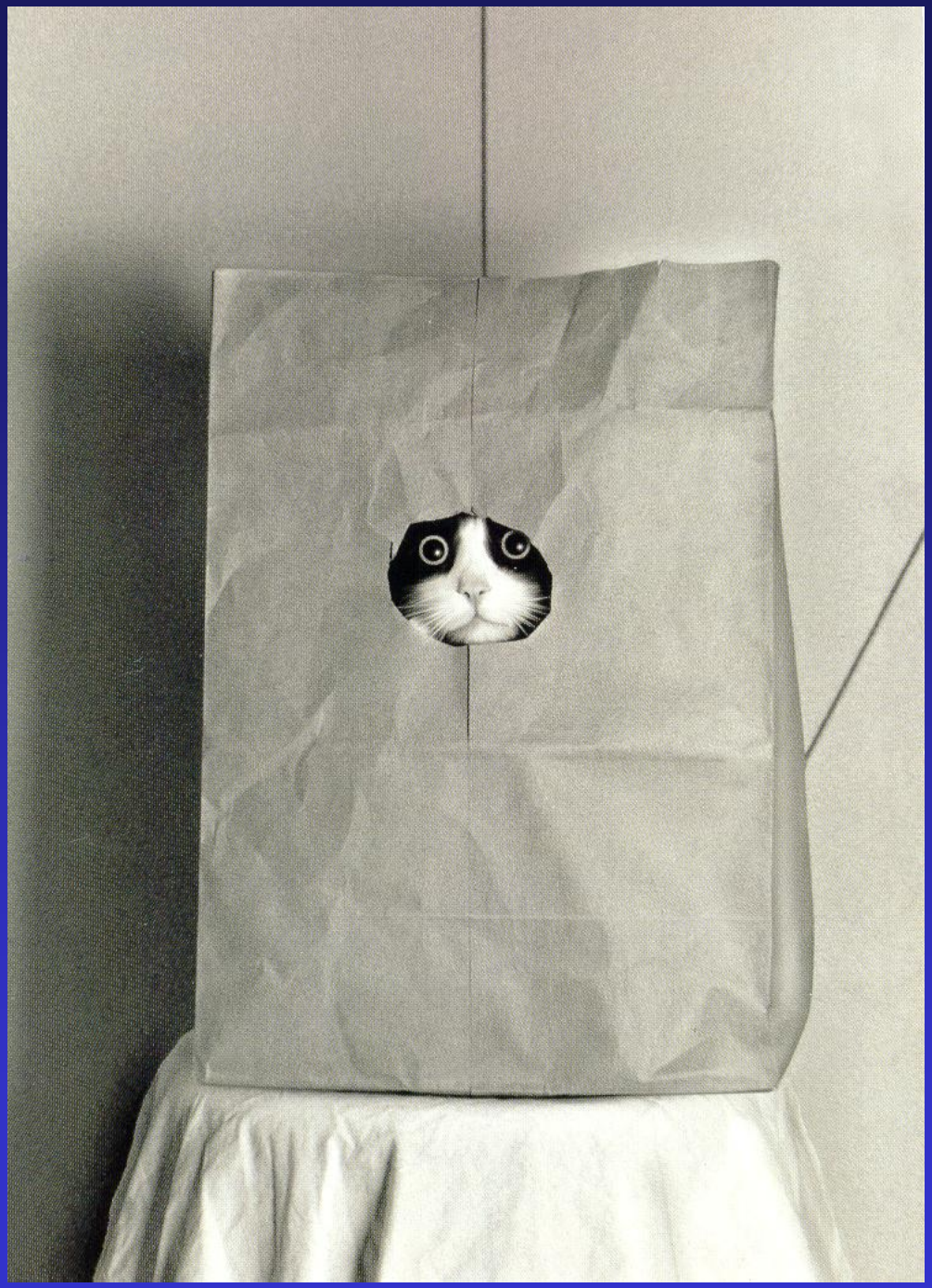
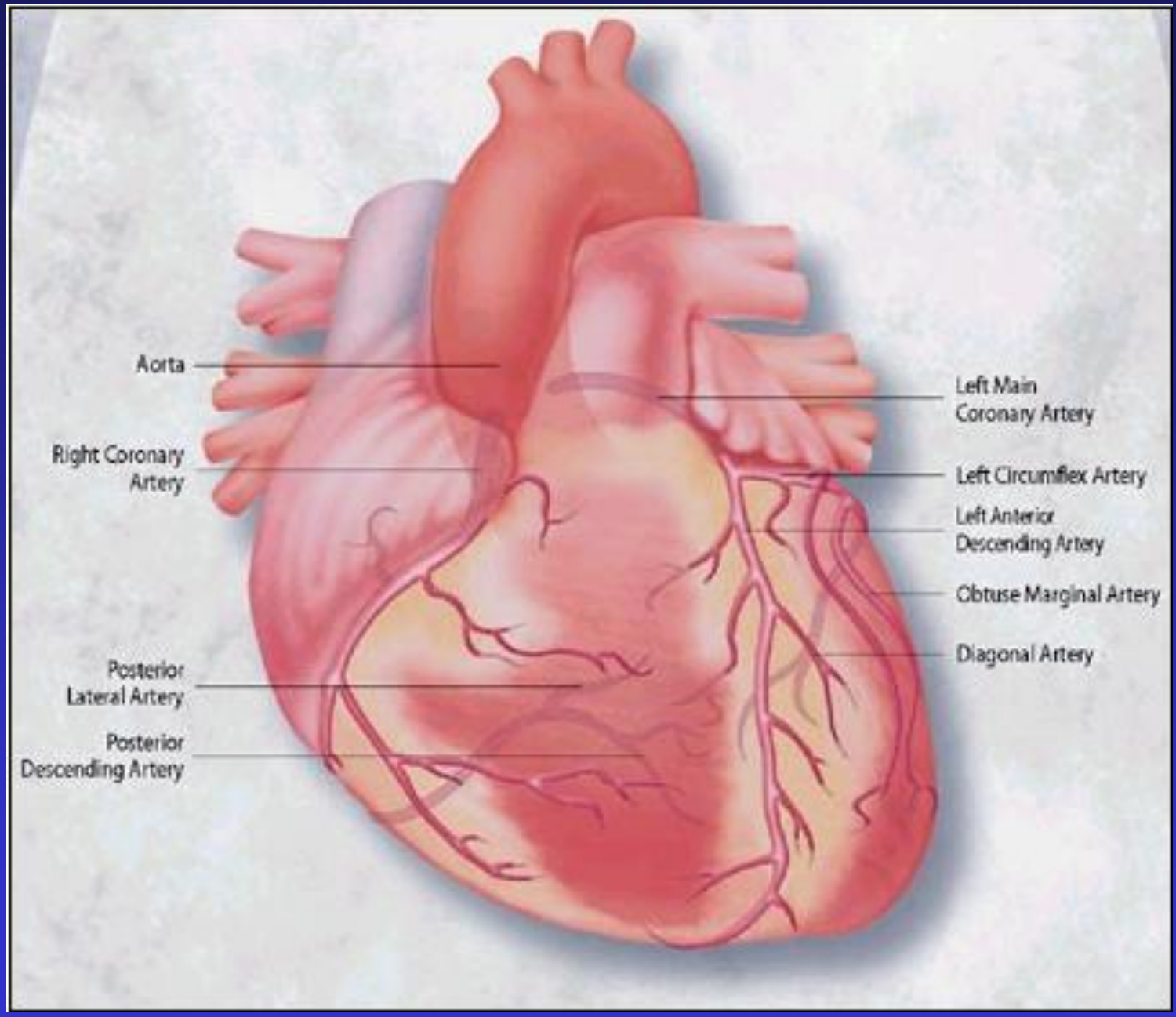


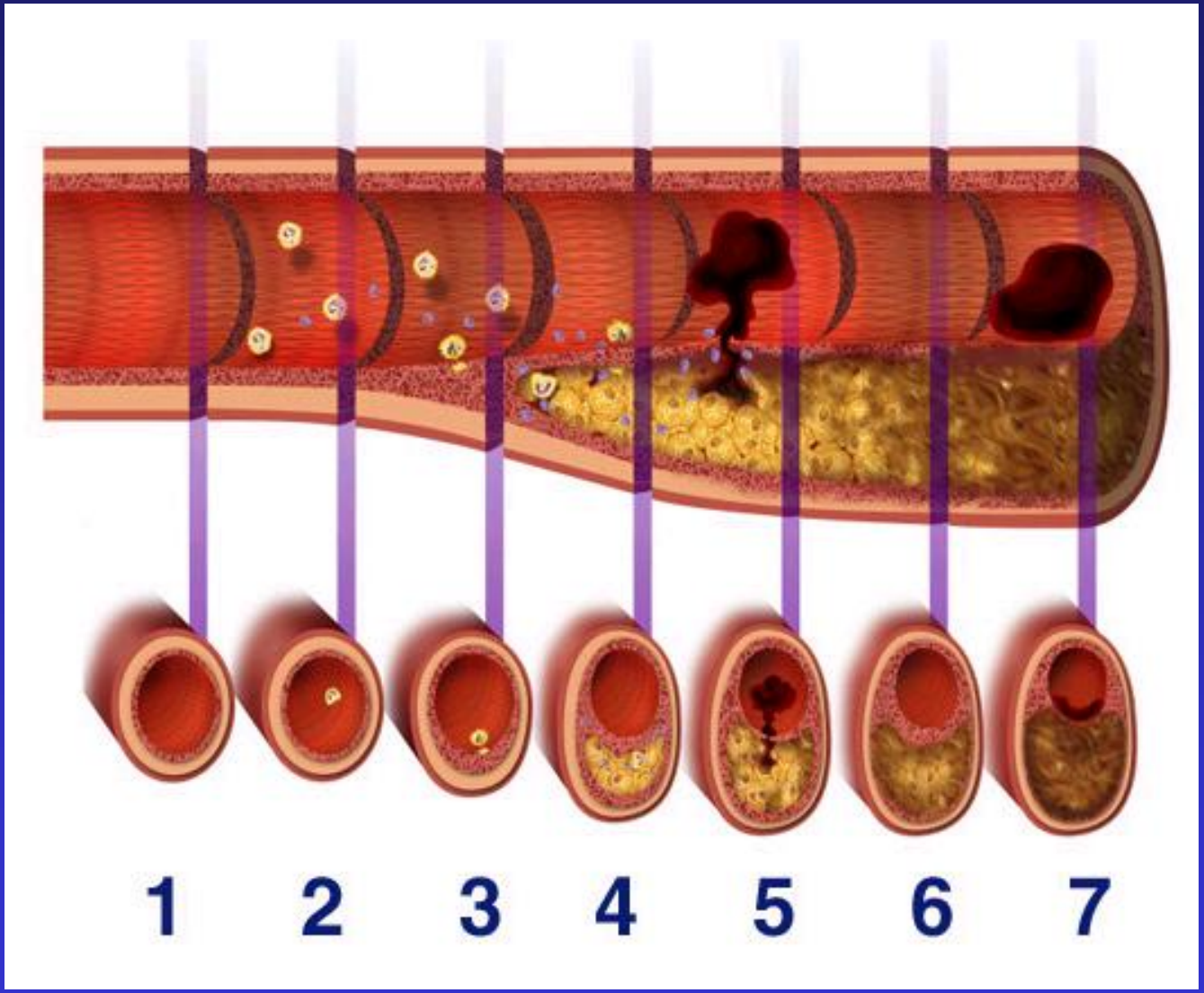
Acute Coronary Syndrome

John Coyle, M.D.

April 30, 2004


Aorta
Right Coronary Artery
Posterior Lateral Artery
Posterior Descending Artery
Left Main Coronary Artery
Left Circumflex Artery
Left Anterior Descending Artery
Obtuse Marginal Artery
Diagonal Artery

Progression of Coronary Artery Disease



Caloric Restriction Society (N = 18)

Dietary differences

Nutritional profile	CR	Control
Total calories (kcal/day)	1112-1958	1976-3537
Fat (%)	28	32
Carbohydrates (%)	46	50
Protein (%)	26	18

Fontana L et al. *Proc Natl Acad Sci* 2004. Available at: http://www.pnas.org.

Caloric Restriction Society (N = 18)

Risk factor	CR	Control	p
BMI	19.6	25.9	0.0001
Total cholesterol (mg/dL)	158	205	0.001
LDL (mg/dL)	86	127	0.0001
HDL (mg/dL)	63	48	0.006
Triglycerides (mg/dL)	48	147	0.0001
Systolic BP (mm Hg)	99	129	0.0001
Diastolic BP (mm Hg)	61	79	0.0001
Fasting glucose (mg/dL)	81	95	0.0001
Fasting insulin (µlU/mL)	1.4	5.1	0.0001
CRP (µg/mL)	0.3	1.6	0.001
Carotid IMT (mm)	0.5	0.8	0.0001

Fontana L et al (Wash. U., St. Louis). *Proc Natl Acad Sci* 2004. Available at: http://www.pnas.org.

State Bird of Oklahoma

Atherosclerotic Plaques Are **Common**

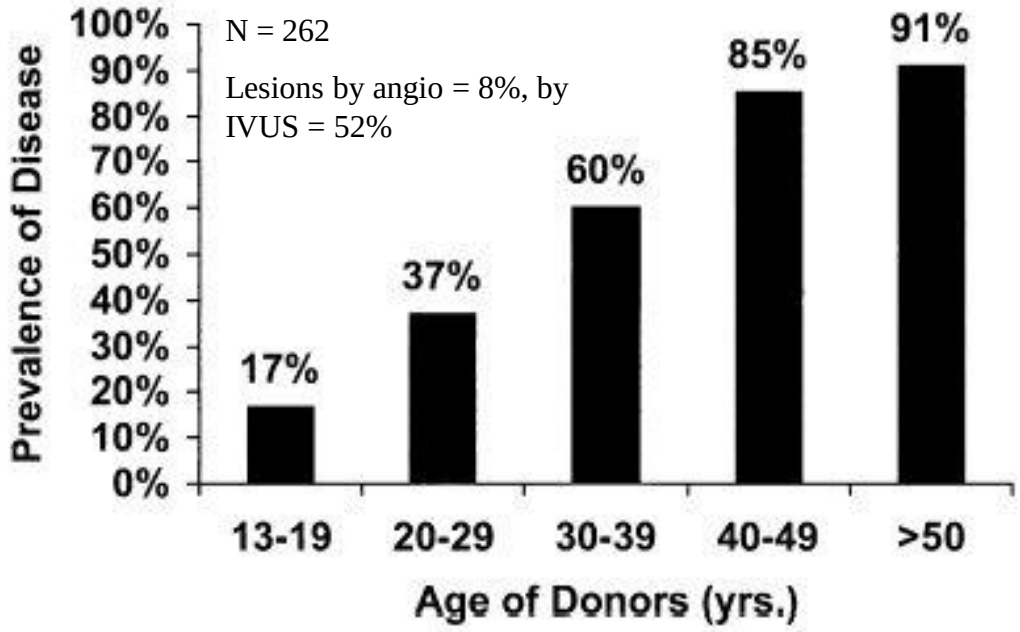


Figure 7. Prevalence of coronary disease in transplant donors. These data demonstrate an aggressive increase in the likelihood of an atheroma of at least 0.5 mm in thickness in individuals as young as 13 years of age. yrs. = years. Tuzcu EM, Kapadia SR, Tutar E, et al High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. Circulation 2001;103:2705–10. Adapted with permission from Lippincott, Williams, and Wilkins.

"With the appearance of the first luminal irregularity, at least 80% of the coronary tree is already arteriosclerotic." Nissen, JACC 41:106S, 2003

Definition:

Acute coronary syndrome (ACS) is a term that refers to the entire spectrum of acute MI, including acute myocardial infarction with and without ST-segment elevation and unstable angina. The final classification of Q-wave or non-Q-wave MI or unstable angina is a retrospective process that is not possible for 24 hours or more after presentation.

Acute Coronary Syndromes

(including Unstable and Intermediate Coronary Syndromes AND/OR Acute Myocardial Infarction):

Symptoms felt to be consistent with acute cardiac ischaemia within 24 hours of hospital presentation

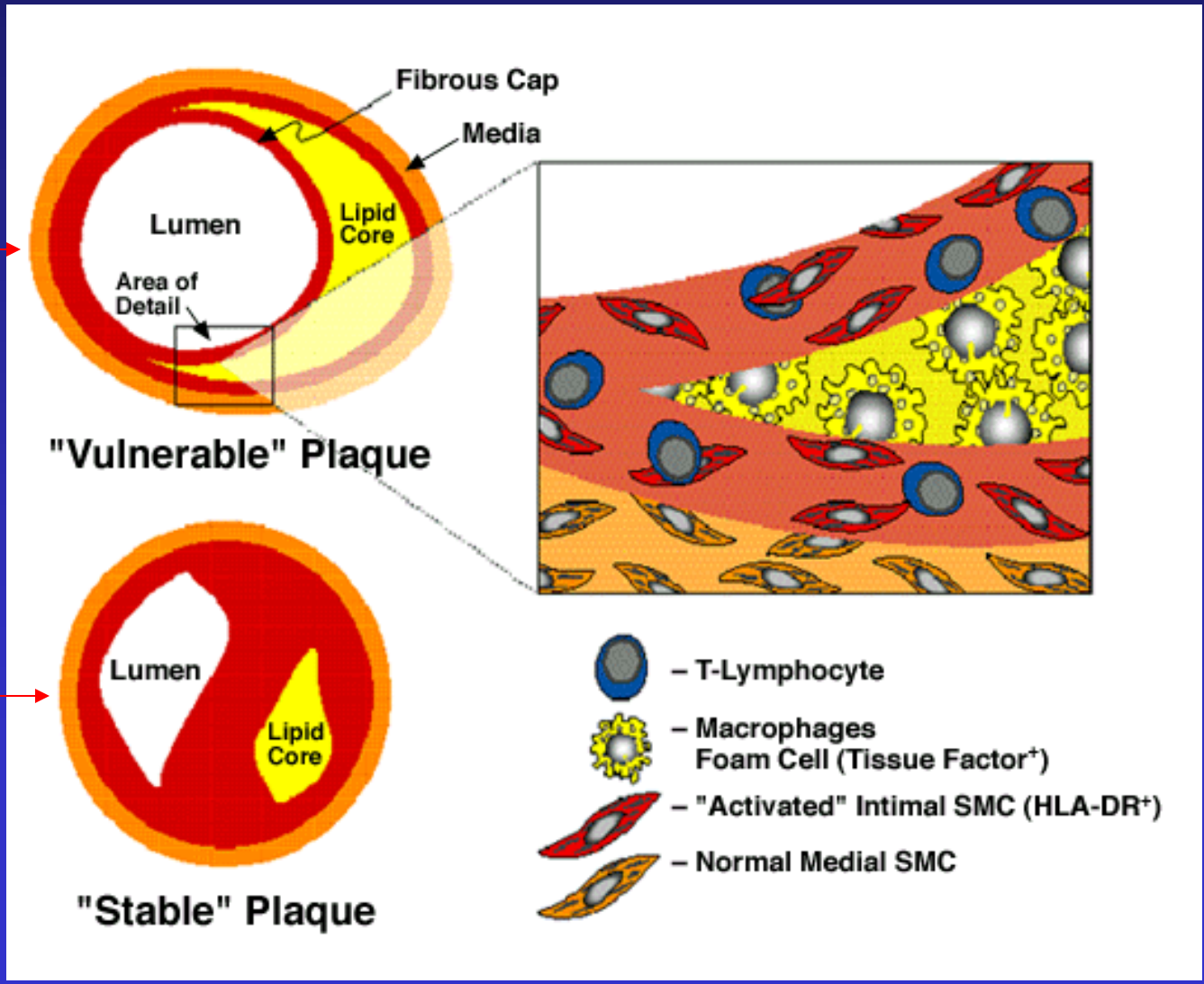
And at least one of the following

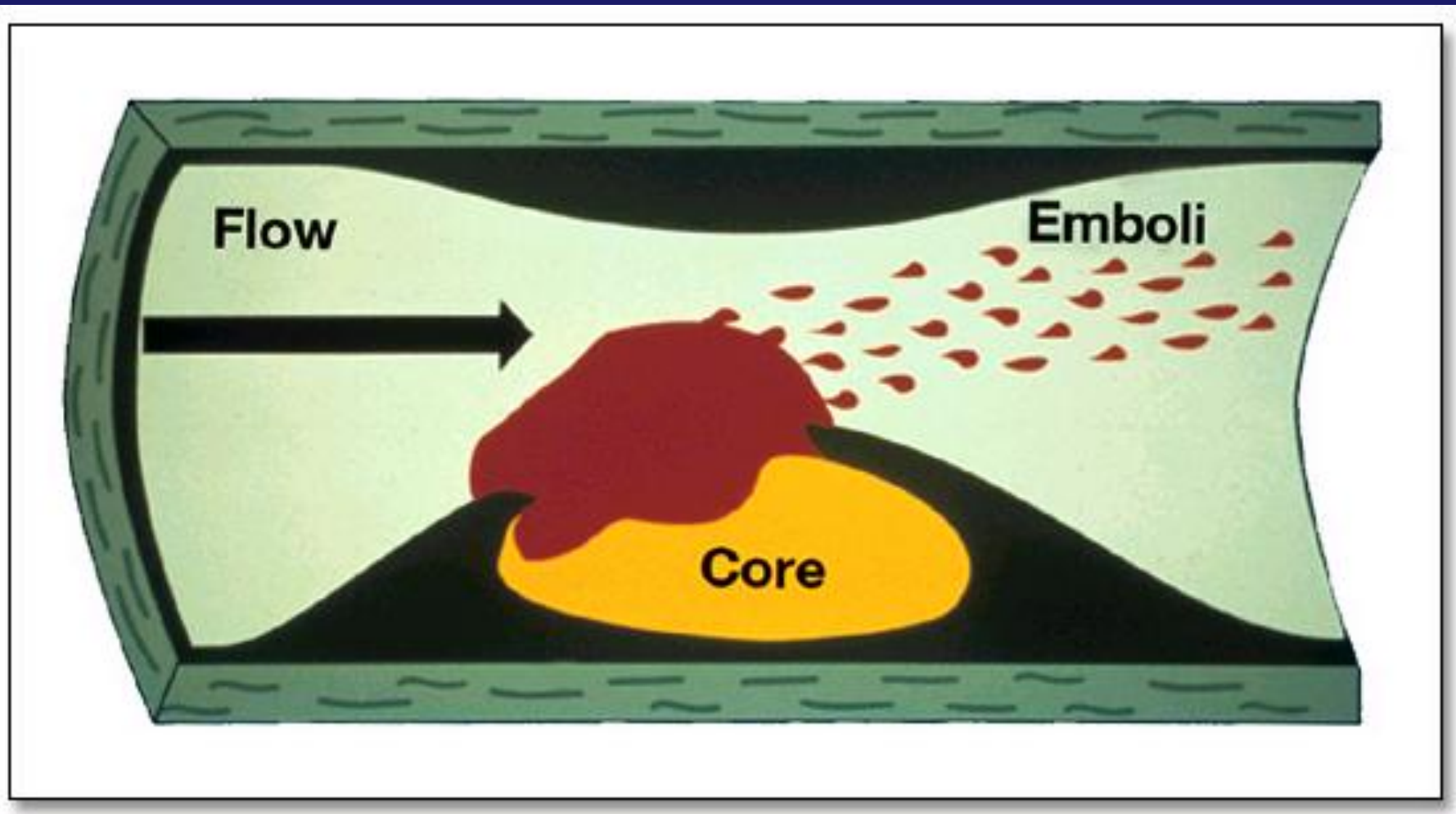
- ECG changes:
  - transient ST segment elevation of 1mm
  - ST segment depression of 1mm
  - new T wave inversion of 1mm
  - pseudo-normalization of previously inverted T waves
  - new Q-waves (1/3 the height of the R wave or > 0.04 seconds)
  - new R wave > S wave in lead V_1 (posterior MI)
  - new left bundle branch block
- Documentation of Coronary Artery Disease:
  - history of MI, angina, CHF felt to be due to ischaemia or resuscitated sudden cardiac death
  - history of, or new, positive stress test with imaging
  - prior, or new, cardiac catheterization documenting coronary artery disease
  - prior, or new, percutaneous coronary intervention or coronary artery bypass surgery
- Increase in Cardiac Enzymes:
  - CK-MB > 2x upper limit of the hospitals normal range OR if no CK-MB available, then total CPK > 2
  - positive troponin I
  - positive troponin T

Mechanism of Thrombus Formation in ACS

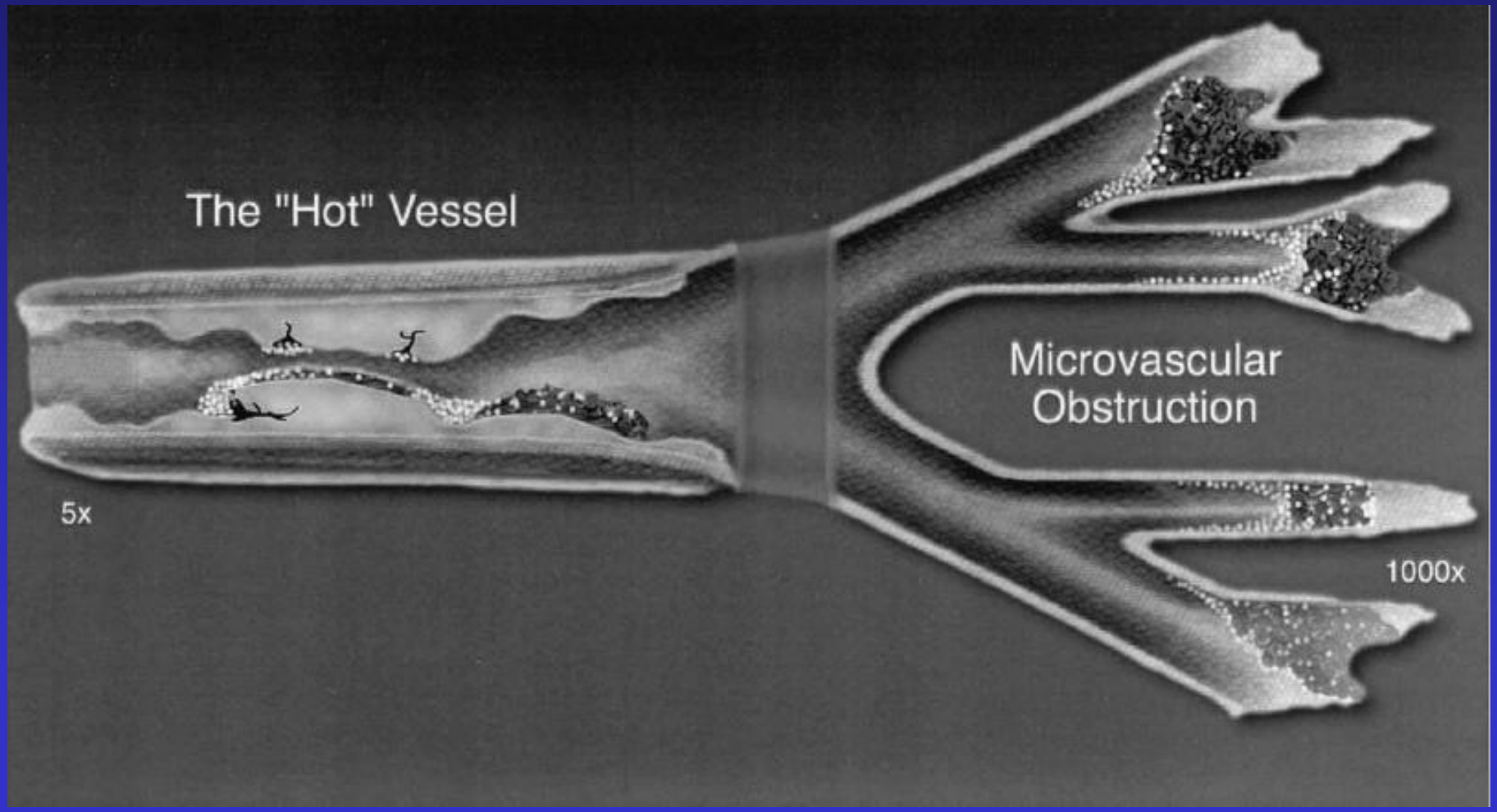
2/3 of cases:
Plaque
RUPTURE

1/3 of cases:
Plaque
EROSION

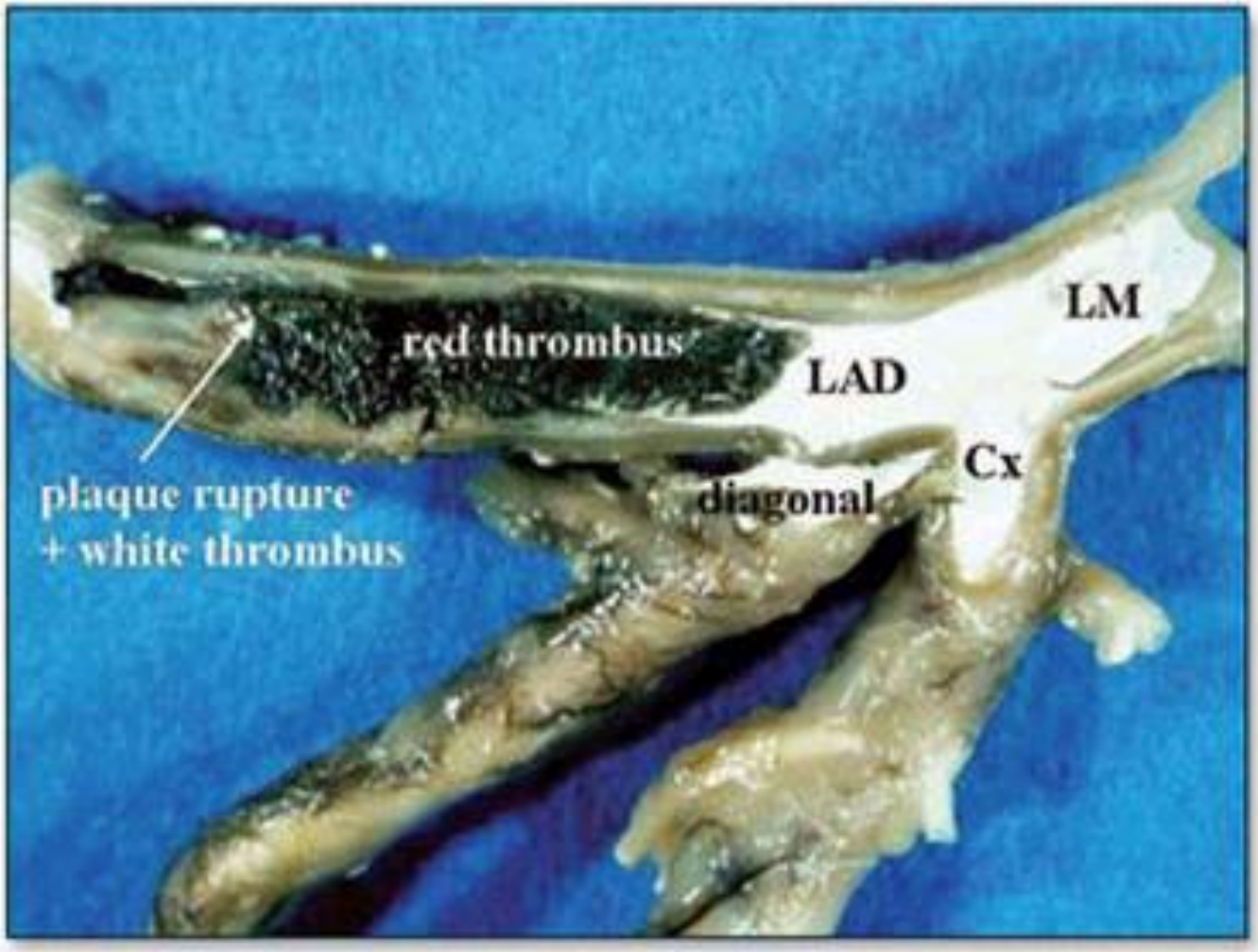



Flow
Emboli
Core

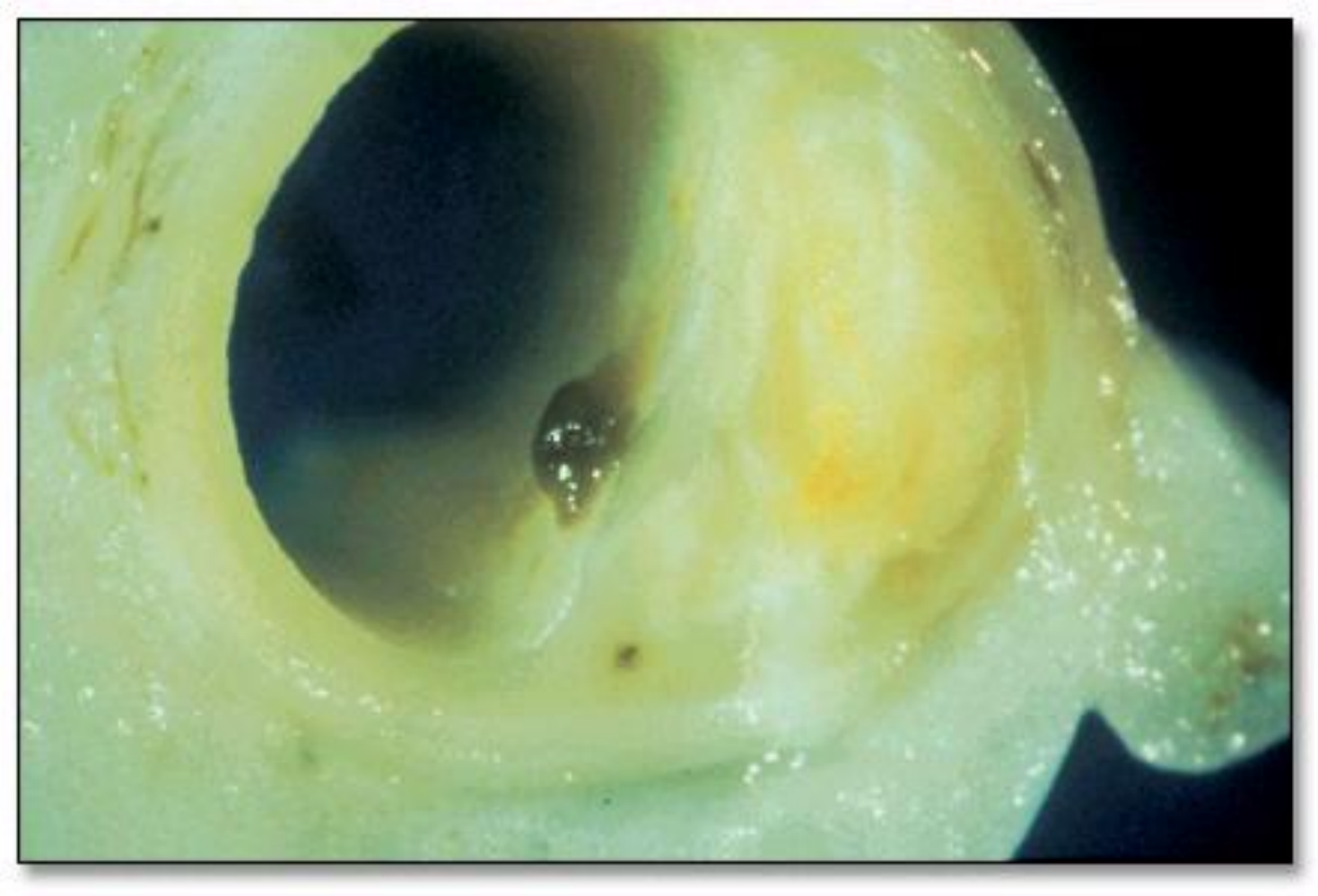
Micro-Emboli and ACS



Secondarily Formed Venous-Type Stagnation Thrombosis

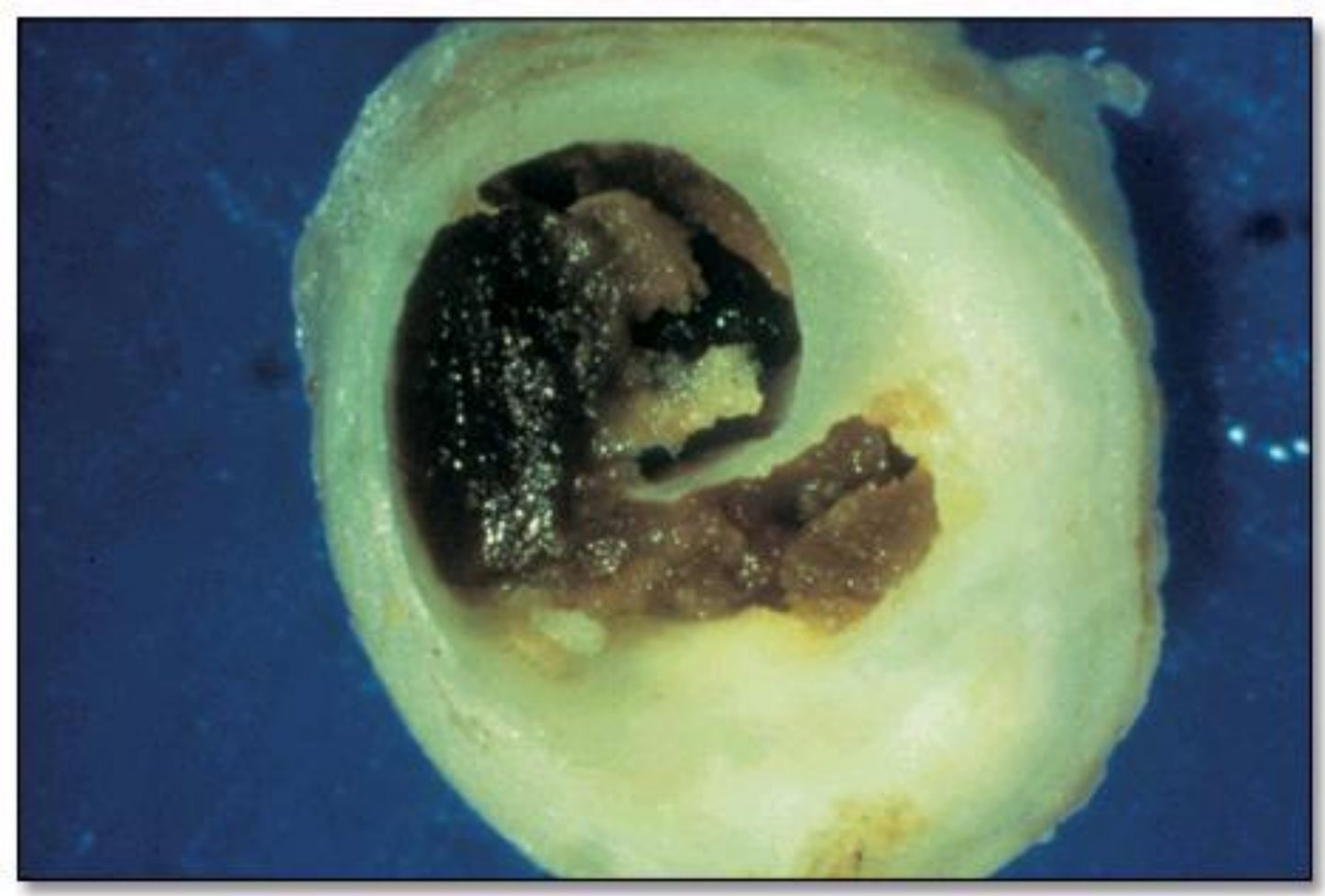


Endothelial EROSION with a Small Thrombus

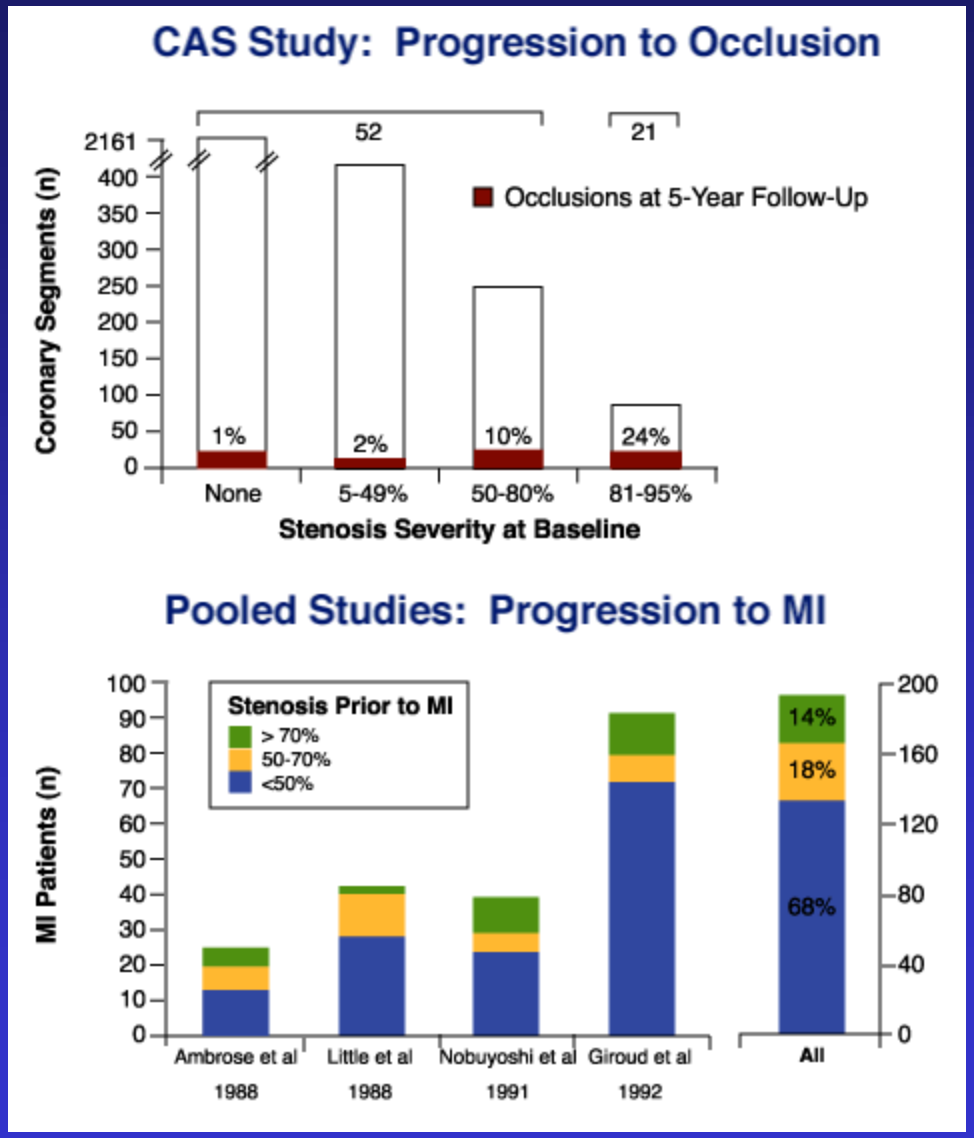


"In clinical trials, about 20% of ACS patients undergoing early angiography exhibit no hemodynamically significant stenosis." Nissen, JACC 41, 206S, 2003

Plaque RUPTURE Causing Major Thrombosis



What Category of Narrowing Produces the Greatest Hazard? Mild.



Chest Pain Checklist for Use by EMT/Paramedic for Diagnosis of Acute Myocardial Infarction and Thrombolysis Screening (ACC/AHA Guidelines)

Check each finding below. If all [yes] boxes are checked and ECG indicates ST elevation or new BBB, reperfusion therapy with thrombolysis or primary PTCA may be indicated. Thrombolysis is generally not indicated unless all [no] boxes are checked and BP ≤ 180/110 mmHg.

	Yes	No
Ongoing Chest Discomfort (≥ 20min and < 12 hrs)	☐	____
Oriented, Can Cooperate	☐	____
Age > 35 y (> 40 if female)	☐	____
History of Stroke or TIA	____	☐
Known Bleeding Disorder	____	☐
Active Internal Bleeding in Past 2 Weeks	____	☐
Surgery or Trauma	____	☐
Terminal Illness	____	☐
Jaundice, Hepatitis, KidneyFailure	____	☐
Use of Anticoagulants	____	☐

Systolic/Diastolic Blood Pressure

Right Arm: _____/_____

Left Arm: _____/_____

	Yes	No
ECG done	☐	____

High-Risk Profile*	Yes	No
Heart Rate ≥ 100bpm	☐	____
BP ≤ 100 mmHg	☐	____
Pulmonary Edema (Rales Greater than One Half Way Up)	☐	____
Shock	☐	____

*Transport to Hospital Capable of Angiography and Revascularization if Needed.

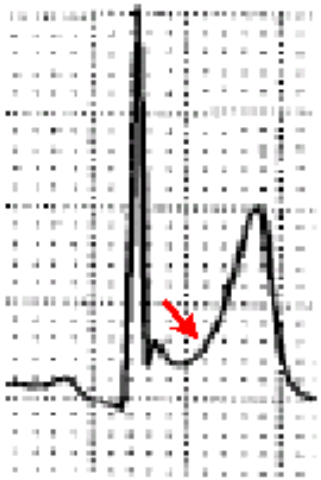
Pain Began	_____	AM/PM
Arrival Time	_____	AM/PM
Begin Transport	_____	AM/PM
Hospital Arrival	_____	AM/PM

EMT = Emergency Medical Technician; ECG = Electrocardiogram; BBB = Bundle Branch Block; PTCA = Percutaneous Transluminal Coronary Angioplasty; BP = Blood Pressure; TIA = Transient Ischemic Attack. Adapted from the Seattle/King County EMS Medical Record.

Sorting Out ST Segment Coving

Downward ST Coving

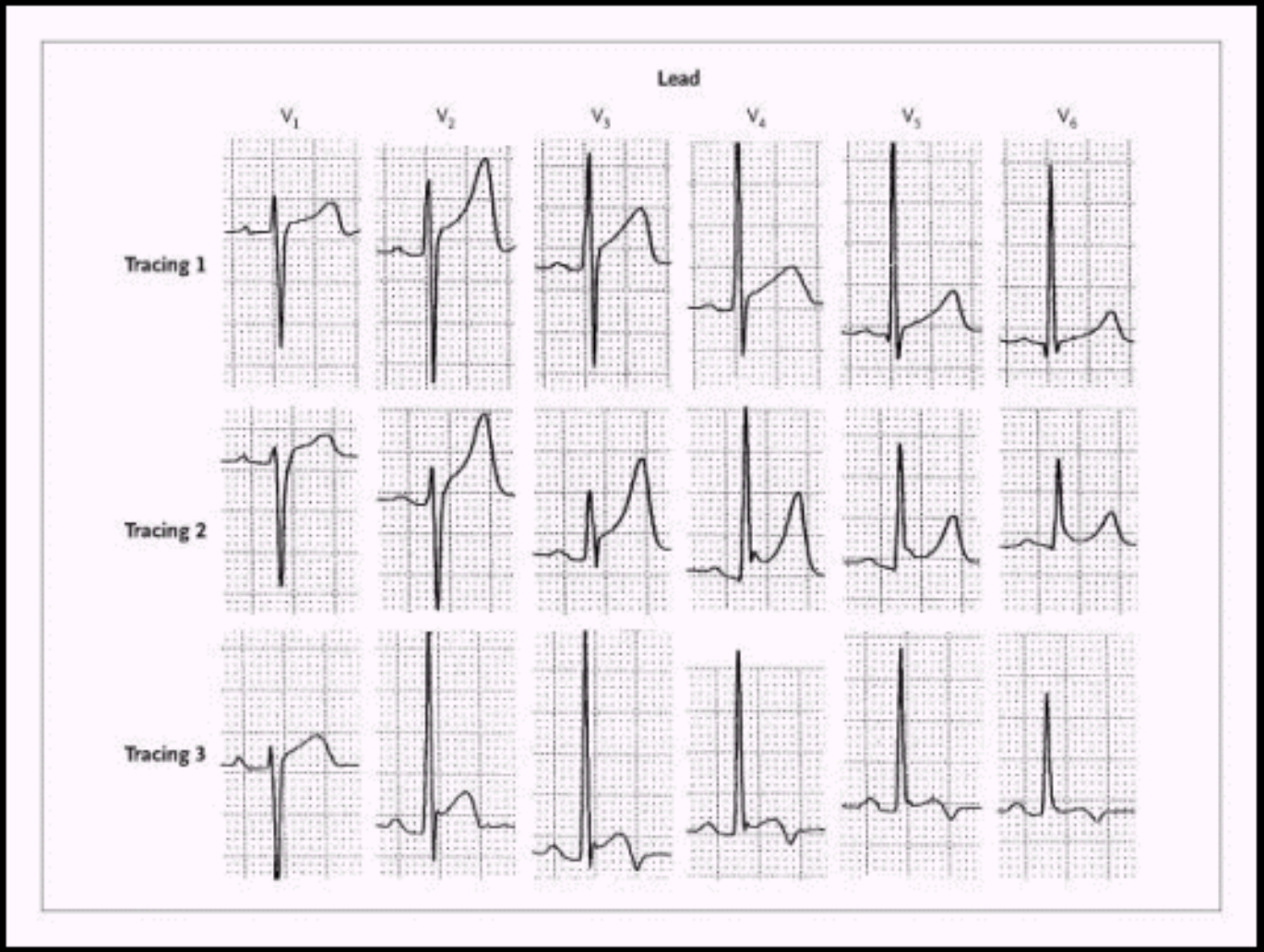
Smile! It's often a Normal Variant.



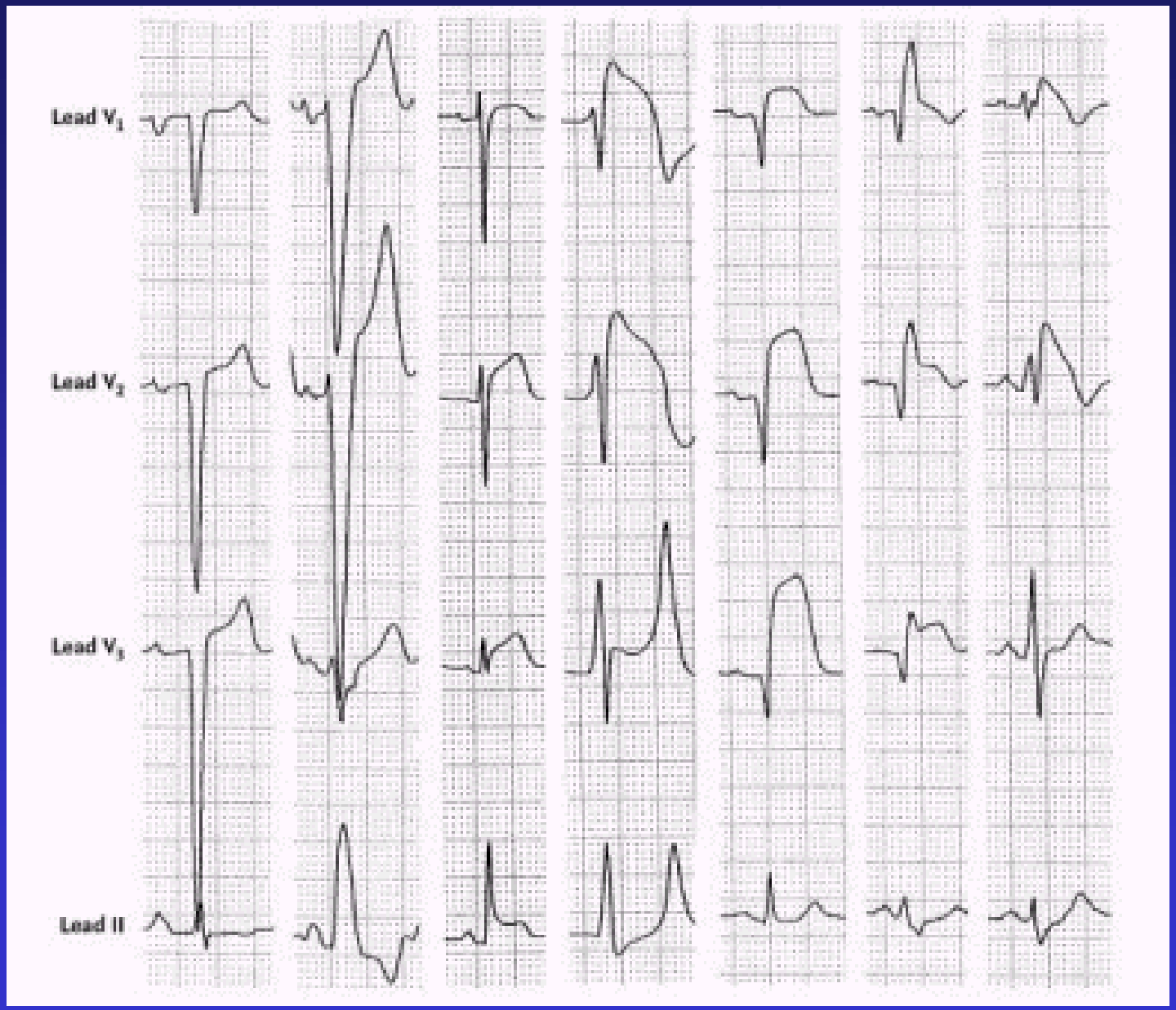
Upward ST Coving

Frown. This could be Trouble.

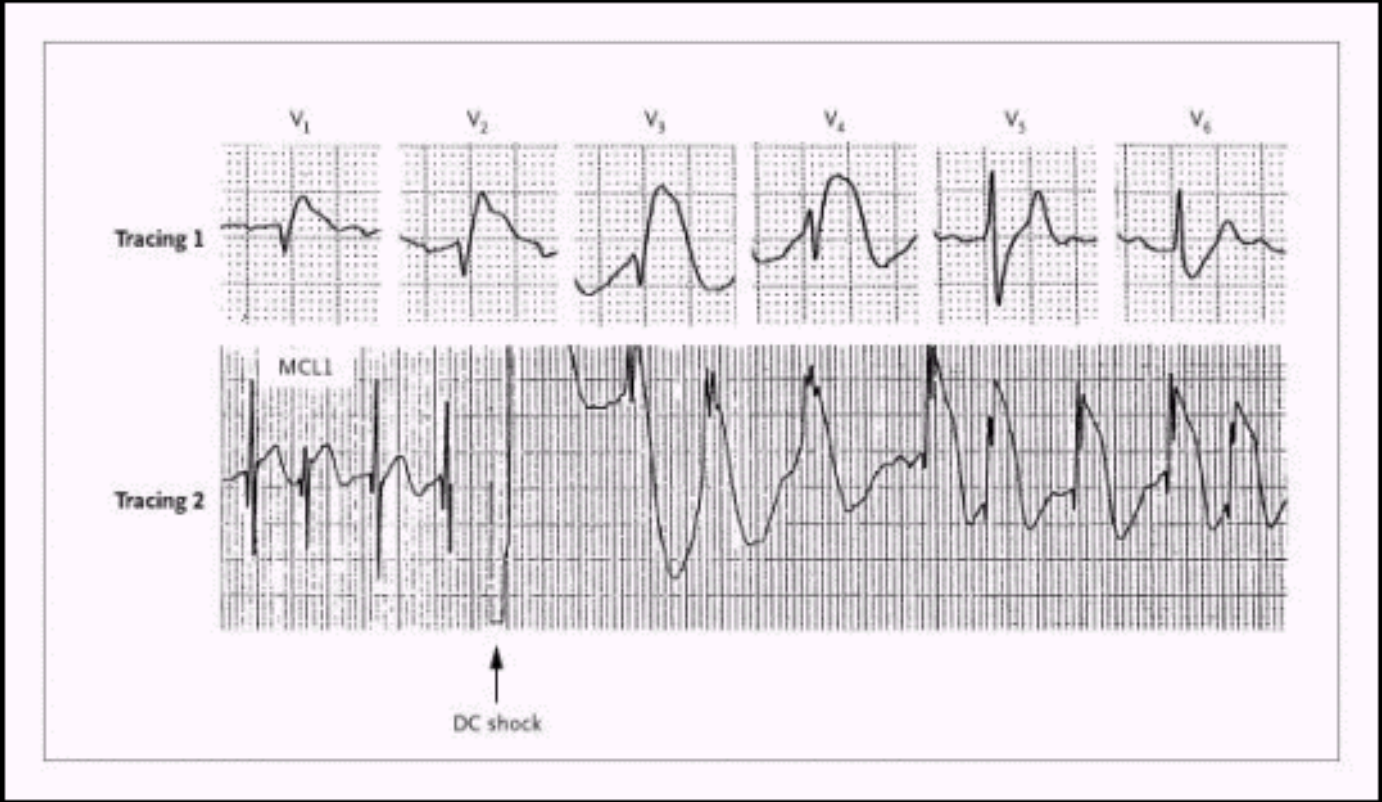
Electrocardiograms Showing Normal ST-Segment Elevation and Normal Variants



Wang, K. et al. N Engl J Med 2003;349:2128-2135

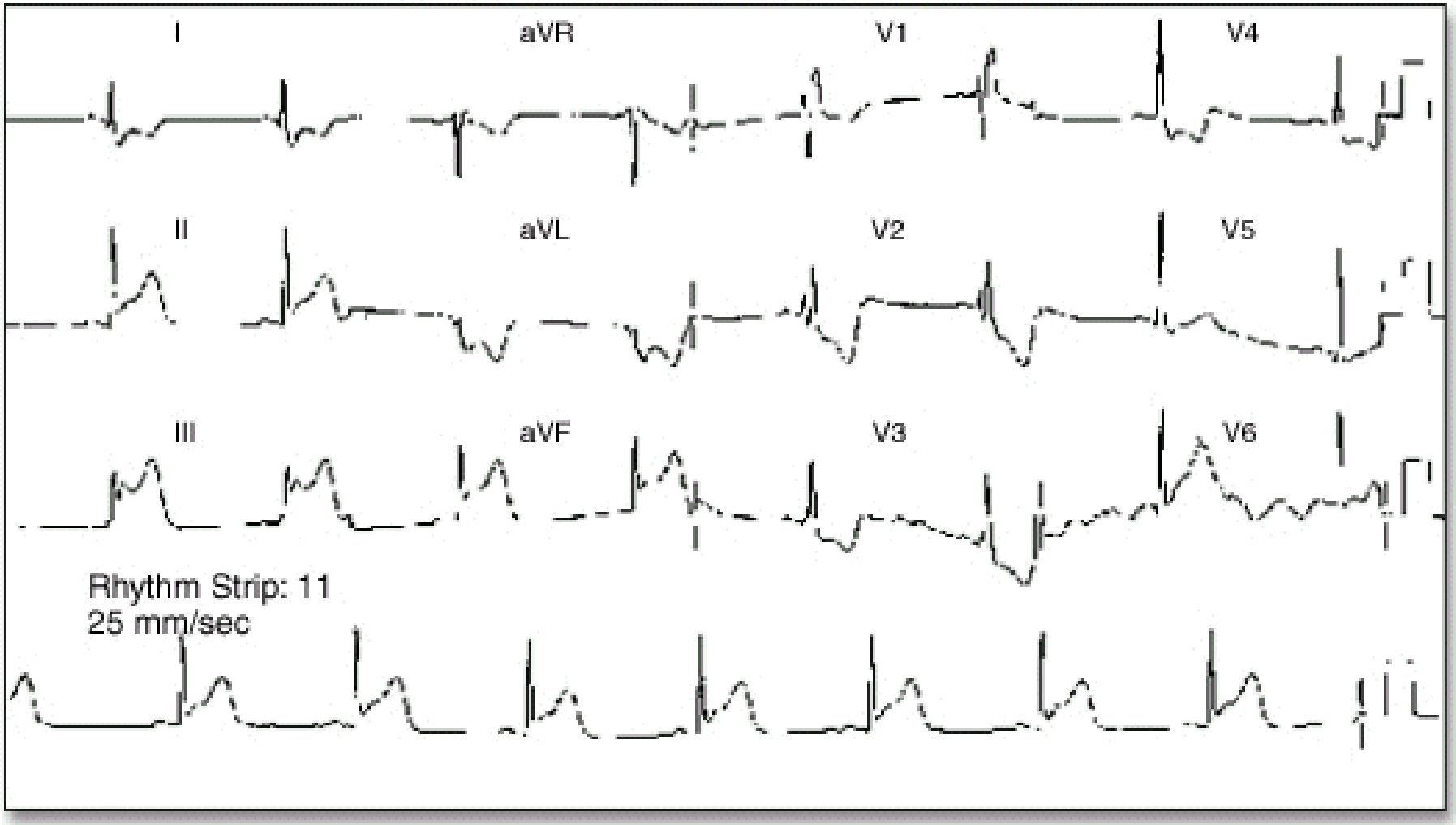

LVH
LBBB
Acute Pericarditis
Hyper-kalemia
Acute ASMI
Acute ASMI
Brugada Syndrome
Lead V1
Lead V2
Lead V3
Lead II

Electrocardiograms from a Patient with Massive Pulmonary Embolism Who Had a Normal Coronary Angiogram (Tracing 1) and a Patient with Transient ST-Segment Elevation Immediately after Direct-Current (DC) Countershock to the Precordium (Tracing 2)

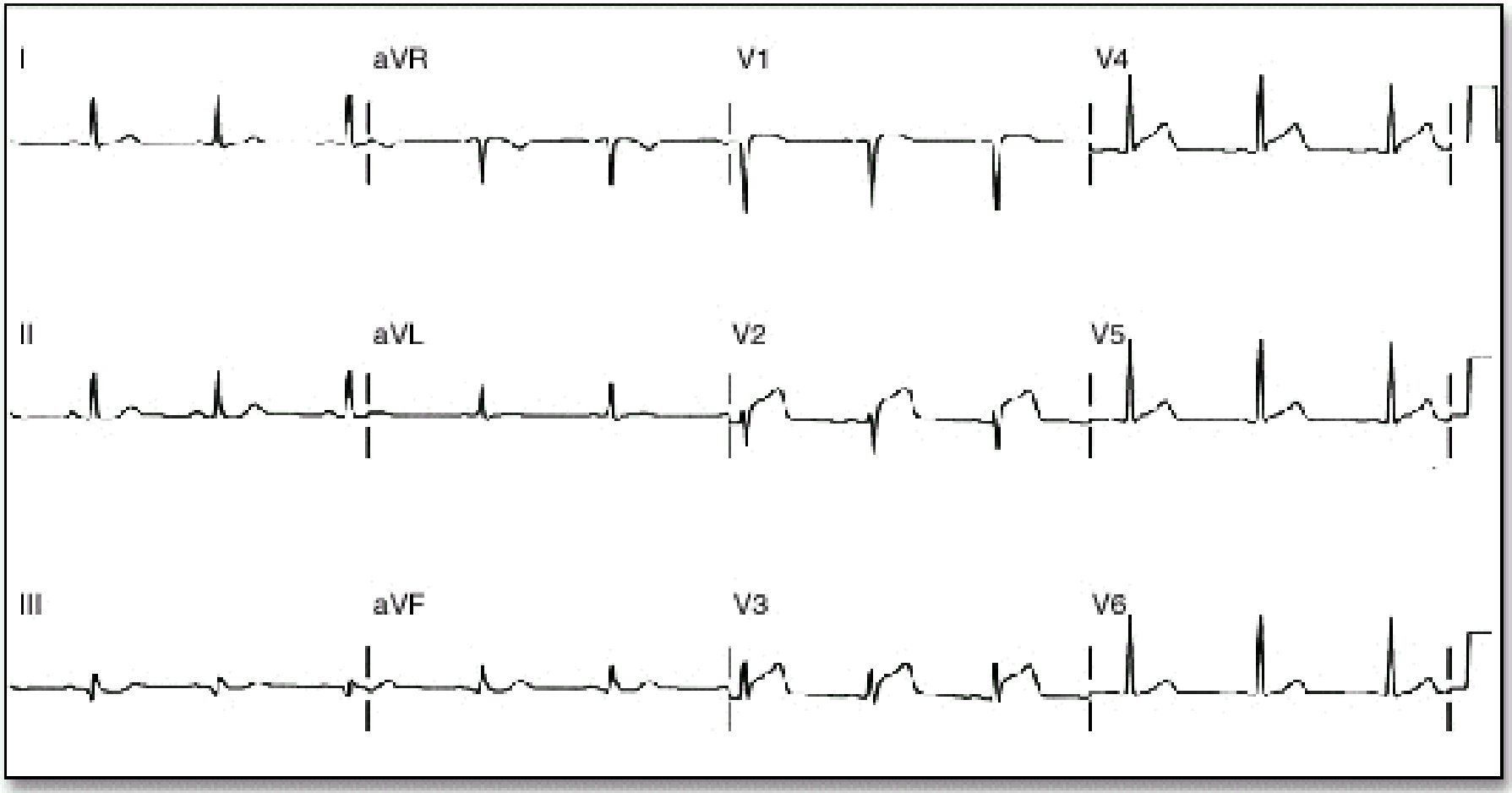


Wang, K. et al. N Engl J Med 2003;349:2128-2135

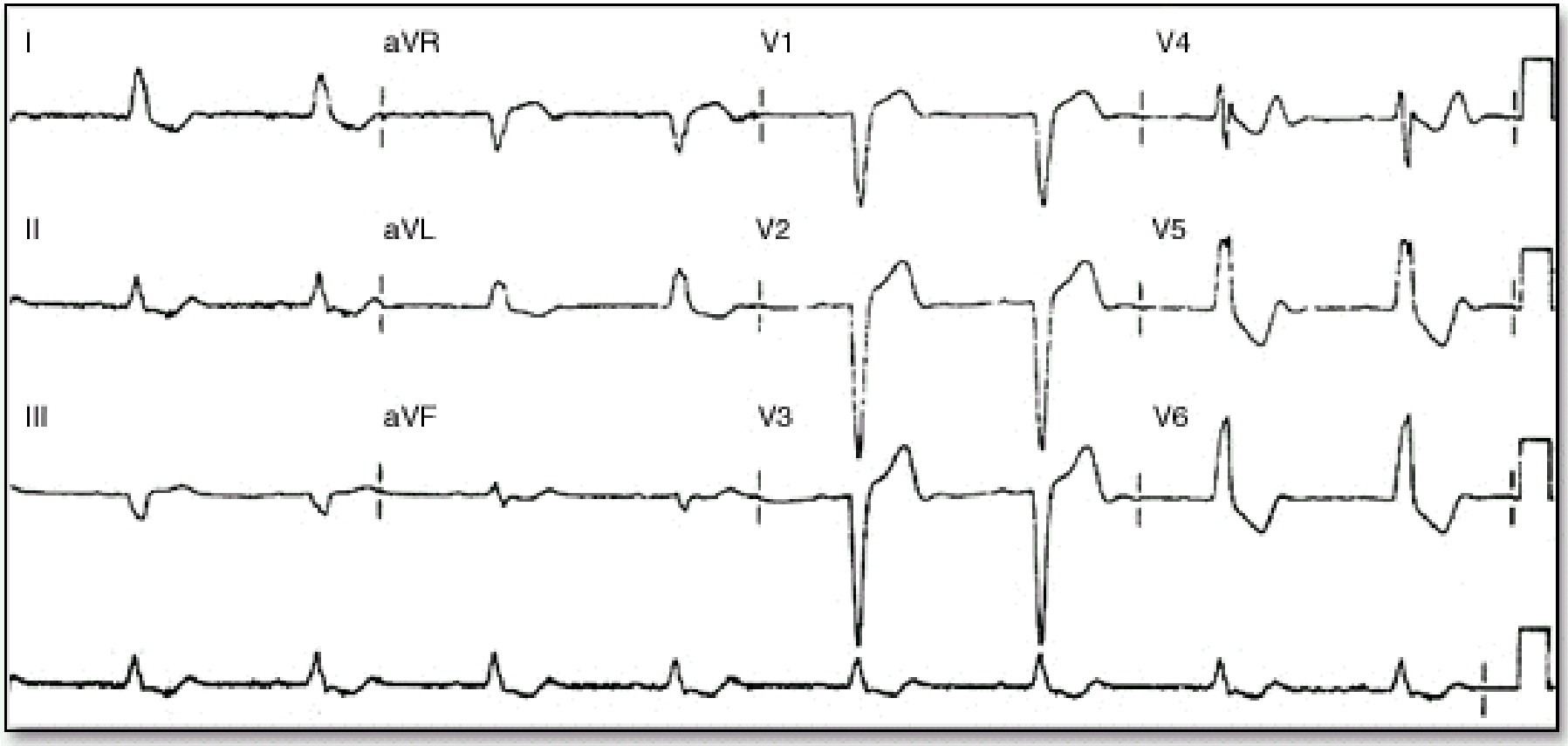
Inferior ST Elevation Infarction



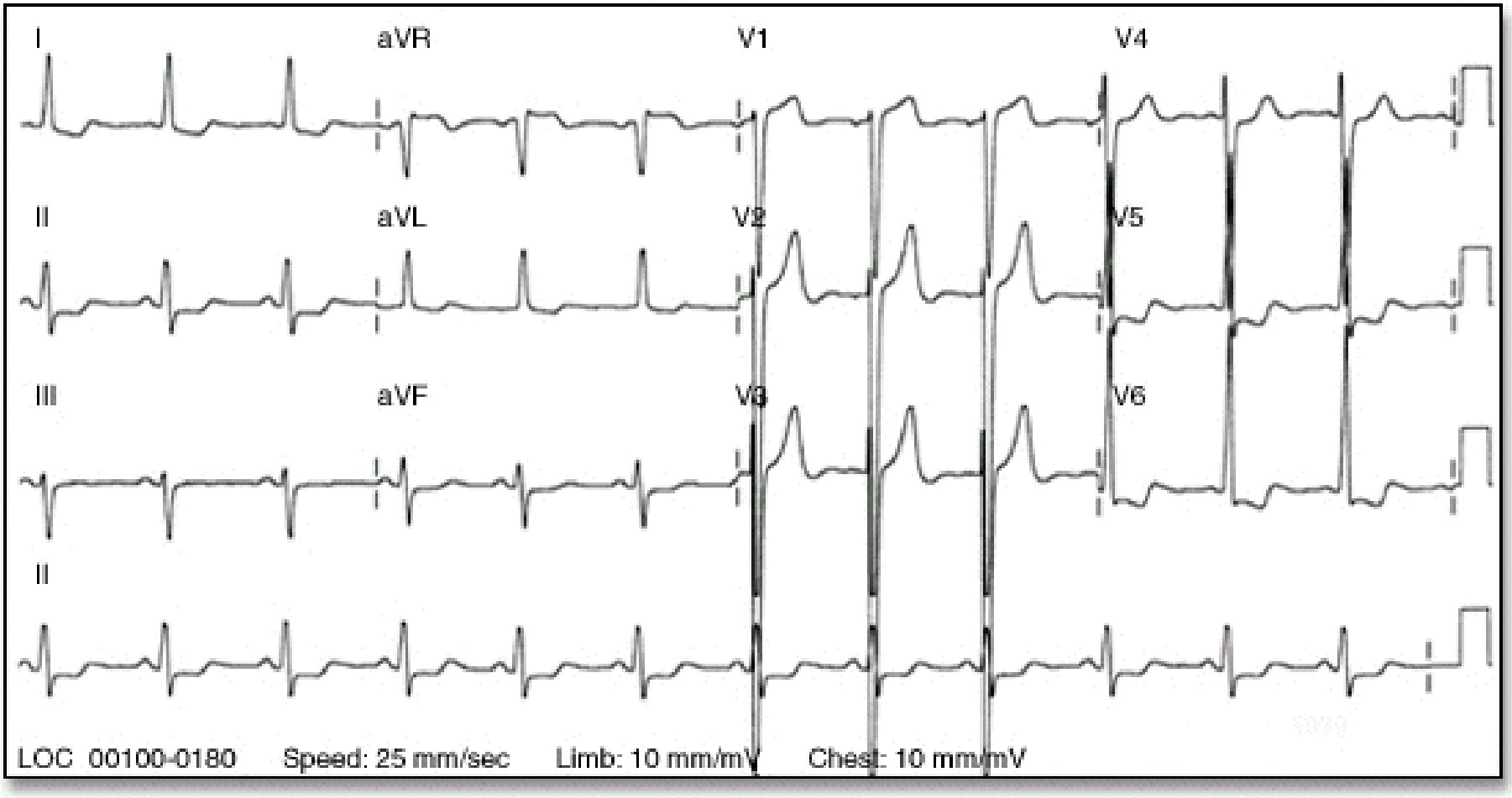
Typical Anterior ST Elevation Infarction



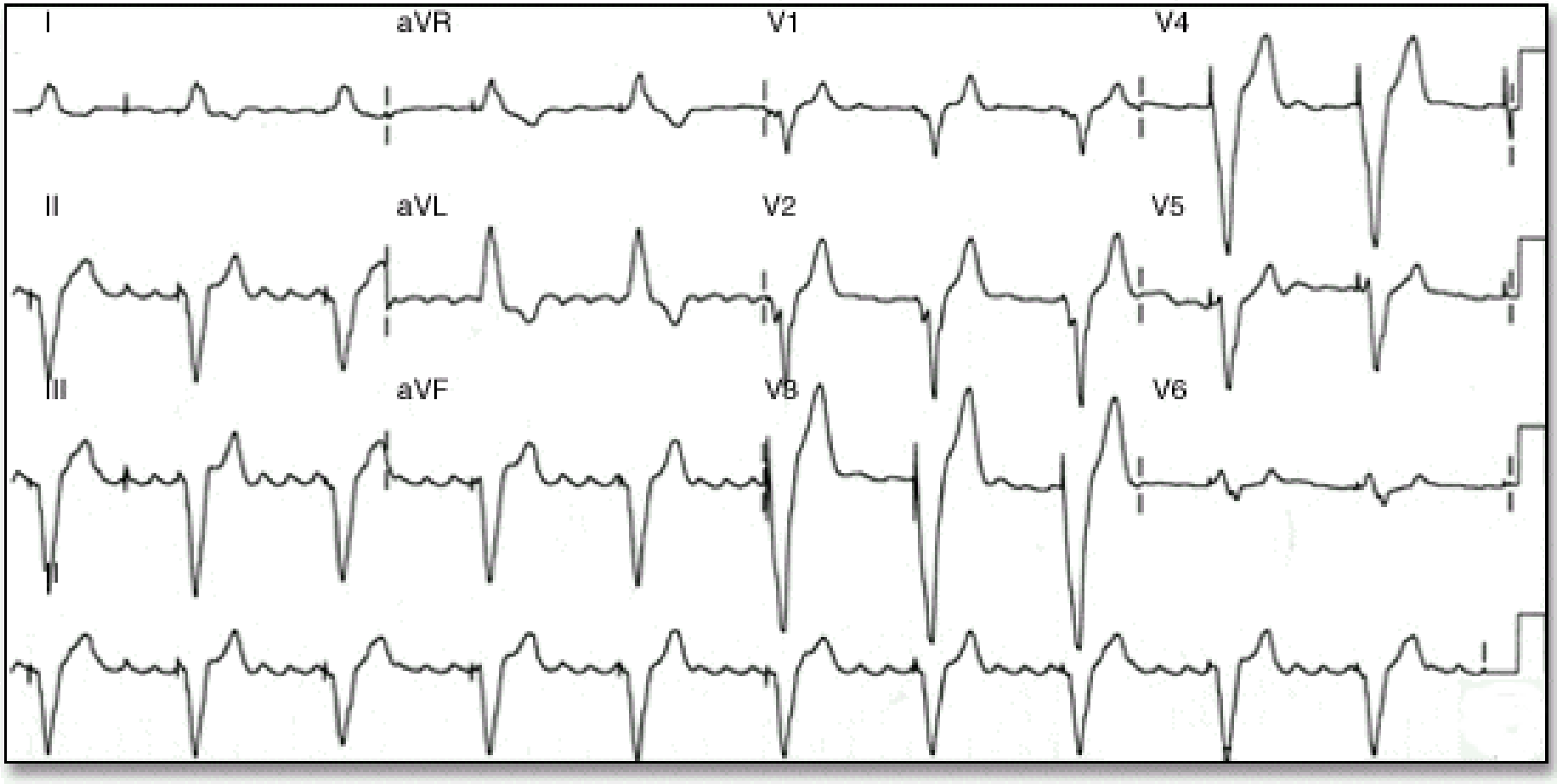
Characteristic Electrocardiogram of Bundle Branch Block



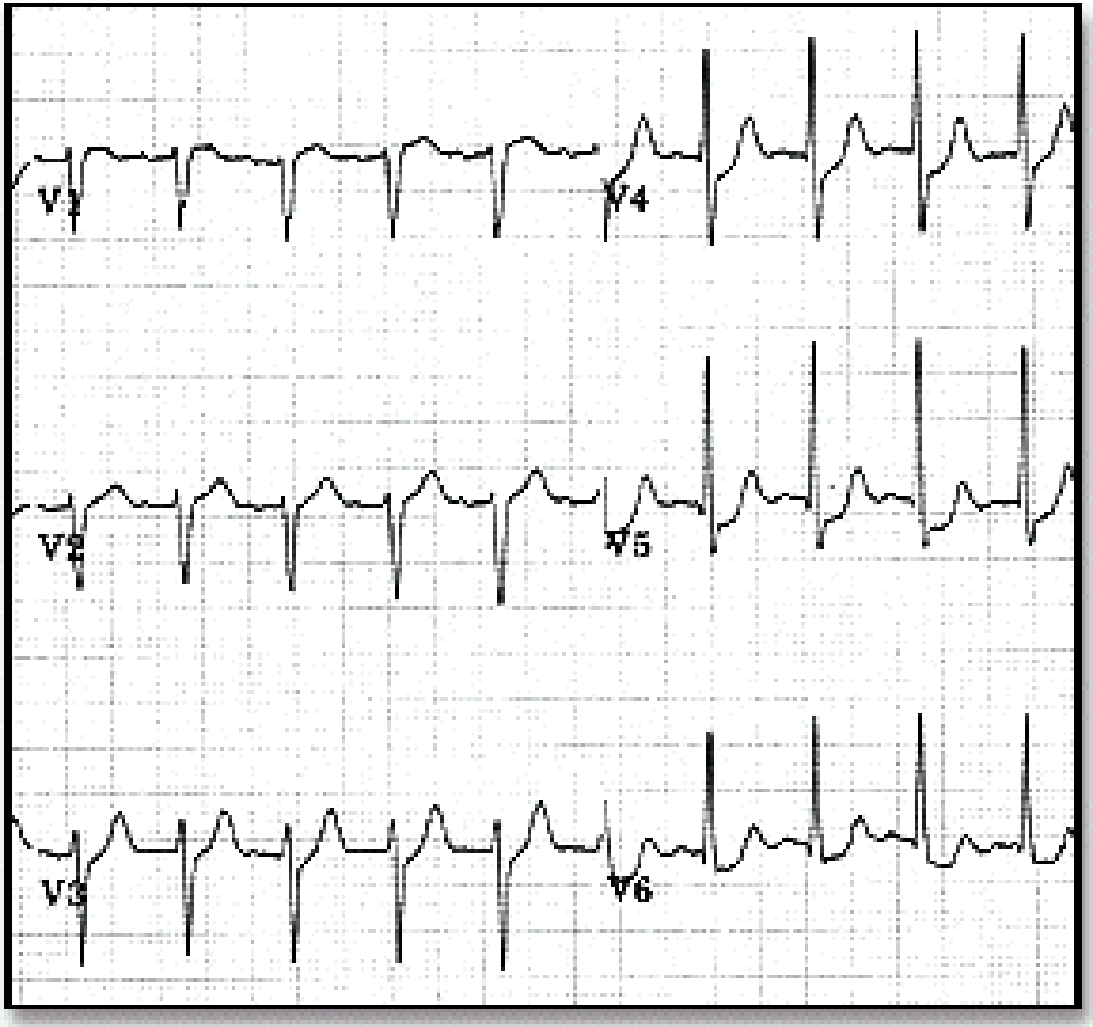
Characteristic Electrocardiogram of Left Ventricular Hypertrophy

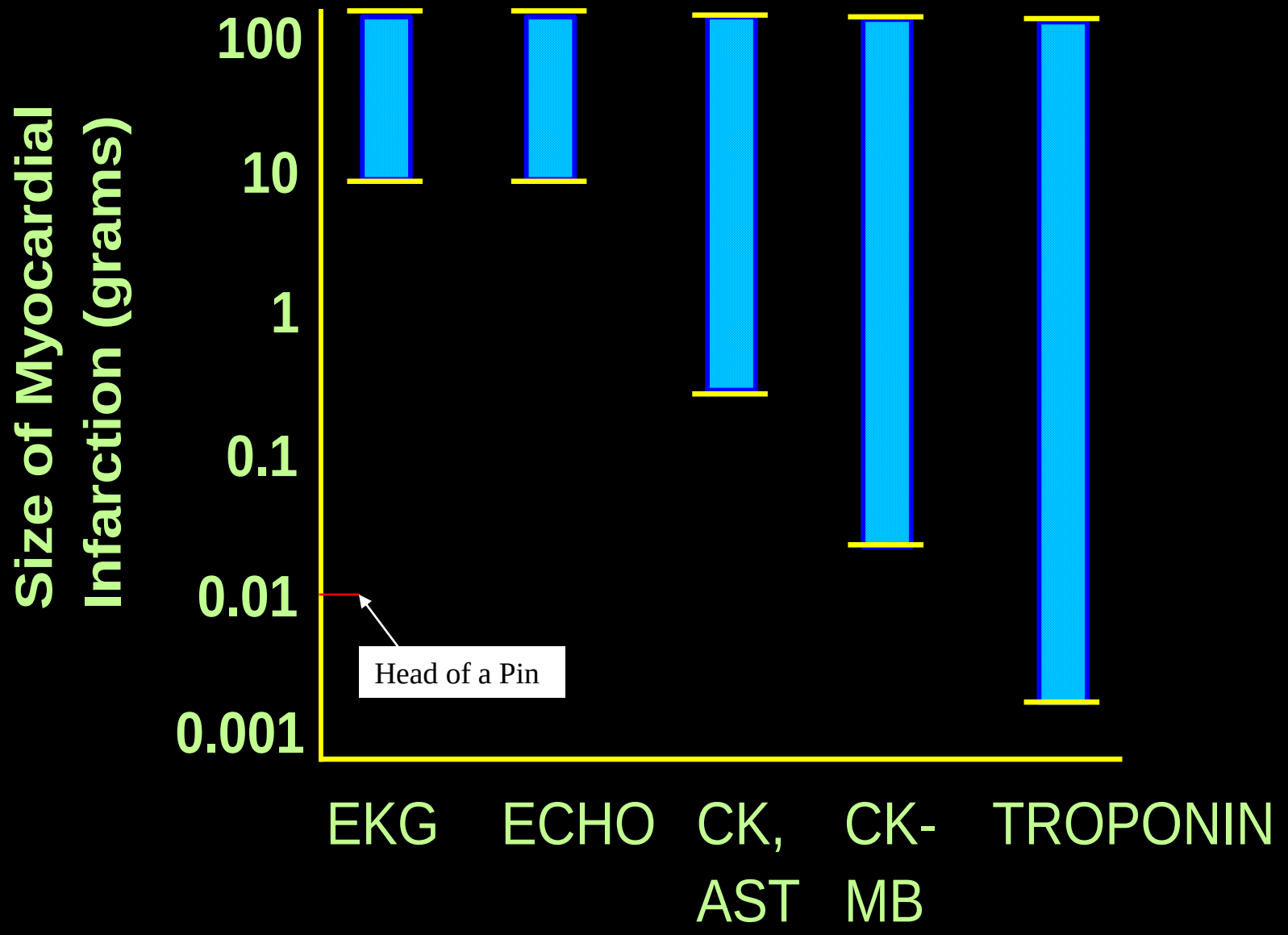


Characteristic Electrocardiogram of Paced Rhythm



Typical ST Depression





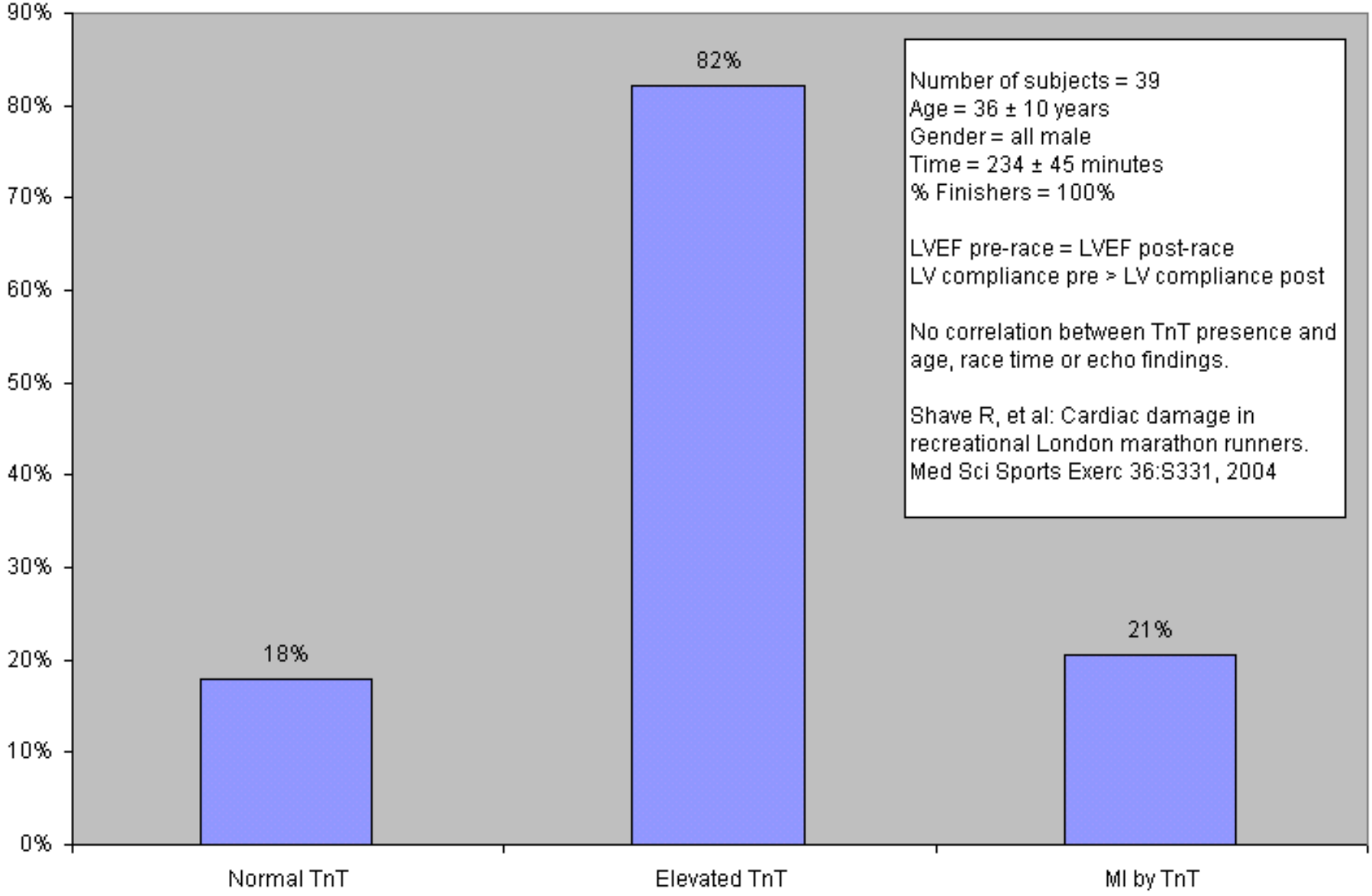
Normal heart weight = 230-340 grams

Reported Cases of Elevated Tpn-I

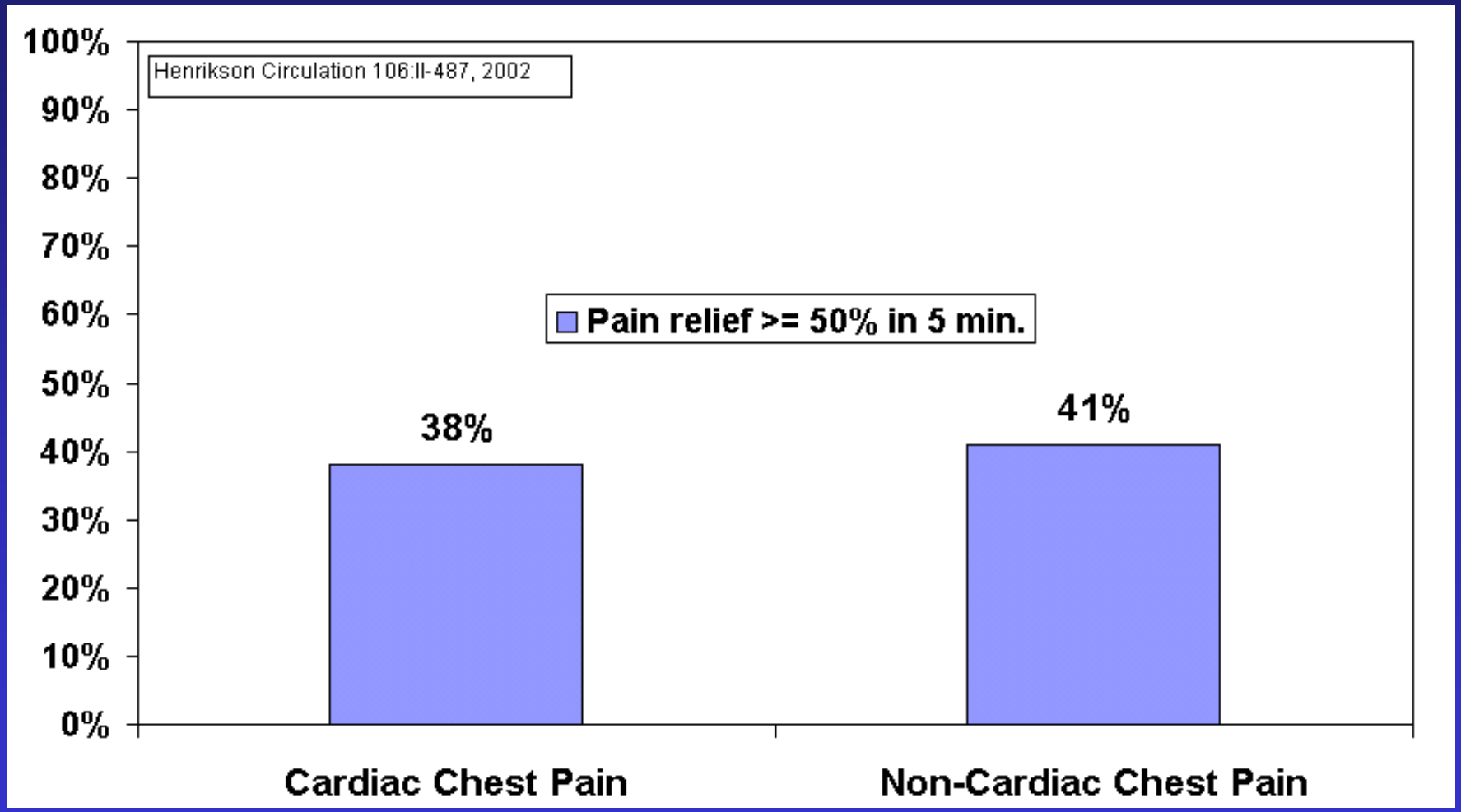
- Acute cardiac graft rejection
- Alk phosphatase elevation
- Cardiac contusion
- Cardiac amyloidosis
- CNS disorders
- Chemotherapy (anthracyclines)
- Cirrhosis of the liver
- Coronary vasospasm
- Heart failure - chronic
- Heart failure - acute - up to 89%
- Hematologic malignancies
- Heterophile antibody
- HIV disease
- Labor and delivery
- LVH
- Myocardial Infarction
- Pericardial effusion
- Pericarditis
- Pre-eclampsia
- Pulmonary embolism
- Renal failure, acute>chronic
- Sepsis/ Septic shock

JP Higgins, 9/02

Elevated Troponin T In Recreational London Marathon Runners



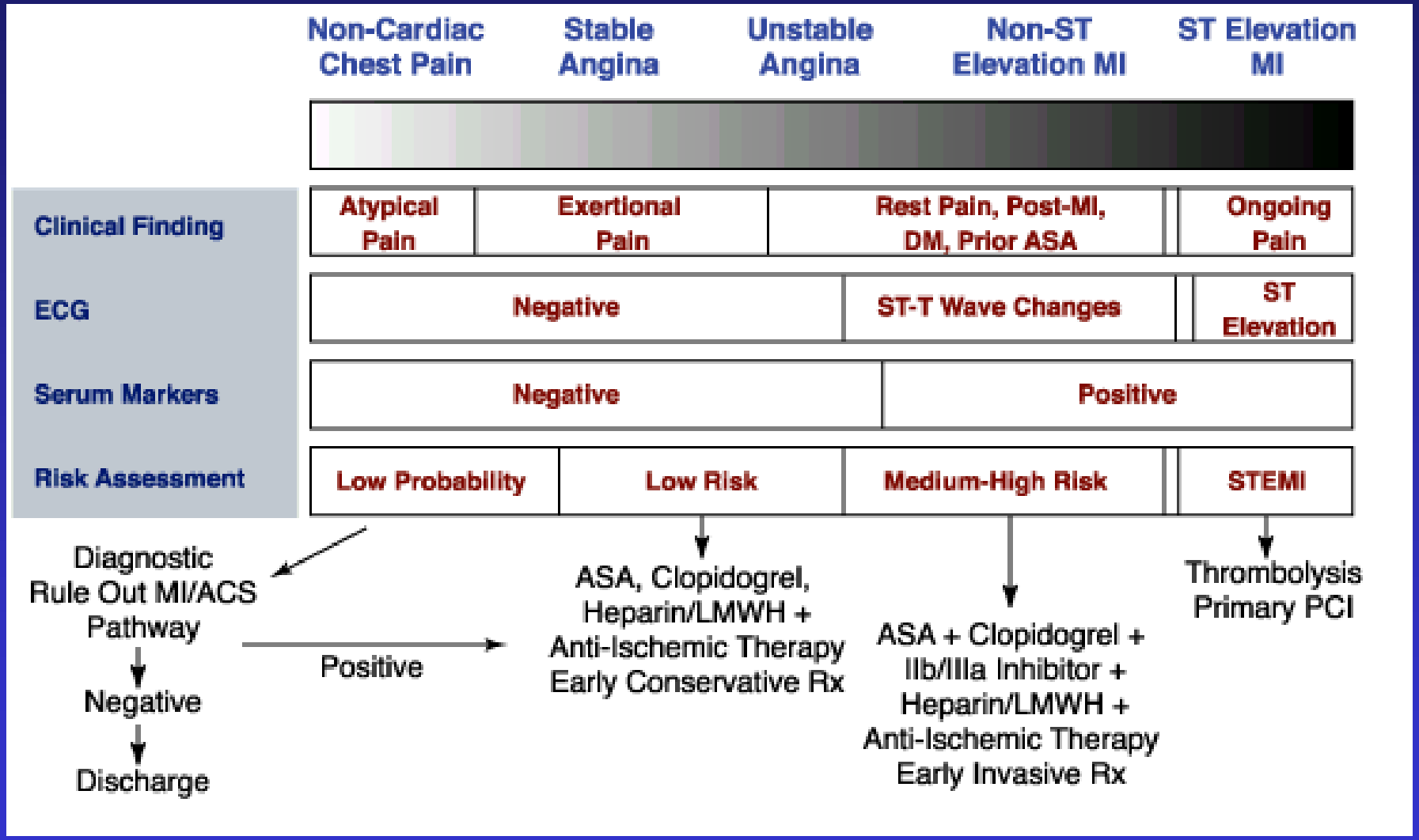
Response of Chest Pain in the E.R. to NTG: Johns Hopkins Hospital - 459 Patients (prospective)



Short-Term Risk of Death or Nonfatal MI in Patients with UA

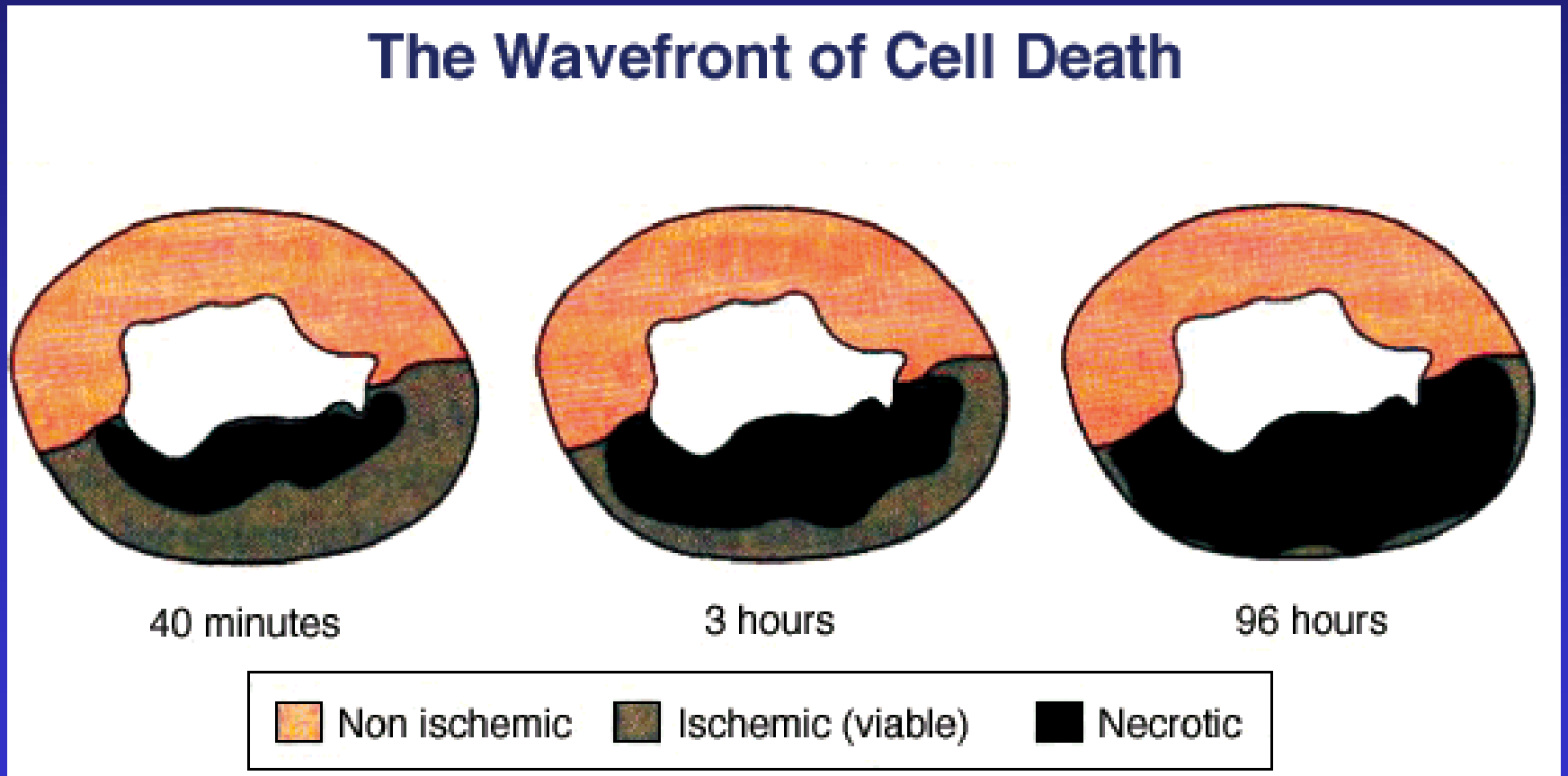
Feature	High-Risk At least 1 of the following features must be present:	Intermediate-Risk No high-risk feature but must have 1 of the following	Low-Risk No high- or intermediate-risk feature but may have any of the following features:
History	Accelerating tempo of ischemic symptoms in preceding 48 h	Prior MI, peripheral or cerebrovascular disease, or CABG, prior aspirin use	
Character of Pain	Prolonged ongoing (>20 minutes) rest pain	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD Rest angina (<20 min) or relieved with rest or sublingual NTG	New-onset CCS Class III or IV angina in the past 2 weeks without prolonged (>20 min) rest pain but with moderate or high likelihood of CAD (see Table 5)
Clinical Findings	Pulmonary edema, most likely due to ischemia New or worsening MR murmur, S_3 or new/worsening rales Hypotension, bradycardia, tachycardia Age > 75 years	Age >70 years	
ECG	Angina at rest with transient ST-segment changes >0.05 mV Bundle-branch block, new or presumed new Sustained ventricular tachycardia	T-wave inversions >0.2 mV Pathological Q waves	Normal or unchanged ECG during an episode of chest comfort
Cardiac Markers	Markedly elevated (e.g., TnT or TnI >0.1 ng/mL)	Slightly elevated (e.g., TnT > 0.01 but <0.1 ng/mL	Normal

Therapy for ACS

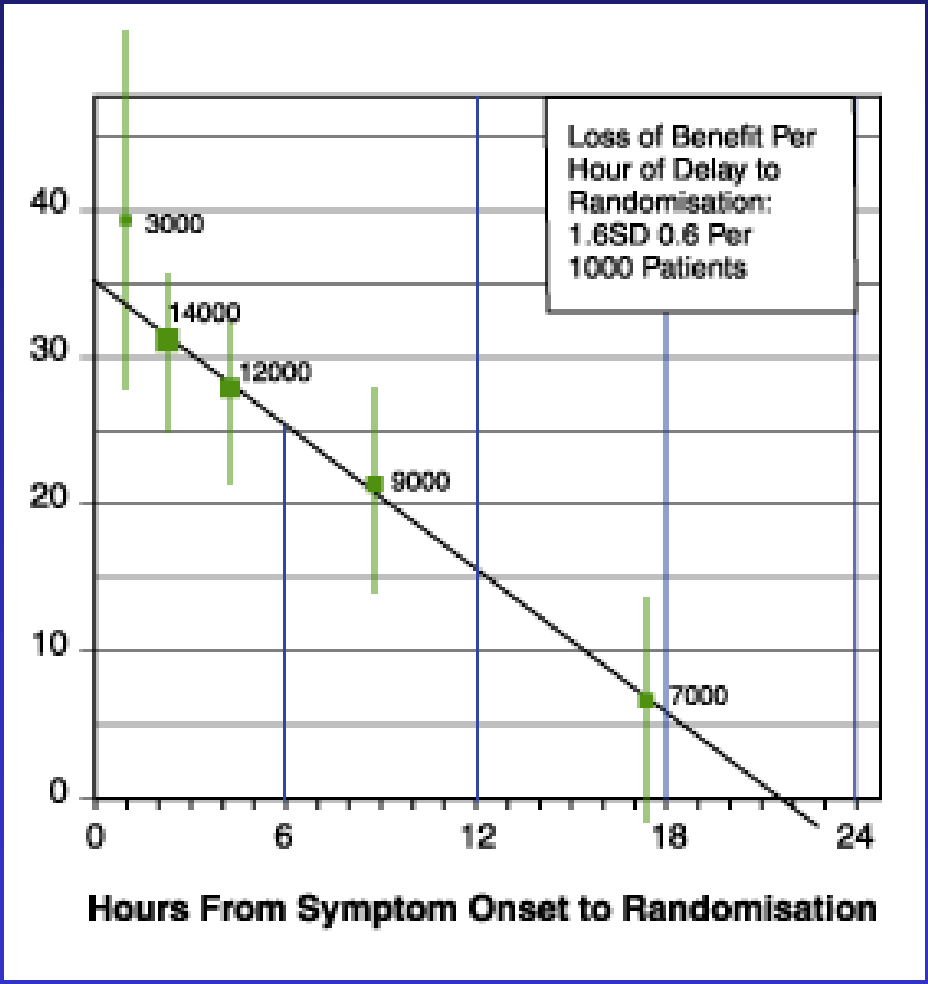


Christopher Cannon, M.D., 2004

Time and Infarction Size



Absolute benefit in terms of lives saved per thousand for patients treated with fibrinolytic therapy for ST elevation or bundle branch block MI



Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1,000 patients. Fibrinolytic Therapy Trialists (FTT) Collaborative Group. Lancet 1994;343:311-22.

Angioplasty vs. Thrombolysis for Acute ST-Elevation MI

Clinical Outcome at 30 Days

Outcome	Referral Hospitals			Invasive-Treatment Centers			All Hospitals		
	Fibrinolysis Group (N=562)	Angioplasty Group (N=567)	p Value	Fibrinolysis Group (N=220)	Angioplasty Group (N=223)	p Value	Fibrinolysis Group (N=782)	Angioplasty Group (N=790)	p Value
	no. (%)			no. (%)			no. (%)		
Death	48 (8.5)	37 (6.5)	0.20	13 (5.9)	15 (6.7)	0.72	61 (7.8)	52 (6.6)	0.35
Reinfarction	35 (6.2)	11 (1.9)	<0.001	14 (6.4)	2 (0.9)	0.002	49 (6.3)	13 (1.6)	<0.001
Disabling Stroke	11 (2.0)	9 (1.6)	0.64	5 (2.3)	0	0.02	16 (2.0)	9 (1.1)	0.15
Composite Endpoint	80 (14.2)	48 (8.5)	0.002	27 (12.3)	15 (6.7)	0.05	107 (13.7)	63 (8.0)	<0.001

Andersen HR, Nielsen TT, Rasmussen K, Thuesen L. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003;349:733-42

Criteria for Emergency Catheterization

- Symptoms or Signs of AMI <12 Hours Duration (1mm ST Elevation in 2 or More Contiguous Leads, New LBBB)
- Acute MI 12-24 Hours Duration With Continued Chest Pain
- Cardiogenic Shock Within 24 Hours (Patient Less than Age 75)
- Thrombolytic Failure Within 12 Hours of Chest Pain Onset
- Suspected Reocclusion After Thrombolytic Therapy
- ECG Evidence of True Posterior MI, Echocardiographic Wall Motion Abnormality, Positive Serum Markers, Refractory Angina, or Hemodynamic Instability/CHF

The SHOCK Trial

Cardiogenic shock: clinical criteria

- **Systolic blood pressure <90 mm Hg for 30 minutes before inotropes/vasopressors,**

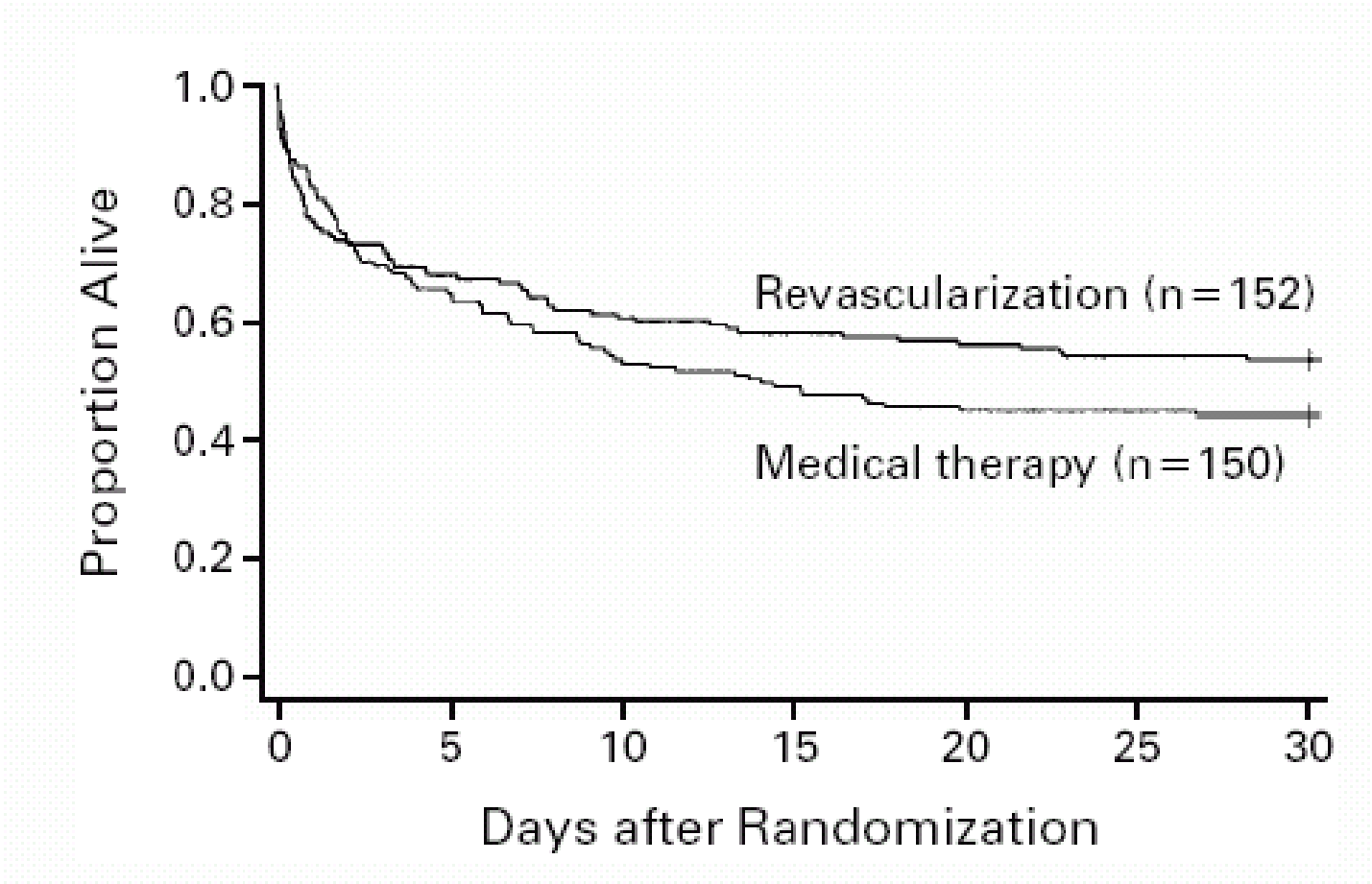
  or **vasopressors or IABP are required to maintain systolic blood pressure >=90 mm Hg**

- **Evidence of decreased organ perfusion**
- **Heart rate >=8O beats per minute (including paced rhythms)**

Cardiogenic shock: hemodynamic criteria

- **PCWP>/=15mmHg**
- **Cardiac Index <=2.2 L/min/m^2**

The SHOCK Trial



PCI and 2B3A Inhibitor Use in ACS

(1) Large-scale clinical trial evidence over the last decade has demonstrated, unquestionably, that **abciximab** plays an important and beneficial role in PCI patients,and this is evident among ACS subgroups in intent-to-stent trials. For **ST-segment elevation MI**, a strategy of interventional procedure with stents and adjunctive abciximab has been shown to be the reperfusion modality of choice when experienced operators and laboratory personnel are available **in a timely manner**. (This approach was shown to be superior to standard thrombolytic therapy in STOP-AMI and superior to direct PCI-stent without abciximab in ADMIRAL.)

(2) Dual therapy of low-dose reteplase and abciximab is safe and effective as shown in GUSTO-V, but because mortality rates did not differ from standard thrombolytic strategies, this approach is not likely to be competitive with a direct PCI strategy.

(3) Abciximab added to combination lytic approaches should be avoided in the elderly (age 75 years) and among patients who are being treated with streptokinase.

(4) The current standard of therapy for moderate-to-high risk non–ST-segment elevation ACS should include the administration of tirofiban or eptifibatide beginning soon after hospitalization, if immediate PCI is not planned.

(5) Because most of the benefits shown in the clinical trials were derived from the complementary use of PCI and intravenous GP IIb/IIIa antagonists, all but low-risk patients should undergo early cardiac catheterization for further risk stratification and possible revascularization while receiving the GP IIb/IIIa inhibitor infusion.

(6) Abciximab should be administered to ACS patients who are taken immediately to the catheterization laboratory or who are not already receiving a IIb/IIIa inhibitor before a planned PCI.

(7) Among patients undergoing primary coronary intervention, abciximab remains the reference standard of GP IIb/IIIa inhibitor initiated in the catheterization laboratory, though with an increased cost.

David J. Moliterno, MD, FACC, Albert W. Chan, MD (Cleveland Clinic): Glycoprotein IIb/IIIa Inhibition in Early Intent-to-Stent Treatment of Acute Coronary Syndromes: EPISTENT, ADMIRAL, CADILLAC, and TARGET (J Am Coll Cardiol 2003;41:49S–54S)


GOOD
NEWS