Acute Coronary Syndrome

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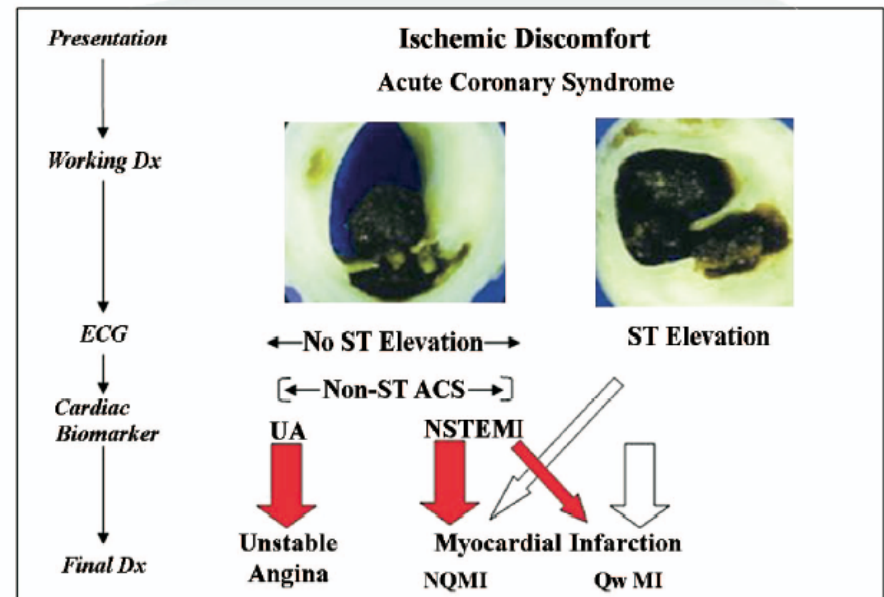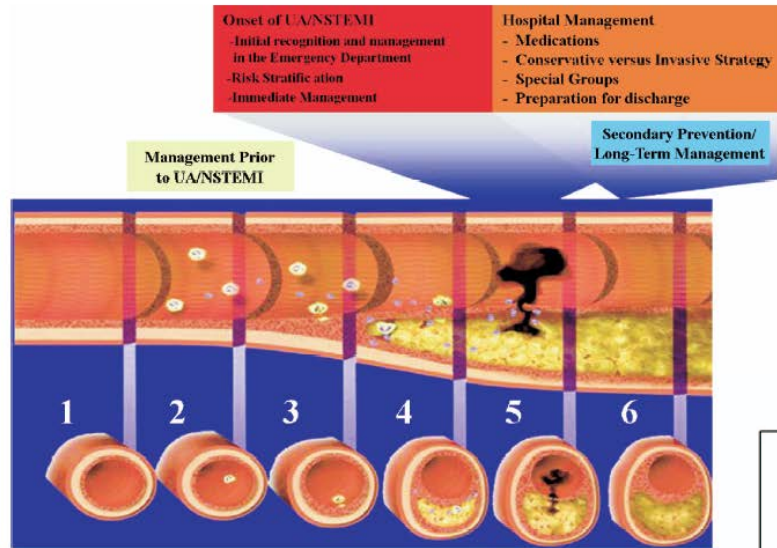Heart & Vascular Center of Arizona

Objectives

1. understand the mechanisms and pathophysiology of acute coronary syndromes

2. be able to rapidly identify high risk and low risk ACS patients

3. discuss current pharmacologic and interventional treatment modalities for ACS
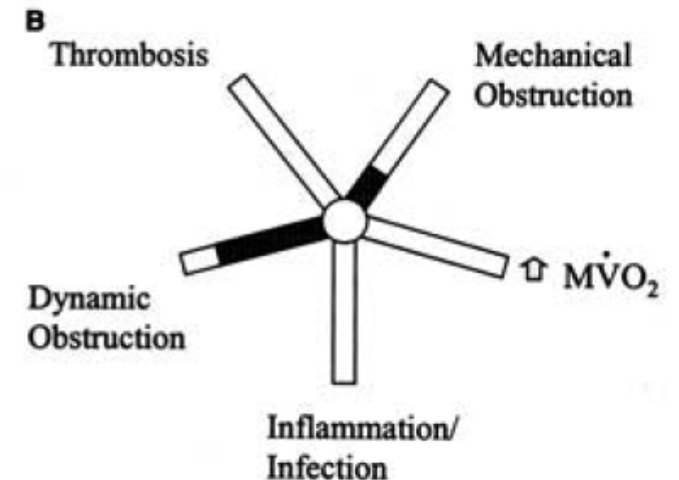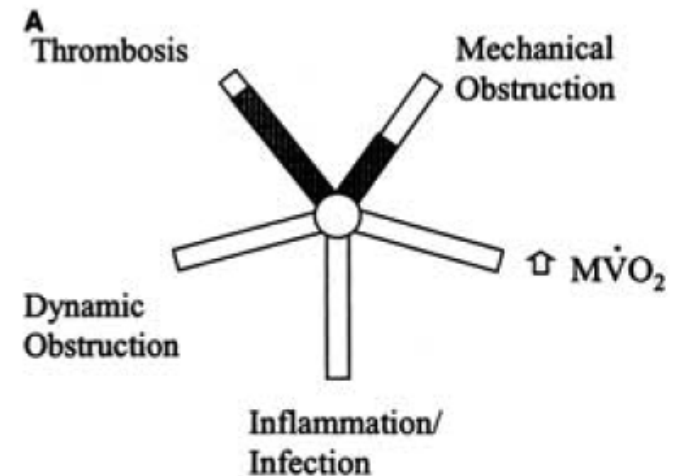
Definitions

Definitions - Biological

Most commonly:
- ruptured plaque
- non-occlusive, platelet-rich thrombus
- distal microembolization

Also may have:
- spasm
- anemia
- tachyarrhythmias
- HTN (high LVEDP)

Goals of Tx

Short Term:

- Address acute hemodynamic status
- Pain relief
- Prevention of acute thrombosis/embolism
- Prevention of arrythmias

Long Term:

- Slow progression of disease
- Prevent future events (death, MI, rehosp, revasc)
- Prevention of angina

Early Clinical Assessment

- Traditional risk factors only weakly predictive of ACS
  - Do predict worse prognosis once ACS has been established

- Clinical symptoms, ECG, biomarkers much more predictive

Early Clinical Assessment

- Atypical symptoms do not necessarily decrease the likelihood of ACS
    - Lee TH, Cook EF, Weisberg M, Sargent RK, Wilson C, Goldman L. Acute chest pain in the emergency room: identification and examination of low-risk patients. Arch Intern Med 1985;145:65-9.
        - Sharp or stabbing pain --> 22% had acute ischemia
        - Pleuritic pain --> 13% had acute ischemia
        - Pain reproduced with palpation --> 7% had acute ischemia

- Older age, male sex, presence of chest or left arm pain, chest pain identified as most important presenting symptom all increase the likelihood of ACS (N Engl J Med 1984;310:1273-8; Med Care 1991;29:610-27)

Early Clinical Assessment ECG

- ECG changes define a gradient of risk
  - BBB, paced rhythm, LVH with repol ("uninterpretable" ECGs)
  - ST segment deviation
  - T wave inversions ≥ 0.2mV
  - Non-specific T wave abnormalities or normal ECG

Early Clinical Assessment ECG
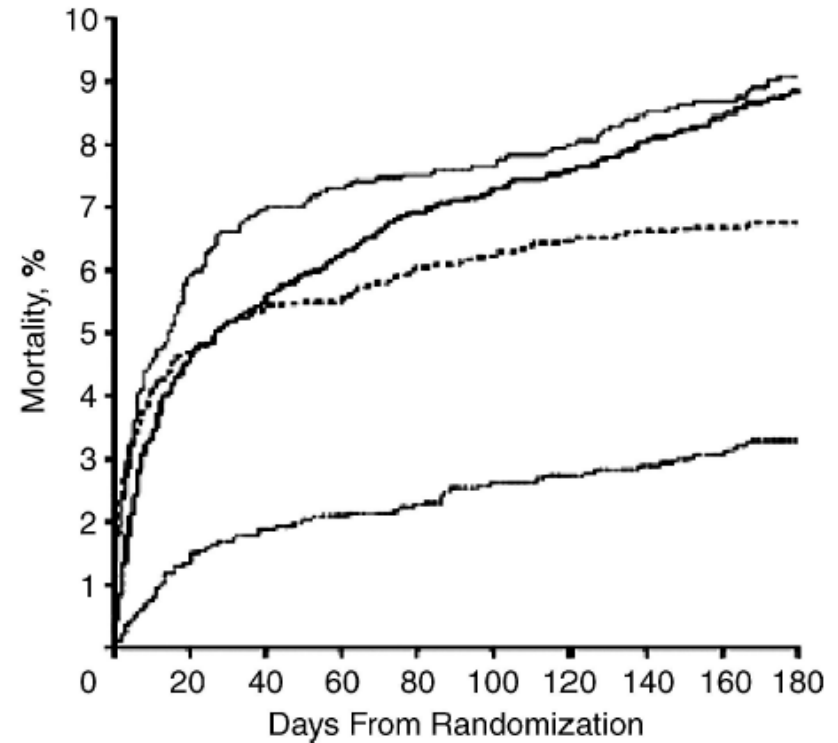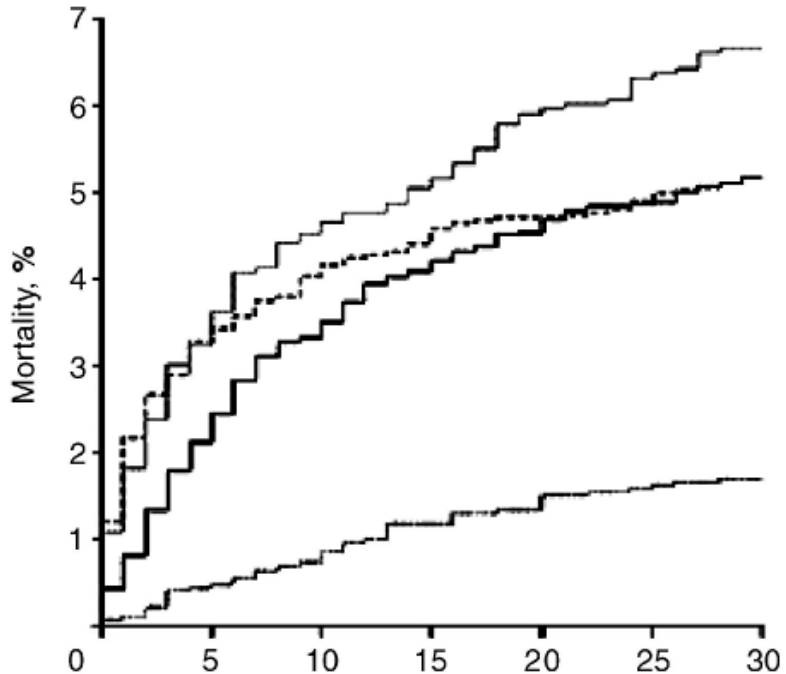
Figure 19. Kaplan-Meier Estimates of Probability of Death Based on Admission Electrocardiogram

- CLASS I

- 1. In patients with chest pain or other symptoms suggestive of ACS, a 12-lead ECG should be performed and evaluated for ischemic changes within 10 minutes of the patient arrival at an emergency facility (21). (Level of Evidence: C)

- 2. If the initial ECG is not diagnostic but the patient remains symptomatic and there is a high clinical suspicion for ACS, serial ECGs (e.g., 15- to 30-minute intervals during the first hour) should be performed to detect ischemic changes. (Level of Evidence: C)

Biomarkers
(BNP)

Mortality at 10 mo (%)

P=.02 P<.0001 P=.001

Q1 Q2 Q3 Q4

ST ↑ MI
825

Non-ST ↑ MI
565

Unstable Angina
1133

de Lemos JA, et al. *N Engl J Med.* 2001;345:1014-1021.
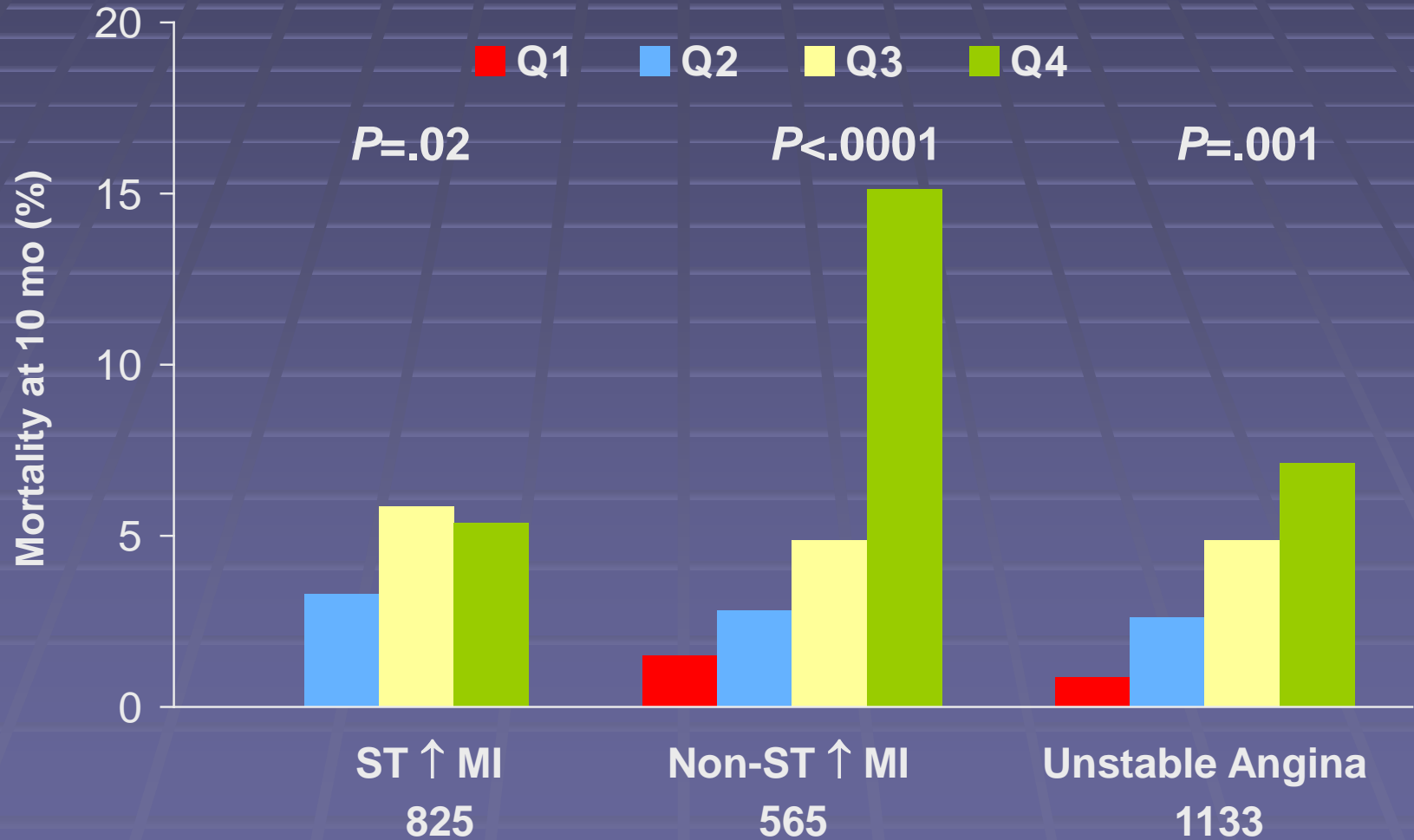
Biomarkers
(troponin, CRP, BNP)
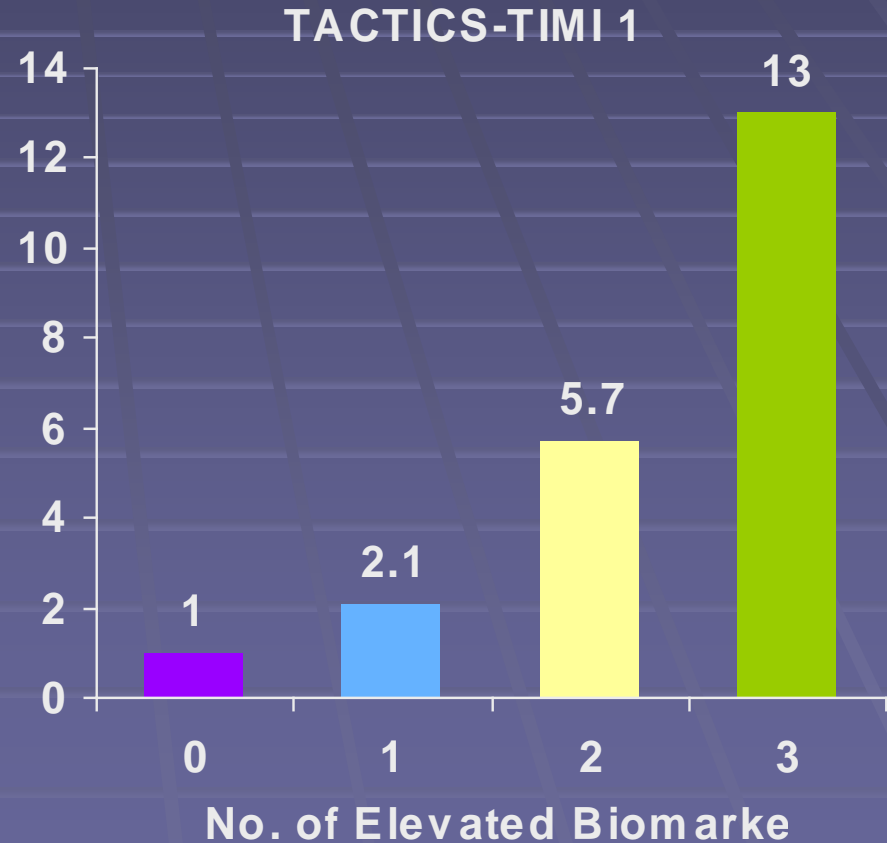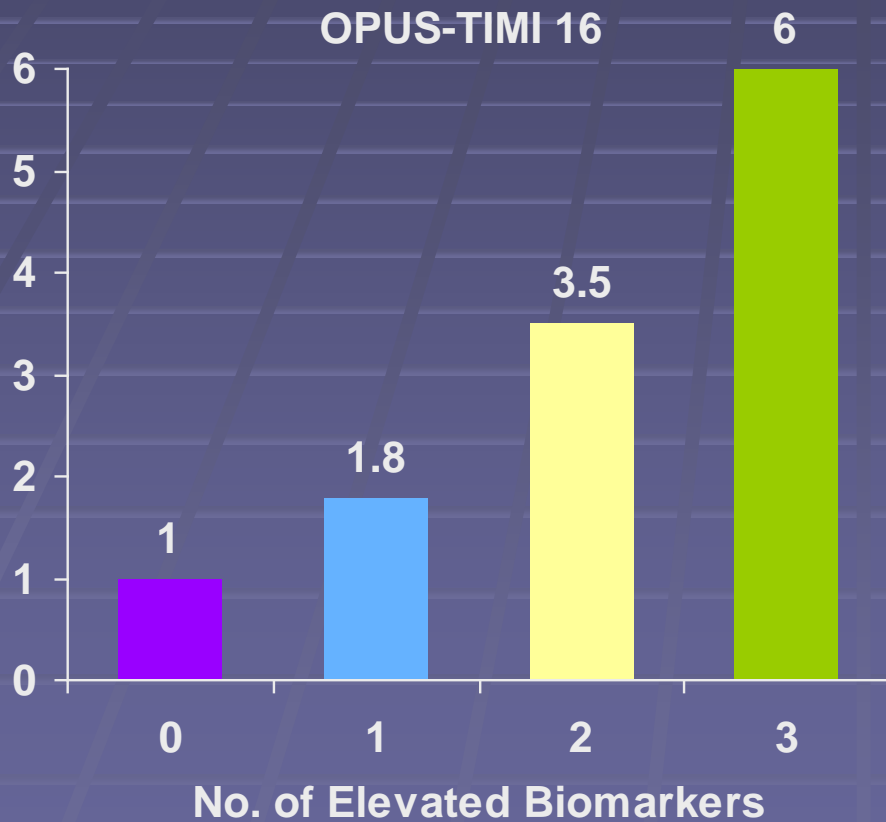
OPUS-TIMI 16

TACTICS-TIMI 1

No. of Elevated Biomarkers

No. of Elevated Biomarke

- The Sanchis score (49), Vancouver rule (50), Heart (History, ECG, Age, Risk Factors, and Troponin) score (51), HEARTS3 score (52), and Hess prediction rule (53) were developed specifically for patients in the ED with chest pain. Although no definitive study has demonstrated the superiority of risk assessment scores or clinical prediction rules over clinician judgment, determination of the level of risk on initial evaluation is imperative to guide patient management, including the need for additional diagnostic testing and treatment. See Section 3.2.2 for a discussion of risk stratification variables.
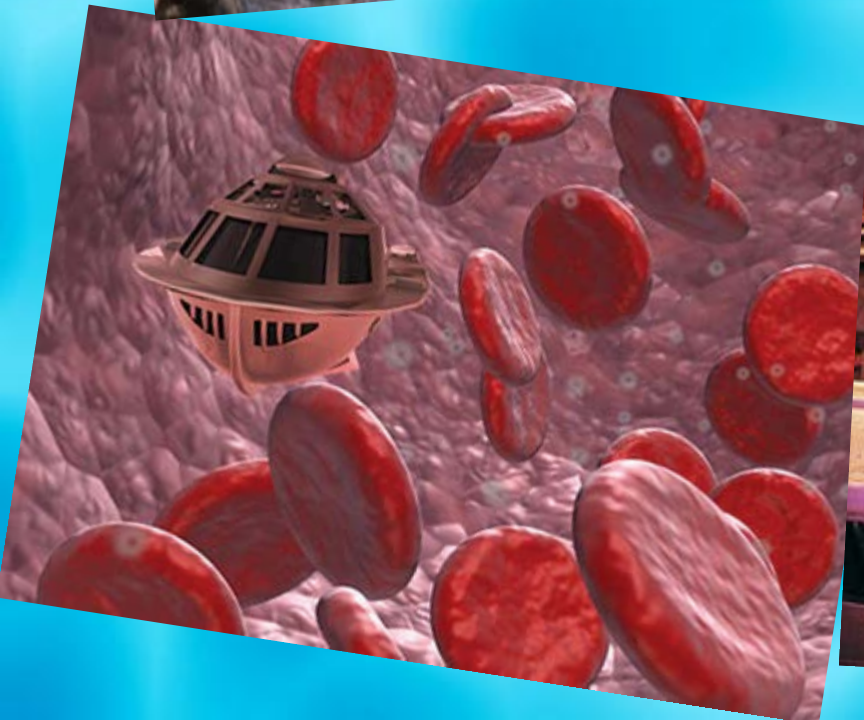
TIMI Risk Score

1) Age ≥65 years

2) ≥3CAD Risk Factors

3) Prior Stenosis >50 %

4) ST deviation

5) ≥2 Anginal events ≤24 hours

6) ASA in last 7 days

7) Elev Cardiac Markers (CK-MB or troponin)

D/MI/Urg Revasc (%) at 14ds

	0/1	2	3	4	5	6/7
Value	4.7	8.3	13.2	19.9	26.2	40.9

Number of Risk Factors
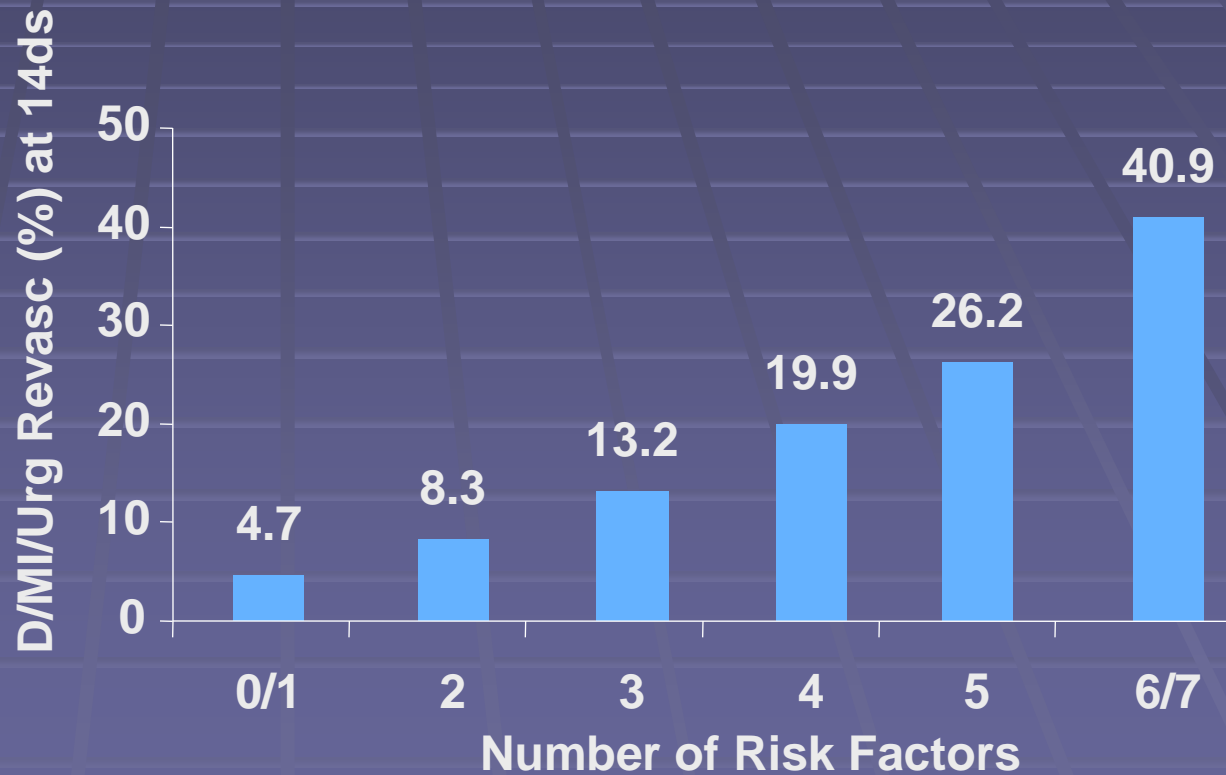
Population (%):	4.3	17.3	32.0	29.3	13.0	3.4

Antman EM, et al. *JAMA.* 2000;284:835-442.

Pharmacological Therapy
antiplatelet agents

- ASA
  - 325mg chewed
  - 81mg if taking Ticagrelor or Prasugrel
- Clopidogrel or Ticagrelor (Prasugrel only after PCI)
  - loading dose
  - delays CABG by 5ds
- IIB/IIIA inhibitors
  - highest risk cohort, ongoing ischemia
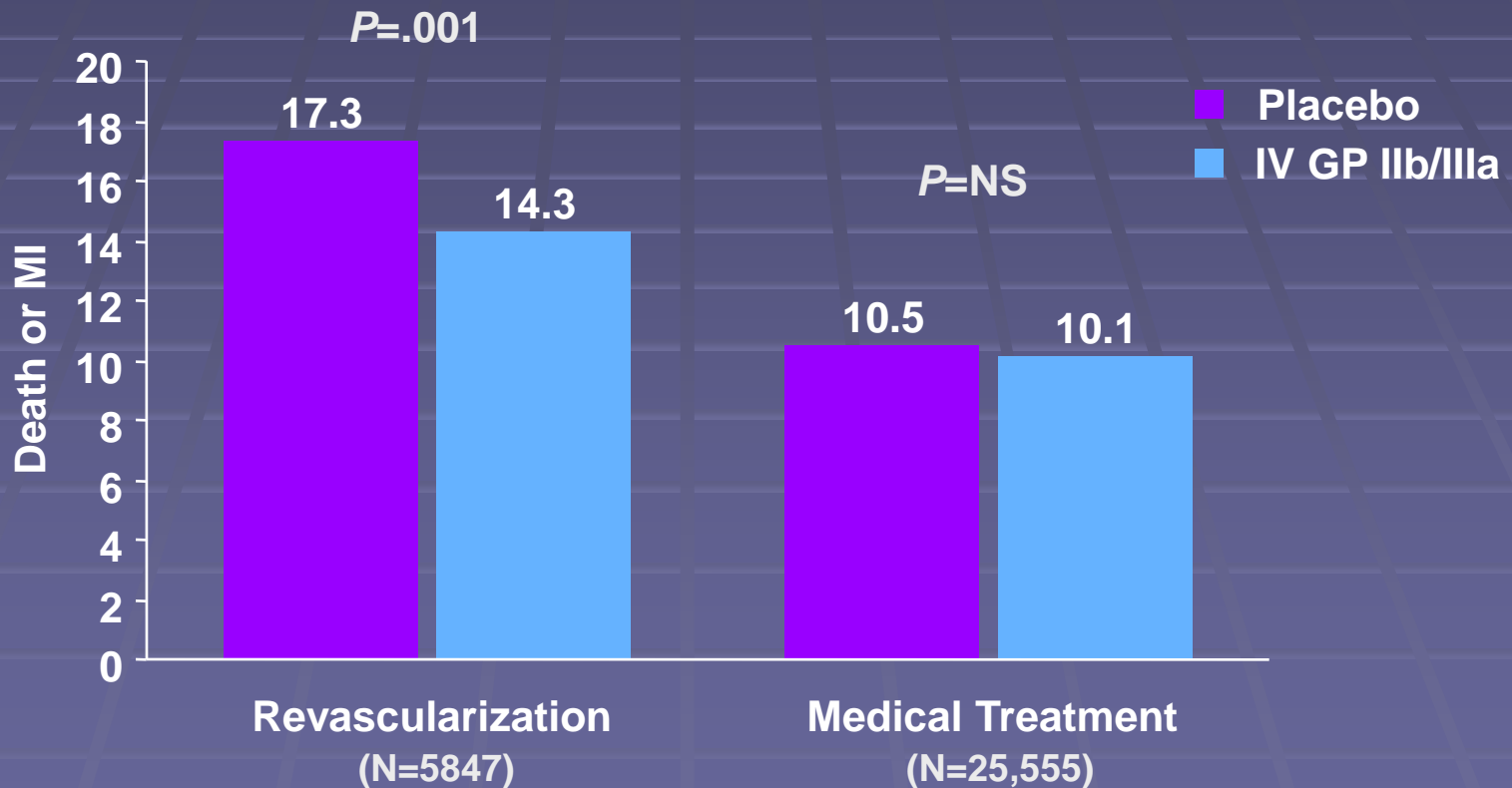 - most benefit if early PCI planned

TABLE 7 Summary of Recommendations for Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS and PCI

Recommendations	Dosing and Special Considerations	COR	LOE	References
Aspirin				
• Non-enteric-coated aspirin to *all* patients promptly after presentation	162 mg-325 mg	I	A	(288-290)
• Aspirin maintenance dose continued indefinitely	81 mg/d-325 mg/d*	I	A	(288-290, 293,391)
P2Y₁₂ inhibitors				
• Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin	75 mg	I	B	(291)
• P2Y₁₂ inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy: – Clopidogrel – Ticagrelor*	300-mg or 600-mg loading dose, then 75 mg/d 180-mg loading dose, then 90 mg BID	I	B	(289,292) (293,294)
• P2Y₁₂ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post-PCI patients treated with coronary stents	N/A	I	B	(293,296,302, 330,331)
• Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy	N/A	IIa	B	(293,294)
GP IIb/IIIa inhibitors				
• GP IIb/IIIa inhibitor in patients treated with an early invasive strategy and DAPT with intermediate/high-risk features (e.g., positive troponin)	Preferred options are eptifibatide or tirofiban	IIb	B	(43,94,295)
Parenteral anticoagulant and fibrinolytic therapy				
• SC enoxaparin for duration of hospitalization or until PCI is performed	• 1 mg/kg SC every 12 h (reduce dose to 1 mg/kg/d SC in patients with CrCl <30 mL/min) • Initial 30 mg IV loading dose in selected patients	I	A	(133,136,309)
• Bivalirudin until diagnostic angiography or PCI is performed in patients with early invasive strategy only	• Loading dose 0.10 mg/kg loading dose followed by 0.25 mg/kg/h • Only provisional use of GP IIb/IIIa inhibitor in patients also treated with DAPT	I	B	(292,293, 310,311)

GP IIb/IIIa Antagonists in ACS: Death or MI at 30 Days in PCI/CABG < 5 Days Cohort vs Medical Treatment Cohort

P=.001

P=NS

- **Placebo**
- **IV GP IIb/IIIa**

Death or MI

17.3
14.3
10.5
10.1

Revascularization
(N=5847)

Medical Treatment
(N=25,555)

ACS, acute coronary syndrome; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; NS, not significant.
Boersma E, et al. *Lancet*. 2002;359:189-198.

Pharmacological Therapy
antithrombotic agents

- Heparin
    - Easiest to reverse
- LMWH
    - Easiest to dose
    - Less HIT
- Direct thrombin inhibitors (lepirudin, bivalrudin, etc.)
    - For pts with HIT

Pharmacological Therapy
antiplatelet & antithrombotic agents

Trials	N	Active	Placebo	Risk ratio (95% CI)	p
ASA vs placebo		% Death or MI		5-day to 2-year endpoint	
Lewis et al. (VA)	1266	5.0	10.1		0.005
Cairns et al.	555	10.5	14.7		0.137
Théroux et al.	239	3.3	11.9		0.012
RISC group	388	7.4	17.6		0.003
All ASA vs. placebo	2448	6.4	12.5		0.0005
UFH + ASA vs ASA				1-week endpoint	
Théroux et al.	243	1.6	3.3		0.40
RISC group	399	1.4	3.7		0.140
ATACS group	214	3.8	8.3		0.170
Gurfinkel et al.	143	5.7	9.6		0.380
All UFH vs ASA	999	2.6	5.5		0.018
LMWH + ASA vs ASA				1-week endpoint	
Gurfinkel et al.	141	0.0	9.6		NA
FRISC group	1498	1.8	4.8		0.001
All hep. or LMWH vs ASA	2629	2.0	5.3		0.0005
GPIIb/IIIa anta. + UFH vs UFH				30-day endpoint	
CAPTURE	1265	4.8	9.0		0.003
PARAGON*	1516	10.6	11.7		0.410
PRISM-PLUS	1570	8.7	11.9		0.034
PRISM†	3232	5.8	7.1		0.110
PURSUIT	9461	3.5	3.7		0.042
All GPIIb/IIIa vs UFH‡	17044	5.1	6.2		0.0022

0.2   0.6   1.0   1.4   1.8   2.2   2.6

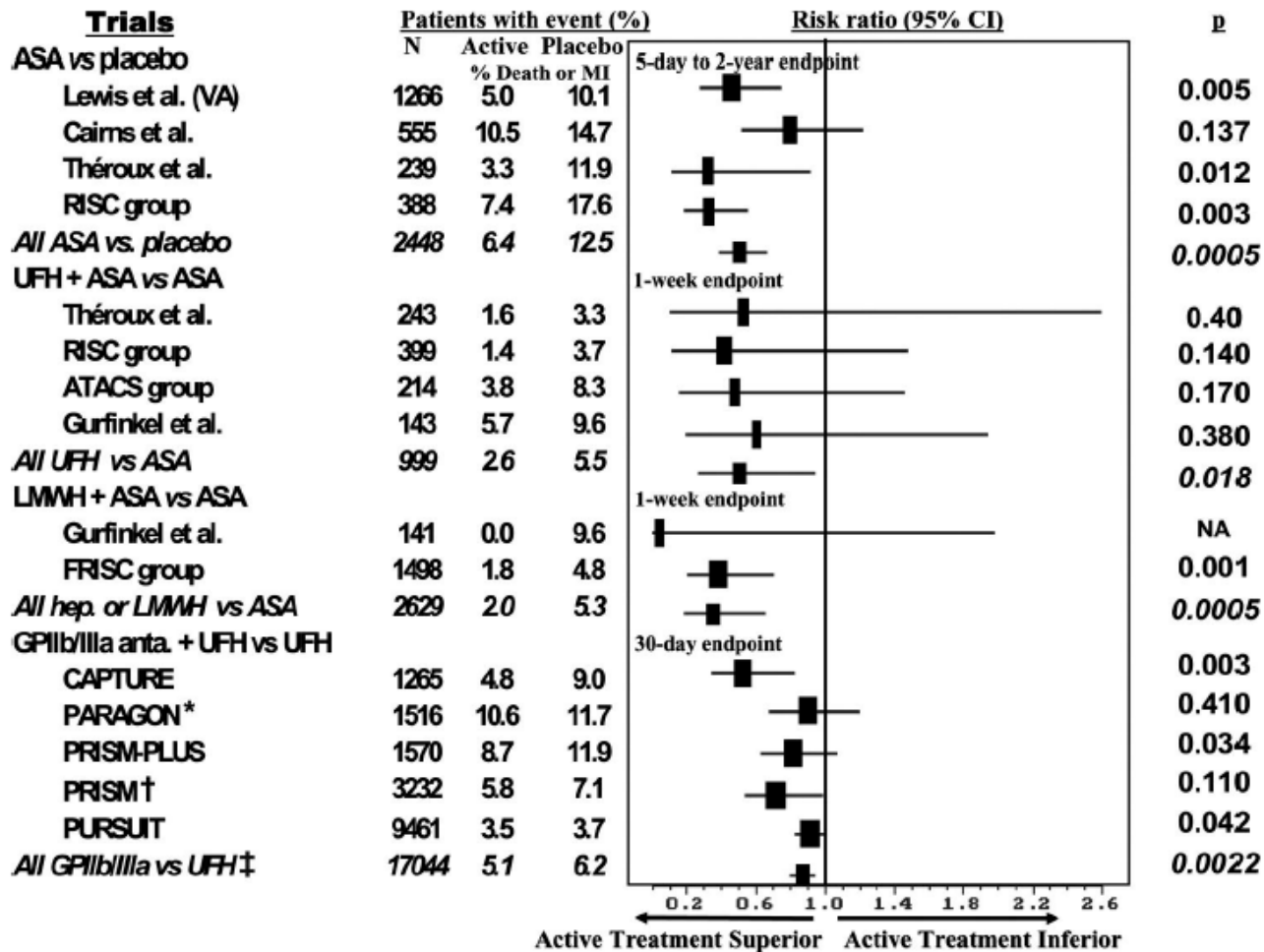← Active Treatment Superior   Active Treatment Inferior →

Figure 10. Older Trials of Antiplatelet and Anticoagulant Therapy in UA/NSTEMI

Pharmacological Therapy
Nitrates

- benefits
  - pain, HTN, decrease preload
  - no documented mortality benefit

- reflex increase in HR and contractility
  - should be used with beta blockers

- contraindications
  - severe AS, RV infarct, recent sildenafil

Pharmacological Therapy
Beta Blockers

- Benefits
  - ↓ MVO2, ↑ diastolic coronary perfusion
- IV (5mg IV Q5min X 3)
- PO (12.5-25mg PO Q6 X 48hrs)
- BID dosing for maintenance outpt tx
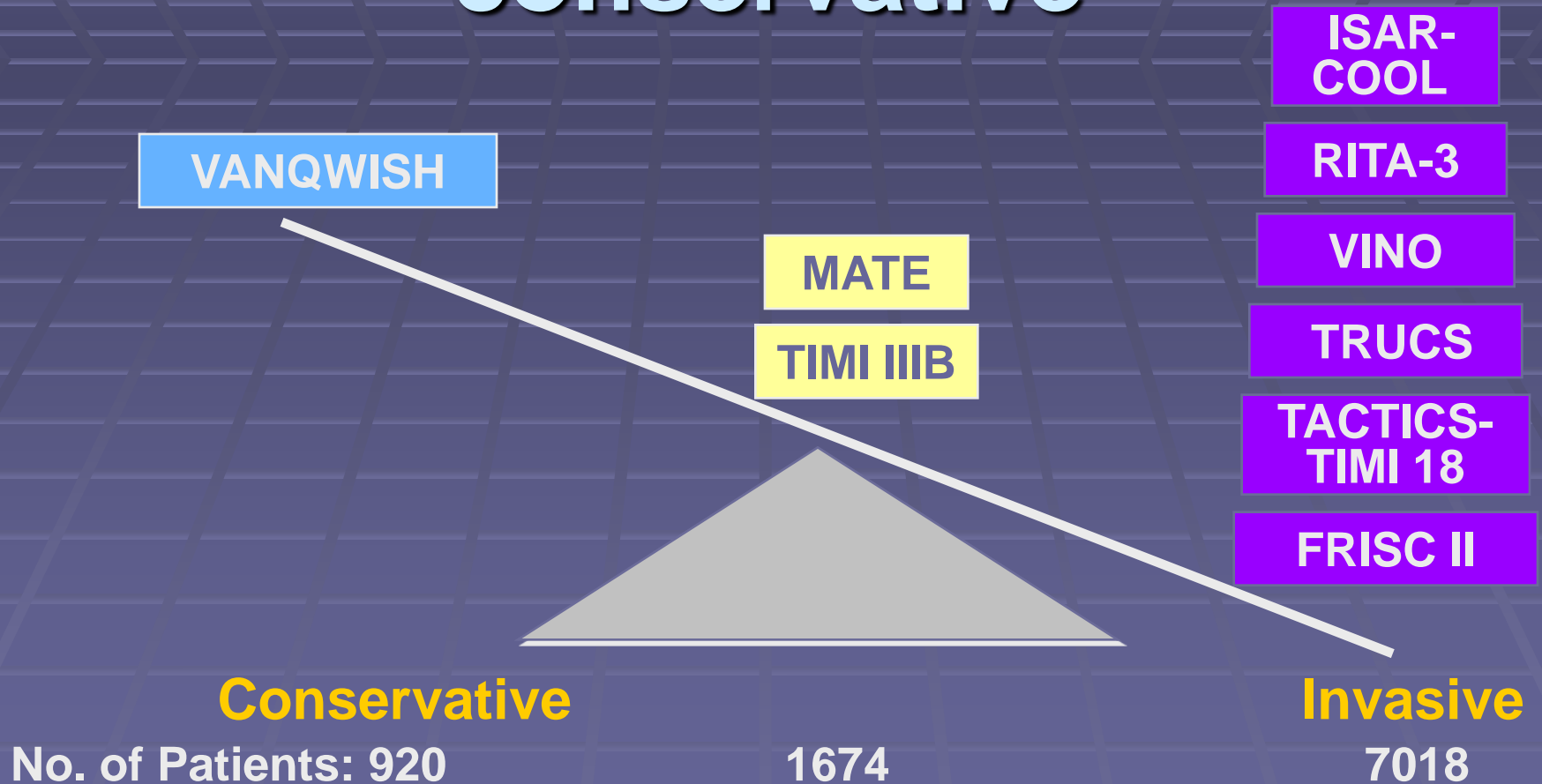- Caution in LV dysfunction, active heart failure, shock/low-output

- Most data from AMI, chronic stable angina, s/p recent MI, heart failure.
  - Little data specifically in ACS

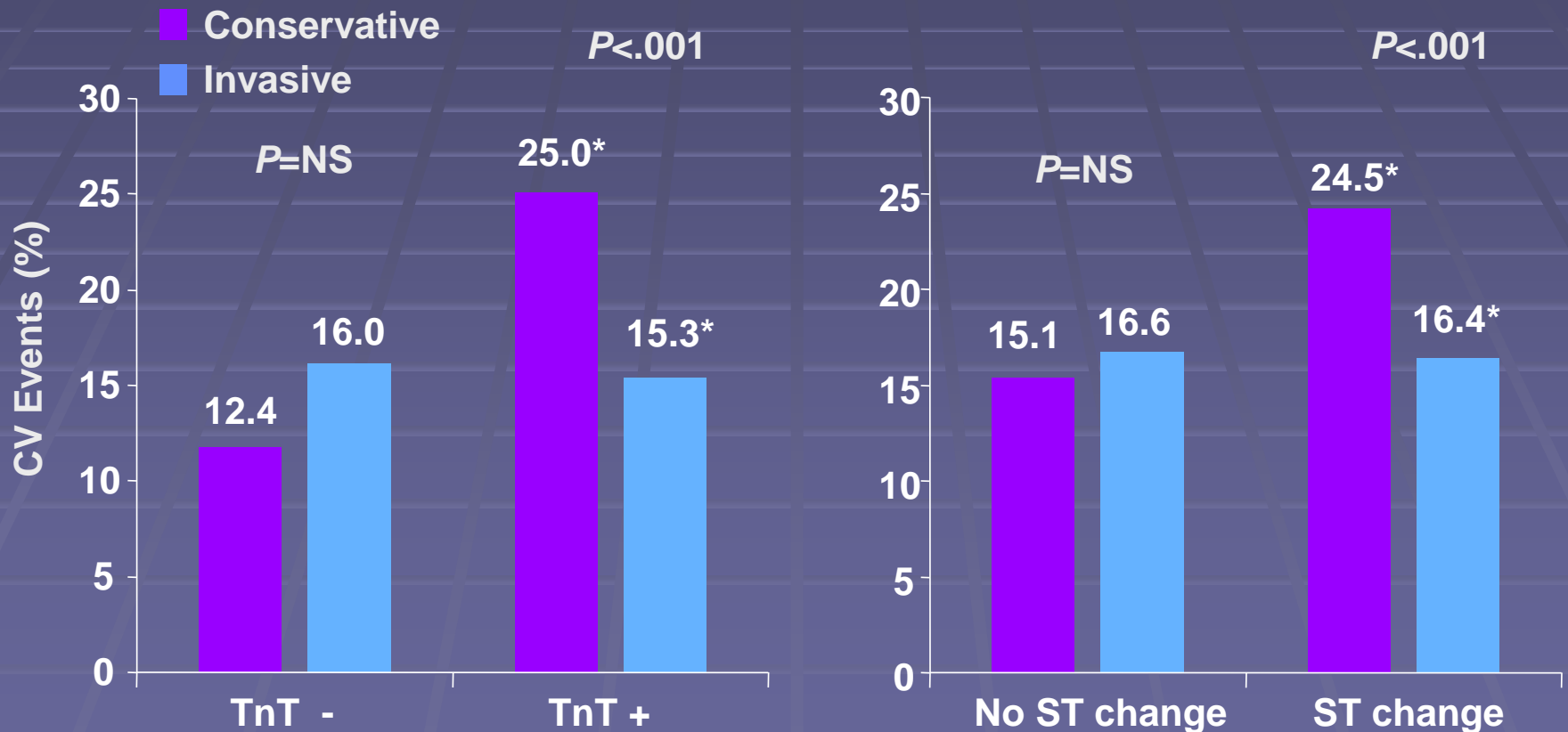# Pharmacological Therapy
Calcium Channel Blockers

- May use diltiazem or verapamil acutely for pts in whom beta blockers are contraindicated

- Caution in LV dysfunction

- Short-acting dihydropyridines *without beta blockade* showed increased events

Early invasive vs conservative

VANQWISH

MATE

TIMI IIIB

ISAR-COOL

RITA-3

VINO

TRUCS

TACTICS-TIMI 18

FRISC II

Conservative

Invasive

No. of Patients: 920   1674   7018

Early invasive vs conservative

TACTICS - TIMI 18

Conservative
Invasive

CV Events (%)

P=NS
P<.001

12.4
16.0
25.0*
15.3*

TnT - | TnT +

P=NS
P<.001

15.1
16.6
24.5*
16.4*

No ST change | ST change

TnT, troponin T; ST, ST segment.
Morrow DA. *JAMA*. 2001;286:2405-2412; Cannon CP. *N Engl J Med*. 2001;344:1879-1887.

Case 1

- 72yo male h/o HTN, hyperchol, AF, COPD, DM, LVEF 45%, mod MR
- CP rad L arm, R arm, jaw, assoc with SOB, nauaea, several hours off and on
- Insulin, lasix, dig, quinapril, simva, warfarin
- Trop 0.05, 1.64, 1.97, 1.52
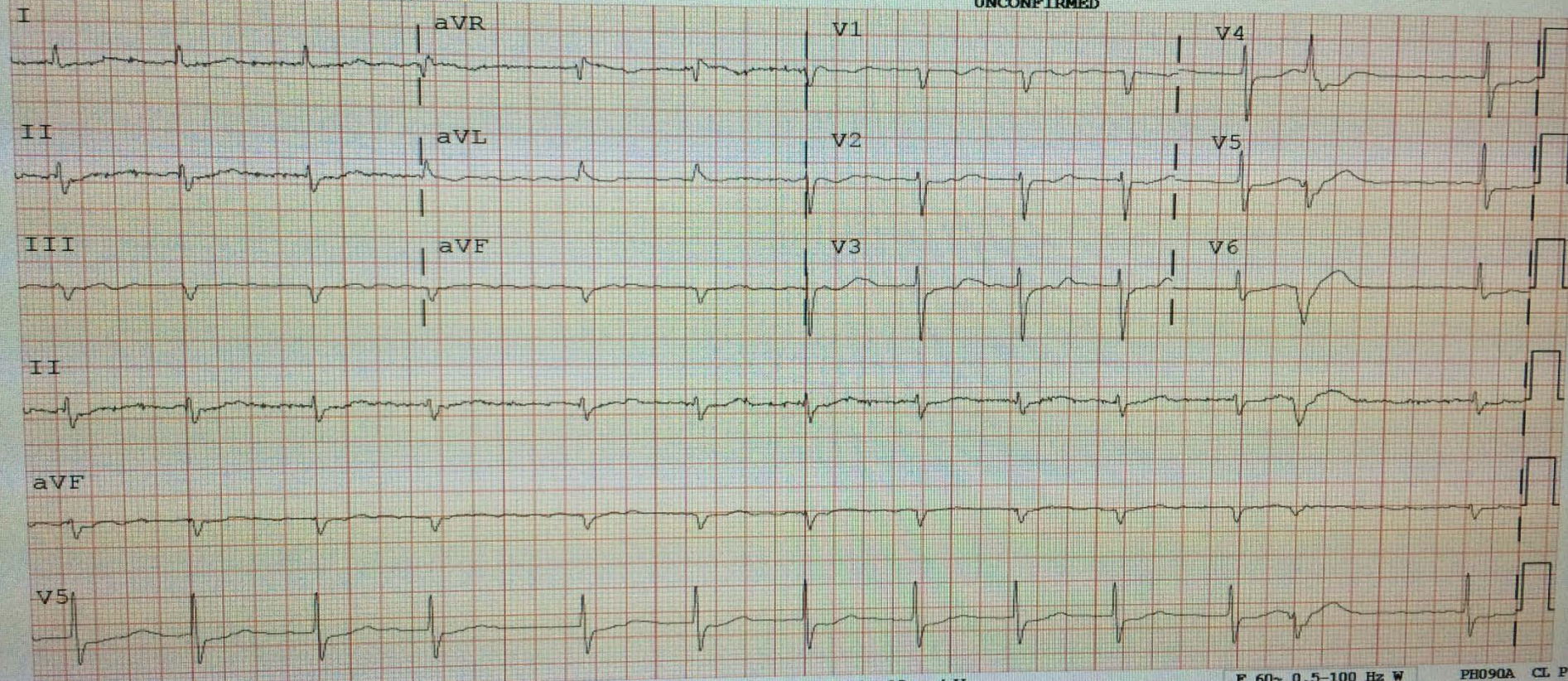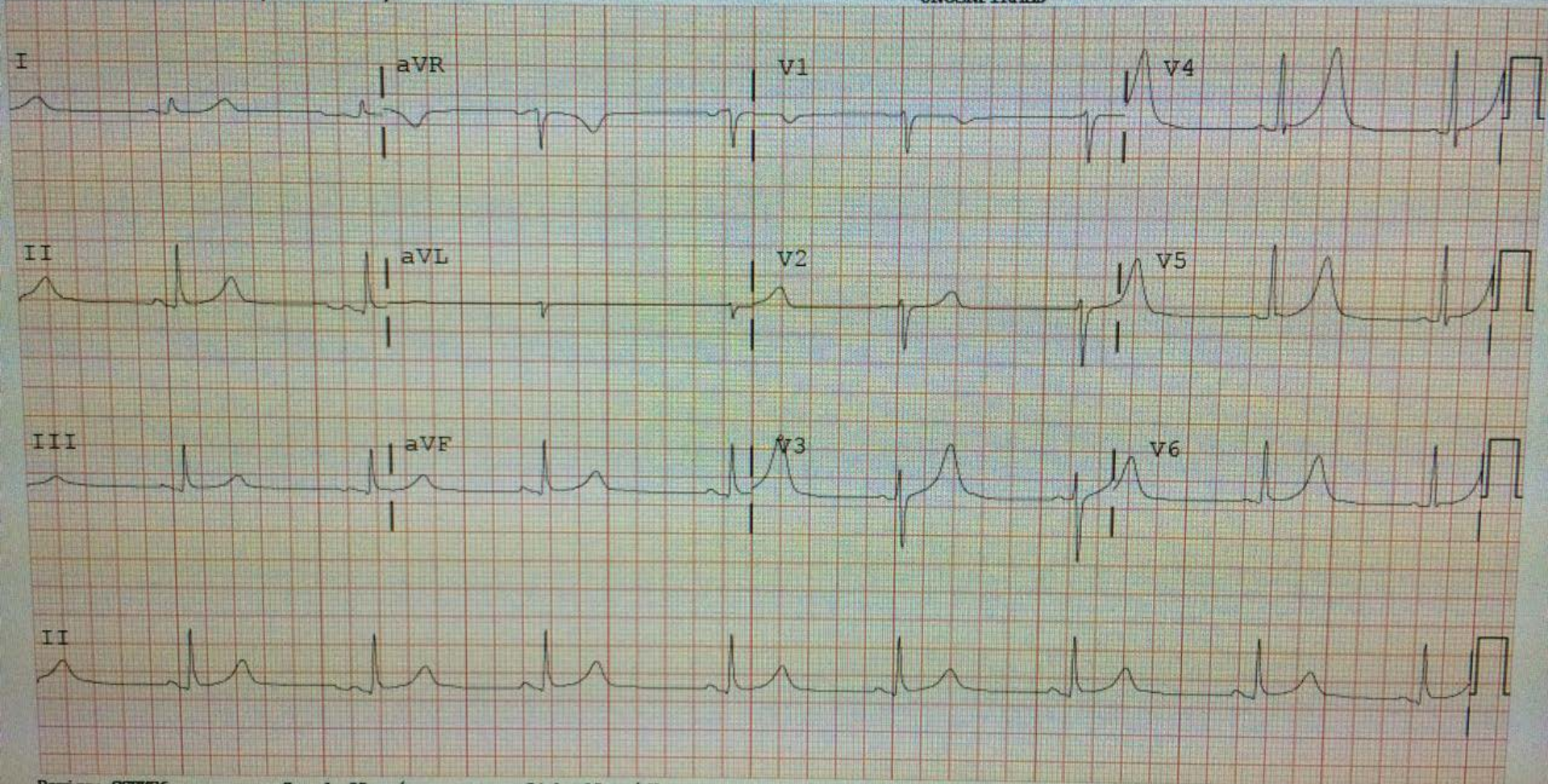
Case 1

- Tx with Lovenox, metoprolol, clopidogrel
- 95% LCx lesion, successful PCI

Case 2

- 34yo male h/o STEMI s/p PCI 2yrs ago, uses "spice," med noncompliance

- CP while wrestling with his dogs, central chest, sharp, radiated to neck, waxed/waned few hours
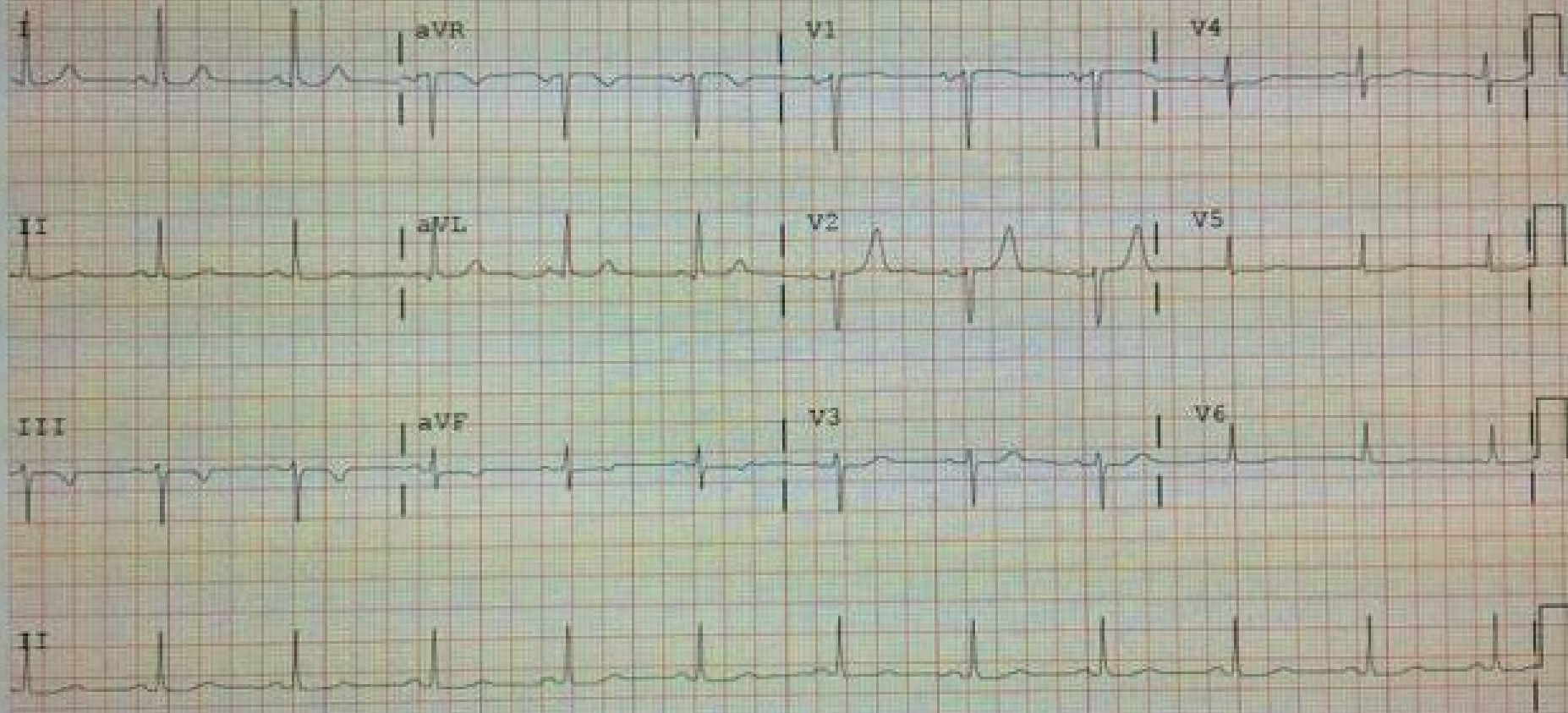
- Trop 0.05, 1.64, 1.97, 1.52

Case 2

- Tx with metoprolol, asa, clopidogrel, atorva
- Cath showed patent stent, normal LVEF, no PCI done

Case 3

- 84yo female h/o CAD s/p PCI, DM, HTN, CVA, CKD, recent echo with nl LVEF
- c/o inc SOB past 2 wks, worse this AM, + orthopnea and PND
- asa, carvedilol, clopidogrel, furosemide, isosorbide, rosuvastatin, losartan, insulin
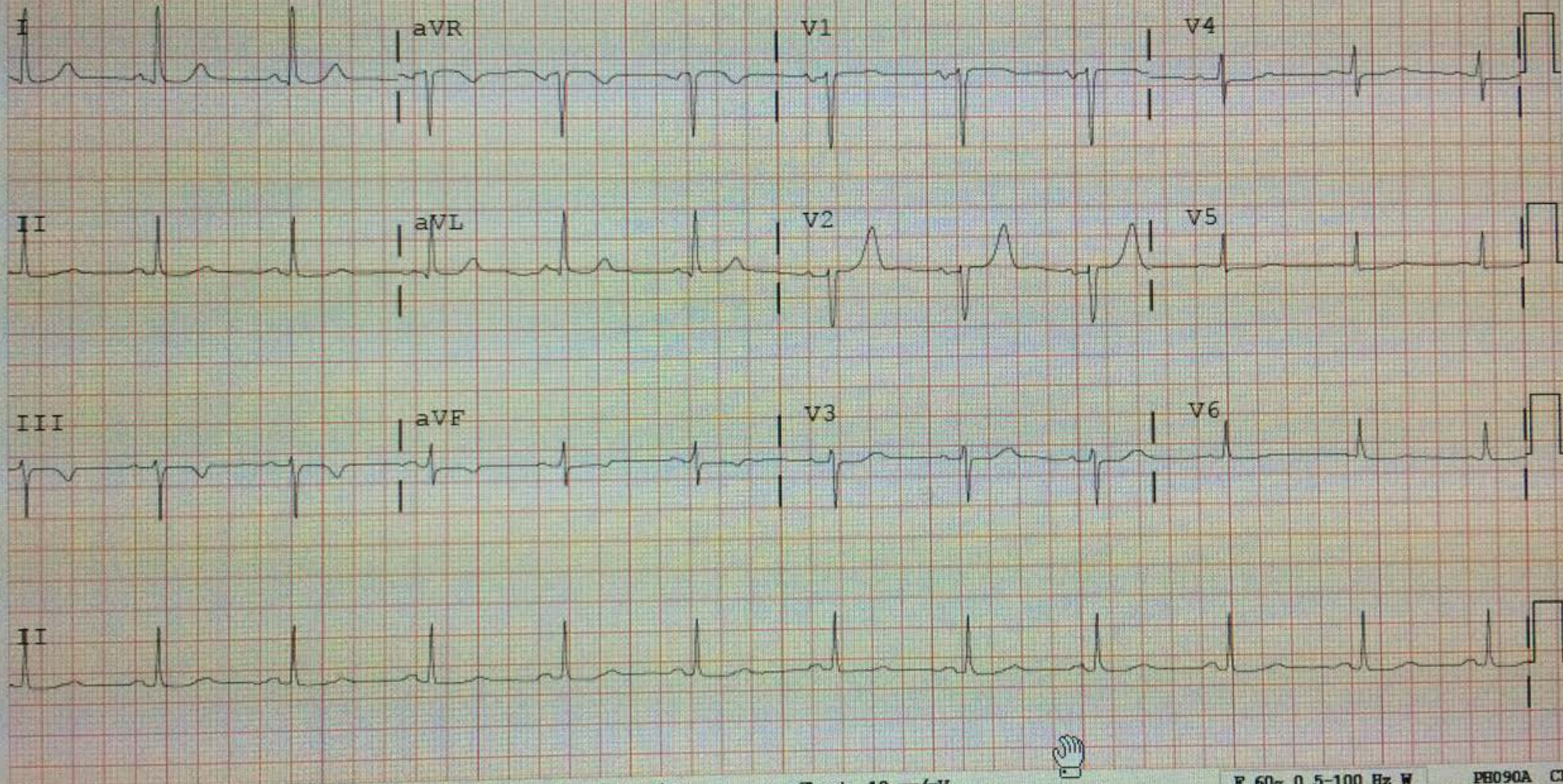- Trop 0.16, 0.14
- NT-proBNP 58,358
- Cr 1.9

Case 3

- Tx with diuretics
- Stress test showed scar without ischemia
- No cath done

Case 4

- 89 yo male h/o CAD s/p PCI, HTN, hyperchol, RA, is a "DNR"
- CP past 3 wks, several times per day, relieved with NTG, radiates shoulders/arms, both exertional and at rest, neg stress test at VA 8 wks ago
- asa, dilt, isosorbide, metoprolol, prava, mtx
- Trop 0.08, 0.09, 0.11

Case 4

- Tx with clopidogrel, atorva

- Stress test with anterior and lateral ischemia

- Cath showed severe stenosis of distal LM, ostial LCx, prox-mid LAD. Surgical opinion obtained, Tx with multivessel PCI