PCI in Acute MI

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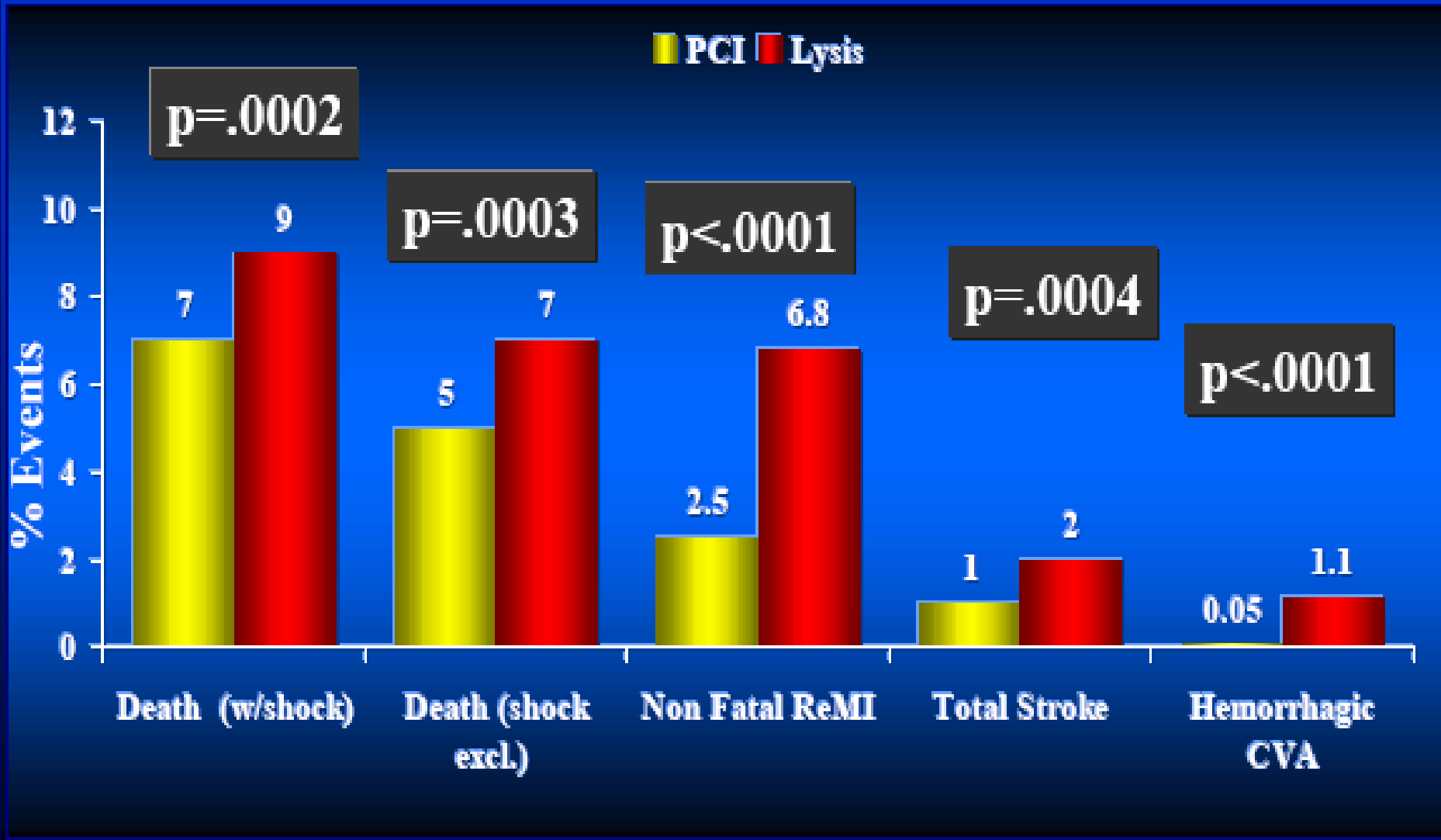
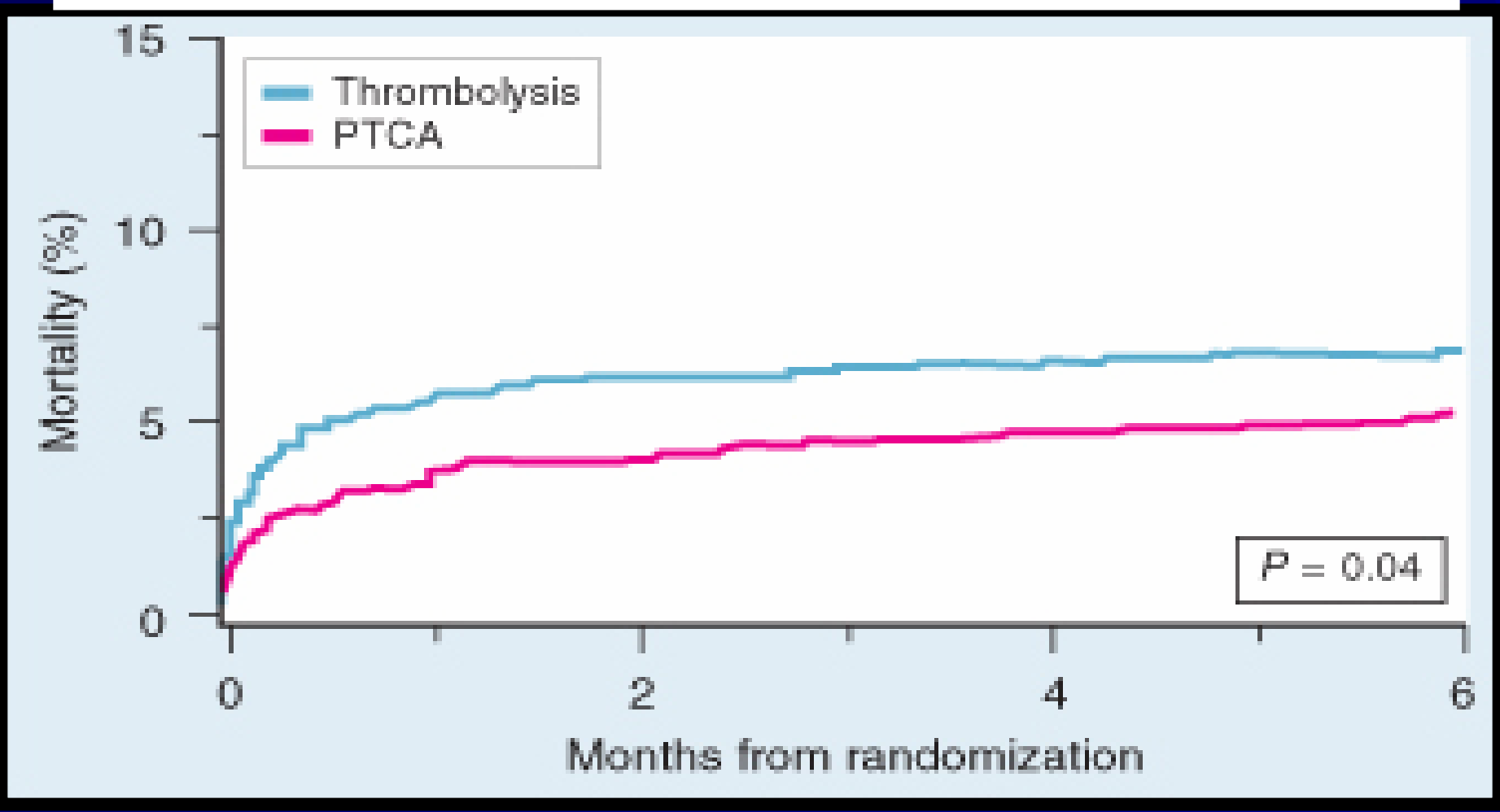
Meta-Analysis of 23 Randomized Trials of PCI vs Lysis (n=7739)



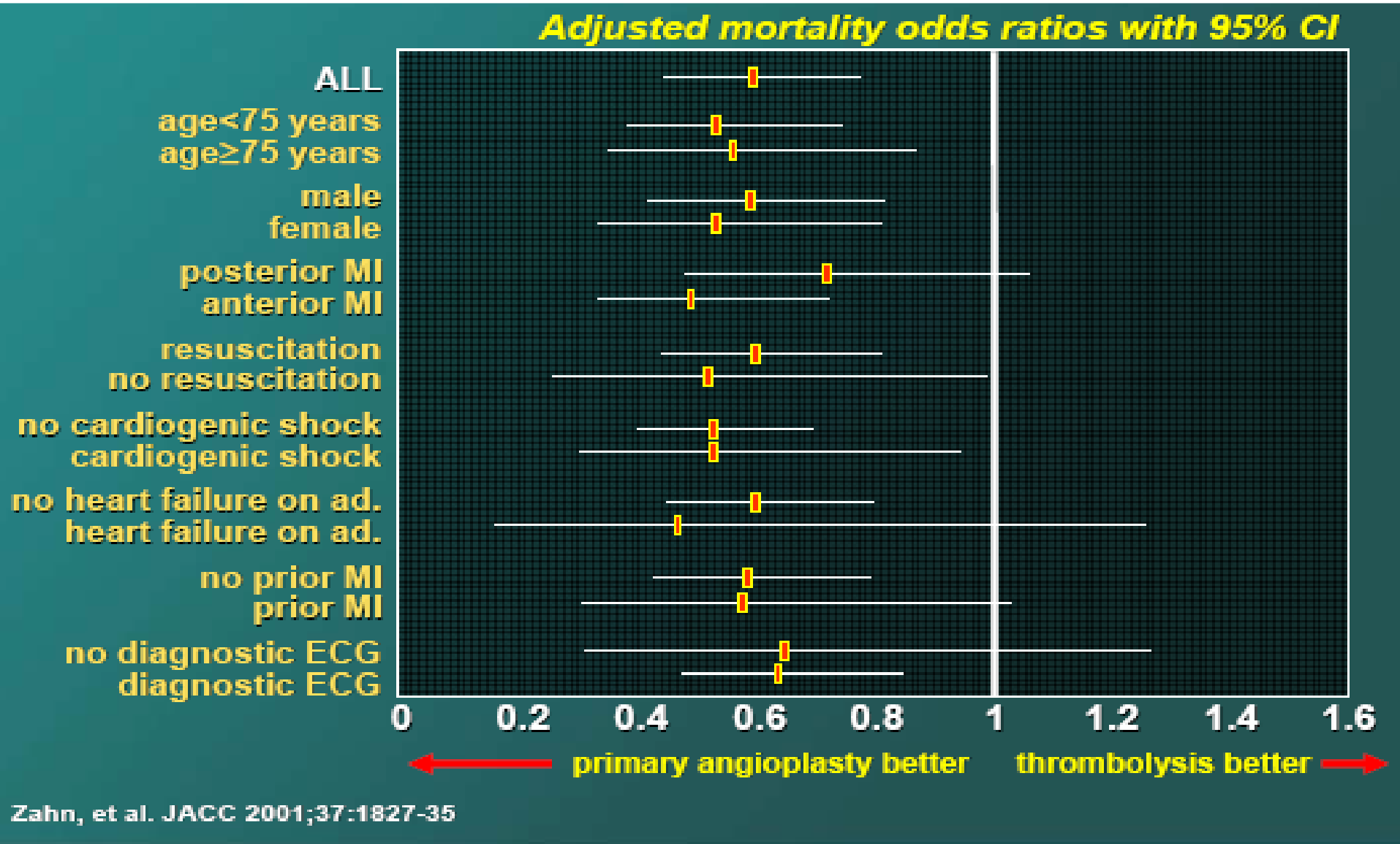
Mortality: PCI versus Thrombolysis



Mortality over 6 months from Primary PCI Trialists analysis of 11 randomized trials.

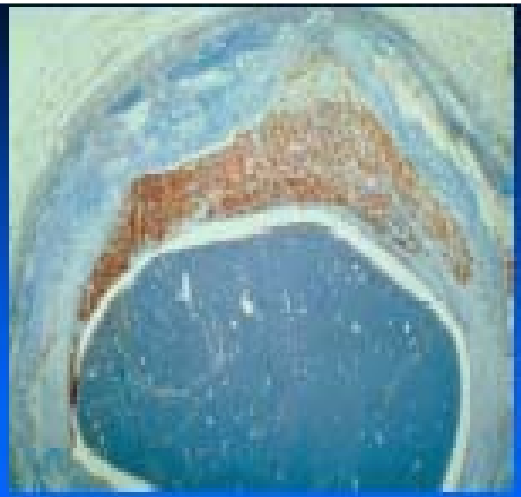
Grines C et al. Am Heart J 145:47, 2003

Which pts for PCI ?



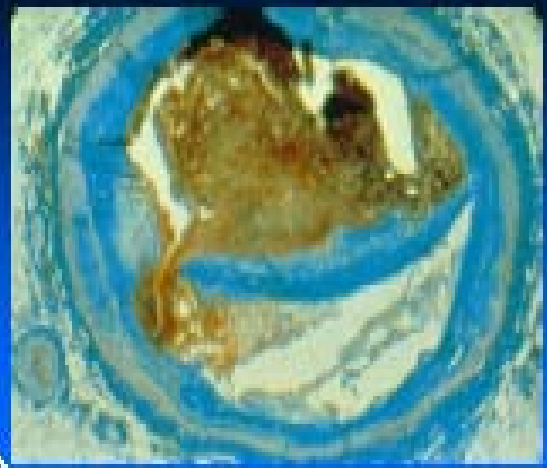
Zahn, et al. JACC 2001;37:1827-35

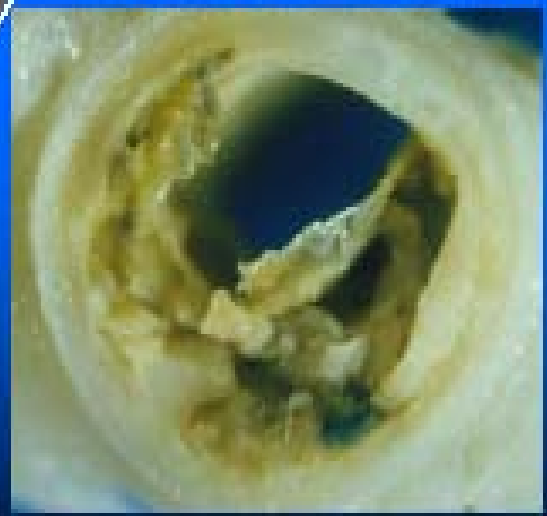
Vulnerable and Ruptured Plaques

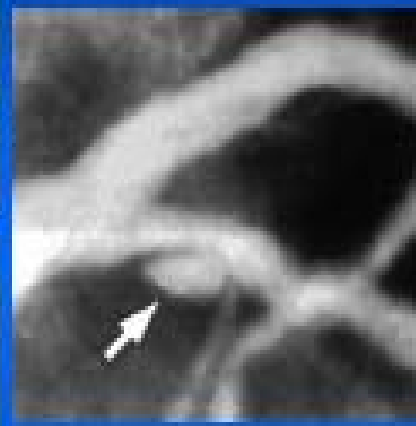


Vulnerable plaque

rupture



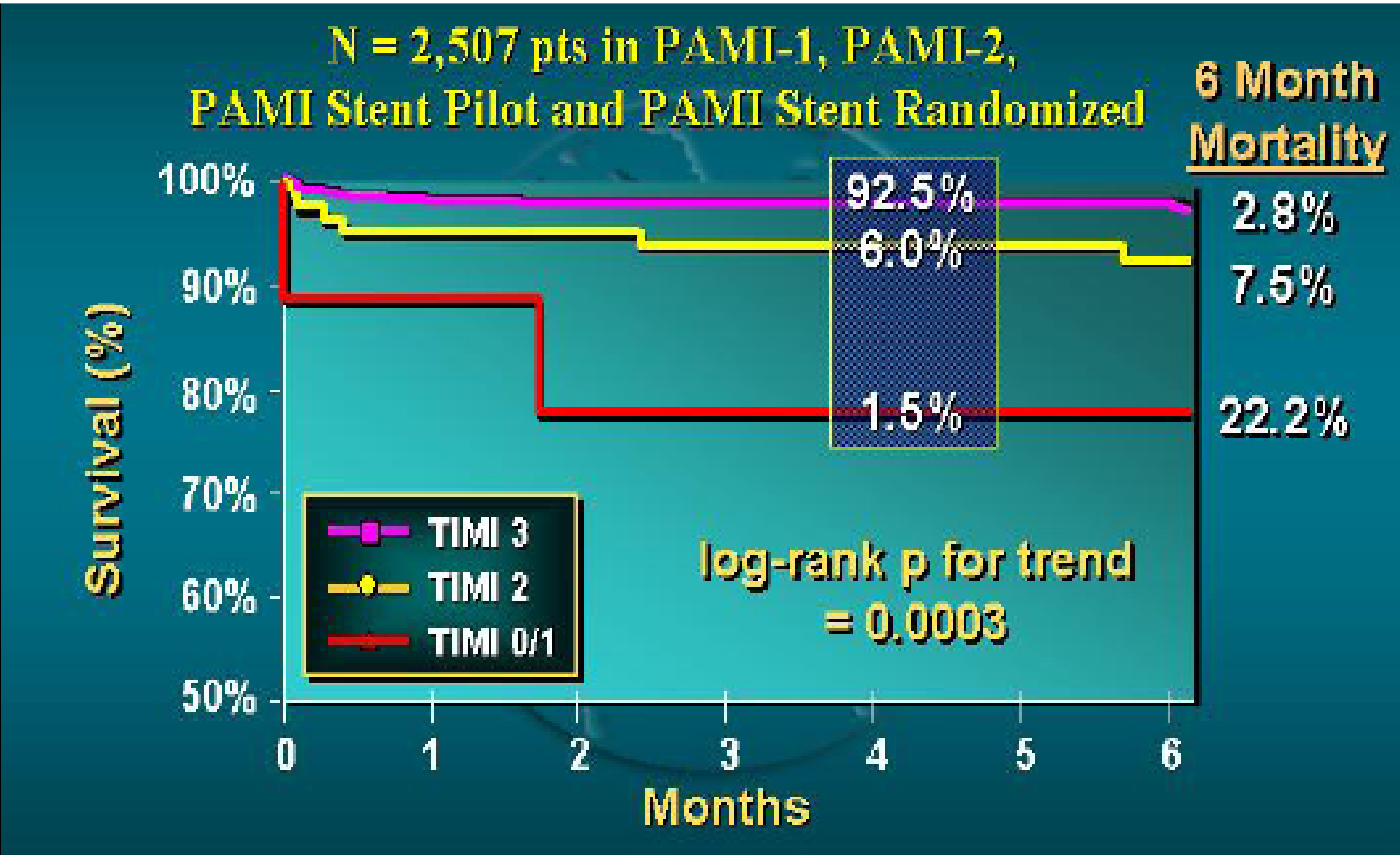




Advantages of Primary PCI Compared to Thrombolysis

- Superior TIMI flow rates.
- Reduced Re-occlusion.
- Reduced rate of: Re-Ischemia, Re-MI, Death & Stroke.
- Shorter length of hospital stay.
- Allows reperfusion when lytics contraindicated.

Effect of post PCI TIMI flow



Myocardial Blush

TIMI Myocardial Perfusion

Grades	Definition
Grade 0	Minimal or no myocardial blush.
Grade 1	Dye stains the myocardium and this stain persists on the next injection.
Grade 2	Dye enters the myocardium but washes out slowly so that dye is strongly persistent at the end of the injection.
Grade 3	There is normal entrance and exit of dye in the myocardium so that dye is mildly persistent at the end of the injection.

Angiographic NO-Reflow

A predictor of adverse long-term outcome in pts treated by PCI for first AMI

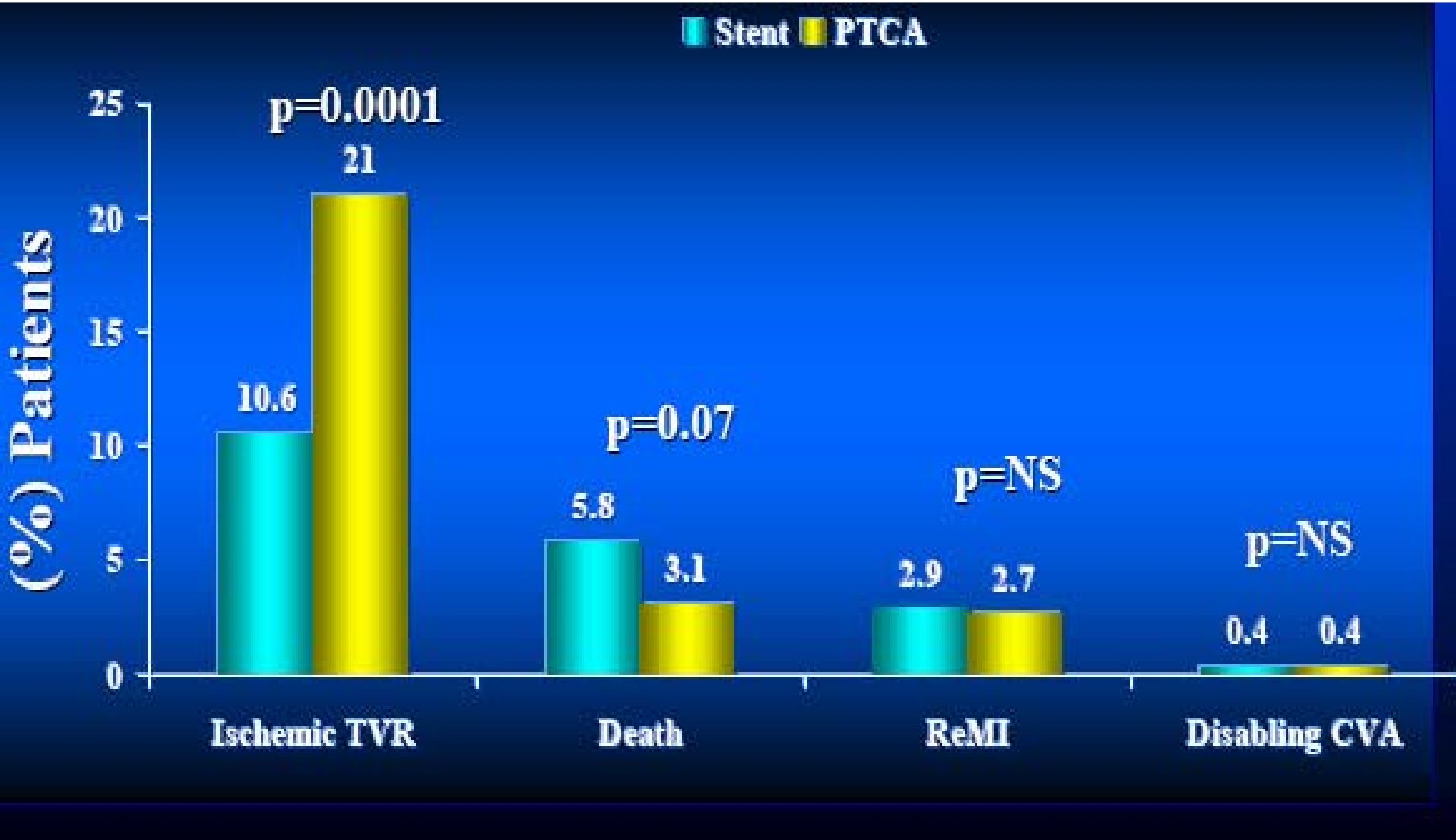
Follow-up 5.2±1.2 years

	No-Reflow n=27	Reflow n=90	P-value
CHF	41%	7%	0.001
Death	37%	10%	0.002

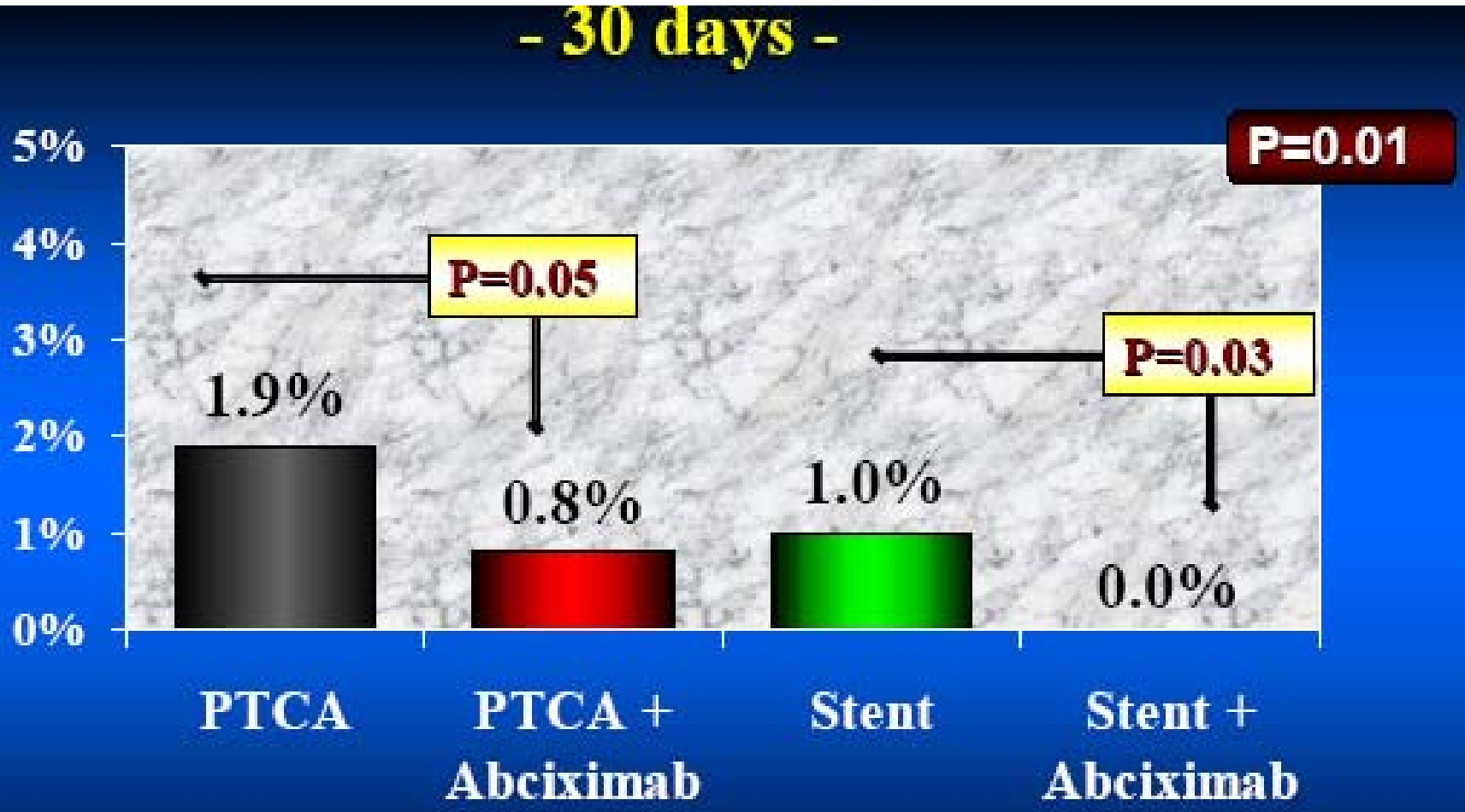
No-Reflow is an independent predictor of:

1. cardiac death; OR=5.25; P=0.002
2. and cardiac events; OR=3.7; P=0.001
3. Higher LVEDP and lower LVEF

Stent PAMI
One Year Events

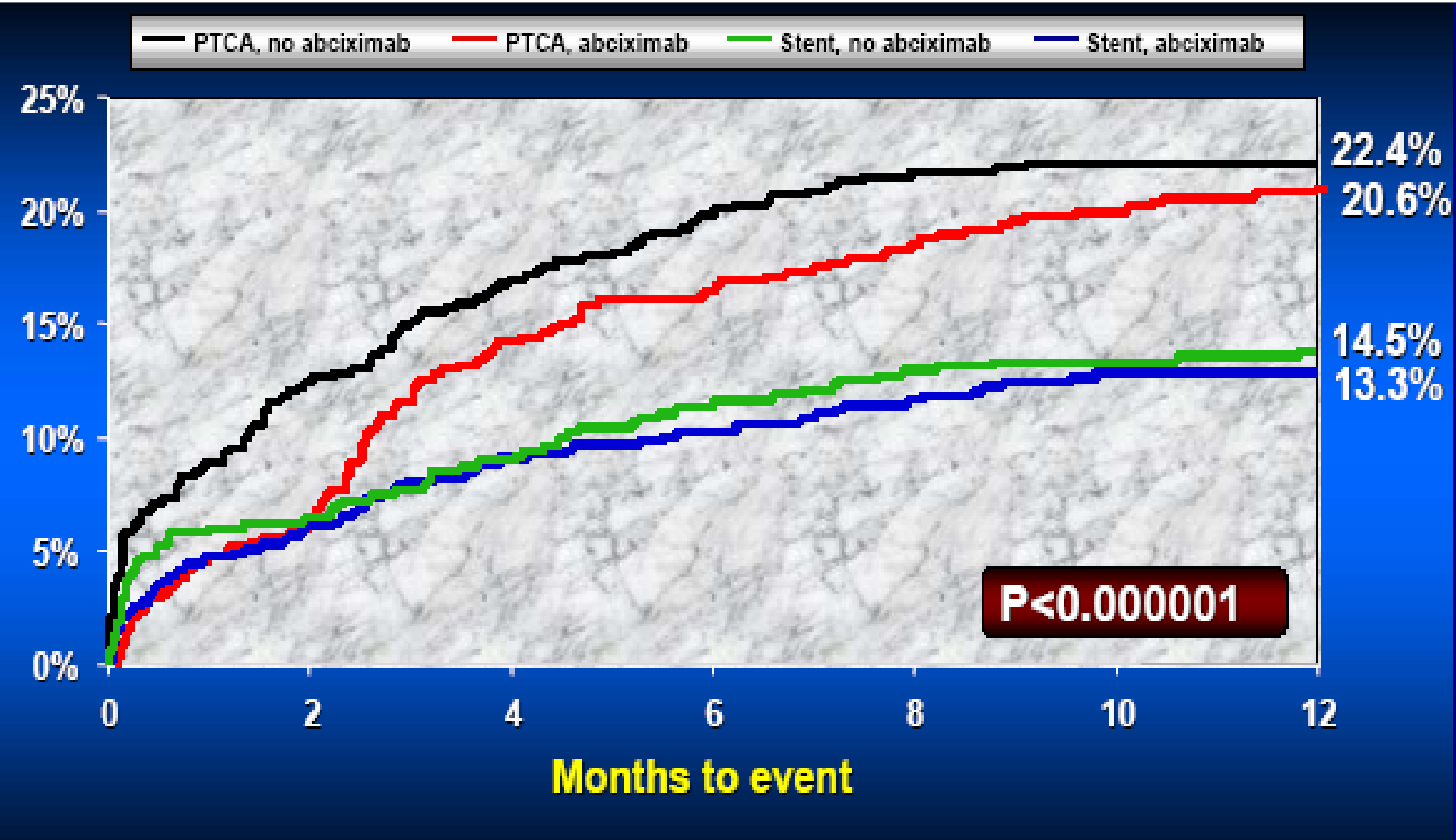


CADILLAC: Subacute Thrombosis

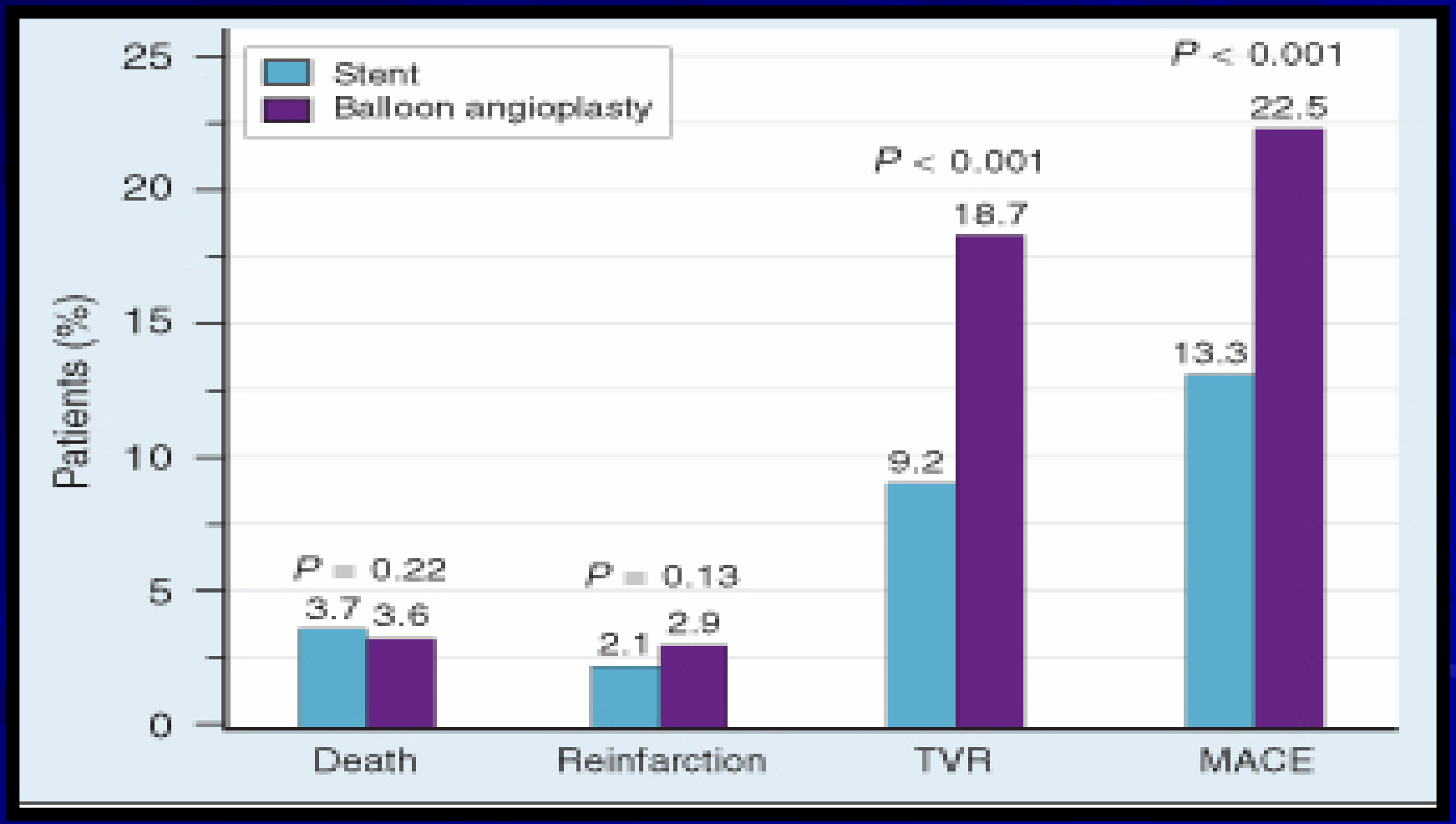


Kaplan Meier estimates

CADILLAC: 12 Month MACE



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



Am J Cardiol 88:297, 2001

Exclusion for Stenting in AMI trials

- If stent would protrude in LM.
- Likely occlusion of large side branch.
- Vessel tortuosity or heavy calcification that may prevent proper deployment.
- No-reflow or huge thrombus [globular filling defects with length> 2 times coronary diameter].

Causes of Failure to Re-Perfusion with Normal Epicardial Flow

- Microvascular spasm or stunning.
- Endothelial cell swelling.
- Microvascular compression: cell edema and elevated LVEDP.
- Loss of microvascular integrity.
- Platelet, WBC plugging of small vessel [embolization or in situ thrombosis].
- Free radicals.

Enhancing Myocardial Recovery (Mechanical)

- IABP
- X-sizer
- AngioJet
- Distal protection

Enhancing Myocardial Recovery (Mechanical)

- IABP
  1. Increase coronary flow.
  2. Decrease LVEDP.
  3. Unload LV.

PAMI 2

- Prophylactic IABP after primary PCI for stable high risk AMI pts.

> 70y

3 VD

EF < 45%

SVG

Suboptimal results

Malignant ventricular arrhythmia

PAMI 2

- 211 pts : IABP for 36-48 h
- 226 pts : conservative

No benefit of IABP in these pts (death, re-MI, IRA-occlusion, heart failure).

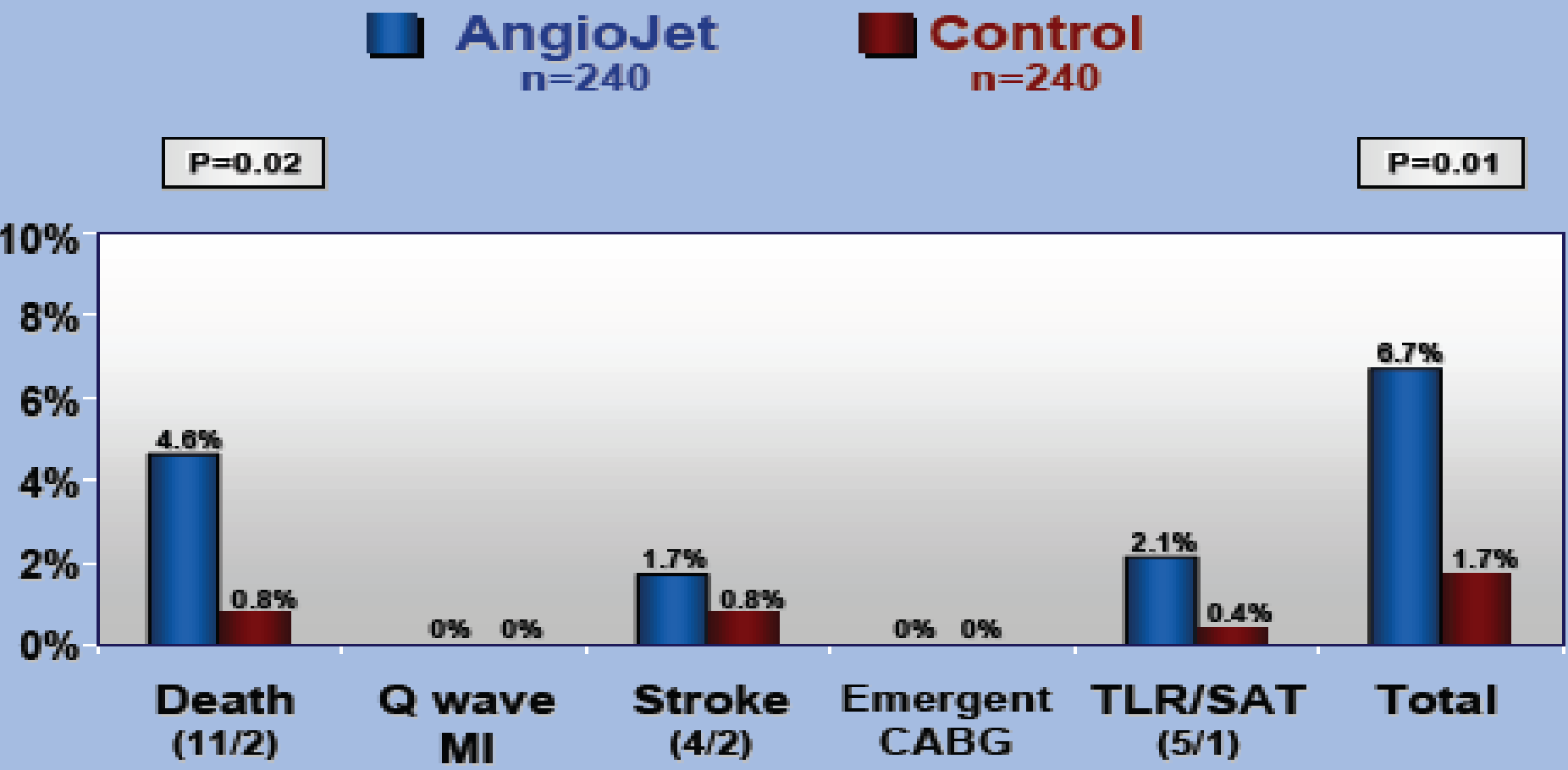
Increase stroke rate with IABP.

Enhancing Myocardial Recovery (Mechanical)

- AngioJet
- X-sizer
- Distal Protection

AngioJet AMI

MACE by 30 Days



X-SIZER in AMI Patients for Negligible Embolization and Optimal ST Resolution

	No-X-Sizer n=101	X-Sizer n=100	P-value
No flow	16%	4.1%	0.01
Distal emboli	10%	2.1%	0.006
PCI time (min)	45±25	55±28	0.003
PCI success*	79%	87%	NS

* TIMI 3 & < 30% Stenosis

EKG resolution Pre Vs. Post (Sum ST)

	No X-sizer	X-Sizer	p value
Patients (N=185)*	96	89	
ST segment resolution (mm)			
Median	4.95	7.50	0.036**
Mean (SD)	6.81±9.23	8.54±10.14	
ST segment resolution >50% (%)	53.1	67.4	0.052**
ST segment resolution score			
Median	0.56	0.66	0.028**
Mean (SD)	0.42±0.49	0.52±0.50	

Conclusion

Reducing thrombus burden prior to PCI with X-Sizer leads to better Myocardial Reperfusion as shown by:

1. Higher ST segment resolution
2. Lower rate of distal embolization, slow/no-reflow

Enhancing Myocardial Recovery (Mechanical)

- Distal Protection

  No proven benefit in most studies

Enhancing Myocardial Recovery

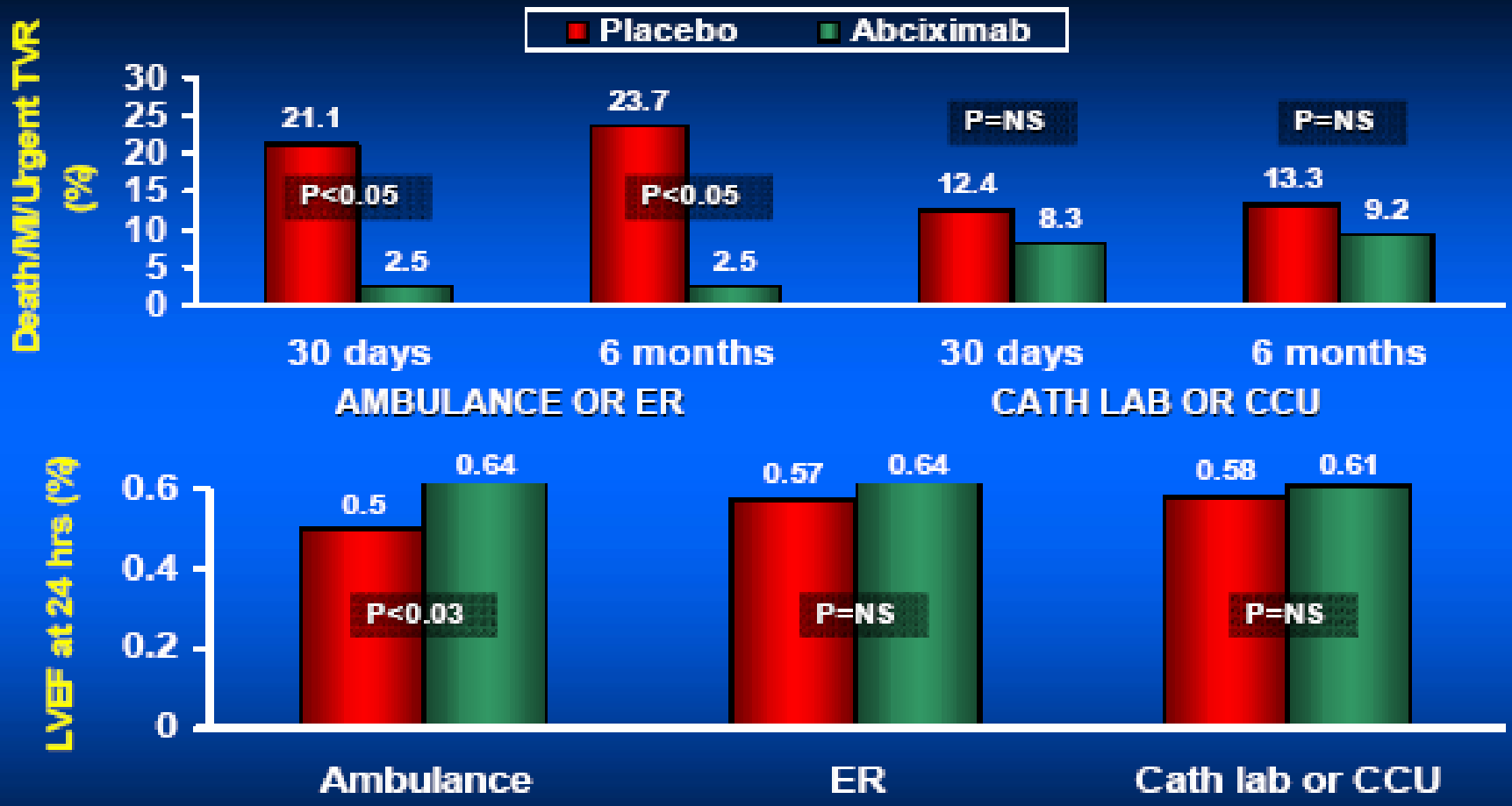
Pharmacology adjuncts to mechanical reperfusion

- Reduce distal embolization / platelet plugging: GP 2b/3a inh, adenosine.
- Decrease microvascular resistance: Verapamil, Adenosine, Nicorandil
- Prevent reperfusion injury.

Effect of IIb/IIIa Agents on Infarct Size or LV Function

Study	Test	Results
ISAR-2 (Circ 1998;98:2695)	LV gram - 14 days (n=151)	Improved wall motion and EF
ADMIRAL (NEJM 2001;25:1895)	LV gram 24 hrs & 6 mos.	Improved EF
RAPPORT (AJC 1999;84:728)	Area under CK curve (measured 2, 6, 12, 18, 24, 30, 40 hrs) (n=483)	No difference
CADILLAC (NEJM 2002;in press)	Paired LV gram Acute & 6 mos. (n=436)	No difference in EF or wall motion

ADMIRAL:
Outcomes Based on Site of Initiation of Abciximab



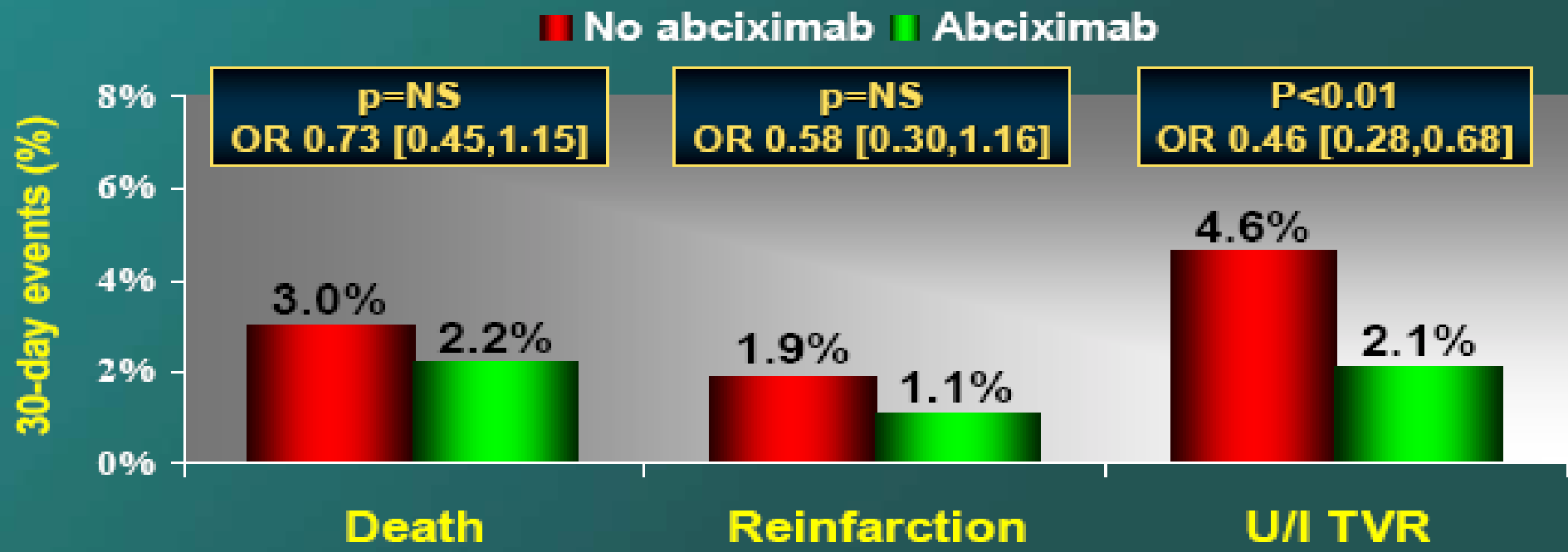
Expected TIMI-3 flow rate with abciximab = 25%
Can this account for 10-fold improvement in outcome and 14-point increase in EF?

GP 2B/3A Inhibitors in PCI-AMI

Abciximab in Primary PCI

3,666 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], ACE [400])



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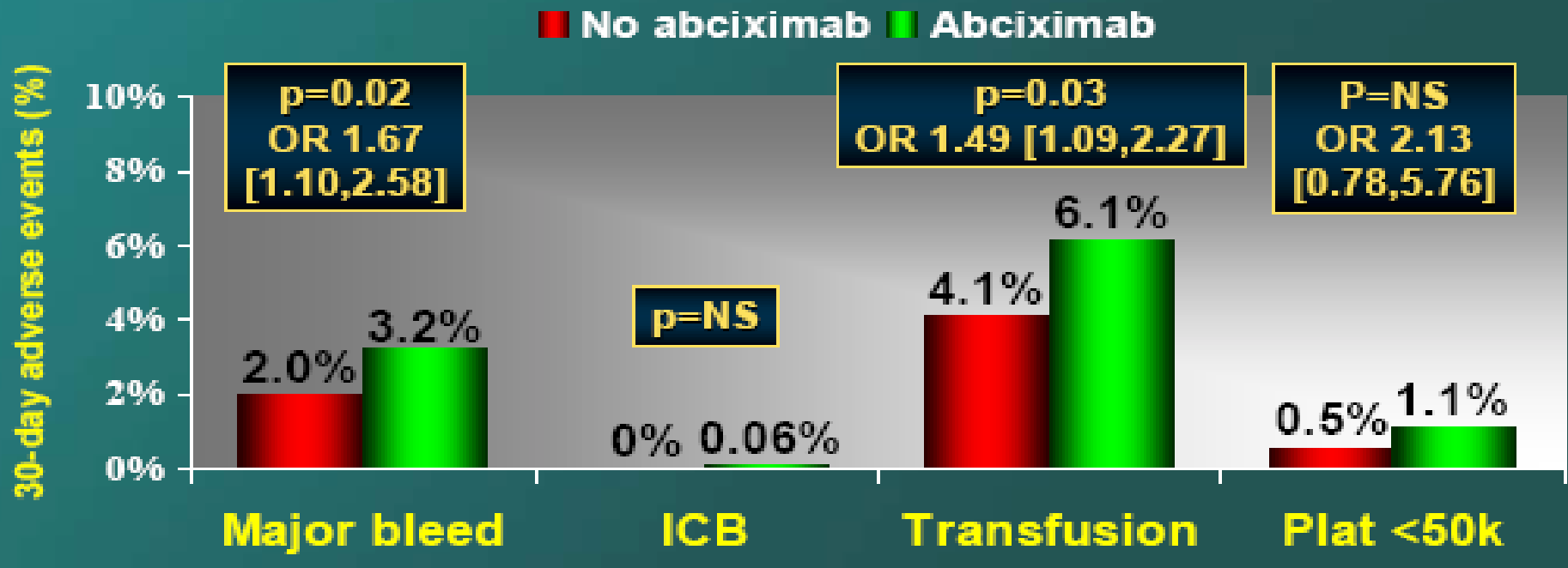


Enhancing Myocardial Recovery (agents)

- Adenosine

54 Ant AMI [<3h] randomized to IC 4mg AD vs Saline.

End points: No-reflow, LV function, MACE.

Marzilli , Circulation 2000;101:2154

Enhancing Myocardial Recovery (agents)

- Adenosine

1. No-reflow: 26% vs 4%; p=0.02.
2. Death: 18% vs 0%; p=0.02.
3. Improve LV function: 36% vs 64%; p=0.001.
4. Q-wave MI: 85% vs 60%; p=0.04.

Marzilli , Circulation 2000;101:2154

Enhancing Myocardial Recovery (Nicorandil)

- **Intravenous nicorandil before PCI**
- Nicorandil, a hybrid of an adenosine triphosphate-sensitive K channel opener and nitrates .
- Based on 368 patients followed up to five years.
- In this double-blind trial, 368 patients with first STEMI were randomized to receive either 12-mg nicorandil or placebo as a single intravenous injection just before undergoing PCI.

***Circulation* 2005; 12:1284-1288.**

Components and composite primary end point, nicorandil vs placebo

Variable	Nicorandil, n (%)	Placebo, n (%)	HR (95% CI)	p
CVS death	6 (3.2)	10 (5.5)	0.59 (0.22-1.64)	0.31
Hospital for CHF	6 (3.2)	20 (10.9)	0.29 (0.11-0.71)	0.0072
Primary end point	12 (6.5)	30 (16.4)	0.39 (0.20-0.76)	0.0058

Circulation 2005; 12:1284-1288.

Enhancing Myocardial Recovery (Nicorandil)

- In addition, postprocedural TIMI-3 flow was obtained in 89.7% of the nicorandil group vs 81.4% of the placebo group (p=0.025).
- An ST-segment resolution of more than 50% after PCI was attained in 79.5% of the nicorandil group vs 61.2% of the placebo group (p=0.0002).

***Circulation* 2005; 12:1284-1288.**

Enhancing Myocardial Recovery (agents)

- Na/H exchanger

1. ESCAMI: Eniporide.
2. GUARDIAN: Cariporide

No benefit .

Future Directions

- **Adjunctive pharmacologic agents:**
  1. New anti-thrombin.
  2. Facilitated PCI.
  3. Drug coated stent (heparin, DES).
- **Myocardial preservation:**
  1. Hypothermia
  2. Super saturated oxygen.

Future Directions

- **Adjunctive pharmacologic agents:**
  1. New anti-thrombin.
  2. **Facilitated PCI.**
  3. Drug coated stent (heparin, DES).
- **Myocardial preservation:**
  1. Hypothermia
  2. Super saturated oxygen.

Comparison of primary and facilitated PCI for ST-elevation AMI: quantitative review of randomised trials.

METHODS:

- 17 trials of patients with STEMI assigned to facilitated (n=2237) or primary (n=2267) PCI.
- Short-term outcomes (up to 42 days) of death, stroke, non-fatal reMI, urgent TVR, and major bleeding.
- Grade 3 flow rates for prethrombolysis and post-TIMI were also analysed.

Lancet. 2006;367:579-88.

Comparison of primary and facilitated PCI for ST-elevation AMI: quantitative review of randomised trials.

- **Results: The facilitated approach resulted in**

3. **Significantly more patients assigned to the facilitated approach than those assigned to the primary approach *died* (5% vs 3%; OR=1.4, 1.01-1.87).**
4. **Higher non-fatal reinfarction rates (3% vs 2%; OR=1.71, 1.16-2.51).**
5. **Higher urgent TVR rates (4% vs 1%; OR= 2.39, 1.23-4.66).**

Lancet. 2006;367:579-88.

Comparison of primary and facilitated PCI for ST-elevation AMI: quantitative review of randomised trials.

Conclusion

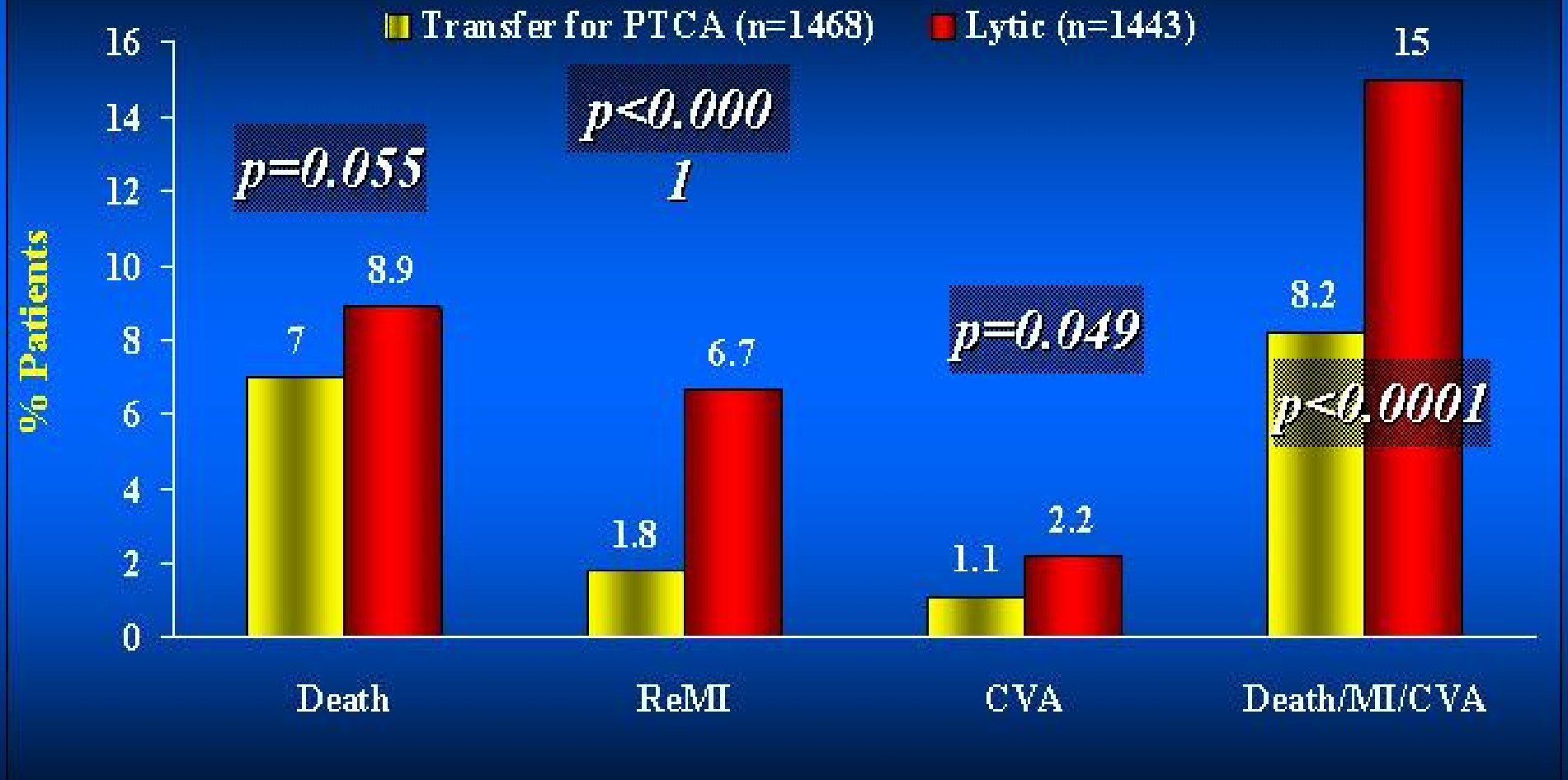
1. **Facilitated PCI offers no benefit over primary PCI in STEMI treatment and should not be used outside the context of randomised controlled trials.**
2. **Furthermore, facilitated interventions with thrombolytic-based regimens should be avoided**

Lancet. 2006;367:579-88.

Transfer for PCI

- Why ?
- Is it safe?
- Which hospital ?

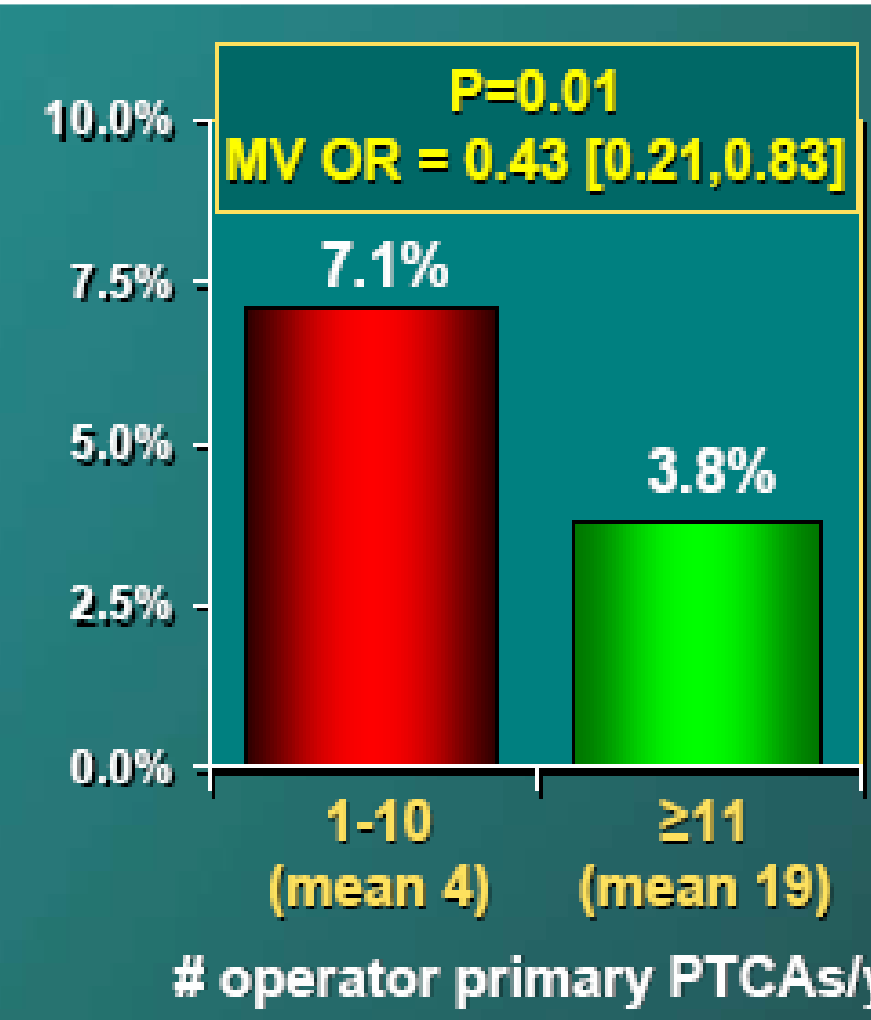
Transfer for Primary PTCA vs On-Site Lytics (Pooled Data from 5 Randomized Trials*)

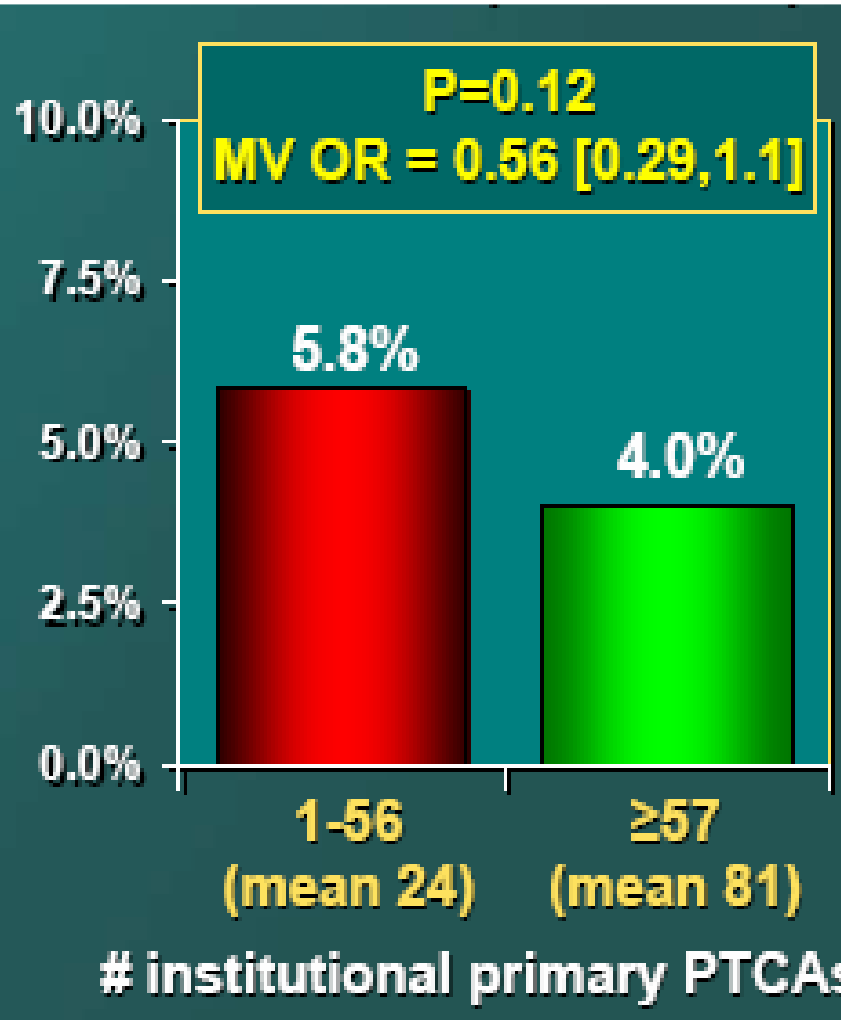


Safety of Transfer

- 1468 pts randomized to transfer for PCI
  (Air PAMI, LIMI, PRAGUE I and II, DANAMI-II)
- 2 deaths (0.1%)
- 13 ventricular fib (0.8%)

Relationship between operator & hospital volume [primary PCI] & hospital death [1995 NY database]





Vakili and Brown, Circulation 2001;104:2171-2176

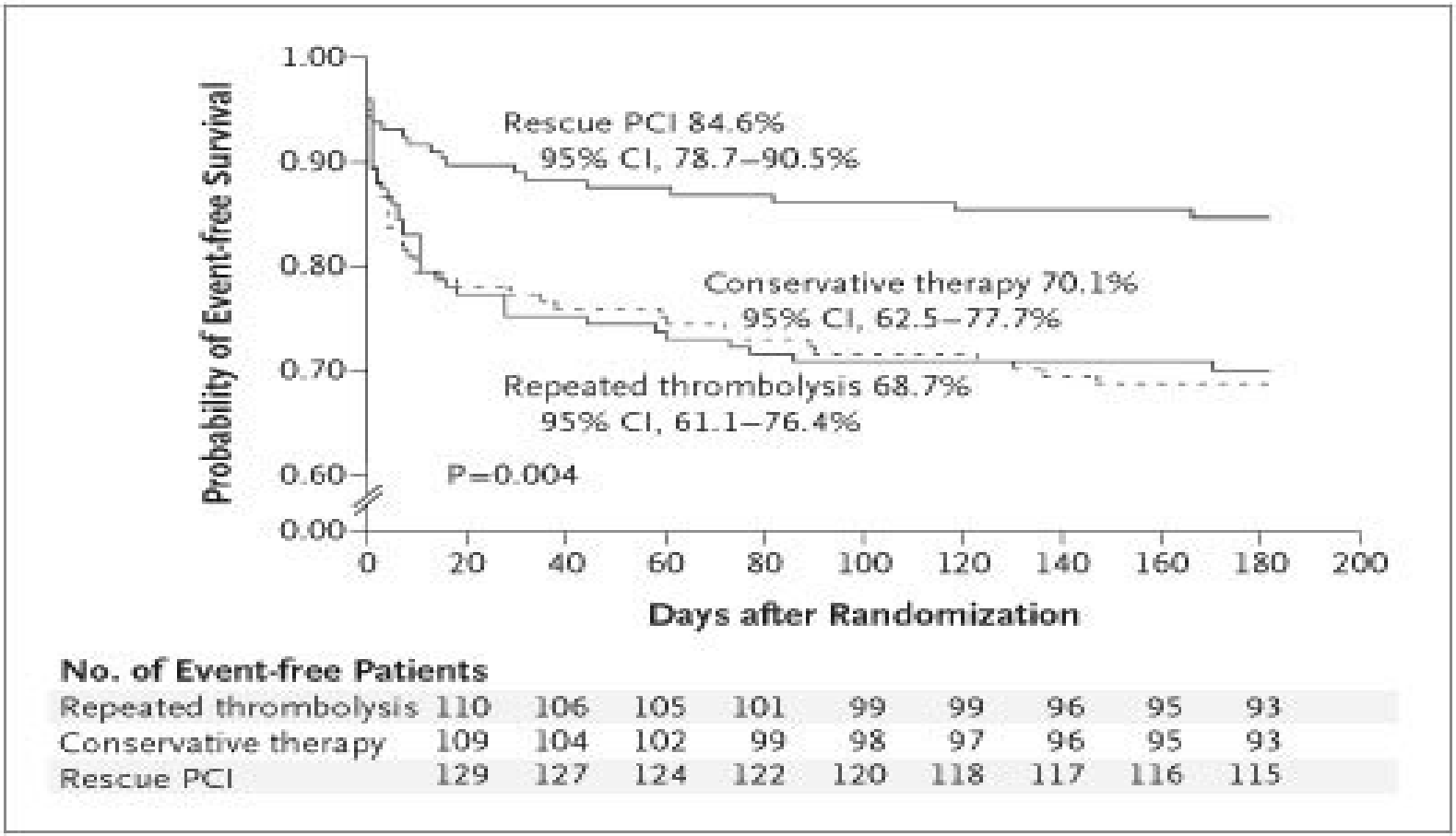
Rescue Angioplasty after Failed Thrombolytic Therapy for AMI

- **Methods**

1. **Multicenter trial in the UK involving 427 pts with STE-AMI in whom reperfusion failed to occur (less than 50 percent ST-segment resolution) within 90 minutes after thrombolytic treatment.**
2. **The patients were randomly assigned to repeated thrombolysis (142 patients), conservative treatment (141 patients), or rescue PCI (144 patients).**
3. **The primary end point was a composite of death, re-MI, CVA, or severe CHF within six months.**

Gershlick, A. H. et al. N Engl J Med 2005;353:2758-2768

Kaplan-Meier Estimates of the Cumulative Rate of the Composite Primary End Point within Six Months



No. of Event-free Patients									
Repeated thrombolysis	110	106	105	101	99	99	96	95	93
Conservative therapy	109	104	102	99	98	97	96	95	93
Rescue PCI	129	127	124	122	120	118	117	116	115

Gershlick, A. H. et al. N Engl J Med 2005;353:2758-2768

Rescue Angioplasty after Failed Thrombolytic Therapy for AMI

Conclusions

1. **Event-free survival after failed thrombolytic therapy was significantly higher with rescue PCI than with repeated thrombolysis or conservative treatment.**
2. **Rescue PCI should be considered for patients in whom reperfusion fails to occur after thrombolytic therapy.**

Gershlick, A. H. et al. N Engl J Med 2005;353:2758-2768

Multi-vessel disease AMI

- Multiple lesion angioplasty ?
- To open Non-IRA ?

Multiple Lesion Angioplasty in the Setting of Acute MI: Stent PAMI Subanalysis

Clinical Outcomes @ 1 Year

	Revascularized (N = 101)	Control (N = 372)	p Value
Death	10 (9.9%)	16 (4.3%)	0.029
Reinfarction	3 (3.0%)	16 (4.3%)	0.78
I – TVR	16 (16%)	66 (18%)	0.65
Disabling stroke	1 (1.0%)	2 (0.5%)	0.51
MACE	27 (27%)	88 (24%)	0.52
Any PCI	35/94 (37%)	120/352 (34%)	0.57
Any CABG	7/91 (7.7%)	25/350 (7.1%)	0.86

ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction

- ***Class III***
  This classification applies to patients with AMI who

Undergo elective angioplasty of a non–IRA at the time of AMI

Elderly patients
SENIOR PAMI

1. In a cohort of elderly patients ≥70 years of age
2. All patients had AMI symptoms between 30 minutes and 12 hours and were eligible for lytic therapy.
3. Excluded pts: SBP>180 mm Hg or DBP>100 mm Hg
4. Taking warfarin
5. The study was stopped early because of recruitment issues, 47 patients short of the planned enrollment of 530 patients.

Grines C. TCT 2005; October 16-21, 2005; Washington, DC.

SENIOR PAMI: 30-day events

End point	PCI (n=252)	Lytic (n=229)	p
Death or disabling stroke*	11.3%	13%	0.57
Death/CVA Re-MI	11.6%	18%	0.05
Death	10%	13%	0.48
Disabling stroke	0.8%	2.2%	0.26
Reinfarction	1.6%	5.4%	0.39

*Primary end point

Grines C. TCT 2005; October 16-21, 2005; Washington, DC.

SENIOR PAMI: 30-day events in pts aged 70-80 years

End point	PCI	Lytics	p
Death or disabling stroke	7.7%	12%	0.18
Death/CVA/ Re-MI	7.7%	17%	0.01
Death	7.1%	11.3%	0.17

Grines C. TCT 2005; October 16-21, 2005; Washington, DC.

Elderly patients :SENIOR PAMI

1. In a subgroup analysis of pts stratified by age, the SENIOR PAMI investigators did find an advantage of primary PCI over lytic therapy.
2. Among patients 70-80 years old, there was a nonsignificant 38% reduction in death, a nonsignificant 36% reduction in death/cerebrovascular accident, and a statistically significant 55% reduction in the combined end point of death/CVA/reinfarction.
3. Among those older than 80 years, there was no advantage of one strategy over the other.

Grines C. TCT 2005; October 16-21, 2005; Washington, DC.

DES in AMI

- Randomized trials have demonstrated that DES reduce the incidence of ISR for de novo lesions within native coronary arteries
- These studies did not include patients with AMI.

Until ACC 2006 meeting

TYPHOON: Clinical and angiographic results

End point	Cypher	BMS	p
Target vessel failure* (%)	7.3	14.3	<0.0036
MACE (%)	5.9	14.6	<0.001
TVR (%)	5.6	13.4	<0.001
TLR	3.7	12.6	<0.0001
Binary restenosis (%)	3.5	20.3	0.001
Late loss (mm)	0.13	0.83	<0.0001
% diameter stenosis	16.4	37.1	<0.0001

*A composite of TVR, MI, cardiac death

Spaulding C. ACC 2006 Scientific Sessions; 2006; Atlanta, GA.

PASSION: Clinical results

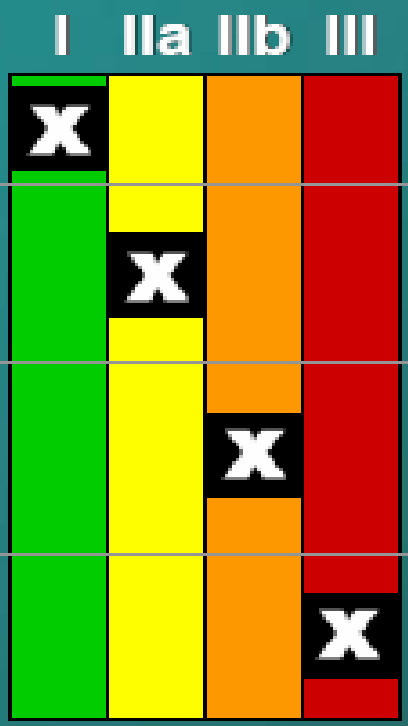
End point	Taxus	BMS	Hazard ratio (95% CI)	p
MACE	8.7%	12.6%	0.68 (0.41-1.10)	0.12
Death/MI	4.8%	6.5%	0.74 (0.38-1.45)	0.39
TLR*	6.2%	7.4%	0.68 (0.36-1.28)	0.23

*Defined as ischemia-driven PCI of target lesions, plus a 5-mm margin from the proximal and distal stent edges, or CABG of target vessel.

Dirksen MT. ACC 2006 Scientific Sessions; 2006; Atlanta, GA.

2004 ACC/AHA STEMI guidelines

Classification of Recommendations



- Intervention is useful and effective
- Weight of evidence/opinion is in favor of usefulness/efficacy
- Usefulness/efficacy is less well established by evidence/opinion
- Intervention is not useful/effective and may be harmful

X = Level of Evidence

- **A** Effect consistent among multiple (3–5) population risk strata
- **B** Limited (2–3) population risk strata evaluated
- **C** Very limited (1–2) population risk strata evaluated

2004 ACC/AHA STEMI guidelines

Primary PCI

Class I

A

- **STEMI (including posterior MI or presumably new LBBB) within 12 hours of symptom onset**
  - **Door to balloon <90 minutes**
  - **Skilled operator (>75 PCIs per year)**
  - **Skilled team (>200 PCIs and >36 primary PCIs per year)**
  - **Surgical facilities available**

2004 ACC/AHA STEMI guidelines

Primary PCI: specific consideration

Class I

- B — Door to balloon goal <90’
- B — If presentation <3 hours, and
  - (Door to Balloon) – (Door to Needle) <1 hour ⇒ Primary PCI generally preferred
  - (Door to Balloon) – (Door to Needle) >1 hour ⇒ Thrombolysis generally preferred
- B — If presentation >3 hours, then primary PCI is generally preferred
- A — Primary PCI is preferred for cardiogenic shock (IA) and severe CHF and/or Killip class III (IB)
- B

2004 ACC/AHA STEMI guidelines

Primary PCI: specific consideration

Class IIa

B

- Patients ≥75 years old who develop cardiogenic shock within 36 hours of MI onset who can be revascularized within 18 hours of shock

C

- Symptom onset 12-24 hours with:

C

  - Severe CHF and/or Killip class III, or

C

  - Hemodynamic or electrical instability, or
  - Persistent ischemia

2004 ACC/AHA STEMI guidelines

Primary PCI: specific consideration

Class IIb

C

- **The benefit of primary PCI for STEMI pts eligible for fibrinolysis is not well established when performed by an operator who performs <75 PCI procedures per year**

2004 ACC/AHA STEMI guidelines

Primary PCI: specific consideration

Class III

C

- **PCI should not be performed in a non infarct artery at the time of primary PCI in patients without hemodynamic compromise**

C

- **Primary PCI should not be performed in asymptomatic patients >12 hours after onset of STEMI if they are hemodynamically and electrically stable**

2004 ACC/AHA STEMI guidelines

Primary PCI without on site surgery

Class

IIb B

- May be considered in STEMI by skilled physicians (>75 PCI/yr) and team (>36 pPCI/yr) as long as door to balloon is <90' and:
  - There exists a proven plan for rapid transport with appropriate hemodynamic support capability to a cardiac surgery OR in a nearby hospital

III C

- Otherwise

2004 ACC/AHA STEMI guidelines

Choice of reperfusion therapy depends on:

- **Time from onset of symptoms**
  - **Lytic therapy within 2º can abort MI**
  - **Reperfusion rates after lytics are time dependent; much less so with primary PCI**
- **Risk of STEMI (mortality)**
  - **The higher the risk, the more PCI is favored**
- **Risk of bleeding**
  - **The higher the risk, the more PCI is favored**
- **Time required for transport to a skilled PCI lab**

2004 ACC/AHA STEMI guidelines

Thrombolytic therapy is generally favored:

- **Early presentation**
  - **<3° from sx onset to ER, plus delay to invasive strategy**
- **Invasive strategy is not an option**
  - **Cath lab unavailable**
  - **Vascular access difficult**
  - **Skilled PCI lab unavailable**
    - **Operator >75 PCIs per yr; team >36 primary PCIs per yr**
- **Delay to invasive strategy**
  - **Prolonged transport**
  - **(Door to Balloon) – (Door to Needle) >1 hour**
  - **Door to Balloon >90 minutes**

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Primary PCI is generally favored:

- **Skilled PCI lab is available with surgical back-up**
  - **(Door to Balloon) – (Door to Needle) <1 hour**
  - **Door to Balloon <90 minutes**
- **High risk STEMI**
  - **Cardiogenic shock or Killip class III**
- **Contraindications to fibrinolysis, including increased risk of bleeding and ICH**
- **Late presentation (symptom onset to ER >3º)**
- **Diagnosis of STEMI is in doubt**

ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction

- **Strict performance criteria must be mandated for primary angioplasty programs so that such delays in revascularization and performance by low-volume operators/centers do not occur.**

1- Balloon dilation within 90 ±30 minutes of admission and diagnosis of AMI.

2- A documented clinical success rate with TIMI 2-3 flow attained in >90% of pts without emergency CABG, stroke, or death.

3- Emergency CABG rate<5% among all patients undergoing the procedure.

4- Actual performance of angioplasty in a high percentage of patients (85%) brought to the laboratory.

5- Mortality rate<10% .

Otherwise, the focus of treatment should be the early use of thrombolytic therapy

2004 ACC/AHA STEMI guidelines

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