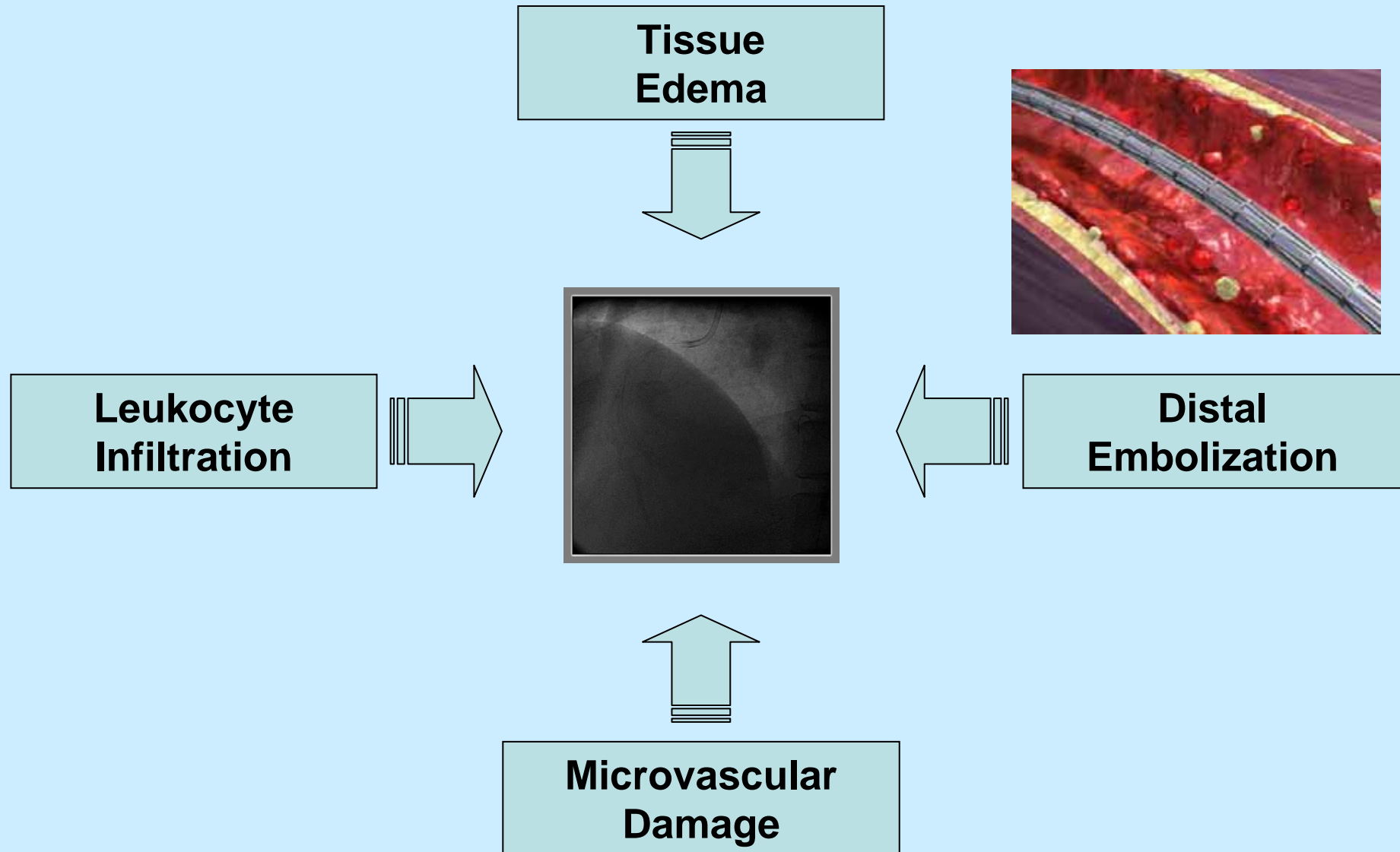


Percutaneous Coronary Intervention and Distal Injury in AMI

Seung-Jea Tahk, MD., PhD.
Ajou University Medical Center
Suwon, KOREA

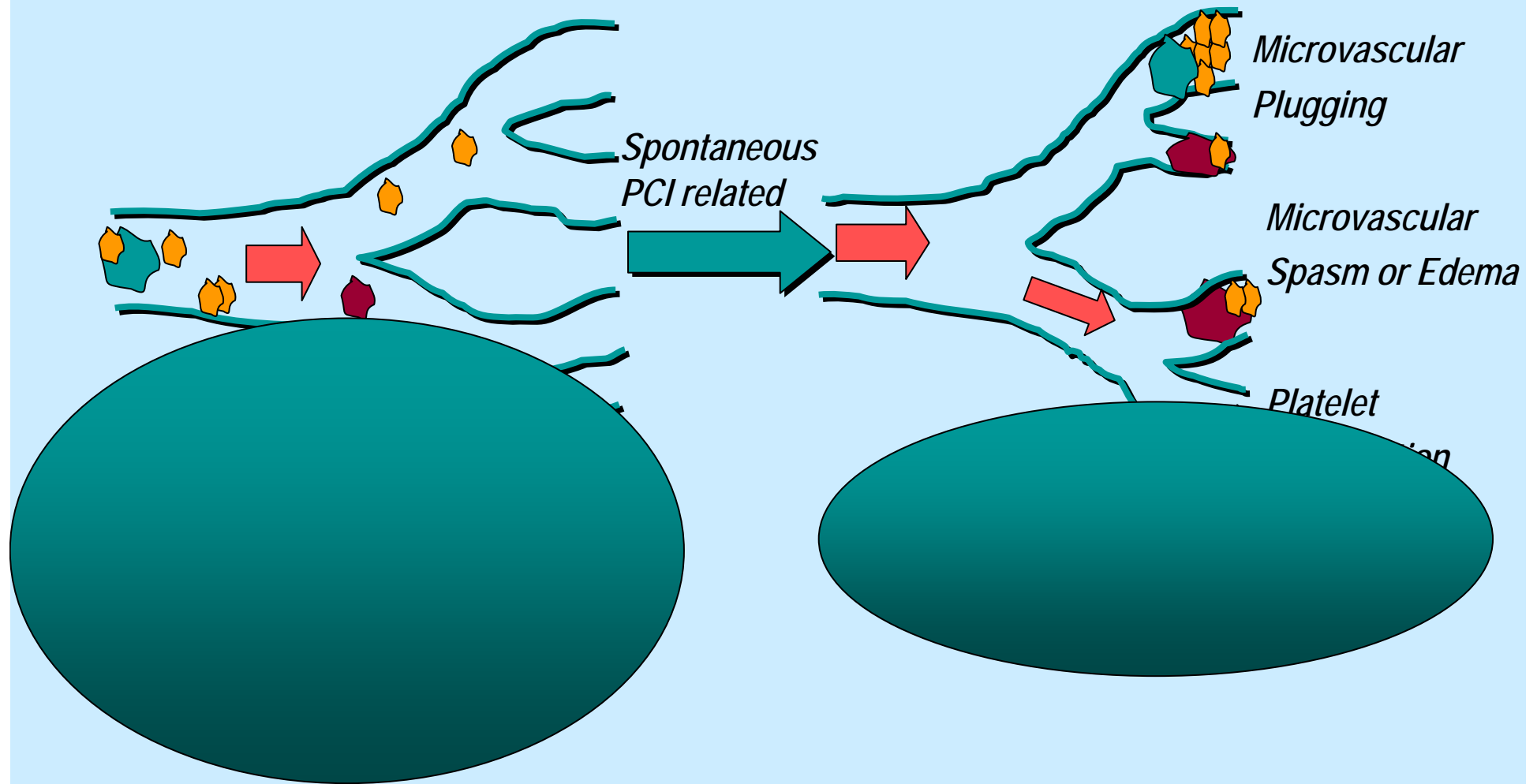
Slow Flow or No Reflow after Primary PCI: 5-30%



Distal injury during PCI

- **Potential mechanism of distal injury during PCI**
- **Evidences of distal injury**
- **Clinical consequences of distal injury**
- **How to prevent distal injury ..**

Potential mechanism of distal injury during PCI



Modified from Hori M, et al. Am J Physiol, 1986

Evidences of embolization: Autopsy study

- **32 patients with AMI treated PTCA or thrombolytics or both, who died within 3 weeks after intervention.**
- **At autopsy, emboli were observed in 26 (81%) of patients.**
- **Among 83 emboli, 95% was thrombotic.**
- **The greatest number of emboli was associated with intervention in LAD, multiple intervention, medial dissection..**

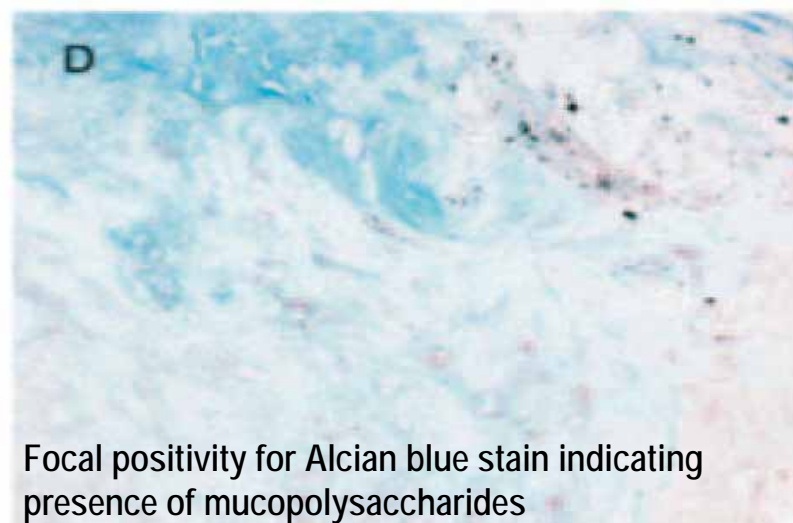
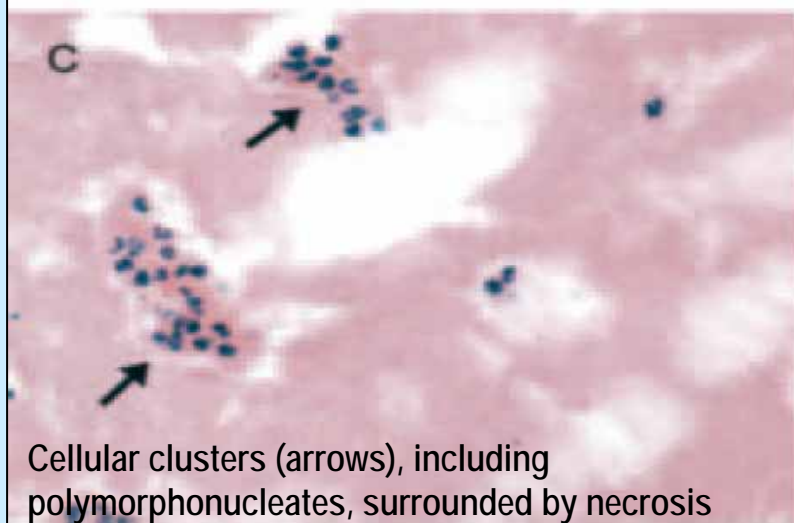
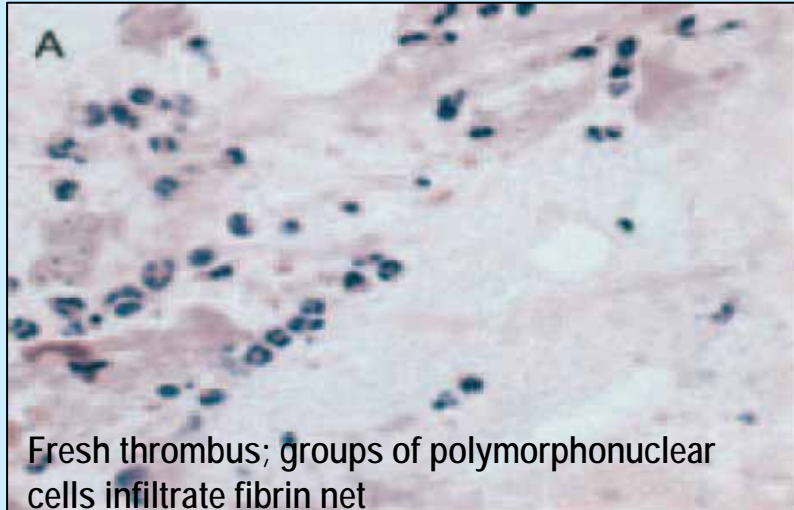
Saber et al. J Am Coll Cardiol 1993;22:1283-1288

Materials retrieved during primary PCI



Histopathologic Analysis

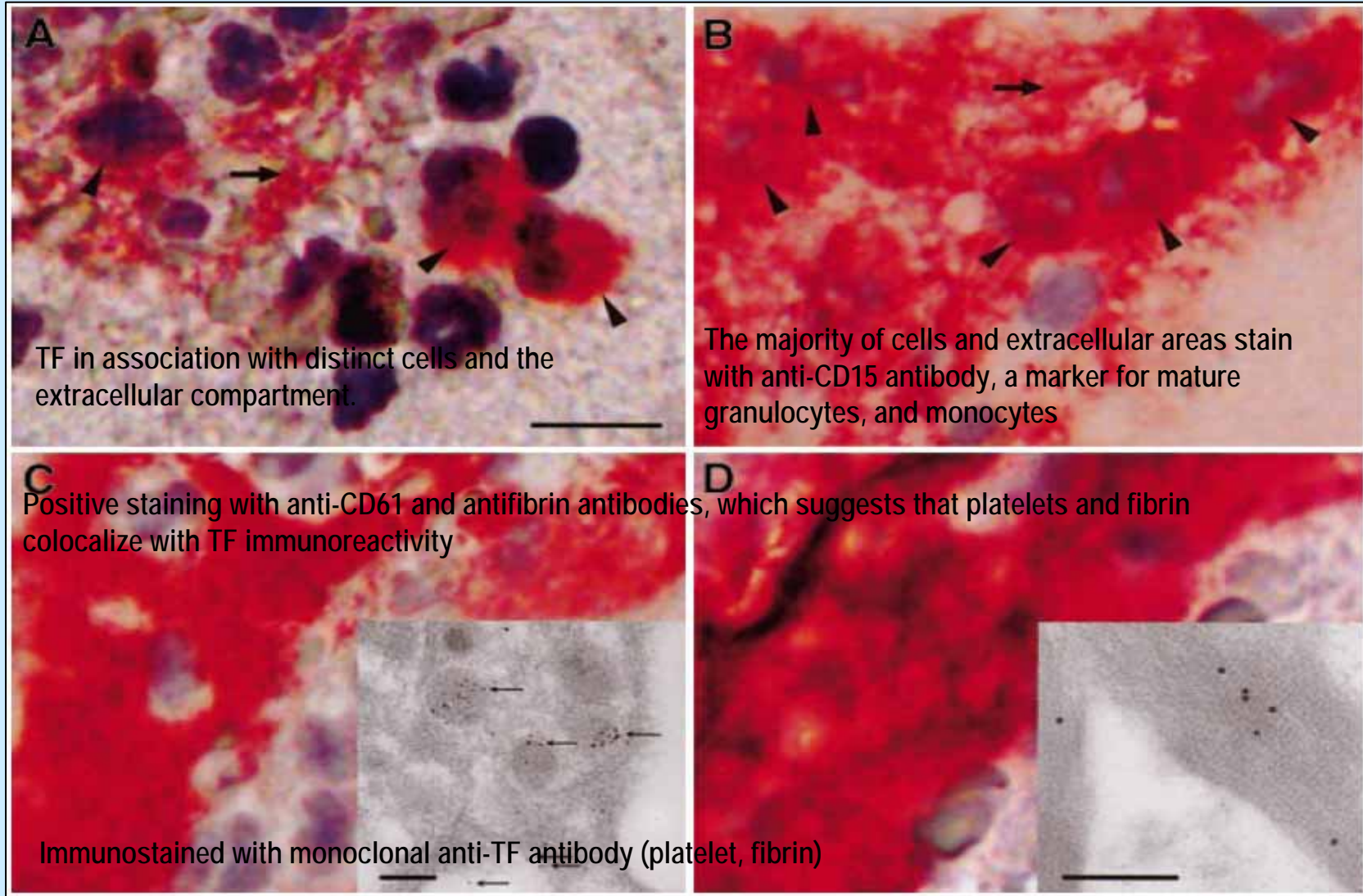
Particulate Trapped in the Filter Wire



U. Limbruno U et al. Circulation 2003;108:171-176

Immunohistochemical and Immunoelectron Microscopic Analyses

Particulate Trapped in the PercuSurge GuardWire: Patients with no reflow

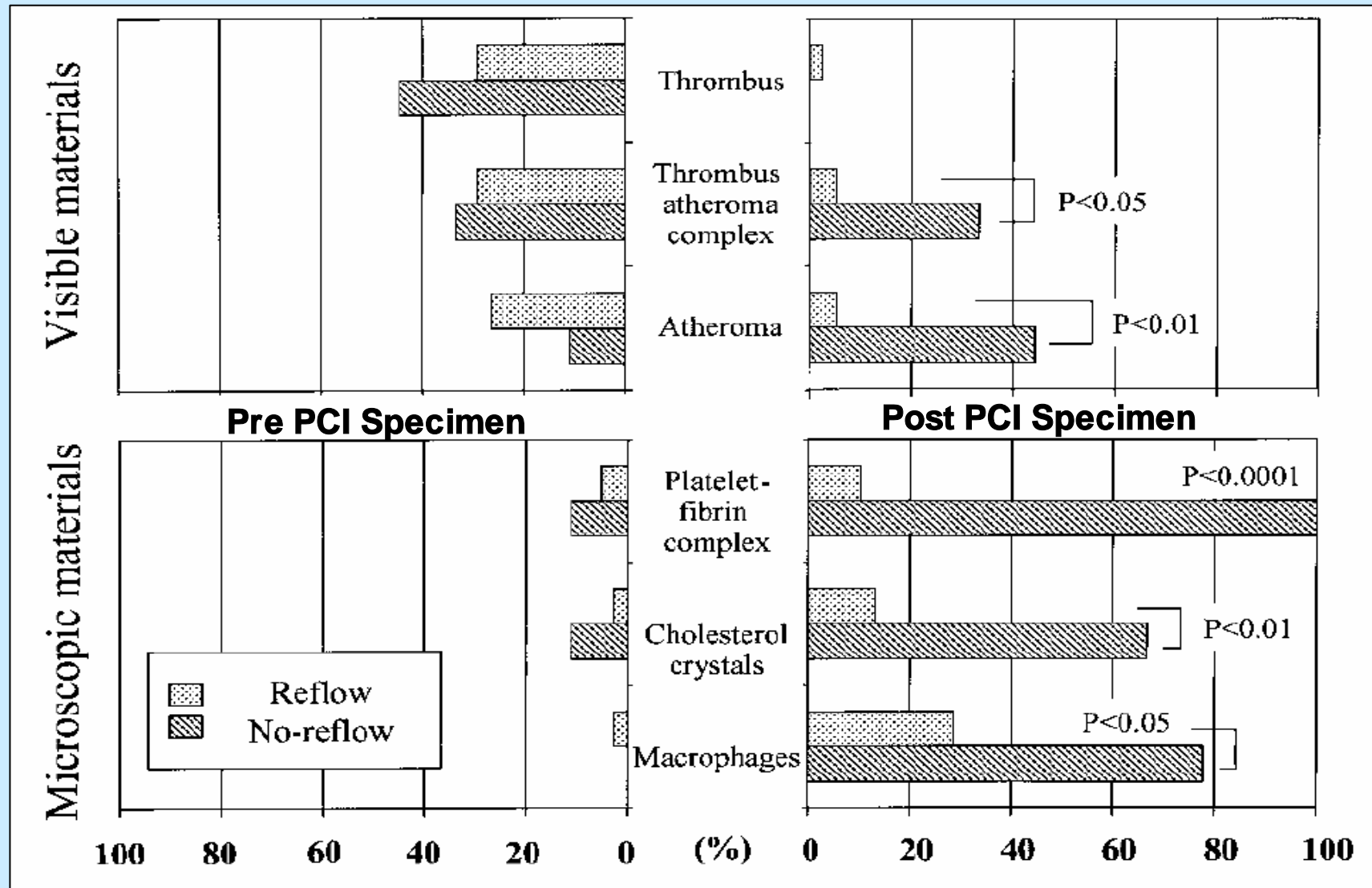


Bonderman et al. Blood 2002;99:2794-2800

ANGIOPLASTY
SUMMIT 2006

Character of retrieved materials and no-reflow

No-reflow versus reflow patients

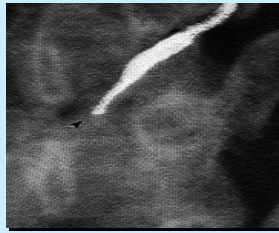


Angiographic distal macroembolization during Primary PCI

- Incidence: before 4.8% → after 15.2%
- Predictor of more myocardial damage and worse prognosis.

	Embolization	NO	p value
TIMI 3 Flow (%)	70	90	0.01
Myocardial Blush (%)			
0/1	68	17	0.01
2	32	55	0.05
3	0	28	0.05
ST Segment Resolution >50% (%)	64	90	0.001
LVEF at discharge (%)	42 ± 14	52 ± 9	0.005
5-year Clinical FU			
Mortality (%)	44	9	0.001
Death/Recurrent MI (%)	52	14	0.001

Henrique et al. AJC 2003; 91: 708
Henrique et al. Eur H J 2002; 23: 1112



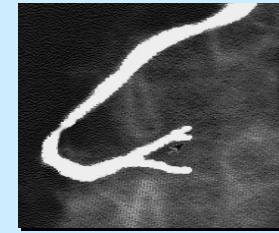
TIMI 0
Occlusion



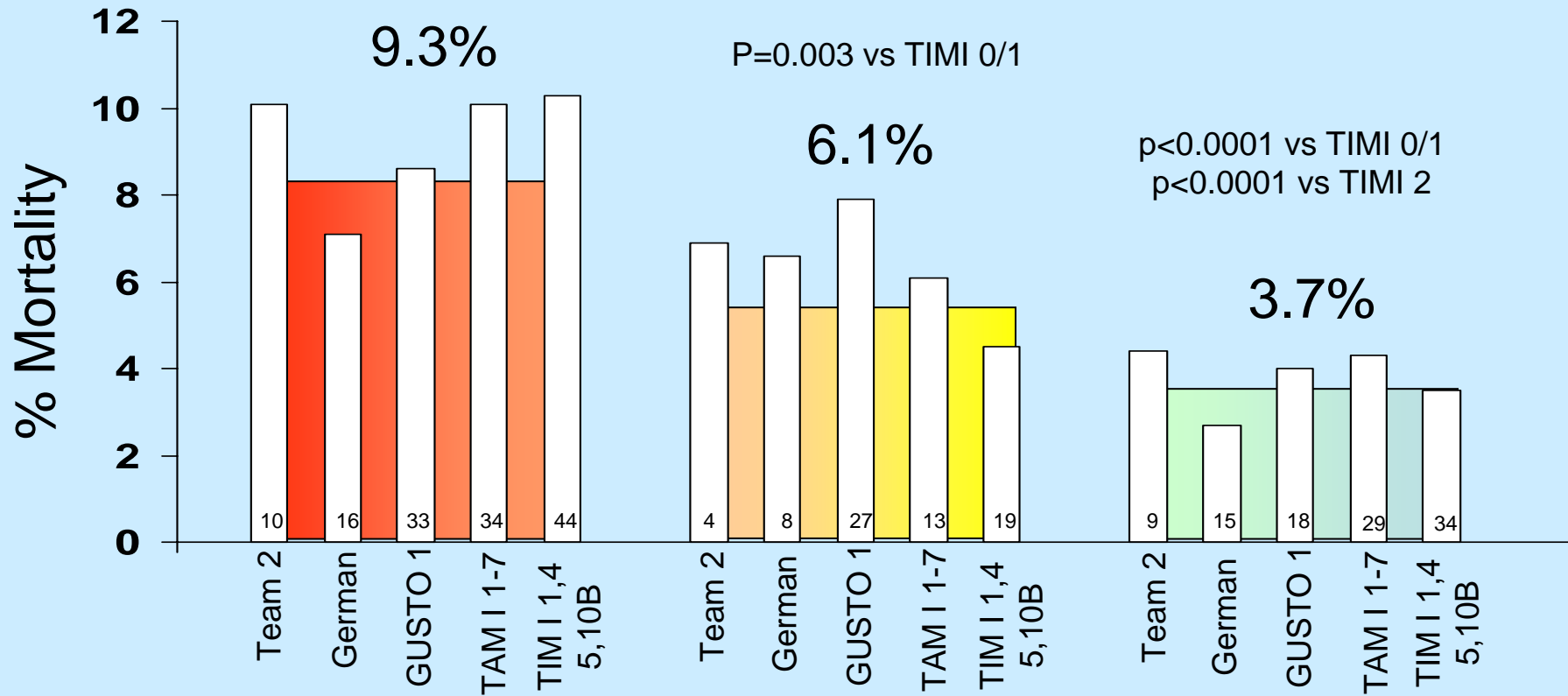
TIMI 1
Penetration



TIMI 2
Slow Flow



TIMI 3
Normal Flow



Gibson 1998, Sample Size of Pooled Analysis: 5,498

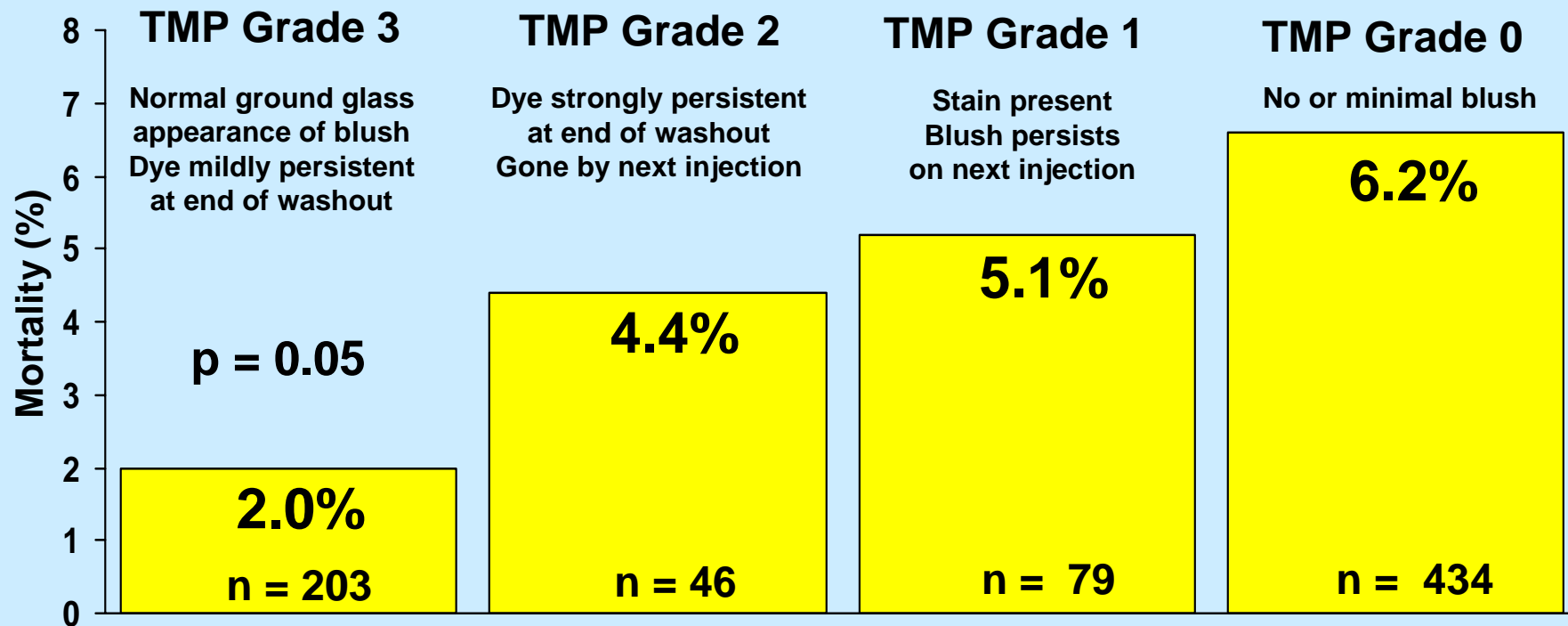
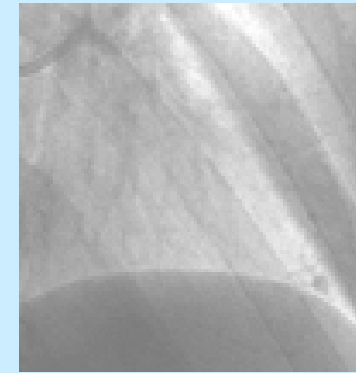
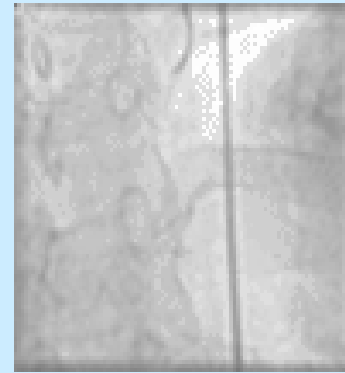
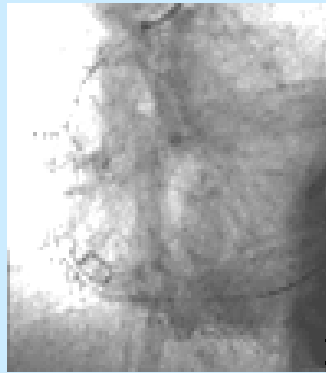
TIMI flow and mortality: CADILLAC

TIMI PreStent	TIMI Final	NO	12mo Mortality
3	3	687	3.3%
0-2	3	54	9.3%
0-2	0-2	17	5.9%
3	0-2	14	21.4%

Deterioration in TIMI flow occurred in 1.8% of stent patients

Grines et al. JACC 2001; 37: 342A

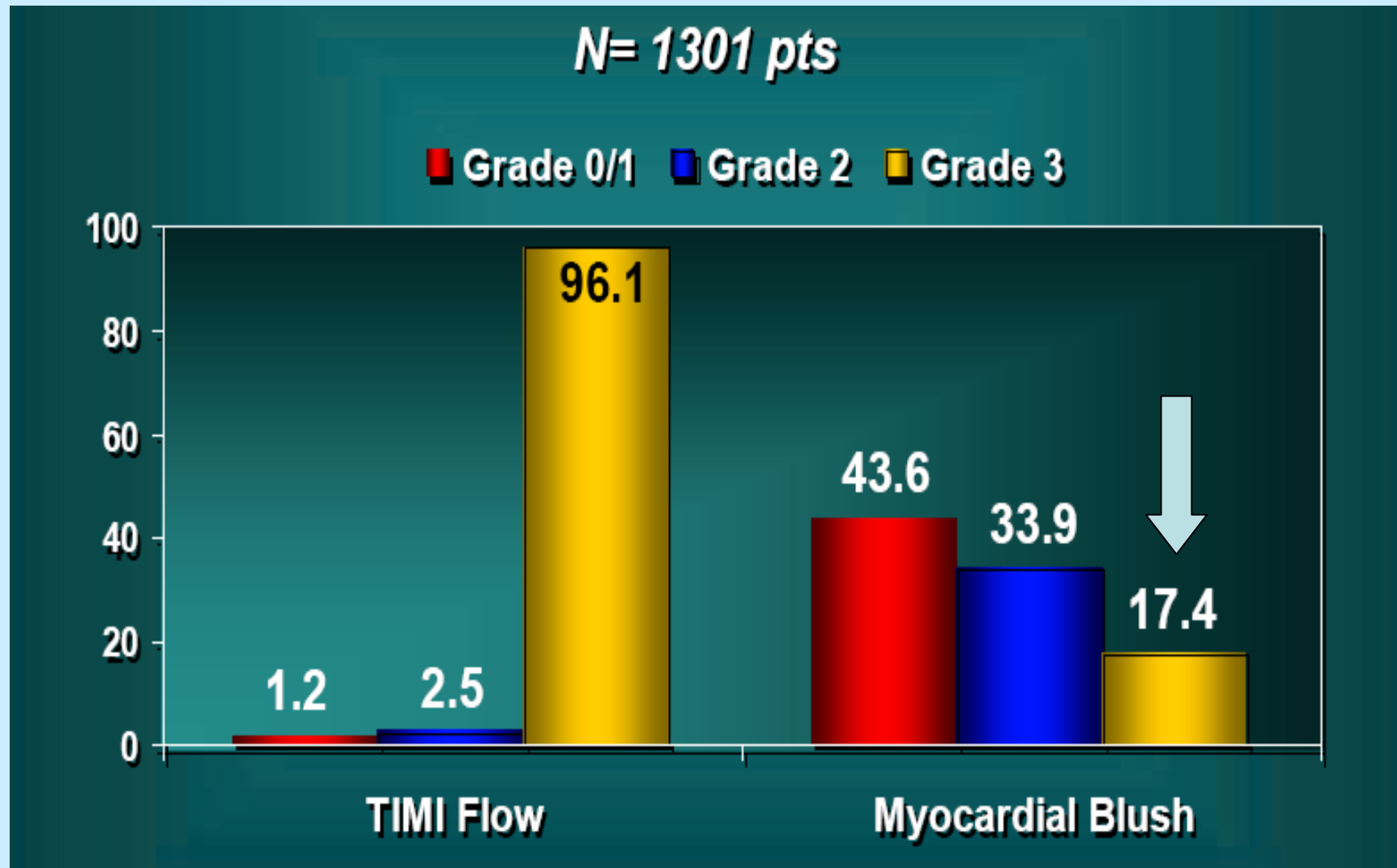
TIMI Myocardial Perfusion (TMP) Grades



Gibson et al., *Circulation* 2000;101:125

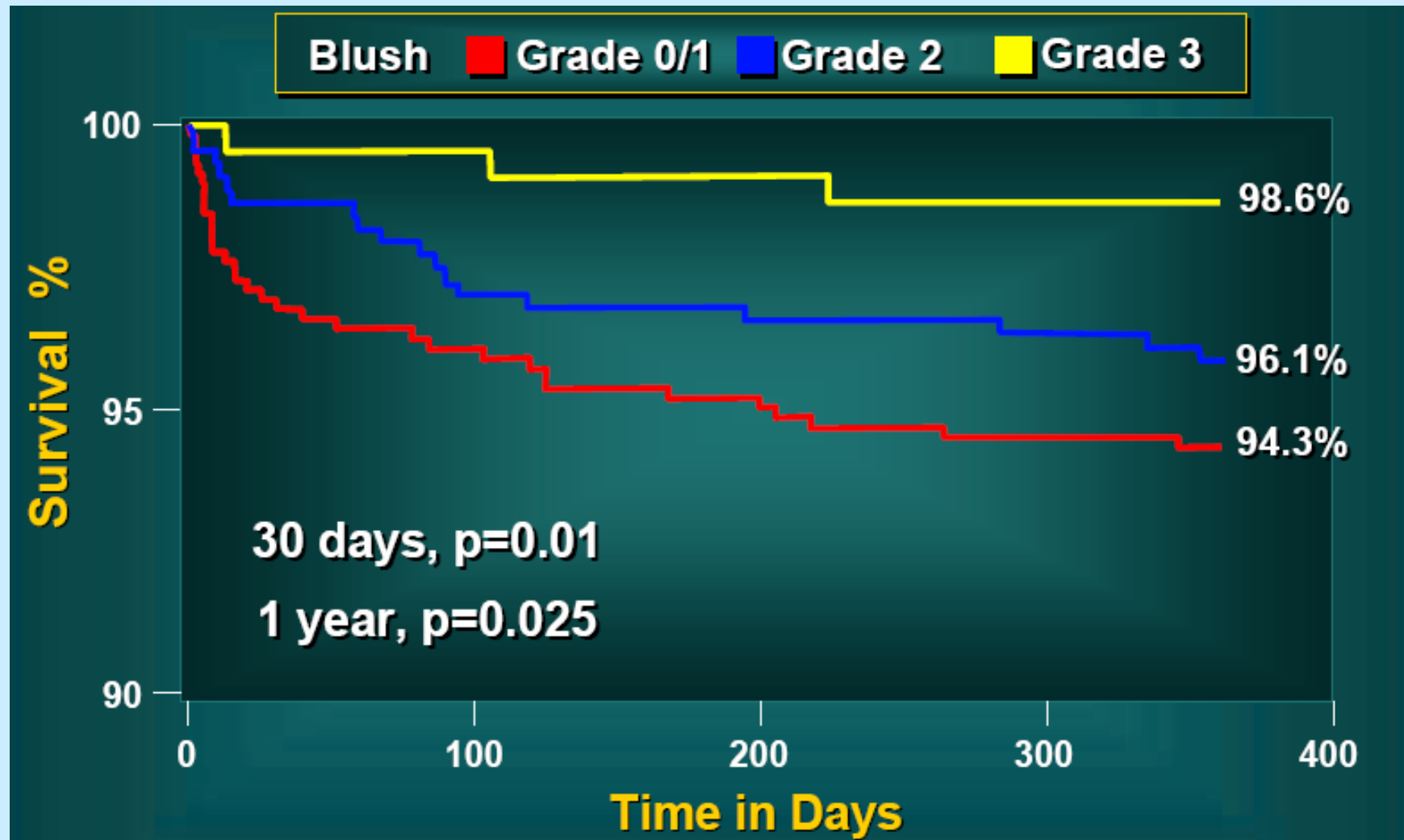
Achieving Tissue Level Reperfusion: CADILLAC

Final TIMI Flow and Myocardial Blush Score

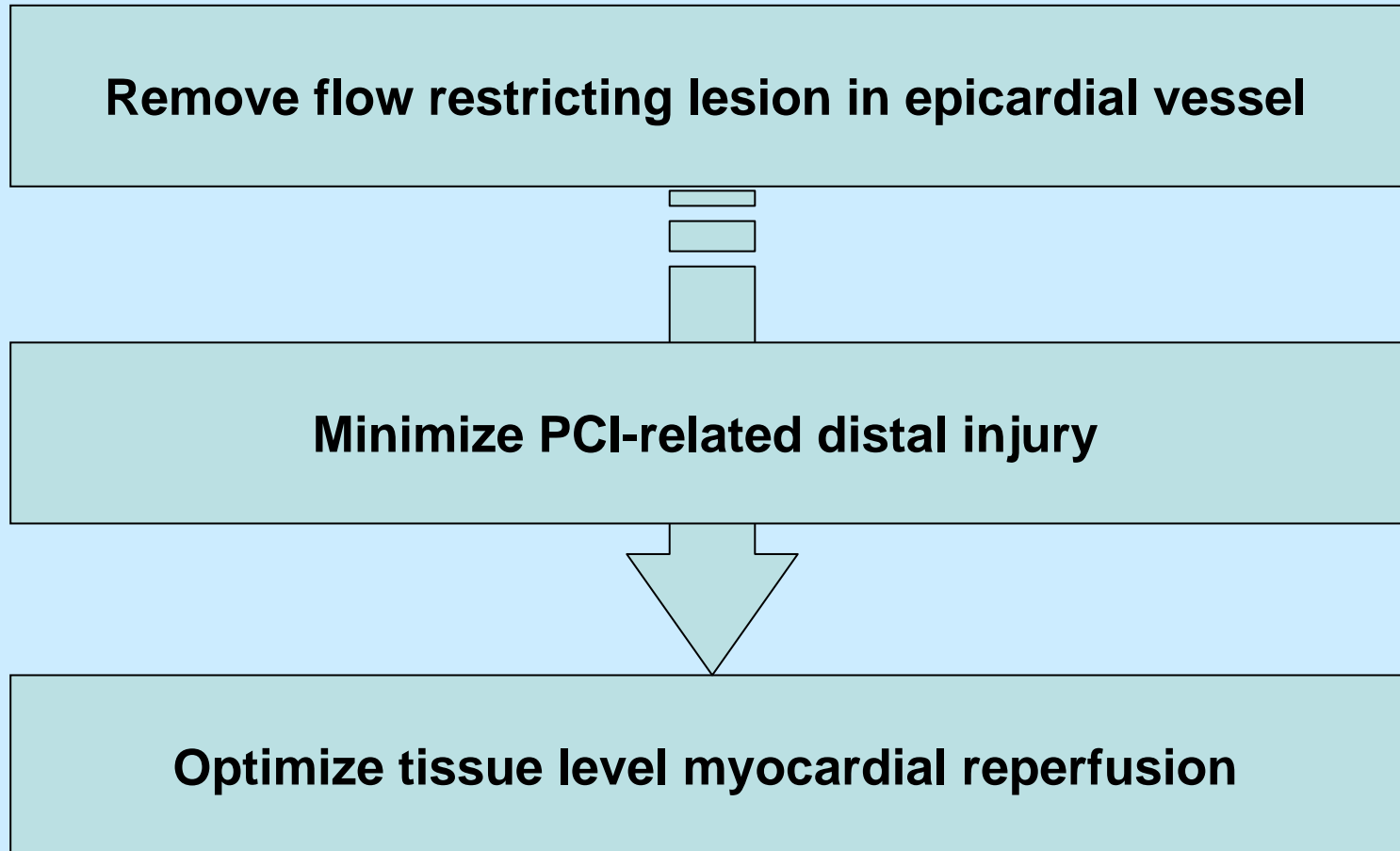


Survival Rate and Tissue Level Reperfusion: CADILLAC

Survival in Patients with Final TIMI 3 Flow



The objects of primary PCI



Risk factors to microvascular injury during PCI

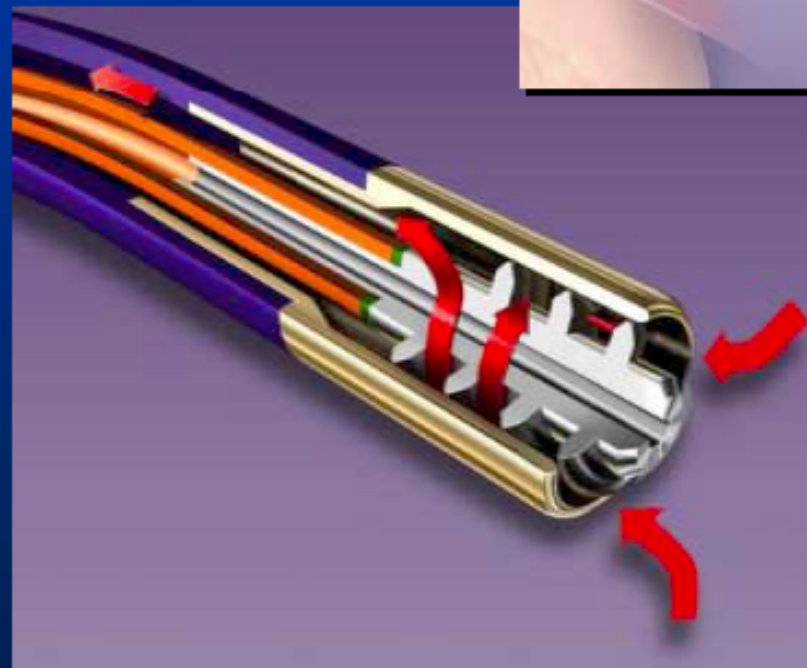
- **Lesion characteristics**
 - **The diffuseness of disease**
 - **Friability of the atheromatous lesion**
 - **Presence of platelet-thrombus**
- **Invasiveness of the revascularization technique**

How to reduce distal injury during primary PCI ..

- **Procedural factor: as simple as possible**
- **Distal Protection Devices**
 - **Balloon occlusion devices**
 - **Filter devices**
- **Adjunctive pharmacotherapy**
- **Thrombectomy**
 - **Mechanical**
 - **Rheolytic**

X-SIZER® Catheter System

- Self-contained, over-the-wire system
- Cutting and aspiration mechanical thrombectomy
- 1.5mm and 2.0mm diameter
- 7F and 8F guide catheter compatible

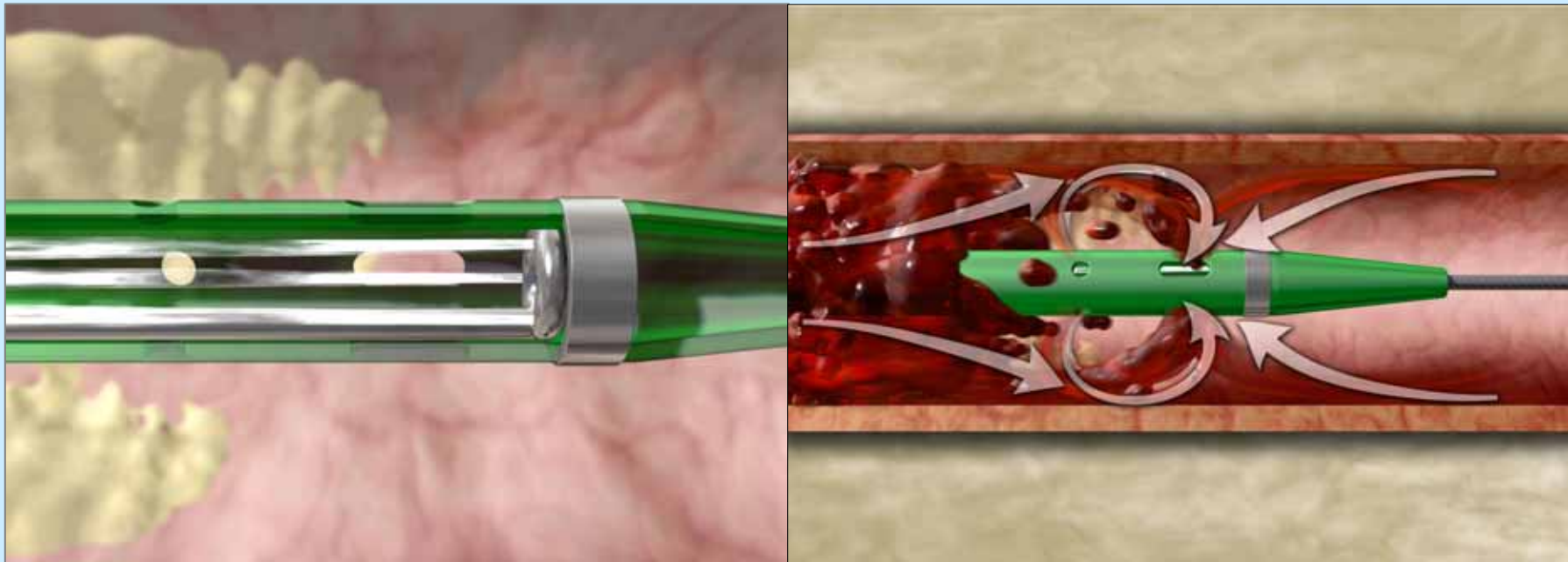


eV3

AngioJet® Mechanism of Action

The Bernoulli Effect explains the relationship between velocity and pressure.

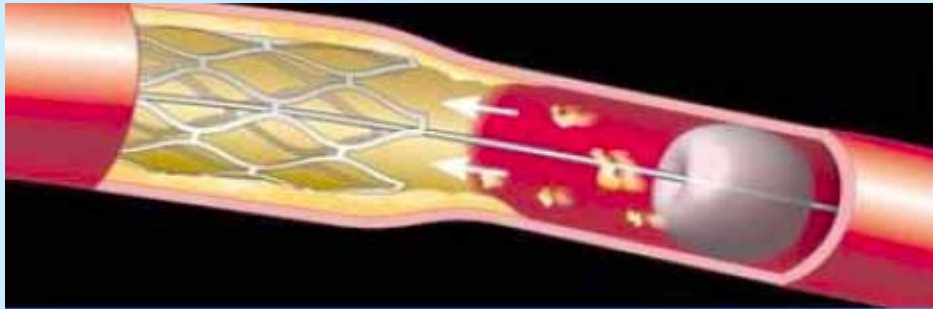
"Where the speed is highest, the pressure is lowest--creating a vacuum."



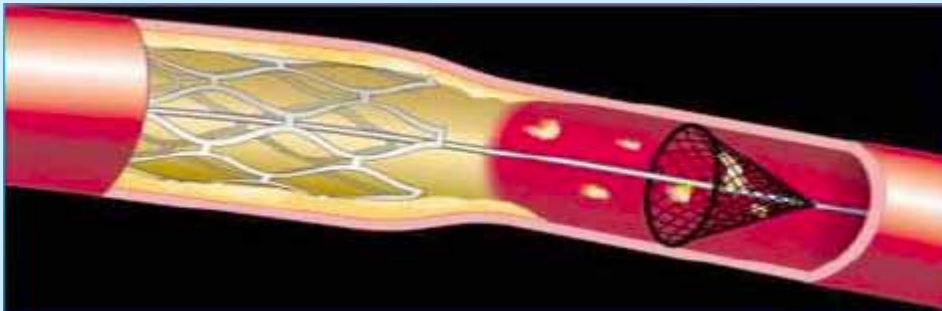
Saline jets travel backwards at half the speed of sound to create a low pressure zone.

Thrombus is drawn into the catheter where it is fragmented by the jets and evacuated from the body.

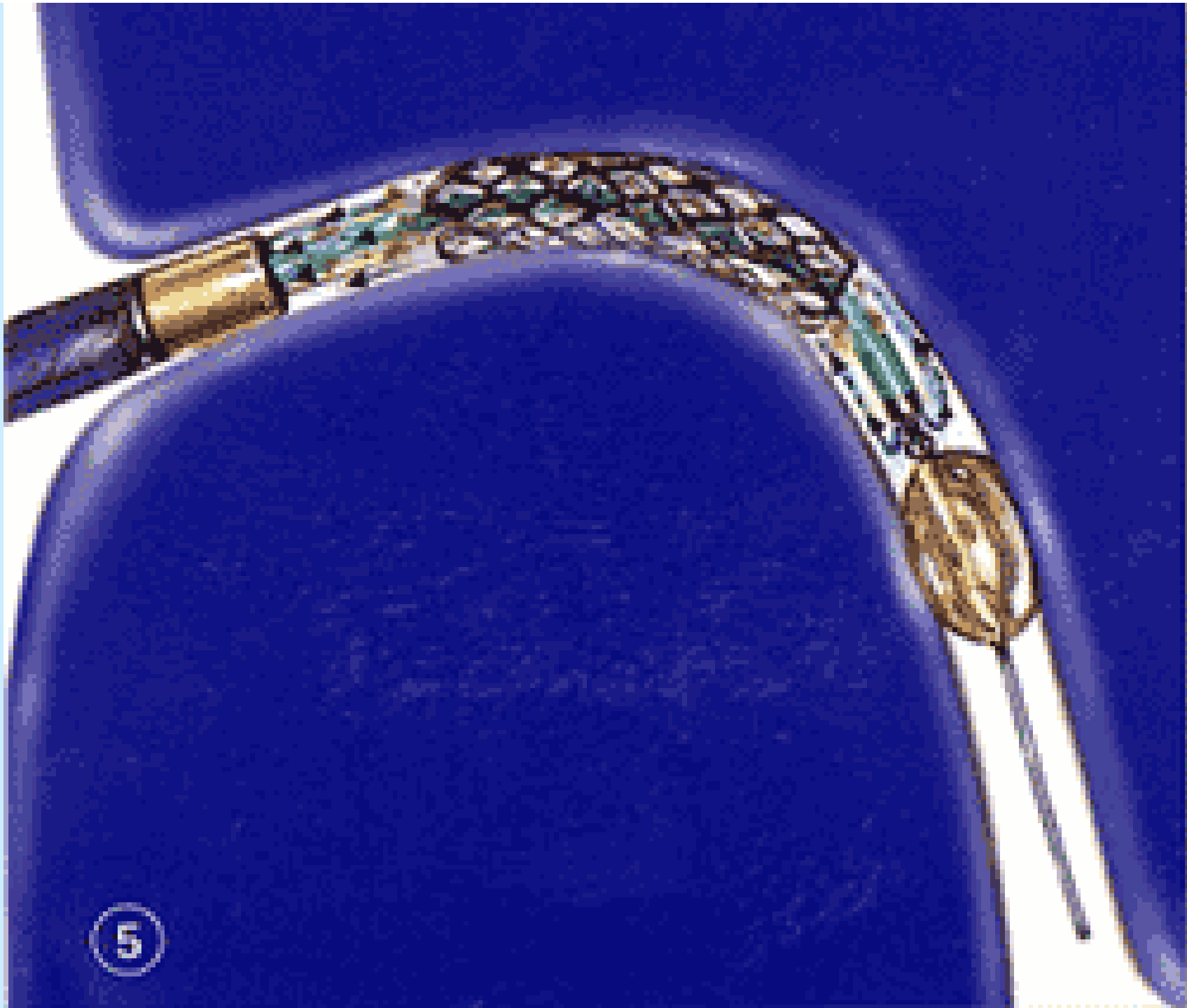
Distal protection devices



**Distal balloon occlusion and
Aspiration system**



Distal filter devices



5

Comparison of distal protection devices

Balloon Occlusion	Filter
Advantages	
<ul style="list-style-type: none"> ✓ Good apposition ✓ Small profile, flexible, steerable ✓ No limit in capture efficacy and capacity ✓ Block small particle and vasoactive substance 	<ul style="list-style-type: none"> ✓ Continuous myocardial perfusion with less ischemia ✓ Good forward contrast flow facilitate accurate PCI
Disadvantages	
<ul style="list-style-type: none"> ✓ Block myocardial perfusion with more ischemia ✓ Poor forward contrast flow may hamper accurate PCI ✓ Direct flow toward side branch 	<ul style="list-style-type: none"> ✓ Possibility of poor apposition ✓ Large profile, less flexible and steerable ✓ Limit in capture efficacy and capacity: <i>limit in capacity with extruded debris, dislodged during retrieval, small particle and vasoactive substance can pass</i> ✓ Debris can block forward flow

Thrombectomy and Distal Protection in AMI

Study/Investigator	Pts no.	Results/Benefits
Mechanical Thrombectomy (X-Sizer)		
M Napodano	92	blush score, ST resolution
G Beran	66	cTFC, ST resolution
T Lefevre (XAMINE ST)	200	blush score, ST resolution
Rheolytic Thrombectomy (AngioJet)		
D Antoniucci	100	cTFC, ST resolution, infarct size
A Ali	273	TIMI flow, ST resolution, LVEF, mortality
Andrew	101	TIMI, cTFC, blush score
Distal Occlusion Balloon and Aspiration (GuardWire)		
EMERALD	501	No benefit
HS Yip	199	TIMI, blush score, 30-day mortality
ASPARAGUS	329	slow flow/no reflow, embolism, prox. RCA
SJ Tahk (Korean)	116	TIMI, TMPG, flow pattern
Filter Devices		
Limbruno	106	TIMI, blush score, distal embolization, cTFC, ST resolution, LVWMSI, LVEF
PROMISE	200	No benefits

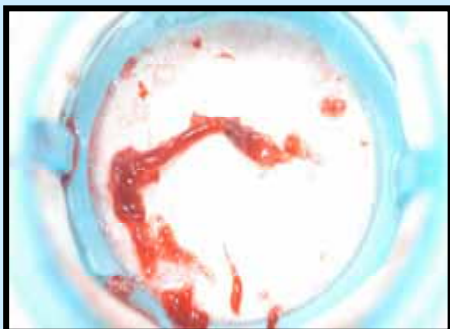
Korean Randomized Multicenter Study

Distal Protection during Primary Stenting in Acute STEMI

- Ajou University Medical Center * *SJ Tahk, MH Yoon, SY Choi*
- Keimyung University Dongsang Medical Center *KB Kim, SH Hur*
- Seungkyunkwan University Samsung Medical Center * *HC Geon*
- Seoul National University Bundang Hospital *IH Chae*
- Seoul National University Hospital * *MM Lee, BK Ku*
- YeungNam University Hospital *YJ Kim, GR Hong*
- Yonsei University Cardiovascular Center * *YS Jang*
- Yonsei University Wonju Christian Hospital *JH Yoon, SW Lee*

* *Doppler Center*

Primary Stenting with Distal Protection



GuardWire® Temporary Occlusion and Aspiration System (Medtronic AVE)

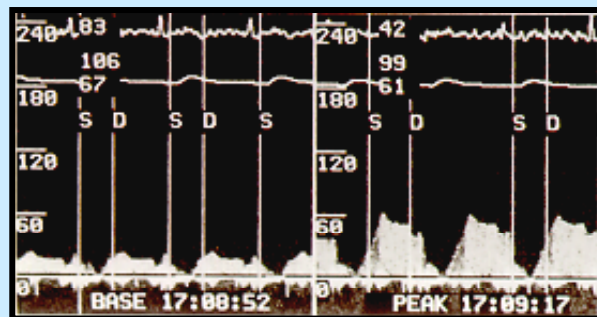
GuardWire Temporary Occlusion Catheter

Export® Aspiration Catheter



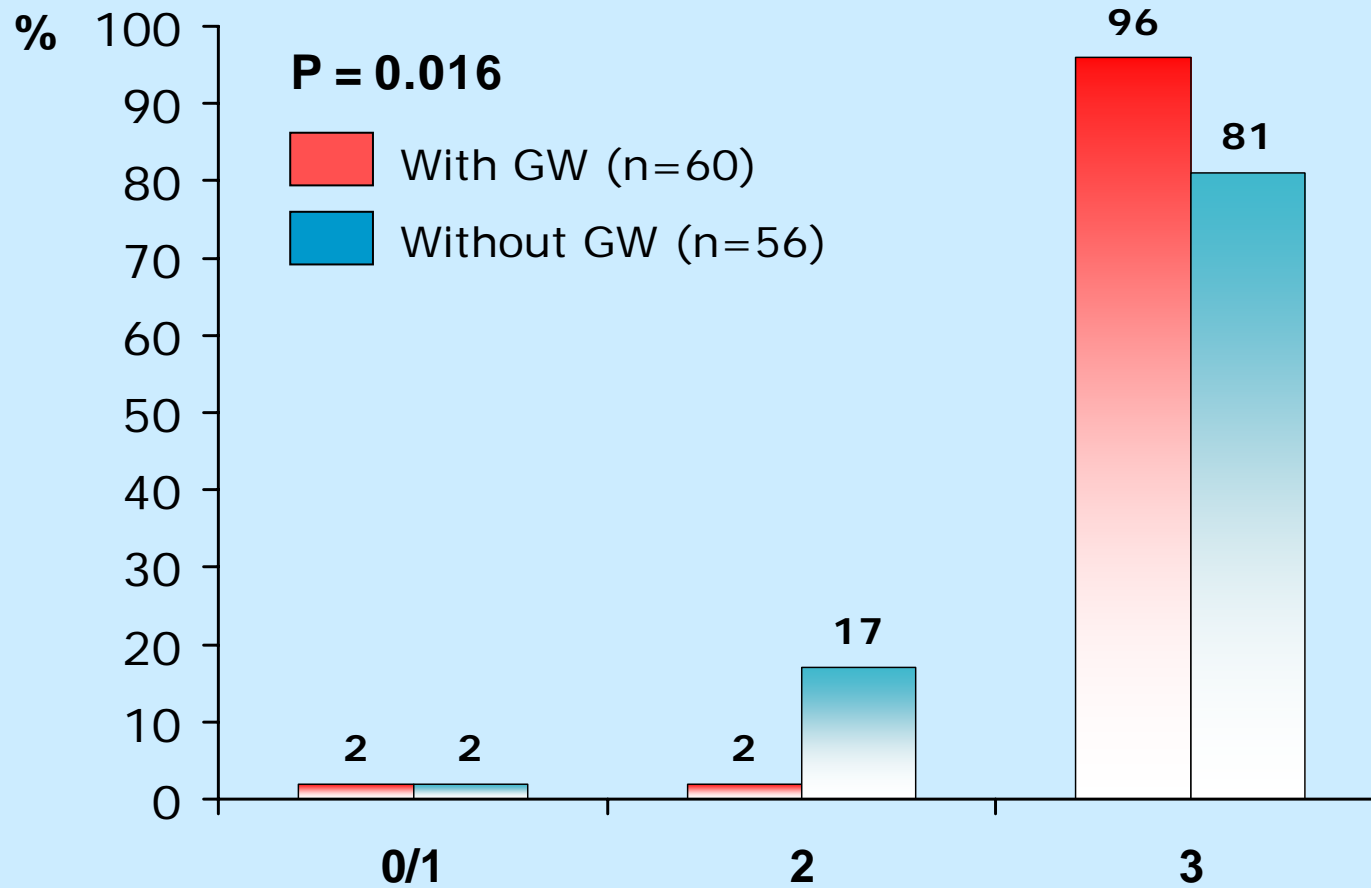
Doppler Guide Wire
FloWire™ (Endosonic)
FloWire XT (JOMETRICS)
FlowMap® System

Intracoronary Adenosine 24-48µg



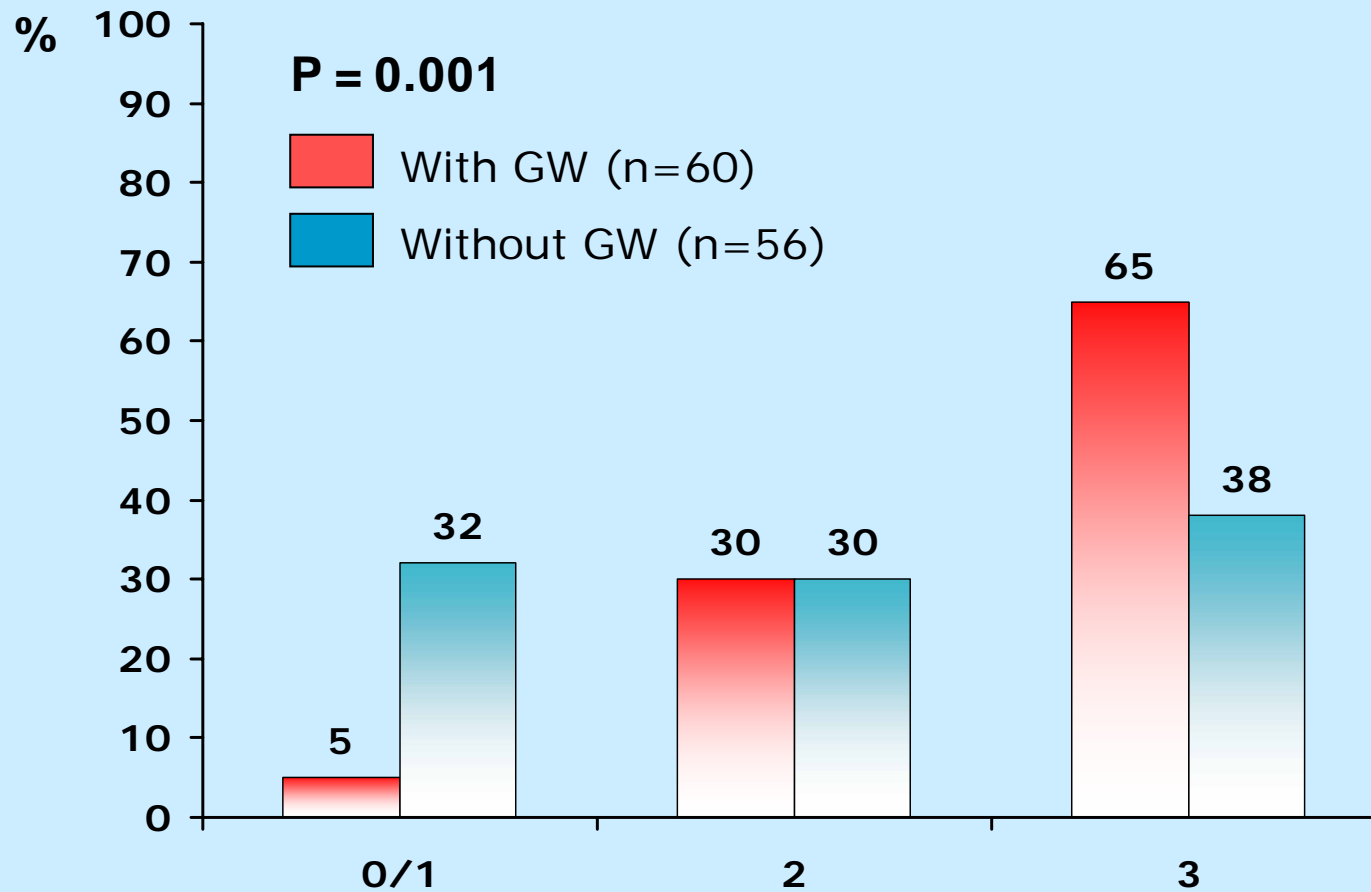
Thrombus aspiration was not permitted before stenting
Additional ballooning after stenting was permitted only with GuardWire protection

Post Stent Angiographic TIMI Score



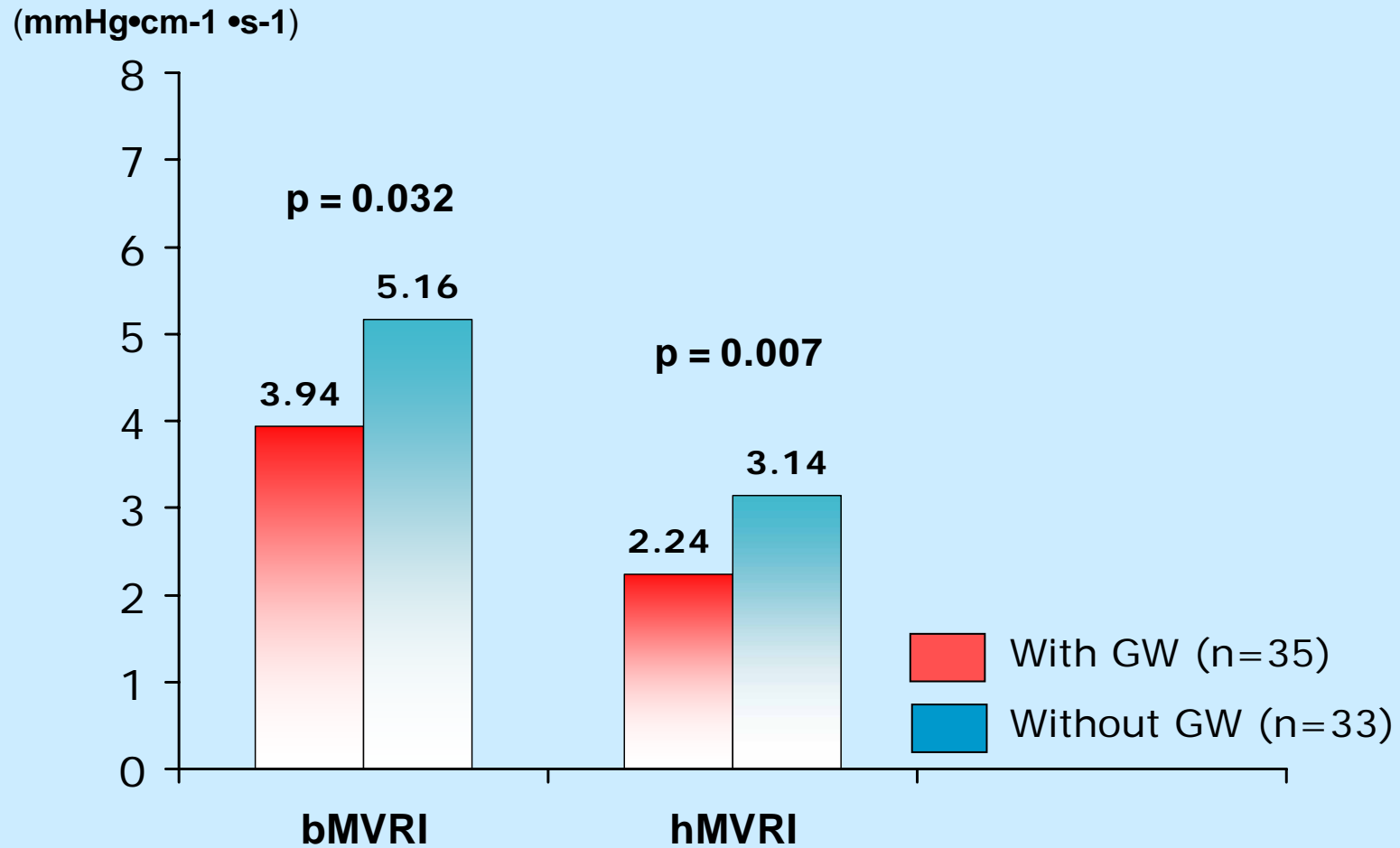
SJ Tahk, et al. AHA 2004

Post Stent Angiographic TMP Grades



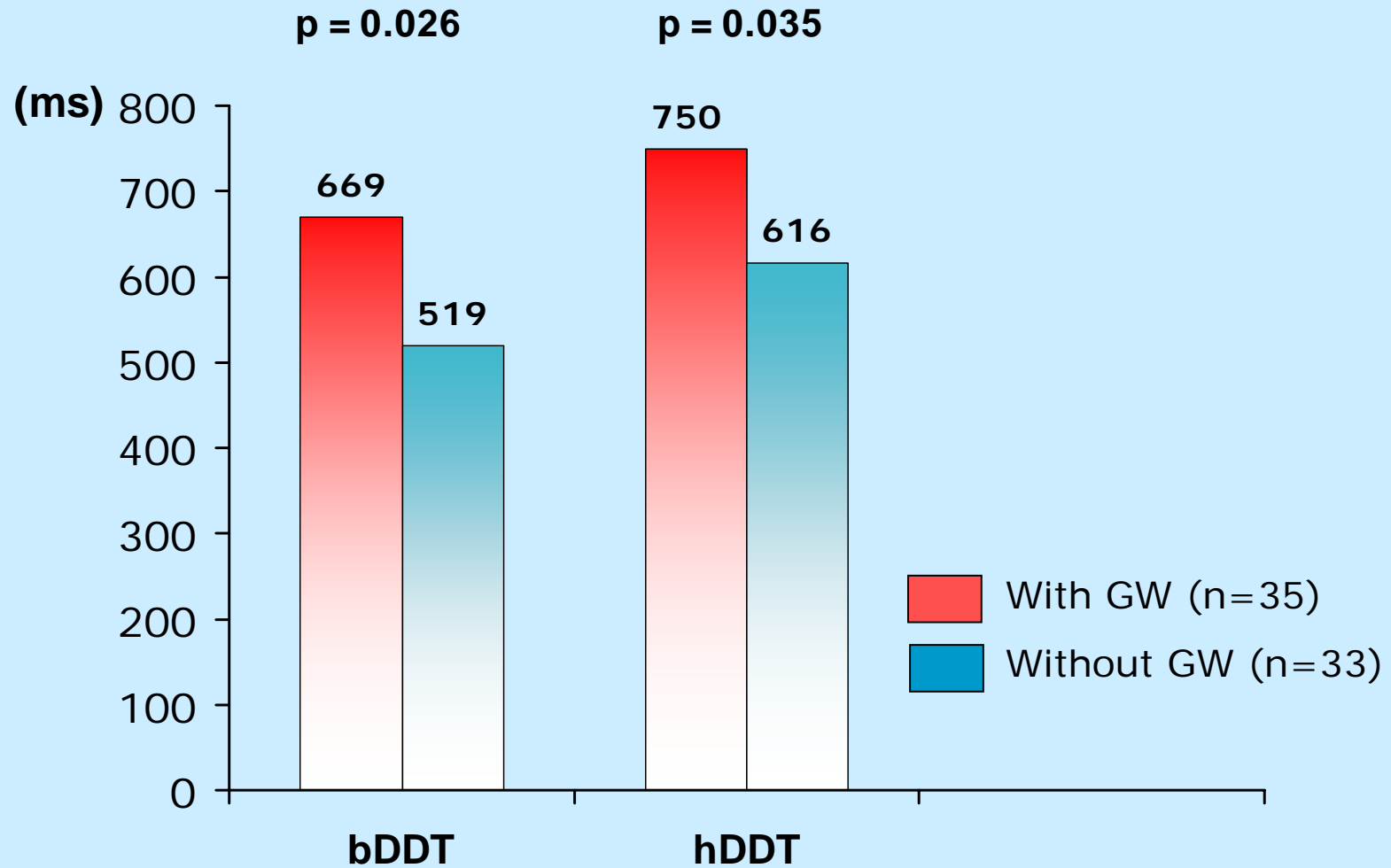
SJ Tahk, et al. AHA 2004

Microvascular Resistance Index



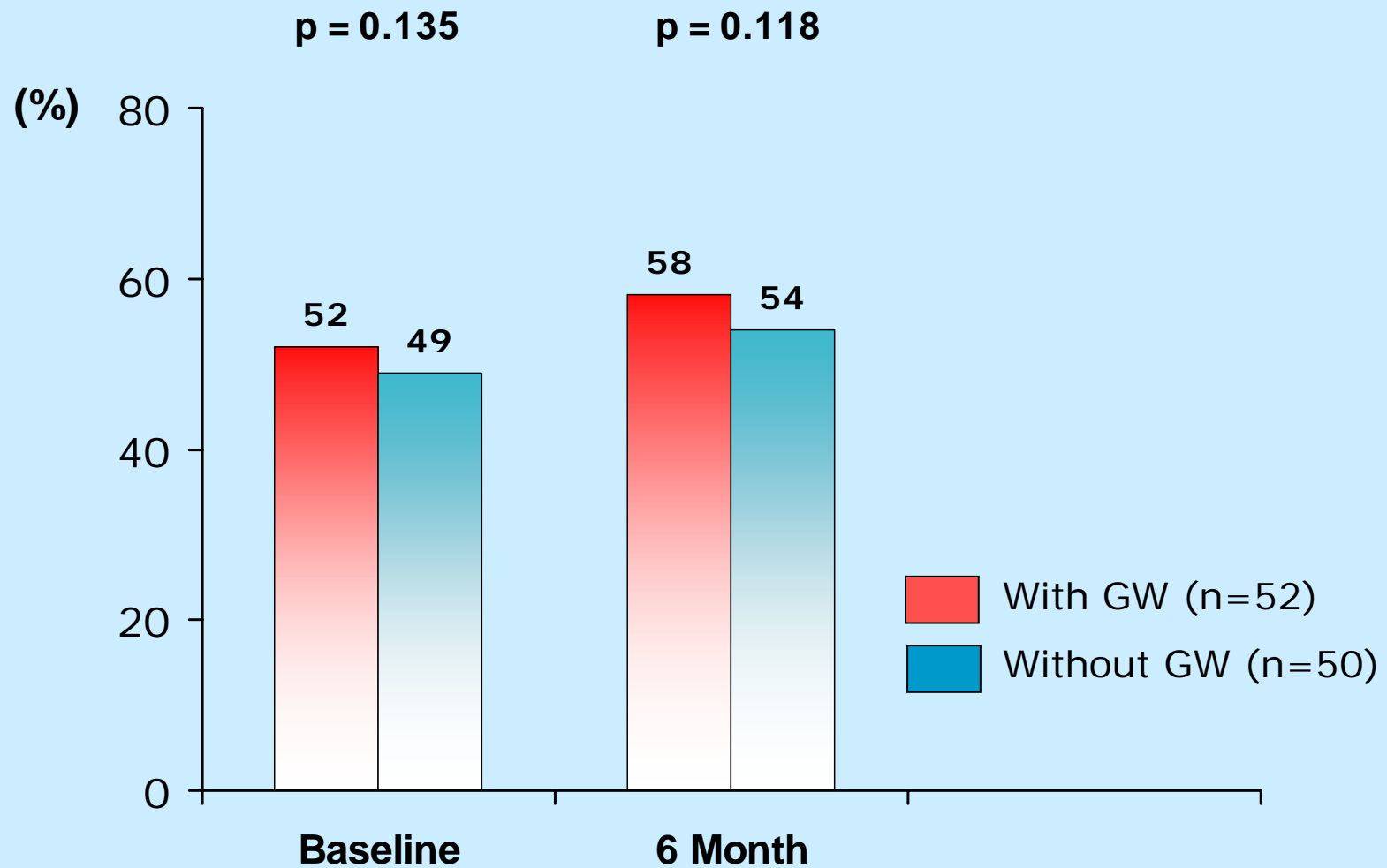
SJ Tahk, et al. AHA 2004

Deceleration Time of Diastolic Flow Velocity



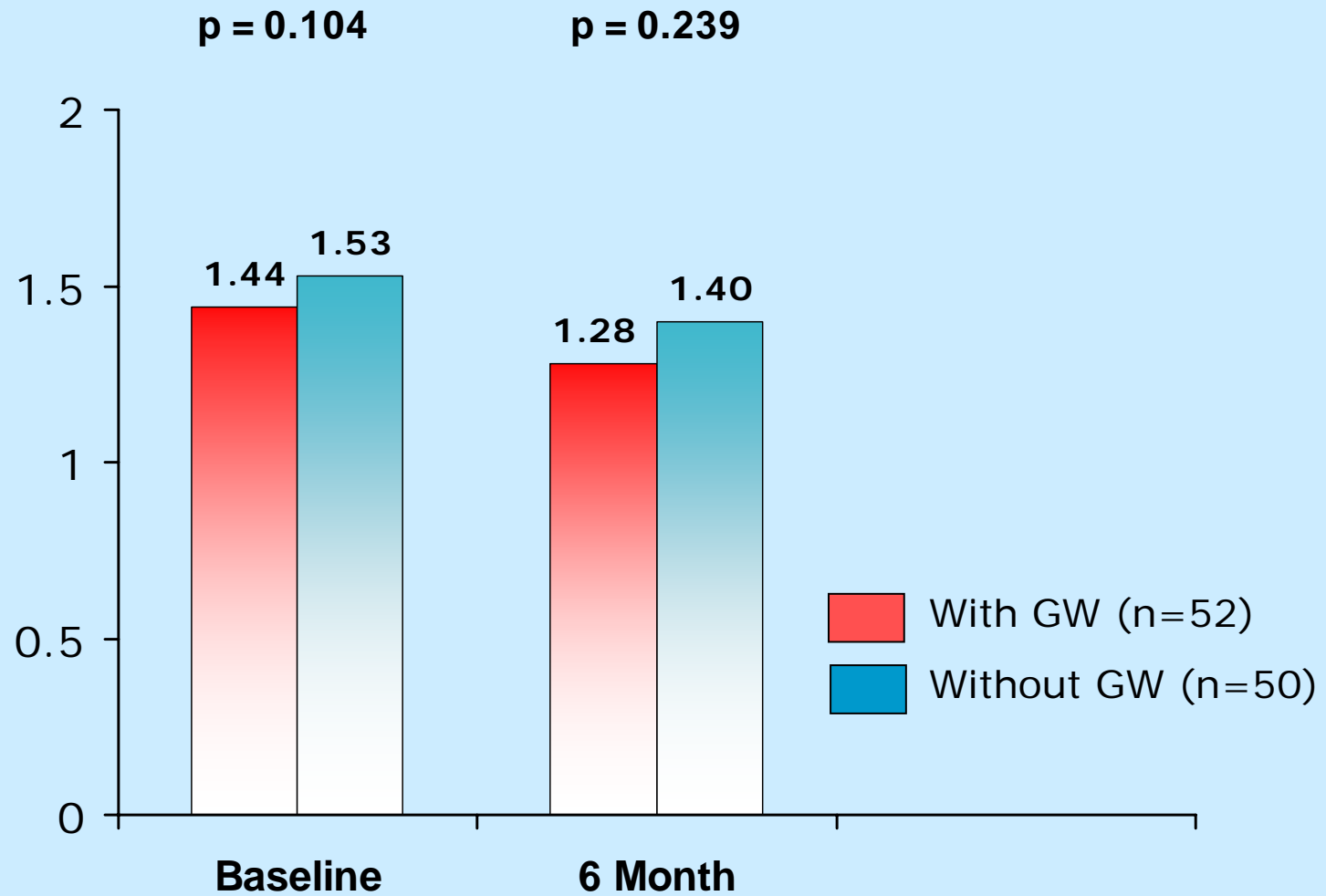
SJ Tahk, et al. AHA 2004

Left Ventricular Ejection Fraction



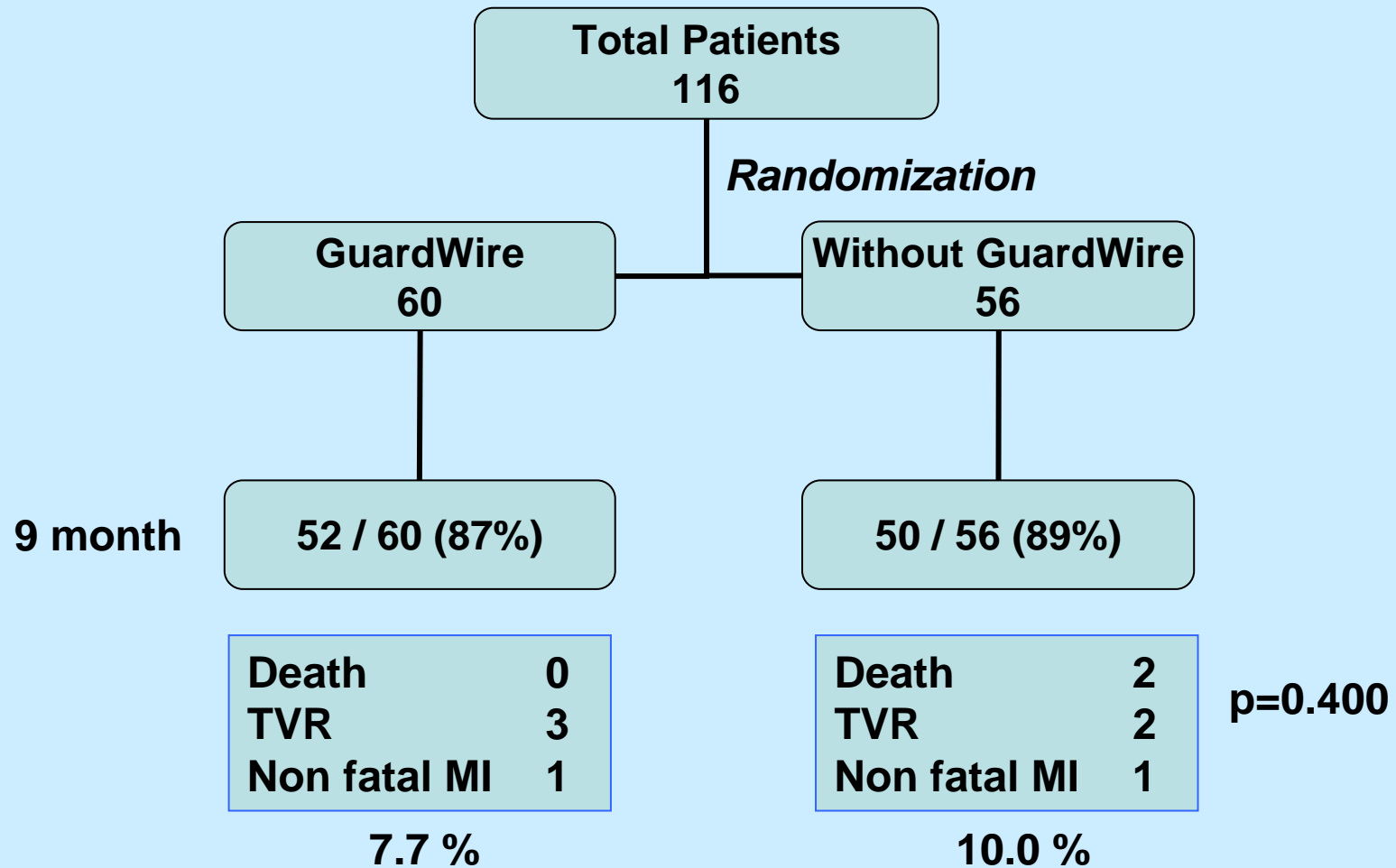
SJ Tahk, et al. AHA 2004

Wall Motion Score Index

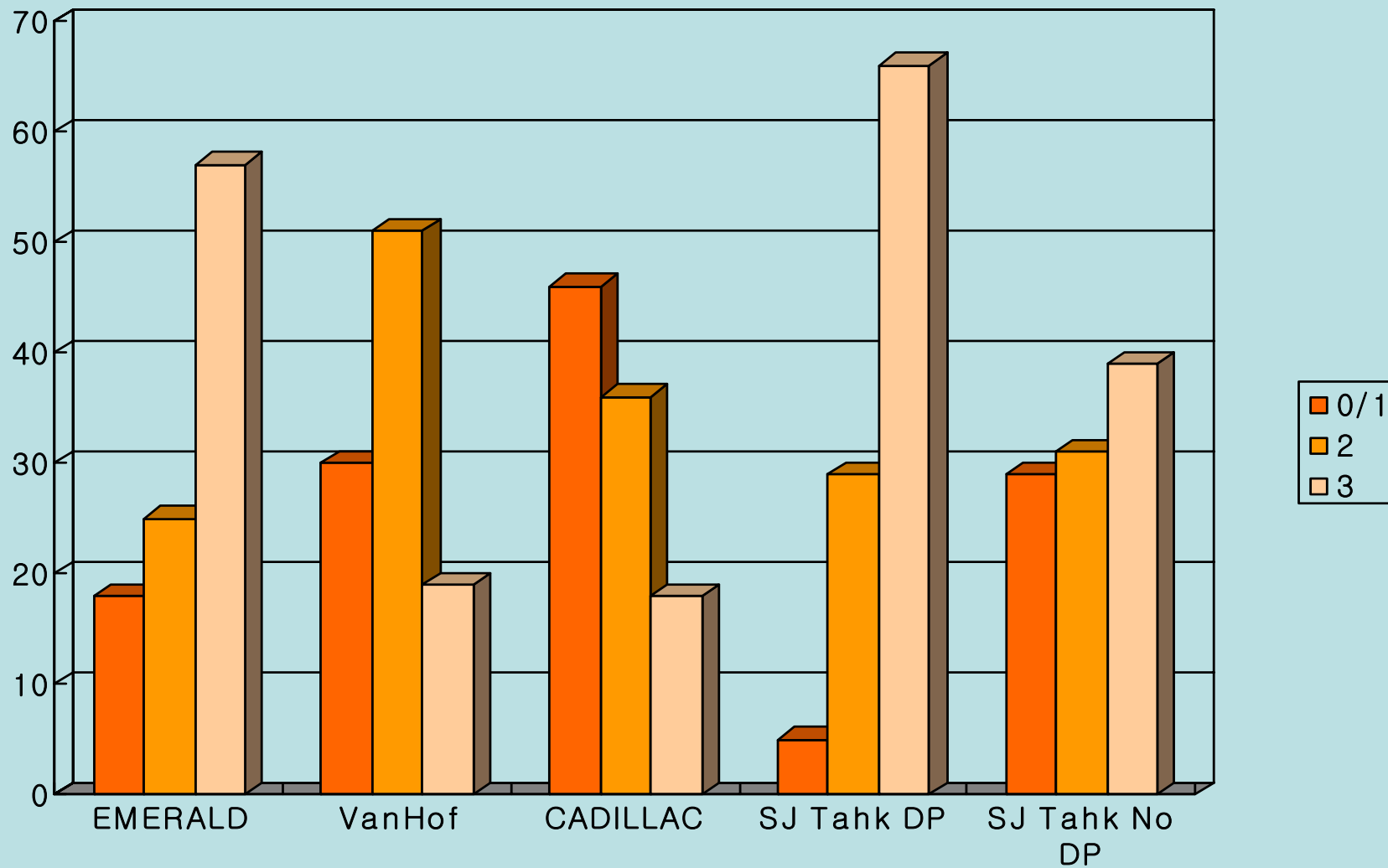


SJ Tahk, et al. AHA 2004

Major Adverse Cardiovascular Events

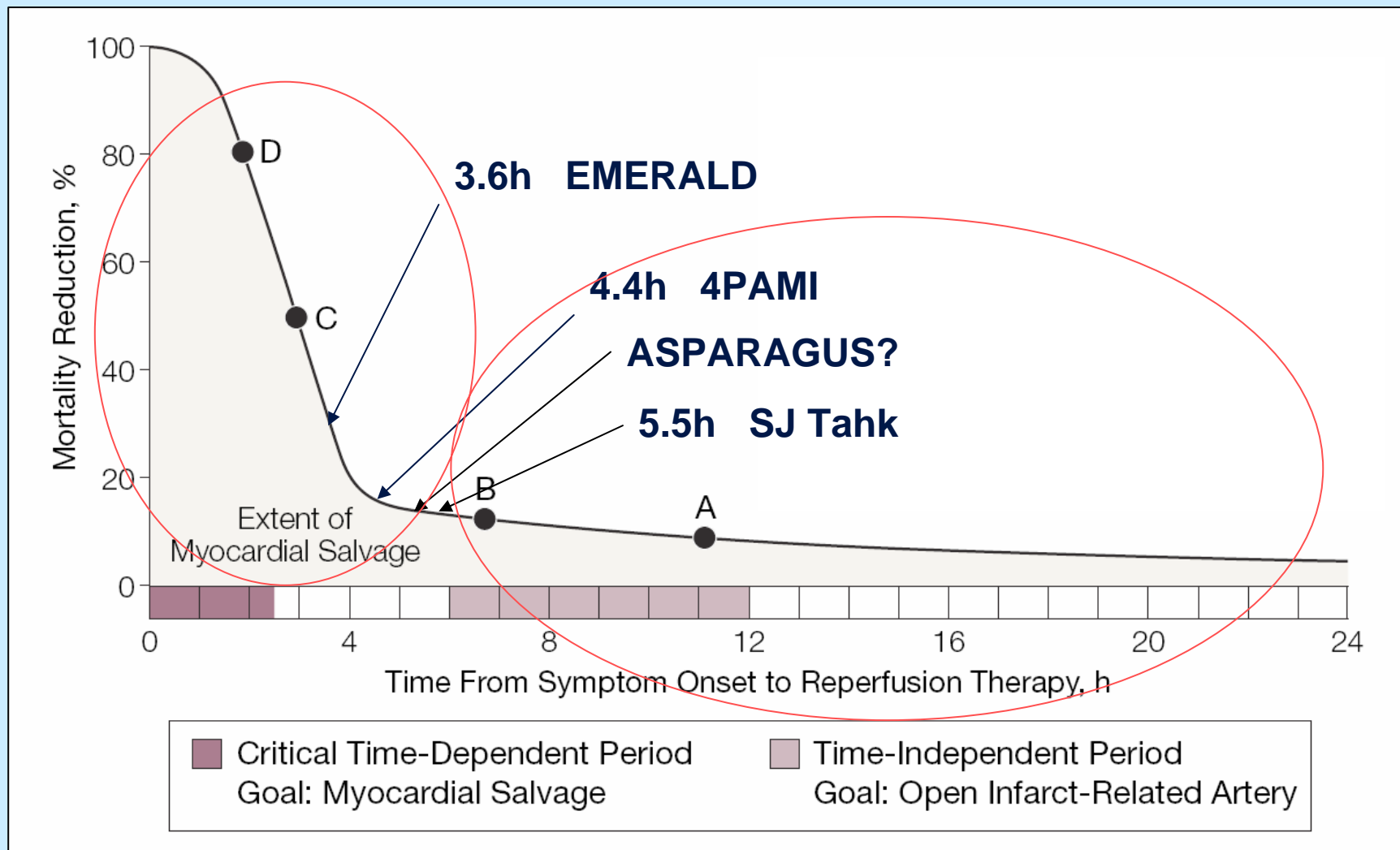


Final TMP Grade after primary PCI: What makes difference?



Time from onset to reperfusion

Mortality reduction as a benefit of reperfusion therapy



Modified from Gersh BJ, et al. JAMA 2003:824-826

Why were distal protection studies negative?

- **Patient related issues?**

- There may be a certain patient/lesion subtype that would benefit.
- Large vessels, proximal occlusion, heavy thrombotic load?
- Ischemic time, pre PCI flow, LV function?
- Concurrent use of GP IIb/IIIa inhibitors reduce device effect?

- **Device related issues?**

- The device efficacy
- Embolization occurred during device passage?
- Difficult to handle
- Device related delays and ischemia?
- Couldn't protect proximal side branches/bifurcations

Why were distal protection studies negative?

- **Misconception related issues?**

- What is major cause of distal injury?
- Vasospasm (neurohumoral substances)
- Interstitial edema
- Inflammation
- Myonecrosis with capillary leak

Adjuvant pharmacological treatments may be needed..

- GP inhibitors, adenosine, CCB, nicorandil, etc...

- **Procedural or operator related issues?**

- Operators on the learning curve
- Incomplete protection during the whole procedure

Pharmacologic Facilitation of primary PCI

- **Facilitated PCI .. should be considered as**
- **The pharmacologically advancing the opening of the epicardial artery in AMI patients who undergo immediate PCI may be associated with restoration not only epicardial flow but also tissue-level reperfusion.**
- **Therefore, facilitated PCI should be considered in a broader and appropriate context as PCI performed after pretreatment with antithrombotic drugs to reduce infarct size and mortality.**

Facilitated PCI .. results of small RCTs

- **Pharmacologic facilitation before primary PCI improve coronary flow at the time of intervention and may increase the time window to PCI.**
- **Fibrin-specific agents or combination of fibrinolytic and glycoprotein IIb/IIIa inhibitor are preferred.**
- **Facilitated PCI is more effective and safe than thrombolytic therapy alone. However, it showed limited benefit compared with primary PCI alone.**
- **The role of facilitated PCI needs to be established in large multicenter randomized clinical trials.**

Meta analysis of 4RCTS with abciximab

RAPPORT, ISAR-2, ADMIRAL, CADILLAC: quite different view..

- **Meta analysis of interventional RCTs evaluating adjuvant abciximab therapy in AMI has found a 46% significant reduction in the combination of death, reinfarction, and ischemic TVR, and a trend toward reduction in combination of death and reinfarction. This benefit is maintained at 6-month follow-up.**

Kandzari DE, et al. Am Heart J 2004:457-462



- **In the setting of primary PCI, four clinical trials involving over 3,000 pts demonstrated that GP IIb/IIIa inhibition results in a significant decrease in the need for urgent TVR, but not in reductions of death or recurrent MI. Thus, GP IIb/IIIa inhibition may provide only limited benefits in acute STEMI.**

Eisenberg MJ, et al. J Am Coll Cardiol 2003:1-6

Primary PCI .. GP IIb/IIIa inhibitors

ACC/AHA Practice Guideline 2004

6.3.1.6.8.2.3. Glycoprotein IIb/IIIa inhibitors.

Class IIa

- **It is reasonable to start treatment with abciximab as early as possible before primary PCI (with or without stenting) in patients with STEMI. (Level of Evidence: B)**

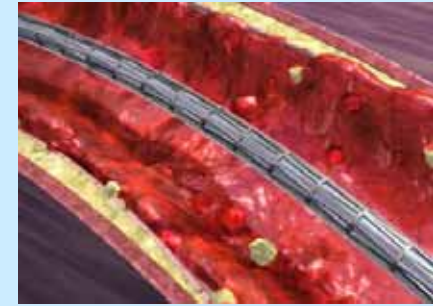
Class IIb

- Treatment with tirofiban or eptifibatide may be considered before primary PCI (with or without stenting) in patients with STEMI. *(Level of Evidence: C)*
- Five randomized trials compared abciximab to placebo control in a collective total of 3666 patients undergoing primary PCI for STEMI (34-36,38,582). A total of 1843 patients received abciximab, a relatively small data set on which to base recommendations for treatment. In addition, in the setting of primary PCI, periprocedural recurrent MI is not easily measured, so the benefit of antiplatelet therapy with GP IIb/IIIa inhibitors is harder to determine.
- The Writing Committee believes that it is reasonable to start treatment with abciximab as early as possible in patients undergoing primary PCI (with or without stenting), but given the size and limitations of the available data set, assigned a Class IIa recommendation.

Conclusions

- **Various degree of distal embolization and additional myocardial damage occur during primary PCI.**
- **3 randomized clinical trials proved no clinical benefits of distal protection devices.**
- **However, many other small clinical trials revealed beneficial effects in flow patterns and clinical outcomes.**

Conclusions



- **What more proof do you need?**
- **Distal protection may be beneficial in patients with ...**
 - **Proximal occlusion with large ischemic area**
 - **Heavy thrombus burden**
 - **Poor pre PCI coronary flow**
 - **Lower ejection fraction**
 - **Late presentation with longer ischemic time**
- **What we have to elucidate in the future are the efficacy of distal protection in a certain patient or lesion subtype**
- **We need more data. It is not the time to conclude, but the time to start.**