2005 춘계 대한 순환기학회

Acute Coronary Syndrome: Interventional Strategy

Youngkeun Ahn, MD, PhD, FACC, FSCAI

Department of Cardiology
Program in Gene and Cell Therapy,
The Heart Center of Chonnam National University,
GwangJu, Korea

STEMI

Interventional Management

Case presentation

57 yo wm presents with severe chest pain to a local hospital (cath lab is not available) at 1 AM. ECGs reveal an anterior wall MI.

Current treatment guidelines recommend:

A. Administer IV lytic, evaluate response to reperfusion; consider transfer if lytic therapy fails

B. Transfer for emergency angio and possible PCI

C. Administer lytic therapy; proceed with emergency transfer for cath/PCI

ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction)

Developed in Collaboration With the Canadian Cardiovascular Society

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Achieve Coronary Patency

Initial Reperfusion Therapy

- Defined as the initial strategy employed to restore blood flow to the occluded coronary artery

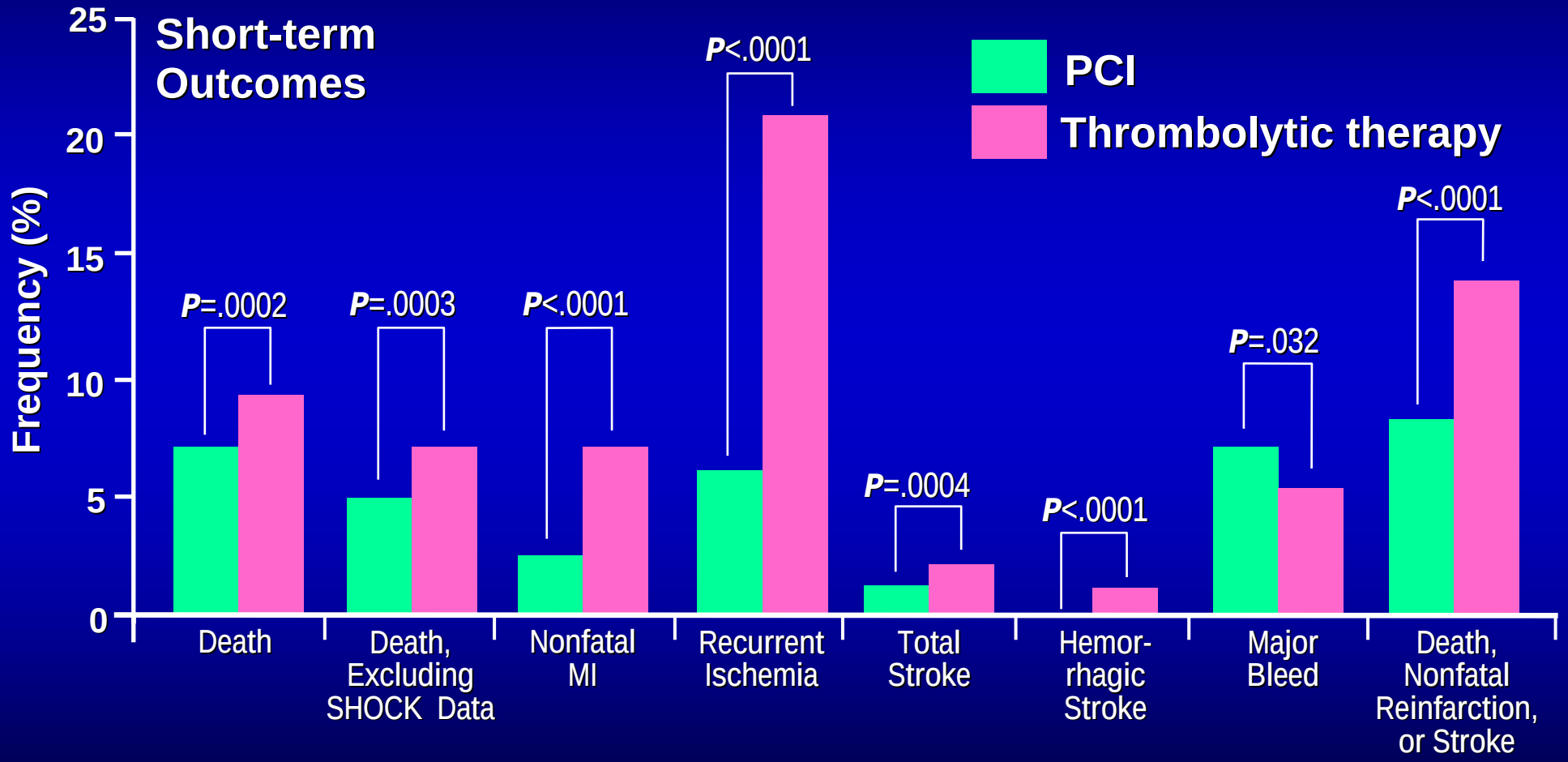
3 Major Options

- Pharmacological reperfusion
- **PCI**
- Acute surgical reperfusion
- **Rescue or Faciliated PCI**

Recent Influences of Practice

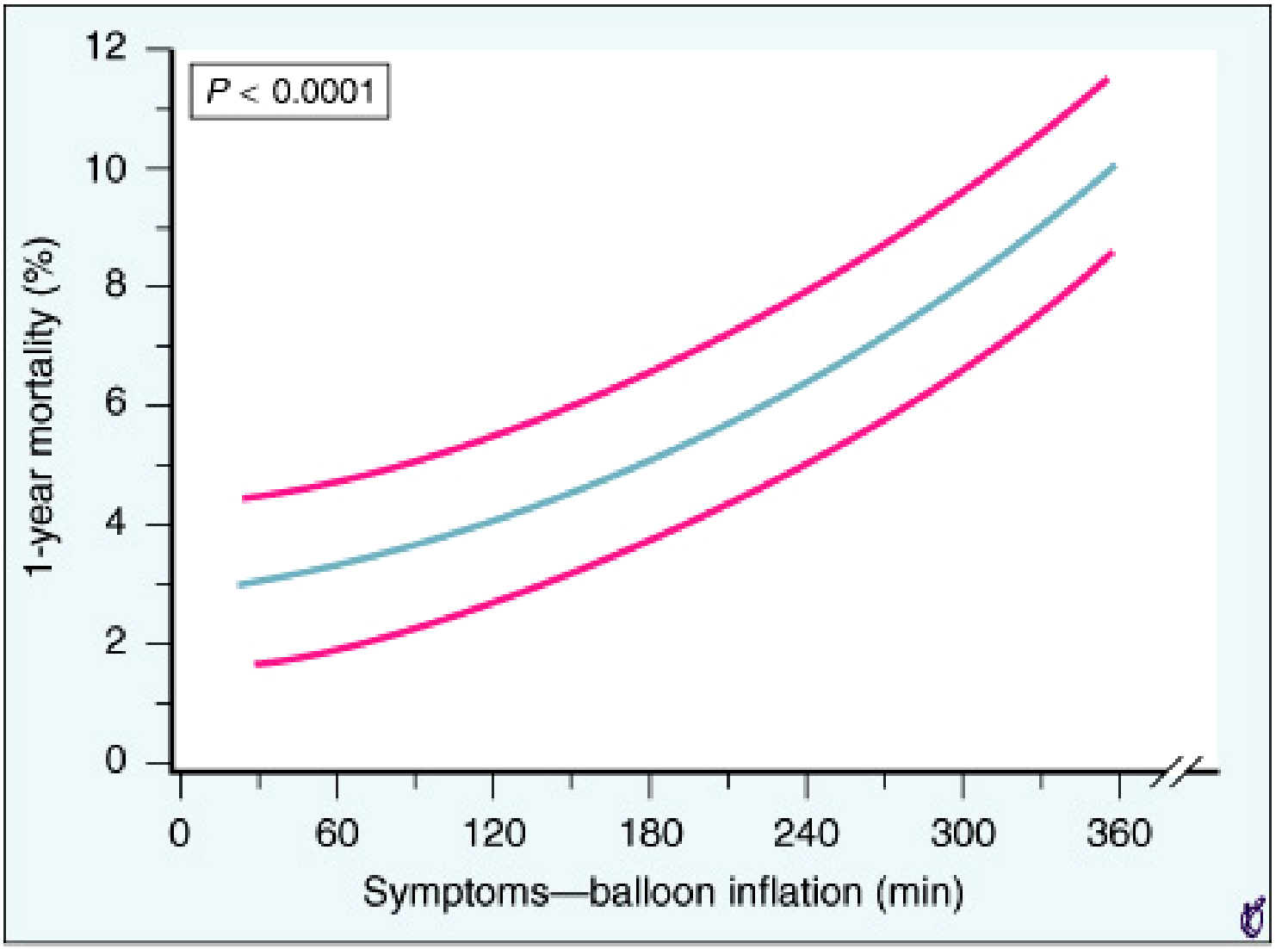
- Superiority of Primary Percutaneous Coronary Intervention (PPCI) over fibrinolysis if Door-to-Balloon completed in a timely fashion

Primary PCI vs Thrombolysis in STEMI: Meta-Analysis

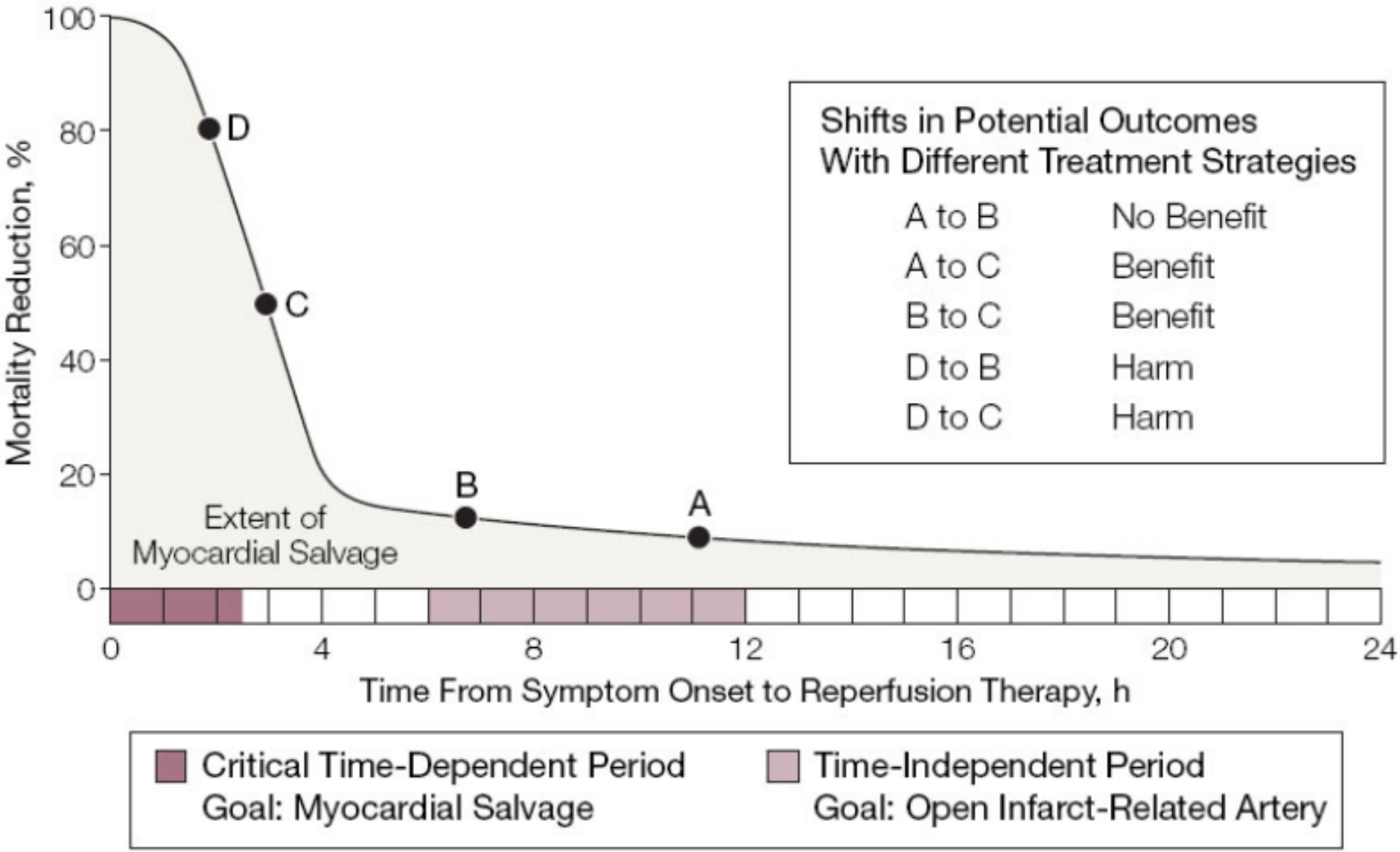


Adapted with permission from Keeley EC, et al. Lancet. 2003;361:13-20

For every 30-minutes delay from onset of symptoms to primary PCI, there is an 8% increase in the relative risk of 1-year mortality

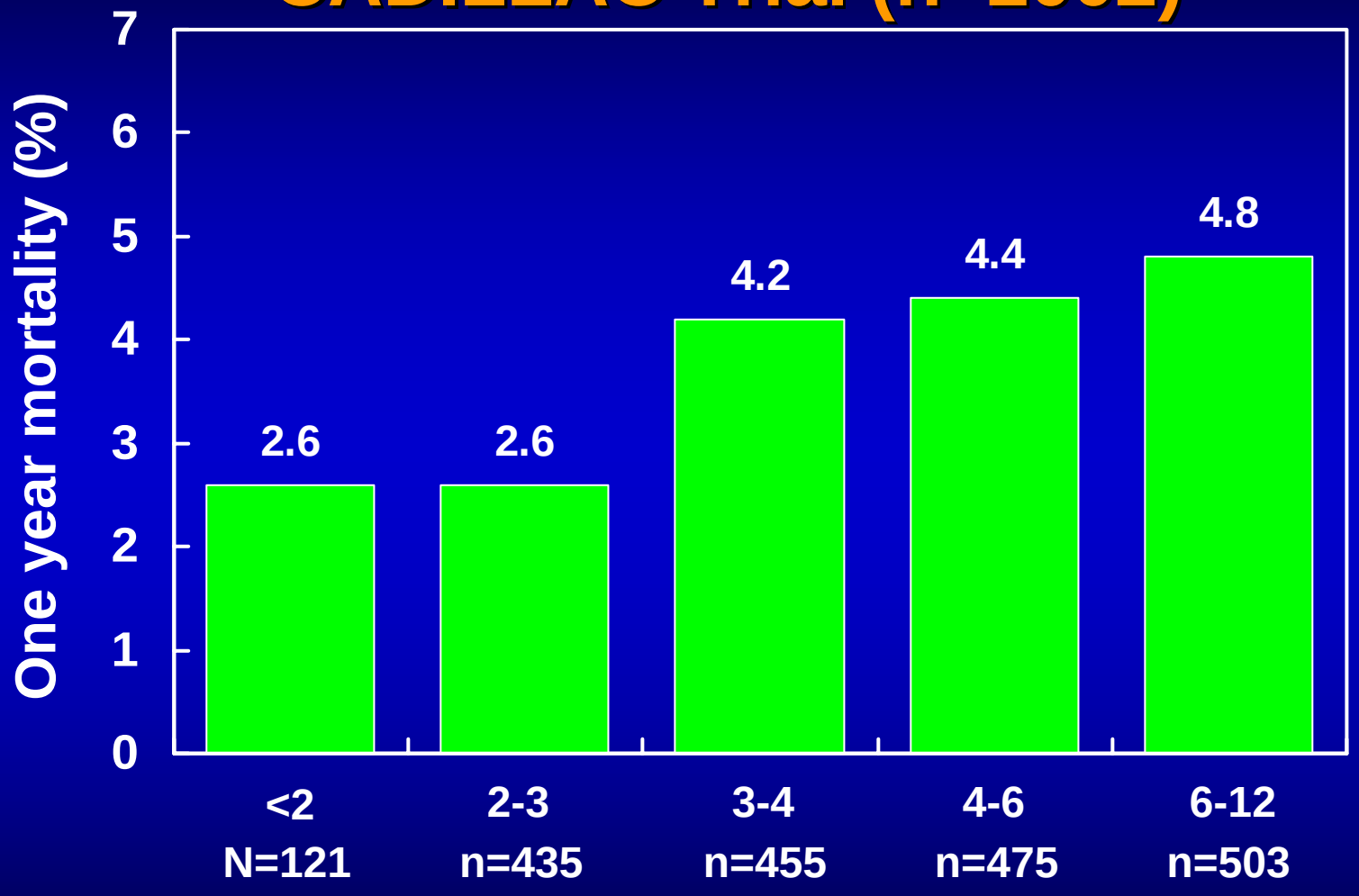


De Luca G et al., Circulation 109;1223, 2004


100
80
60
40
20
0
Mortality Reduction, %
D
C
B
A
Extent of
Myocardial Salvage
Shifts in Potential Outcomes
With Different Treatment Strategies
A to B No Benefit
A to C Benefit
B to C Benefit
D to B Harm
D to C Harm
0
4
8
12
16
20
24
Time From Symptom Onset to Reperfusion Therapy, h
Critical Time-Dependent Period
Goal: Myocardial Salvage
Time-Independent Period
Goal: Open Infarct-Related Artery

Time to Reperfusion and One Year Mortality

CADILLAC Trial (n=2002)



Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications. Brodie. ACC 2003

Importance of Early Reperfusion Therapy in STEMI

Outcomes Dependent Upon:

- Time to treatment-TIME IS STILL MUSCLE
- Early and full restoration in coronary blood flow
- Sustained restoration of flow

Patients Transported by EMS After Calling 9-1-1

Call 911
Call Fast

Onset of STEMI Symptoms → 9-1-1 EMS Dispatch → EMS on-scene
•Encourage 12-lead ECG
•Consider prehospital fibrinolytic if capable and EMS-to-needle < 30 min

EMS Triage Plan

Hospital Fibrinolysis: Door-to-needle within<30 min

- Not PCI Capable Hospital
- Interhospital Transfer
- PCI Capable Hospital

Goals

Patient	Dispatch	EMS on scene	EMS transport
5 min after Symptom onset	1 min	Within 8 min	EMS transport:EMS to Balloon within 90 min Patient self-transport: Hospital Door-to-Balloon within 90 min

Total ischemic time: Within 120 min*

* Golden hour = First 60 min

Adapted from Panel A Figure 1 Antman et al. JACC 2004;44:676.

Determine Whether Fibrinolysis or an Invasive Strategy is Preferred

Fibrinolysis is generally preferred if:

- ***Early presentation*** (3 hours or less from symptom onset & delay to invasive strategy; see below)

- ***Invasive strategy is not an option***
  - Catheterization lab occupied/not available
  - Vascular access difficulties
  - Lack of access to a skilled PCI lab-
    - Operator experience > 75 PPCI cases per year/
    - Team experience >36 PPCI cases per year

- ***Delay to invasive strategy***
  - Prolonged transport
  - (Door-to Balloon) – (Door-to- needle) time is > 1 HR
  - Medical contact-to- balloon time is > than 90 min

An invasive strategy is generally preferred if:

- ***Skilled PCI laboratory available with surgical backup***
  - Medical contact-to- balloon time is < than 90 min
  - (Door-to Balloon) – (Door-to- needle) time is < 1 hr

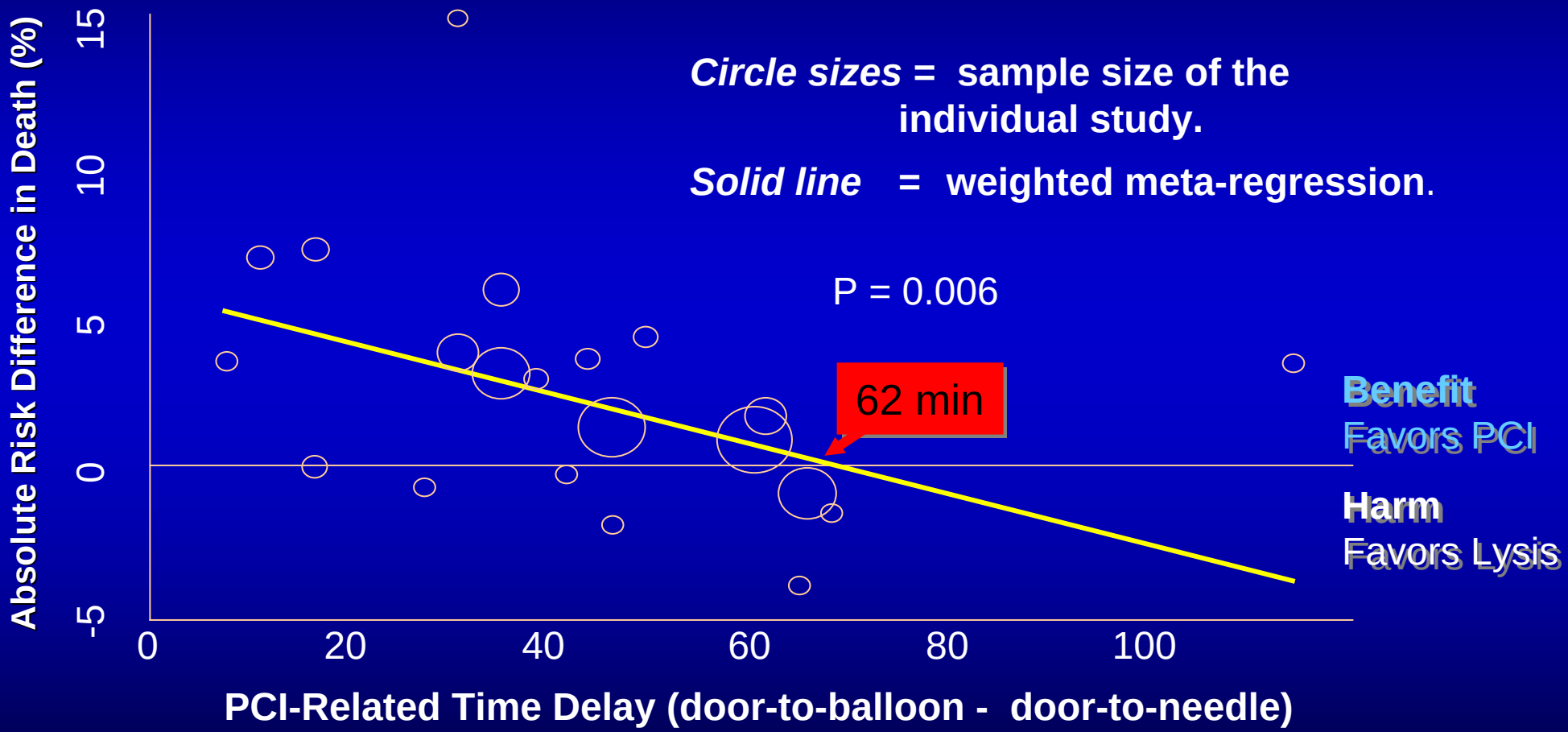
- ***High risk from STEMI***
  - Cardiogenic shock
  - Killip class greater than or equal to 3

- ***Contraindications to fibrinolysis, including increased risk of bleeding and ICH***

- ***Late presentation***
  - Symptom onset was more than 3 hours ago

- ***Diagnosis of STEMI is in doubt***

Mortality rates with primary PCI as a function of PCI-related time delay

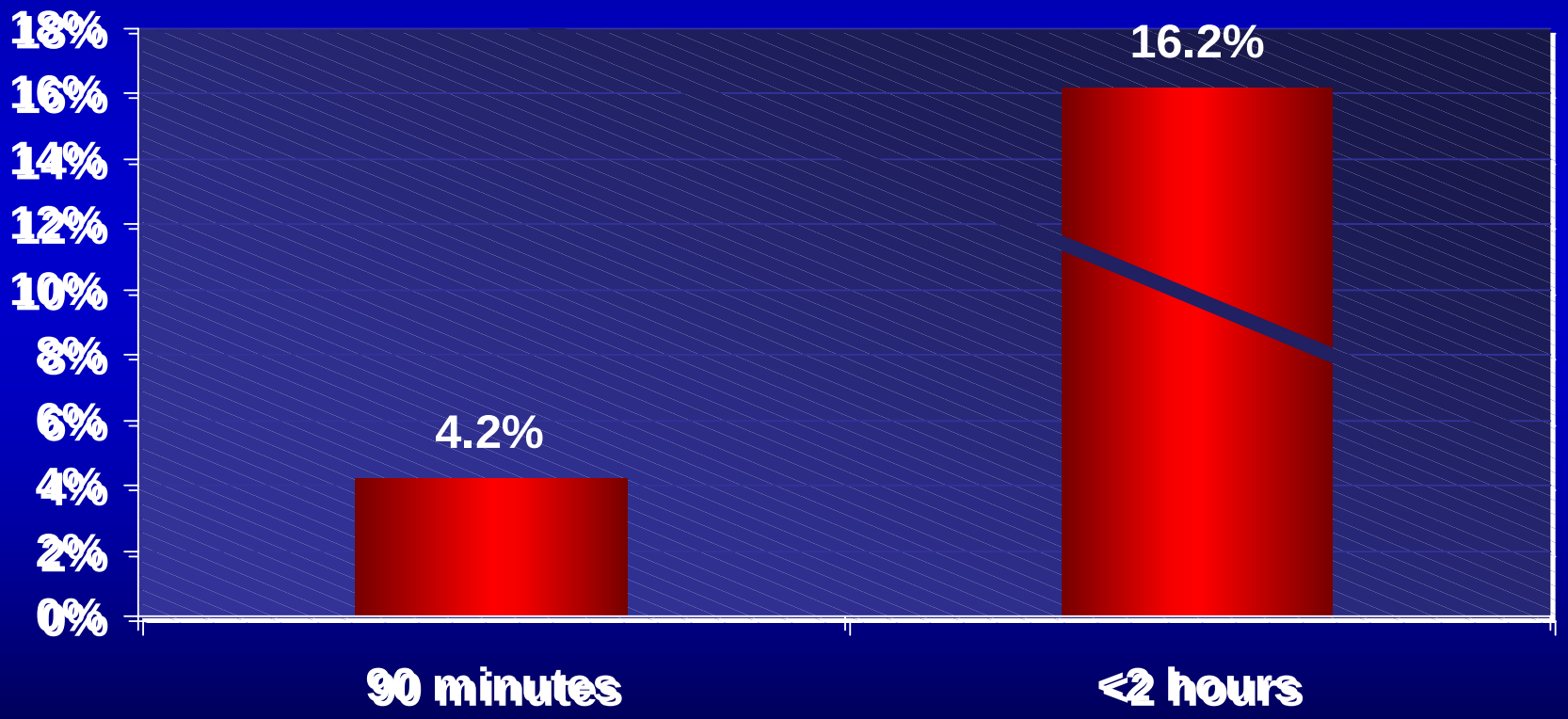


For Every 10 min delay to PCI: 1% reduction in mortality difference towards lytics

Nallamothu BK, Bates ER. Am J Cardiol. 2003;92:824-6

Times to Treatment in Transfer Patients Undergoing PPCI for AMI: NRMI 3/4 Analysis

- Analysis of 4278 pts transferred for PPCI



Initial Door to Balloon InflationTime

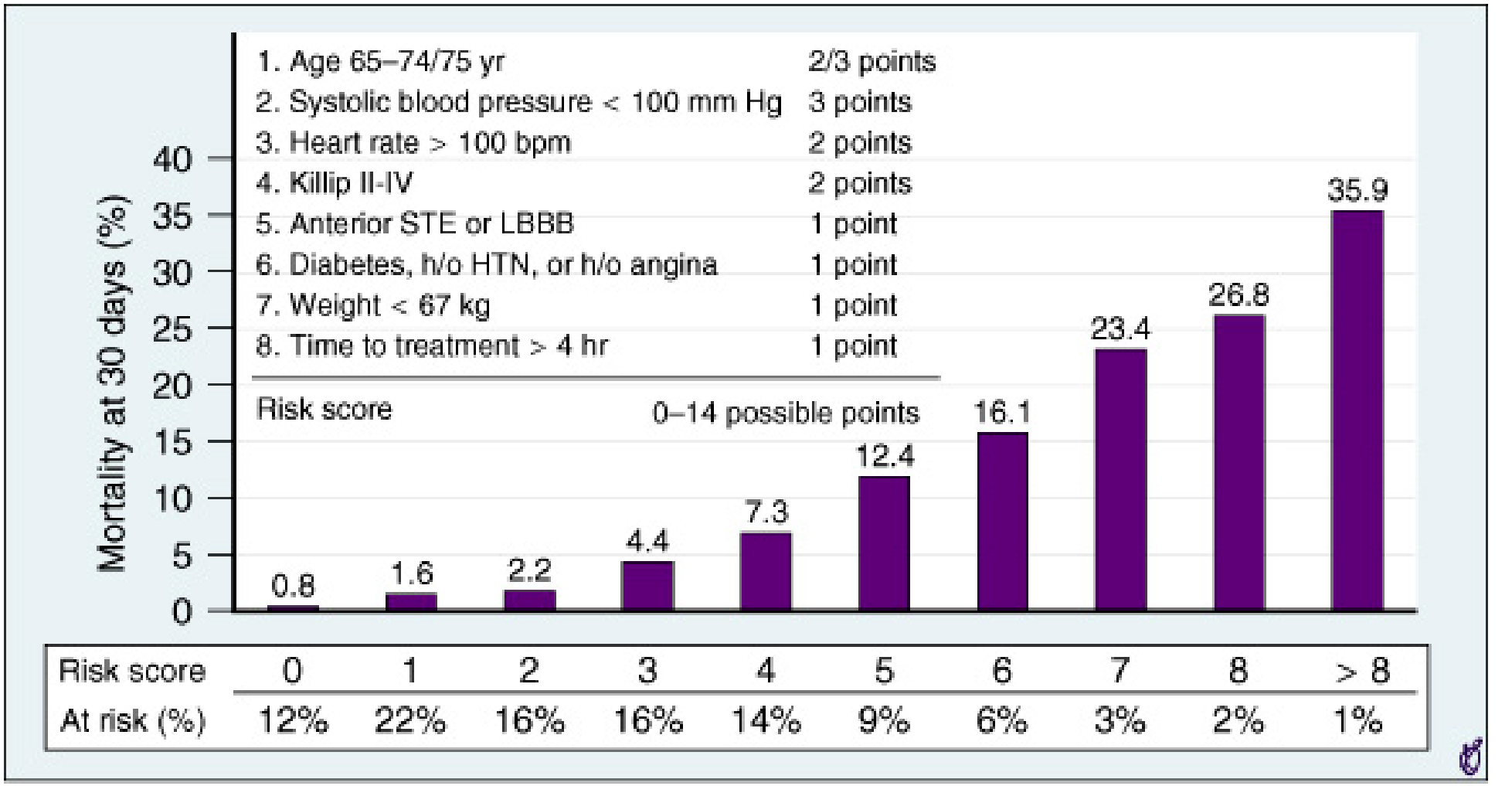
Nallamothu, Circulation. 2005; 111:761-767

Randomized controlled trials of Inv versus N-Inv management of patients with ST-segment elevation acute myocardial infarction

First author (reference)	Year	Sample size	1-y Cumulative incidence rate (%)											
			CATH (inhospital)		CATH		PCI		CABG		Reinfarction		Death	
			Inv	N-inv	Inv	N-inv	Inv	N-inv	Inv	N-inv	Inv	N-inv	Inv	N-inv
CATH within 2.75 h in invasive arm														
European Cooperative Study*														
Simoons [6]	1988	367	98.4	†	†	†	91.8	–	4.9	3.8	6.6	9.8	8.2	3.3
TIMI II A‡														
Rogers[8]	1990	586	99.0	†	†	†	75.8	23.9	19.1	18.3	9.5	9.6	8.2	10.2
CATH within 18-48 h in invasive arm														
TIMI II A†														
Rogers[8]	1990	586	90.2	†	†	†	64.3	23.9	14.0	18.3	6.5	9.6	7.7	10.2
SWIFT														
SWIFT Trial Study Group[10]	1991	800	95.0	13.4	–	–	42.6§	3.0§	14.9§	1.7§	15.1	12.9	5.8	5.0
TIMI II														
Williams[11]	1992	3339	97.2	27.5	98.0	45.2	61.2	20.5	17.5	17.3	9.4	9.8	6.9	7.4
GRACIA*														
Fernàndez-Aviles[13]	2002	500	100	19.0	–	–	79.0¶	19.0	3.0	–	–	–	2.5	2.0
CATH ≥72 h in invasive arm														
Barbash et al[9]	1990	201	94.8	37.5	–	–	54.6	24.0	11.3	3.8	3.0	3.8	8.2	3.8

Beck CA et al., Am Heart J 2005;149:194-9.

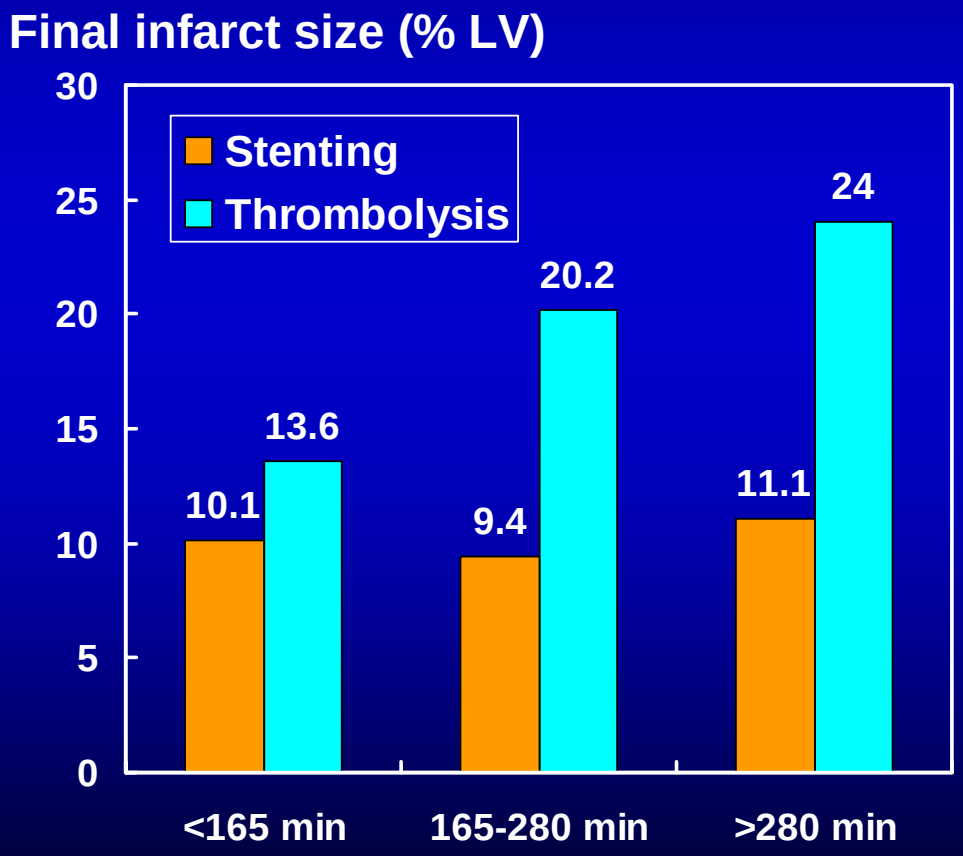
TIMI risk score for STEMI predicting 30-D mortality

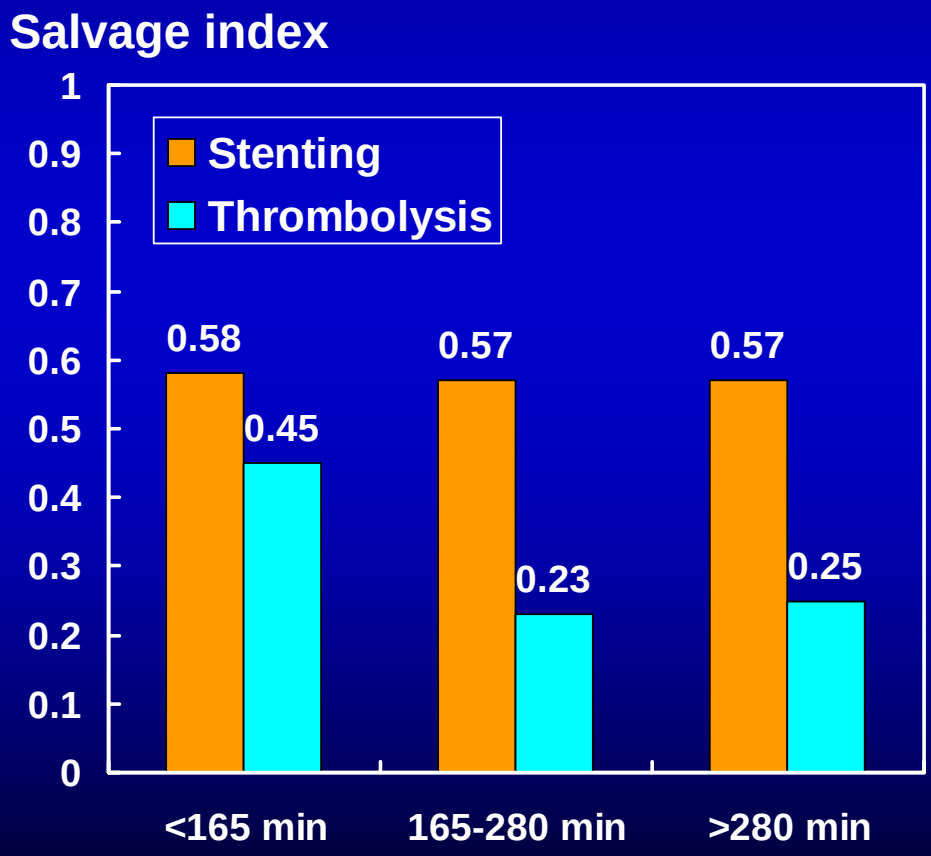


KTIMI II substudy. Circulation 102:2031, 2000

Selection of Reperfusion Strategy (STEMI)

Time from onset of symptoms to initiation of reperfusion therapy

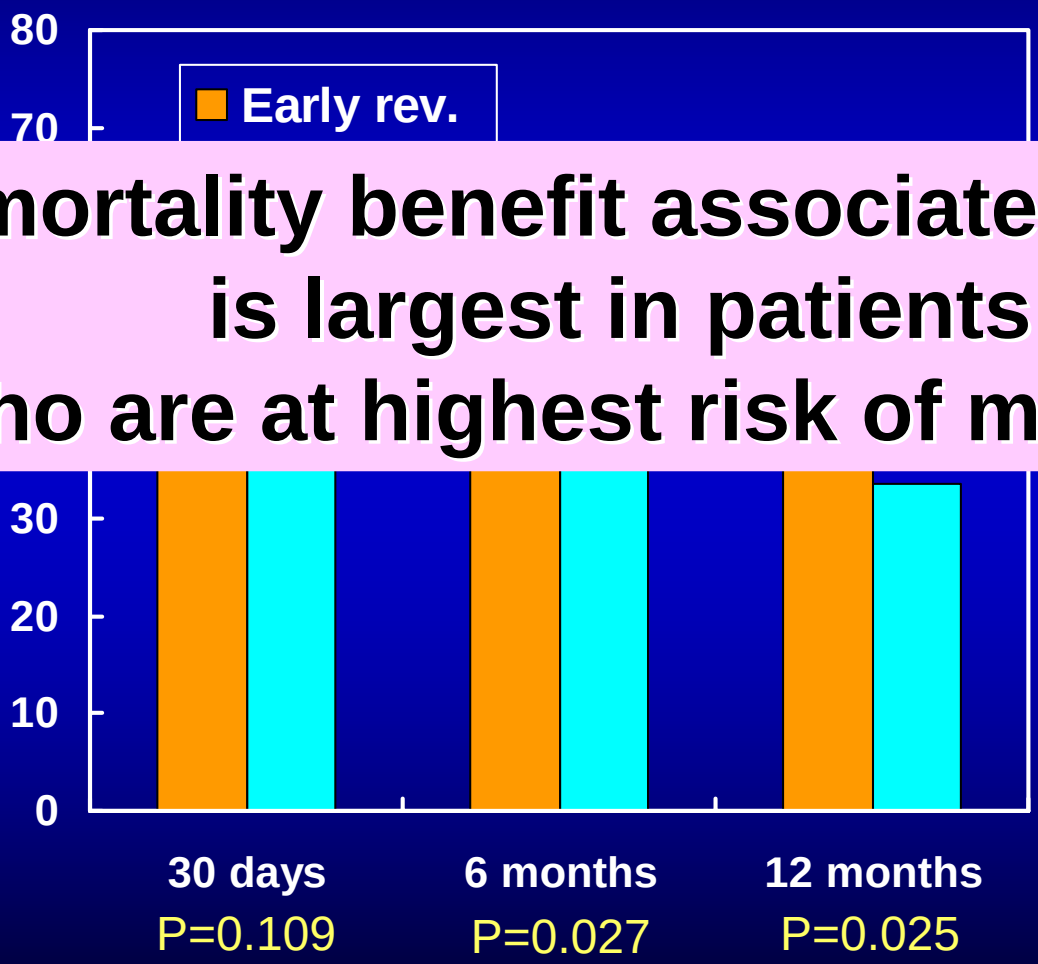




Shomig A et al. Circulation 108:1084, 2003

Selection of Reperfusion Strategy (STEMI)

Risk of the STEMI



The mortality benefit associated with PCI is largest in patients who are at highest risk of mortality

SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK. Hochman JS et al. JAMA 285:190, 2001

Selection of Reperfusion Strategy (STEMI)

Risk of bleeding

- **Increased risk of bleeding:**
  Advanced age, low body weight, hypertension

Selection of Reperfusion Strategy (STEMI)

Time required for transportation to a skilled PCI center

Goal:

Media campaign
Patient education

Greater use of 9-1-1
Prehospital Rx

Prehospital ECG
to initiate Rx

MI protocol
Critical Pathway
Quality Improvement
Program

Bolus Lytics
Dedicated PCI Team

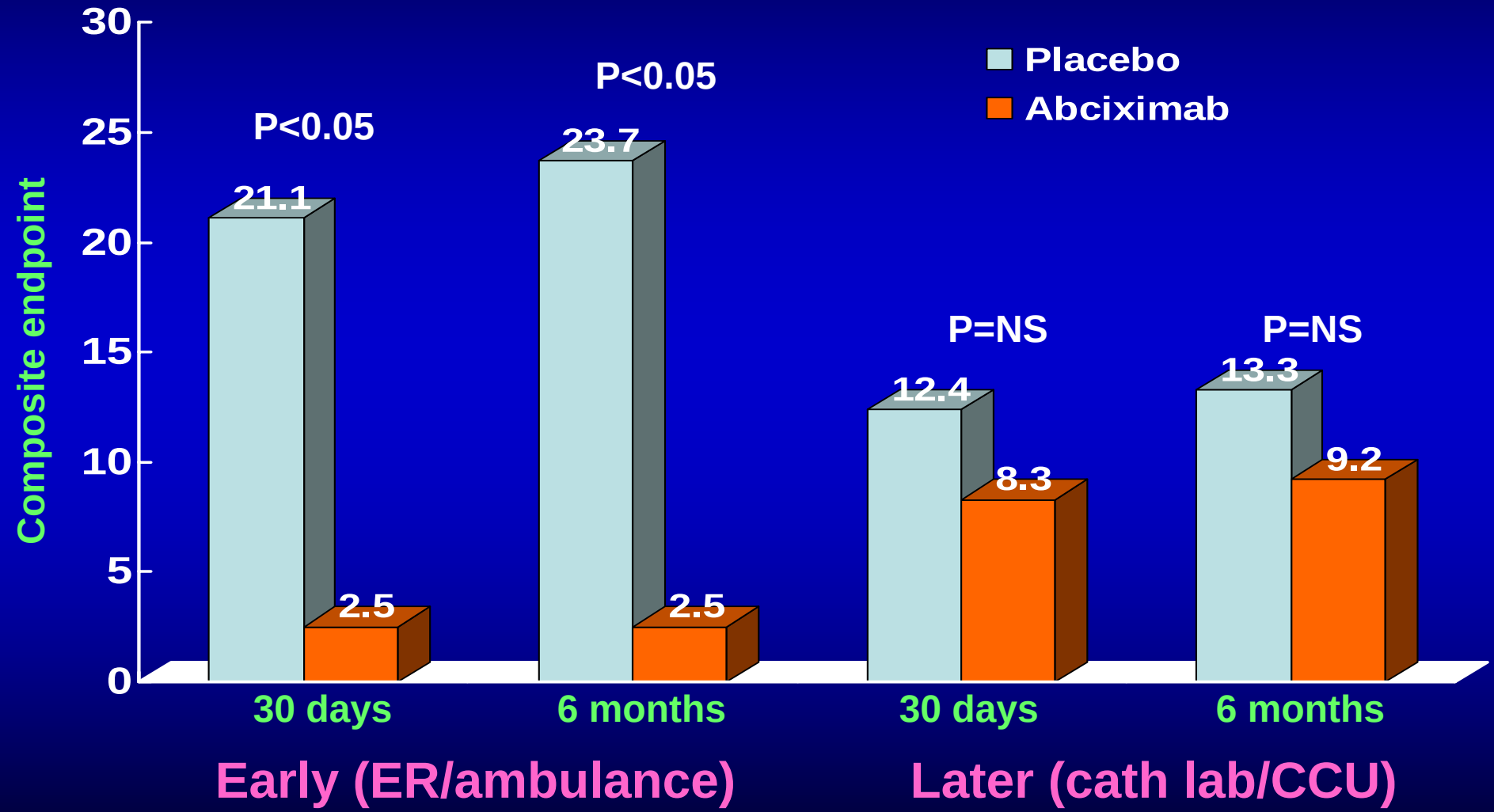
Methods of
Speeding Time
to Reperfusion

Glycoprotein IIb/IIIa Inhibition

Strong theoretical basis for utilization of GP IIb/IIIa inhibition during catheter based reperfusion therapy

- **Passivate unstable mechanically injured atherosclerotic arterial wall**
- **Avert thrombus formation on acutely deployed stents**
- **Prevent microembolization with subsequent no reflow**

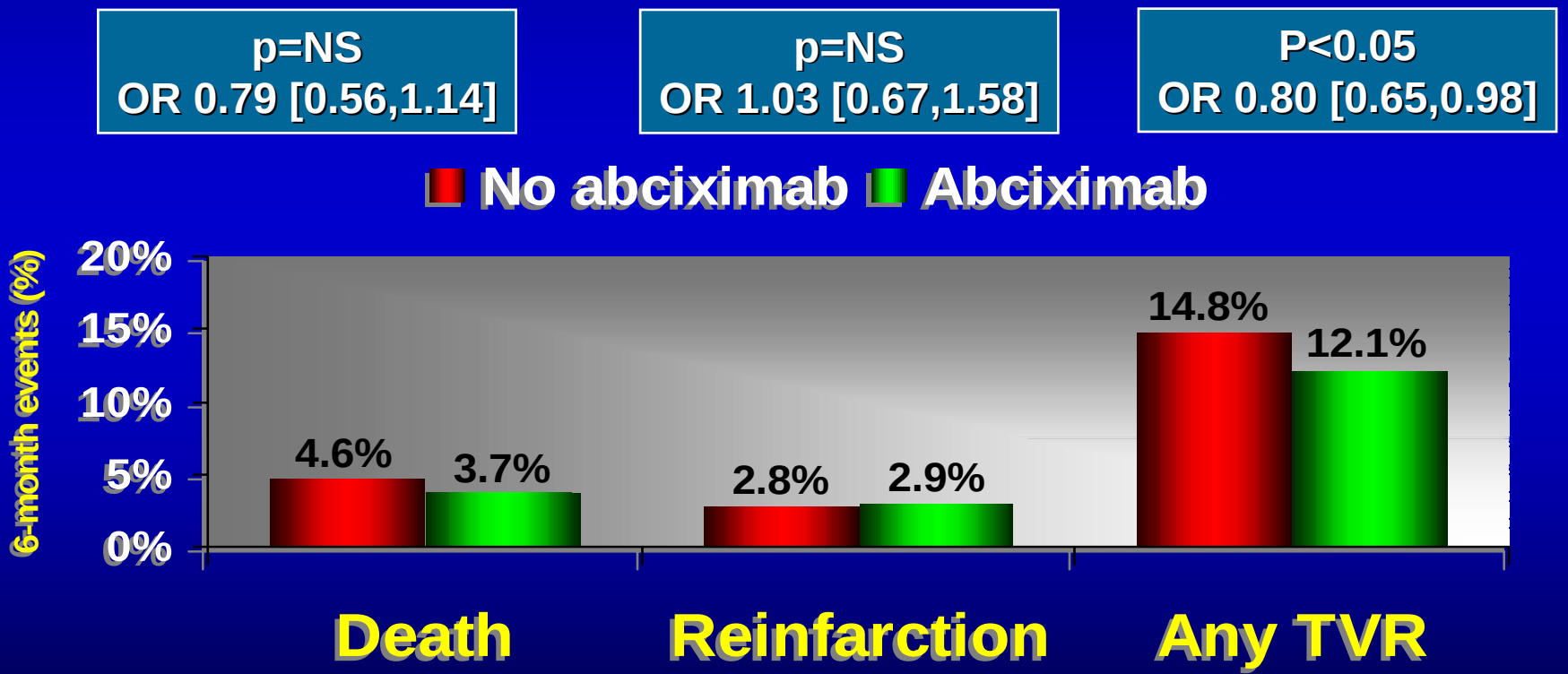
The incidence of death, reinfarction, or TVR in Abciximab before Direct angioplasty and stenting in Myocardial Infarction Regarding Acute and Long-term results (ADMIRAL trial)



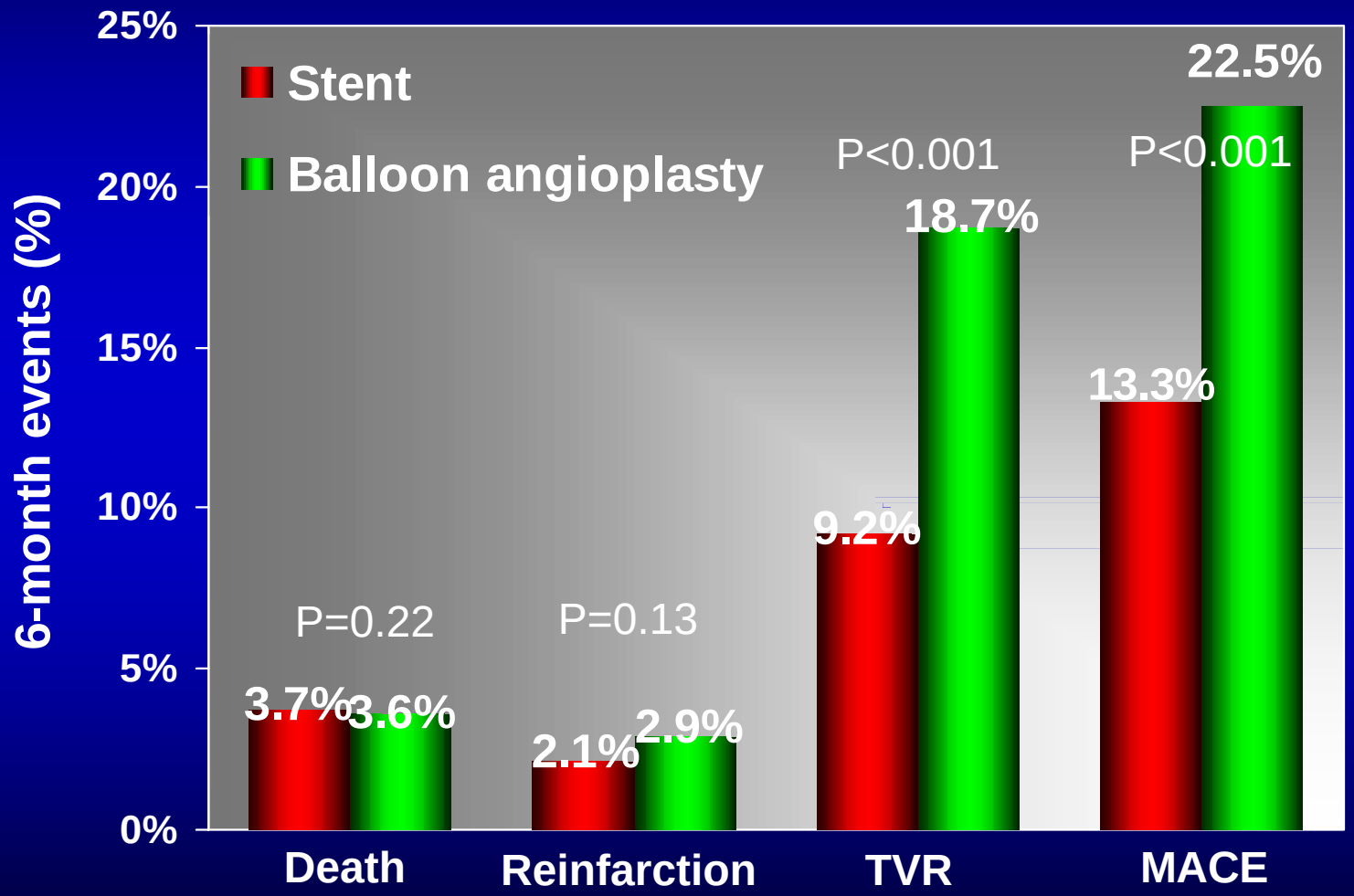
Montalescot G, NEJM 344:1895, 2001

GP IIb/IIIa Inhibition in Primary PCI

3,266 pts with AMI within 12° undergoing primary PTCA or stenting randomized to abciximab vs. placebo or control (RAPPORT [n=483], ISAR-2 [401], ADMIRAL [300], CADILLAC [2,082])

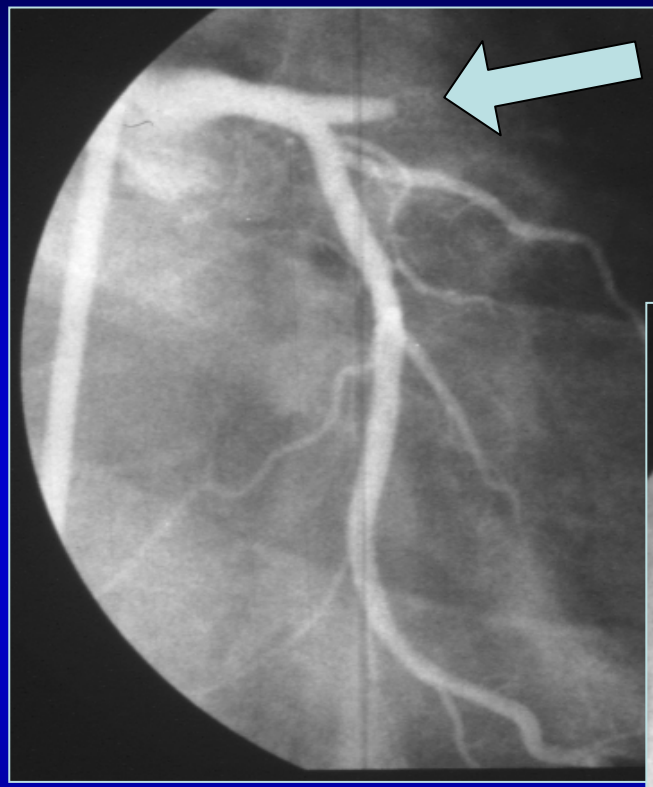


Results of meta-analysis comprising primary stenting with primary balloon angioplasty

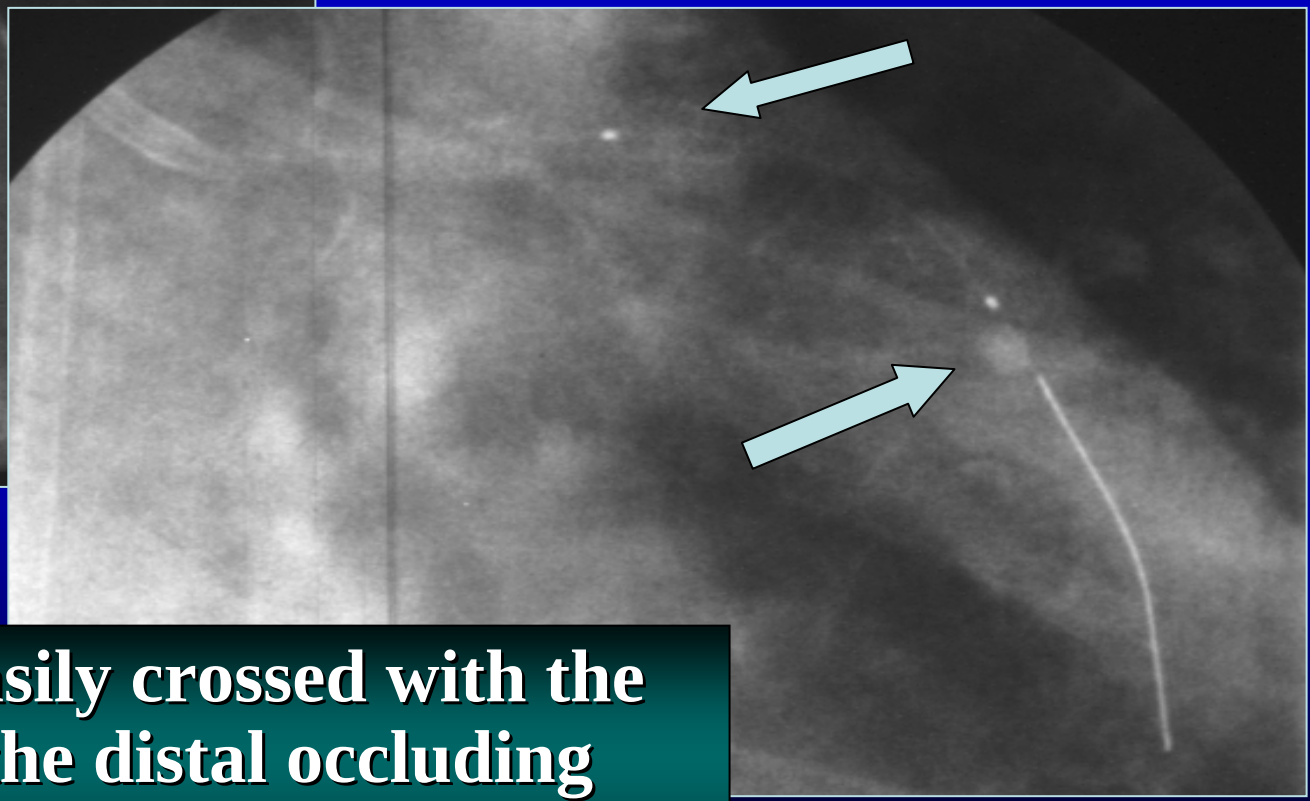


From Stent-PAMI and CADILLAC

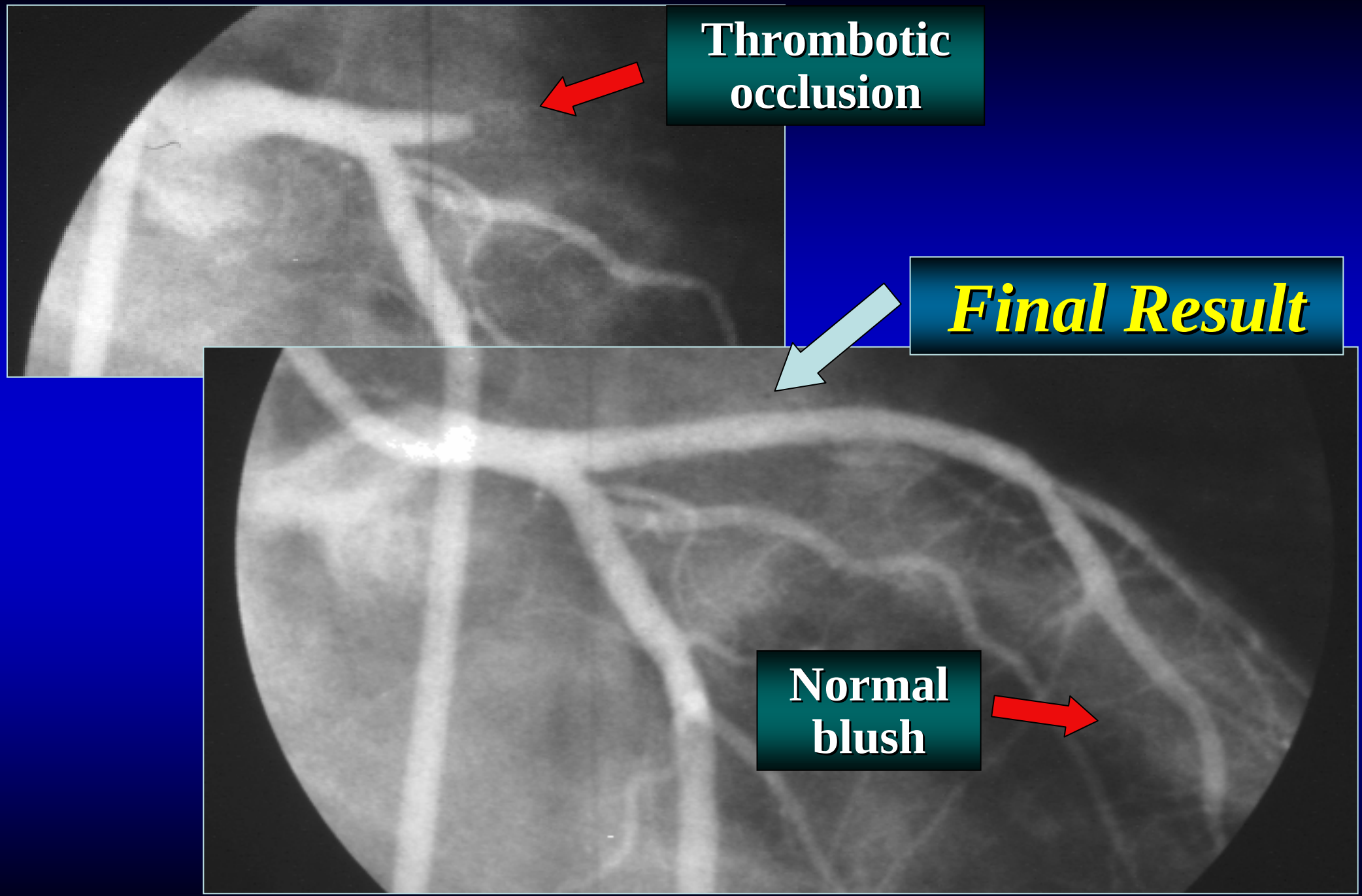
Utilization of transluminal extraction catheter device



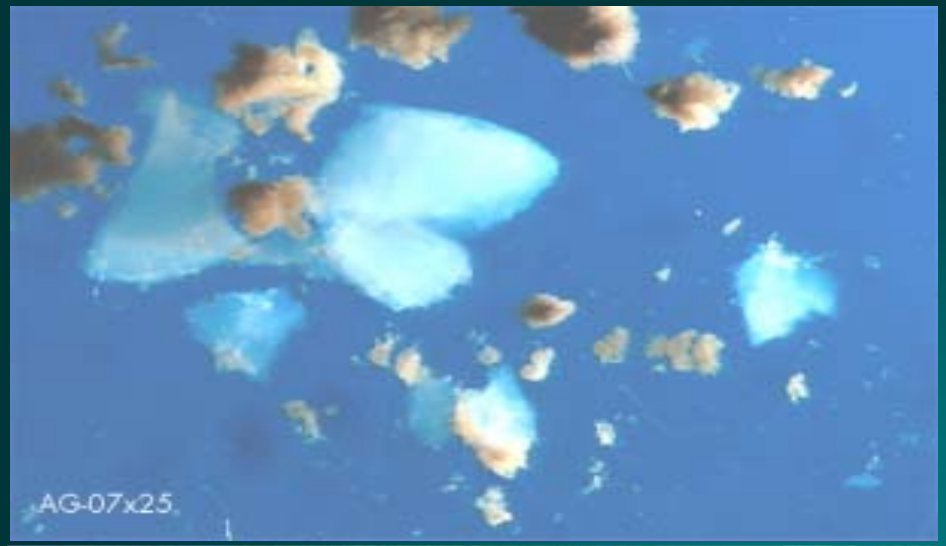
AMI
Thrombotically Occluded Proximal LAD

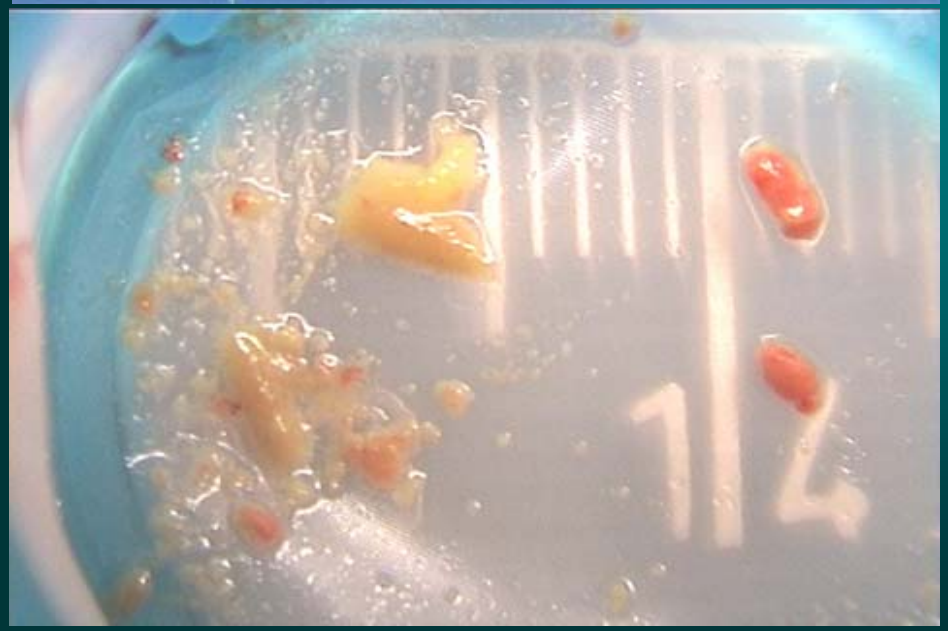


The thrombus is easily crossed with the GuardWire and the distal occluding balloon is inflated


Thrombotic occlusion
Final Result
Normal blush

PercuSurge Distal Protection in AMI





Rescue Angioplasty

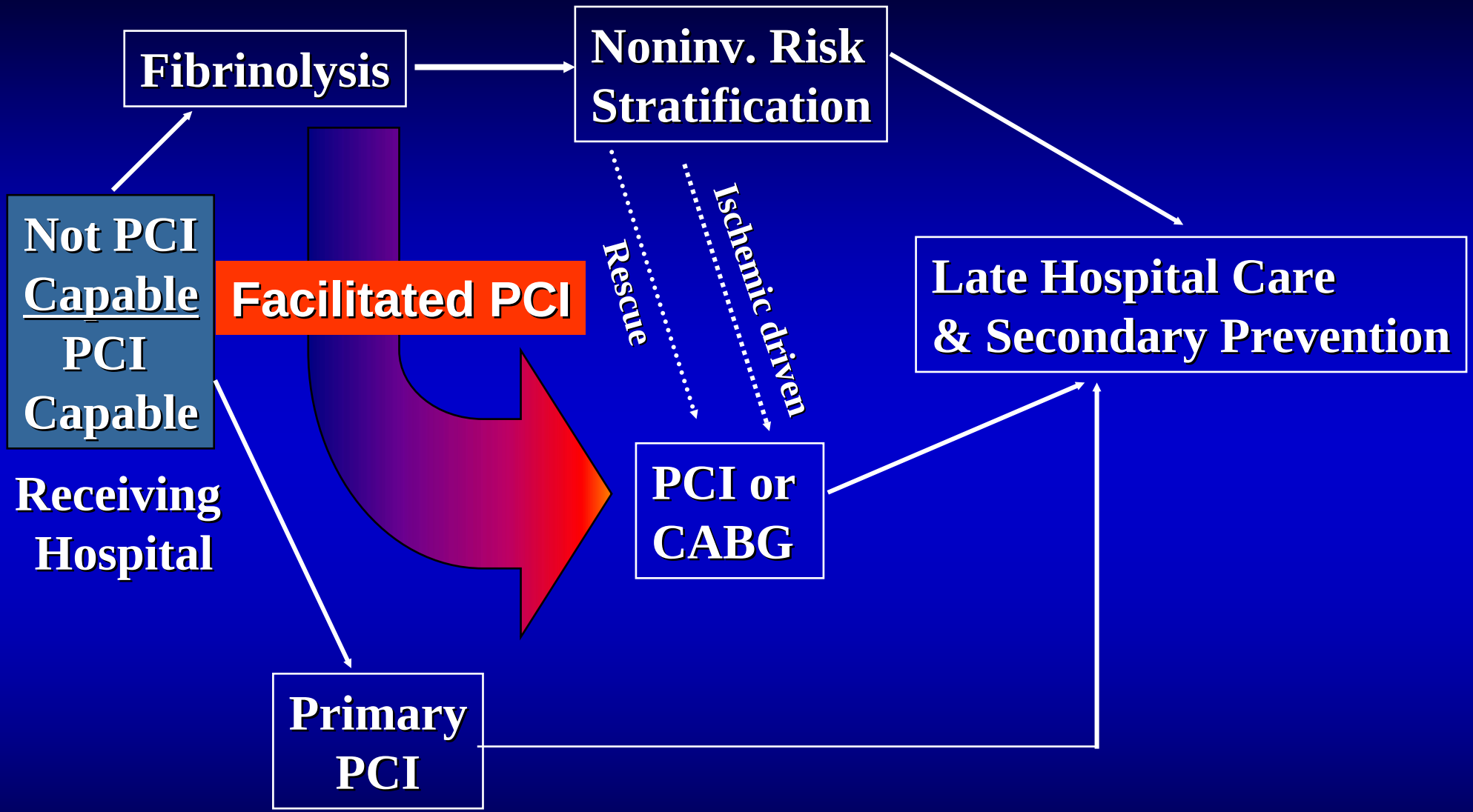
Analysis of four small randomized trials

Determination of status of infarct artery perfusion

- **Utilization of clinical features**
- **Baseline/60-minute biomarkers**
- **ST segment resolution**

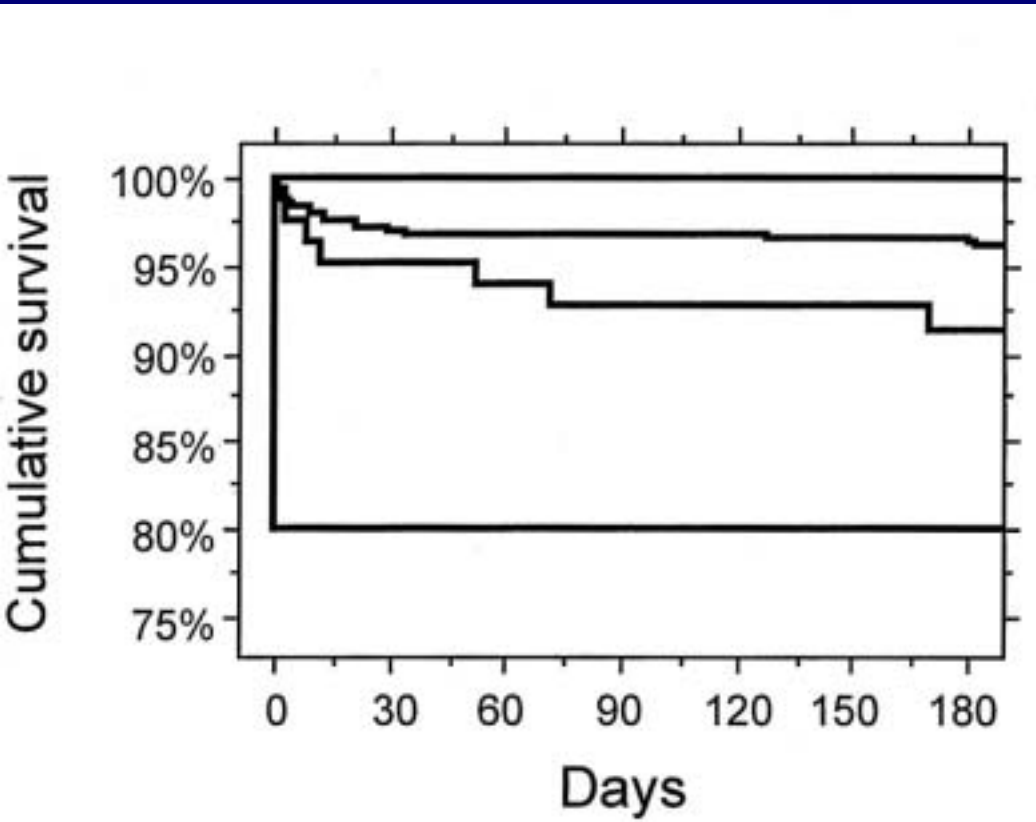
Reduced mortality

(8.5% vs. 12.2%, p=0.26)



Adapted from Panel B Figure 1
Antman et al. JACC 2004;44:676.

PAMI trial



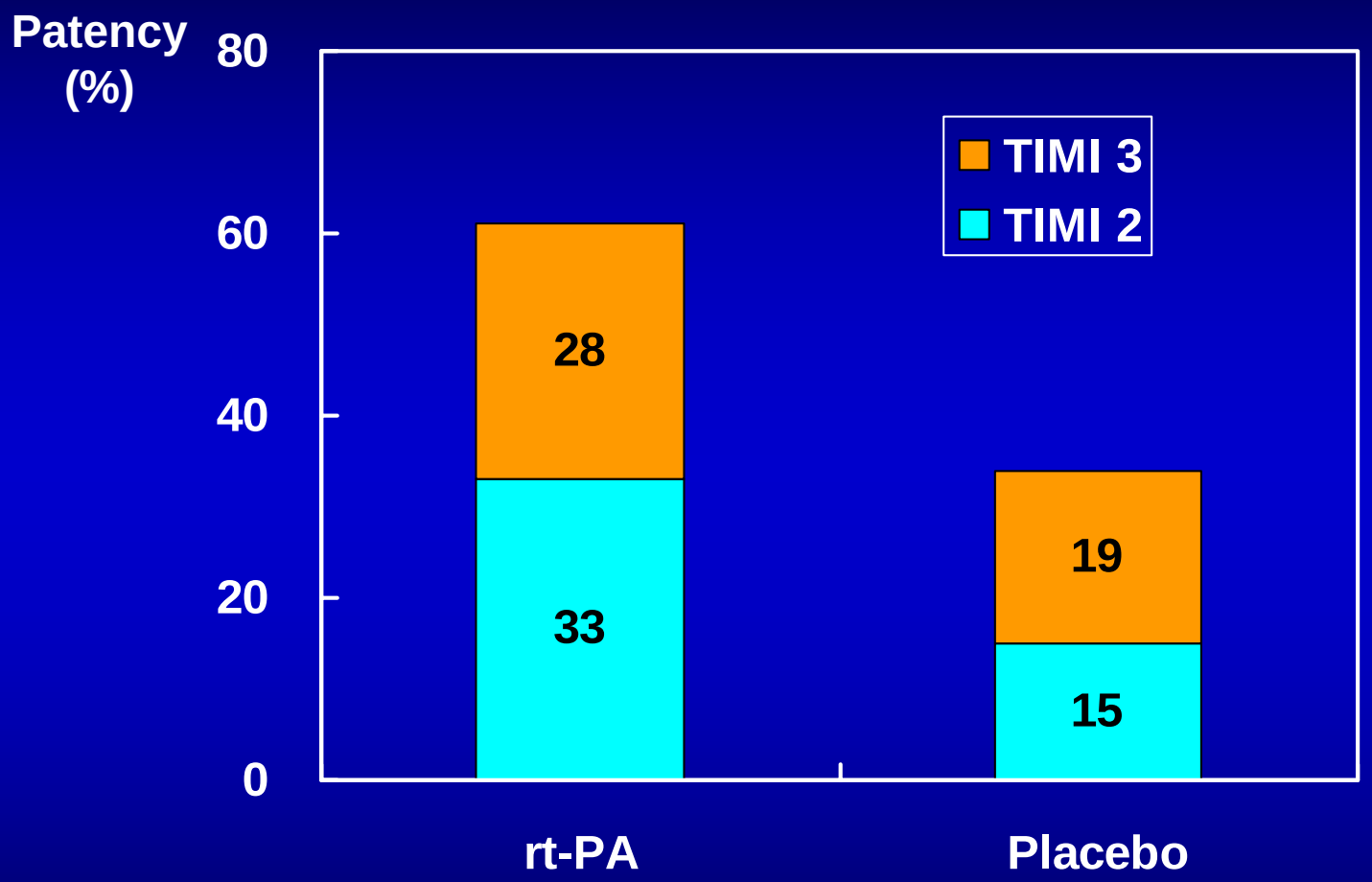
TIMI flow pre	TIMI flow post	N (%) patients	6 month mortality	
3	3	368 (15.8%)	0%	p=0.004
0-2	3	1,786 (76.8%)	3.6%	p<0.001
0-2	0-2	166 (7.1%)	8.6%	
3	0-2	7 (0.3%)	20.0%	

p<0.001

Spontaneous reperfusion (TIMI-3 flow) on initial angiography prior to intervention had improved LV function c/ less heart failure, HOT, hospital mortality

Primary angioplasty in myocardial infarction. Stone GW et al., Circulation 104:636, 2001

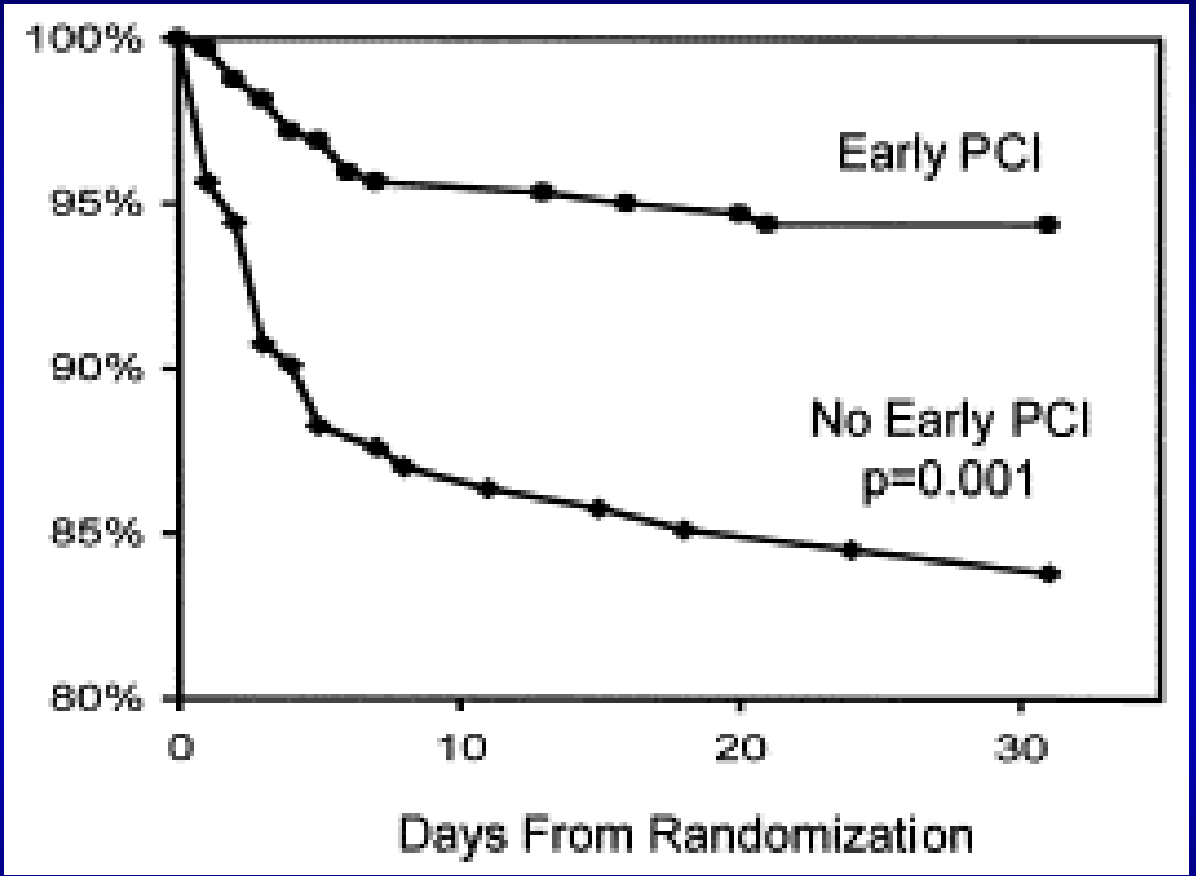
PACT trial



Infarct-related artery patency at time of initial coronary angiography (33% vs. 15% in TIMI 3)

Plasminogen-activator angioplasty compatibility trial. Ross AM et al. JACC 34:1954, 1999

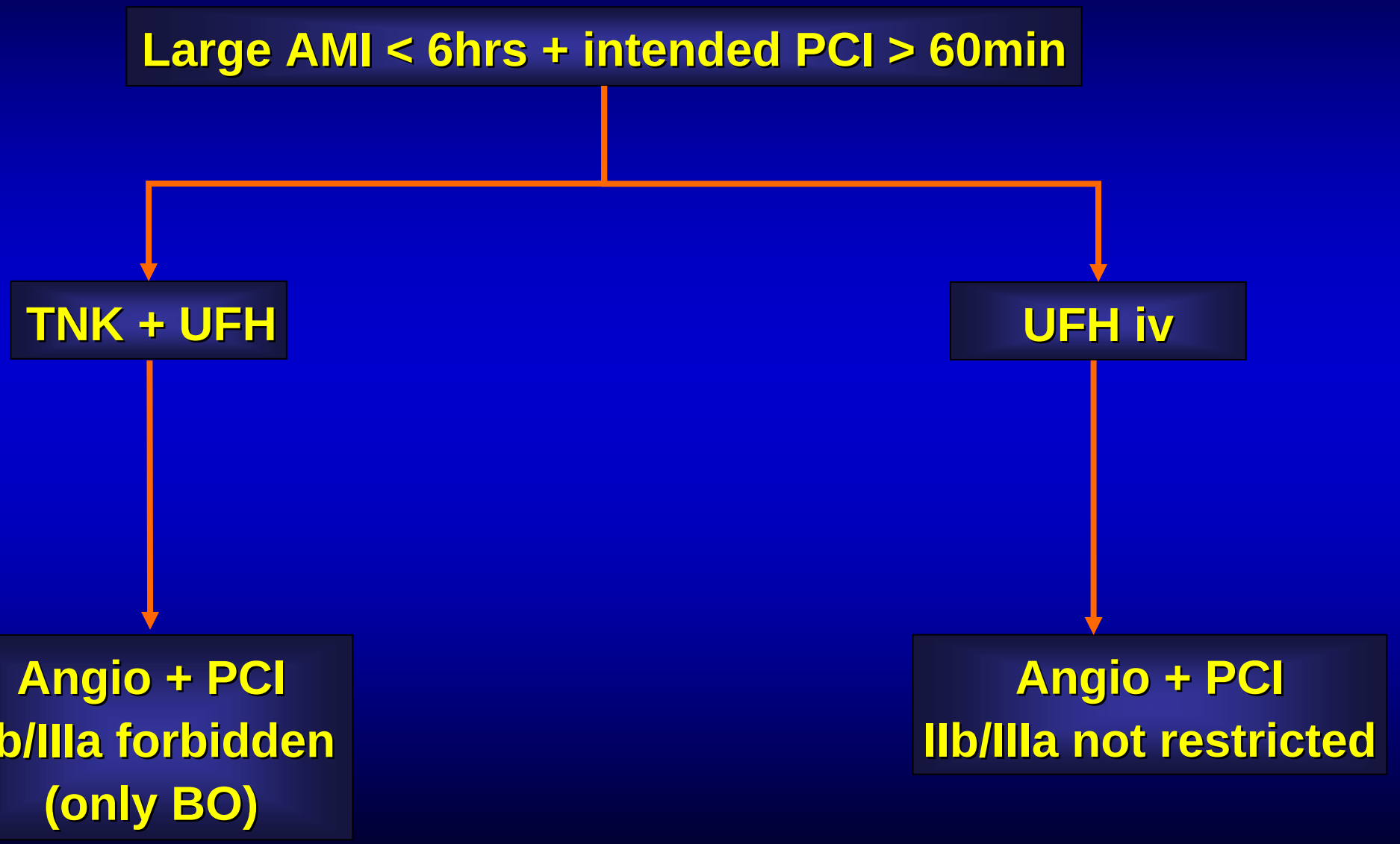
SPEED trial



Freedom from the composite of death, reinfarction, or urgent revascularization for severe ischemia at 30 days

Strategies for patency enhancement in the emergency department. Hermann HC et al. JACC 36:1489, 2000

ASSENT-4



Assessment of the Safety and Efficacy of a New Thrombolytic Regimen

Vasodilator adenosine, Nicorandil

Intravenous nicorandil can preserve microvascular integrity and myocardial viability in patients with reperfused anterior wall myocardial infarction.

J Am Coll Cardiol. 1999;33:654-60

Nicorandil improves cardiac function and clinical outcome in patients with AMI undergoing primary PCI.

Am Heart J. 2004;148:E15

Intracoronary administration of adenosine with nicorandil improve no-reflow in patients with AMI during PCI and short-term clinical outcome

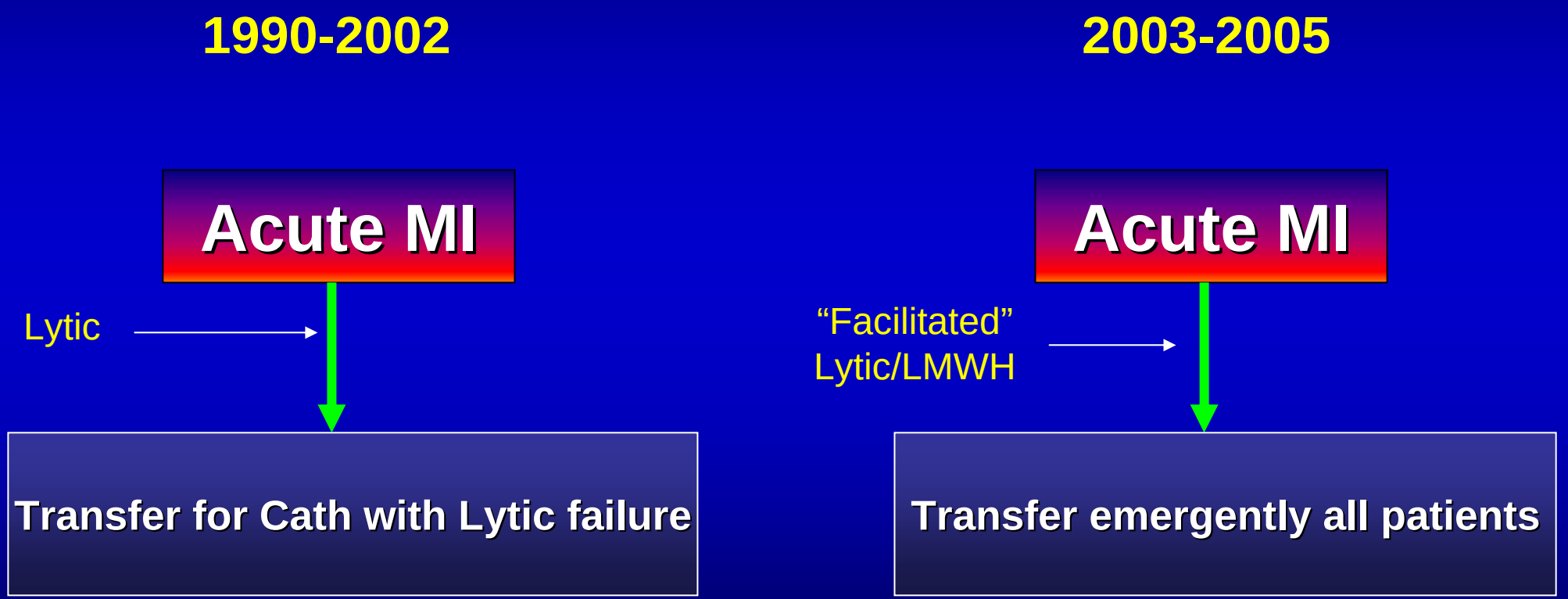
Circ J. 2004;68:928-32

Effect of Nicorandil on No-reflow during PCI

	GroupI AND+NCR(n=25)	Group II AND only(N=25)	p
TFG			
Before PCI	0.5± 0.6	0.4± 0.5	0.574
After PCI	2.0± 0.9	2.6± 0.6	0.024
⊿ TFG	1.5± 1.1	2.2± 1.0	0.033
TFC			
Before PCI	102.5± 35.7	107.8± 31.4	0.587
After PCI	56.9± 35.0	44.6± 20.8	0.141
⊿ TFC	45.6± 24.9	63.6± 23.2	0.014
Blush score 3 after PCI (%)	44	64	0.014
Cardiogenic shock(%)	20	12	0.014

CNUH data. Circ J. 2004;68:928-32.

Change in Approach to AMI



Synopsis of primary angioplasty strategy in STEMI

- Primary angioplasty strategy provides a greater chance for restoring blood flow and stabilization of infarct artery
- The expanded latitude of temporal benefit for primary angioplasty may mitigate logistical constraints of this approach
- Stents enhances durability of procedure. Early administration of GP IIb/IIIa inhibitors may augment results of primary stenting
- There is considerable promise for evolution of science of microcirculatory and myocardial protection during infarction

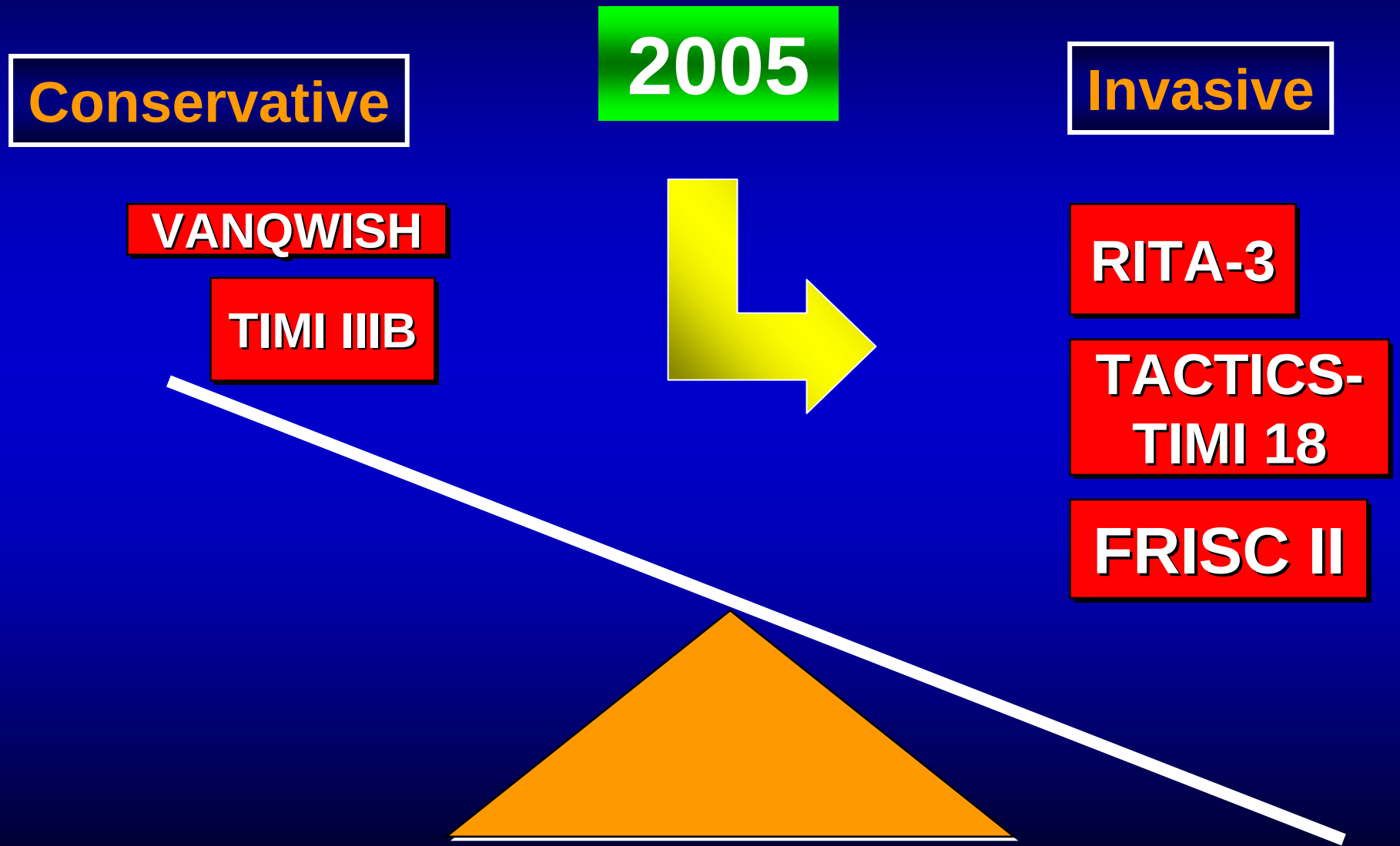
UA/NSTEMI

Interventional Management

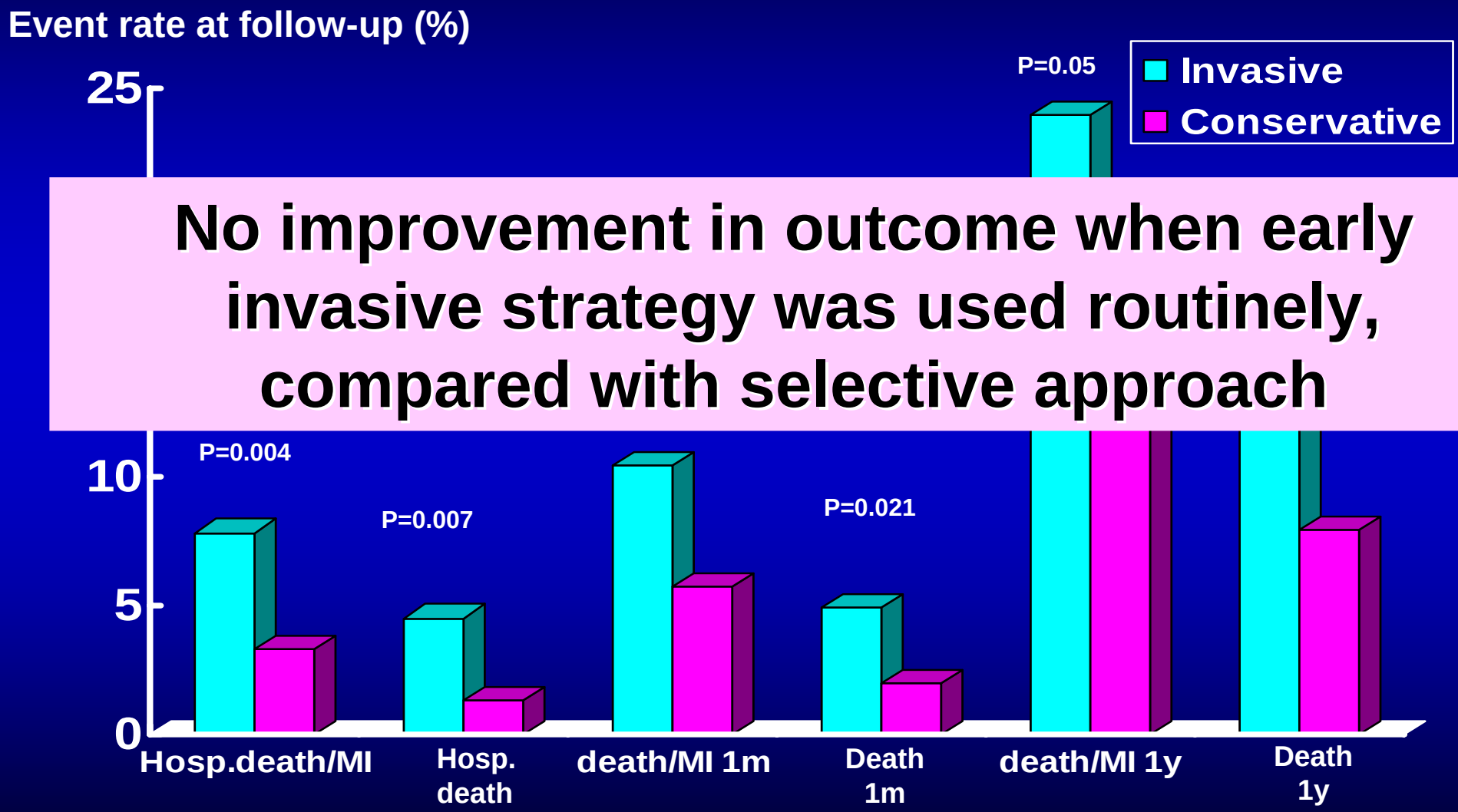
- **Early invasive strategy**: routine early cardiac catheterization and revascularization with PCI or bypass surgery, depending on coronary anatomy

- **Conservative approach**: initial medical management with catheterization and revascularization only for recurrent ischemia either at rest or in a noninvasive stress test

Optimal Strategy for UA/NSTEMI



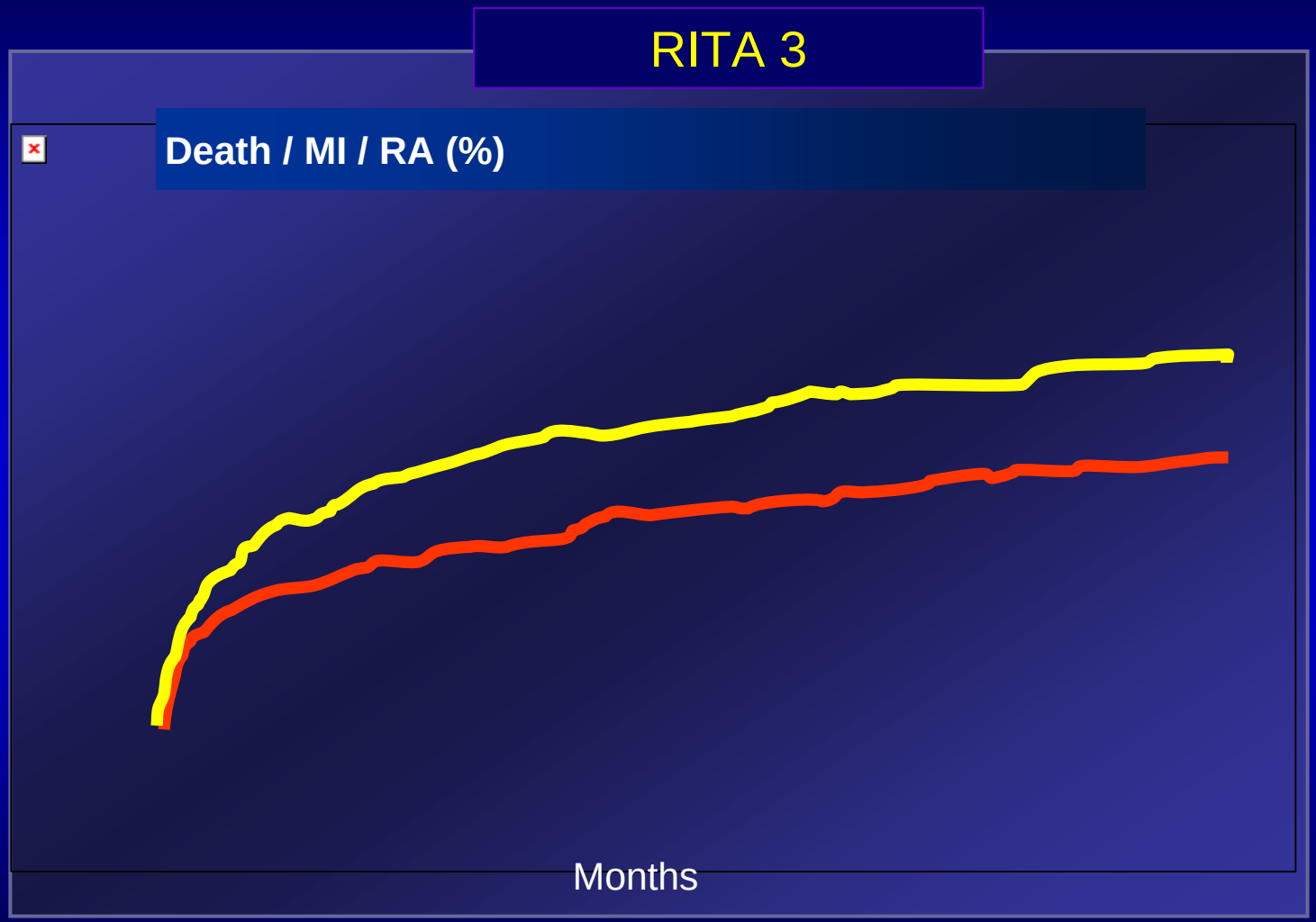
VANQWISH trial



No improvement in outcome when early invasive strategy was used routinely, compared with selective approach

Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital
N Eng J Med 1998;338:1785-1792

RITA 3

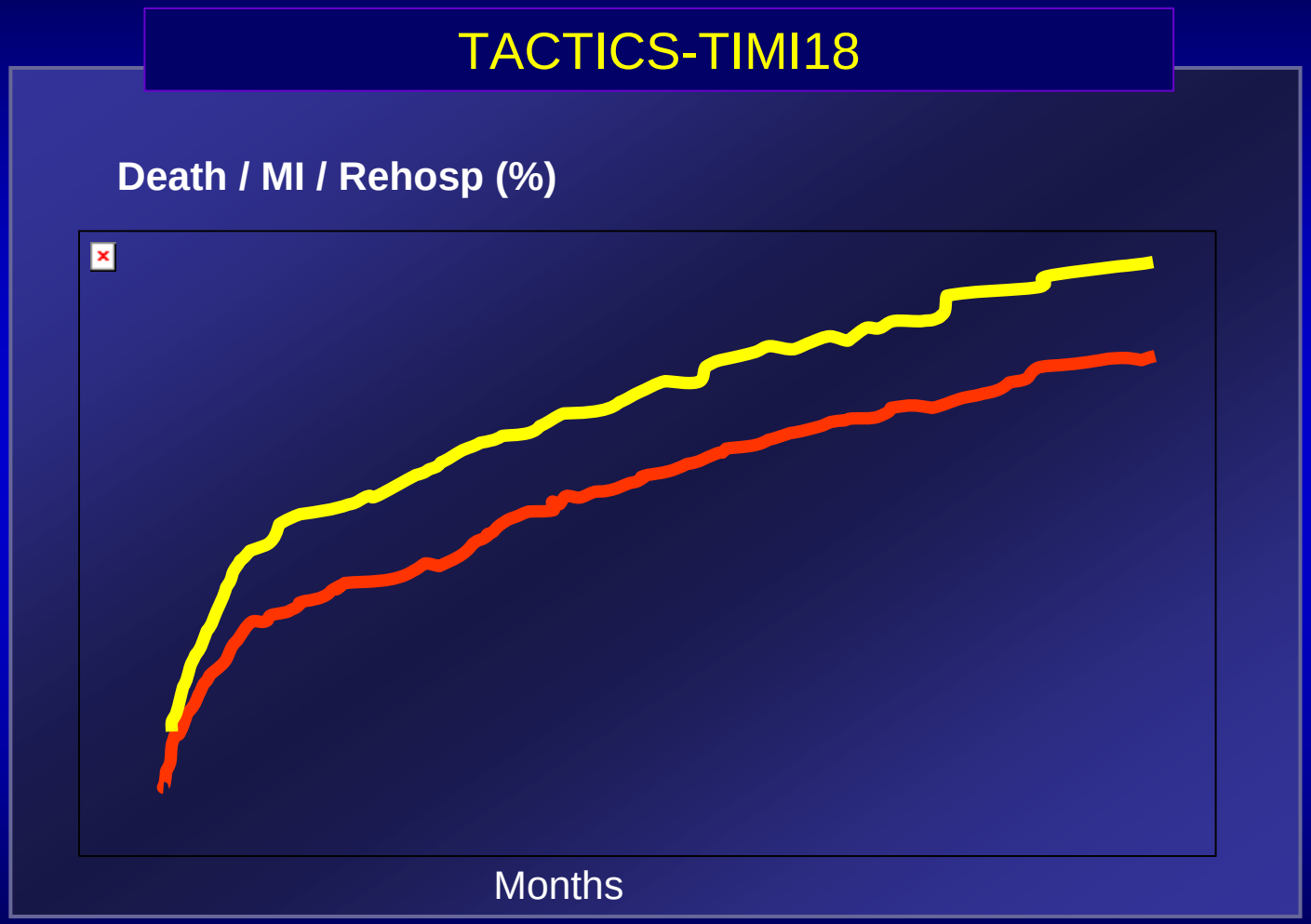


Conservative
Invasive

- 1810 UA/NSTEMI
- Early Invasive vs. conservative

The British Heart Foundation Randomised Intervention Treatment of Angina
Fox KAA. Lancet 2002;360:743

TACTICS-TIMI 18



Conservative
Invasive

- 2220 UA/NSTEMI
- Tirofiban for 48h
- Early invasive vs. conservative

Treatment Angina with aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction
Cannon CP et al. NEJM 2001;344:1879

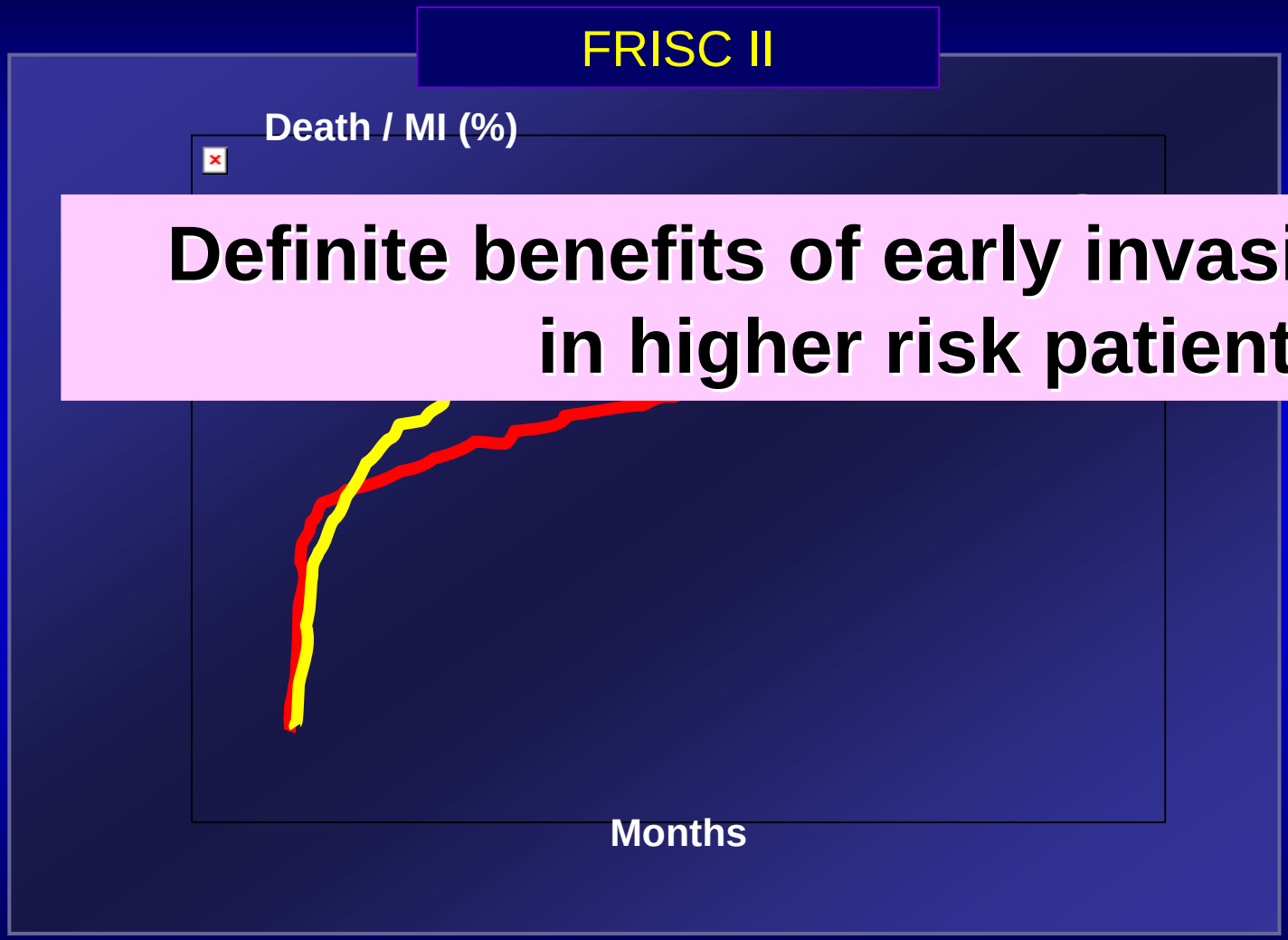
Results according to the risk

From TACTICS-TIMI 18

Variable	No (%)
Diabetes	613 (28)
No diabetes	1607 (72)
Creatine kinase MB ≤5 ng/ml	1297 (61)
Troponin T >0.1 ng/ml	748 (41)
Troponin T ≤0.1 ng/ml	1078 (59)
TIMI risk score	
0–2 (low)	555 (25)
3–4 (intermediate)	1328 (60)
5–7 (high)	337 (15)

No difference in low risk group !

FRISC II

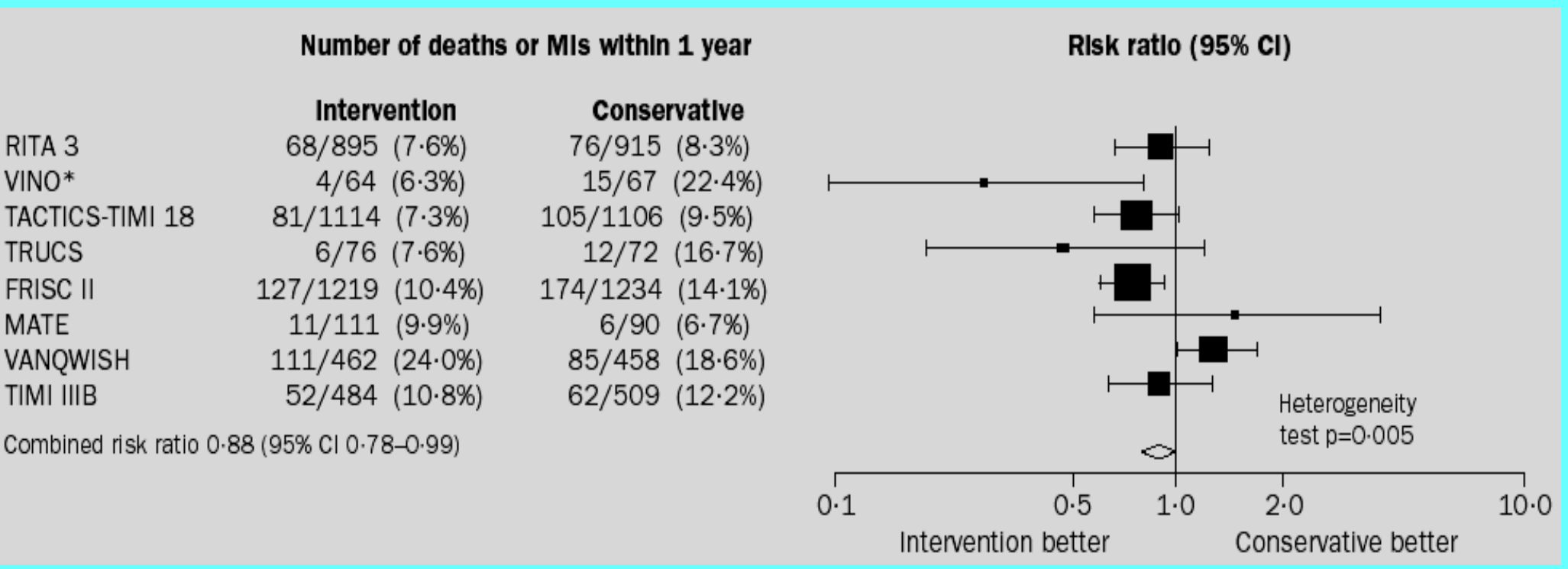


Definite benefits of early invasive strategy in higher risk patients

- Dalteparin for 72h
- Early invasive vs. Conservative
- Daltepairin for 3 m vs. placebo

FRagmin and Fast Revascularization during InStability in Coronary artery disease
Wallentin L et al. Lancet 2000;356:9

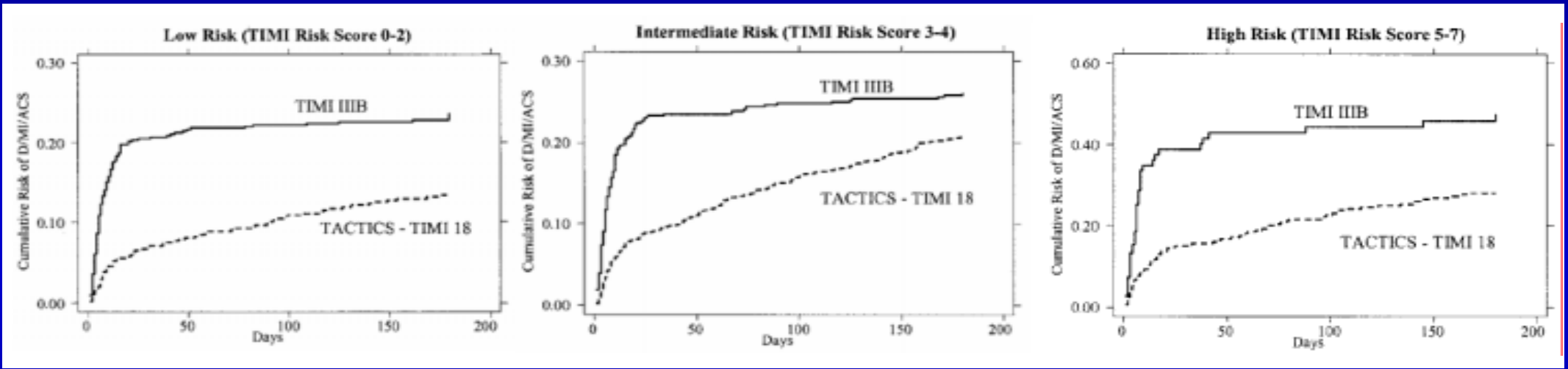
Incidence of MI or Death in 8 Trials



6-month outcomes in TACTICS-TIMI 18 and VINO.

Lancet 2002;360:743-51

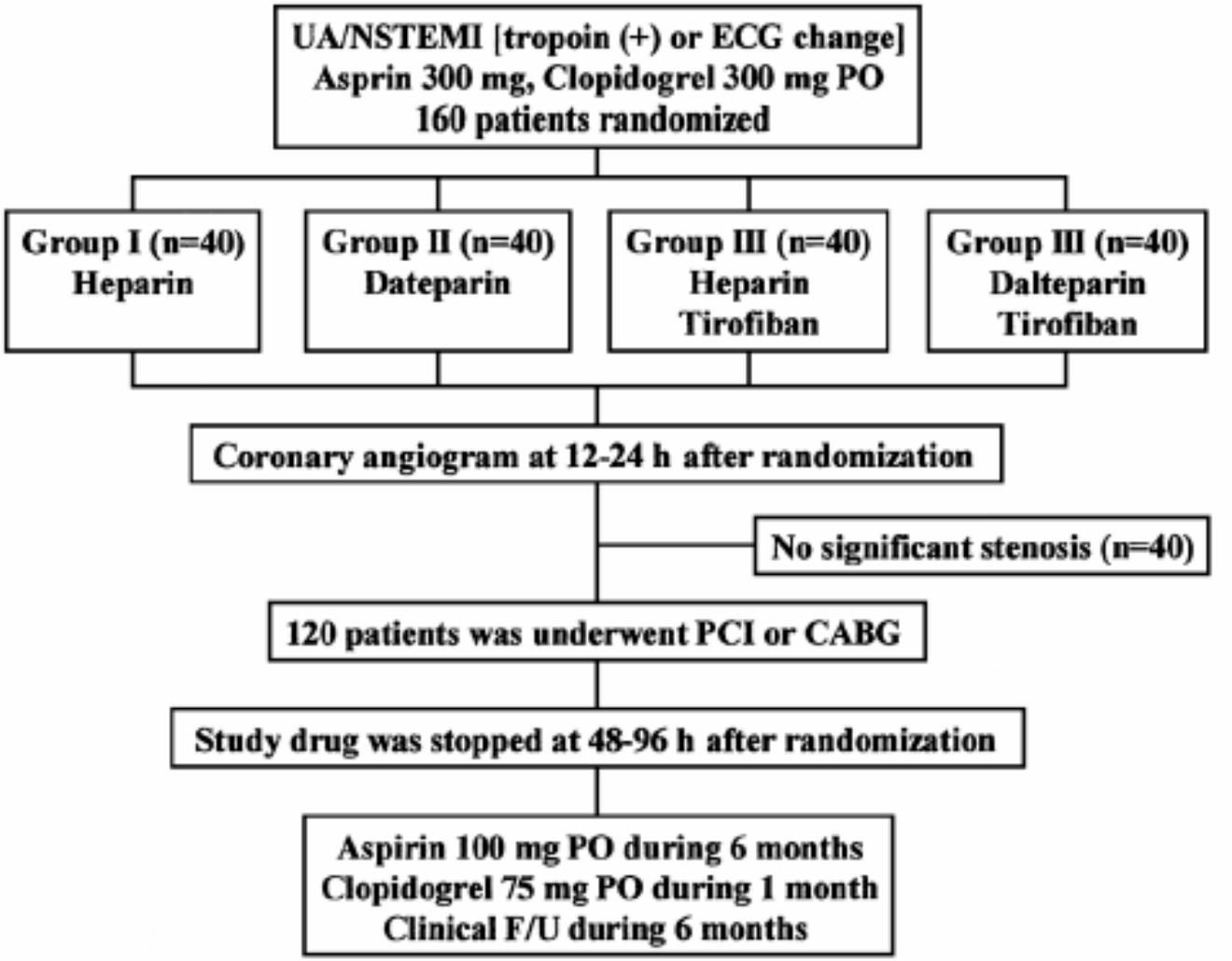
Glycoprotein IIb/IIIa inhibition and stenting were associated with lower rates of death, MI, and rehospitalization: a greater benefit of an early invasive strategy



Kaplan-Meier curves of cumulative incidence of composite end point of death, MI, or rehospitalization for ACS in TIMI IIIB (solid lines) vs TACTICS-TIMI 18 (dashed lines) among patients matched for baseline TIMI risk score category.

Sabatine MC et al. Circulation 2004;109:874-80

Long-Term Clinical Outcomes of Platelet GP IIb/IIIa Inhibitor Combined With LMWH in Patients With ACS



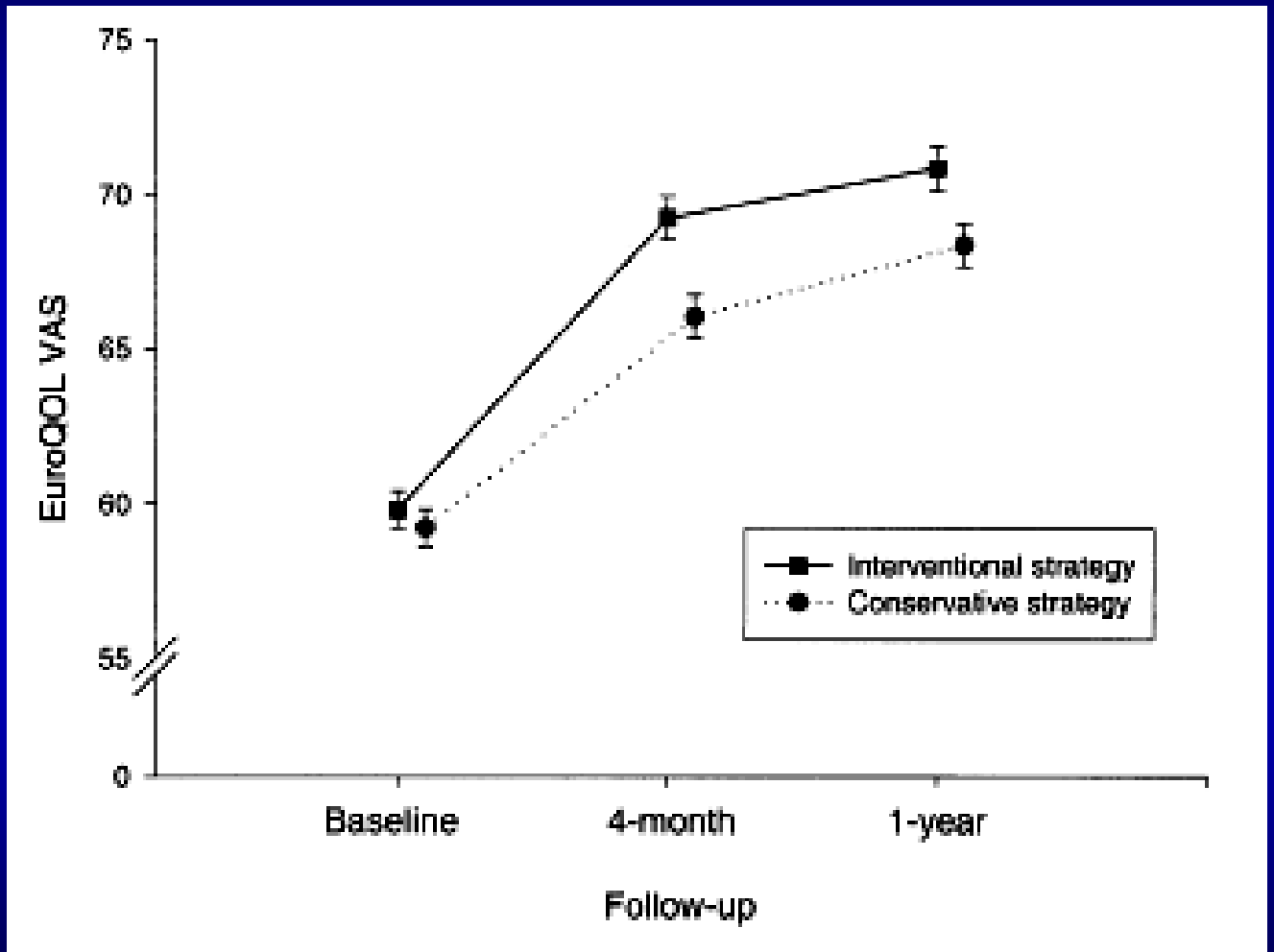
CNUH data. Circ J 2005;69:159-164

	I (n=32)	II (n=29)	III (n=28)	IV (n=31)	Total (n=120)
In-hospital					
Revascularization	1	1	0	0	2
Myocardial infarction	1	0	0	0	1
Cardiac death	0	0	0	1	1
One-month late					
Revascularization	1	0	1	0	2
Myocardial infarction	0	0	0	0	0
Cardiac death	1	0	0	0	1
Six-months late					
Revascularization	6	7	3	3	19
Myocardial infarction	0	1	0	0	1
Cardiac death	0	0	0	0	0
Total MACE	10 (31.3%)	9 (31.0%)	4* (14.3%)	4* (12.9%)	27 (22.5%)

**p=0.02; groups I and II vs groups III and IV respectively.*

CNUH data. Circ J 2005;69:159-164

Early interventional strategy provides greater gains in health-related QOL



Mainly due to angina grade

Kim et al., JACC 2005;45:221-8

Timing of invasive strategy

Event	Delayed	Early	RR (95% CI)	P value
Death and nonfatal MI	24 (11.6)	12(5.9)	1.96(1.01-3.82)	.04
Death	3(1.4)	0		.25
Nonfatal				.12
Q-wave				.54
Non-Q-wave	14(6.8)	8(3.9)	1.72(0.74-4.00)	.21
Major bleeding event	8(3.9)	6(3.0)	1.31(0.46-3.70)	.61
Nadir platelet count <20 x 10^3 /uL	2(1.0)	1(0.5)	1.96(0.18-21.5)	>.99

Optimal timing of invasive approach: within first 48 hours of presentation

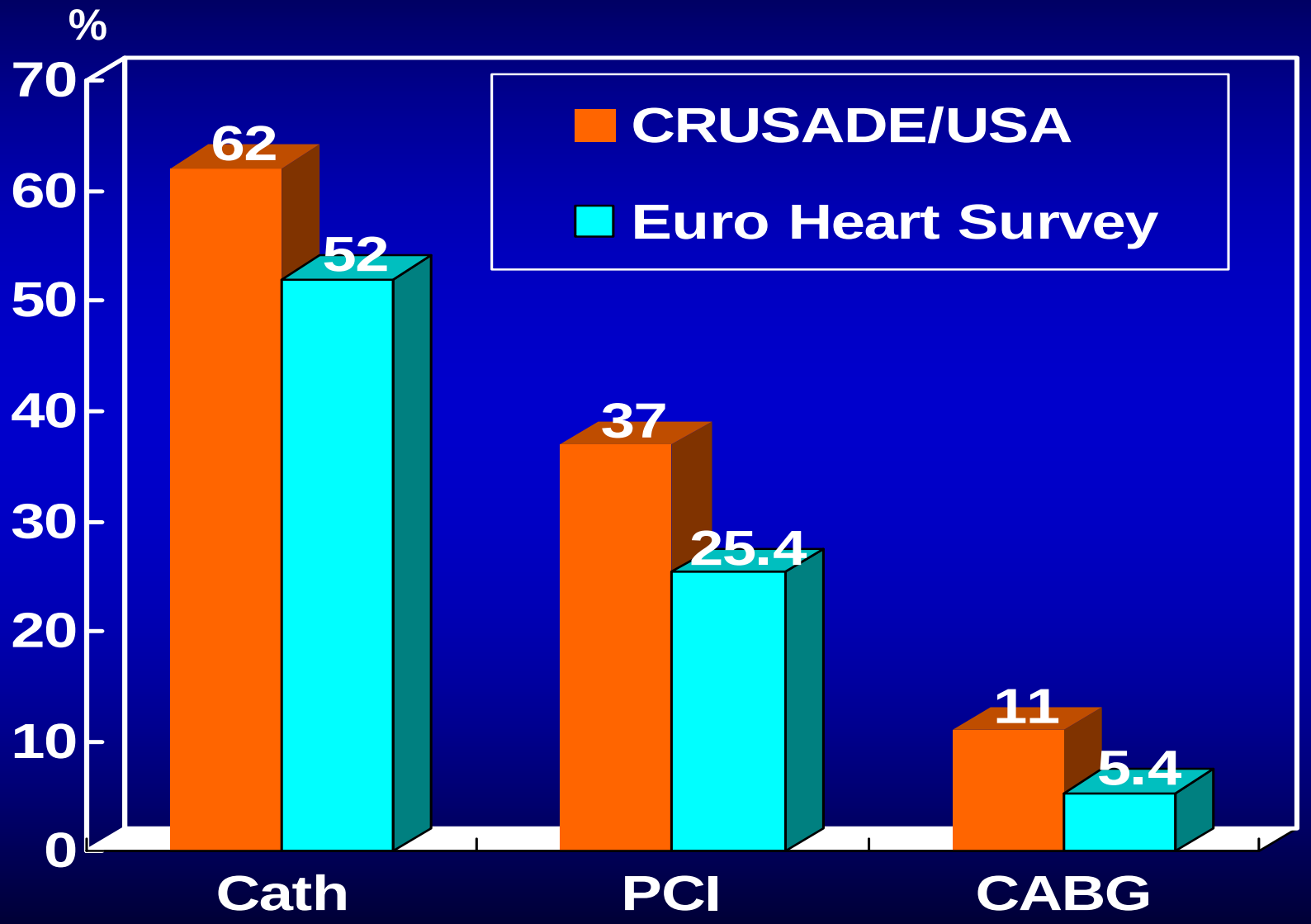
Delayed: antithrombotic pretreatment for 3 to 5 days
Early: early intervention less than 6 hours

Evaluation of prolonged antithrombotic pretreatment before intervention in patients with Unstable coronary syndromes JAMA 2003;290:1593-1599

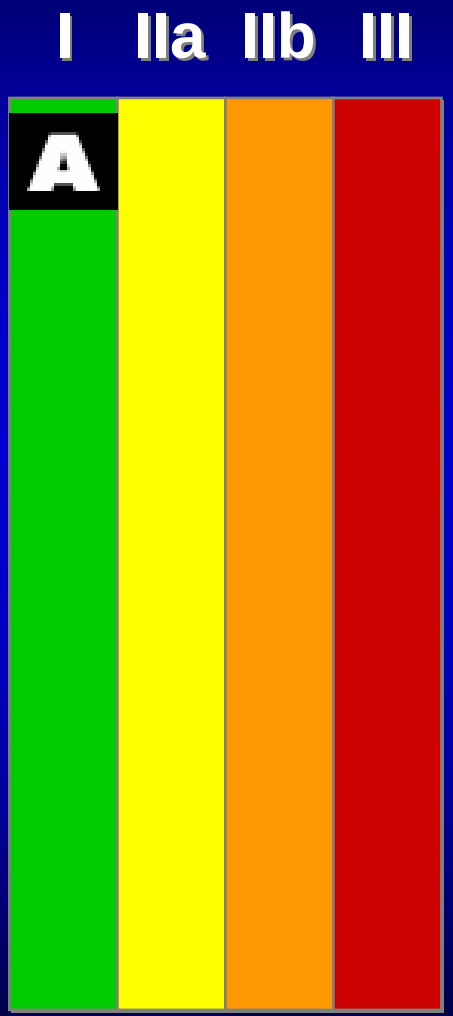
Indications for invasive vs. conservative management

- ST segment changes or positive troponin
- Recurrent ischemia and evidence of CHF
- Cardiogenic shock
- UA/NSTEMI within 6 months of prior PCI or in patients with prior CABG

Current utilization



Conservative vs. Invasive Strategies



Early invasive strategy in high-risk patients with any of the following:

- **Recurrent ischemia, despite meds**
- **Elevated Troponin I or T**
- **New ST-segment depression**
- **New CHF symptoms**
- **High-risk stress test findings**
- **LV dysfunction (EF < 40%)**
- **Hemodynamic instability, sustained VT**
- **PCI within 6 months, prior CABG**

ACC/AHA guideline update for management of UA/NSTEMI. Circulation 2002

Noninvasive test results predicting high risk for adverse outcomes in UA/NSTEMI - 1

Exercise EKG

- Abnormal horizontal or downsloping ST depression c/
- Onset at HR < 120/min or ≤ 6.5 METs
- Magnitude ≥ 2.0 mm
- Postexercise duration of ≥6 min
- Depression in multiple leads

-Abnormal SBP response c/ sustained decrease of 10 mmHg or flat BP response ≤ 130 mmHg, c/ abnormal EKG

- Other
- Exercise-induced ST elevation
- VT

Noninvasive test results predicting high risk for adverse outcomes in UA/NSTEMI - 2

Radionuclide myocardial perfusion imaging

- Abnormal myocardial tracer distribution in more than one coronary artery region at rest or with stress or anterior defect that reperfuses

- Abnormal myocardial distribution c/ increased lung uptake

- Cardiac enlargement

Noninvasive test results predicting high risk for adverse outcomes in UA/NSTEMI - 3

Left ventricular imaging

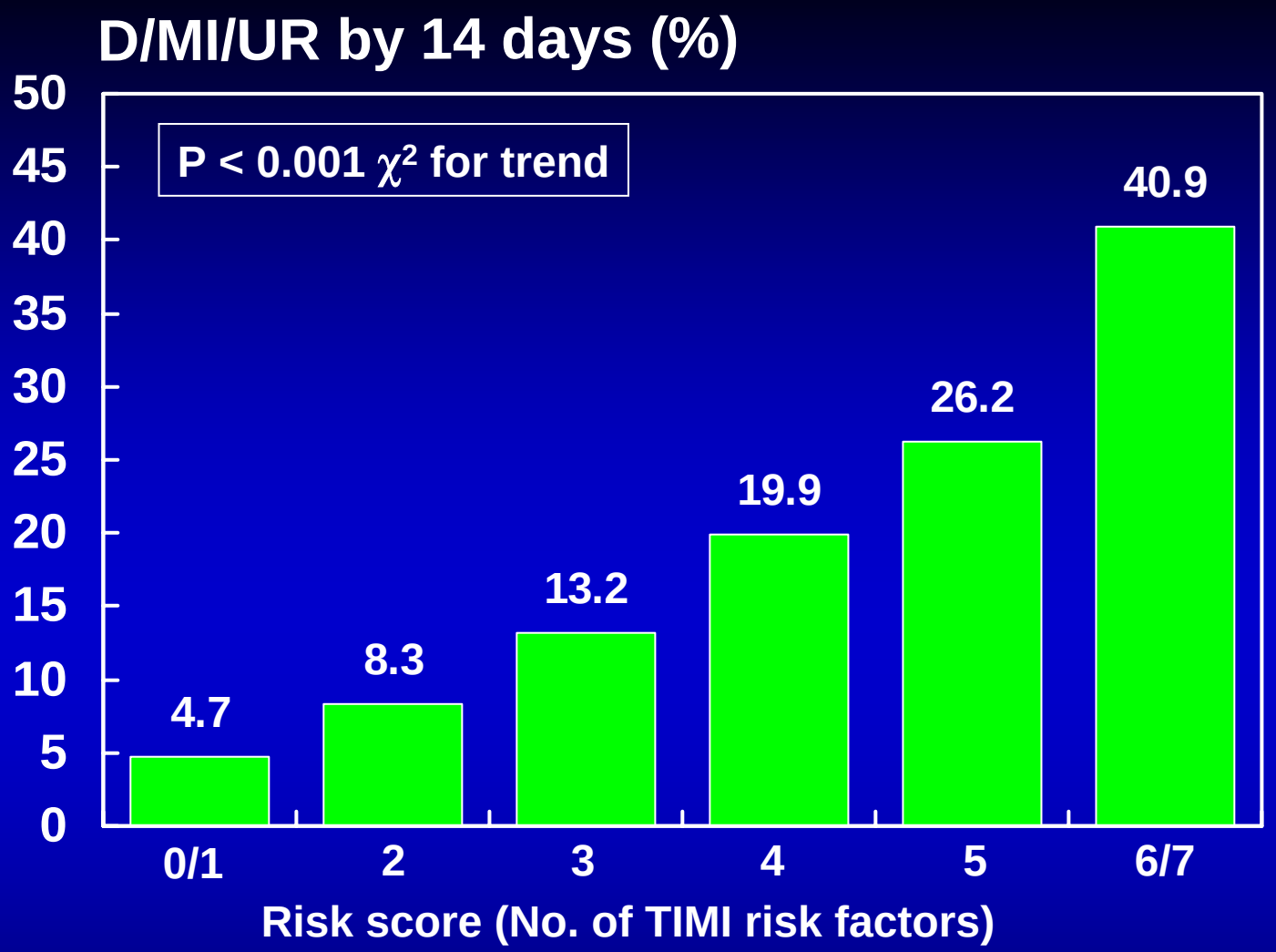
- Stress radionuclide ventriculography

- Exercise EF ≤ 50%
- Rest EF ≤ 35%
- Fall in EF ≥ 10%

Noninvasive test results predicting high risk for adverse outcomes in UA/NSTEMI - 3

Stress echocardiography

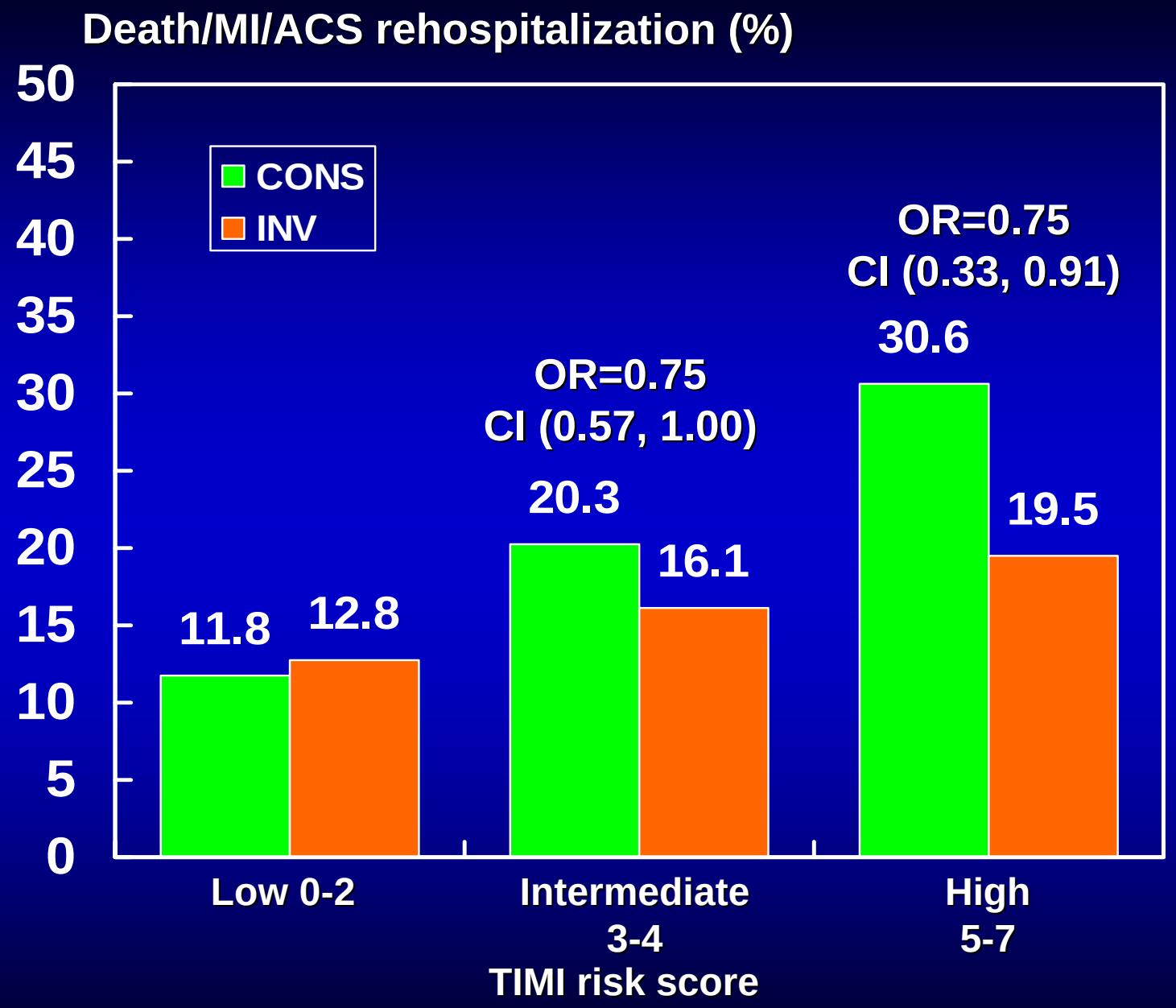
- Rest EF $\leq$ 35%
- Wall motion score index > 1



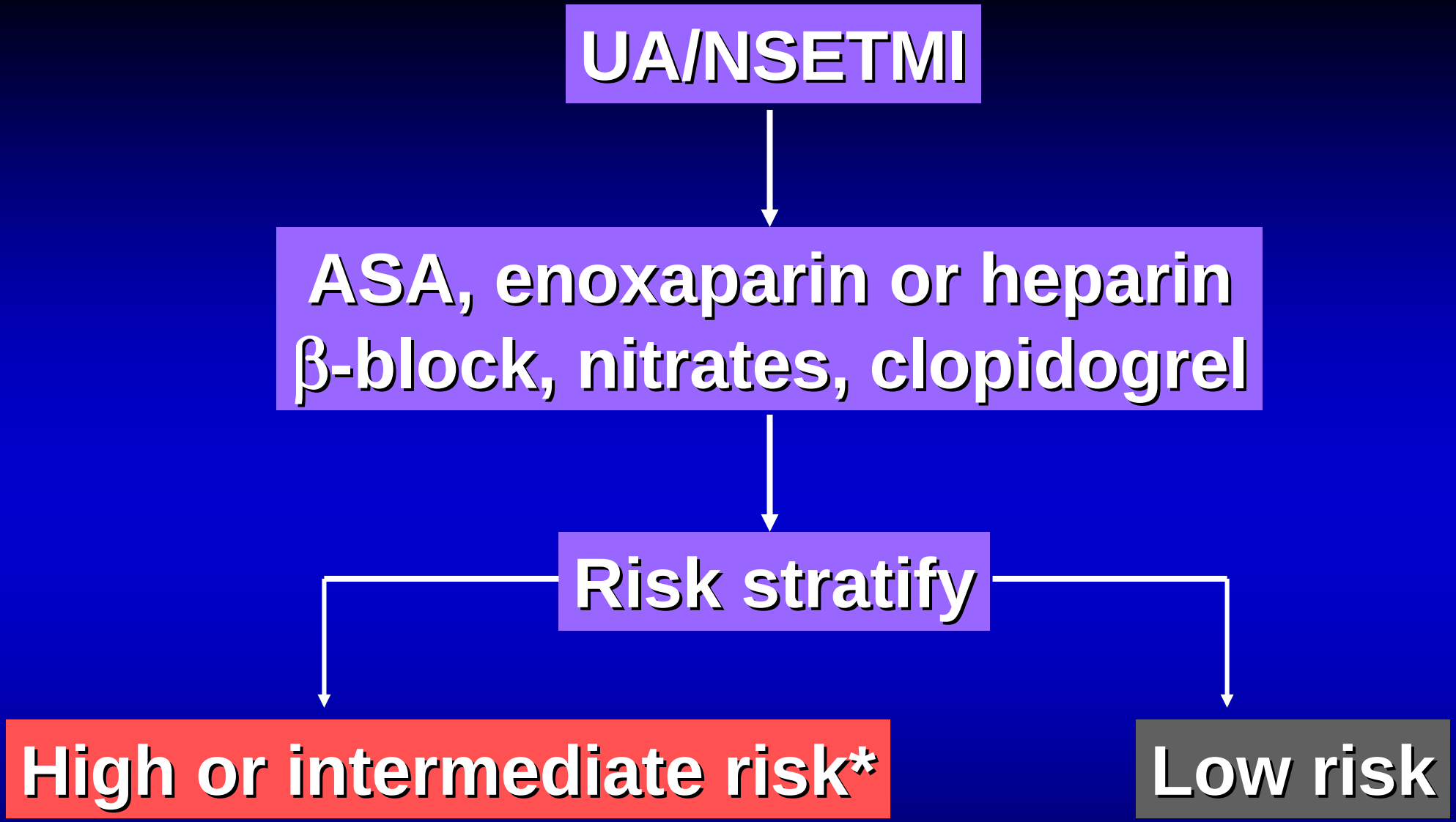
TIMI risk factors

- Age ≥ 65 yrs
- ≥3 CAD risk factors
- Known CAD (> 50% stenosis)
- Prior aspirin
- ≥ 2 anginal episodes in prior 24 hr
- ST deviation ≥ 0.5 mm of presenting ECG
- ↑Cardiac markers

Antman EM, et al. JAMA 284;835, 2000

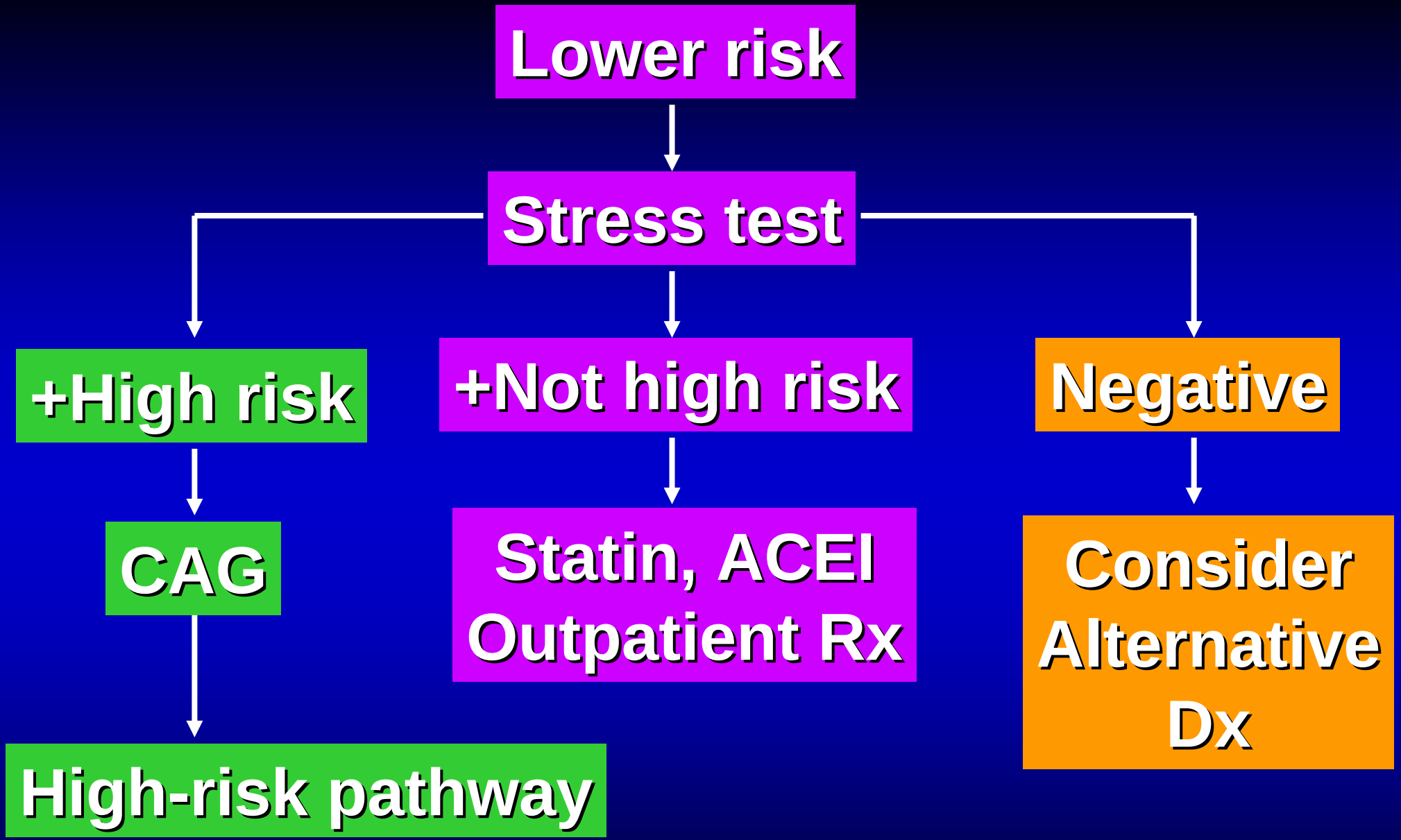


TACTICS-TIMI 18 trial. Cannon CP, et al. NEJM 344;1879, 2001

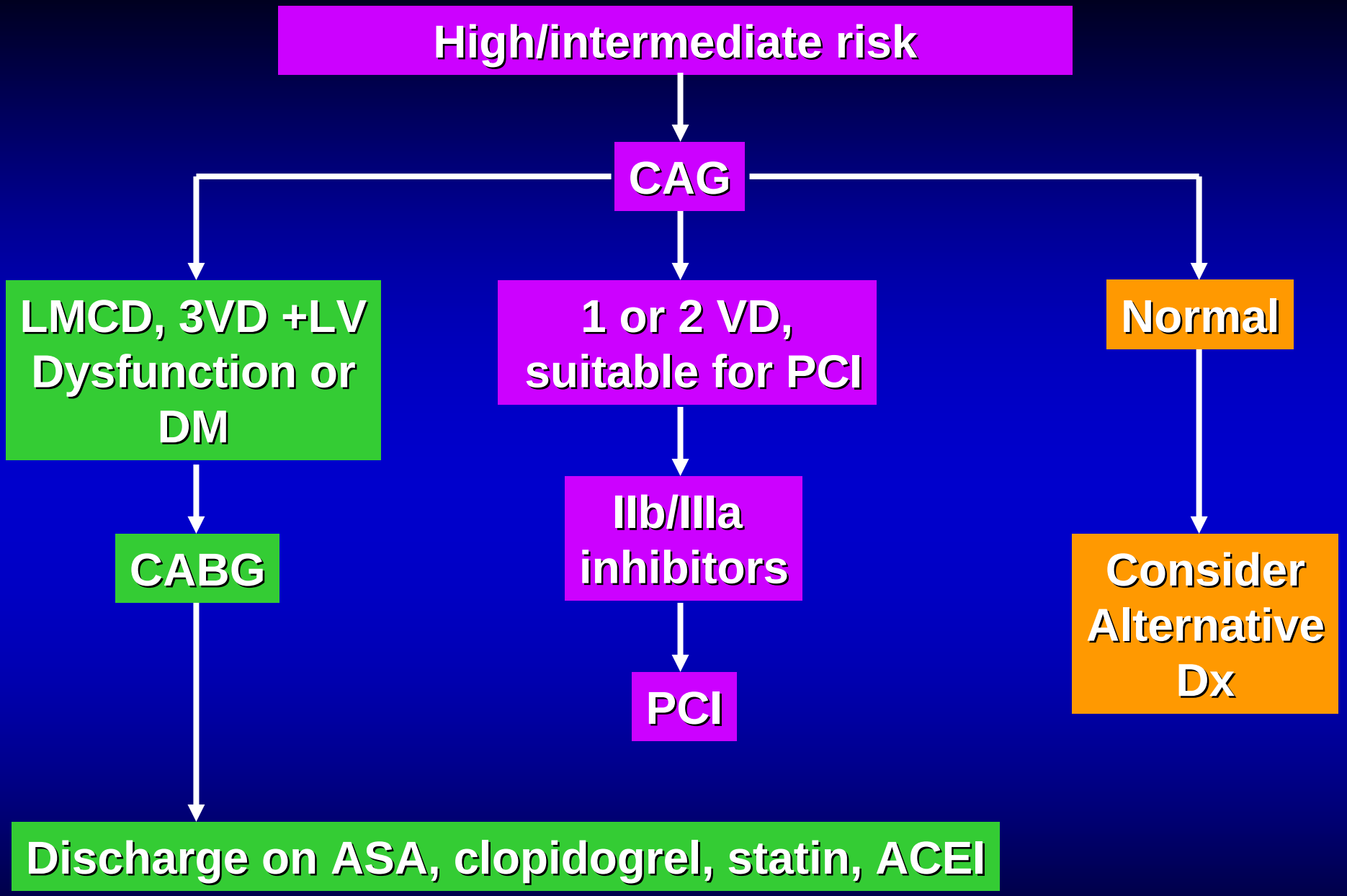


***Recurrent ischemia; ↑Trop; ↓ST; LV failure/dysfunction; hemodynamic instability; VT; prior CABG**

Braunwald E: Application of current guideline to the management of UA/NSTEMI. Circulation 108:III-28, 2003

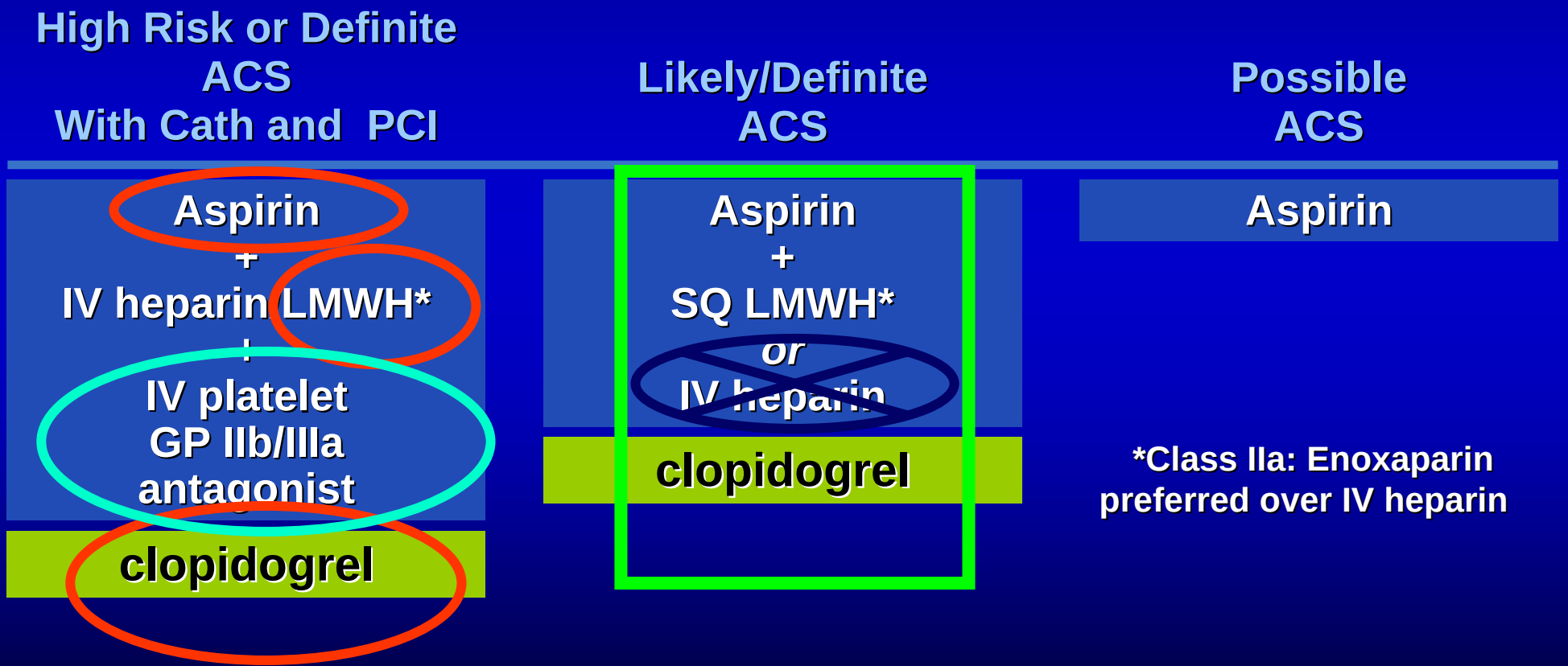


Braunwald E: Application of current guideline to the management of UA/NSTEMI. Circulation 108:III-28, 2003



Braunwald E: Application of current guideline to the management of UA/NSTEMI. Circulation 108:III-28, 2003

ACC/AHA Guideline + 2002 Update:
Recommendations for Antithrombotic Therapy*



Braunwald E et al. J Am Coll Cardiol. 2000;36:970-1062; www.acc.org 3/15/2002

Summary

- Invasive strategy is equally clinically beneficial with early conservative strategy

- For high-risk patients
  (e.g. those with positive troponin, ST segment changes, TIMI risk score > 3),
  GP IIb/IIIa inhibition should be added to the preceding medications, and early invasive strategy is preferred