Insights into Acute STEMI

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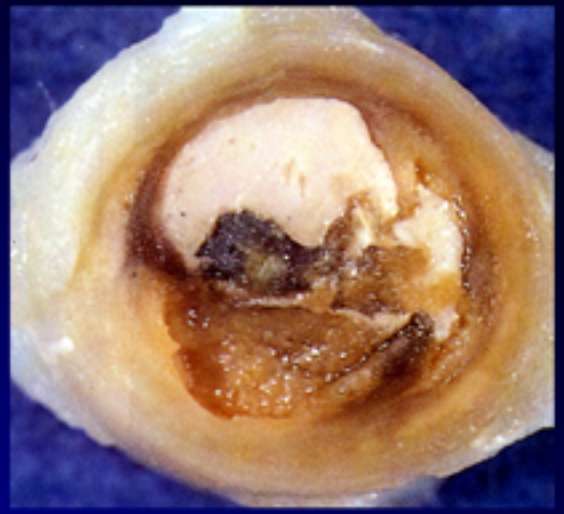
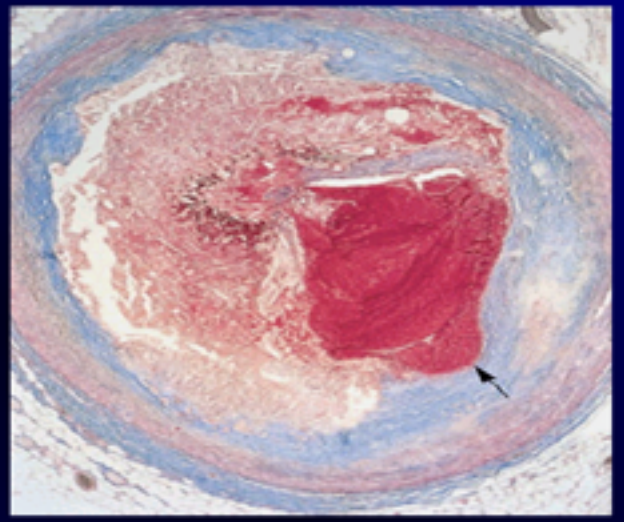
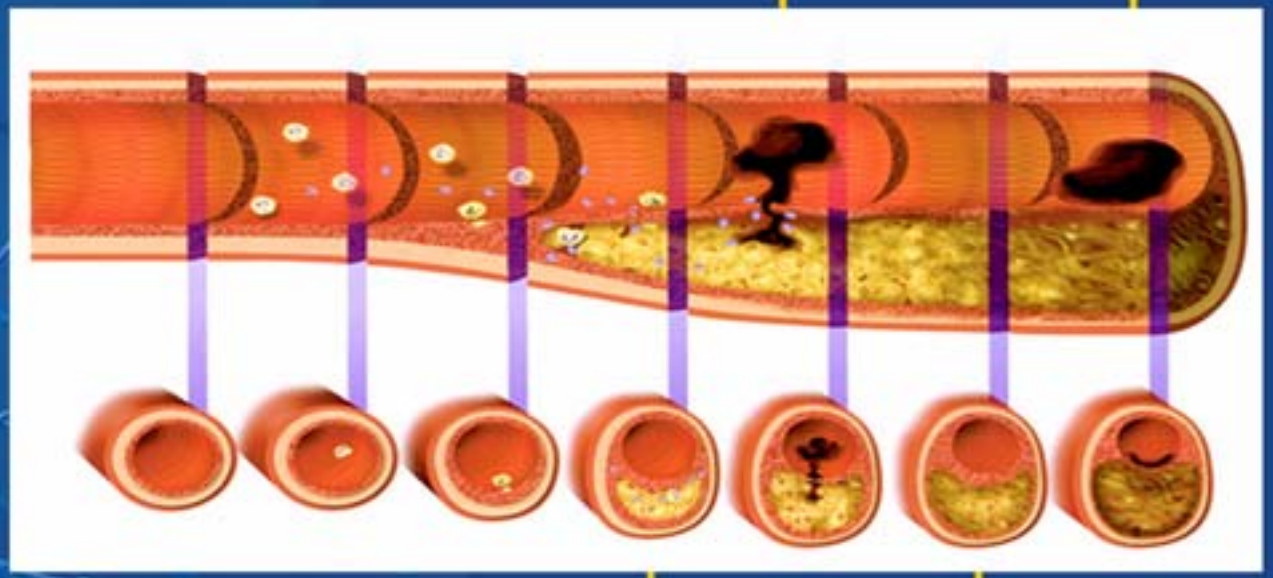
Pathophysiology of AMI





Ruptured fibrous cap with luminal and intraplaque occlusive thrombus

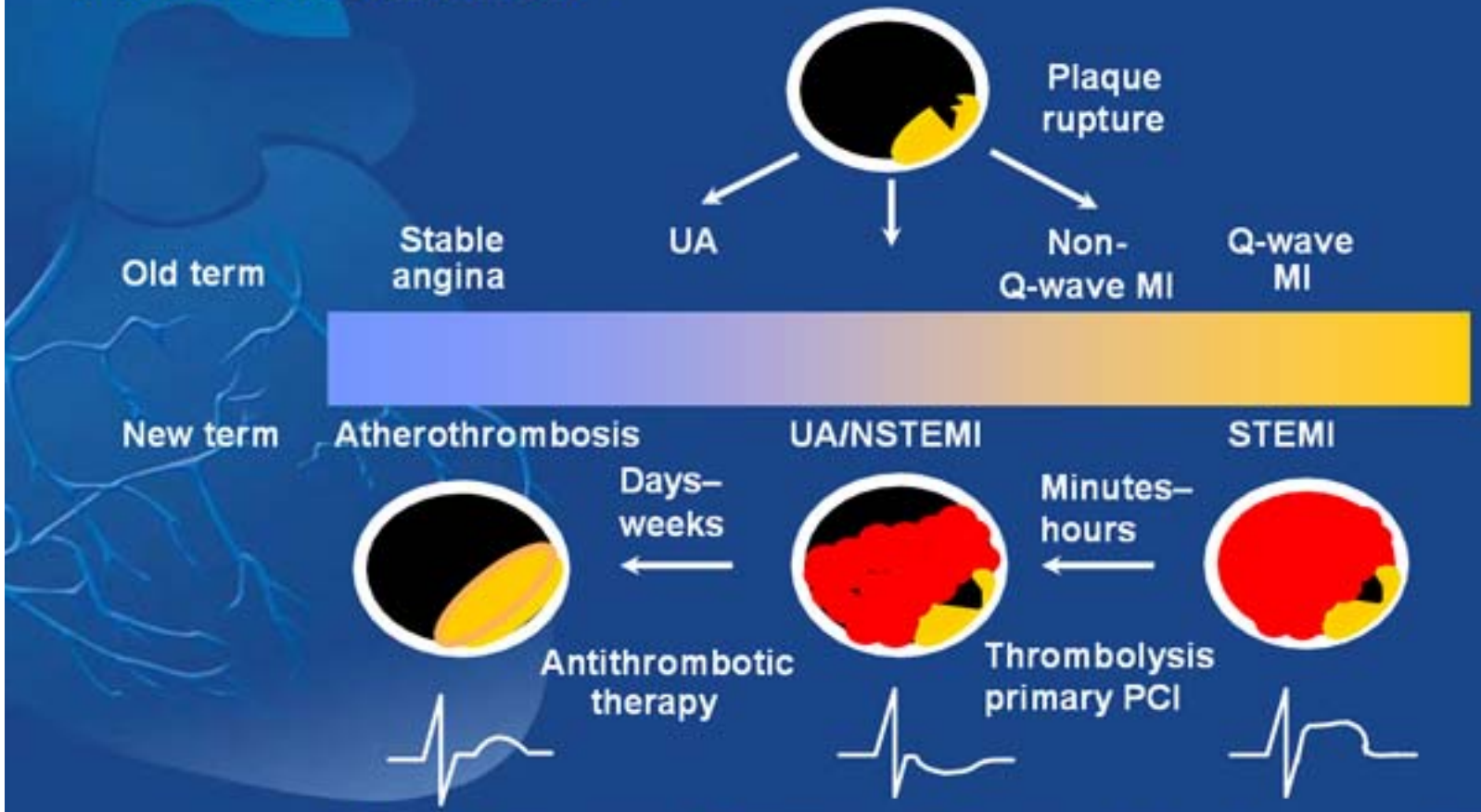
Pathologic Progression to Atherothrombosis[1]



MI=myocardial infarction; ACS=acute coronary syndrome; TIA=transient ischemic attack; CV=cardiovascular

1. Libby P. *Circulation* 2001; 104: 365–372.

ACS is an Important Manifestation of Atherothrombosis[1]

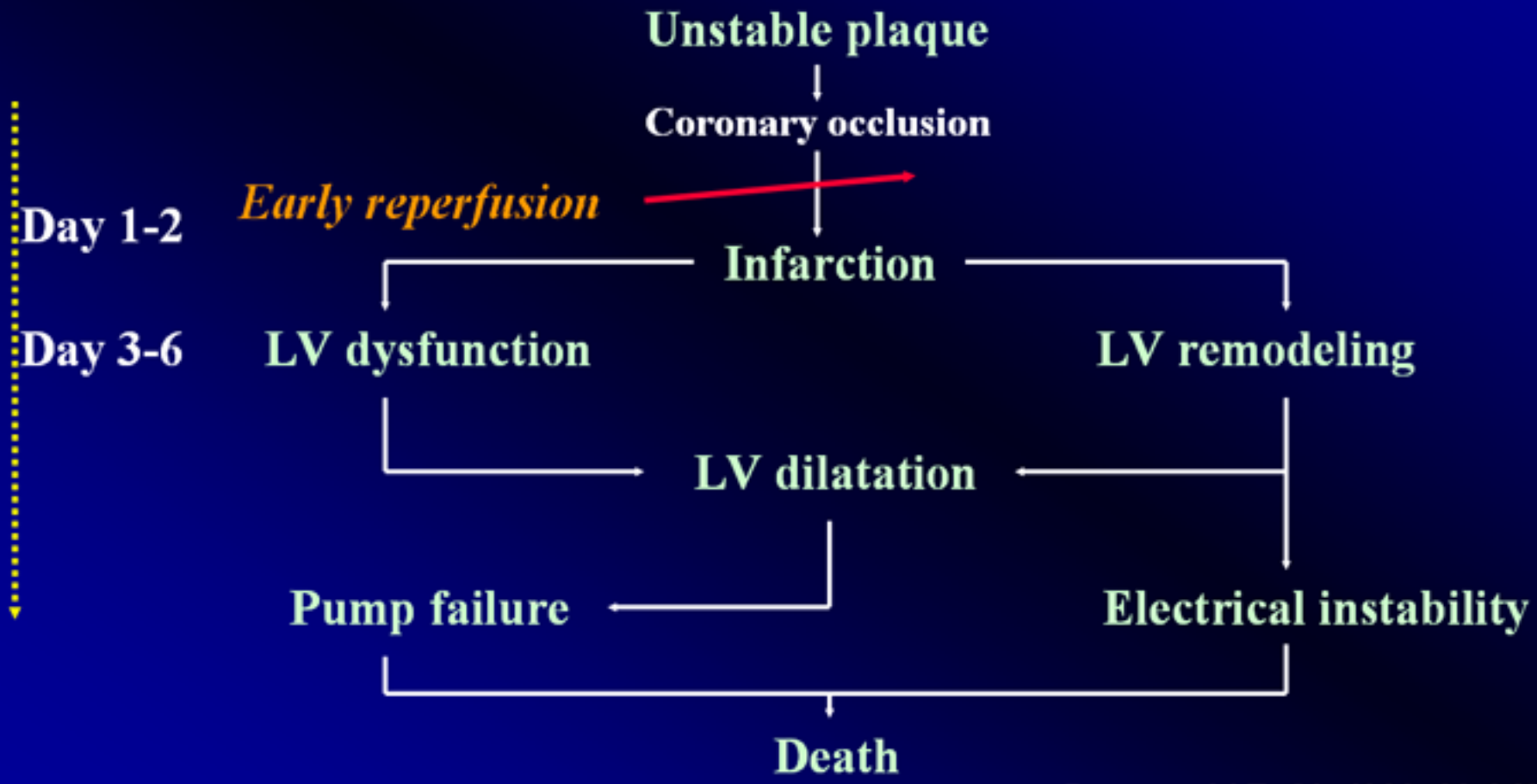


UA=unstable angina; NSTEMI=non-ST-segment elevation myocardial infarction; PCI=percutaneous coronary intervention

1. Cannon CP. *J Thromb Thrombolysis* 1995; 2: 205–218.

Open Artery Hypothesis

From unstable plaque to death



Braunwald E. Cir 1993, 88:2426

High Risk of Mortality Following Acute MI

Approximately 33% of patients with an MI will die before they reach the hospital[1]

	NRMI 3–4 (n=81,679)*[2]	GRACE Registry (n=5,476)[3]
In-hospital mortality	12.3%	7.8%
Reperfused	6.6%	–
Not reperfused	18.7%	–
6-month† mortality	–	4.8%

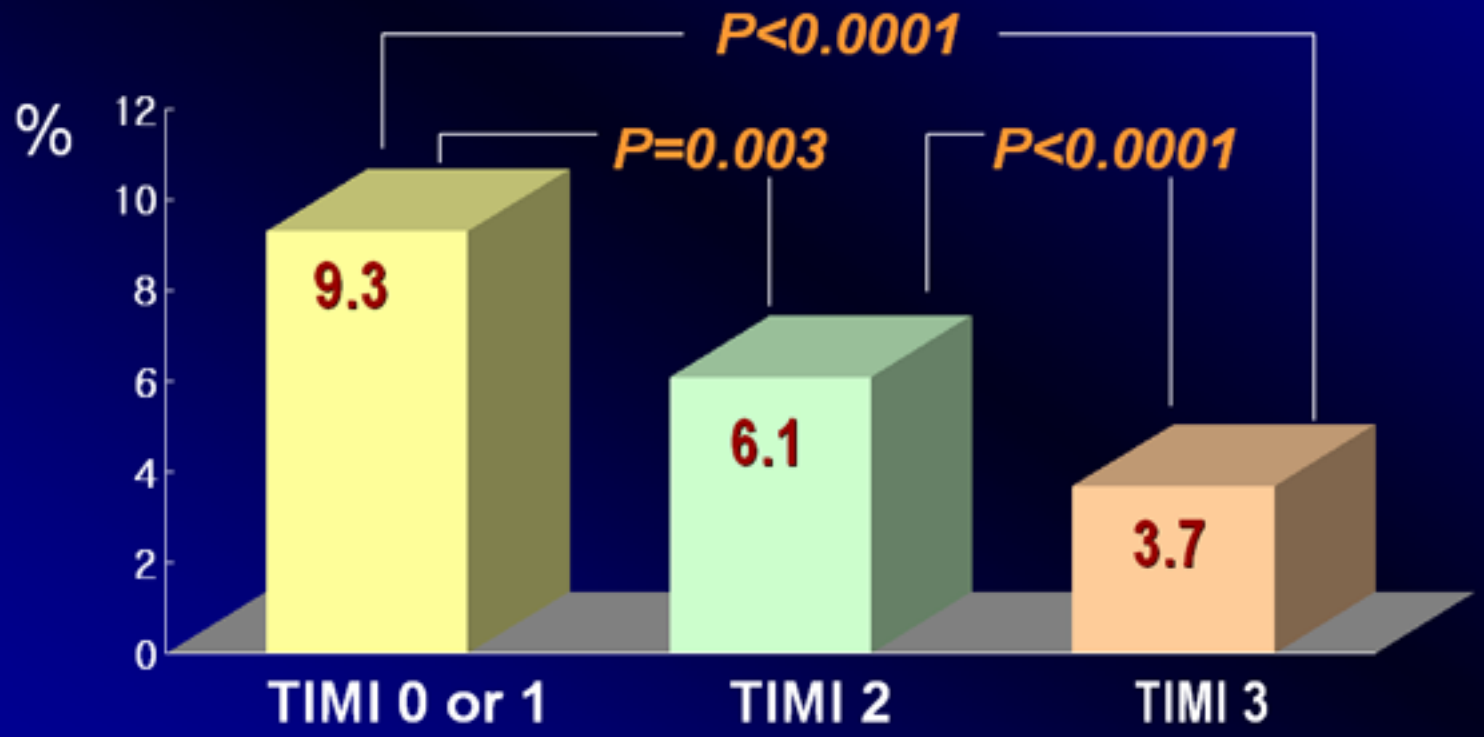
- Within 6 years 18% of men and 35% of women will suffer an additional heart attack[4]

*Patients with STEMI from the NRMI 3–4 database (n=153,486); †post-discharge; GRACE=The Global Registry of Acute Coronary Events; NRMI=National Registry for Myocardial Infarction

1. Boersma E et al. *Lancet* 2003; 361: 847–858.
2. NRMI 3-4. *J Am Coll Cardiol* 2004; 44: 783–789.
3. Goldberg RJ et al. *Am J Cardiol* 2004; 93: 288–293.
4. Antman EM et al. 2004 ACC/AHA STEMI Guidelines. Available at: URL: http://www.accp.org/clinical/guidelines/stemi/index.pdf Accessed February 2005.

TIMI Flow Rate and Mortality

Pooled data from 5498 pts with thrombolysis

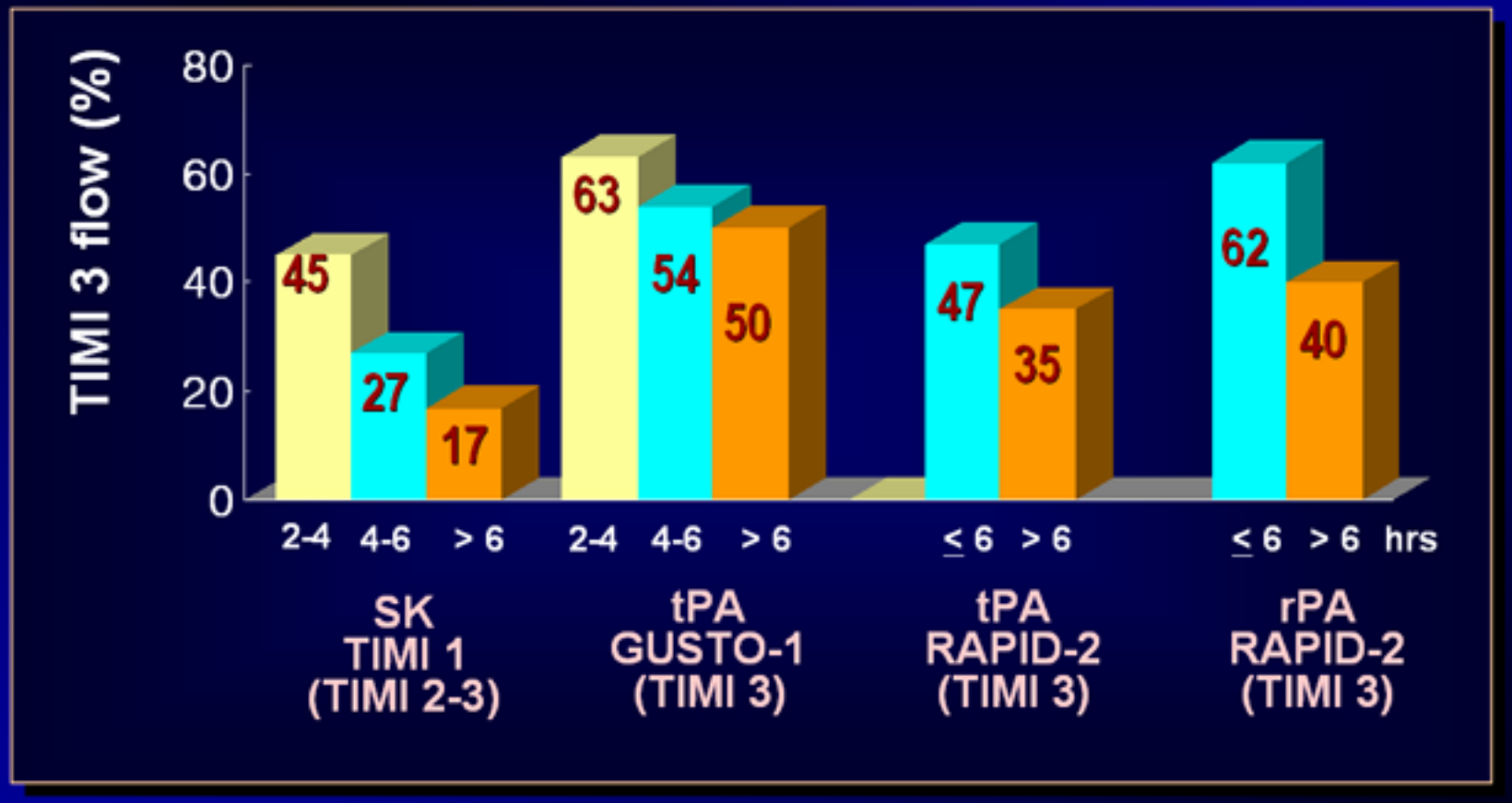


TIMI=Thrombolysis in Myocardial Infarction

Dr. Michael Gibson, 2000

Thrombolysis

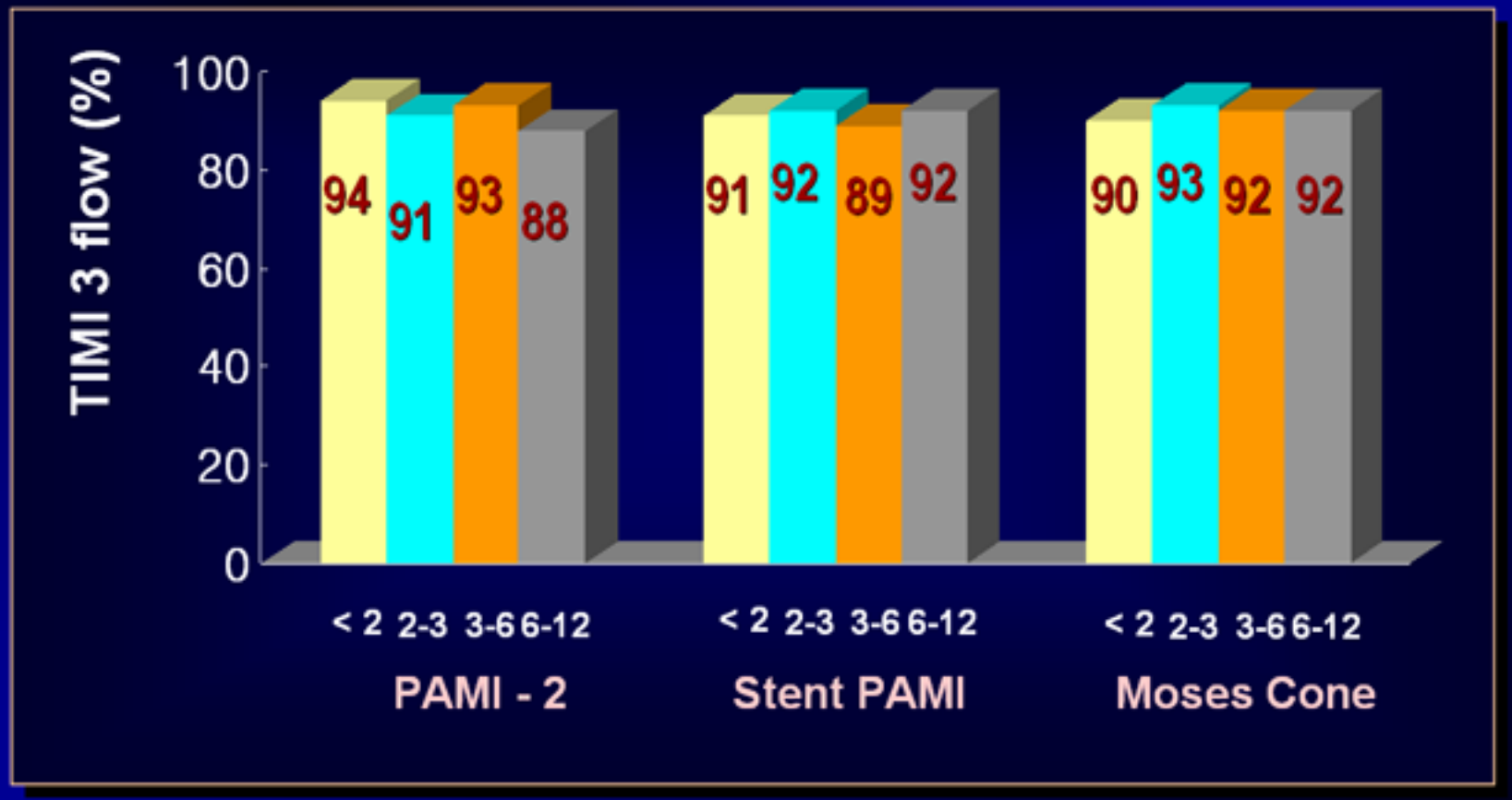
Rapid decrease of reperfusion rate with time



Chesebro JH. Cir 1987;76:142 *Bode C. Cir 1996;94:891*

Primary PTCA

Acceptable reperfusion rate with time



Stone G. Cir 1996;76:142

Brodie BR. JACC 1998;32:1312

Assessing Reperfusion Options for Patients with STEMI[1]

STEP 1: Assess time and risk (time from symptom onset, risk of STEMI, risk of thrombolysis, time for transport to PCI lab)

STEP 2: Determine whether fibrinolysis or invasive strategy is preferred*

Fibrinolysis preferred if:	Invasive strategy preferred if:
• Early presentation (<3 hours) • Invasive strategy not an option • Delay to invasive strategy	• Skilled PCI lab with surgical backup available • High risk (i.e. cardiogenic shock) • Contraindications to fibrinolysis • Late presentation (>3 hours) • Diagnosis of STEMI is in doubt

***If presentation is <3 hours from onset and there is no delay to an invasive strategy, there is no preference for either strategy**

1. Antman EM et al. *Circulation* 2004; 110: 588–636.

Thrombolysis Remains an Important Reperfusion Strategy Worldwide

	GRACE[1] (n=5,476)	EHS[2] (n=3,438)	NRMI 3–4*[3] (n=81,679)
Thrombolytic agent (%)	45.0	35.1	52.0
Catheterization (%)	61.0	53.0	–
PCI	44.4	40.4	–
Primary PCI	–	20.7	48.0
CABG (%)	5.0	3.4	–

*Patients with STEMI from the NRMI 3–4 database (n=153,486); EHS=EuroHeart Survey; CABG=coronary artery bypass graft

1. Goldberg RJ et al. *Am J Cardiol* 2004; 93: 288–293.
2. Hasdai D et al. *Eur Heart J* 2002; 23: 1190–1201.
3. Wiviott SD et al. *J Am Coll Cardiol* 2004; 44: 783–789.

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)	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% 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

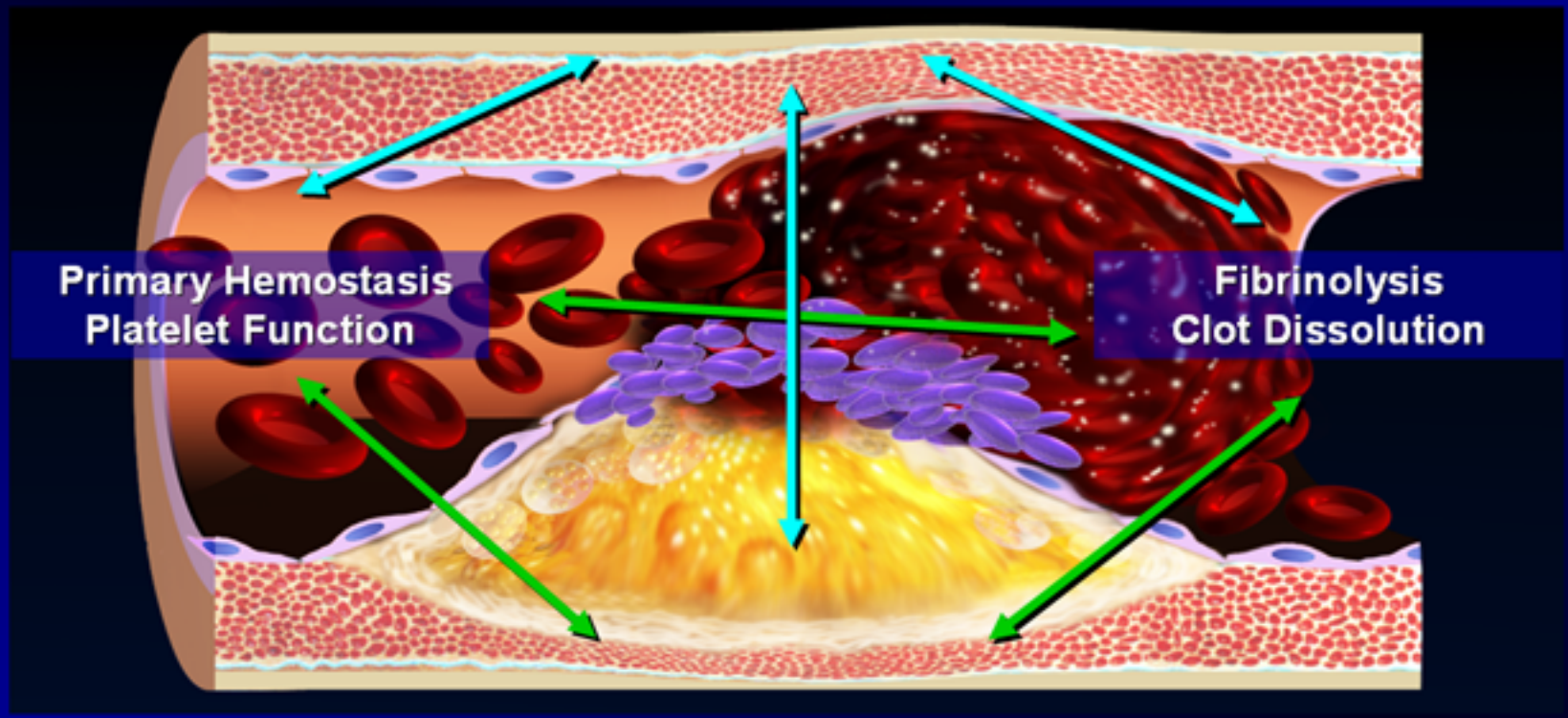
Despite current therapy, 10% of STEMI patients die within one month after hospital discharge[2]

Within 6 years 18% of men and 35% of women will suffer another heart attack[3]

1. Sabatine M et al. *New Engl 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: URL: http://www.accp.org/clinical/guidelines/stemi/index.pdf. Accessed February 2005.

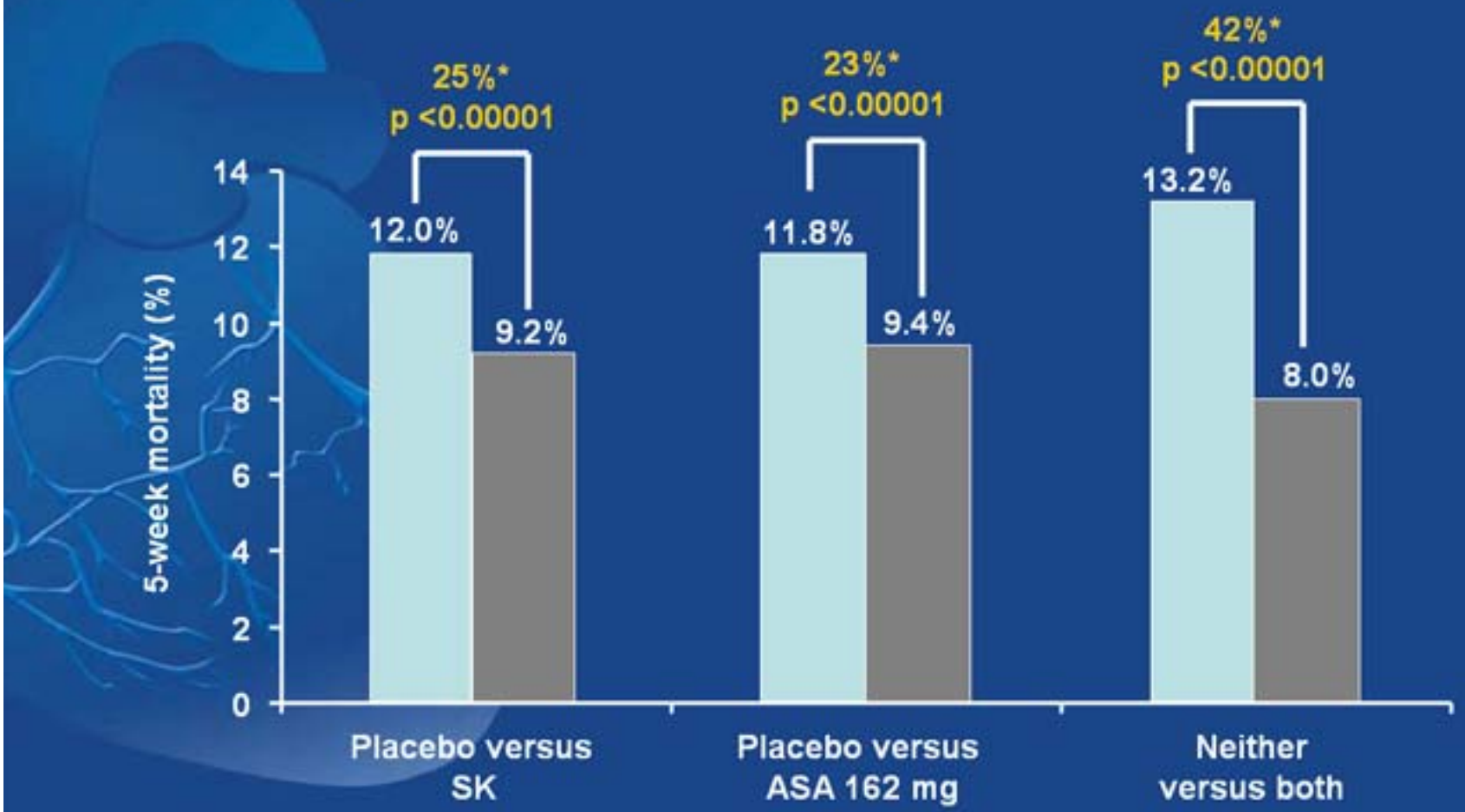
Rationale for Antiplatelet Therapy in Acute MI

Coagulation
Fibrin Formation



Injured Vessel Wall
Endothelium

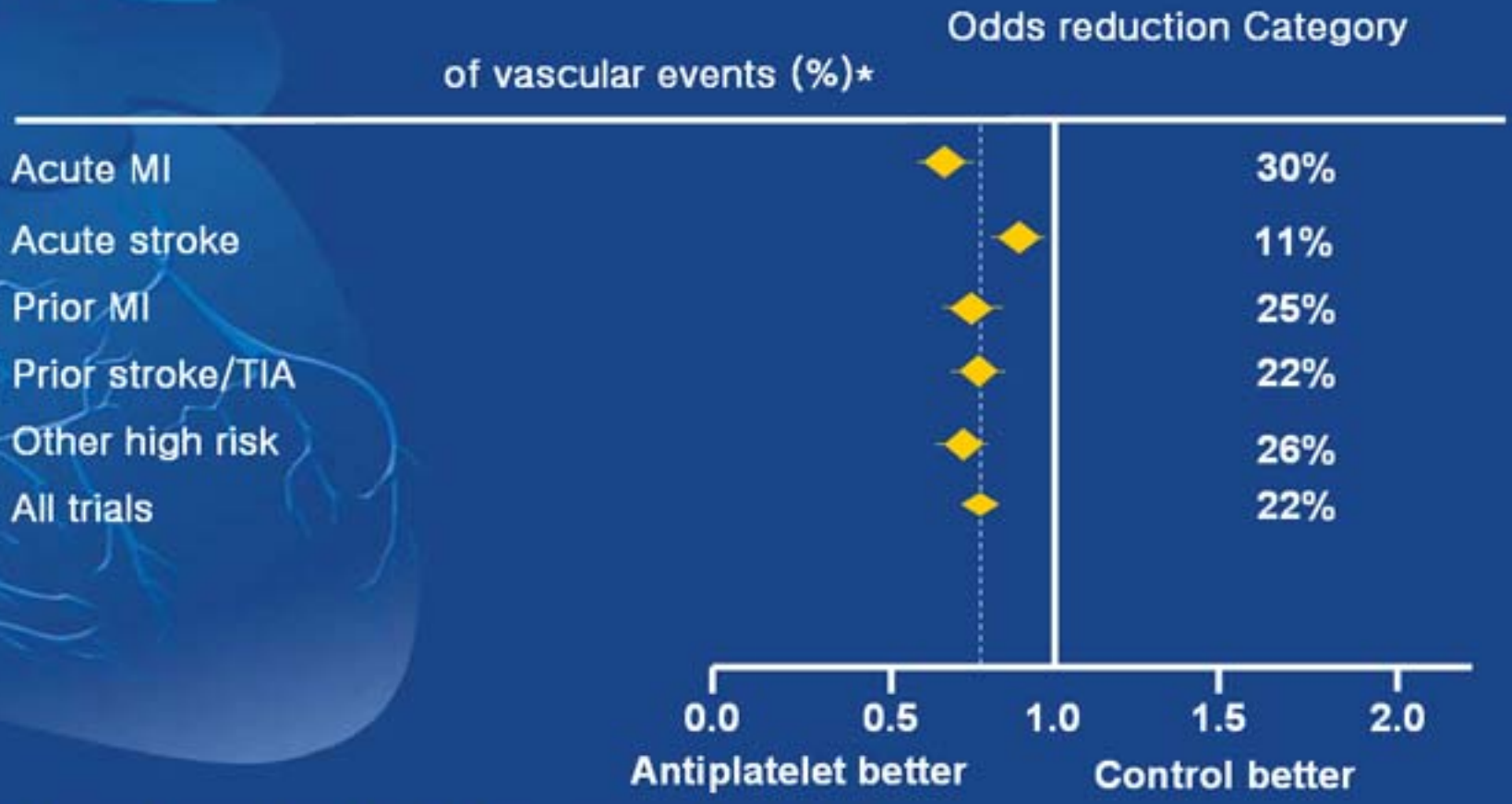
Thrombolysis and ASA in Acute STEMI: ISIS–2[1]



*Odds reduction; ISIS=Second International Study of Infarct Survival

1. ISIS-2 Collaborative Group. *Lancet* 1988; 2: 349–360.

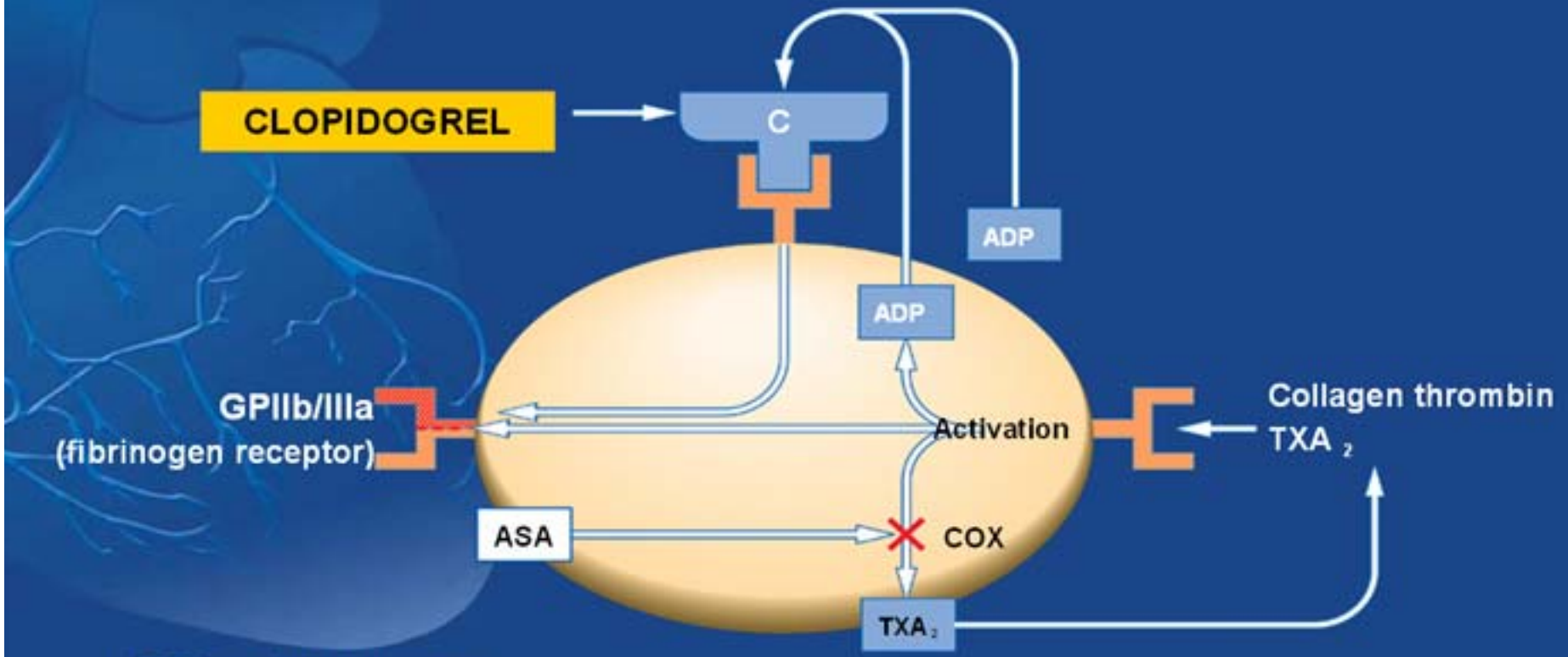
Antiplatelet Therapy is Beneficial[1]



*Vascular events=MI, stroke or vascular death

1. Antithrombotic Trialists' Collaboration. *BMJ* 2002; 324: 71–86.

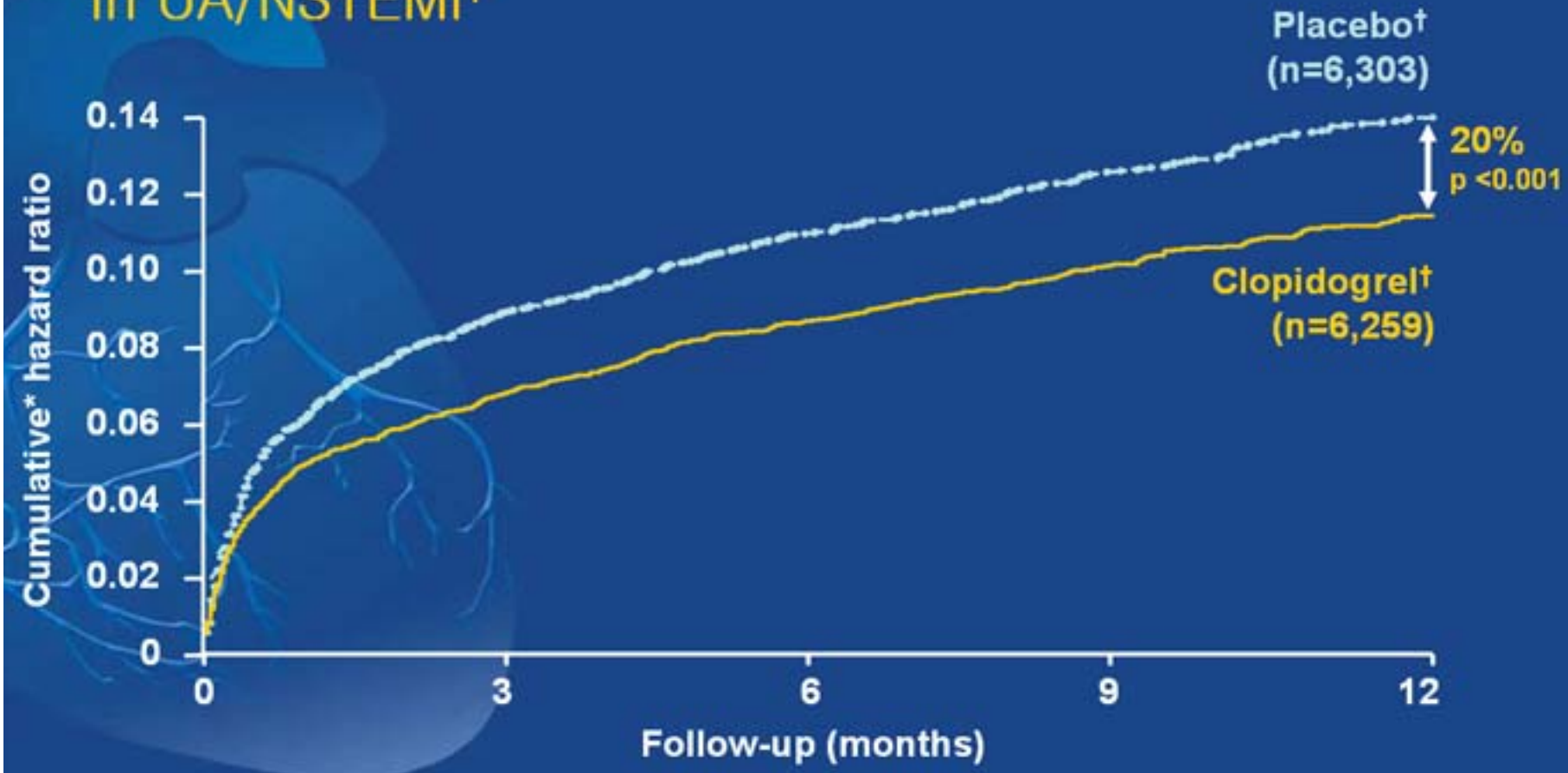
Potent, Specific and Complementary Mode of Action of Clopidogrel[1]



COX=cyclo-oxygenase

1. Jarvis B et al. *Drugs* 2000; 60: 347–377.

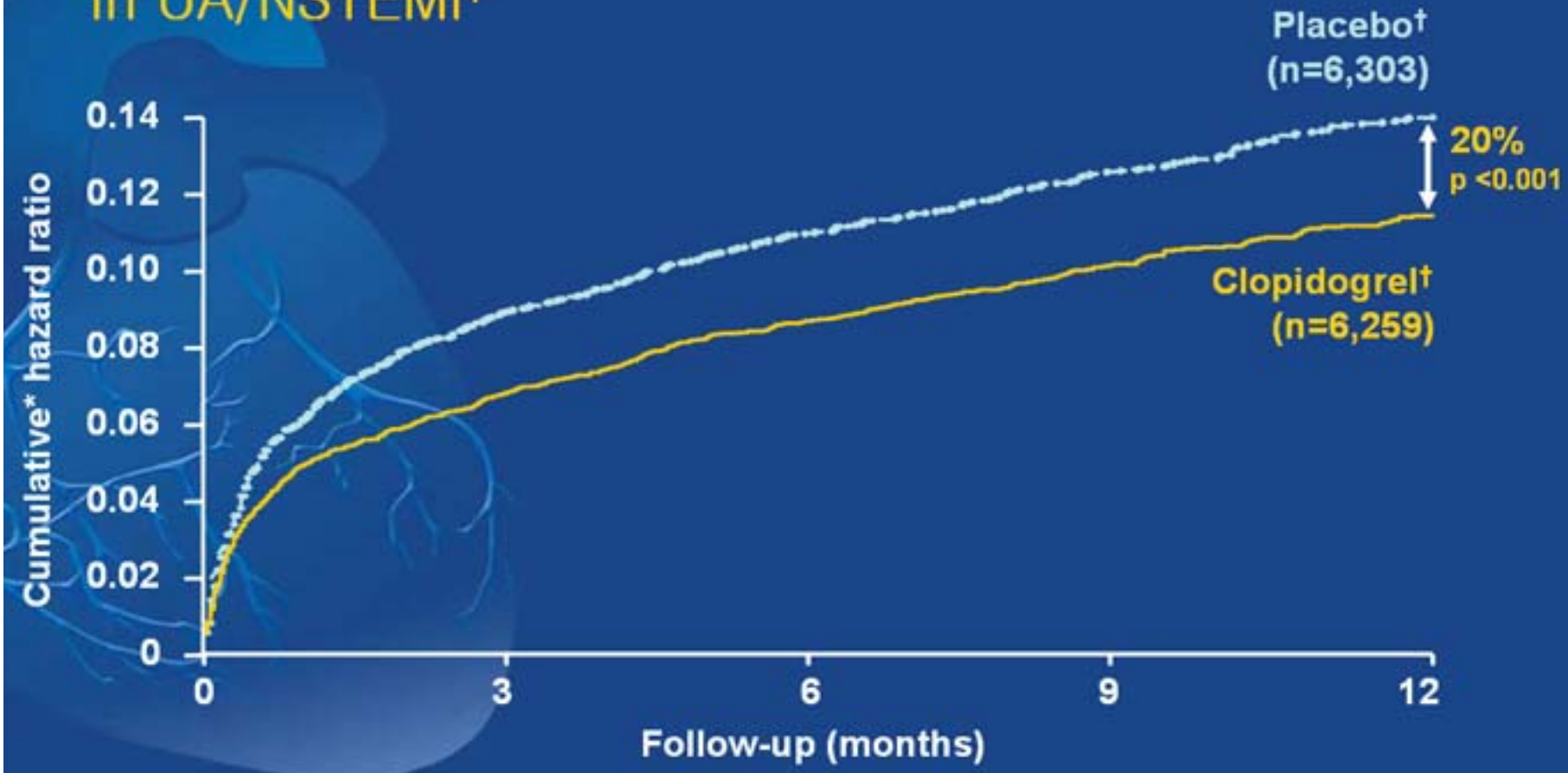
Early and Long-Term Benefits of Clopidogrel in UA/NSTEMI[1]



*Cumulative events: MI, stroke or CV death; †All patients received a background of ASA therapy

1. CURE Trial Investigators. *N Engl J Med* 2001; 345: 494–502.

Early and Long-Term Benefits of Clopidogrel in UA/NSTEMI[1]



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1. CURE Trial Investigators. *N Engl J Med* 2001; 345: 494–502.