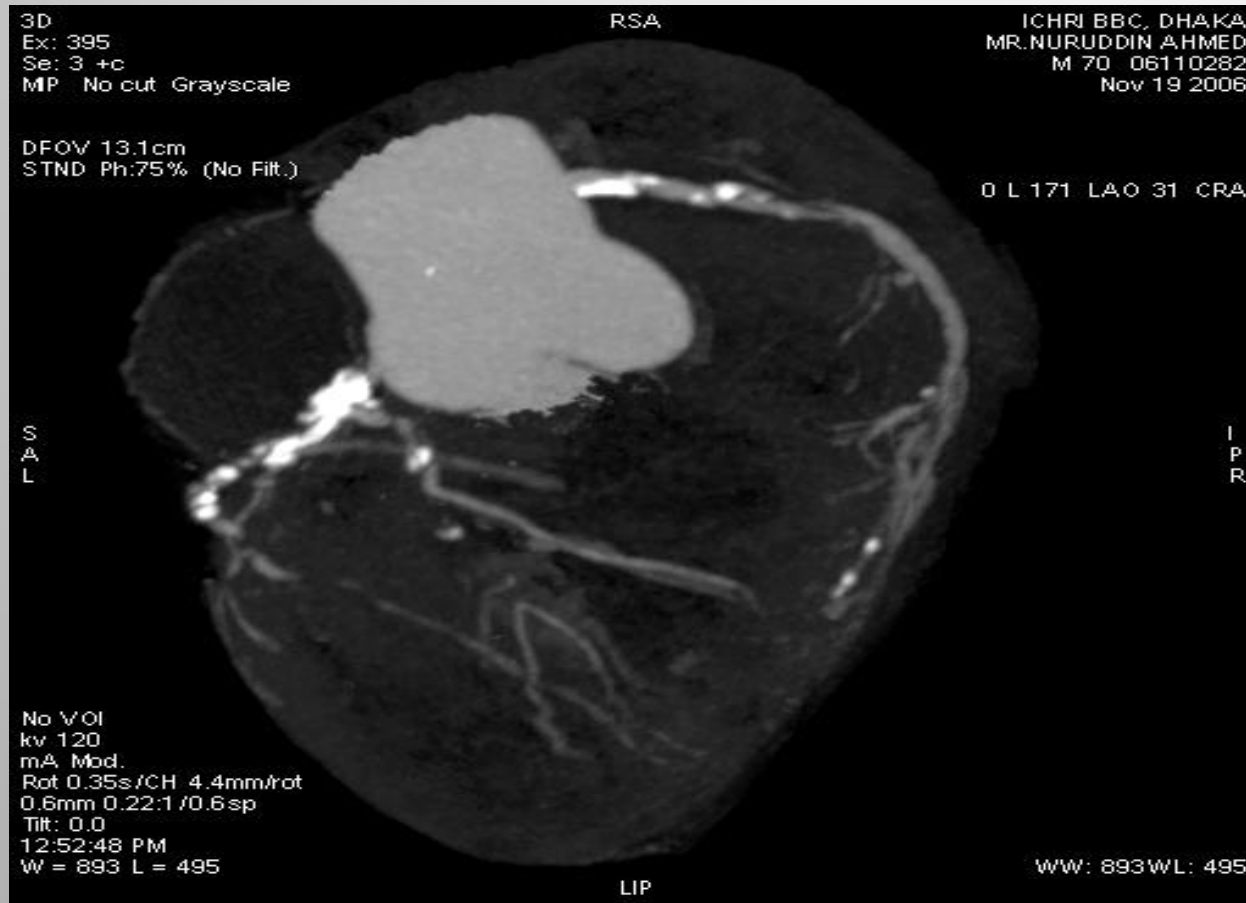
Unstable Lesions are Located Proximally



EBT 5 year All-Cause Mortality



Detection & quantification of calcium within the coronary vessels



Calcification in the vessel wall is an indicator of degree of damage that has occurred to the vessels.

A high calcium score is consistent with a moderate to high risk of coronary artery disease.

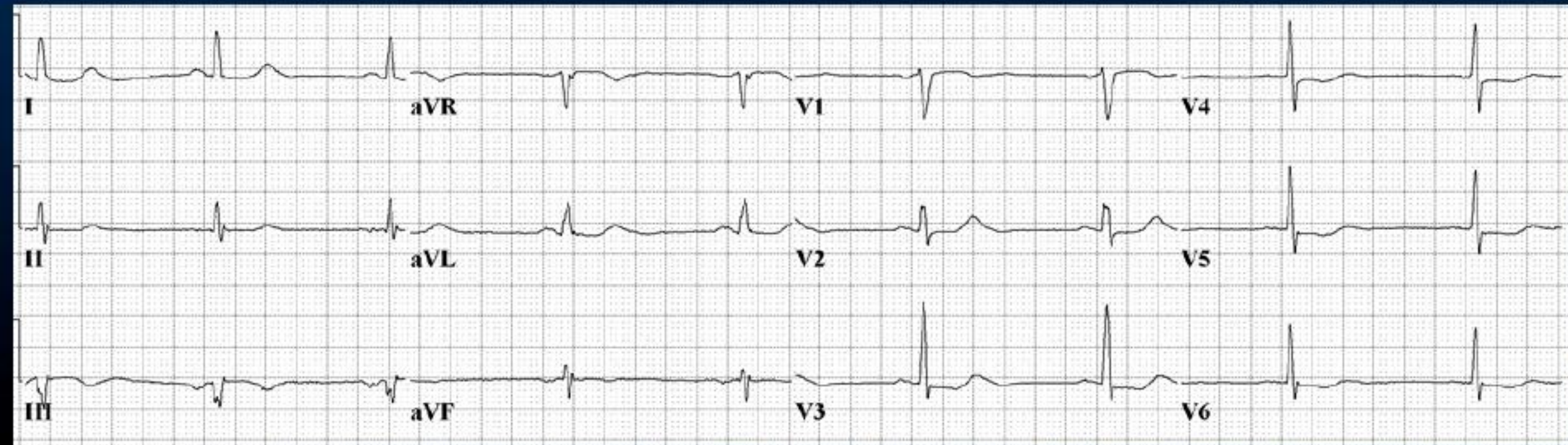
A negative calcium score is predictive of a comparatively very low incidence of coronary artery disease.

The coronary arteries are seen similar to as seen on a regular catheter angiogram.

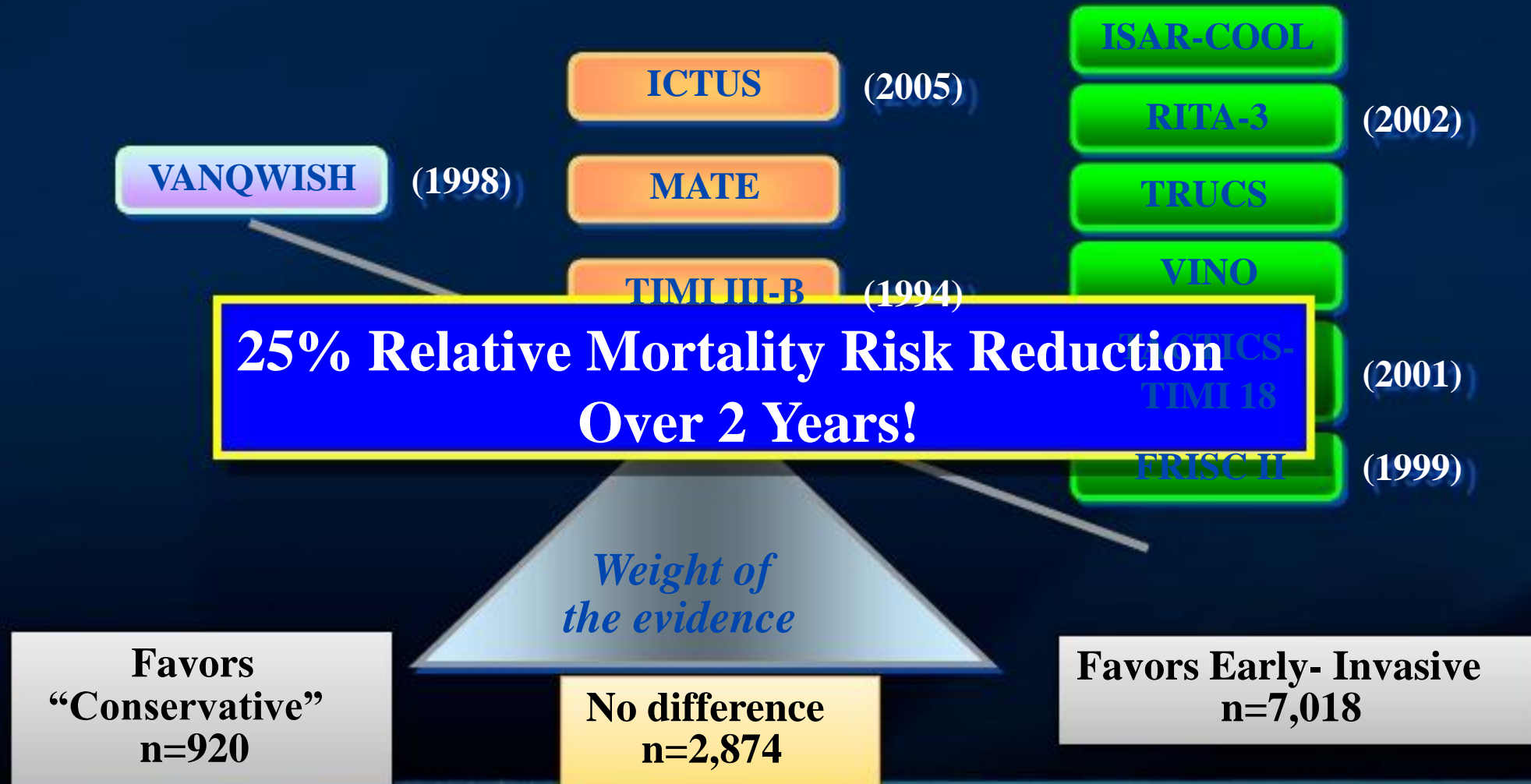
Question 1

A 70yo male presents with intermittent central chest pressure beginning at rest last evening and is now pain free. He takes aspirin for “arthritis” and treatment for diabetes and hypertension.

HR is 90 and BP 112/80. Exam is unremarkable except for expiratory wheeze. ECG shown below. His initial cardiac troponin T is 0.5 ng/mL (normal <0.01) and creatinine 1.8 mg/dL.



Ischemia-Guided vs Early-Invasive Strategy



Non-Coronary Troponin Elevation

Cardiac contusion, or other trauma including surgery, ablation, pacing, etc

Congestive heart failure – acute and chronic

Aortic dissection

Hypertrophic cardiomyopathy

Tachy- or bradyarrhythmias, or heart block

Apical ballooning syndrome

Rhabdomyolysis with cardiac injury

Pulmonary embolism, severe pulmonary hypertension

Renal failure

Acute neurological disease, including stroke

or subarachnoid hemorrhage

Infiltrative diseases, eg, amyloidosis, haemochromatosis, sarcoidosis, and scleroderma

Inflammatory disease, eg, myocarditis or myocardial extension of endo-/pericarditis

Drug toxicity or toxins

Critically ill patients, especially with respiratory failure or sepsis

Burns, especially if affecting >30% of body surface area

Extreme exertion

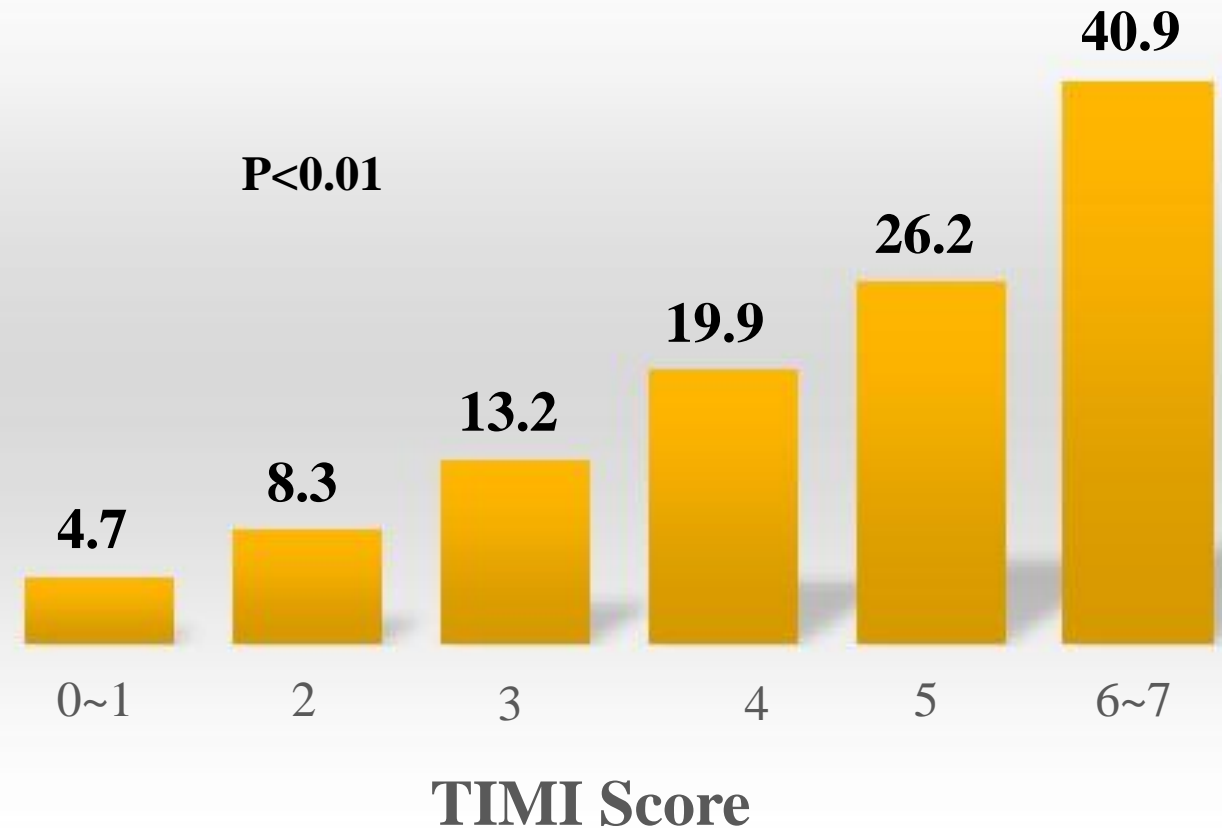
TIMI Risk Score Predicts Outcome*

14-Day Event Rates

TIMI Score (1 pt each)

- ↑cardiac biomarkers
- ≥ 2 CP epsd in 24hrs
- ≥ 3 CAD risk factors
- Age >65
- ASA w/in 7 days
- Prior CAD
- ST-segment deviation

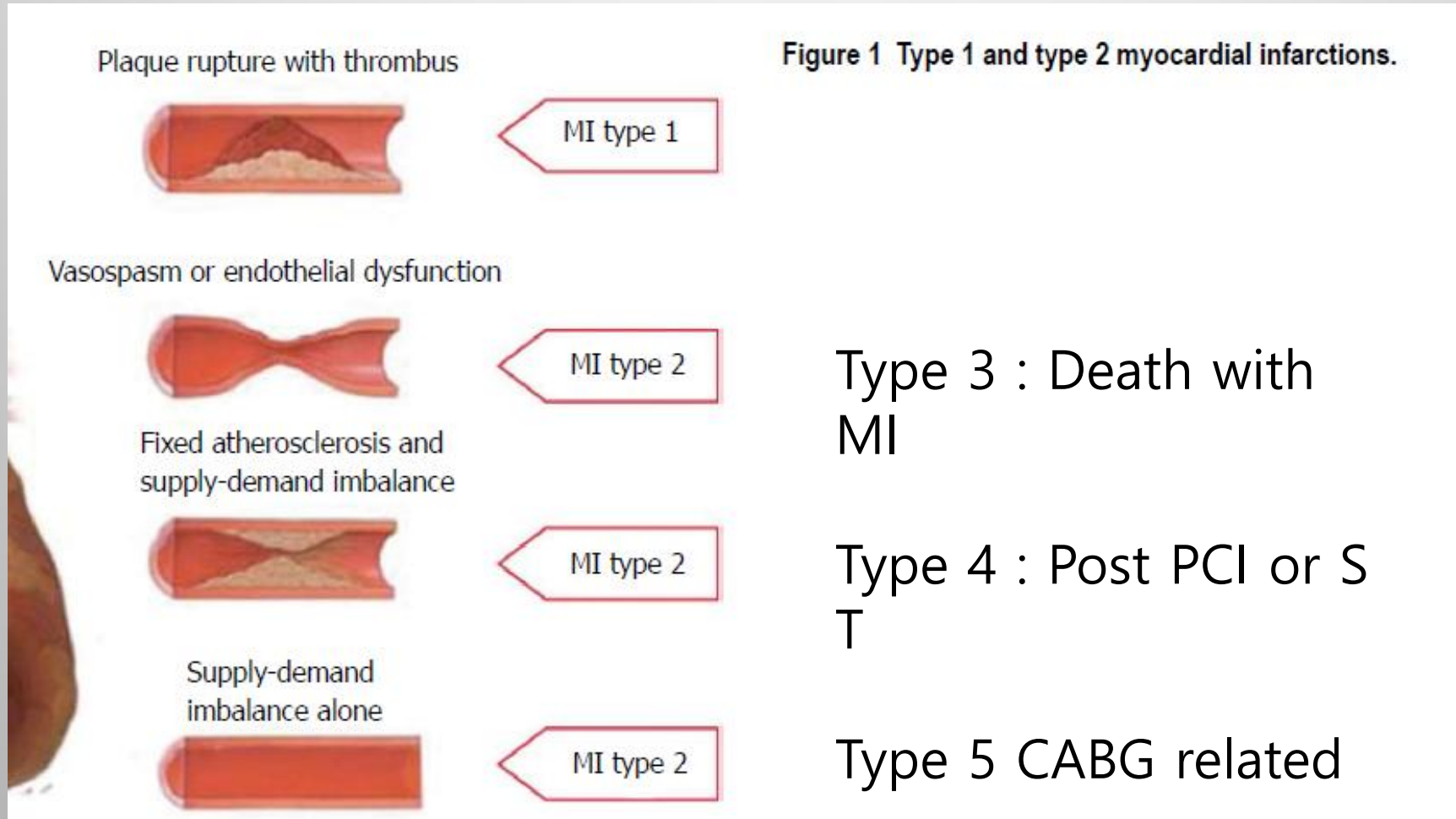
Death, MI, Ischemia requiring
revascularization at 14 days (%)



*TIMI risk score now validated in 6 trials

Antman EM, et al. JAMA 2000; 284:835-842

Universal Definition of MI



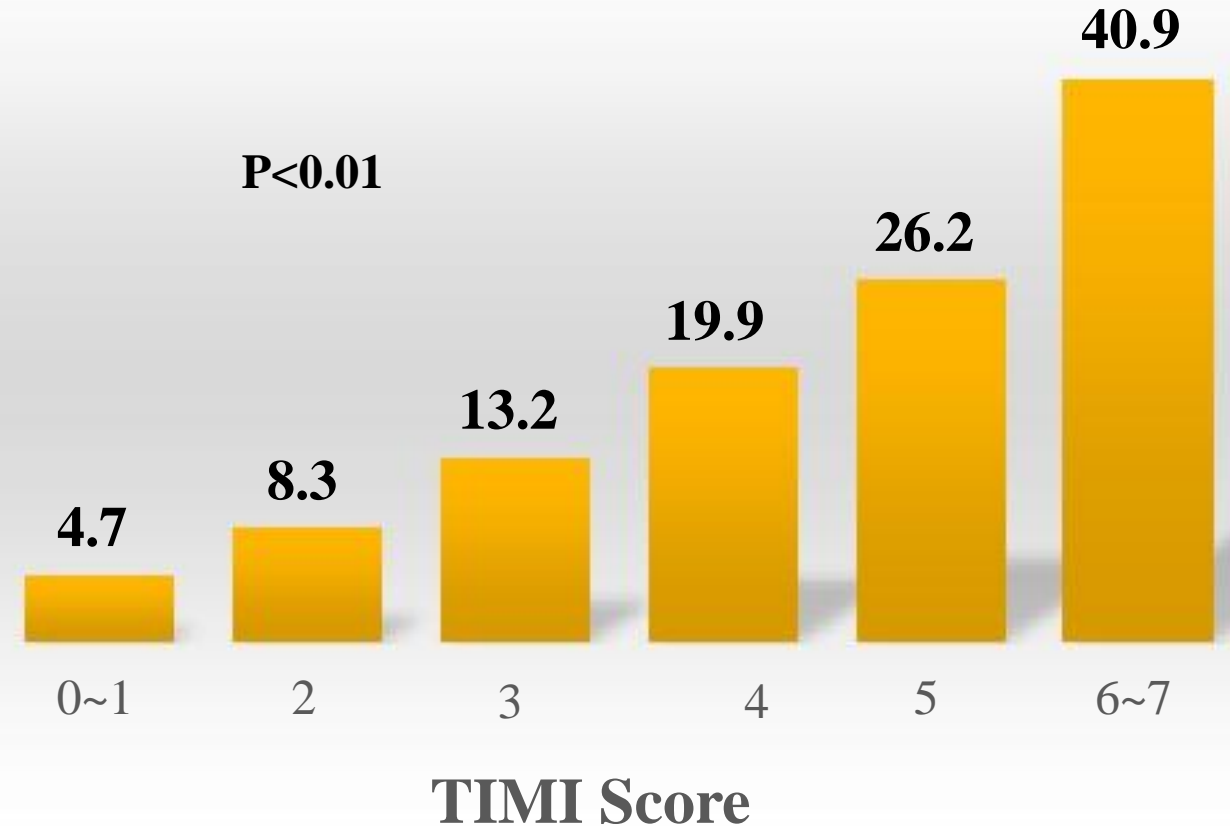
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Death, MI, Ischemia requiring
revascularization at 14 days (%)



*TIMI risk score now validated in 6 trials

Antman EM, et al. JAMA 2000; 284:835-842

Therapy in NSTEMI ACS is Complex

Anticoagulant	UFH	LMWH	Fondaparinux	Bivalirudin
Antiplatelet	ASA (dose)	Clopidogrel (dose)	Prasugrel	Ticagrelor
IV Antiplatelet	None	Abciximab	Tirofiban	Eptifibatide
Cath Strategy	Immediate	Early	Delayed	Never

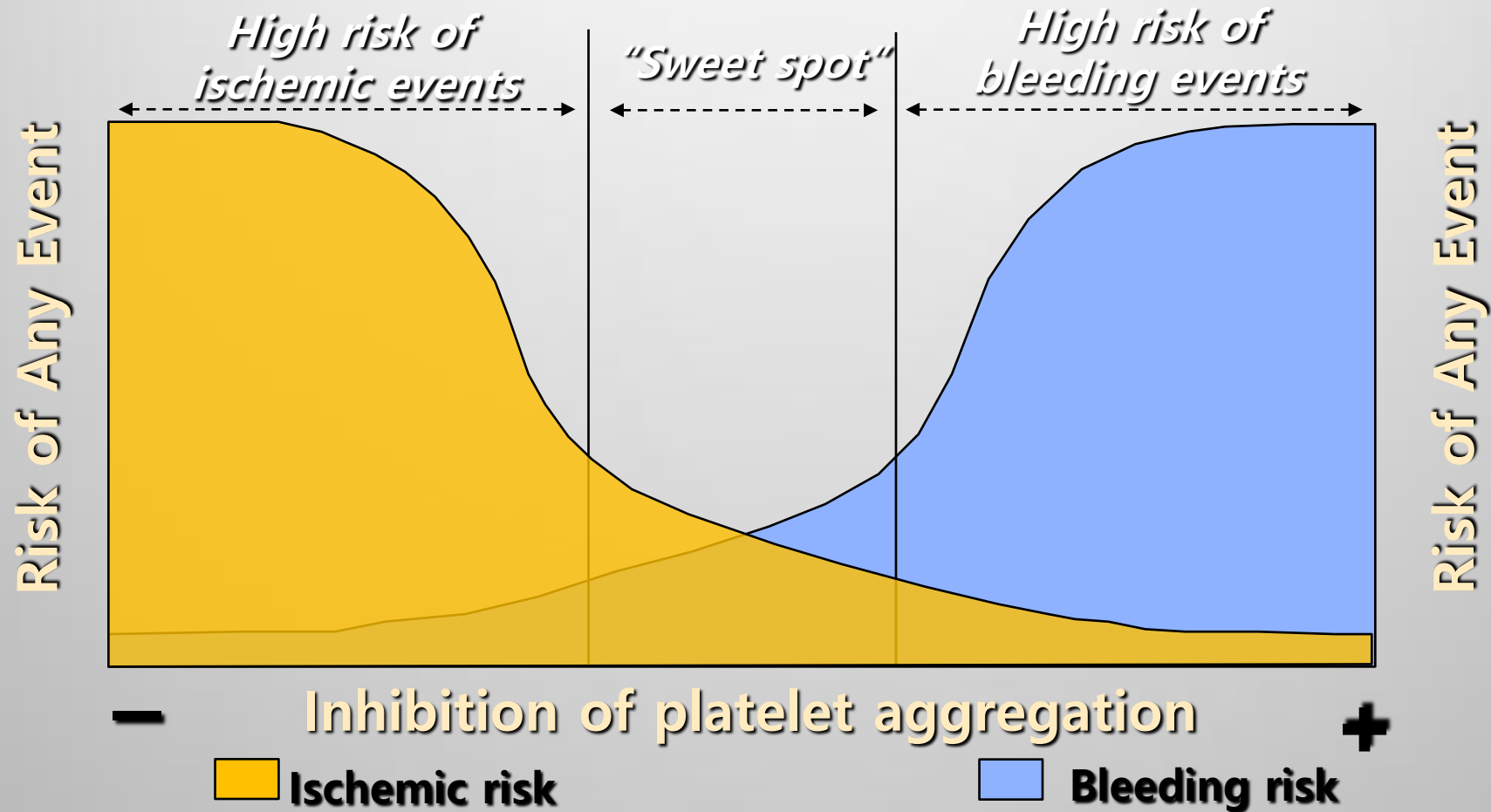
256 Different Combinations with different effects on bleeding and thrombosis risk!

Currently Available Oral Antiplatelet Agents

DRUG	DRUG CLASS	CLINICAL CHARACTERISTICS
Aspirin	COX-1 inhibitor	PO, Irreversible binding
Ticlopidine	P2Y ₁₂ (ADP) receptor antagonist	PO, Irreversible binding
Clopidogrel	P2Y ₁₂ (ADP) receptor antagonist	PO, Irreversible binding
Prasugrel	P2Y ₁₂ (ADP) receptor antagonist	PO, Irreversible binding
Cilostazol	PDE inhibitor; Increase cAMP	PO, Reversible inhibition
Dipyridamole	PDE inhibitor; Increase cAMP	PO, Reversible inhibition

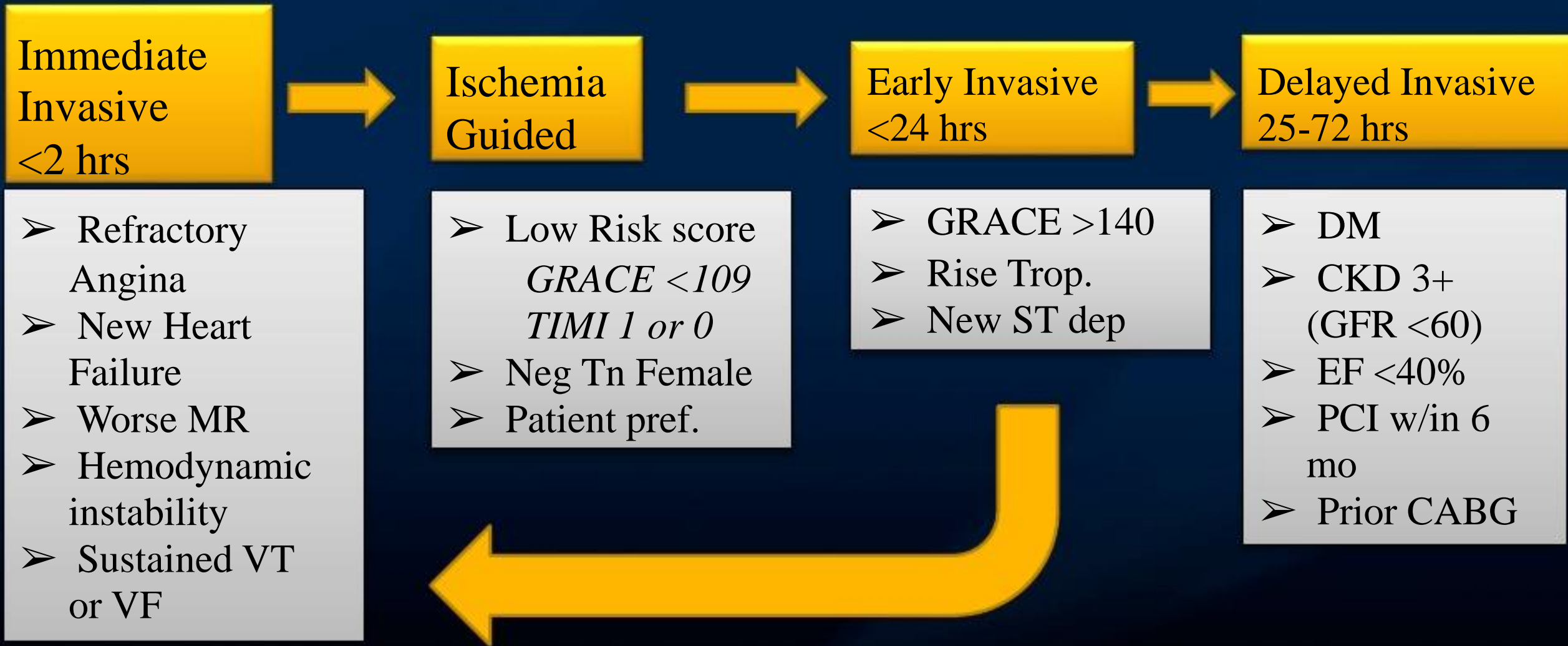
COX = cyclooxygenase; ADP = adenosine diphosphate; PDE = phosphodiesterase

Platelet Inhibition Related to the Risk of Ischemic and Bleeding Events



Early Invasive vs Ischemia-Guided Strategy

Selection Factors and Timing



Conclusion: Therapeutic Treatment Options for ACS

- **STEMI:**

- Thrombolytic therapy
- Percutaneous coronary intervention (PCI)
- Combination of thrombolytics+PCI
- Coronary artery bypass surgery

- **Non-STEMI/USA; Evaluate ; antipalletelet, anticoagulation; GDMT and Decide on Revascularization-Early!**