



Acute Coronary Syndromes and Myocardial Infarction

Scott M. Lilly, MD, PhD

Interventional Cardiology

Associate Professor

Division of Cardiology

The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

 **THE OHIO STATE UNIVERSITY**
WEXNER MEDICAL CENTER

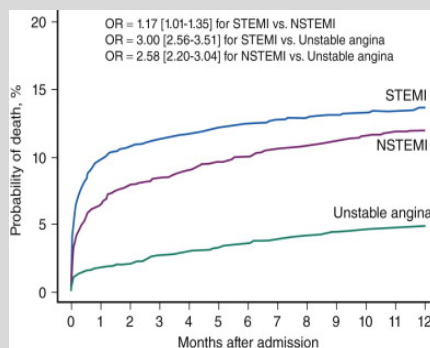
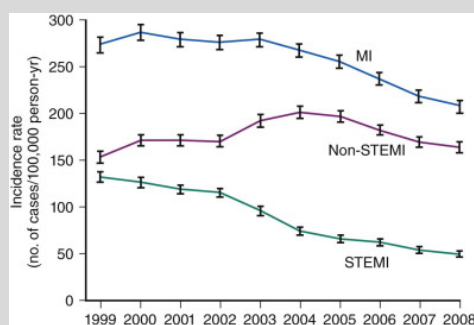
Outline

- EPIDEMIOLOGY AND ATHEROGENESIS
- SPECTRUM OF ACS
- MEDICAL THERAPY
- REVASCULARIZATION – WHO AND WHEN?

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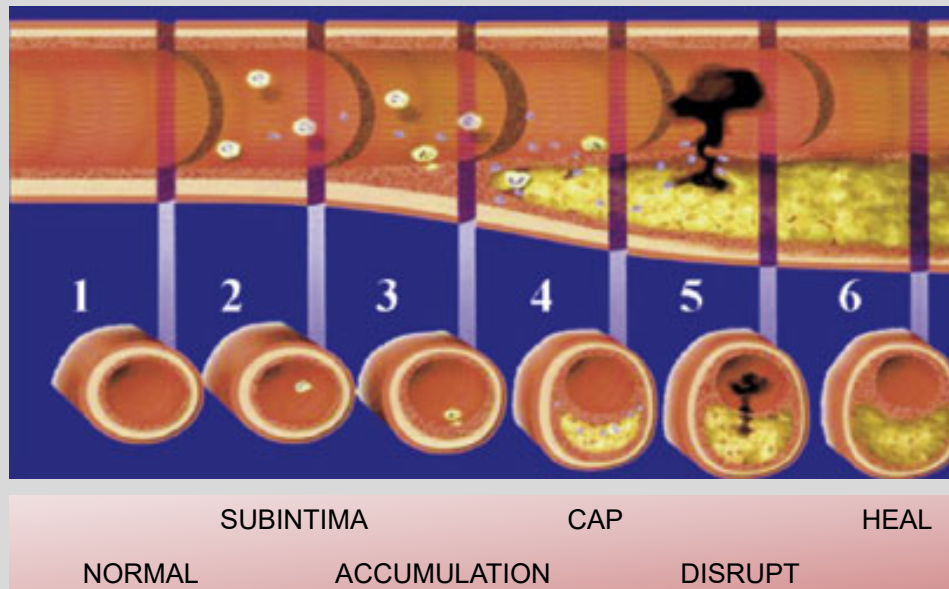
Epidemiology of ACS



- Overall incidence and mortality of ACS is decreasing
- STEMI ~ 30-40% of all AMI, and associated mortality has not changed
 - May reflect broader definition of ACS due to sensitive biomarkers
- Remains a major health problem, with opportunities for uniformity in care

Yeh et al. 2010
 AHA National Discharge Survey
 Ndrepepa et al. 2009

Atherogenesis and ACS



Libby et al. 2001 Circ; Amsterdam et al., 2014 JACC

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Acute Coronary Syndrome

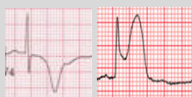
A constellation of symptoms related to **abrupt myocardial ischemia** with **chest pain** being the most common symptom.

ANGINA

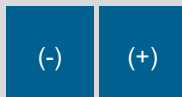
Substernal
Provoked by exertion or emotional stress
Relieved by rest or nitroglycerin

The **spectrum of clinical conditions** includes UA, NSTEMI, STEMI

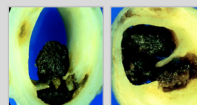
ECG



BIOMARKERS



HISTOLOGY



Possible ACS: Initial Steps

A constellation of symptoms related to **abrupt myocardial ischemia** with **chest pain** being the most common symptom.

ANGINA

Substernal
Provoked by exertion or emotional stress
Relieved by rest or nitroglycerin

- History and Physical
- **Electrocardiogram**
- **Cardiac biomarkers**
- CBC, metabolic panel, PT/INR
- Telemetry
- Chest X-ray
- Supplemental Oxygen
- Analgesia
- Aspirin

Suspected ACS: Evaluation

Differential diagnosis

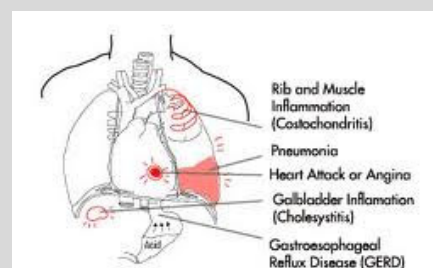
*Aortic dissection, pulmonary embolism,
esophageal rupture, pneumothorax, pneumonia*

Assess Bleeding Risk

Previous bleeding ulcers, melena, on coumadin

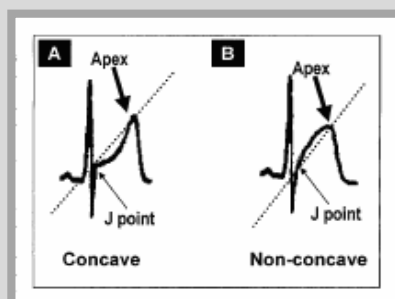
Assess Cerebrovascular Disease

Assess Drug use



“Concave” vs. “Convex” ST Elevation

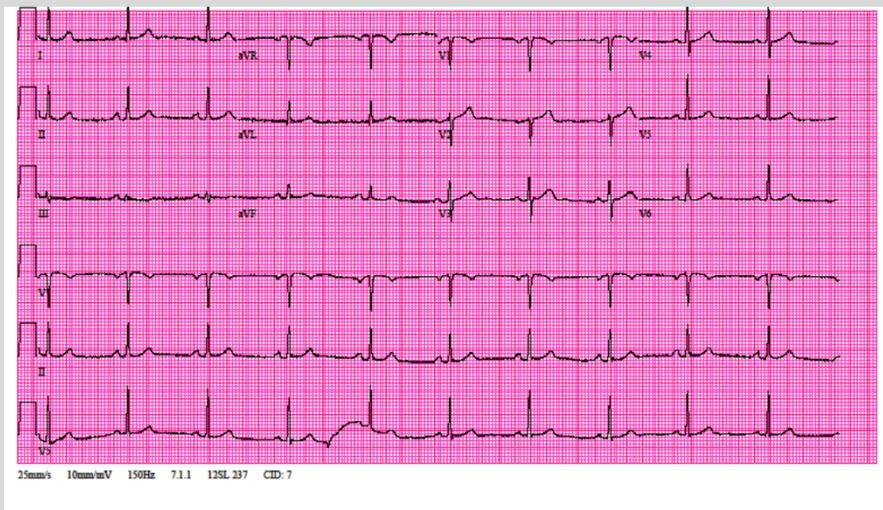
- J-point is the initial part of the ST Segment
- ST Segment is a time of electrocardiographic silence
- Ischemia and injury cause alter the ST segment



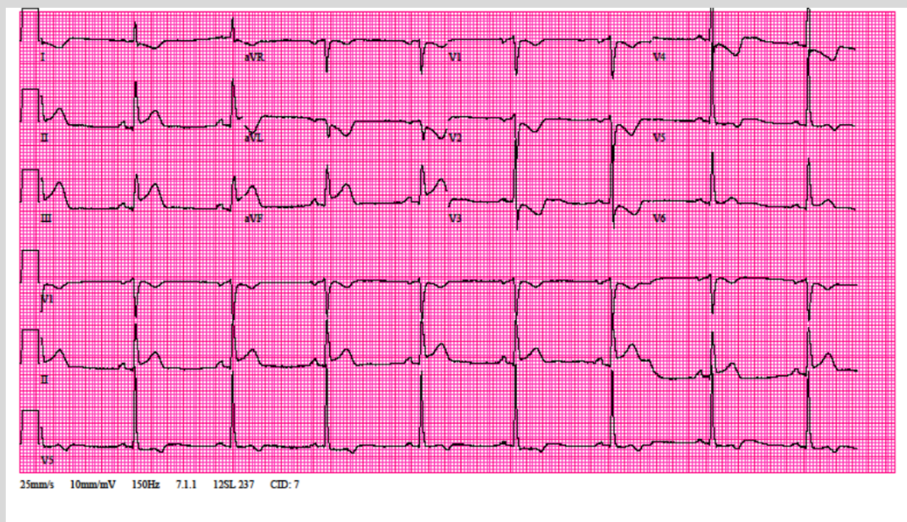
Case

- 56 Year Old Female
 - Called EMS for sharp 8/10 Chest Pain for 3 hours
 - PMH: “mild heart attack in 2003”, COPD
 - Today with different symptoms than in 2003
 - EMS treatment
 - Oxygen
 - Nitroglycerin
 - IV
 - 12 Lead EKG

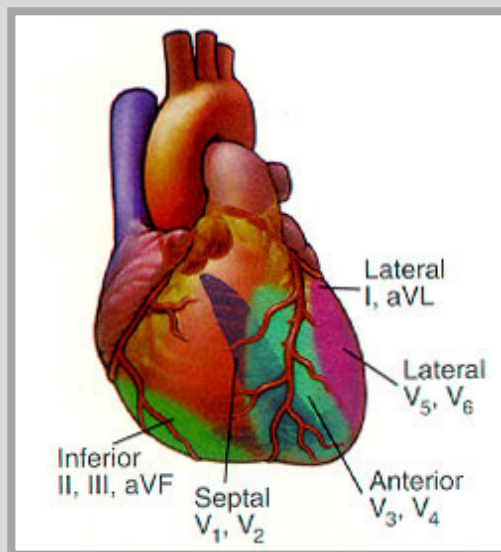
First ED EKG



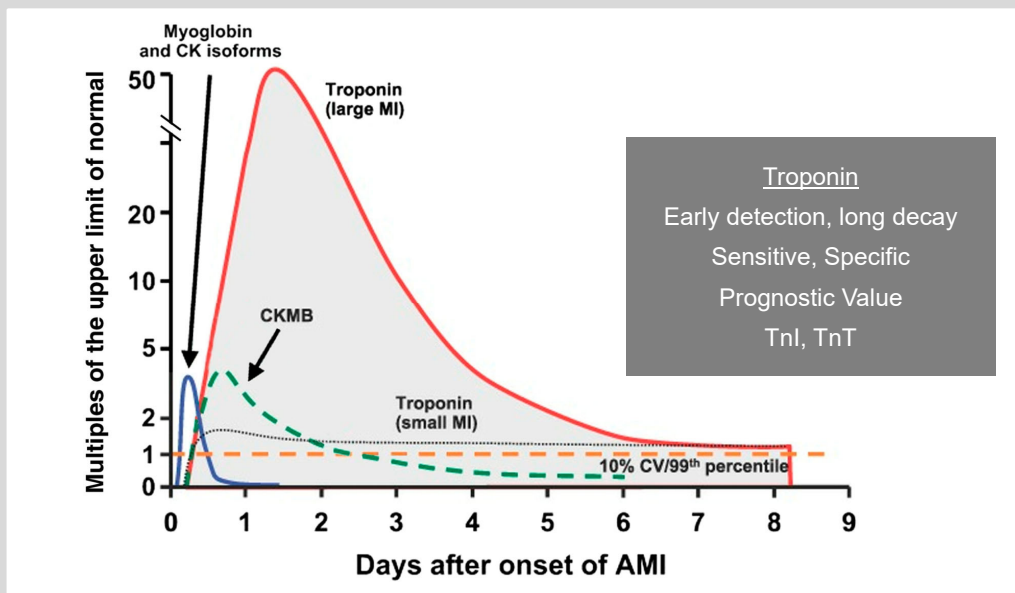
Frequent Repeat EKG Are Important



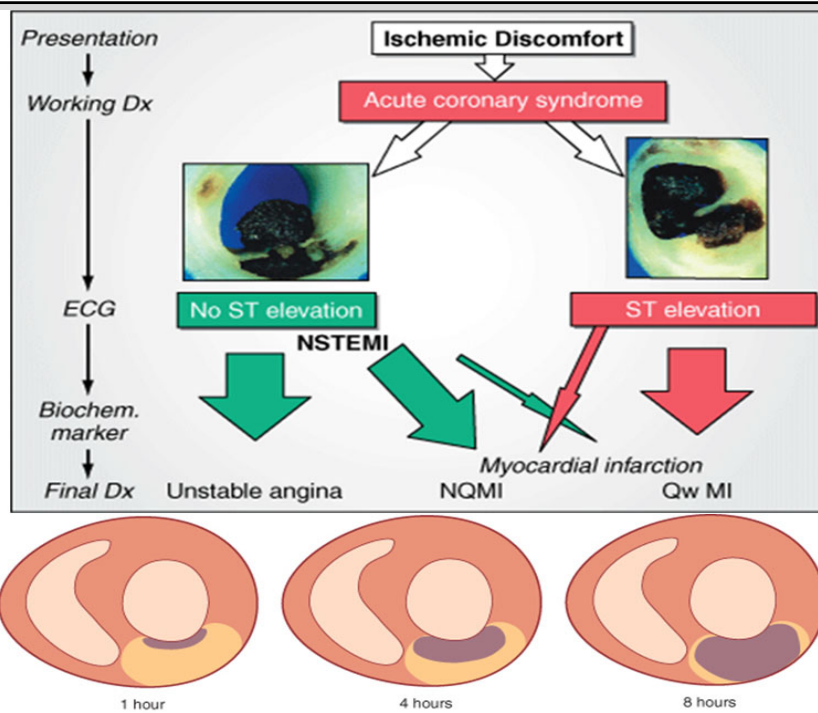
ECG Anatomy



Biomarker Release in ACS



Shapiro et al., JACC 2007



ACC/AHA Guidelines for UA/NSTEMI 2007

The Spectrum of ACS

- **STEMI**
 - ST elevation, **elevated** cardiac enzymes
 - > 1 mm in limb leads, > 2 mm in precordial leads (V2-3)

- **NSTEMI**
 - ST depression, T-wave inversion, **elevated** cardiac enzymes

- **Unstable Angina**
 - Non specific EKG changes, **normal** cardiac enzymes

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- EPIDEMIOLOGY AND ATHEROGENESIS

- SPECTRUM OF ACS

- **MEDICAL THERAPY**

- REVASCULARIZATION – WHO AND WHEN?

Management: Core Measures

- Telemetry
- Serial troponin, CBC, metabolic panel, PT/PTT/INR
- Initial bedrest and NPO; 2 peripheral IVs
- Cardiology Consult
- Oxygen
- Nitroglycerin
- Morphine



INDIVIDUALIZE

Management: Core Measures



James B. Herrick
1861 – 1954

“The importance of absolute rest in bed for several days is clear”



Source for James B. Herrick - Br J Haematol, Volume: 112, Issue: 1, Pages: 3-18, First published: 20 December 2001, DOI: (10.1046/j.1365-2141.2001.02557.x)

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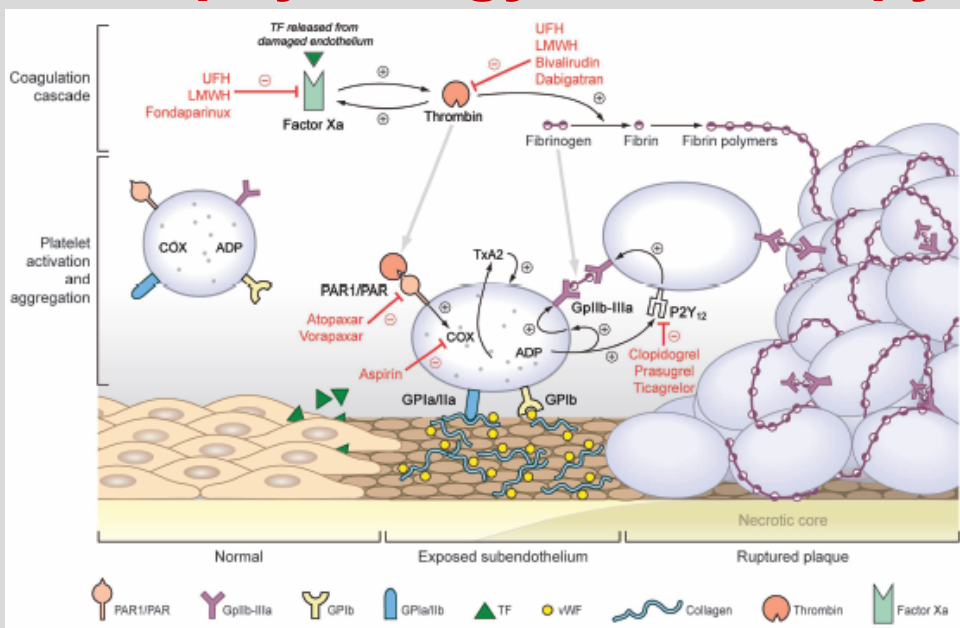
PREVALENCE OF TOTAL CORONARY OCCLUSION DURING THE EARLY HOURS OF TRANSMURAL MYOCARDIAL INFARCTION

MARCUS A. DeWOOD, M.D., JULIE SPORES, C.R.N.A., ROBERT NOTSKE, M.D., LOWELL T. MOUSER, M.D., ROBERT BURROUGHS, M.D., MICHAEL S. GOLDEN, M.D., AND HENRY T. LANG, M.D.



DeWood et al. 1980; NEJM 303:897-902.

Pathophysiology and Therapy



Lilly and Wilensky, Curr Pharm Ther 2011

ACS Management: Drug Therapy

Address Pathophysiology

- Anti-platelet
 - Aspirin
 - ADP-Receptor Inhibitor
 - Clopidogrel
 - Prasugrel
 - Ticagrelor
- Anti-coagulation

Minimize Consequences

- Beta-receptor antagonists
- ACE-inhibitors
- Statins

Management: Drug Therapy

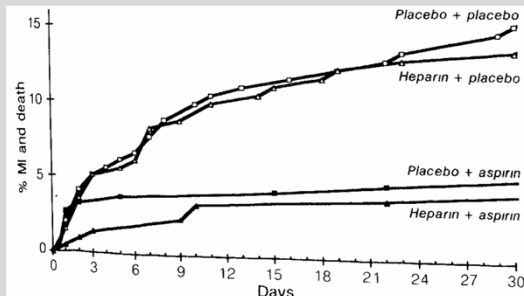
Address Pathophysiology

- **Anti-platelet**
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 - **ADP-Receptor Inhibitor**
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- Anti-coagulation

Minimize Consequences

- Beta-receptor antagonists
- ACE-inhibitors
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Aspirin in ACS

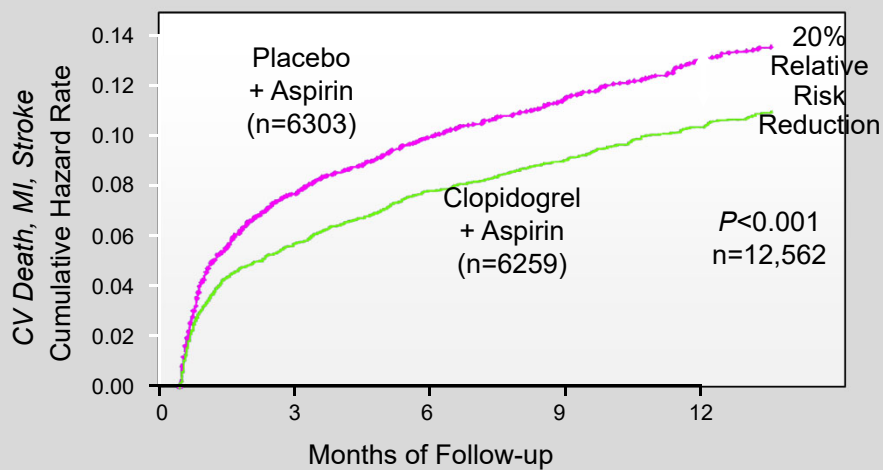


Multiple trials
30-50% ↓ RR in
death, myocardial
infarction

	COR	LOE
Antiplatelet therapy		
Aspirin		
• 162- to 325-mg load before procedure	I	B
• 81- to 325-mg daily maintenance dose (indefinite)*	I	A
• 81 mg daily is the preferred maintenance dose*	IIa	B

O'Gara et al. 2013 ACC/AHA STEMI Guideline.
O'Gara et al., STEMI Guidelines; The RISC Group. Lancet. 1990

CURE: Clopidogrel for UA/NSTEMI

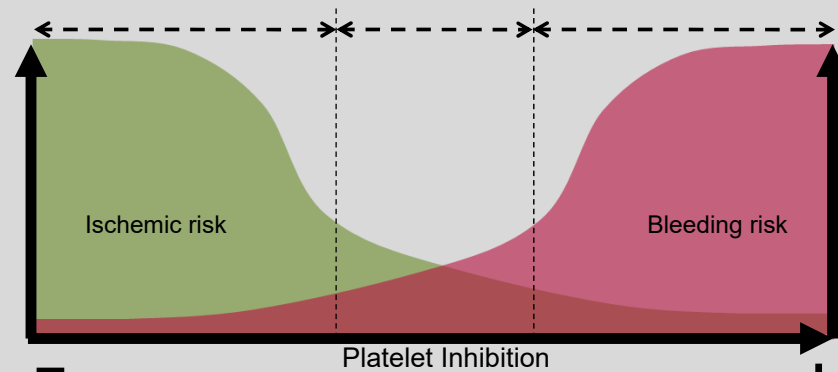


Yusuf S et al. N Engl J Med. 2001;345:494.

ADP-Receptor Inhibitors

	CLOPIDOGREL	PRASUGREL	TICAGRELOR	CANGRELOR
Plt inhibition	40-60%	70%	80-90%	95-100%
Pharmacology	Irreversible, pro-drug	Irreversible, pro-drug	Reversible, active drug	Reversible, active drug
Onset	2-4h h	30 min	30 min	2 min
Duration	3-10 d	5-10 d	3-4 d	60-90 min
Trials	CURE	TRTON TIMI-38	PLATO	CHAMPION PHOENIX
Outcomes	Standard	↓ CV Mort, MI, CVA	↓ CV Mort, MI, CVA**	↓ MI, ST
Dose/Cost	QD/+	QD/++	BID/+++	IV/++++

Balancing Risks



	PRASUGREL	TICAGRELOR	CANGRELOR
Ischemia/MACE	Reduced	Reduced	Reduced
Bleeding	Increased	No increase	Increased
Mortality	No change	Reduced	No change
Exclusions	CVA/TIA, < 60 kg, > 75 yo	ICH	ICH

Management: Drug Therapy

Address Pathophysiology

- Anti-platelet
 - Aspirin
 - ADP-Receptor Inhibitor
 - Clopidogrel
 - Prasugrel
 - Ticagrelor
- **Anti-coagulation**

Minimize Consequences

- Beta-receptor antagonists
- ACE-inhibitors
- Statins

Anti-Coagulation

▪ Unfractionated Heparin

- 50-70 u/kg bolus, 12 units/kg/hr
- PTT 1.5 – 2.0 x institutional control value

Historical Standard

▪ Enoxaparin

- 30 mg iv x 1, 1 mg/kg sc q12h
- Renal and age adjusted

Especially in
Conservatively
Managed

▪ Bivalirudin

- 0.1 mg/kg bolus, 0.25 mg/kg/h
- Renal adjusted

Decreased Bleeding
Rates

▪ Fondaparinux

- 2.5 mg sc x 1

Catheter Thrombosis,
Use Heparin as well

Management: Drug Therapy

- **Beta-blocker (~30%)**
 - Metoprolol (25 mg q6h) or atenolol (25 mg q12h)
 - *Within 24 hours*
 - Escalate to heart rate and blood pressure goals
- **ACE-inhibitors (~ 20%)**
 - Captopril 6.25 mg q6, enalapril 2.5 mg qd, lisinopril 2.5 mg qd
 - *Within 24 hours*
 - Escalate to heart rate and blood pressure goals
 - ARB if ACE-I intolerant
- **Statin therapy**
 - Atorvastatin 80 mg qd
 - *Preferably before PCI*

Summary of Medical Therapy

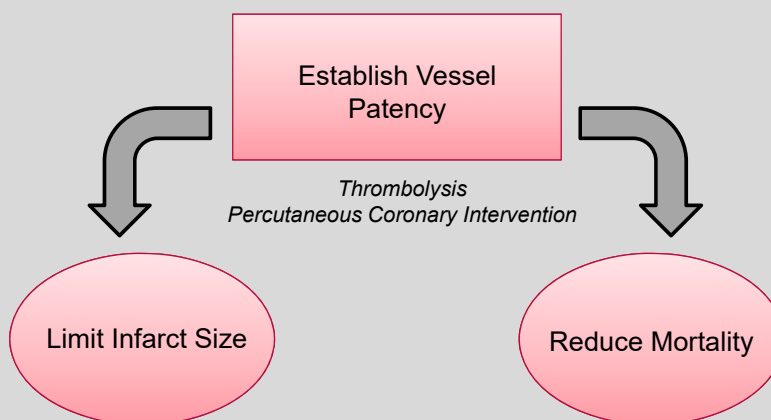
- Aspirin 325 mg
 - Ticagrelor 180 mg or clopidogrel 600 mg
 - Heparin 50-70 u/kg bolus then 12 u/kg/hr infusion
 - Atorvastatin
 - Beta-blocker
 - ACE-inhibitor
- Within 24 hours*

Should you send for urgent angiography?

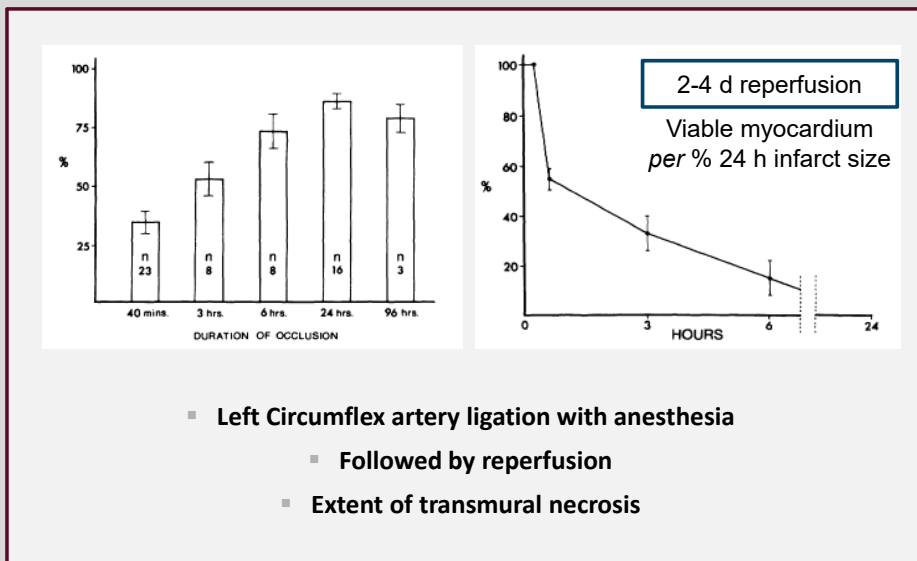
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Evolution of STEMI Therapy



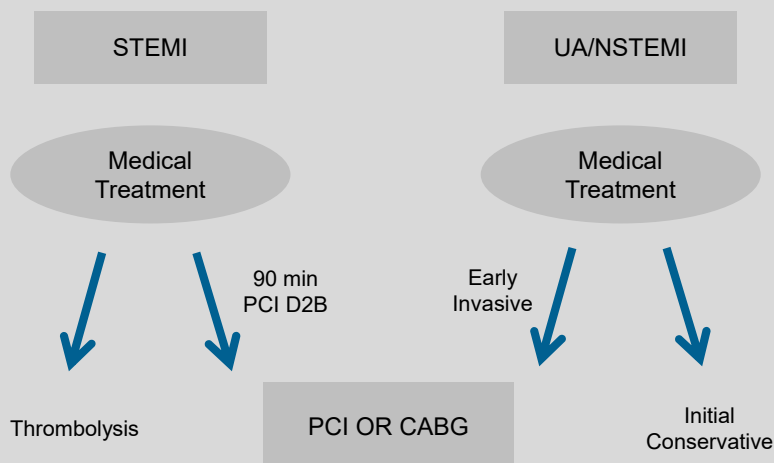
Reperfusion: Time is Myocardium



- Left Circumflex artery ligation with anesthesia
 - Followed by reperfusion
 - Extent of transmural necrosis

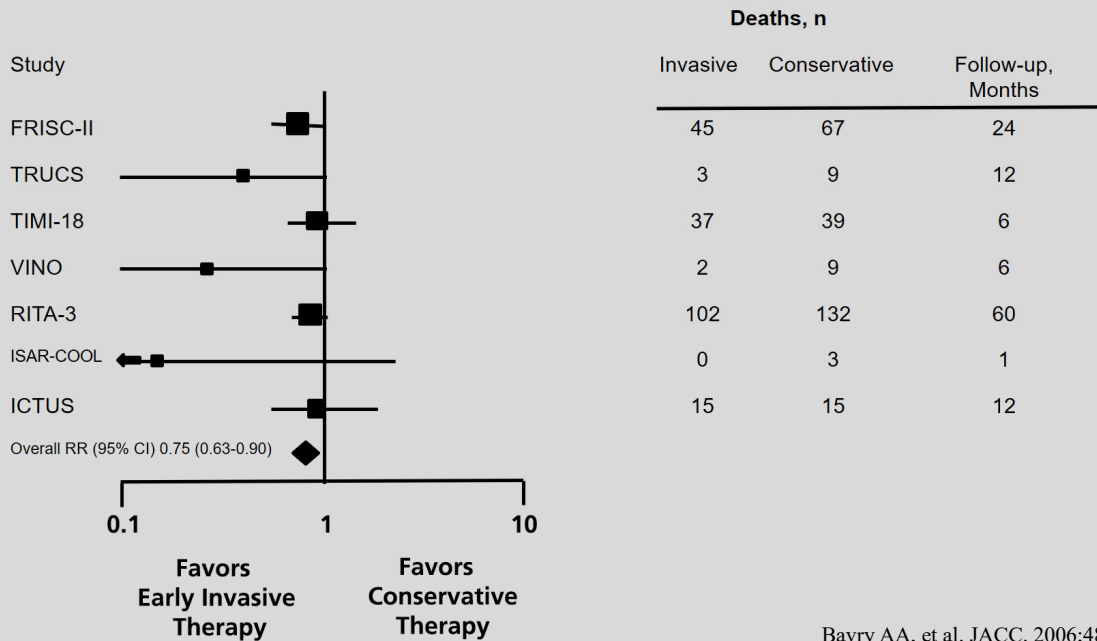
Reimer 1977
Reimer 1977

Reperfusion in ACS



Bowen WE, *N Engl J Med.* 2001;344:1939.

Mortality: Invasive v Conservative - 2 Year Follow-up



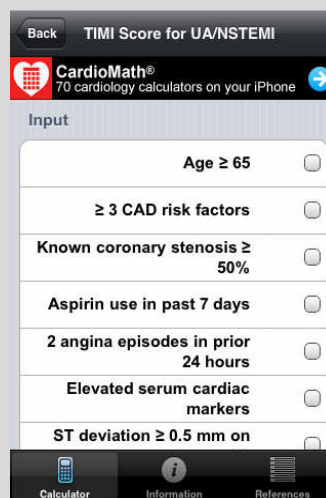
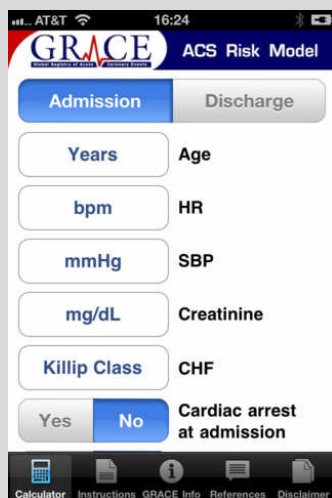
TIMI Risk Score for UA/NSTEMI

HISTORICAL	PTS	RISK OF EVENTS (%) AT 14 DAYS			
Age ≥ 65	1	RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC	
≥ 3 CAD risk factors -FHx, HTN, ↑ chol, DM, smoker	1				
Known CAD	1	0/1	3	5	Low
ASA use in past 7 days	1	2	3	8	
PRESENTATION		3	5	13	Int
Recent (≤24h) angina	1	4	7	20	
↑ cardiac markers	1	5	12	26	High
ST deviation ≥ 0.5 mm	1	6/7	19	41	

RISK SCORE = Total Points (0 - 7)

Antman, et al. JAMA. 2000;284:835-42.

Mobile Risk Calculators



Revascularization Strategy: UA/NSTEMI

EARLY INVASIVE STRATEGY PREFERRED

- Recurrent angina
- Elevated troponin
- Dynamic ST changes
- Signs or symptoms of heart failure
- Hemodynamic or electrical instability
- Prior CABG
- Diabetes
- Mild to moderate renal dysfunction
- Reduced left ventricular ejection fraction
- Intermediate or high risk score

INITIAL CONSERVATIVE STRATEGY REASONABLE

- Low risk score (e.g. GRACE, TIMI)
- Patient or physician preference in the absence of high-risk features

Anderson et al. *J Am Coll Cardiol.* 2012;61:e1-e171

Conclusions

- ▶ ACS represent a spectrum of disorders that identifiable by history, and discernable with biomarkers and ECG.
- ▶ The pathophysiology of ACS is complex, and effective pharmacotherapies interrupt the established cascade.
- ▶ Risk stratification tools for UA/NSTEMI are readily available, and help identify patients that benefit from early revascularization.
- ▶ Procedural and pharmacotherapy developments can be employed to achieve better overall outcomes for patients with ACS.

Thank You



The Ohio State University

Scott M Lilly, MD PhD