Complication of AMI:
Cardiogenic Shock, Stroke, Bleeding

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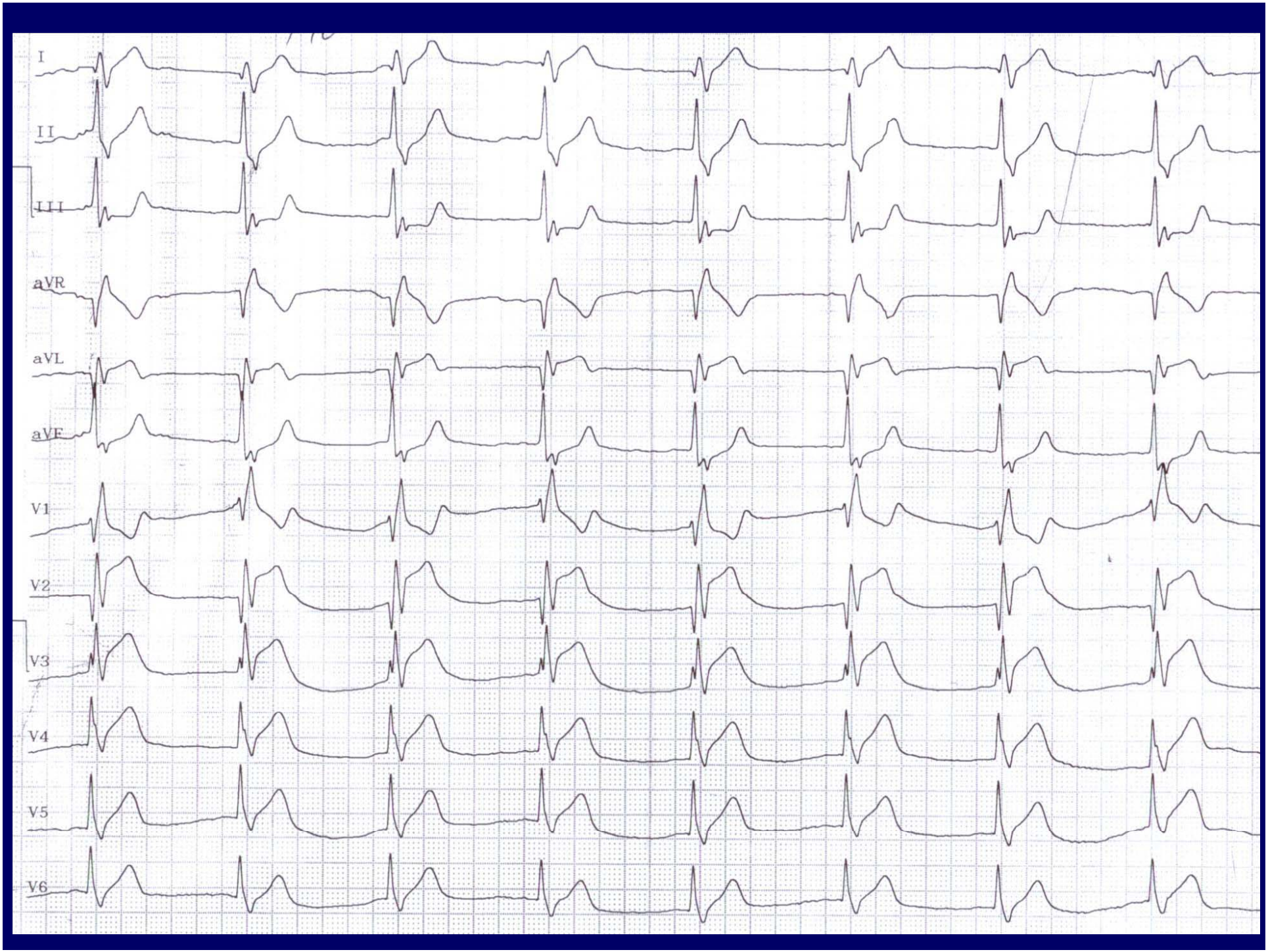
Contents

- Case
- Cardiogenic Shock
- Ischemic Stroke after MI
- Bleeding Complication

Case: Male, 47

- Severe chest pain for 2.5 hrs
- BP < 60 mmHg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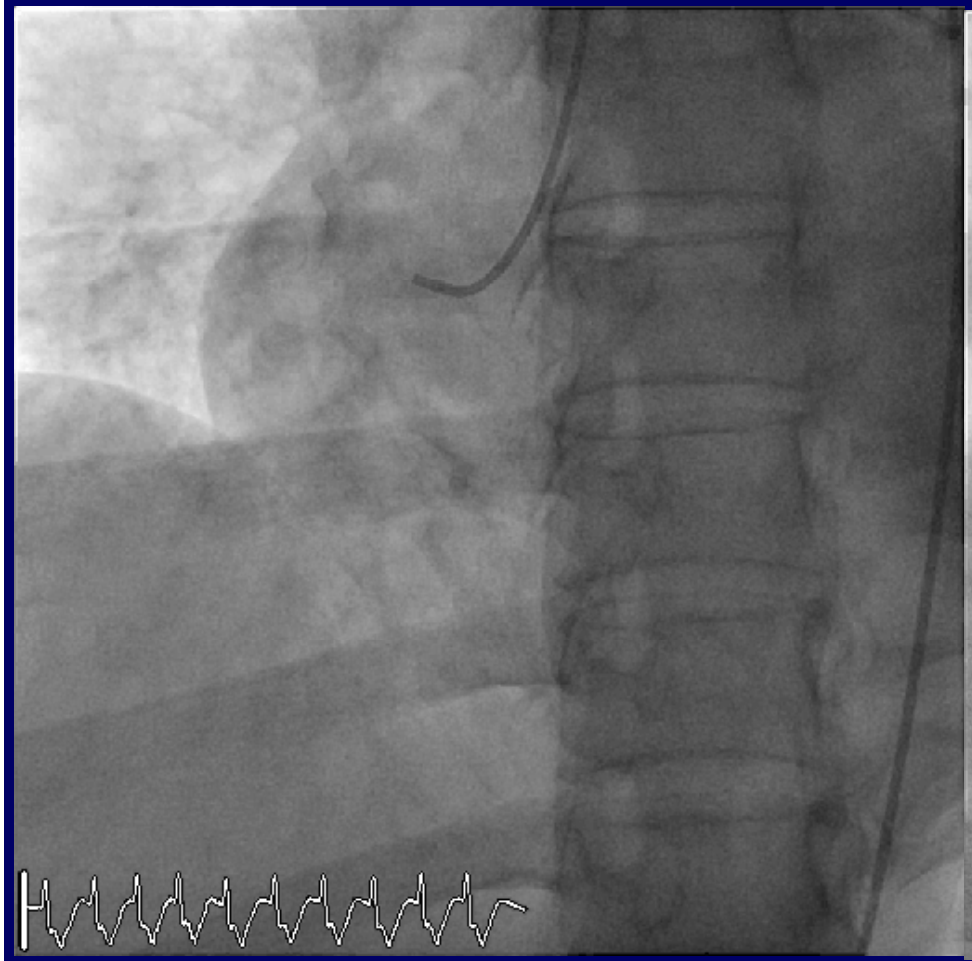
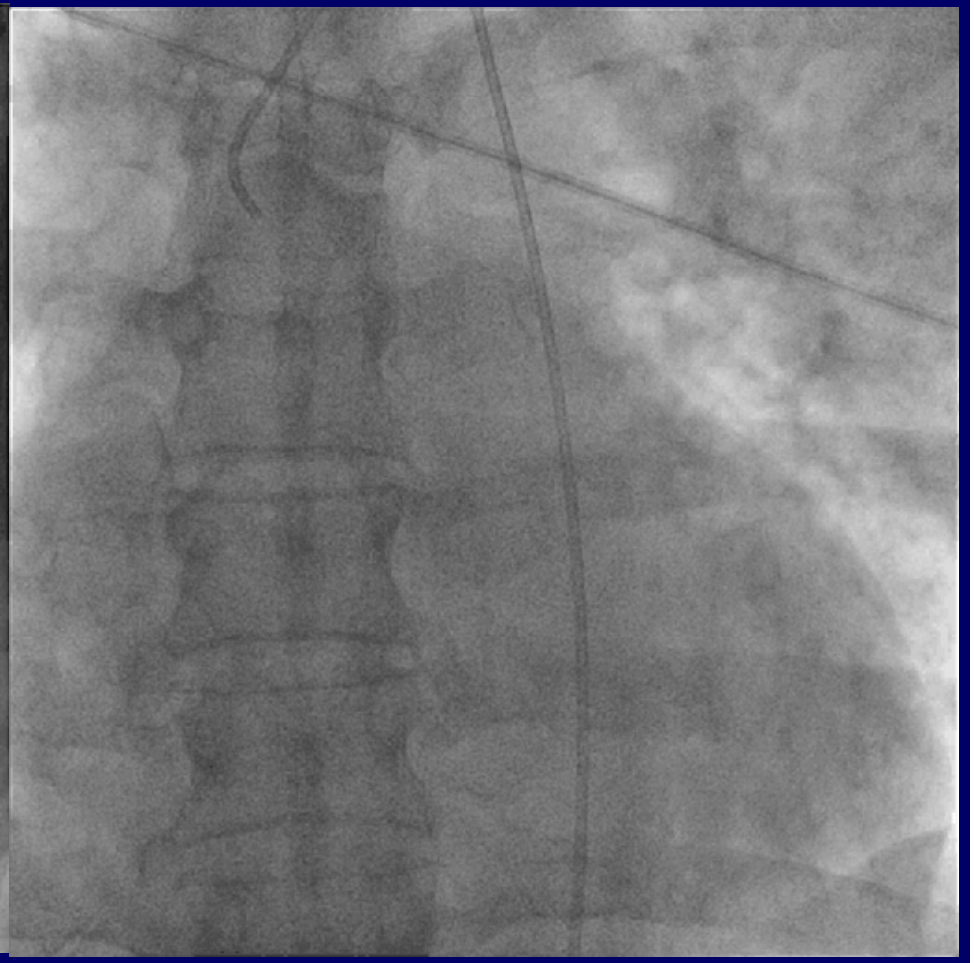
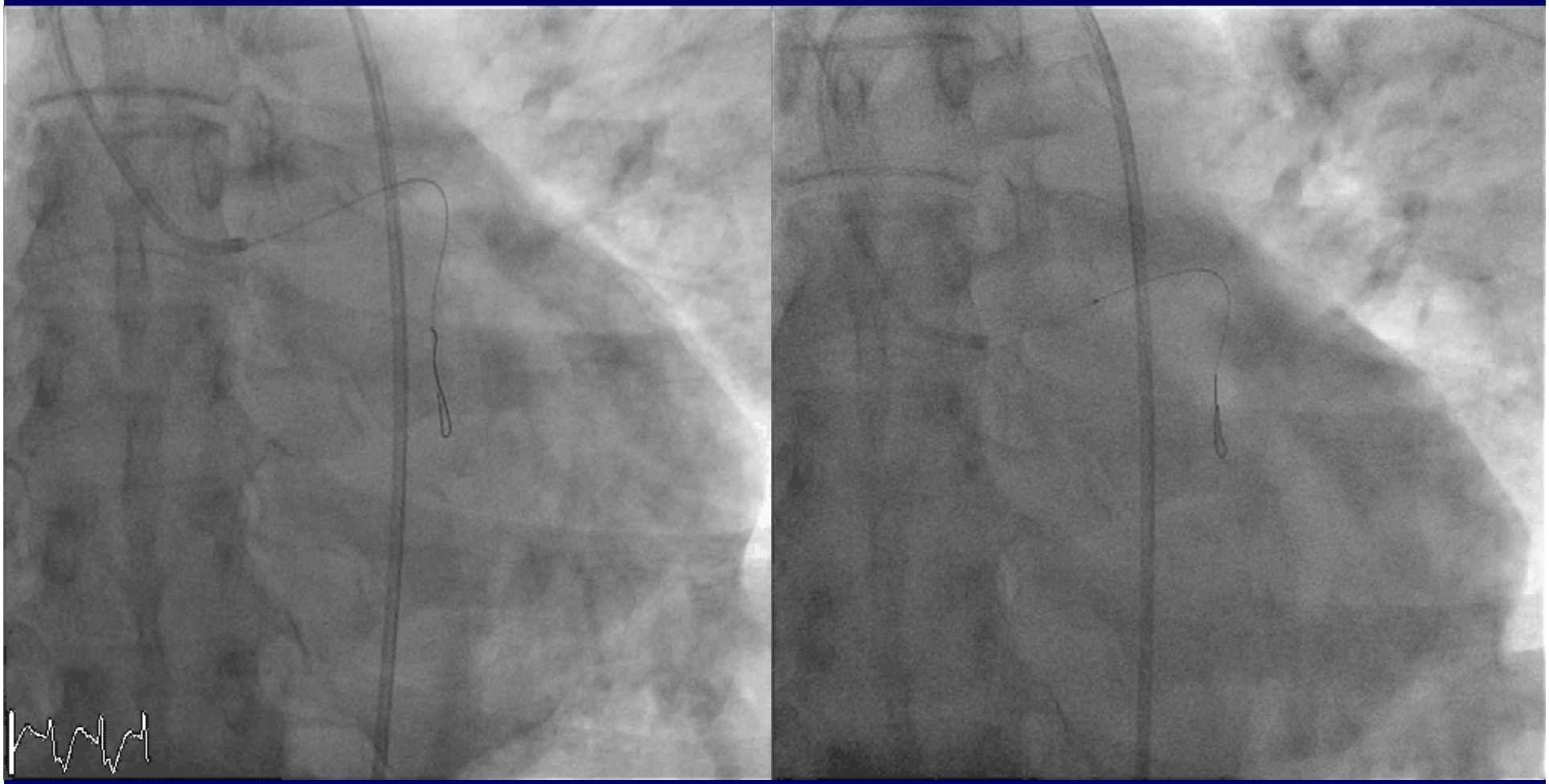
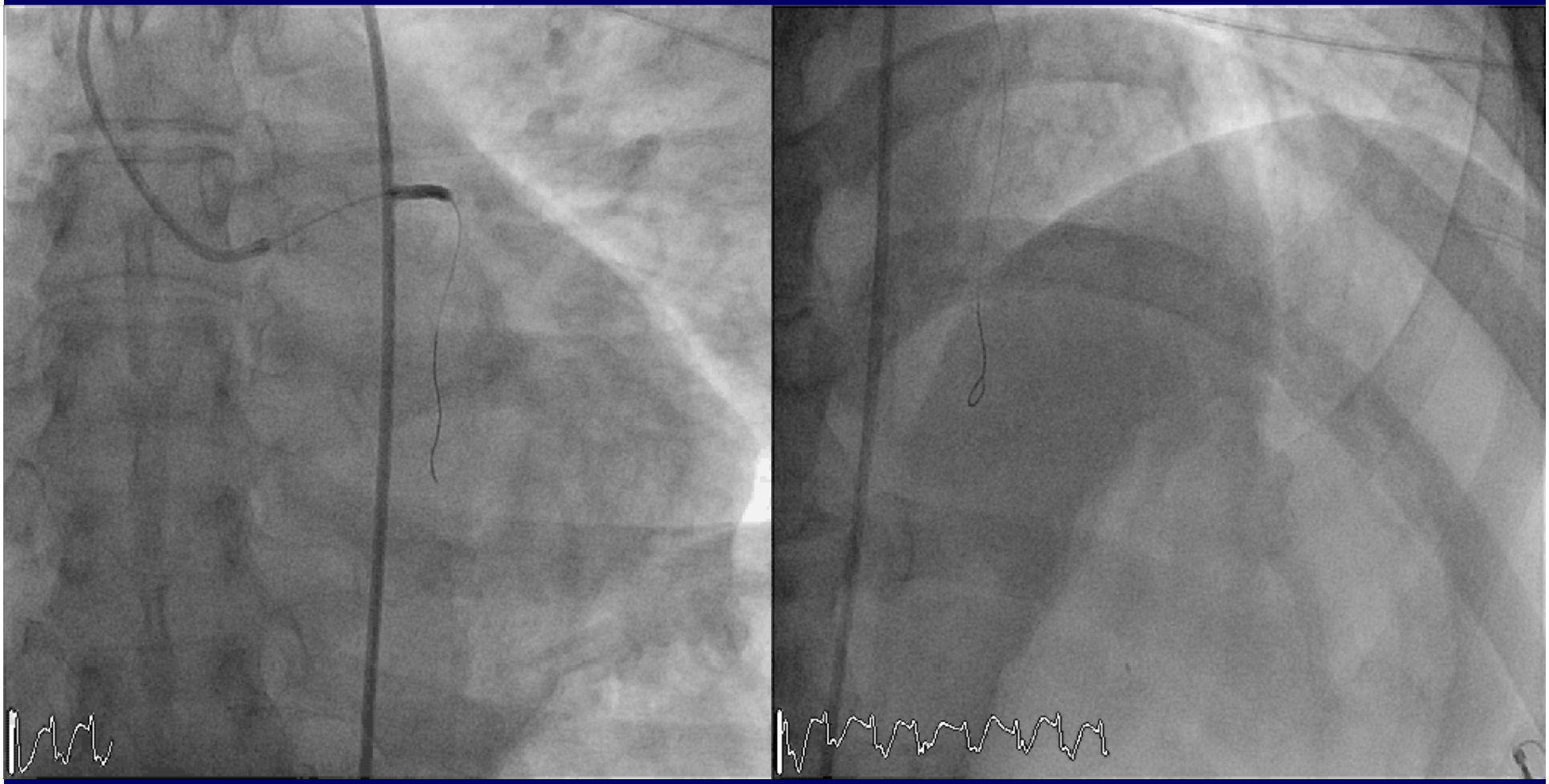
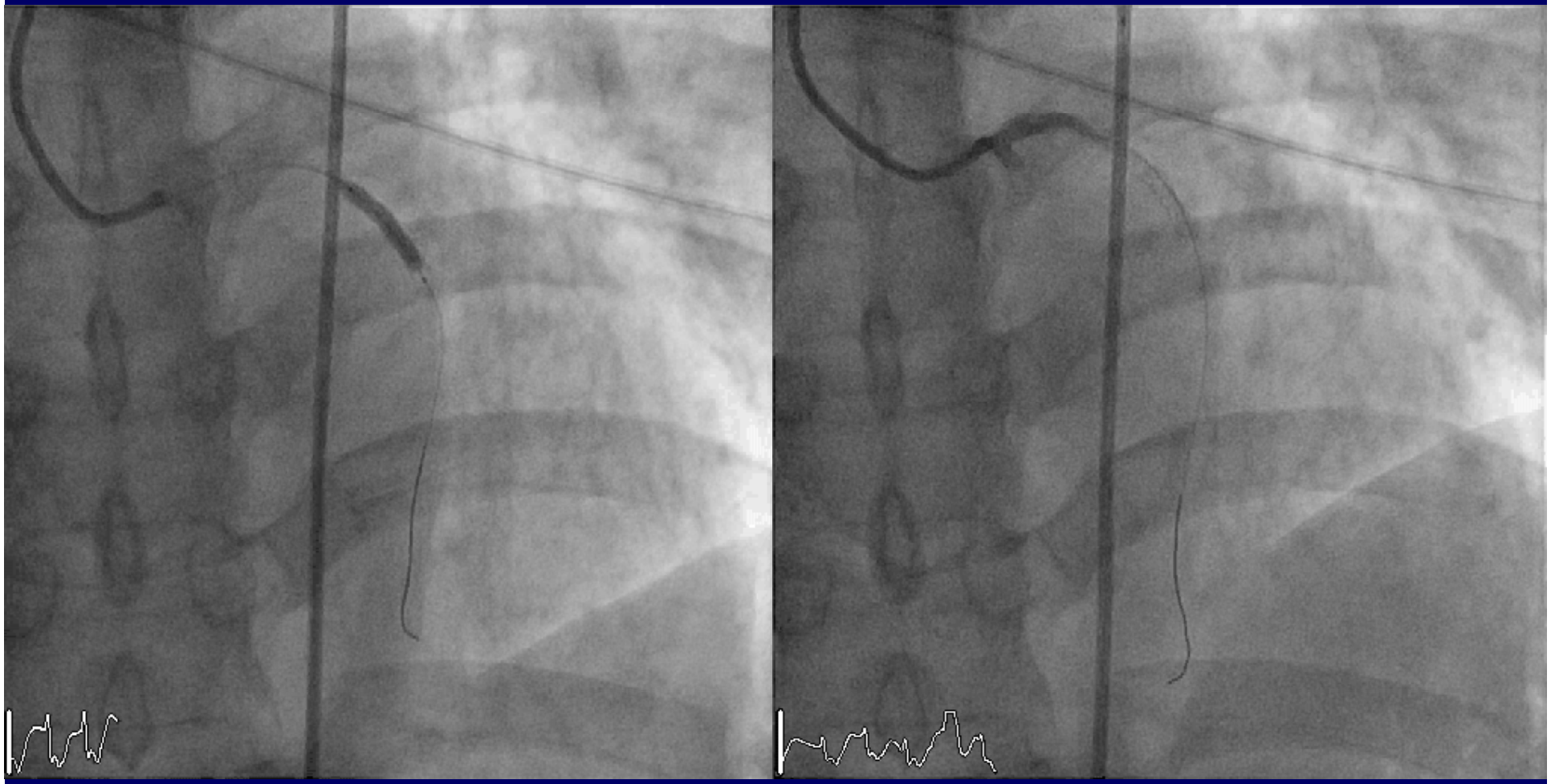
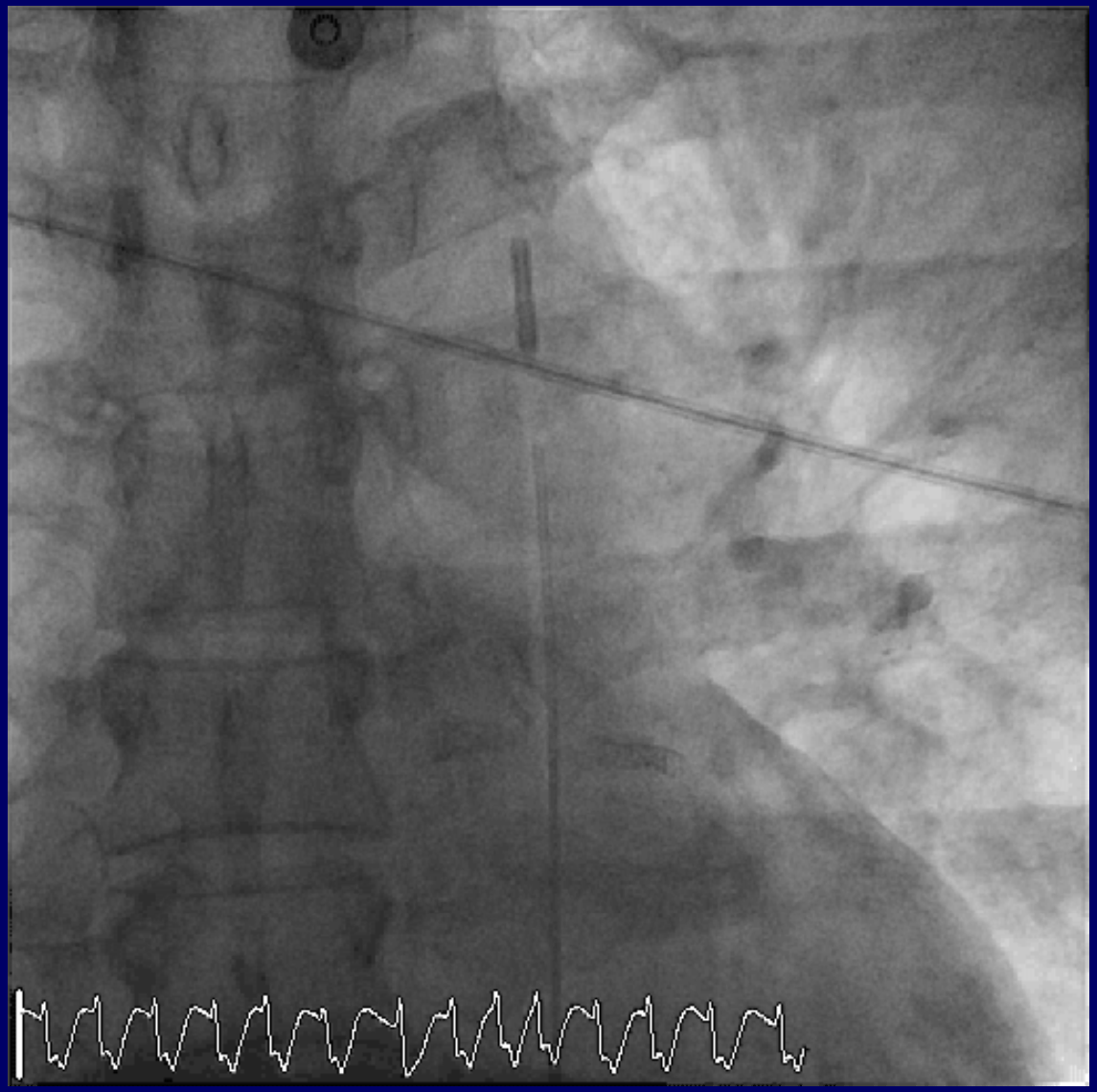






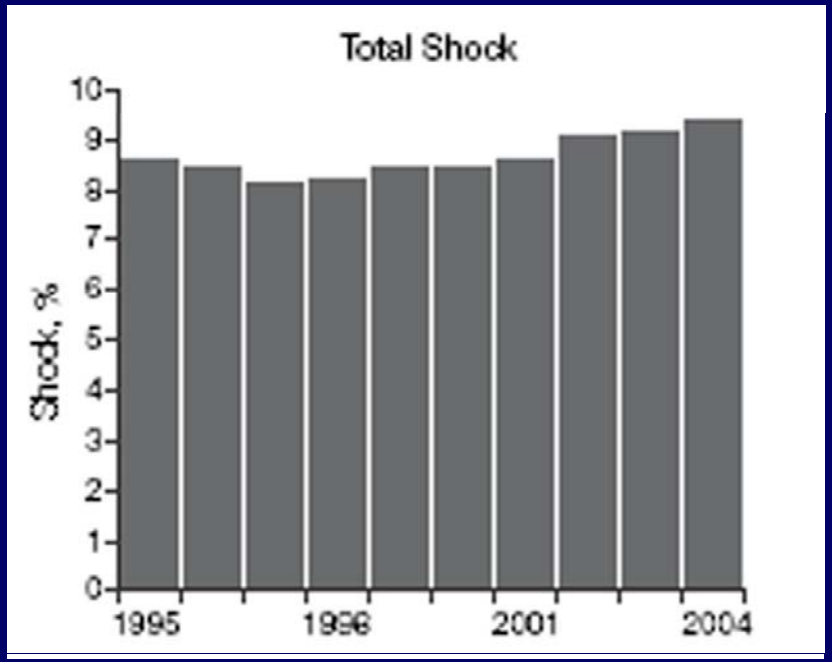






Frequency of CS Has Remained Steady Over Time

Frequency of Cardiogenic Shock



NRMI STEMI Registry1
N=25,311

NRMI Registry[1]

- Inclusion of 293,633 patients from Jan 1995-May 2004 with STEMI or new LBBB
- 775 US Hospitals with on-site PCI
- CS developed in 25,311(8.6%) pts
- CS present on admission in 29%

Worcester Heart Attack Study[2]

- 1975-88 $\rightarrow$7.5%

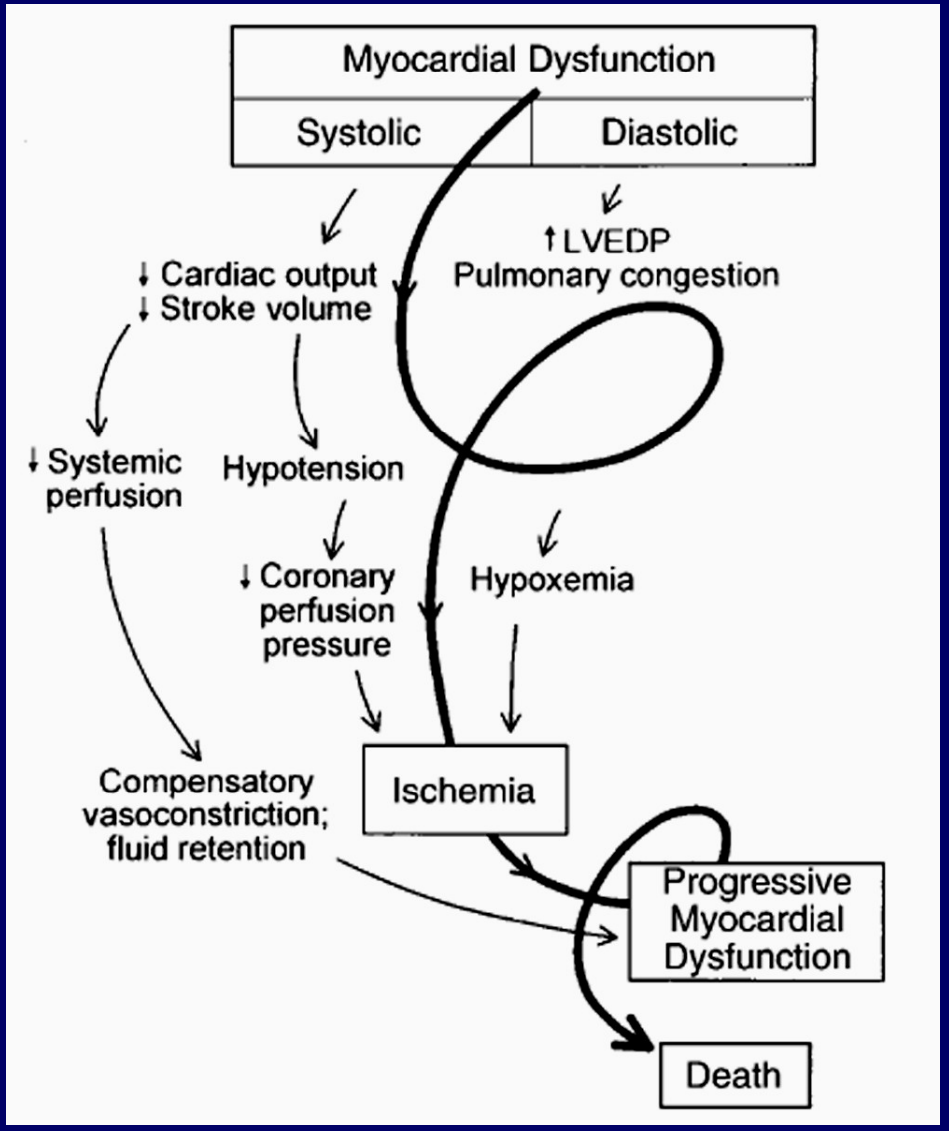
Gusto-1[3]

- 1995 $\rightarrow$ 7.2%

[1]Babaev et al JAMA 2005 294:448
[2]Goldberg RJ NEJM 1991 325:1117
[3]Holmes DR JACC 1995 26:668

Pathophysiology

- When a critical mass of LV is necrotic and fails to pump, stoke volume and CO falls
- Myocardial and coronary perfusion are compromised causing tachycardia and hypotension
- Increased LVEDP further decreases coronary perfusion
- Increase LV wall stress increases myocardial oxygen demand
- Lactic acidosis worsens myocardial performance



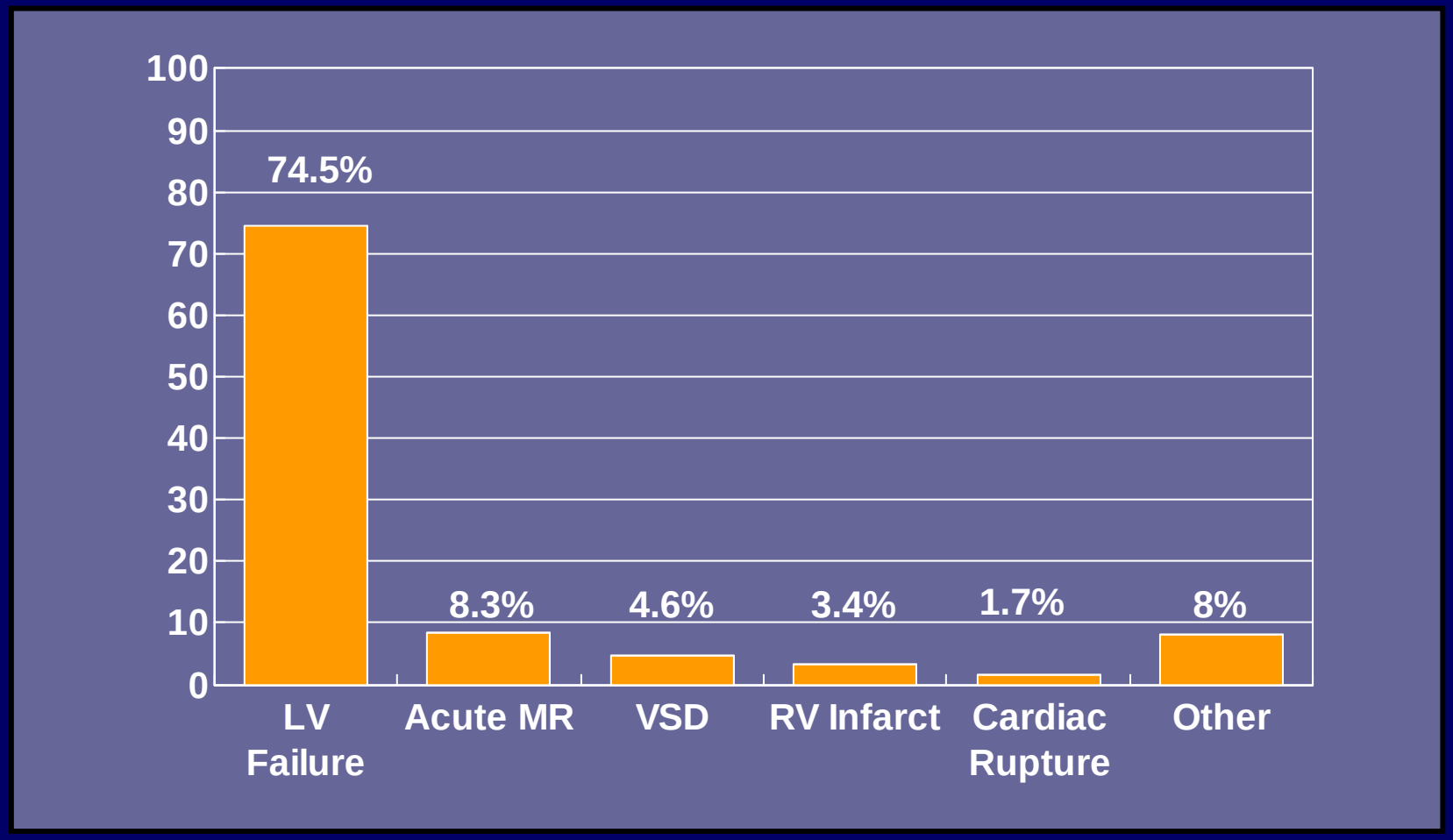
Hollenberg Ann Int Med 1999; 131:47-99

Etiology of Cardiogenic Shock due to AMI

- Loss of LV function
  - Loss of > 40% of myocardial mass
  - Loss of < 40% of LV mass with tachyarrhythmia
- Mechanical defects : 12%
  - Acute VSD
  - Papillary muscle dysfunction, rupture
  - Chordae rupture
  - Free wall rupture
- Right ventricular infarction : 5%

Causes of Cardiogenic Shock

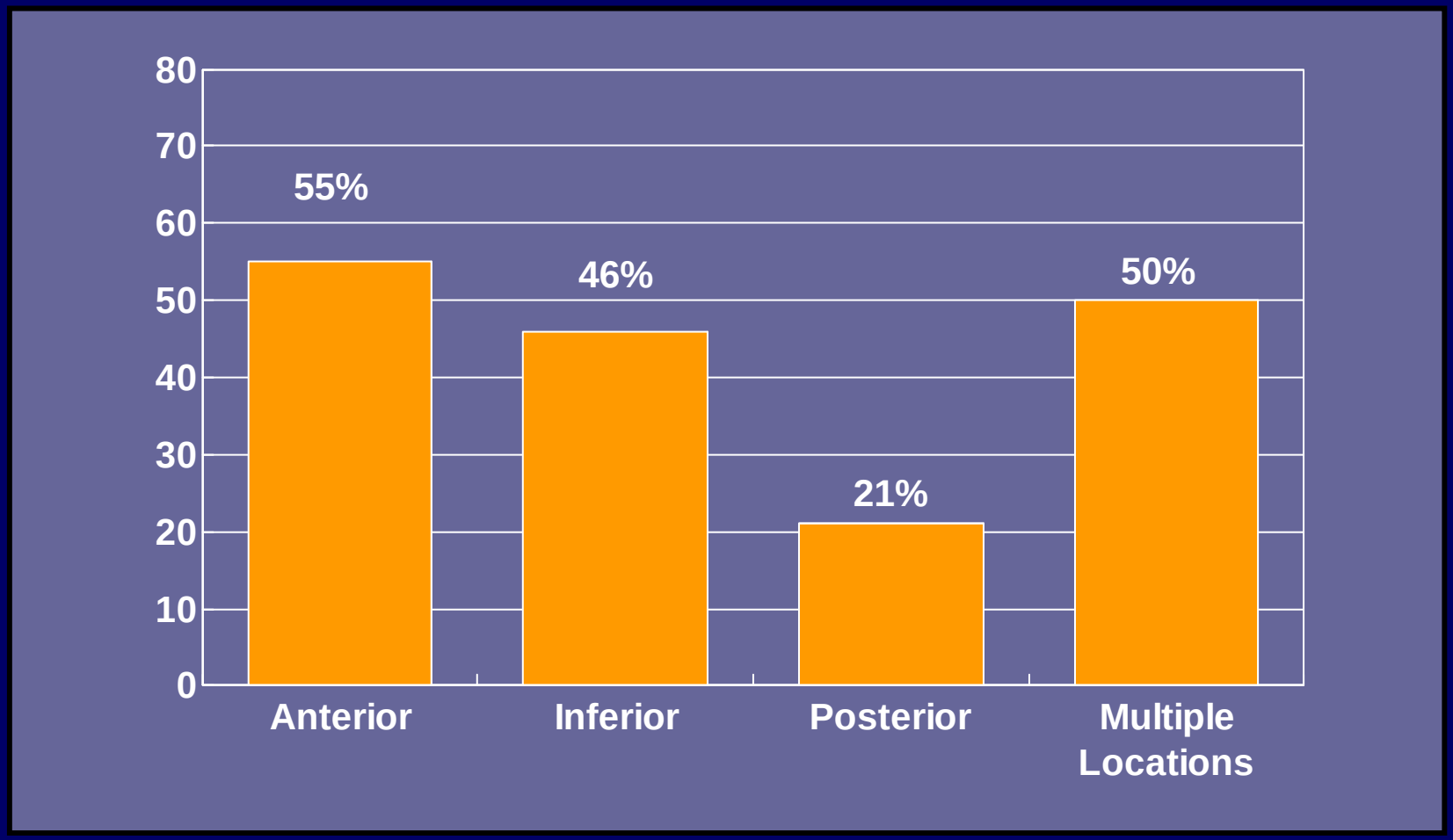
SHOCK Trial and Registry (N=1160)



Hochman Circ 1995; 91:873-81

Infarct Location In Cardiogenic Shock

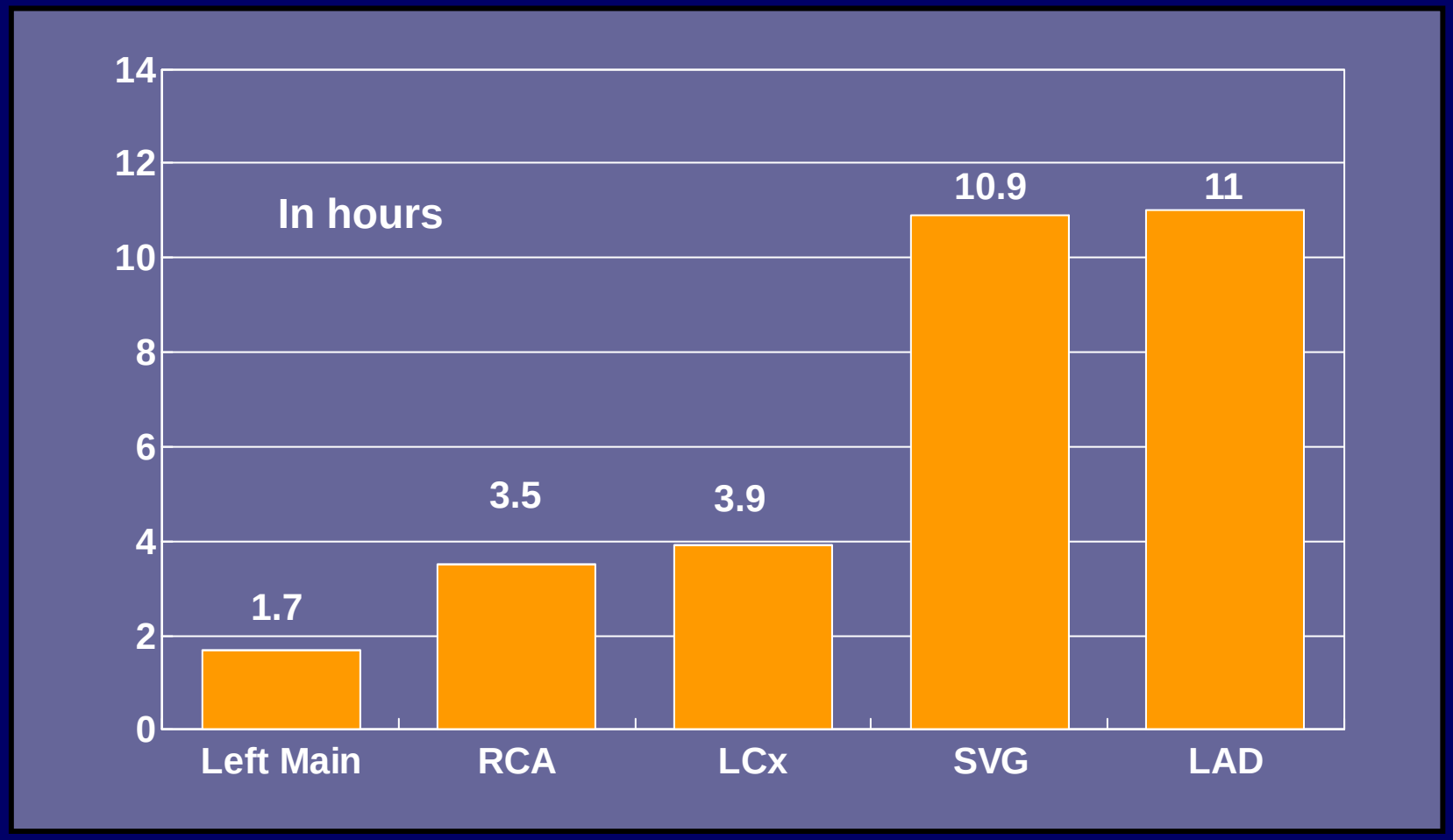
SHOCK Trial (N=1160)



Hochman Circ 1995; 91:873-81

Time of the onset of Cardiogenic Shock

Shock developed a median of 6.2h after MI symptom onset



Webb JACC 2000; 36:1084

Shock Onset after acute MI Occurred within 24 h in 74% of the patients with predominant LV failure

Predictors of Early (<24h) Cardiogenic Shock

- Chest pain at shock onset
- ST-segment elevation in two or more leads
- Multiple infarct locations
- Inferior MI
- Left main disease
- Smoking

Predictors of Late (>24h) Cardiogenic Shock

- Recurrent ischemia,
- Q waves in $\geq$ 2 leads
- LAD culprit vessel

Webb JACC 2000; 36:1084

Clinical Observations from the SHOCK Trial

- The average LVEF is only moderately depressed(30%) with a wide range of EFs and LV sizes noted

  - While most patients were on IABP support and ionotropes, hemodynamic measurements demonstrated persistent hypotension, low CO, and high filling pressures despite a 30% LVEF

- The SVR was not markedly elevated in many cases, with the SVR ranging from 1350-1400 dyness-sec-cm^{-5} despite inotroic support

  - Cardiac power = CI x MAP was the most powerful hemodynamic predictor of mortality

  - The ability to raise SVR may be an important compensatory mechanism to support BP

  - Endogenous/exogenous vasodilators inhibit this response

Hochman Circulation 2003; 107:2998

Cardiogenic Shock: Diagnosis

- Clinical definition[1] is a decreased cardiac output and evidence of tissue hypoperfusion in the presence of adequate filling pressures:

  - Marked and persistent(>30min) hypotension with a systolic BP < 90mmHg

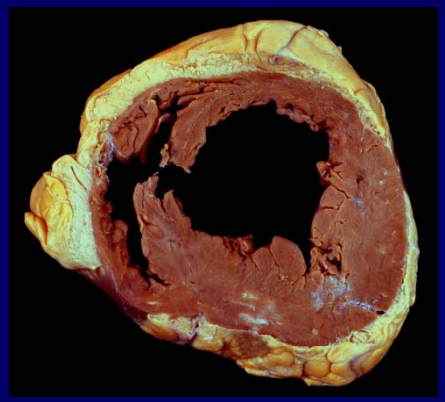
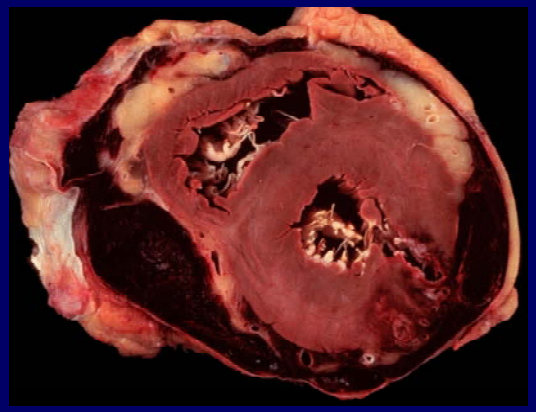
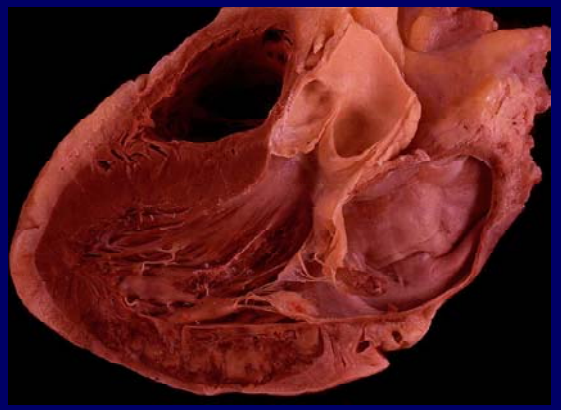
  - Reduction in the cardiac index (<2.2 L/min/M^2)

  - Normal or elevated PCWP (>15 mmHg)

- Circulatory shock[2] is diagnosed by poor tissue perfusion, including oliguria, clouded sensorium, and cool mottled extremities

[1]Forrester JS et al 1976; 295:1404-13
[2] Hollenberg Ann Int Med 1999; 131:47-99

Mechanical Complications Resulting in Cardiogenic Shock

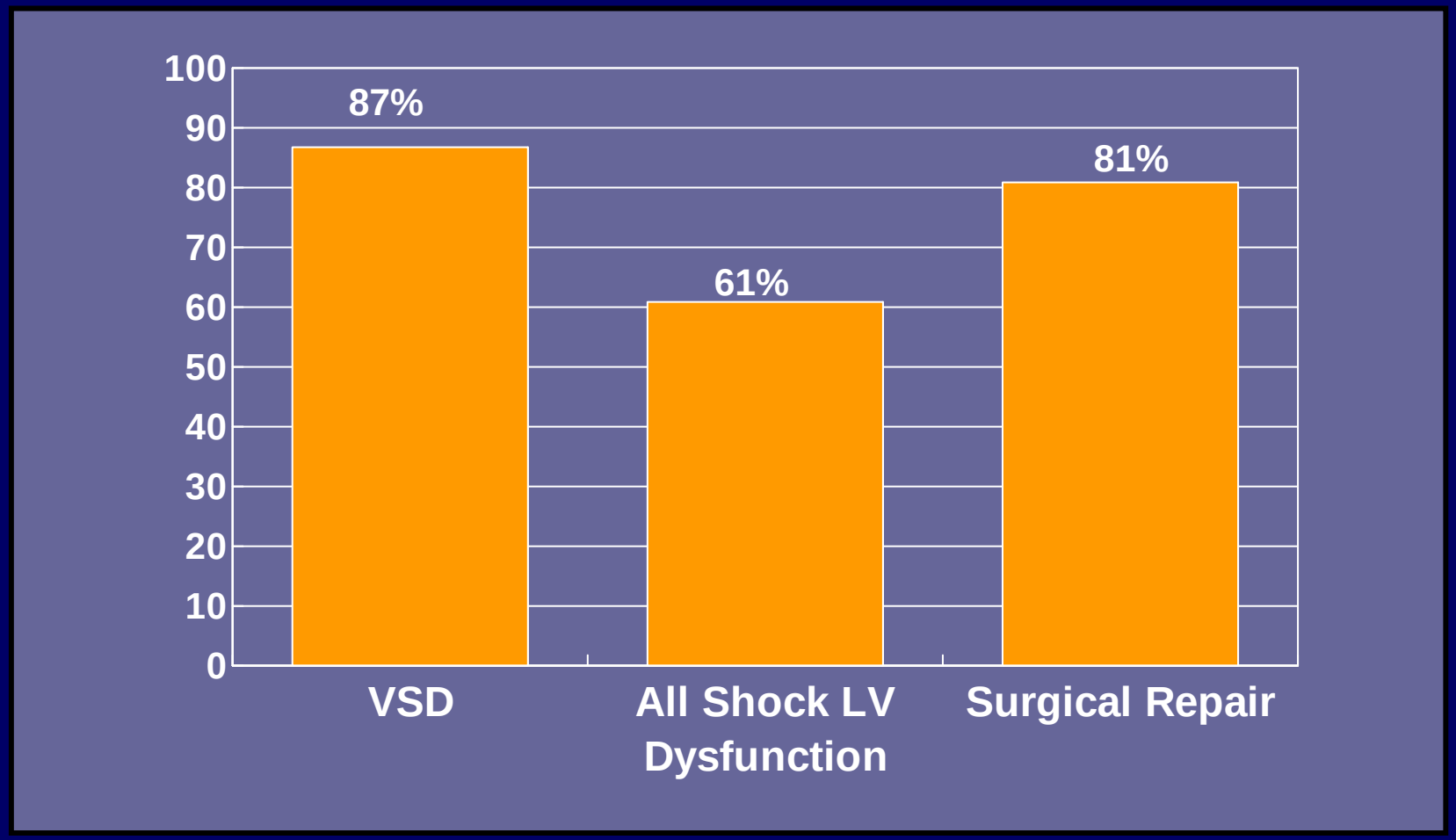
	VSD	Free Wall Rupture	MR due to papillary Muscle dysfunction
			
Incidence	1-2%	1-6%	1-2%
Timing	3-5 days after MI	3-6 days after MI	3-5 days after MI
Phy Exam	Murmur 90%	JVD, EMD	Murmur 50%
Thrill	Common	No	Rare
Echo	Shunt	Pericardial Effusion	Regurgitation Jet
PA cath	O_2 step up > 9%	Equal Diastolic Pressures	c-v wave in PCW

Http:www.americanheart.org/stemi

Images: Courtesy of W D Edwards(Mayo Foundation)

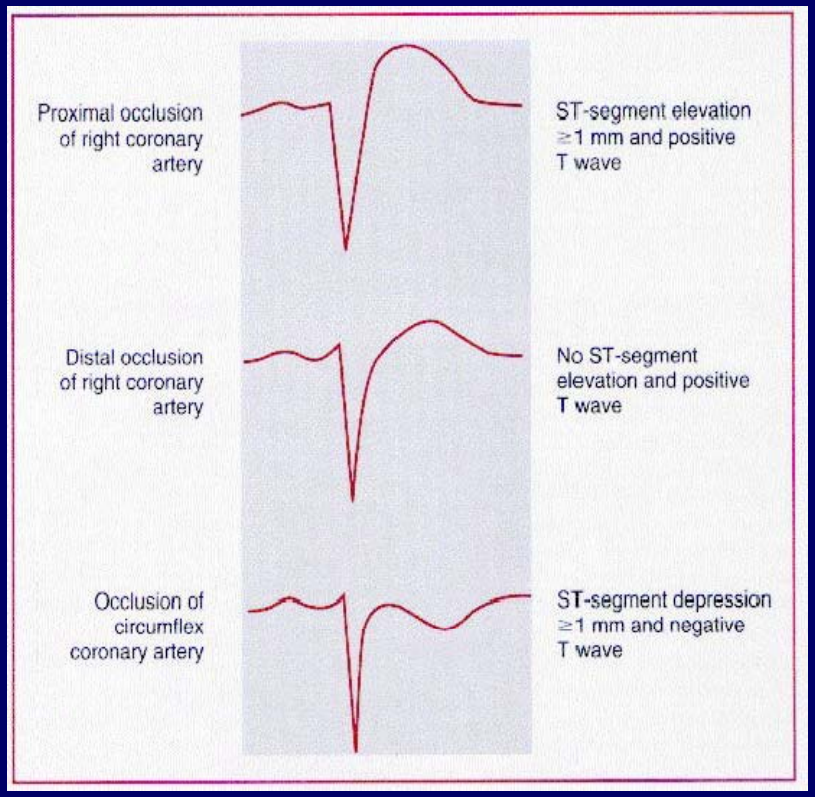
Data : Lavocitz. CV Rev Rpt 1984;5:948: Birnbaum. NEJM 2002;347:1426

Ventricular Septal Defect:
In-Hospital Mortality in the SHOCK Trial



Menon V et al 2000;36:1110-6

Right Ventricular Infarction: Diagnosis



V_4R

Clinical findings:

- **Shock with clear lungs, elevated JVP**
- **Kussmaul sign**

Hemodynamics:

- **Increased RA pressure (y descent)**
- **Square root sign in RV tracing**

ECG:

- **ST elevation in R sided leads**

Echo:

- **Depressed RV function**

Rx;

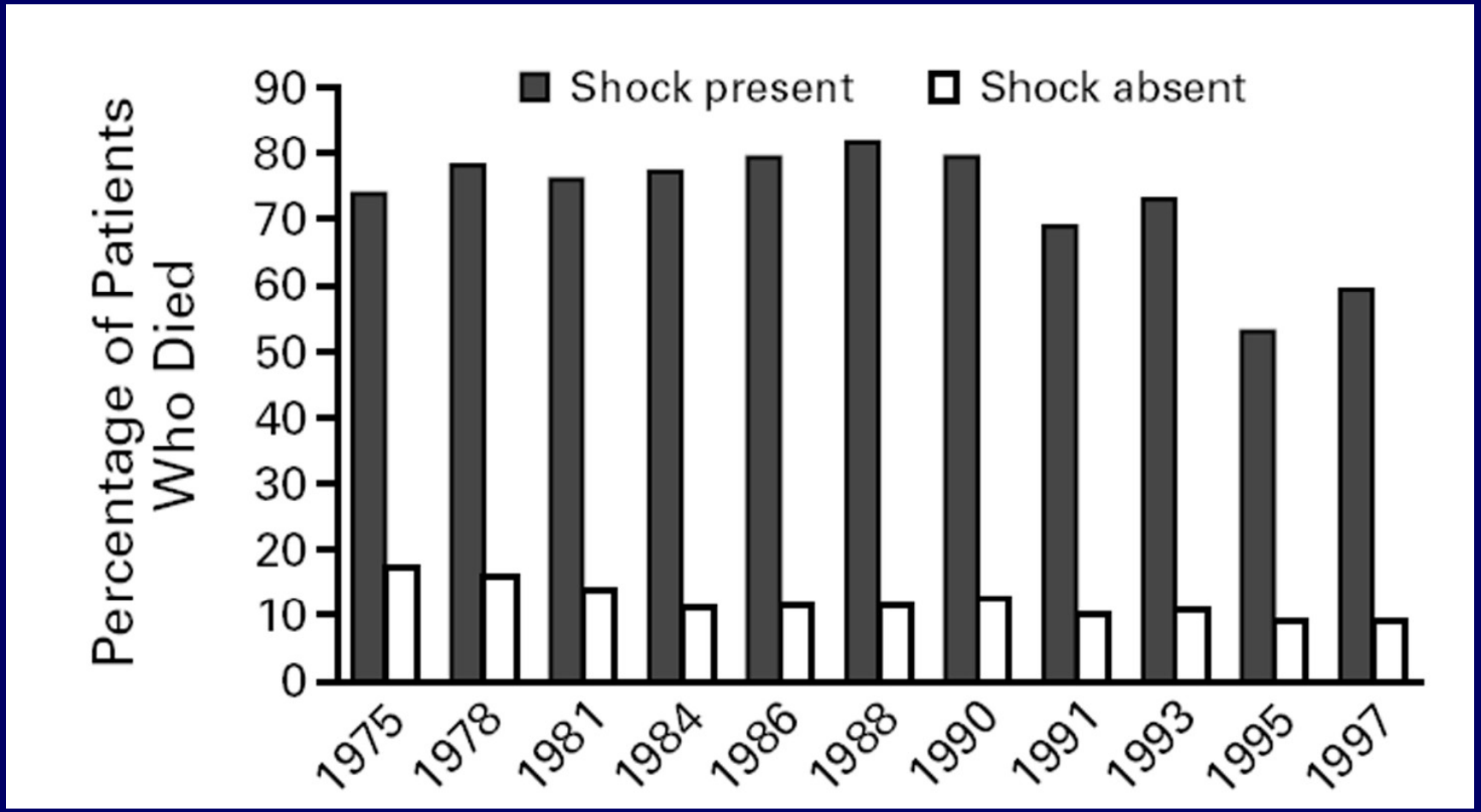
- **Maintain RV preload**
- **Lower RV afterload (PA---PCW)**
- **Inotropic support**
- **Reperfusion**

Modified from Wellens. N Engl J Med 1999;340:381.

http:www.americanheart.org/stemi

Mortality Rates Have Progressively Fallen Over Time

Worcester Heart Attack Registry (N=644)



Goldberg RJ NEJM 1999; 340:1162

The Shock Trial has been the most important study for management guidelines in patients with cardiogenic shock

The New England
Journal of Medicine

VOLUME 341 AUGUST 26, 1999 NUMBER 9

EARLY REVASCULARIZATION IN ACUTE MYOCARDIAL INFARCTION COMPLICATED BY CARDIOGENIC SHOCK

JUDITH S. HOCHMAN, M.D., LYNN A. SLEEPER, SC.D., JOHN G. WEBB, M.D., TIMOTHY A. SANBORN, M.D., HARVEY D. WHITE, D.SC., J. DAVID TALLEY, M.D., CHRISTOPHER E. BULLER, M.D., ALICE K. JACOBS, M.D., JAMES N. SLATER, M.D., JACQUES COL, M.D., SONJA M. MCKINLAY, PH.D., AND THIERRY H. LEJEMTEL, M.D., FOR THE SHOCK INVESTIGATORS*

Hochman et al NEJM 1999;341:625

The SHOCK Trial (n=302)

Randomization from Apr 1993-Mov 1998

Emergency Revascularization N=152	Medical Therapy N=150
• Angioplasty or CABG within 6 hours after randomization • IABP recommended in all pts	• IABP • Thrombolytic Therapy • Delayed Revascularization after 54 hours following randomization, if appropriate

- Primary Endpoint : Overall 30 day mortality
- Seconday Endpoints : 6 month and 1 year mortality

Hochman et al NEJM 1999;341:625

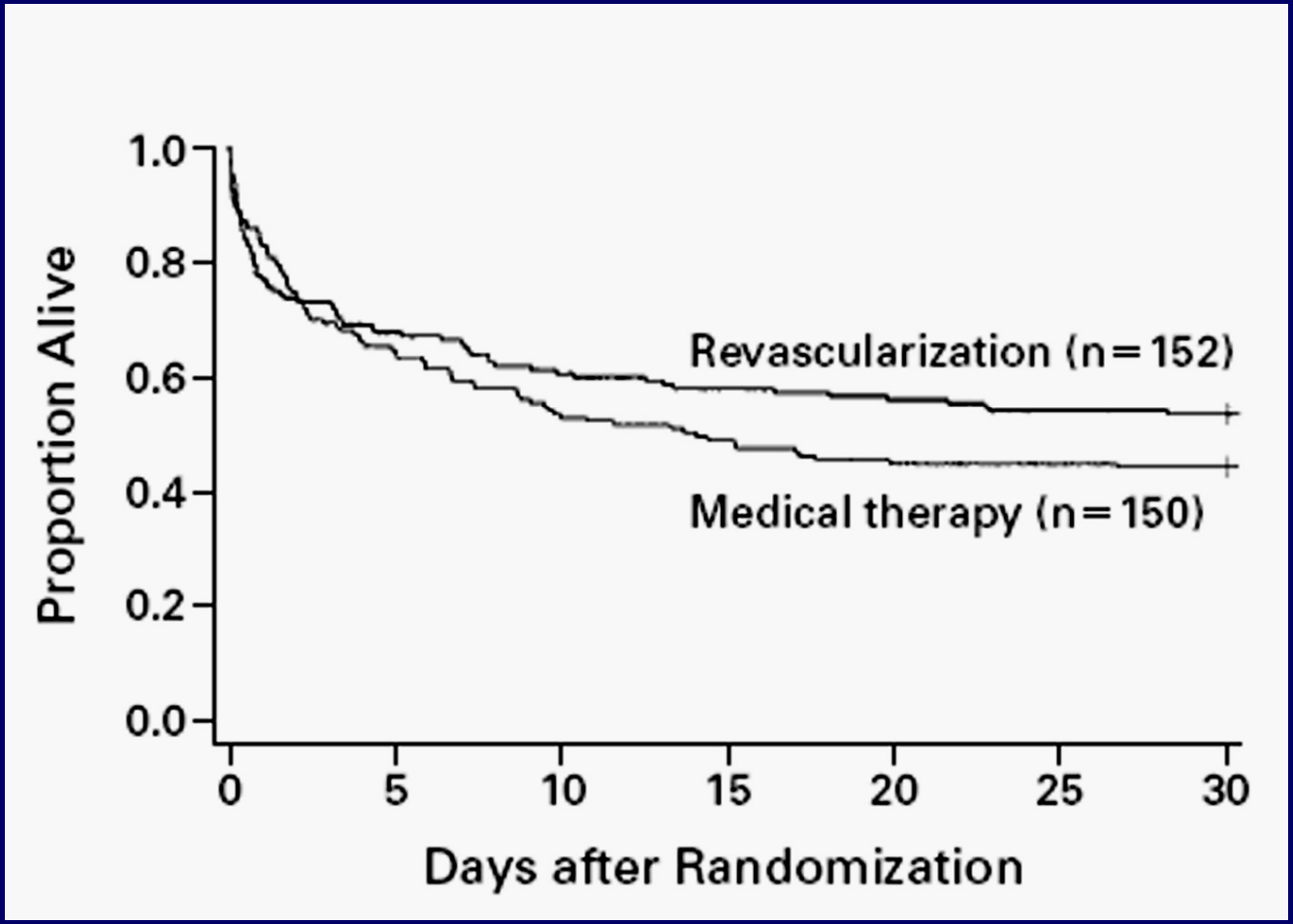
The Shock Trial:

Treatment

TREATMENT	REVASCULARIZATION (N=152)	MEDICAL THERAPY (N=150)
CPR, VT, or VF before randomization (%)*	32.7	23.9
Thrombolytic therapy (%)	49.3	63.3
Inotropes or vasopressors (%)	99.3	98.6
Intraaortic balloon counterpulsation (%)	86.2	86.0
Pulmonary-artery catheterization (%)	93.4	96.0
Left ventricular assist device (%)†	3.6	0.9
Heart transplantation (%)	2.0	0.7
Coronary angiography (%)	96.7	66.7
Angioplasty (%)	54.6	14.0
Stent placed‡	35.7	52.3
Platelet glycoprotein IIb/IIIa receptor antagonist§	41.7	25.0
Coronary-artery bypass grafting (%)	37.5	11.3
Angioplasty or coronary-artery bypass grafting (%)	86.8	25.3
Median time from randomization to revascularization (hr)¶	1.4 (0.6–2.8)	102.8 (79.0–162.0)

Hochman et al NEJM 1999; 341:625

Shock Trial : 30 day mortality (1º Endpoint)



Hochman et al NEJM 1999; 341:625

Shock Trial : 30 Day and 6 Month Mortality

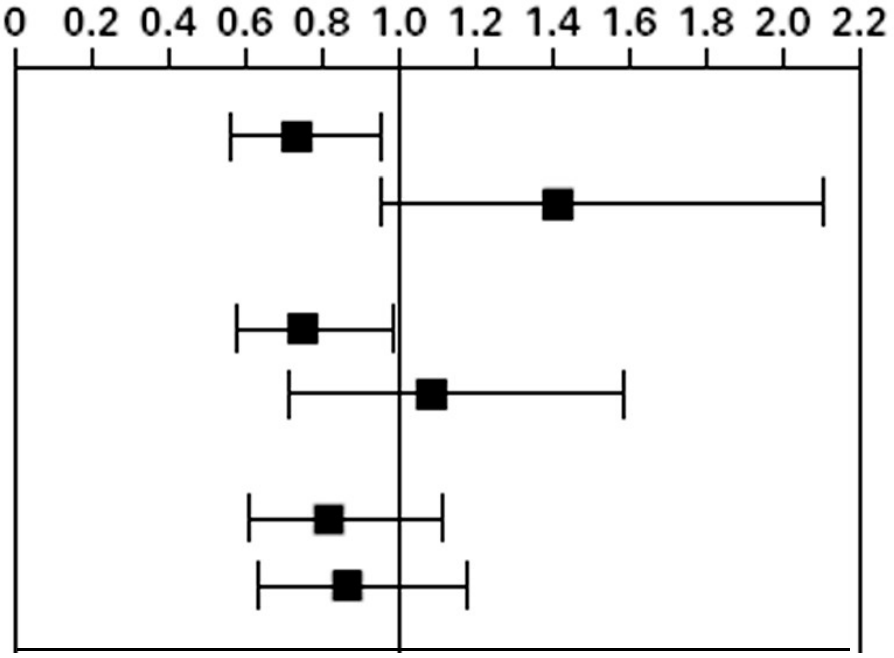
TABLE 4. MORTALITY AMONG STUDY PATIENTS.*

OUTCOME AND SUBGROUP	REVASCULARIZATION	MEDICAL THERAPY	DIFFERENCE BETWEEN GROUPS (95% CI)	RELATIVE RISK (95% CI)	P VALUE
	percent (number in subgroup)		percent		
30-day mortality					
Total	46.7 (152)	56.0 (150)	−9.3 (−20.5 to 1.9)	0.83 (0.67 to 1.04)	0.11
Age <75 yr	41.4 (128)	56.8 (118)	−15.4 (−27.8 to −3.0)	0.73 (0.56 to 0.95)	0.01†
Age ≥75 yr	75.0 (24)	53.1 (32)	+21.9 (−2.6 to 46.4)	1.41 (0.95 to 2.11)	
6-mo mortality‡					
Total	50.3 (151)	63.1 (149)	−12.8 (−23.2 to −0.9)	0.80 (0.65 to 0.98)	0.027
Age <75 yr	44.9 (127)	65.0 (117)	−20.1 (−31.6 to −7.1)	0.70 (0.56 to 0.89)	0.003†
Age ≥75 yr	79.2 (24)	56.3 (32)	+22.9 (0.7 to 46.6)	1.41 (0.97 to 2.03)	

Hochman et al NEJM 1999; 341:625

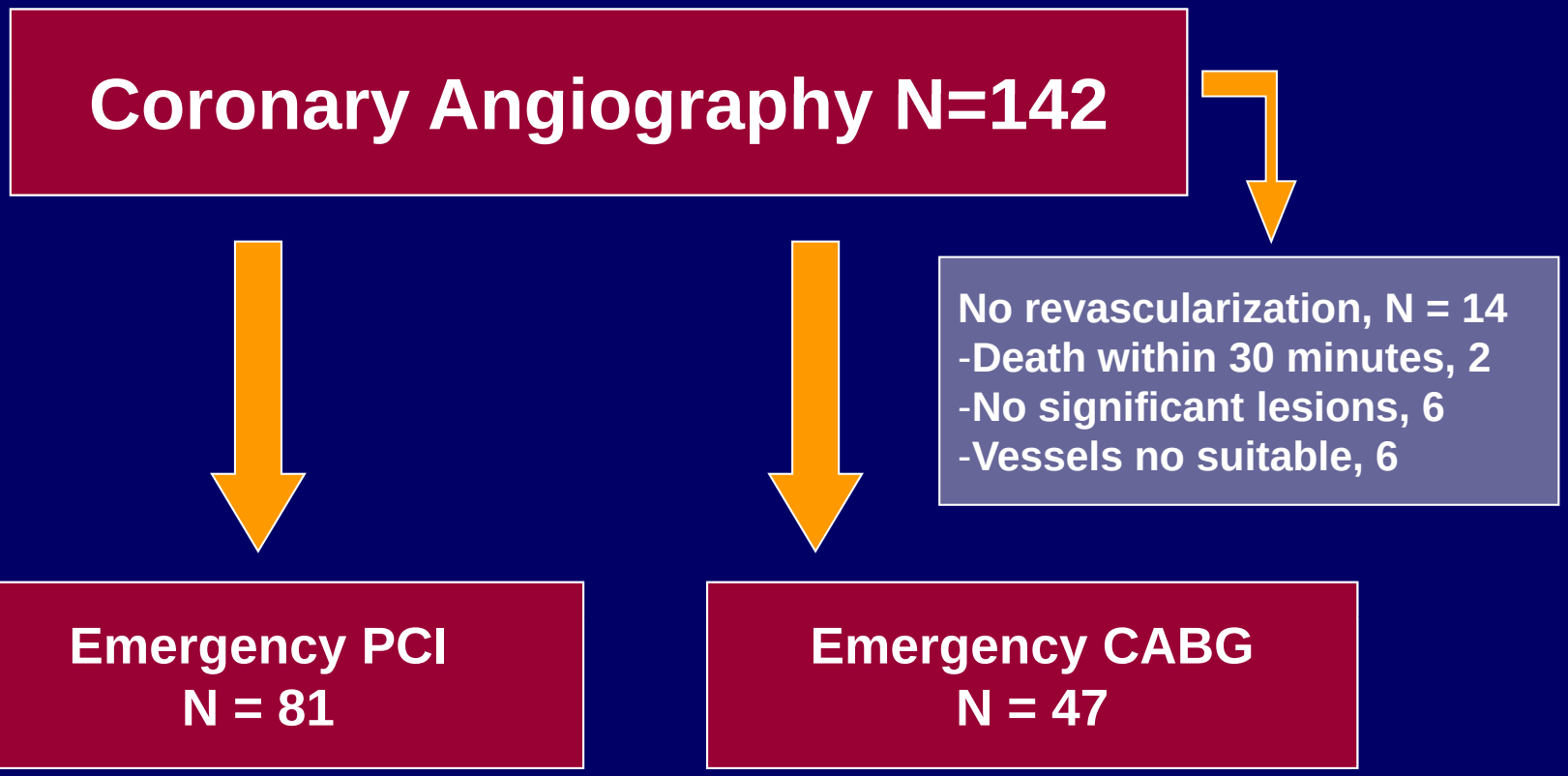
Shock Trial : Subgroup Analyses
Cautionary Note : The Elderly ?

SUBGROUP	NO. OF PATIENTS
Age <75 yr	246
Age ≥75 yr	56
Men	205
Women	97
Transfer admission	167
Direct admission	135



Hochman et al NEJM 1999; 341:625

PCI vs CABG in the Shock Trial

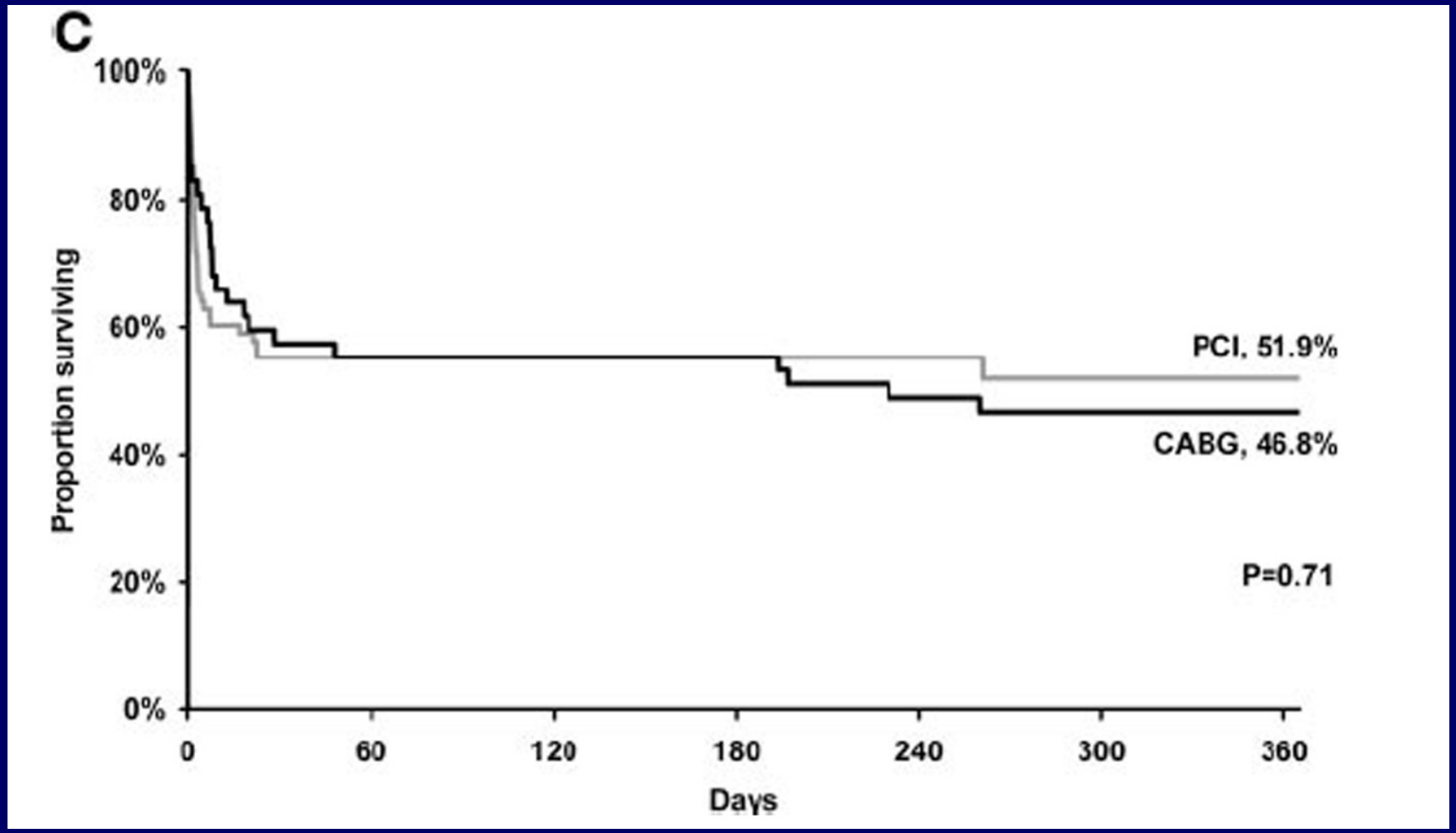


White HD et al Circulation 2005;112:1992

PCI vs CABG in the Shock Trial

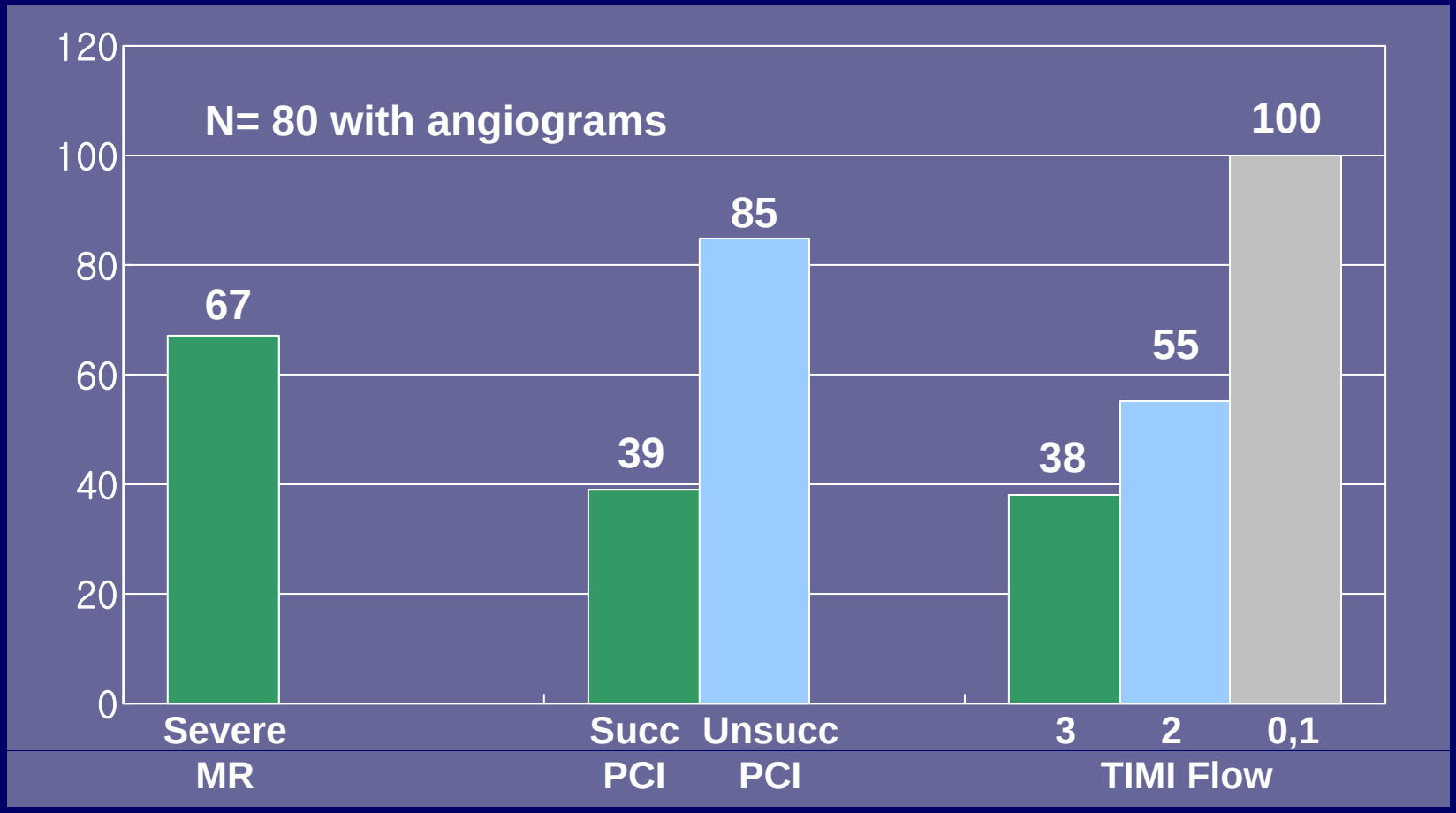
	PCI-Treated N=81	CABG-Treated N=47	P Value
Age(years)	64.8	65.3	NS
Diabetes(%)	26.9	48.9	0.02
PVD(%)	13.8	21.2	0.39
Left Main > 50%	13.0	41.3	0.001
3V CAD	60.3	82.6	0.01
Jeopardy Score	7.1	9.9	<0.001
Angio to revasc, hrs	0.9	2.77	----

PCI v. CABG in the Shock Trial



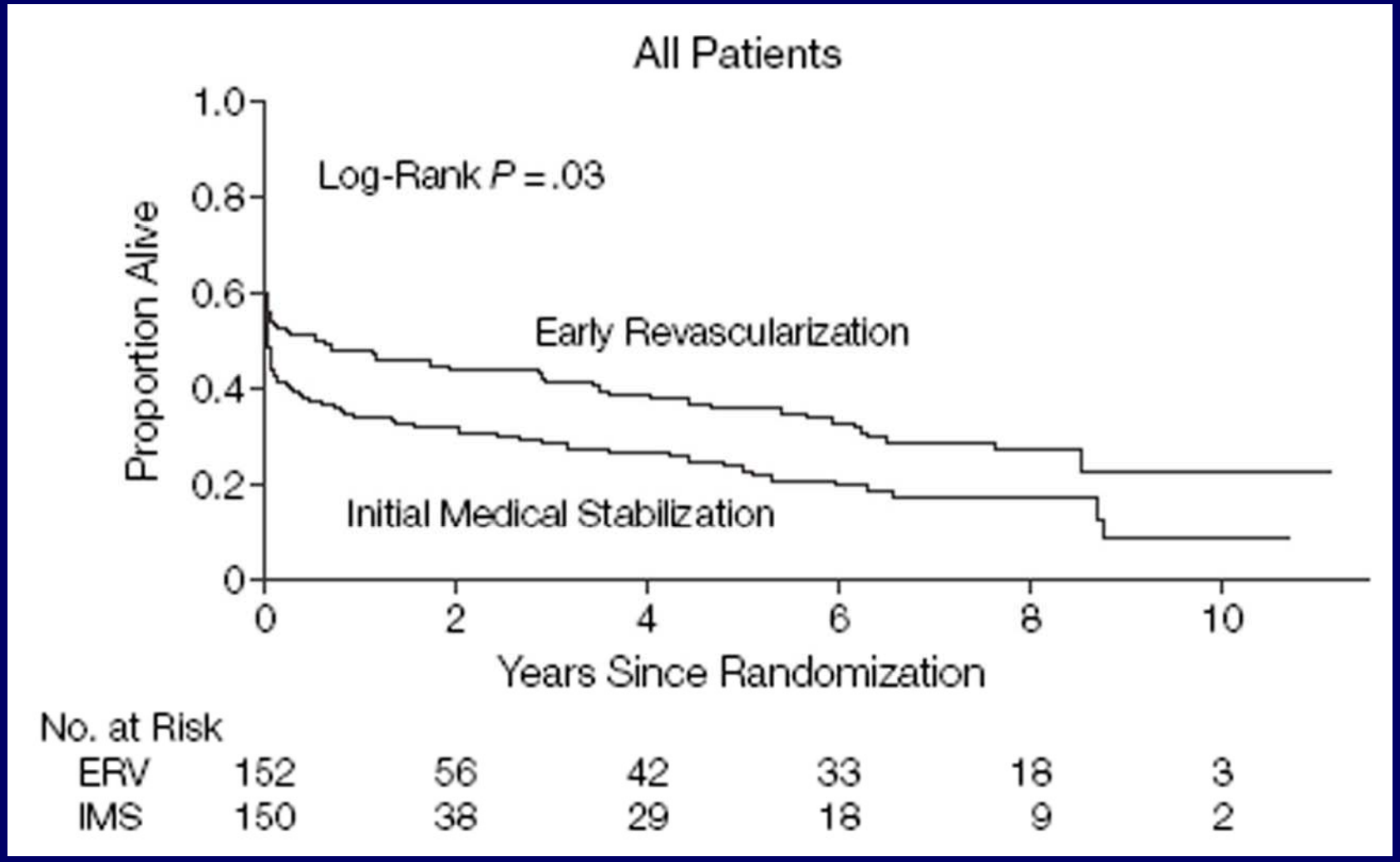
White HD et al Circulation 2005;112:1992

Shock Trial: Mortality Rates with PCI
Overall Mortality = 50%



Webb et al JACC 2003;42:1380

6 Yr Outcome of SHOCK All Patients



Hochman et al JAMA 2006;295:2511

Intra-Aortic Balloon Pump Support

- Reduces afterload
- Augments diastolic perfusion pressure
- Improvement in cardiac output and coronary blood flow
- No Change in myocardial oxygen demand
- Essential as a support device for PCI or bridge to CABG
- ACC-AHA Class I recommendation
- IABP support was associated with a ↓ in mortality:
  - * NRMI-2 with lysis, from 67% to 49%[2]
  - * SHOCK Trial, from 63% to 47%

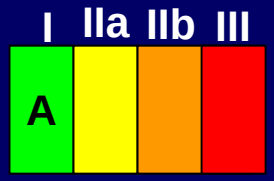
[1]Hollenberg Ann Int Med 1999; 131:47-99 [2]Barron AHJ 2001; 141:933

Clinical Observations from the SHOCK Trial

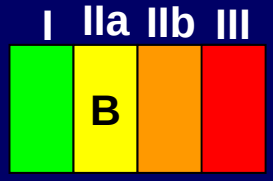
- The Classic notion that cardiogenic shock develops only when 40% of the myocardium is irreversibly damaged is inconsistent with
  - 50% survival in PCI-treated patients
  - Improved LVEF in patients undergoing revascularization
  - NYHA Class I symptoms in 58% of patients after survival of the cardiogenic shock
- Resolution of the ischemia and neurohumeral- inflammatory mediates may result in resolution of the cardiogenic shock
- The range of LVEFs, LV size, and SVR in patients with cardiogenic shock indicate that the pathogenesis may be multifactorial.

Hochman Circulation 2003; 107:2998

ACC/AHA Guidelines for PCI in Patients with Cardiogenic Shock

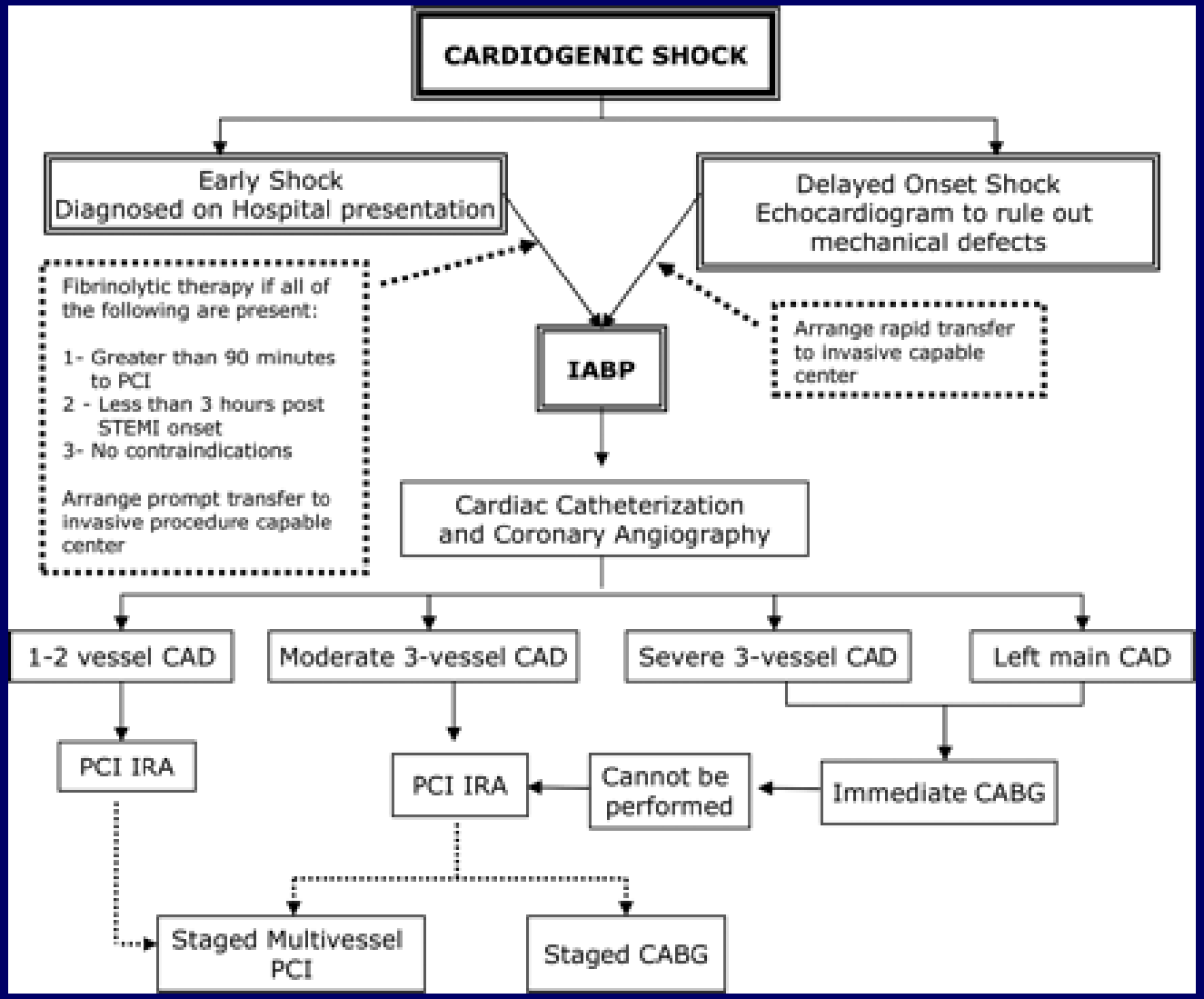


Primary PCI is recommended for patients less than 75 years with ST elevation or LBBB or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.

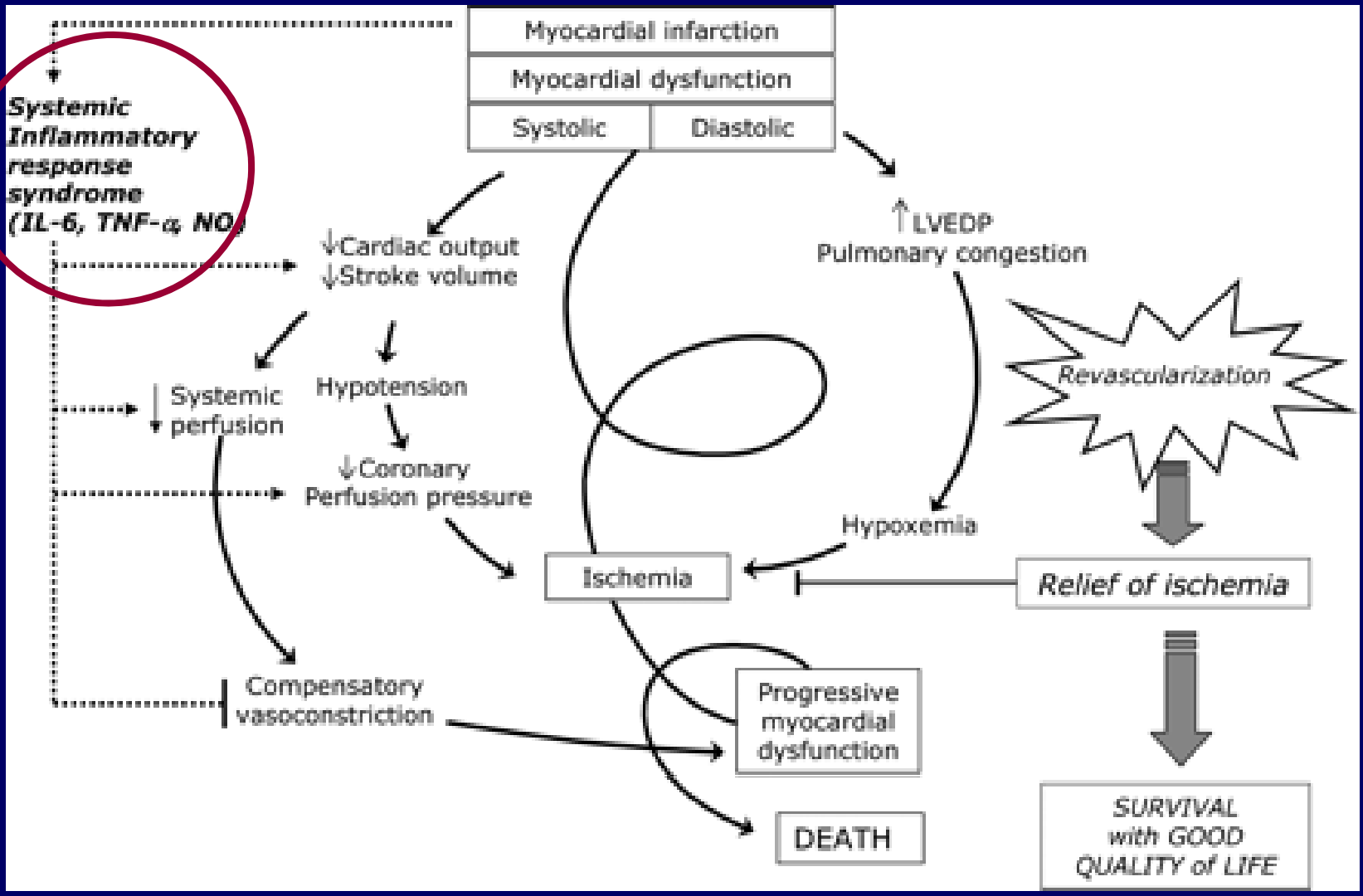


Primary PCI is reasonable for selected patients 75 years or older with ST elevation or LBBB or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock

Algorithm for Revascularization Strategy in Cardiogenic Shock



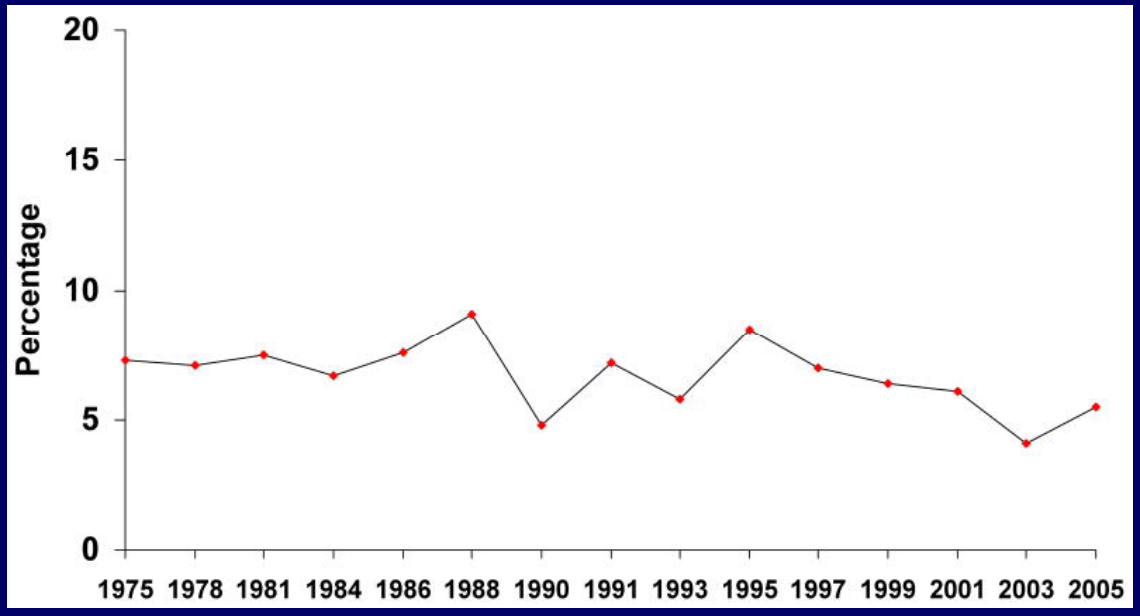
ACC/AHA guideline



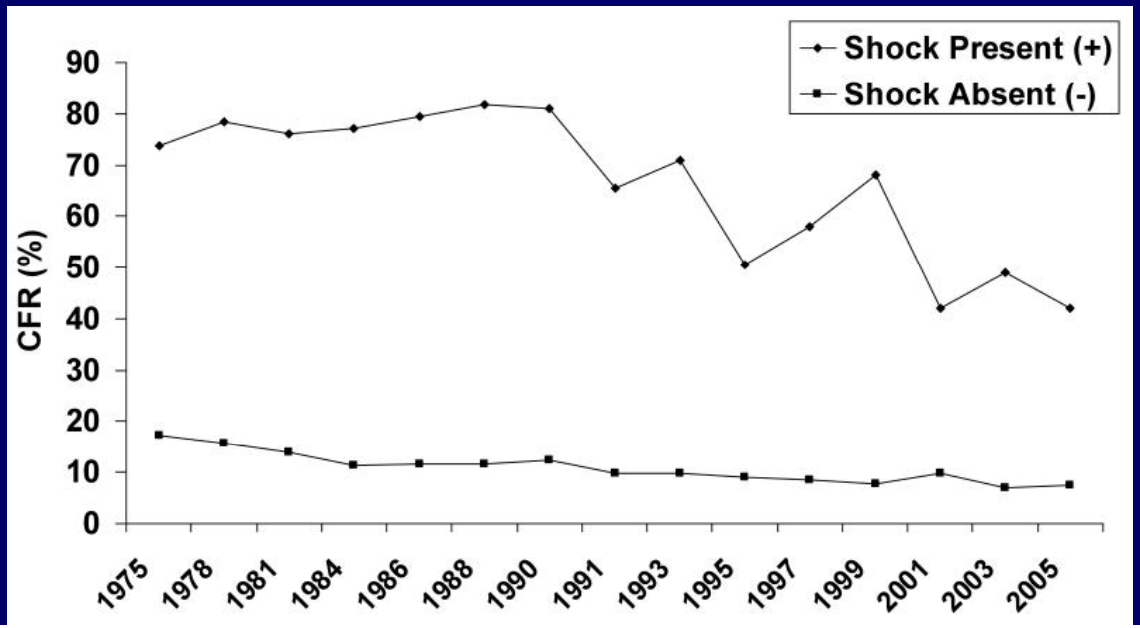
Reynolds HR, & Hochman JS. Circulation 2008
Salem R & Mebazaa. Critical Care 2007

25 yr Trend of Cardiogenic Shock

Incidence



Mortality



Goldberg RJ, et al
Circulation 2009

Summary

- CS is a treatable illness with a reasonable chance for full recovery
  : Although very high risk for early death, great potential exist for salvage.
- An early invasive approach can increase short & long term survival and can result in excellent quality of life.
- Prevention with very early reperfusion therapy remains the major goal.

Reynolds HR & Hochman Circulation 2008

Ischemic Stroke After AMI

: Population based study

Mooe T et al. Stroke. 1997 Apr;28(4):762-7.

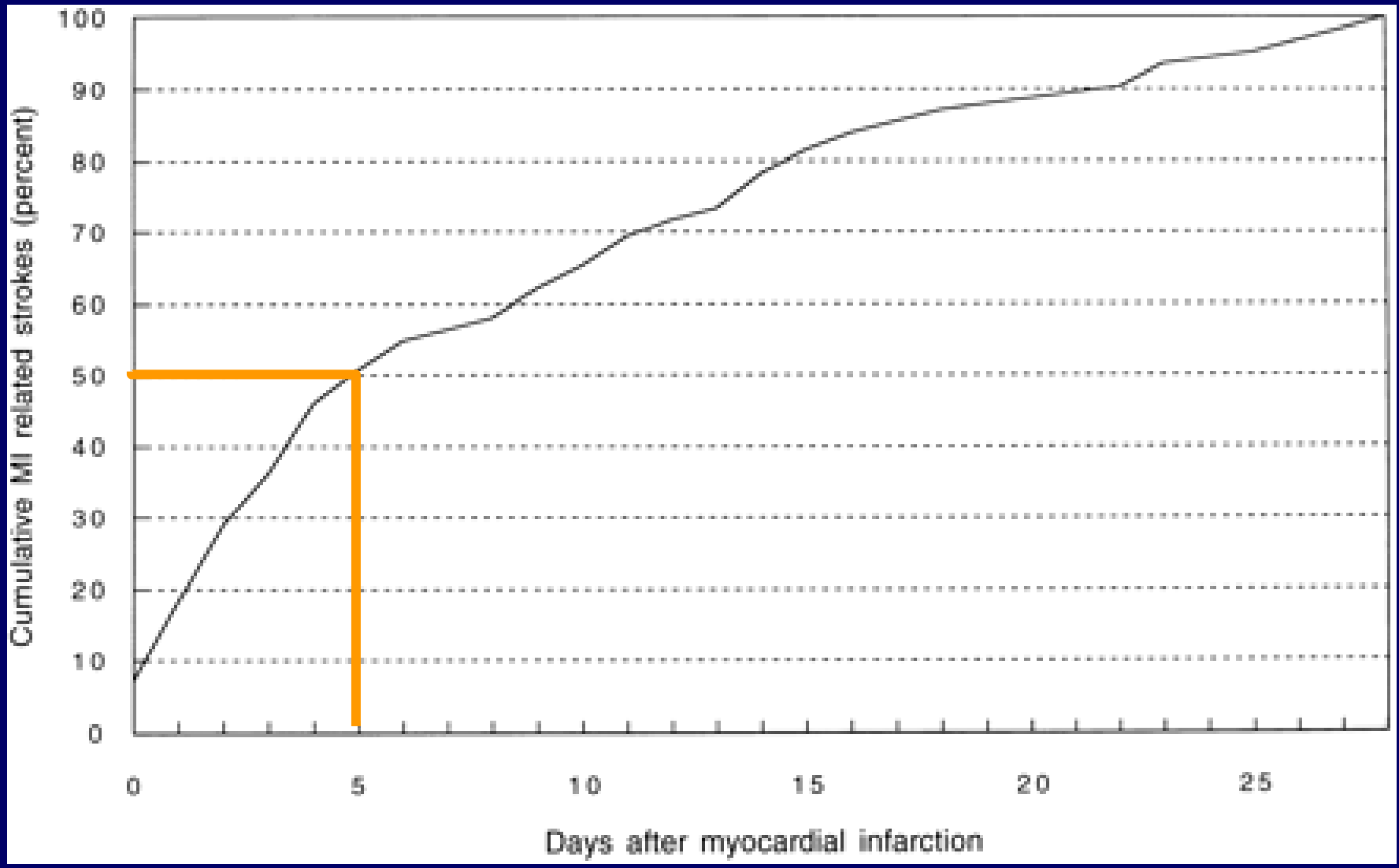
Modern Sweden MONICA study

- 124 cases, stroke within a month after AMI
- Half of stroke (63) < 5 days of MI
- Odds ratio
  - Hx of Hypertension 1.7
  - Previous stroke 2.4
  - Chronic atrial fibrillation 3.0
  - New onset atrial fibrillation 3.5
  - ST segment elevation 2.4
  - Anterior wall infarction 1.5

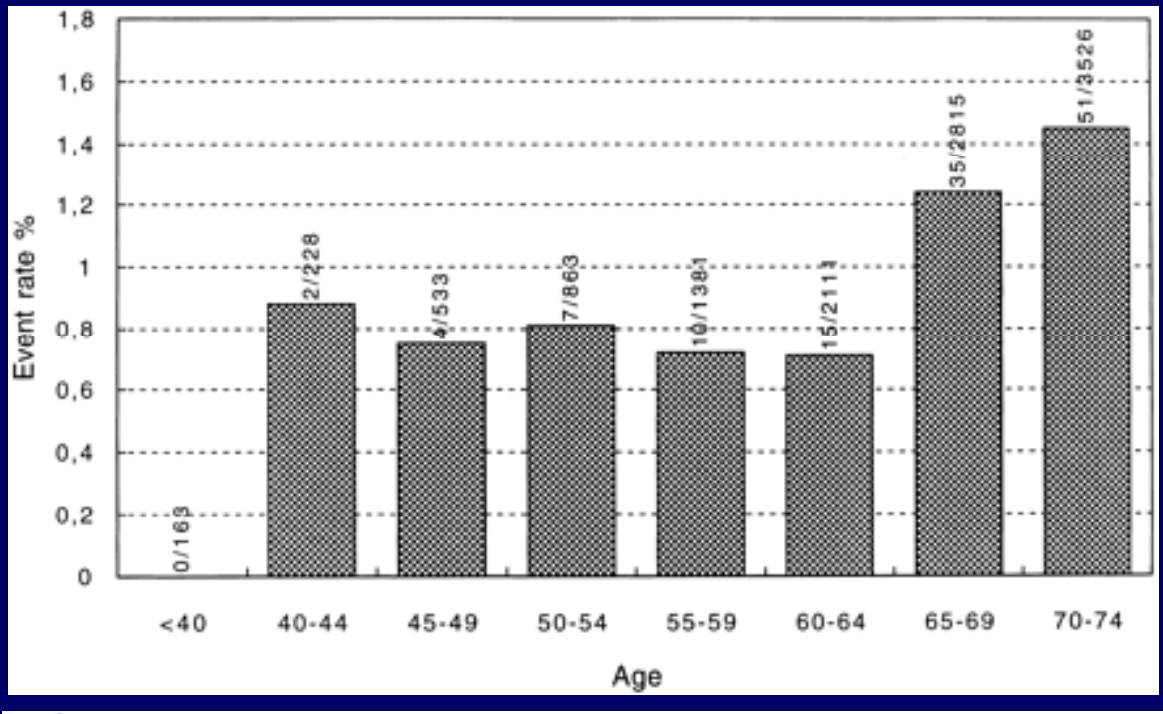
MI related ischemic stroke

- 빈도: 0.9- 2.4%, 국내 2.9%(김등, 1999년)
- 기전
  - 좌심실내 혈전, 색전증
  - 심방세동과 연관된 색전증
  - 경동맥협착과 동반된 응고성향 (hypercoagulability)
- 예측인자: 고혈압, 뇌졸중병력, 심부전

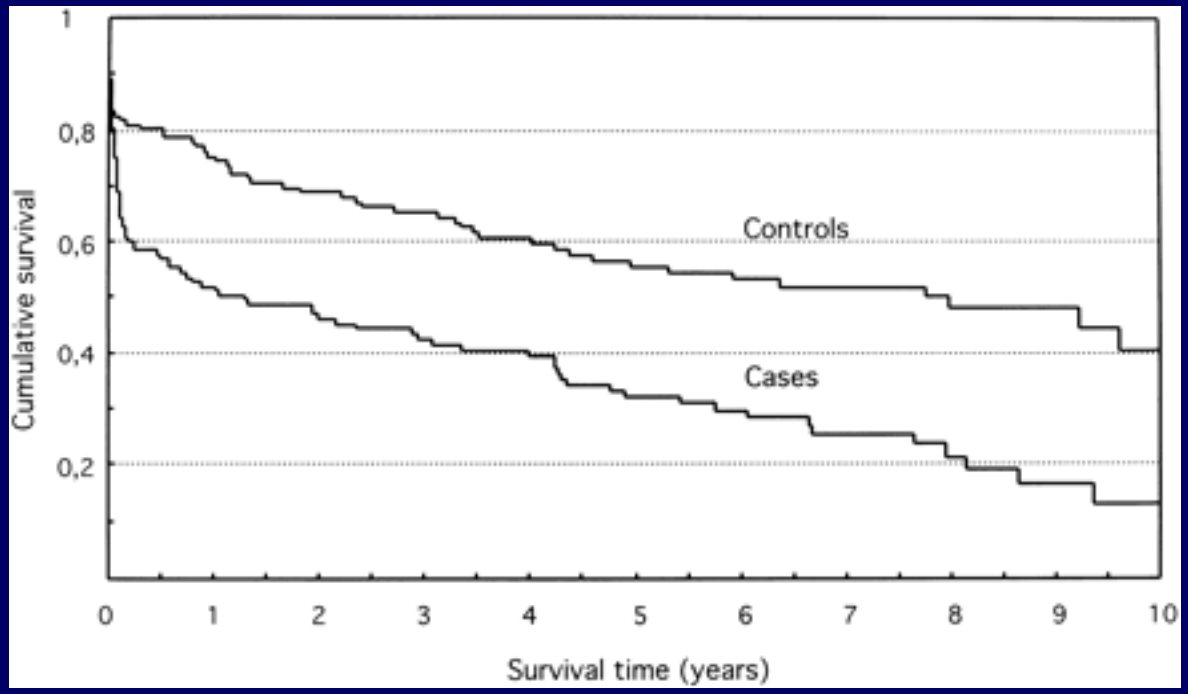
Cumulative MI-related Event within 28 days



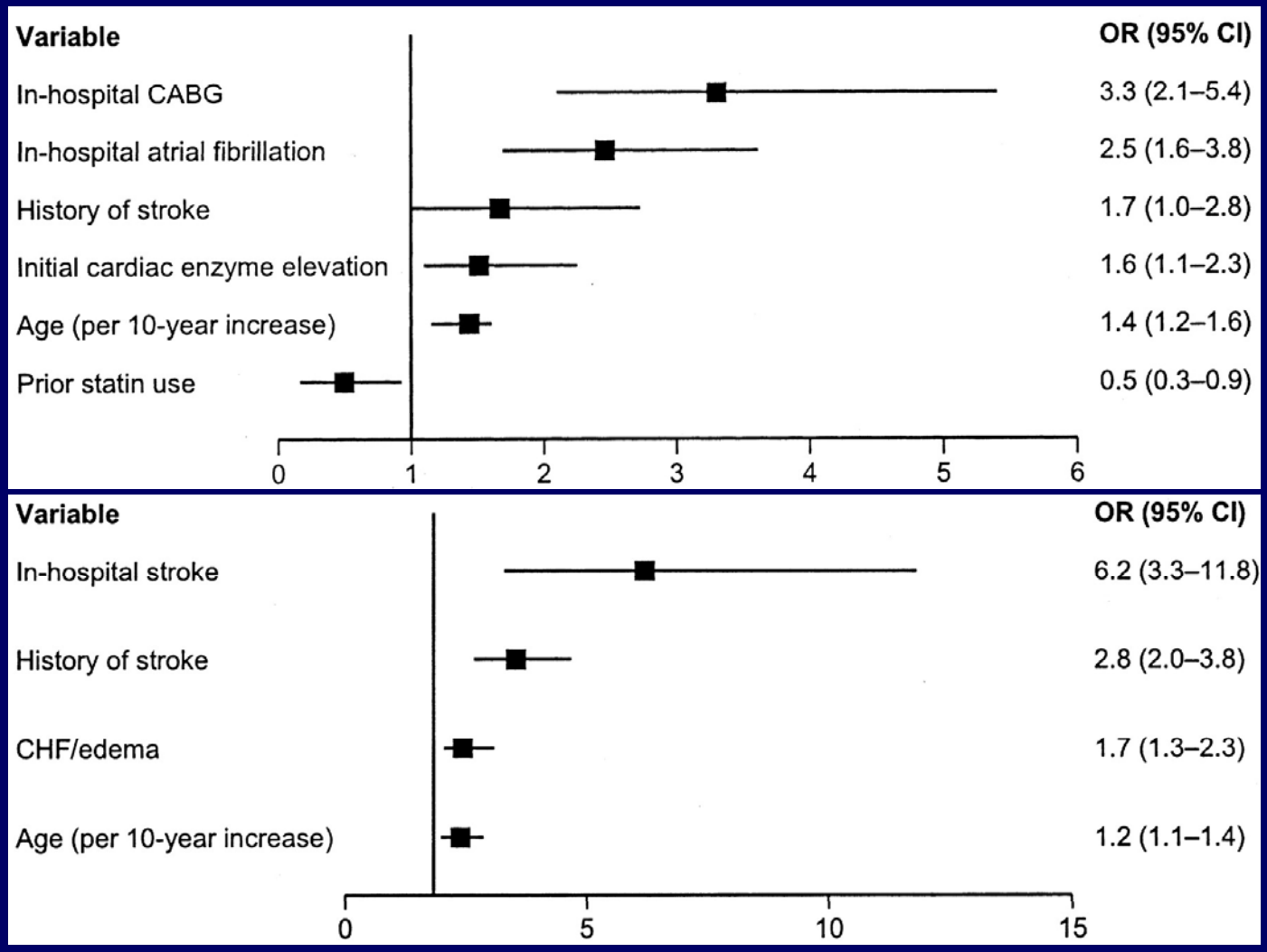
Event rate in different age groups



Long term survival in case & control



Predictors of In-Hospital & Post-Discharge Stroke in ACS Patients



Budaj, A. et al. Circulation 2005;111:3242-3247

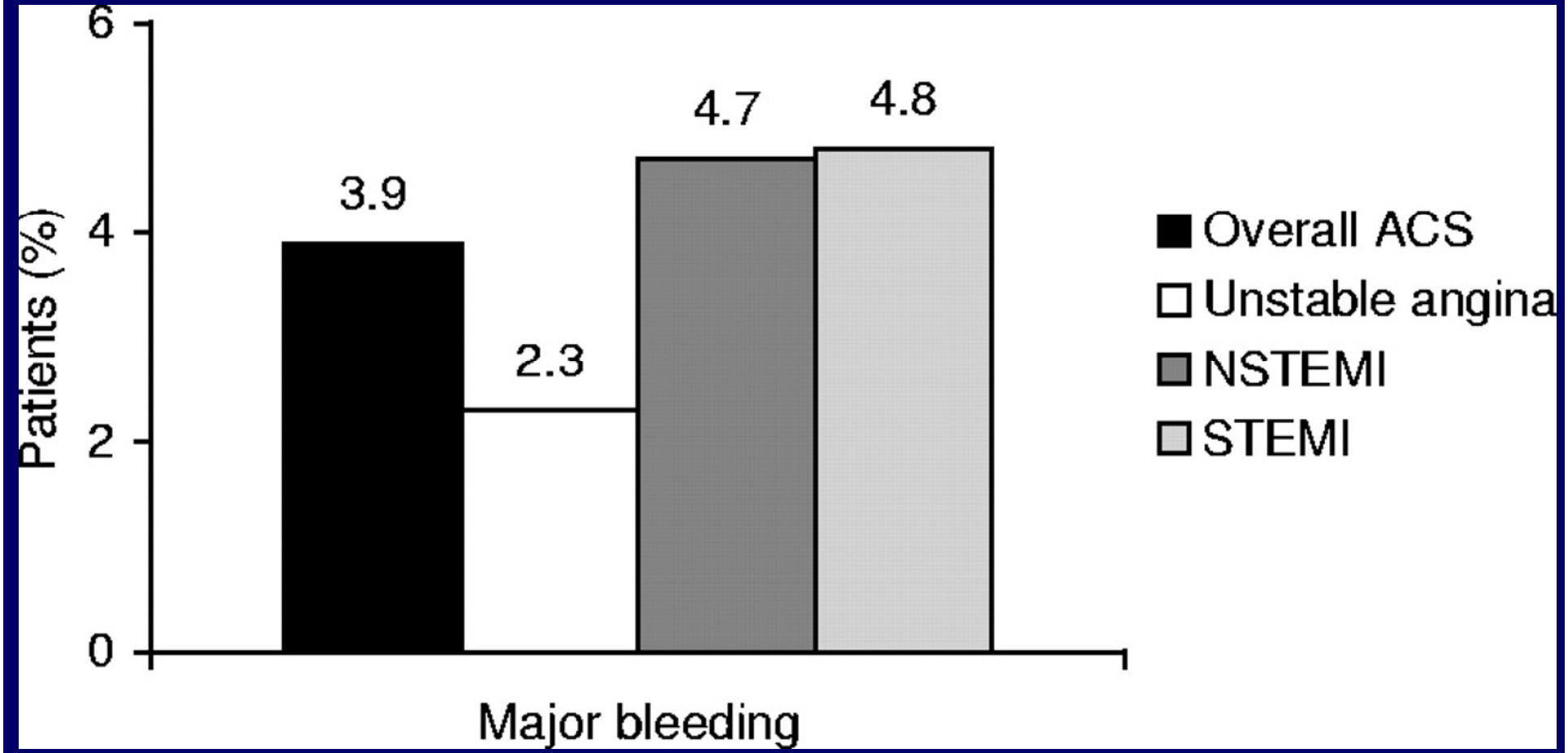
MI related ischemic stroke:Summary

- Incidence: 0.9-2.4, Decreasing trend?
- Few data available, and need updated data
- LV thrombus related embolism is not major mechanism, but atrial fibrillation, either chronic or acute is important predictor.
- 50% > onset within 5 days of AMI
- Mortality is increased with MI related stroke patients

Bleeding Complication

Frequency of Major Bleeding in ACS Patients

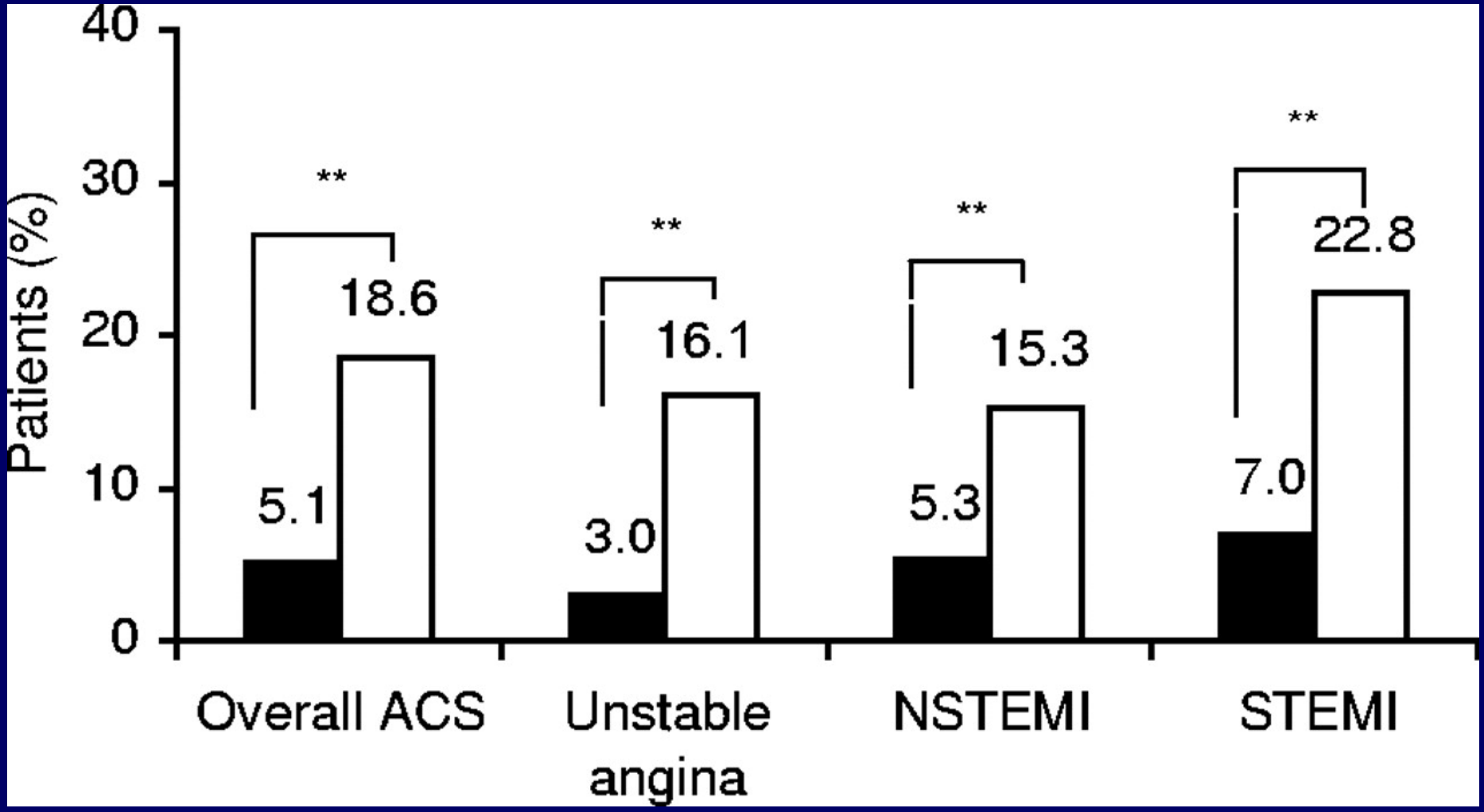
: the Global Registry of Acute Coronary Events (GRACE)



GRACE

Moscucci M, et al. Eur Heart J 2003 24:1815-1823

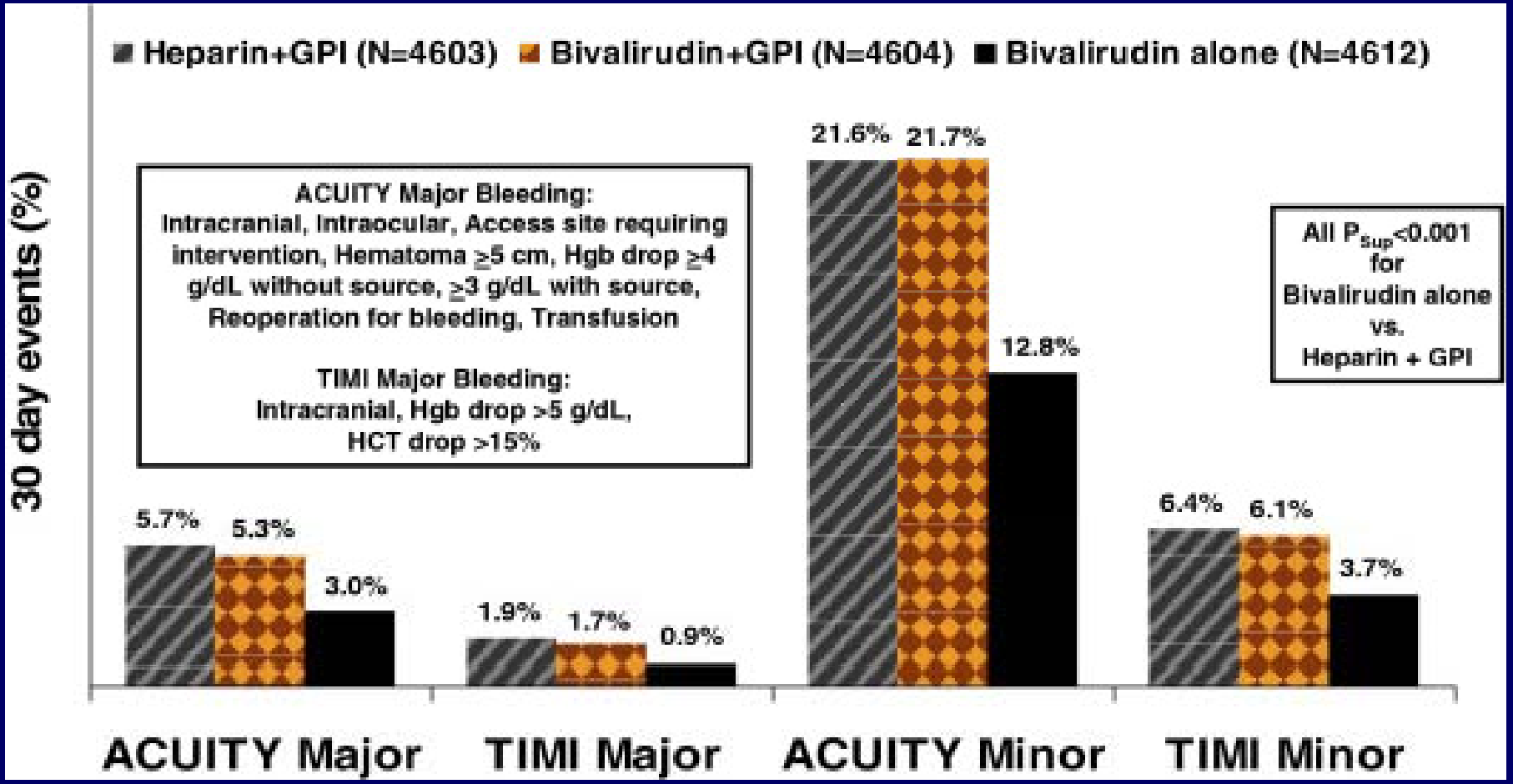
Bleeding & In-hospital Death



GRACE

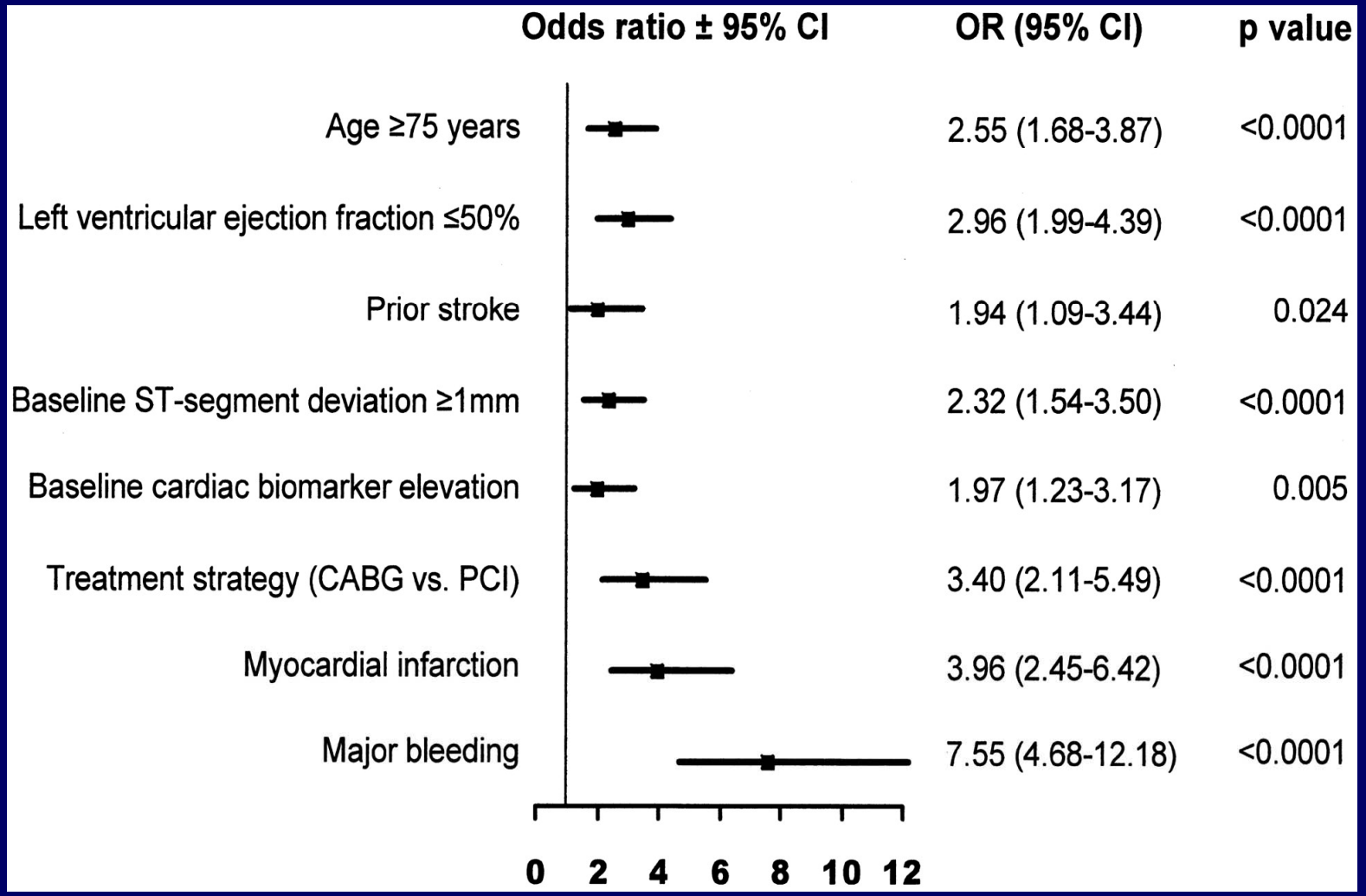
Moscucci M, et al. Eur Heart J 2003 24:1815-1823

Variation in Rates of Bleeding in NSTEMI



Manoukian SV et al, Am J Cardiol 2009

Independent Predictors of Mortality

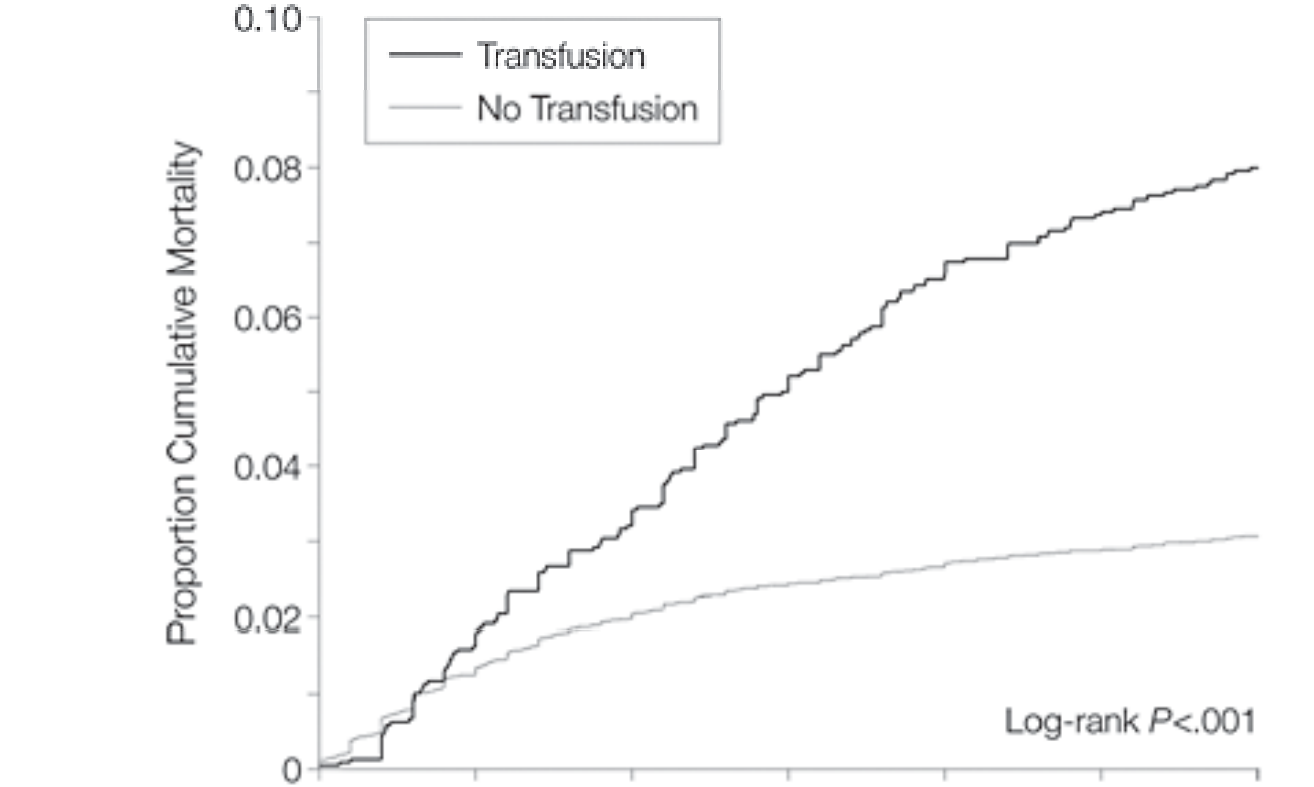


Manoukian SV et al, JACC 2007

Manoukian SV. Am J Cardiol 2009

ACUITY trial

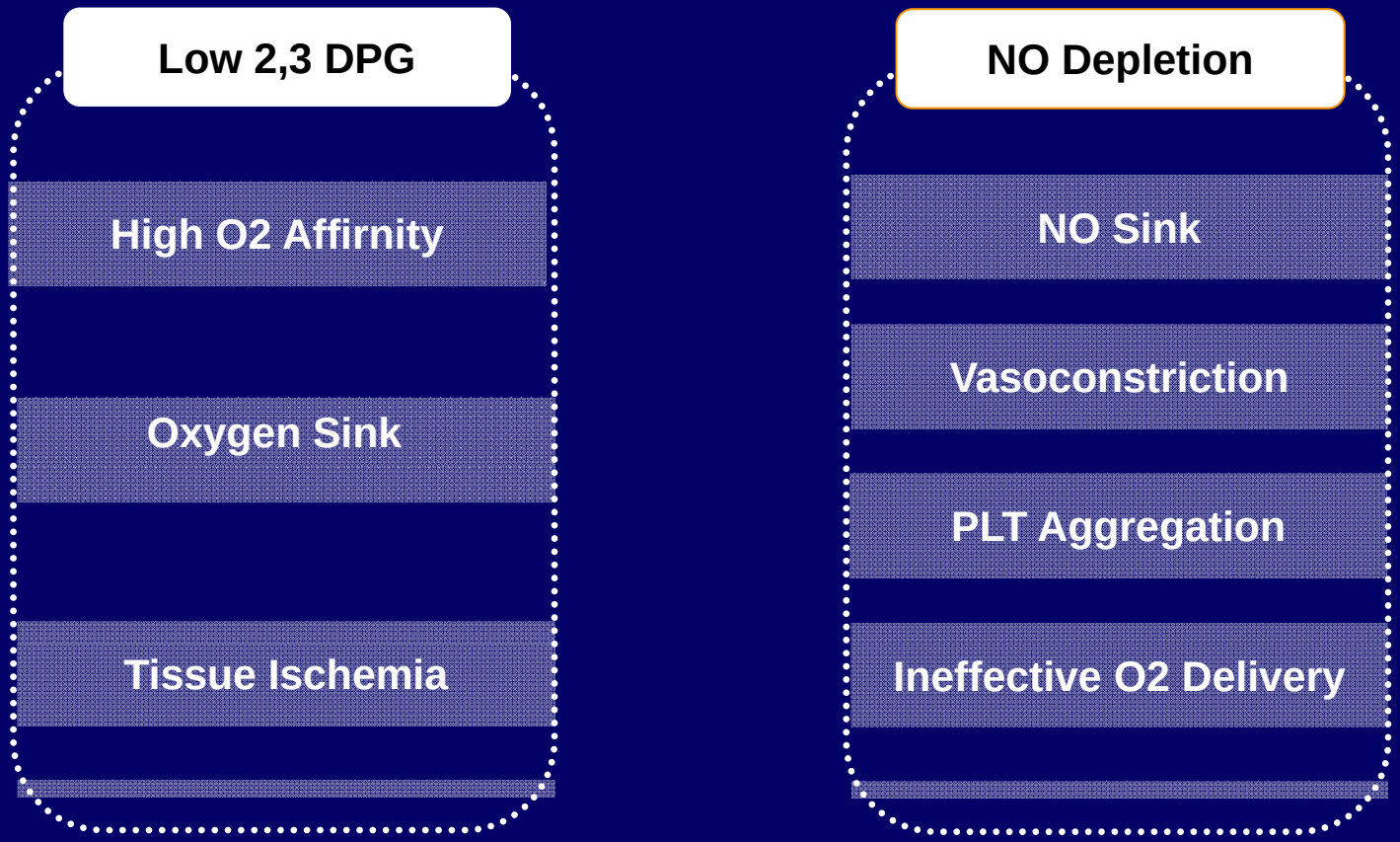
Blood Transfusion & 30 day Mortality



No. at Risk							
Transfusion	2398	2356	2317	2274	2237	2221	2189
No Transfusion	21 684	21 408	21 248	21 162	21 102	21 062	20 884

Rao SV, et al. JAMA 2004;292:1555-1562.

Possible Adverse Effect of Transfusion : Properties of Packed RBC

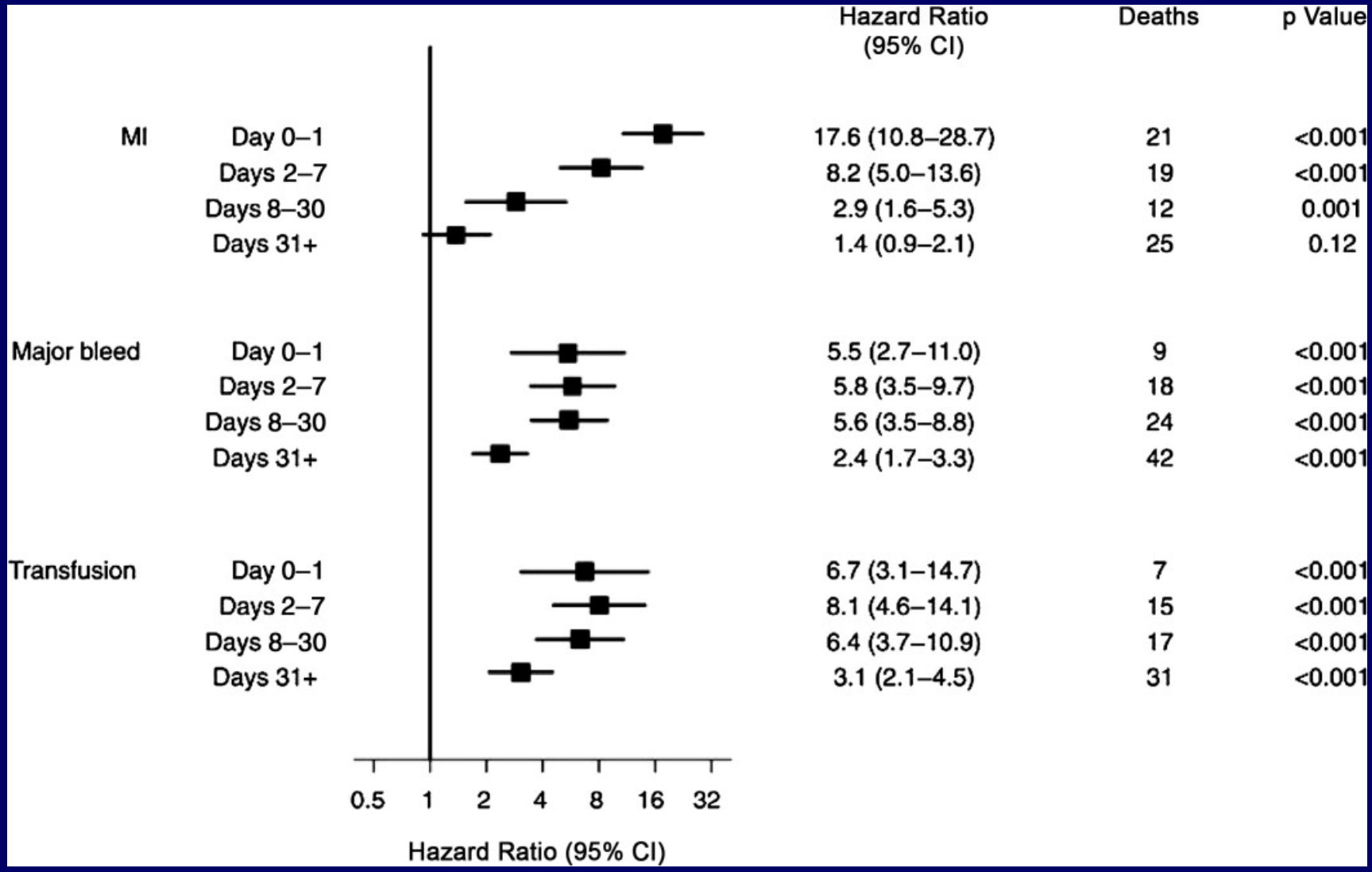


Possible Explanation for Bleeding & Adverse Cardiovascular Outcomes

- Reduced myocardial oxygen delivery
  - Hypotension, Anemia
- Premature discontinuation of antithrombotic drugs
- Platelet activation and increased thrombotic risk
- Deleterious effects of blood transfusion
  - Platelet aggregation
  - Vasoconstriction
  - Inflammation

Fitchett. Can J Cardiolo 2007

Influence of Recurrent MI, Major Bleeding & Transfusion on 1-yr mortality in NSTEMI



Meran R et al, Eur Heart J 2009

Access Site Hematoma Requiring Blood Transfusion & Mortality

NHLBI Registry Data,

Yatskar L et al. CCI 2007;69:961-966

Access Site Hematoma Requiring Blood Transfusion & Mortality

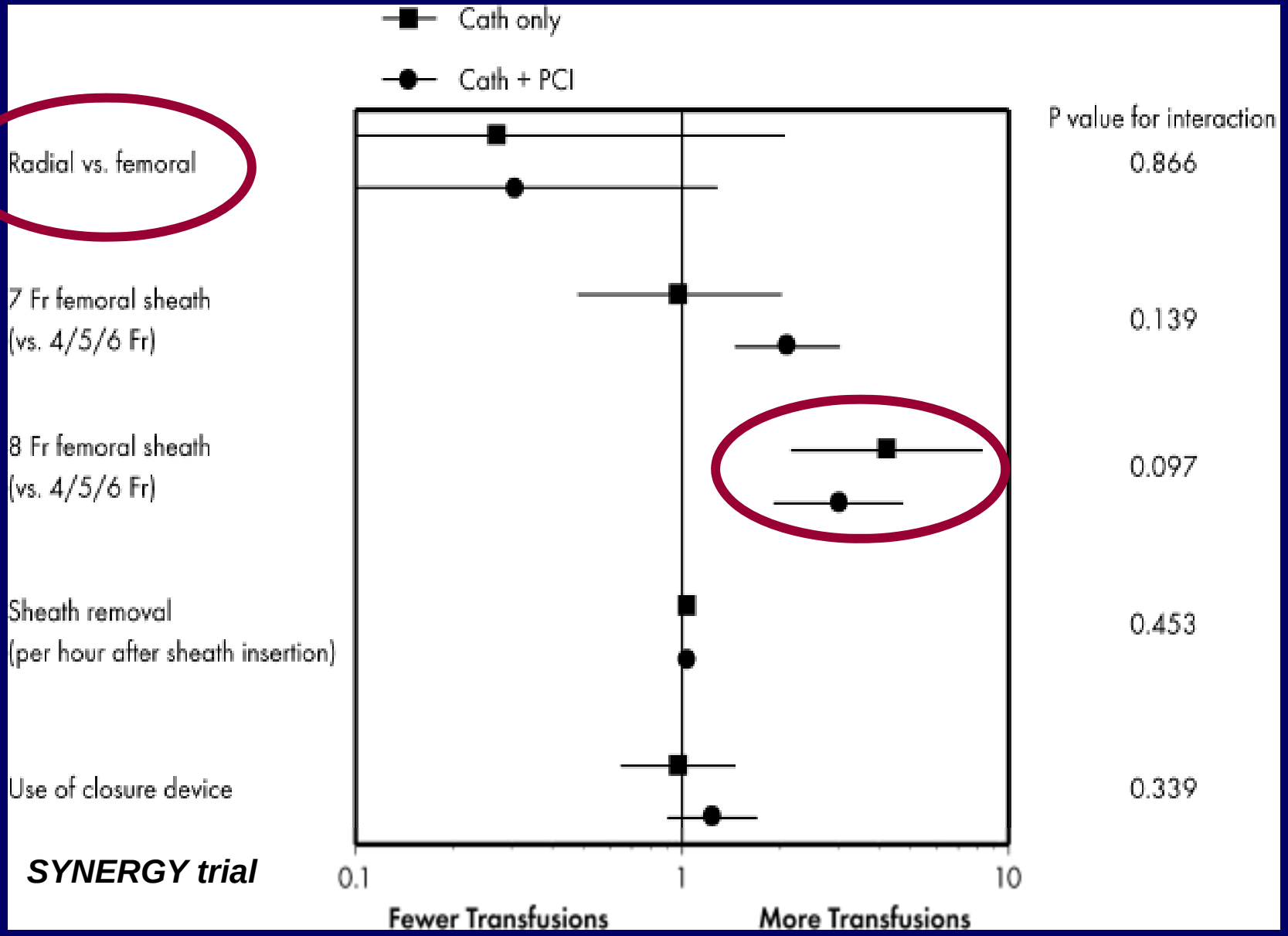
No Transfusion		Transfusion	
Death (IH)	1.2 %	Death (IH)	9.9 %
Death (1Yr)	4.7 %	Death (1Yr)	18.8 %

NHLBI Registry Data, CCI 2007;69:961-966

Risk Factors Associated with HRT

- Age >65
- Female
- IIb/IIIa
- Prior MI
- Thrombolytics
- 3 VD
- Stable Angina
- Cardiogenic shock
- Emergency Procedures
- Renal Insufficiency
- Peripheral Vascular Disease
- Procedural aspirin

Predictors of Transfusion Requirement



SYNERGY trial

A Strategy to Reduce Bleeding

1. Define bleeding risk individual (age, sex, BW, CCR, Hx of bleeding)
2. Appropriate dosing of antithrombotic drugs
3. Avoid combination of antithrombotic agents unless proven medication.
4. Use drugs with proven reduced impact on bleeding
5. Privilage radial over femoral vascular access or use closure device

Crucial Band

Modified from brachial usage

It’s time to consider Transradial PCI in AMI !!

Thank you for your attention