

# IAM COM SUPRA DESNIVELAMENTO DO SEGMENTO ST

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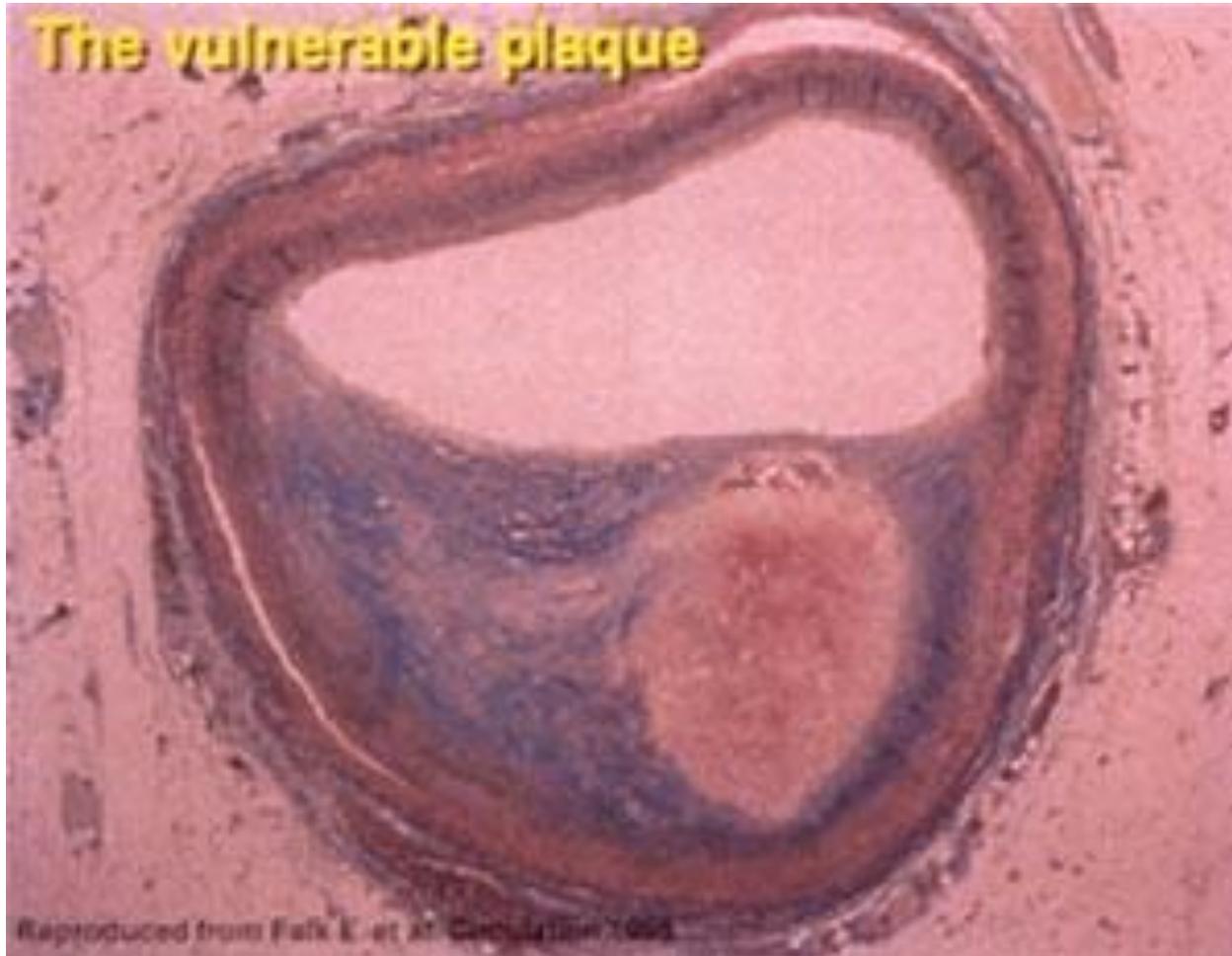
Hospital São Lucas

Hospital Unimed

# Definição

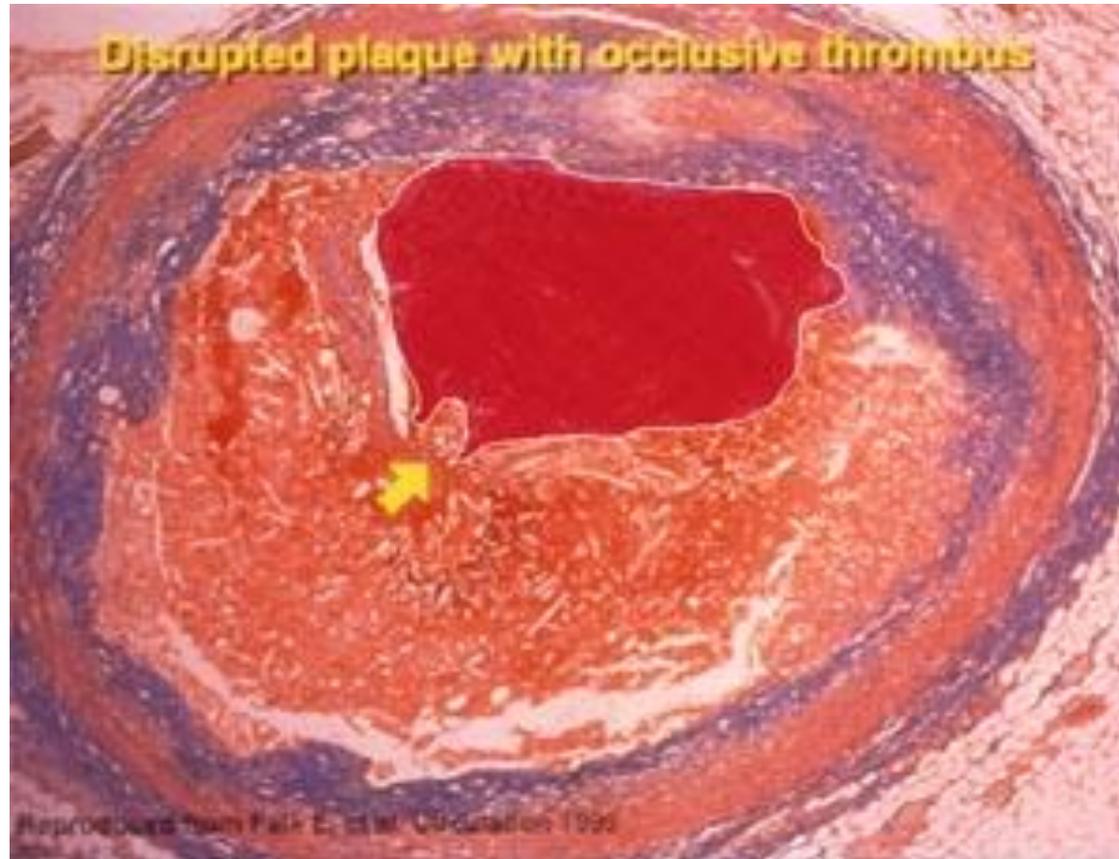
- Situação de urgência ou emergência clínica em que o paciente apresenta sintomas decorrentes de isquemia miocárdica causada pela redução relativa ou absoluta do fluxo coronário que se instalou de forma aguda e abrupta.

# Fisiopatologia



Falk E, et al. *Circulation*. 1995;92:657-671.

# Fisiopatologia



Falk E, et al. *Circulation*. 1995;92:657-671.

## Dor Torácica Aguda (EUA)

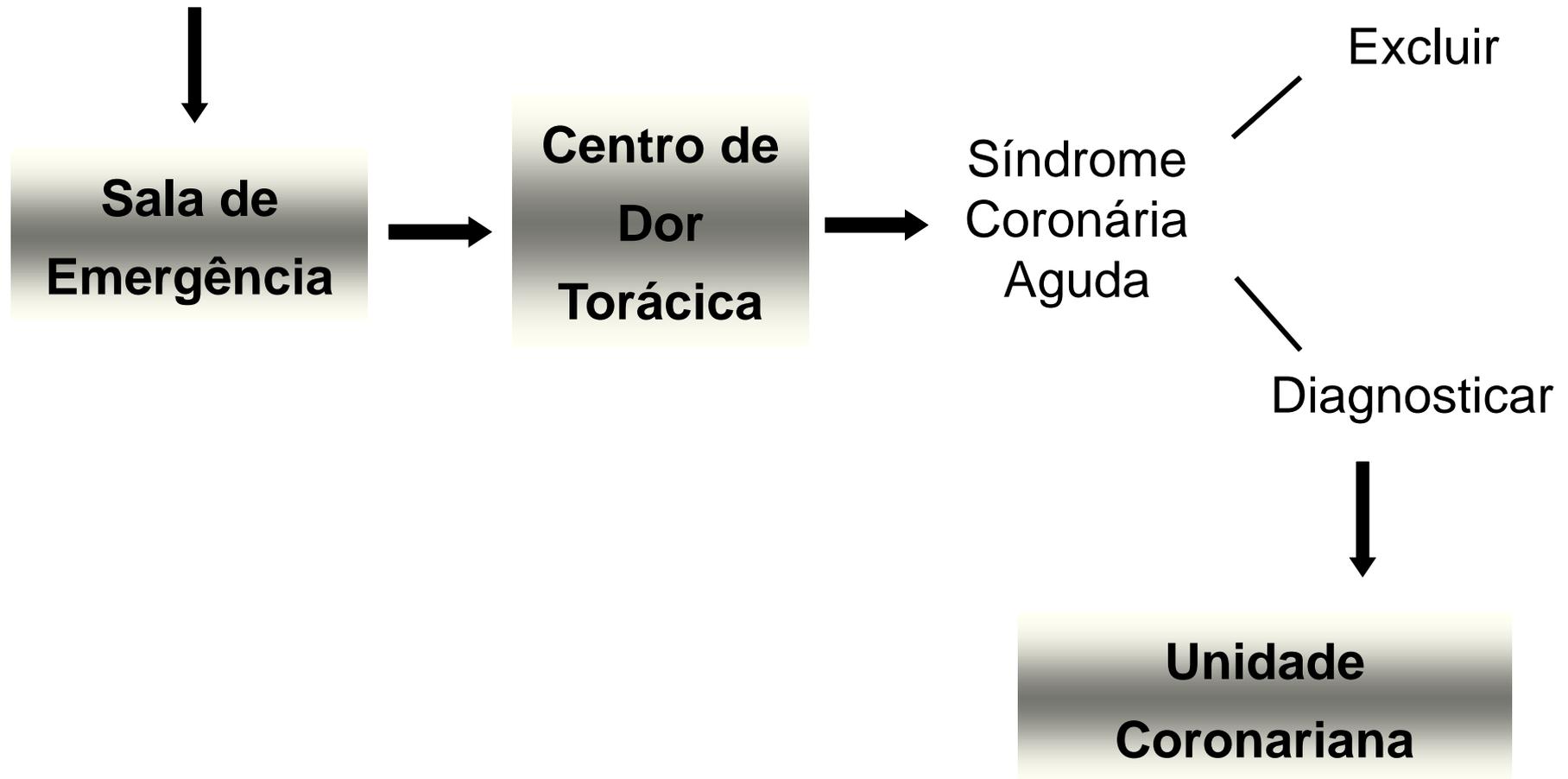
- 5 – 8 milhões casos / ano em departamentos de emergência
- IAM: 10 – 15 %
- Angina instável: 10 – 15 %
- 70 % sem isquemia
- Taxa admissão: 50 – 60 %
- Média internação: 2,8 dias
- Custo médio / internação: US\$ 3.800,00
- Custo total: 10 – 13 bilhões de dólares

## Infartos agudos não diagnosticados

- 2 – 8 % dos casos atendidos
- Destes:
  - 30 % retornam à mesma sala de emergência
  - 6 % óbito em casa
  - 14 % retorna à outra sala de emergência
  - 50 % sem diagnóstico

# CENTROS DE DOR TORÁCICA

**Dor Torácica Aguda**



# DOR TORÁCICA

História dirigida  
Exame físico

- AAS (☒)
- Clopidogrel (☒)
- Nitrato (☒)
- O2 nasal (☒)
- Analgesia (☒)

10 minutos  
!

**ECG**

**SEM alterações**

**Alterações  
isquêmicas**

**SCA com  
supra de ST**

30 minutos

Observação entre  
8-12 h com ECGs  
e enzimas seriados

Internação para  
estabilização

Excluir  
contra-  
indicações  
para  
trombolíticos

**ANGIOPLASTIA  
CORONARIA**

# Síndromes Coronárias

# Classificação Clínica

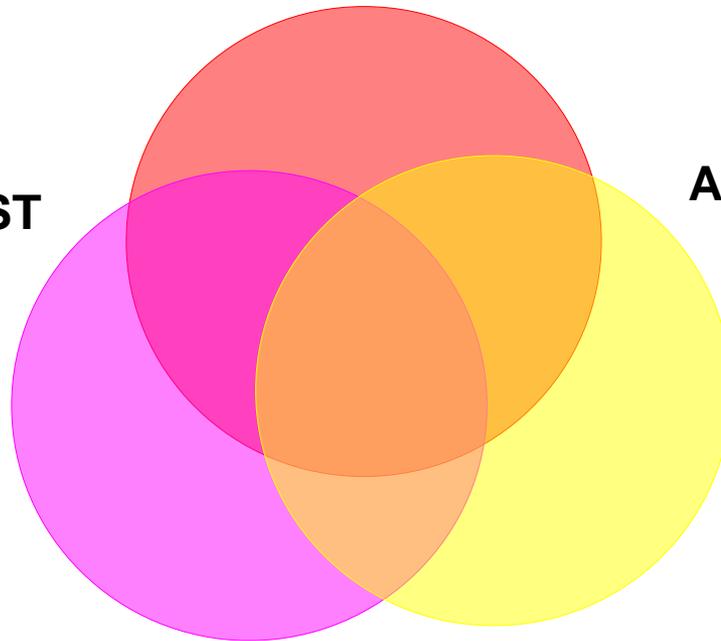
- Síndrome Coronária Aguda com Supra de ST
- Síndrome Coronária Aguda sem Supra de ST
  - Angina Instável
  - Infarto Agudo do Miocárdio sem supra de ST

# SÍNDROMES CORONÁRIAS AGUDAS

**IAM COM SUPRA DE ST**

**IAM SEM SUPRA DE ST**

**ANGINA INSTÁVEL**



“É inevitável na natureza das síndromes de ter uma matriz , uma essência compartilhada de sintomas , e de ter variância de sintomas em torno das bordas da referida essência.”

Antonio R. Damasio

Neurologista e Neurocientista

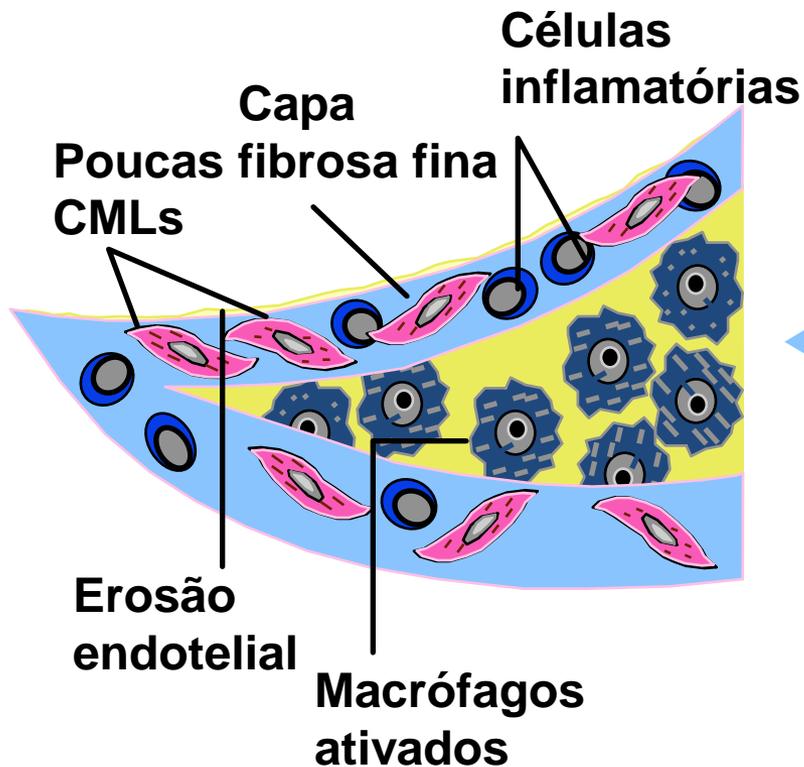
University of Southern California, Div. of Neurology

*in* Descartes' Error: emotion, reason and the human brain

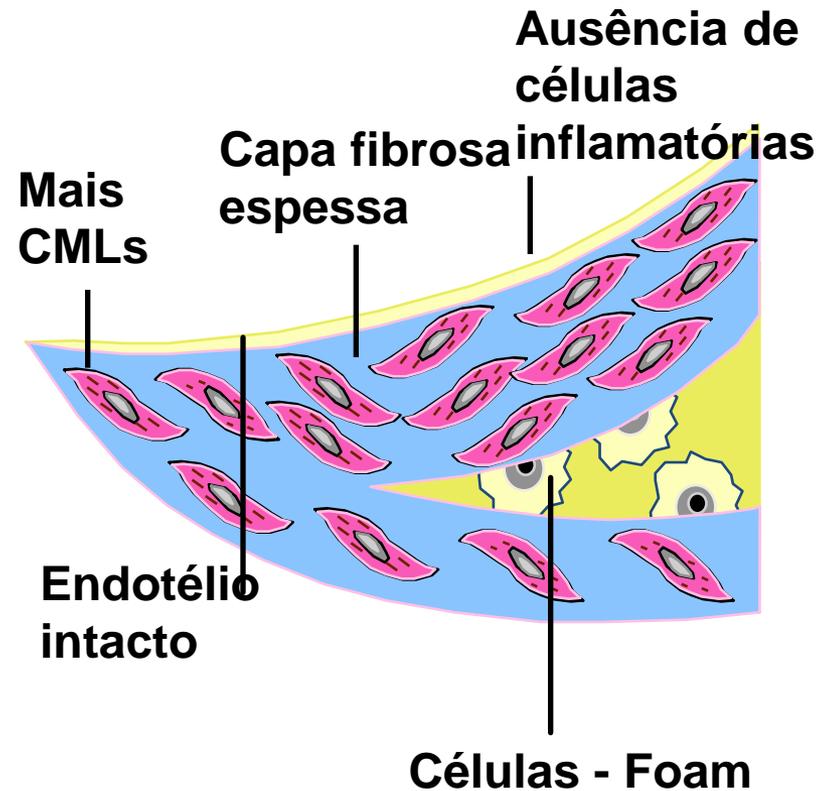
2nd Edition, Penguin Books.

# Características das Placas Instáveis e Estáveis

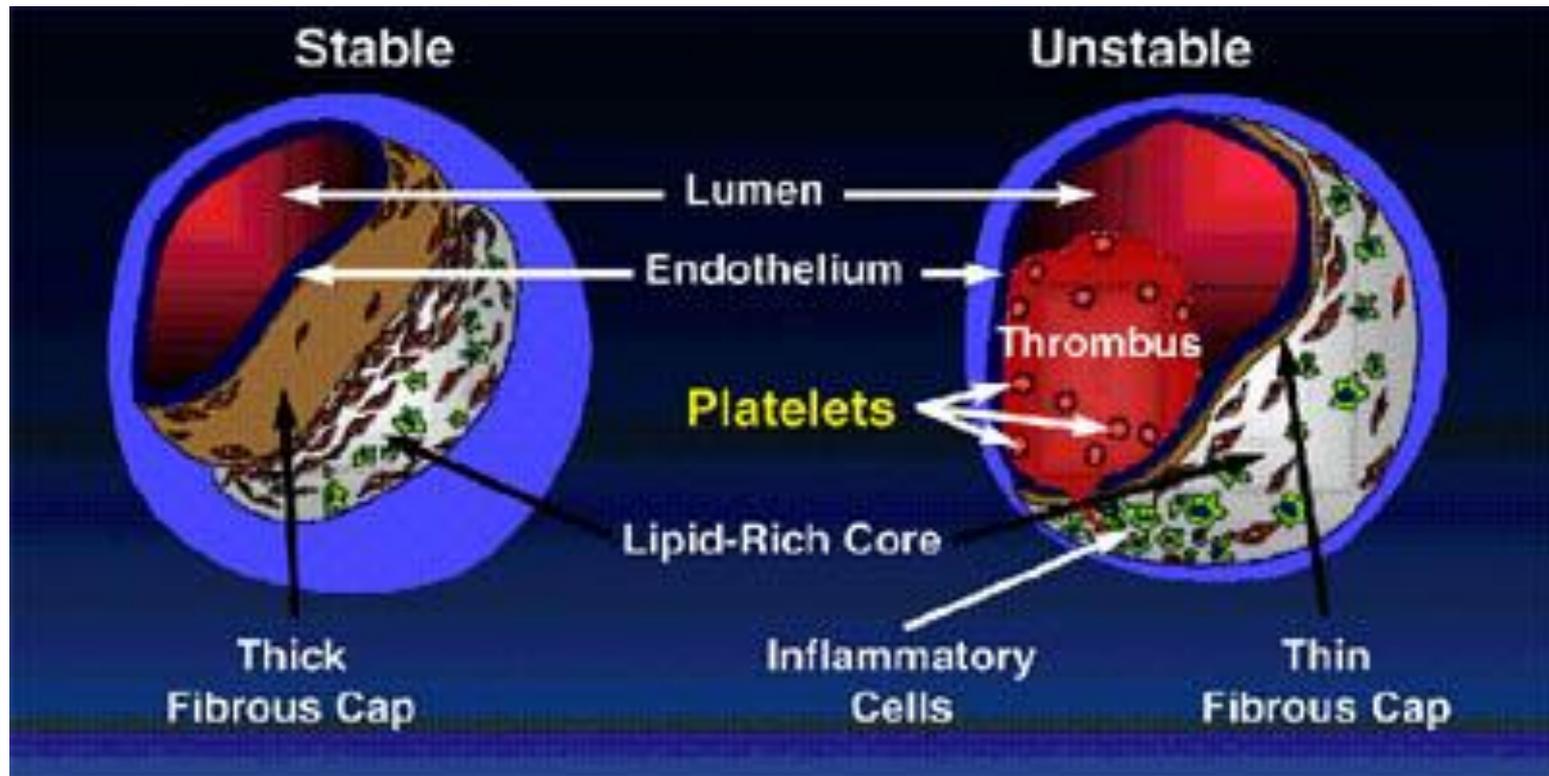
**Instável**



**Estável**



# Atherothrombosis: Thrombus Superimposed on Atherosclerotic Plaque



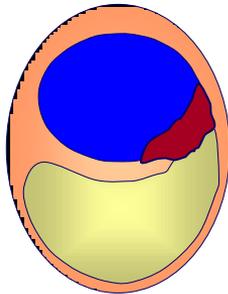
Adapted with permission from Falk E, et al. *Circulation*. 1998;92:657-671. Slide reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# Formação trombótica na SCA

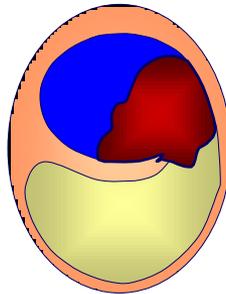
Ruptura/Fissura/Erosão da Placa



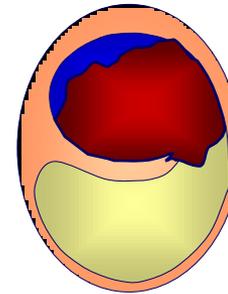
Formação Trombótica



AI



IAM SEM SUPRA DE ST



IAM COM SST

# História Clínica

- Características da dor
  - Tipo
  - Tempo
  - Duração
  - Irradiação
  - Fatores desencadeantes
  - Fatores de melhora
- Dor epigástrica
- Sintomas associados
- História pregressa

# FATORES DE RISCO MAIORES

- ✓ HAS
- ✓ Diabetes Mellitus
- ✓ Dislipidemia
  - ✓ Elevação de LDL
  - ✓ Diminuição do HDL
- ✓ Tabagismo
- ✓ História familiar de coronariopatia

# FATORES DE RISCO MENORES

- ✓ Idade
  - ✓ Homens > 60 anos
  - ✓ Mulheres > 70 anos
- ✓ Sexo Masculino
- ✓ Obesidade
- ✓ Sedntarismo
- ✓ Stress
- ✓ SAOS

# Exame Físico

## DEFINE O RISCO

- ✓ Frequência Cardíaca
- ✓ Pressão arterial
- ✓ Frequência Respiratoria e Sat. perif de O2
- ✓ Ausculta pulmonar e cardíaca
- ✓ Análise de pulsos periféricos
- ✓ Semiologia Abdominal
- ✓ Avaliação Neurológica

# DOR TORÁCICA AGUDA



## DIAGNÓSTICO DIFERENCIAL

- Síndrome Coronária aguda (com ou sem supra de ST)
- Dissecção da aorta
- Pericardite aguda
- Embolia pulmonar
- Pneumotórax
- Dor músculo-esquelética
- Herpes Zoster
- Psicogênica
- Dor origem digestiva (doença péptica, espasmo esofágico, pancreatite, cólica biliar, colecistite aguda)
- Dor origem pulmonar (infecção, pleurite)

## DIAGNÓSTICO DIFERENCIAL

### OUTRAS CAUSAS CARDÍACAS

- Coronariopatia crônica (Angina estável)
- Prolapso valvar mitral
- Estenose aórtica
- Cardiomiopatia hipertrófica
- Doença de Chagas

# EXAMES COMPLEMENTARES

- ✓ ELETROCARDIOGRAMA
- ✓ Marcadores de necrose miocárdica
  - ✓ CPK / CK-MB (atividade) / CK-MB (massa)
  - ✓ TROPONINA I & T
  - ✓ MIOGLOBINA
- ✓ ECOCARDIOGRAMA
- ✓ CINEANGIOCORONARIOGRAFIA

# IAM com supra de ST



## Elevação ST

**Elevação do ponto J do segmento ST em 0,1 mV em 2 ou mais derivações contíguas exceto em V2 e V3**

**V2 e V3: 0,2 mV em homens  $\geq$  40 anos  
0,25 < 40 anos e 0,15 mV em mulheres**

## QRS

**Ondas Q (isolada não é critério)**

**BRE agudo (considerar como supra de ST)**

# Marcadores de necrose miocárdica

**Não esperar enzimas para  
fazer o diagnóstico diante  
de um ECG com supra**

# Terapêutica

## Princípios fundamentais

- Aumentar a oferta de O<sub>2</sub>
- Diminuir o consumo de O<sub>2</sub>
- Atuação no coágulo sanguíneo e nos fatores de coagulação
- Controle da dor

# MORFINA

- Indicações
  - Dor torácica isquêmica
  - IAM sem hipotensão
  - Edema agudo de pulmão
- Dose
  - 4 a 8 mg EV
  - Incrementos de 2 mg em intervalos de 5 a 15 min
- Precauções
  - Não administrar em pacientes hipotensos
  - Se ocorrer hipotensão, administrar 250 a 500 ml de SF 0,9%

# Oxigenioterapia

- **SCA sem complicações**
  - Oxigênio a 4 l/min por cateter nasal nas primeiras 2-3 horas
  - Provavelmente sem benefício após 3-6 horas
- **SCA (congestão pulmonar evidente,  $SaO_2 < 90\%$ )**
  - Máscara facial de O<sub>2</sub> a 10 l/min; ajuste conforme a necessidade
  - Continuar a terapêutica até que o paciente esteja estável
  - Considerar a VNI em edema pulmonar ou intubação

# Beta-bloqueadores

- **Indicações**

- Síndromes Coronárias agudas

- **Efeitos**

- ↓ Consumo de oxigênio miocárdico
- ↓ A mortalidade e o reinfarto não fatal
- ↓ A incidência de FV primária

- **Precauções**

- Insuficiência moderada de VE
- DPOC grave, história de asma

- **Contra-indicações**

- FC < 60 bpm
- PAS < 100 mmHg
- Insuficiência grave de VE
- BAV de segundo ou terceiro graus

**Dose:**

**Metoprolol 5 mg EV de 5/5' até totalizar 15 mg**

**se PAS > 100 mm Hg e FC > 60 bpm)**

**Seguir com 50 a 100 mg VO de 12/12 horas; ou Atenolol 25 a 50 mg VO de 12/12 horas**

# Nitratos

- **Indicações**
  - Síndromes Coronárias Agudas
    - Cuidado no infarto inferior
  - Hipertensão
  - Congestão pulmonar
- **Doses**
  - IV: Nitroglicerina: 12,5 a 25  $\mu\text{g}$  em bolo e infusão de 10 a 20  $\mu\text{g}$  /min
  - SL: Nitroglicerina: 0,4 mg. Repetir 2 vezes em intervalos de 5/5'  
Dinitrato de isossorbida: 5 mg SL. Repetir 2 vezes de 5/5'
- **Contra-indicações**
  - PAS < 90 mmHg
  - Bradicardia ou infarto de VD
  - Bradicardia ou taquicardia graves

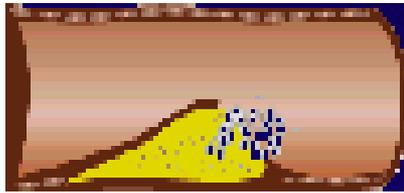
# Inibidores de ECA

- **Indicações**
  - IAM
  - Hipertensão arterial
  - Insuficiência cardíaca
  - Sinais clínicos de disfunção de VE
  - FE do VE < 40%
- **Dose e administração**
  - Não administrar nas primeiras 6 horas do IAM
  - Iniciar após terapia de reperfusão e que o paciente esteja estável sintomática e clinicamente
  - Iniciar com doses baixas
  - Captopril, Enalapril, Ramipril
- **Contra-indicações**
  - Gravidez
  - Angioedema
  - PAS < 100 mm Hg
  - Insuficiência renal clinicamente relevante
  - Estenose de artéria renal bilateral
  - Hipersensibilidade a IECA

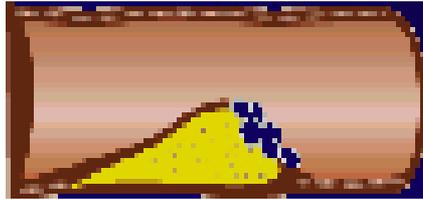
# Adesão, Ativação e Agregação Plaquetária

# Patogenética das Síndromes

## Coronárias Agudas: O papel fundamental das plaquetas



Placa  
Fissura  
ou  
Rotura



Adesão  
Plaquetária



Ativação  
Plaquetária



Agregação  
Plaquetária

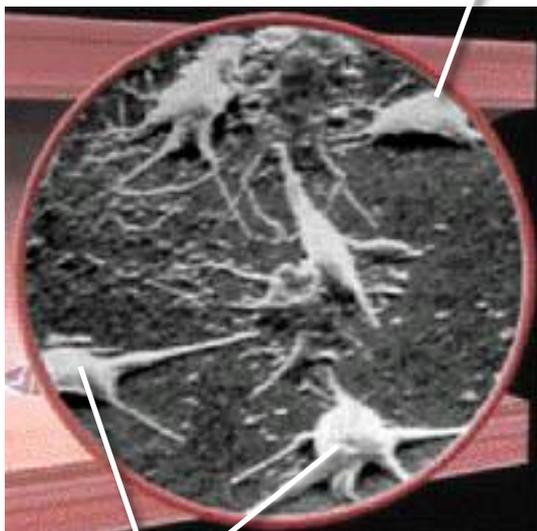


Obstrução  
Trombótica

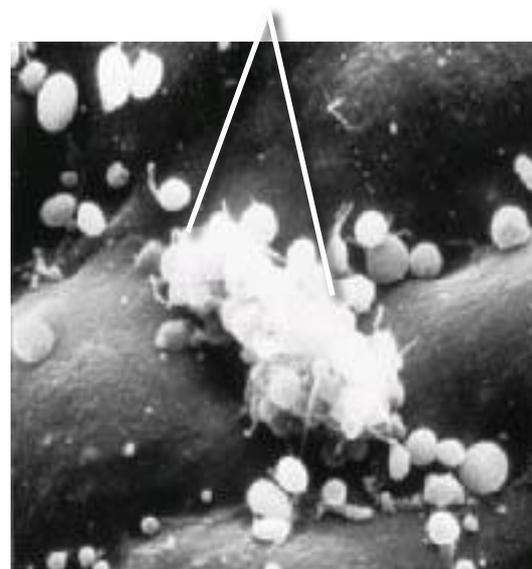


# O Papel das Plaquetas na Aterotrombose

## 1 Adesão



## 3 Agregação



## 2 Ativação

## Targets for antithrombotics

### Anticoagulation

Fondaparinux

LMWH  
Heparin

Bivalirudin

Tissue Factor

Plasma clotting  
cascade

Prothrombin

Factor  
Xa

Thrombin

Fibrinogen

Aspirin

Collagen

ADP

Thromboxane A<sup>2</sup>

Conformational  
activation of GPIIb/IIIa

Clopidogrel  
Prasugrel  
Ticagrelor

GPIIb/IIIa  
inhibitors

Platelet  
aggregation

Fibrin

**Thrombus**

- Indicações
  - Suspeita de dor torácica isquêmica
  - IAM com elevação do segmento ST
  - Angioplastia coronária
- Dose
  - 160 a 325 mg VO, amassada ou mastigada
  - Supositórios de 325 mg se náuseas ou vômitos
- Precauções e Contra-indicações
  - Úlcera péptica ativa
  - Hipersensibilidade ou alergia
  - Desordens hemorrágicas, doença hepática grave

# P2Y<sub>12</sub> Inhibitors

	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Triazolopyrimidine
Reversibility	Irreversible	Irreversible	Reversible
Activation	Prodrug, limited by metabolism	Prodrug, not limited by metabolism	Active drug
Onset of effect	2-4 h	30 min	30 min
Duration of effect	3-10 days	5-10 days	3-4 days
Withdrawal before major surgery	5 days	7 days	5 days

# Tienopiridínicos

- **Indicação**

- IAM com supra de ST
- Angina instável ou IAM sem supra de ST tratada clinicamente
- Angina instável ou IAM sem supra de ST que serão submetidos a ICP

- **Doses de ataque**

- Clopidogrel: 300 a 600 mg via oral
- Ticagrelor : 180 mg via oral
- Prasugrel : 60 mg via oral

\*Manutenção: por um período mínimo de 12 meses

- **Precauções/contra-indicações**

- Sangramento ativo ou distúrbio de coagulação nos últimos 30 dias
- Hemorragia intracraniana, cirurgia ou trauma no último mês
- Hipersensibilidade
- Contagem de plaquetas  $< 150000/\text{mm}^3$

# Anticoagulantes



- **Medicações**
  - Heparina não fracionada (HNF)
  - Heparina de baixo peso molecular (HBPM)
- **Dose**
  - HNF: 80 UI/kg EV em bolo seguido de 18 UI/kg/h EV por 48 horas. Manter KPTT 1,5 a 2 vezes o controle (45 a 70")
  - HBPM: 1 mg/kg SC de 12/12 horas
    - A primeira dose pode ser precedida de 30 mg EV
- **Contra-indicações**
  - **Absolutas**
    - Vigência de hemorragia, TCE recente, hemorragia recente no SNC, coagulopatia grave
  - **Relativas**
    - HAS severa, endocardite bacteriana, hemorragia digestiva recente, retinopatia diabética, plaquetopenia ( $<100.000/\text{mm}^3$ )

# Fibrinolíticos

- **Precauções**

- HAS grave (PA > 180/110 mm Hg)
- Uso de anticoagulantes (RNI > 2,5)
- Trauma recente ( 2-4 sem)
- RCP traumática ou cirurgia maior (< 3 sem)
- Depressão do segmento S-T

- **Contra-indicação de Trombólise**

- AVC hemorrágico prévio
- AVC no último ano
- Sangramento ativo
- Suspeita de dissecação de aorta

# Fibrinolíticos

## – Rt-PA (Alteplase)

- Infusão acelerada (1,5 hora)
- 15 mg ev em bolo
- 0,75 mg/kg em 30' (máx. 50 mg)
- 0,50 mg/kg em 60' (máx. 35 mg)

## – TNK t-PA (Tenecteplase)

- 30 mg se peso < 60 kg
- 35 mg entre 60 e < 70 kg
- 40 mg entre 70 e < 80 kg
- 45 mg entre 80 e < 90 kg
- 50 mg  $\geq$  90 kg

## – Estreptoquinase

- 1.500.000 UI em 1 hora de infusão

# Missed Opportunities for Reperfusion

**ST ↑ or LBBB, <12 hrs from onset, no contraindications**

	<b>ANC (%)</b>	<b>US (%)</b>	<b>AB (%)</b>	<b>EUR (%)</b>
n	269	327	339	739
PCI alone	1.1	17.7	13.9	16.2
Lytic alone	66.9	30.6	53.1	49.4
Both	2.2	18.7	5.0	4.9
Neither	29.7	33.0	28.0	29.5

AB, Argentina/Brazil; ANC, Australia/New Zealand/Canada; EUR, Europe; US, United States

# Independent Predictors of No Reperfusion

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Variable	OR (95% CI)
Prior CABG	<b>2.28</b> (1.35 - 3.87)
History of diabetes	<b>1.46</b> (1.11 - 1.94)
History of congestive heart failure	<b>2.92</b> (1.84 - 4.67)
Presentation without chest pain	<b>2.23</b> (2.13 - 4.89)
*Age $\geq 75$ years	<b>2.37</b> (1.82 - 3.08)

\*As compared to the <55 years age group

# ***Oclusão Coronariana Aguda***



**Necrose Miocárdica**



**Disfunção Ventricular**



**Morte**

**Reperfusion Coronária**



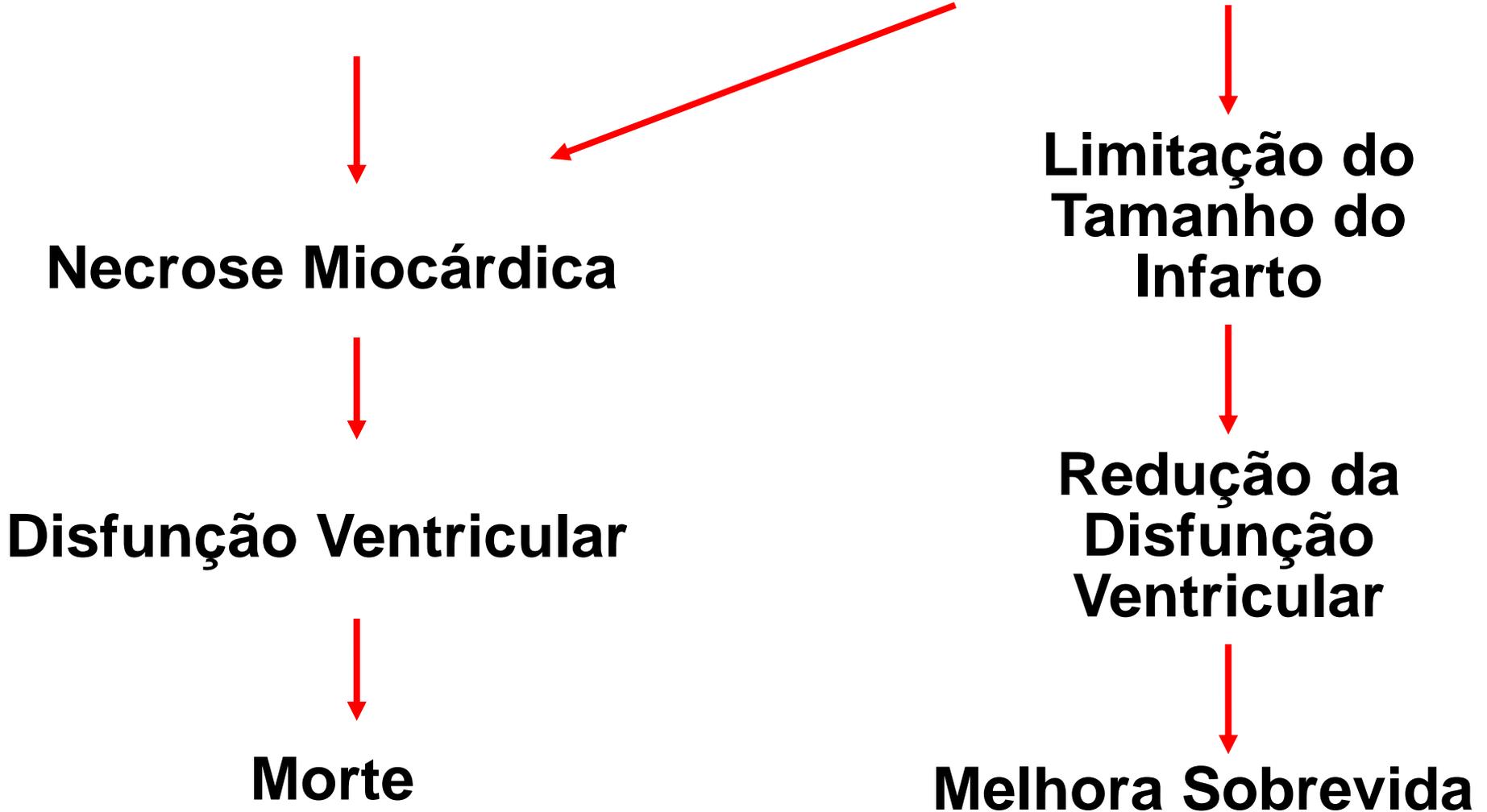
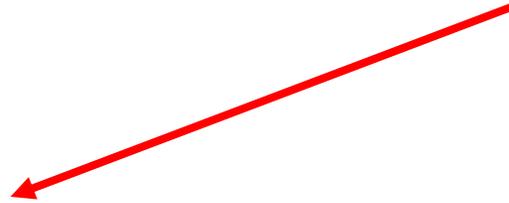
**Limitação do Tamanho do Infarto**



**Redução da Disfunção Ventricular**



**Melhora Sobrevida**



PR 152 INFARTO ANTERIOR, IDADE INDEFINIDA  
QRSd 106 INFARTO INFERO-POSTERIOR, AGUDO  
QT 384 LATERAL TAMBÉM EXISTEM DERIVS ENVOLVIDAS  
QTc 437 OSCILAÇÃO DA LB NAS DERIVS V1,V2

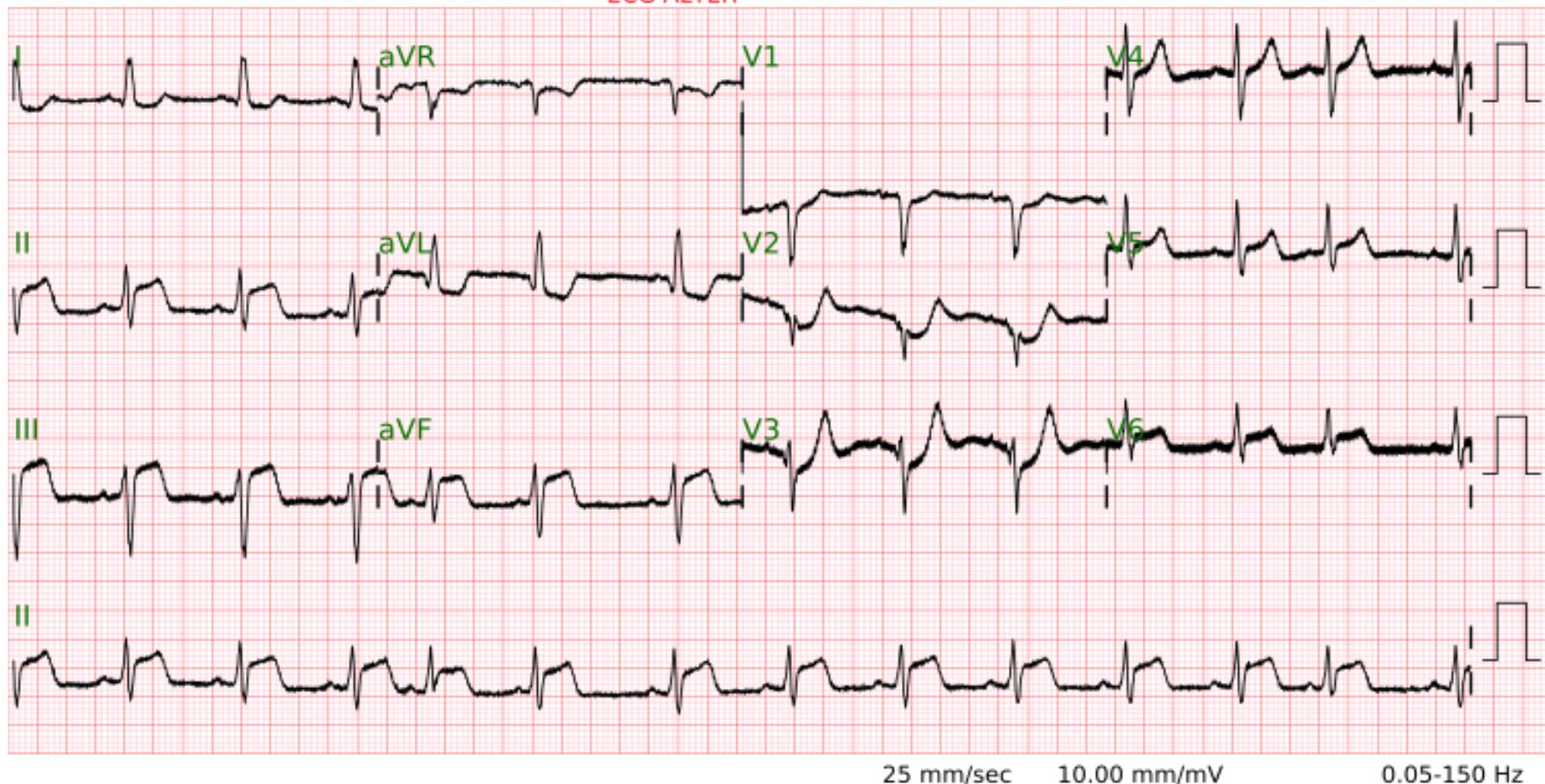
Axes  
P 49  
QRS -1  
T 95

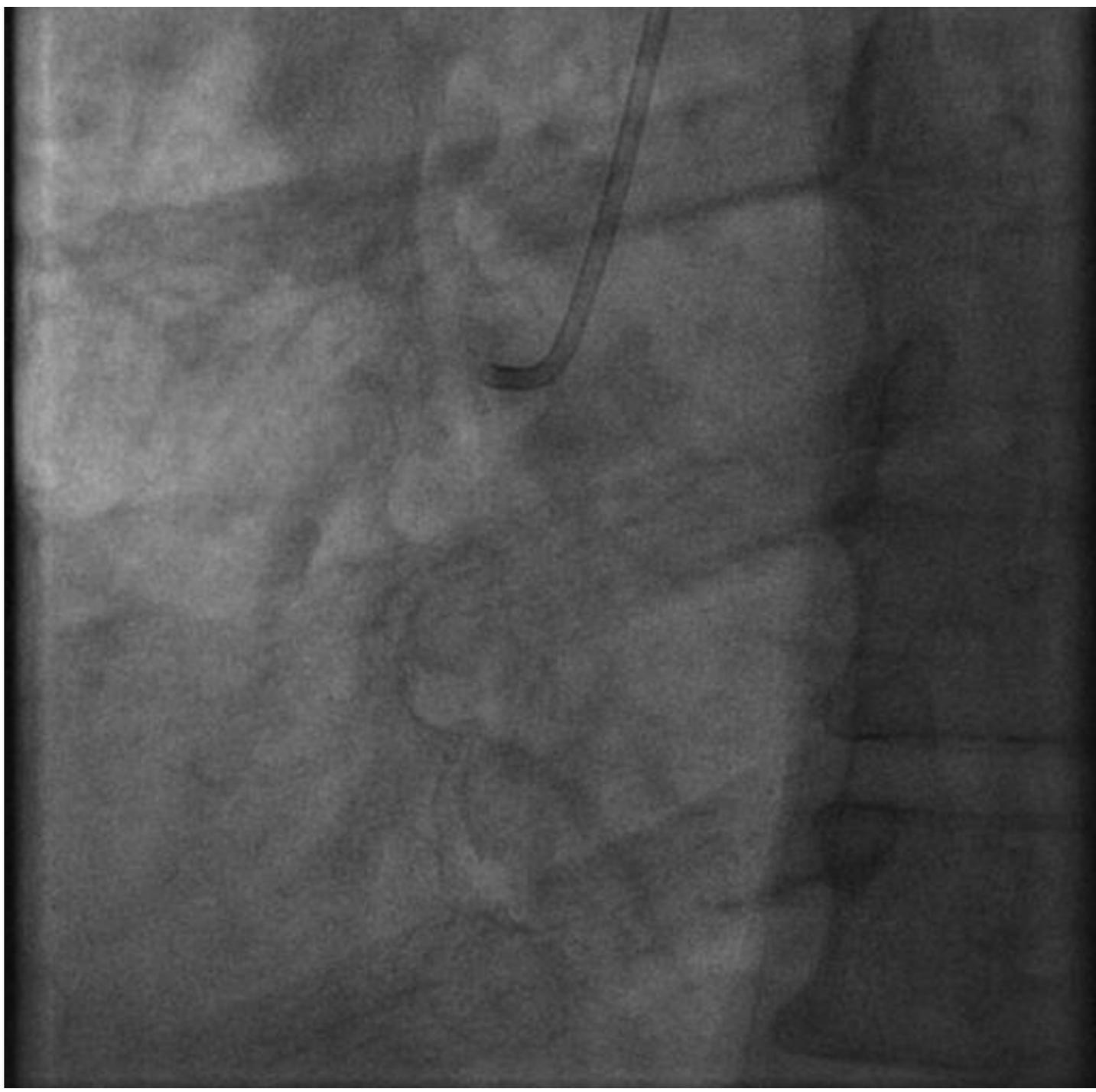
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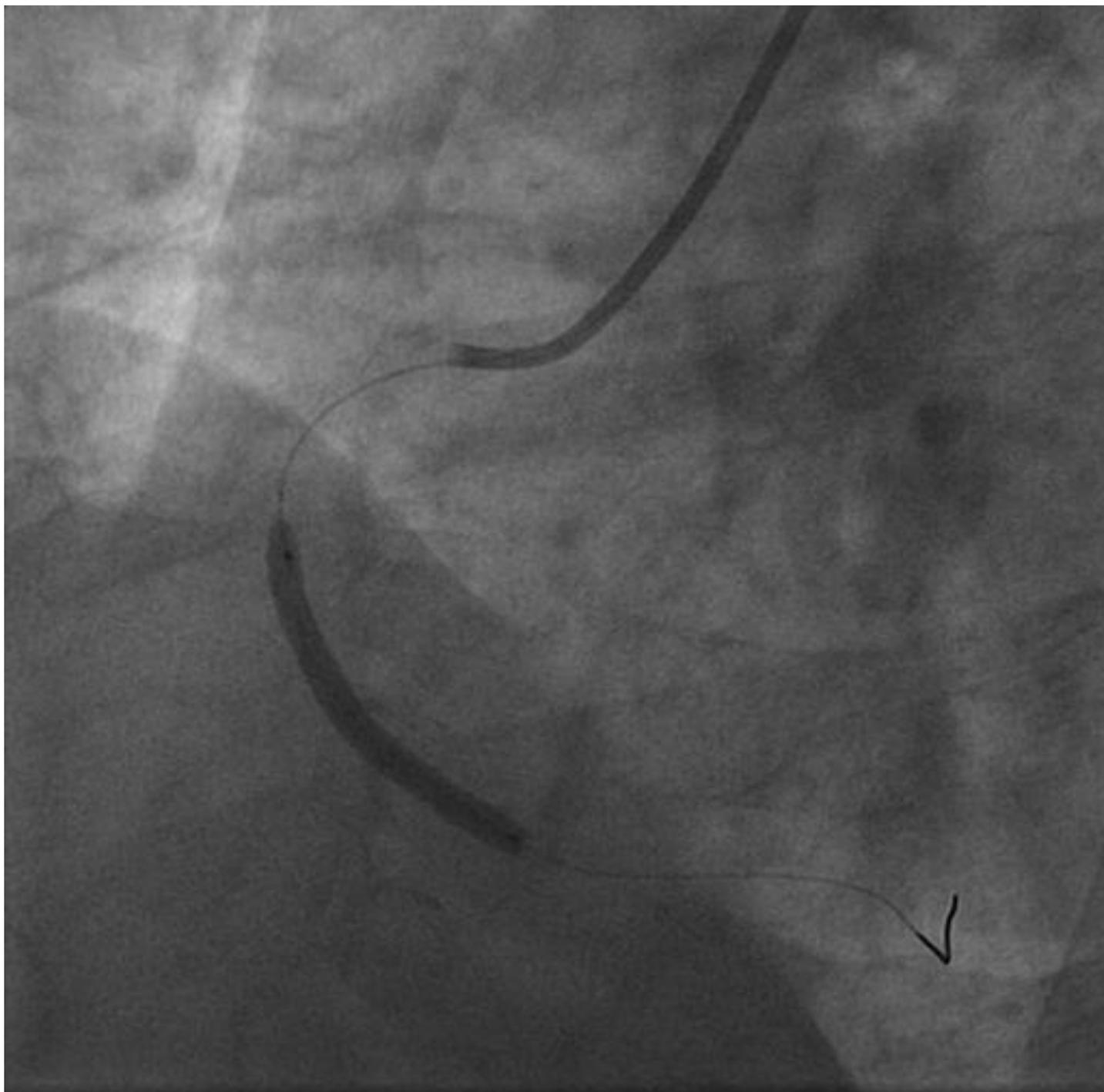


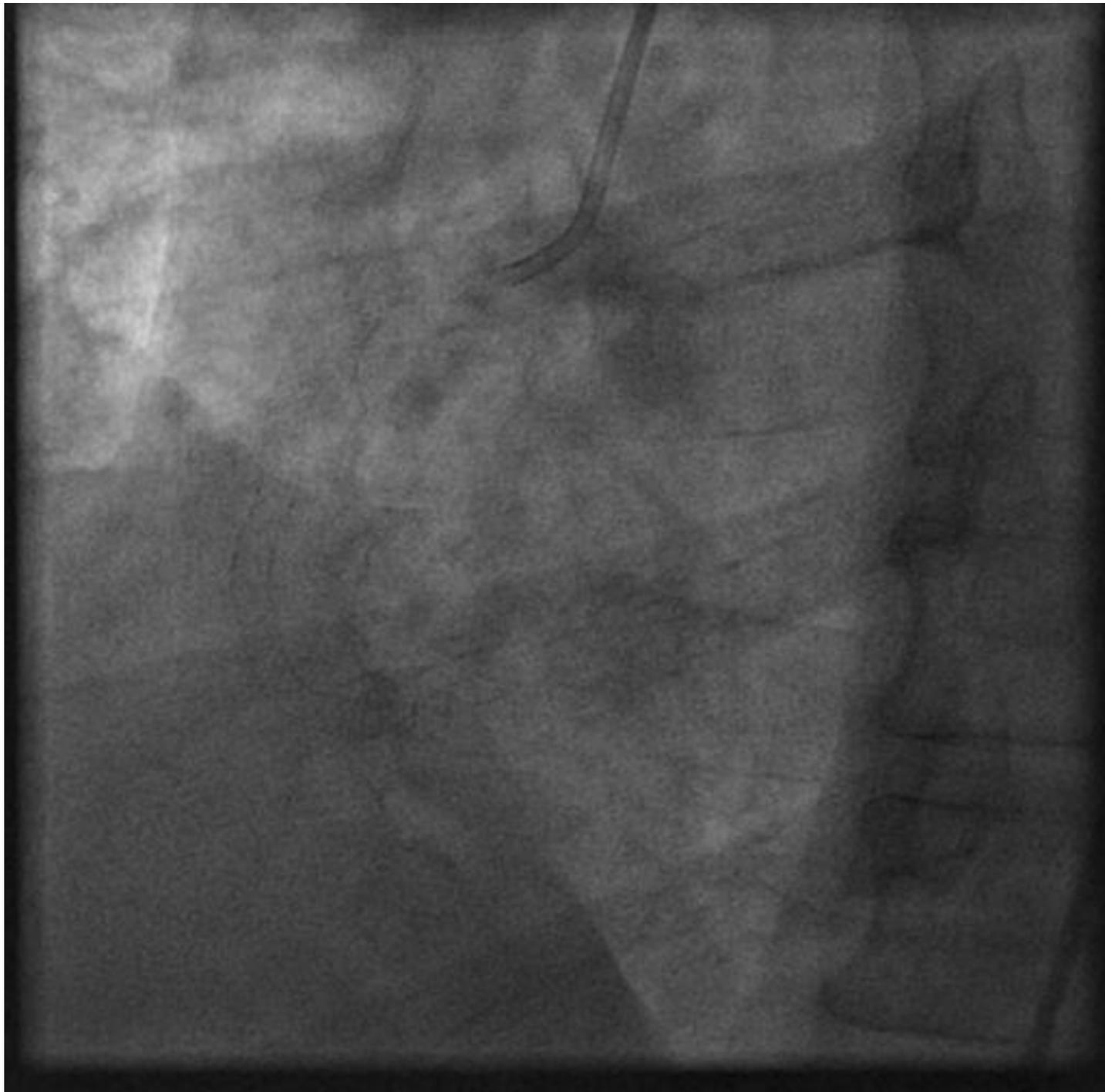
- ECG ALTER -

Diagnóstico não confirmado







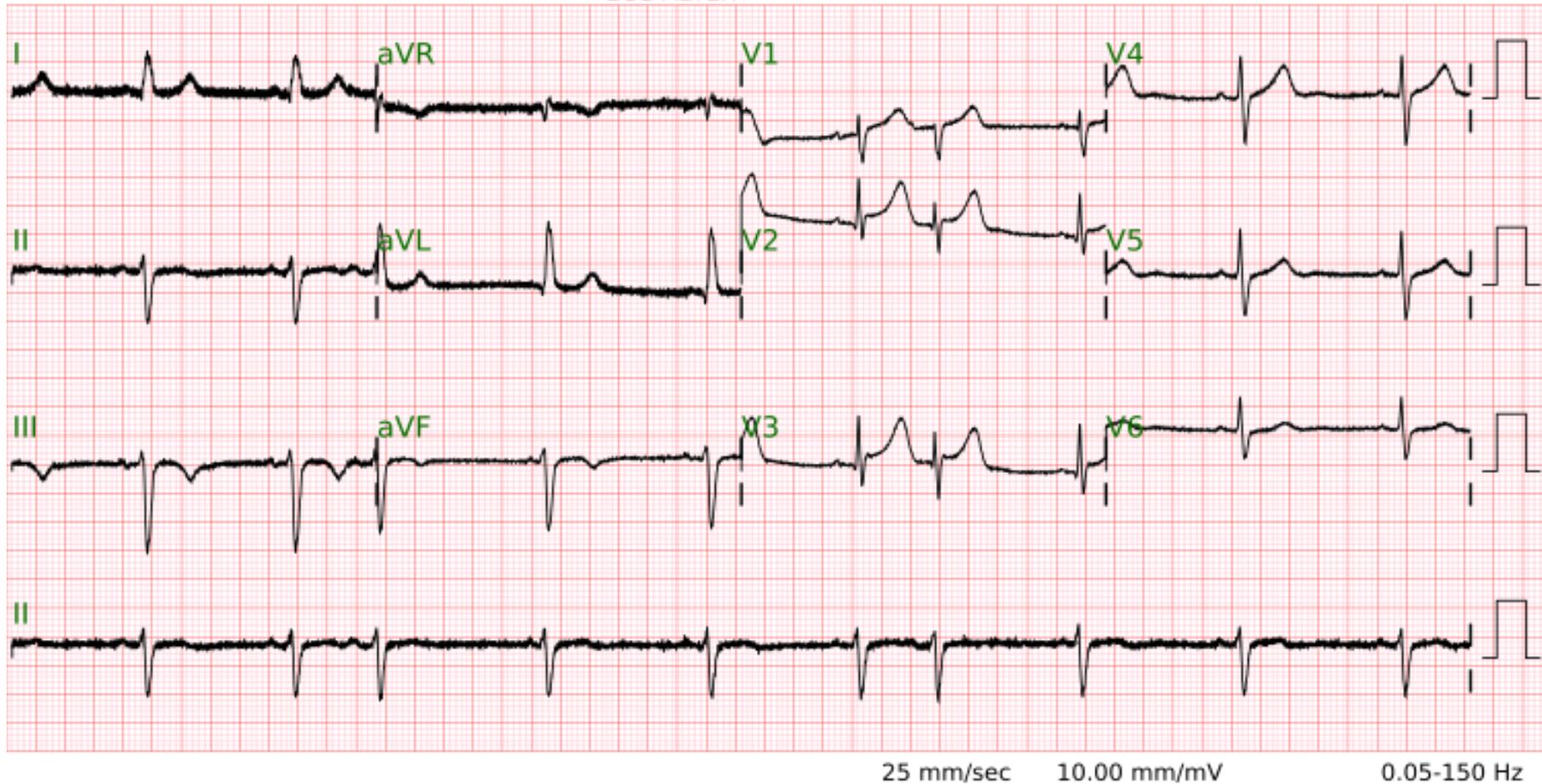


Rate 56 RITMO SINUSAL  
PR 152 EXTRA-SÍSTOLES ATRIAIS MÚLTIPLAS  
QRSd 113 BLOQUEIO FASCICULAR ANTERIOR ESQUERDO  
QT 436 OSCILAÇÃO DA LB NAS DERIVS V2  
QTc 421

## Axes

P 33  
QRS -59  
T -11

- ECG ALTER -



## Expert Consensus Document

### Universal Definition of Myocardial Infarction

Kristian Thygesen; Joseph S. Alpert; Harvey D. White;  
on behalf of the Joint ESC/ACCF/AHA/WHF Task Force  
for the Redefinition of Myocardial Infarction

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# Nova classificação clínica de Infarto Agudo do Miocárdio



## Classificação Descrição

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- 1** IAM espontâneo devido a um evento coronário primário como uma erosão de placa e/ou ruptura, fissura ou dissecção
- 2** IAM secundário a isquemia devido a um desbalanço entre oferta e consumo de O<sub>2</sub> devido a espasmo ou embolização coronária, anemia, arritmias, hipertensão ou hipotensão
- 3** Morte Súbita de origem cardíaca, incluindo parada cardíaca, sempre com sintomas sugerindo isquemia associadamente a uma nova alteração eletrocardiográfica (elevação do segmento ST ou BRE); ou evidência histopatológica ou angiográfica de trombo coronário recente diante da ausência dos biomarcadores acima
- 4a** IAM associado a Interenção Coronária Percutânea
- 4b** IAM associado com trombose intra-stent documentada
- 5** IAM associado c/ cirurgia de revascularização miocárdica

# Extratificação de Risco

# Braunwald Classification of Risk for Patients with Unstable Angina

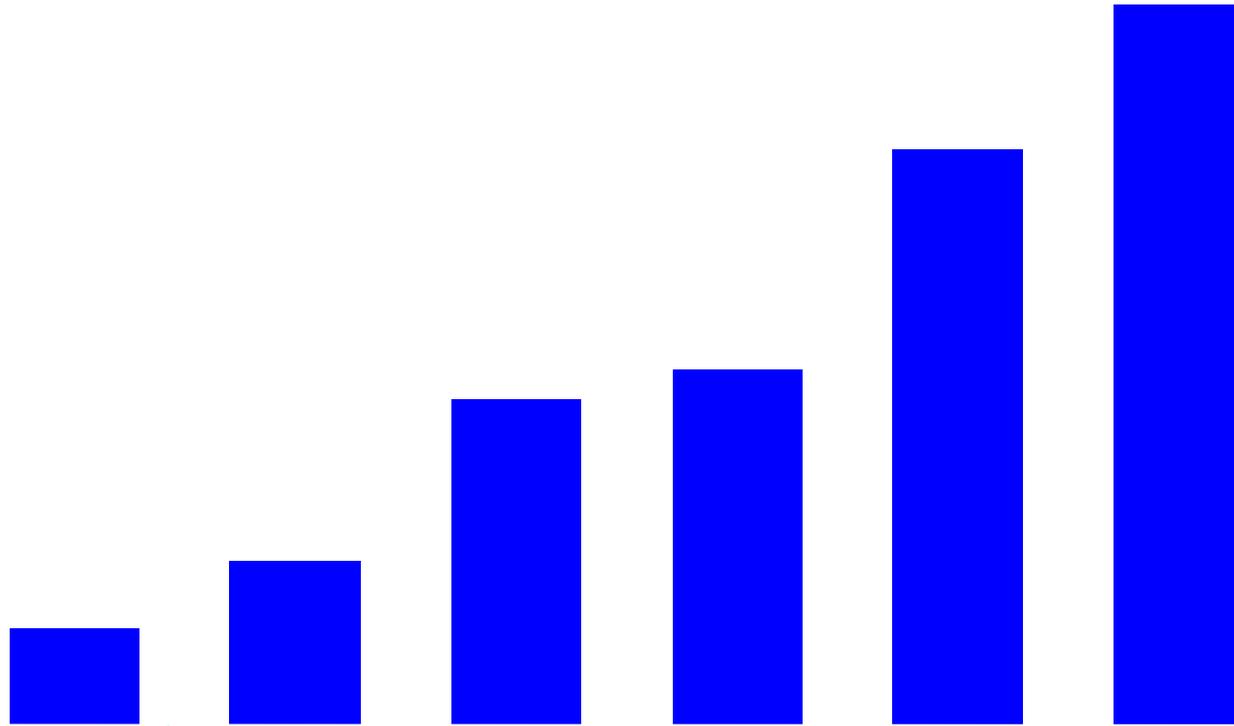


Feature	High Risk	Intermediate Risk	Low Risk
	At least 1 of the following features must be present:	No high-risk feature but must have 1 of the following:	No high- or intermediate-risk feature but may have any of the following features:
History	Accelerating tempo of ischemic symptoms in preceding 48 hrs	Prior MI, peripheral or cerebrovascular disease, CABG, or prior aspirin use	
Character of Pain	Prolonged ongoing (>20 min) rest pain	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD	New-onset or progressive CCS Class III or IV angina the past 2 weeks
Clinical Findings	<ul style="list-style-type: none"> <li>•Pulmonary edema</li> <li>•New or worsening MR murmur</li> <li>•S<sub>3</sub> or new/worsening rale</li> <li>•Hypotension, bradycardia, tachycardia</li> <li>•Age &gt;75 years</li> </ul>	Age > 70 years	
ECG	<ul style="list-style-type: none"> <li>•Angina at rest with transient ST-segment changes &gt;0.05 mV</li> <li>•New or presumed new BBB</li> <li>•Sustained ventricular tachycardia</li> </ul>	<ul style="list-style-type: none"> <li>•T-wave inversions &gt;0.2 mV</li> <li>•Pathological Q waves</li> </ul>	Normal or unchanged ECG during an episode of chest discomfort
Cardiac Markers	Elevated (TnT or TnI >0.1 mg/mL)	Slightly elevated (TnT >0.01 but <0.1 ng/mL)	Normal

# TIMI Risk Score

- Age  $\geq 65$  years
- $\geq 3$  CAD Risk Factors
- Prior Coronary Stenosis  $>50\%$
- ST deviation
- $\geq 2$  Anginal events  $\leq 24$  hours
- ASA in last 7 days
- Elevated Cardiac Markers (CK-MB or troponin)

# Troponin I Levels and Mortality in Patients with NSTEMI-ACS



Troponin I Level

# Prognostic Value of Troponin T or I in ACS: A Meta-Analysis

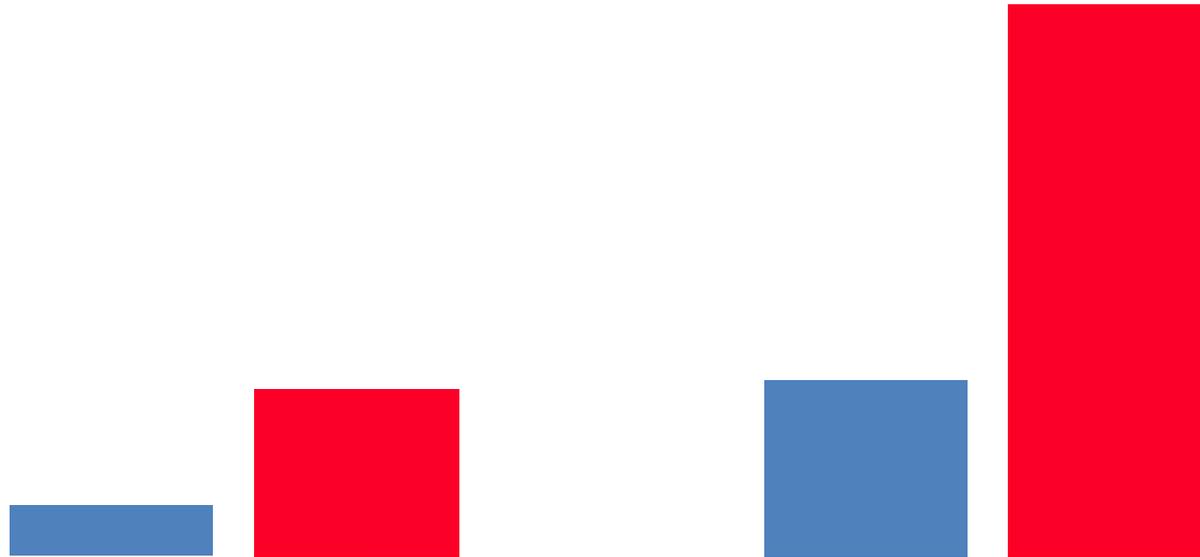
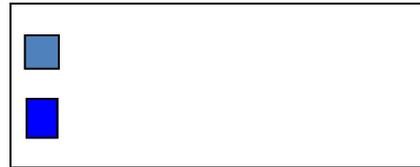


Figure reproduced with permission from Heidenreich PA, Alloggiamento T, Melsop K, et al. The prognostic value of troponin in patients with non-ST elevation acute coronary syndrome: a meta-analysis. *J Am Coll Cardiol.* 2001;38:478-485. Slide modified with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# B-type Natriuretic Peptide (BNP) and Mortality in ACS Patients

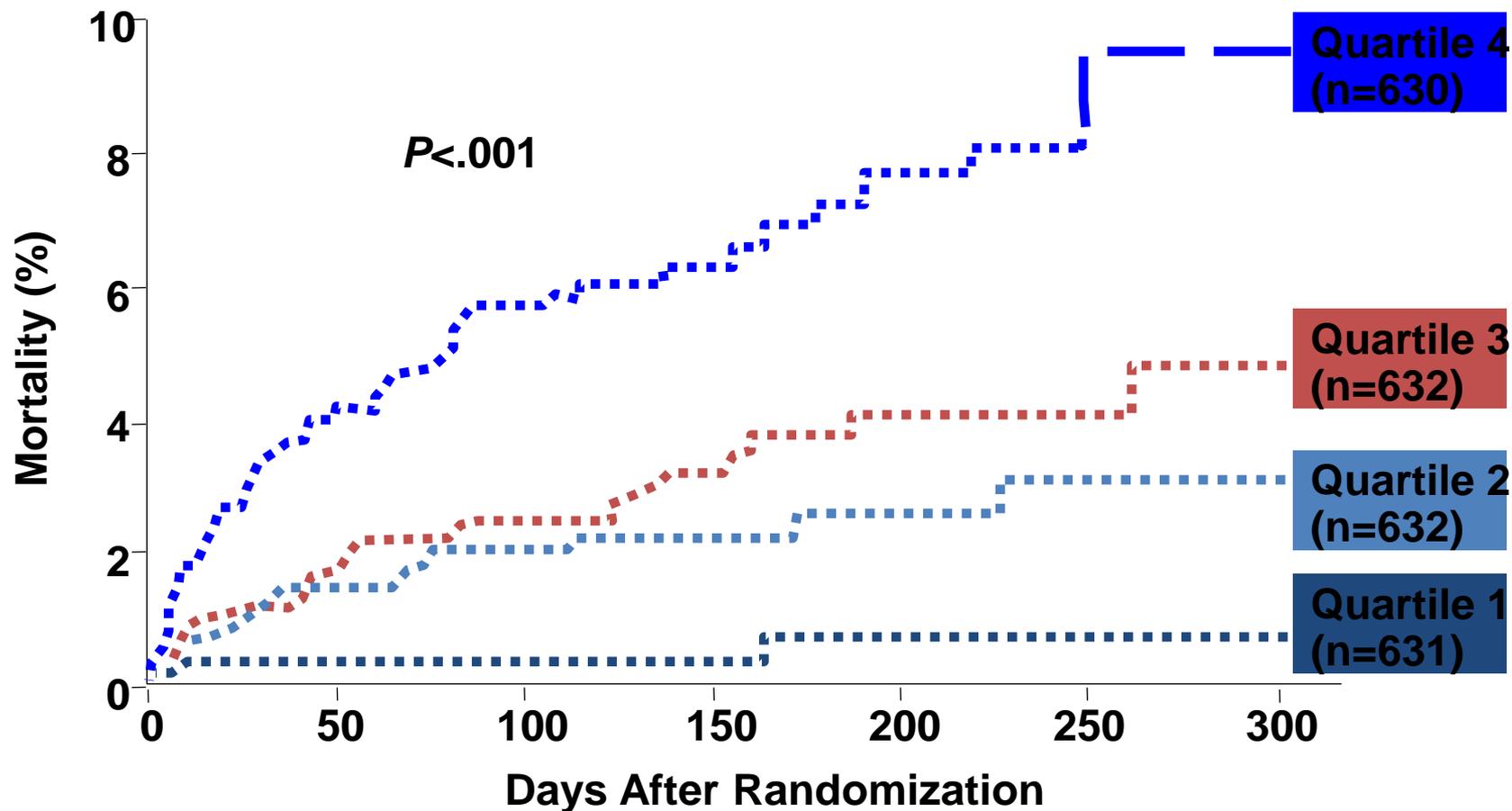


Figure reproduced with permission from de Lemos JA, Morrow DA, Bentley JH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndrome. *N Engl J Med.* 2001;345:1014-1021. Copyright © 2001, Massachusetts Medical Society. All rights reserved.

# Predictive Value of hs-CRP for Mortality from ACS in FRISC Substudy

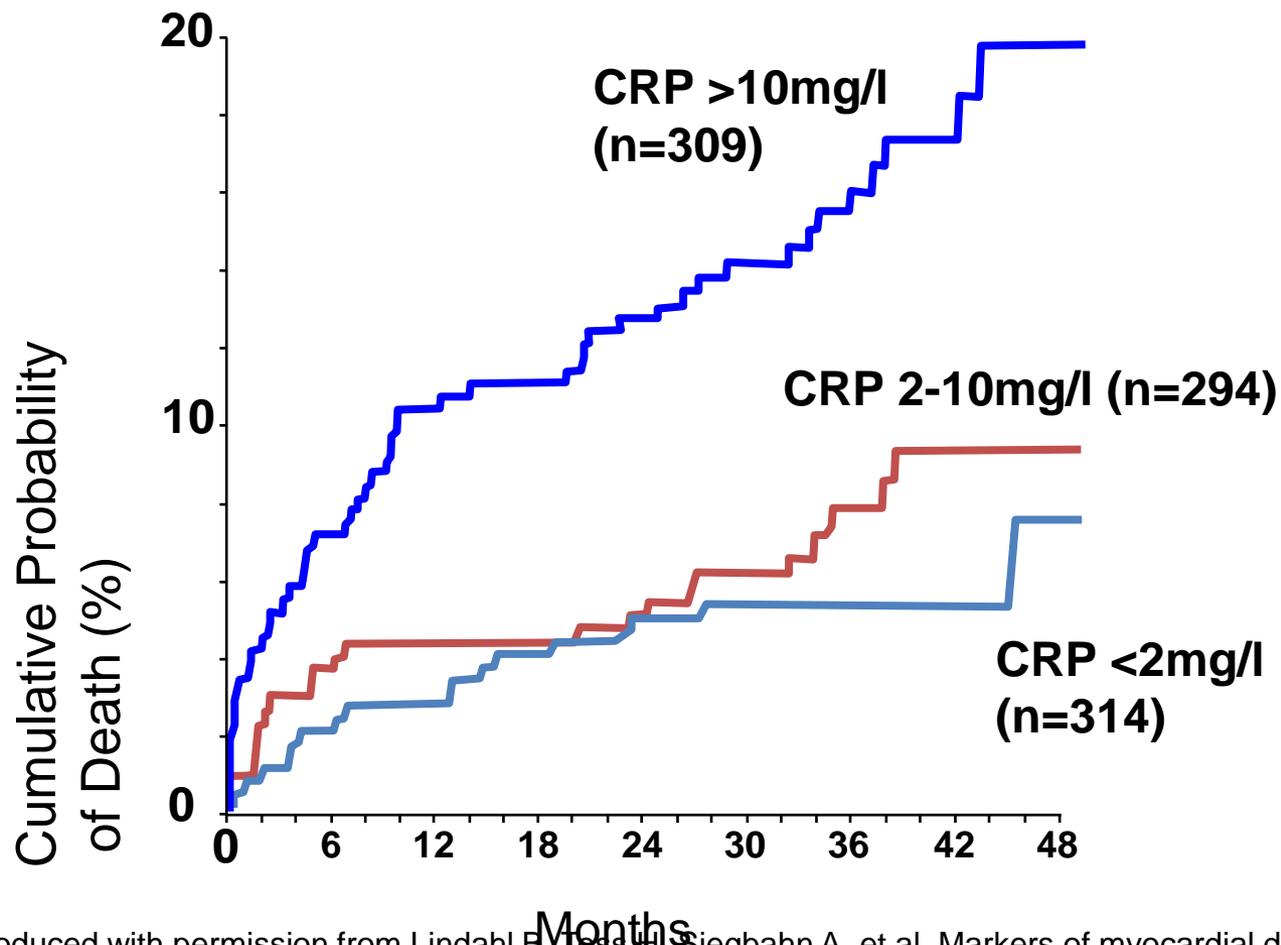


Figure reproduced with permission from Lindahl B, Teis E, Siegbahn A, et al. Markers of myocardial damage and inflammation in relation to long-term mortality in unstable coronary artery disease. FRISC Study Group. Fragmin during Instability in Coronary Artery Disease. *N Engl J Med.* 2000;343:1139-1147. Copyright © 2000, Massachusetts Medical Society. All rights reserved.

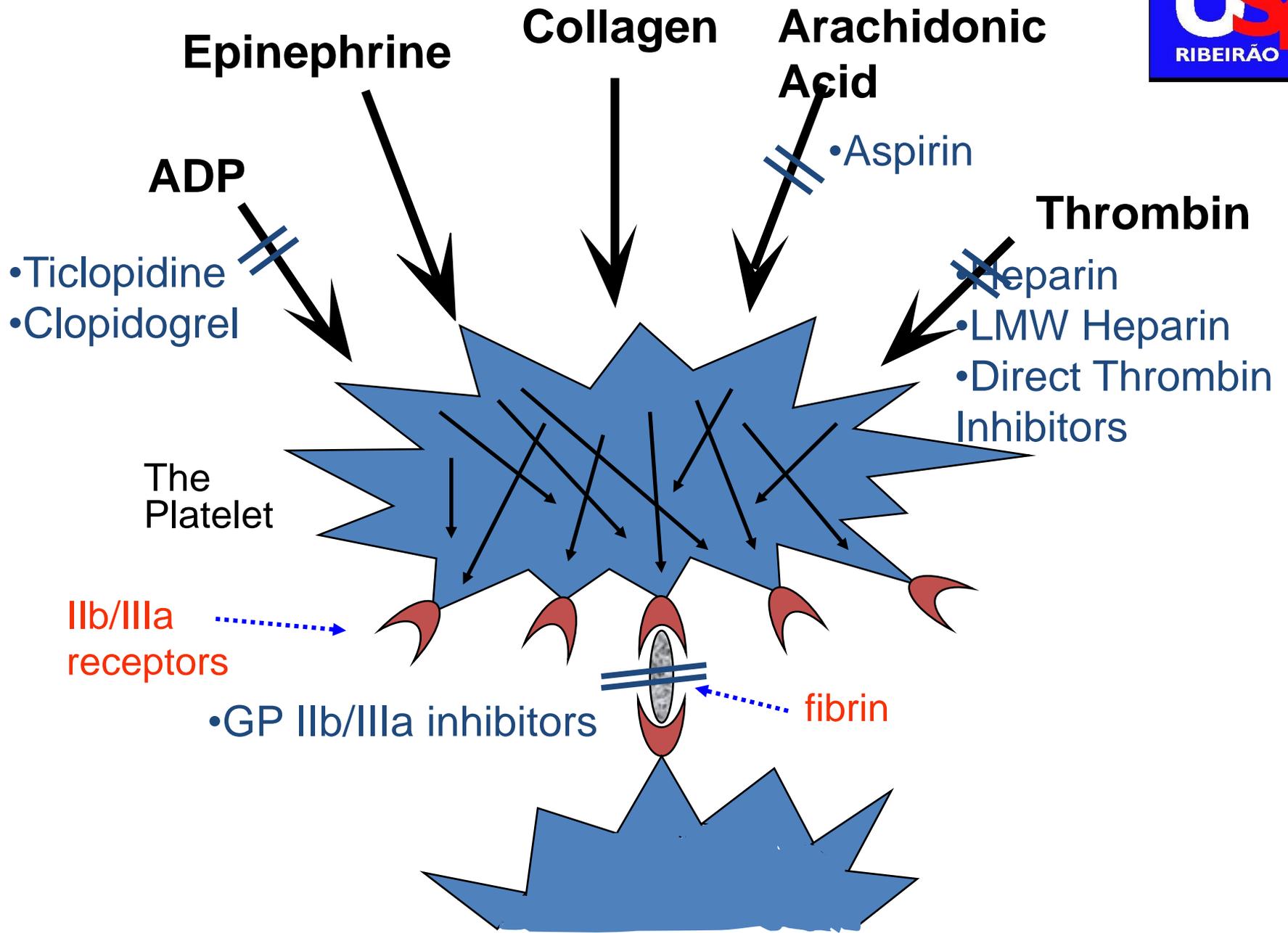
Slide modified with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# Initial Therapies and Management

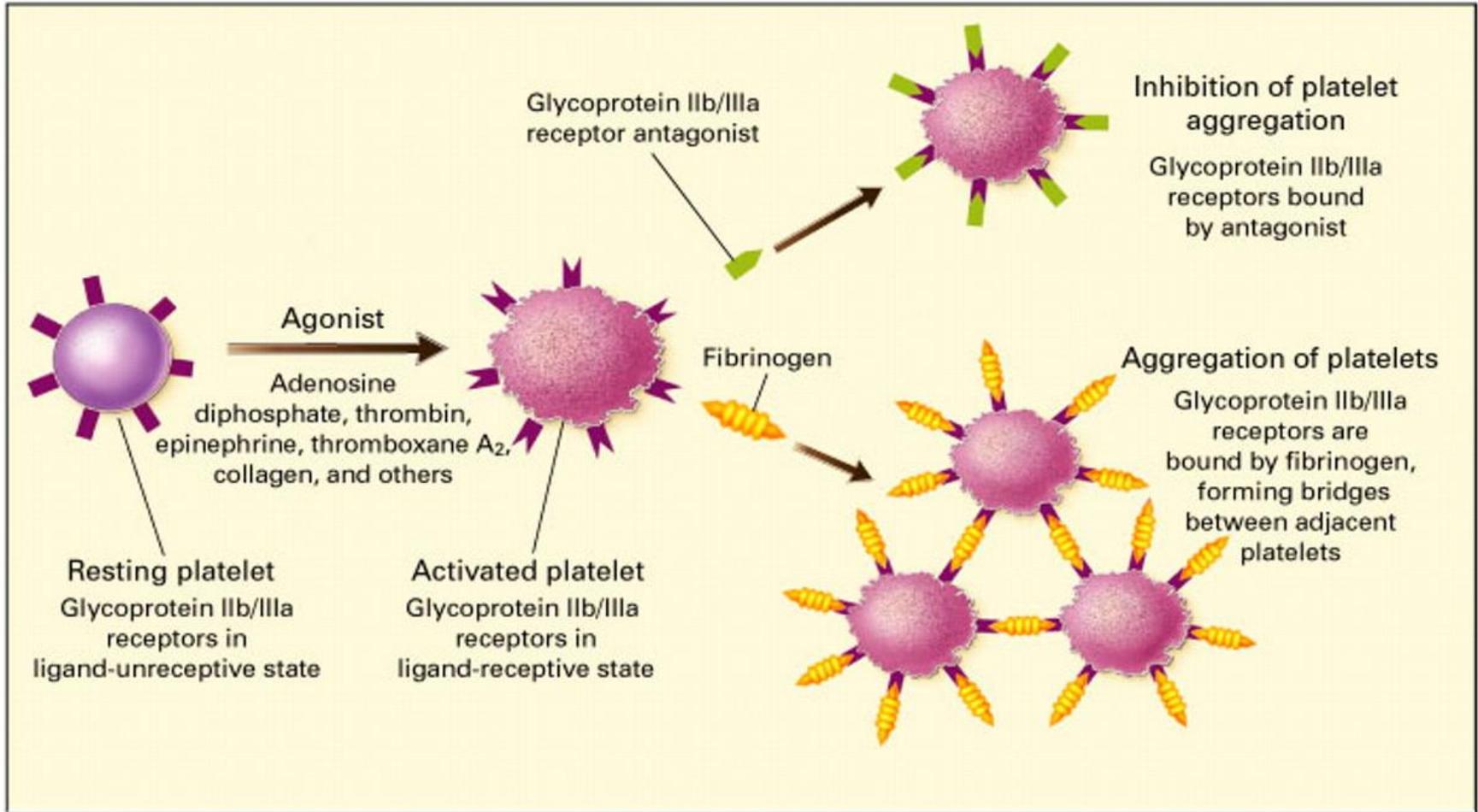
# ACC/AHA Class I Recommendations for Initial Management and Anti-Ischemic Therapy

- Bed rest
- Continuous ECG Monitoring
- Supplemental O<sub>2</sub> to maintain SaO<sub>2</sub> >90%
- NTG (IV or PO as dictated clinically)
- Beta-blockers (PO and/or IV)
- IV Morphine prn pain, anxiety, and/or CHF
- IABP for hemodynamic instability
- ACEI for persistent hypertension in patients with LV systolic dysfunction or CHF

# Platelets and Anti-Platelet Therapies

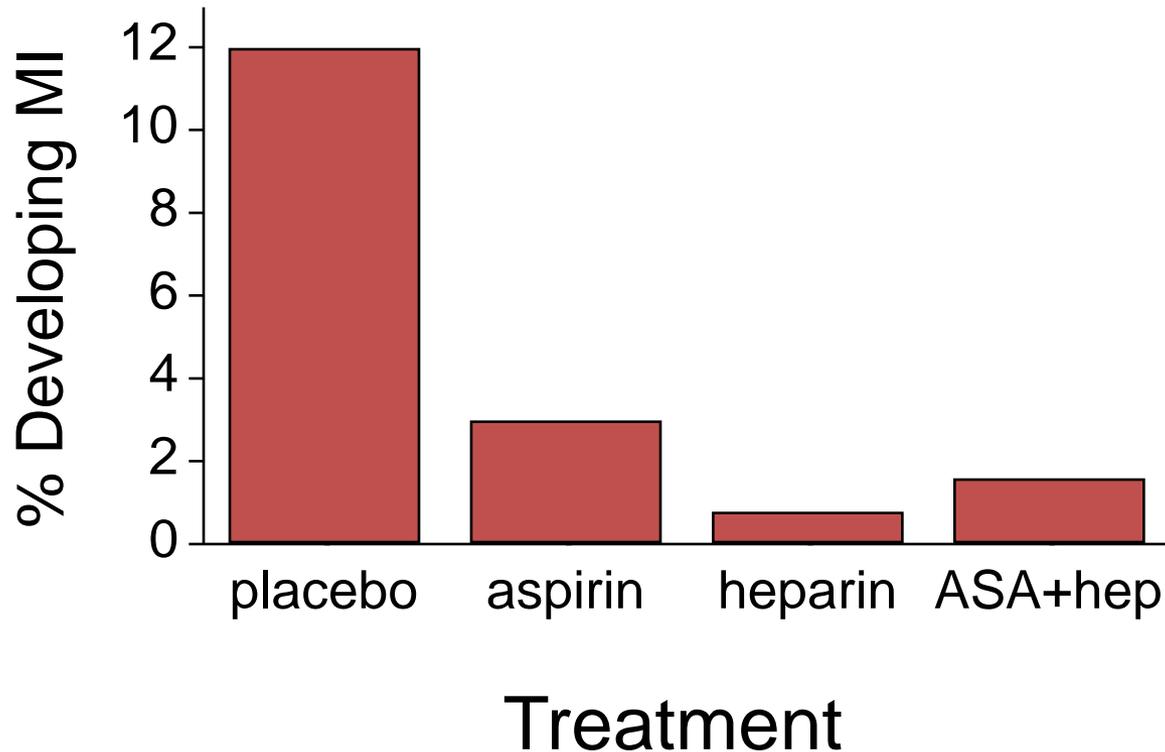


# Platelet Inhibition With GP IIb/IIIa Inhibitors



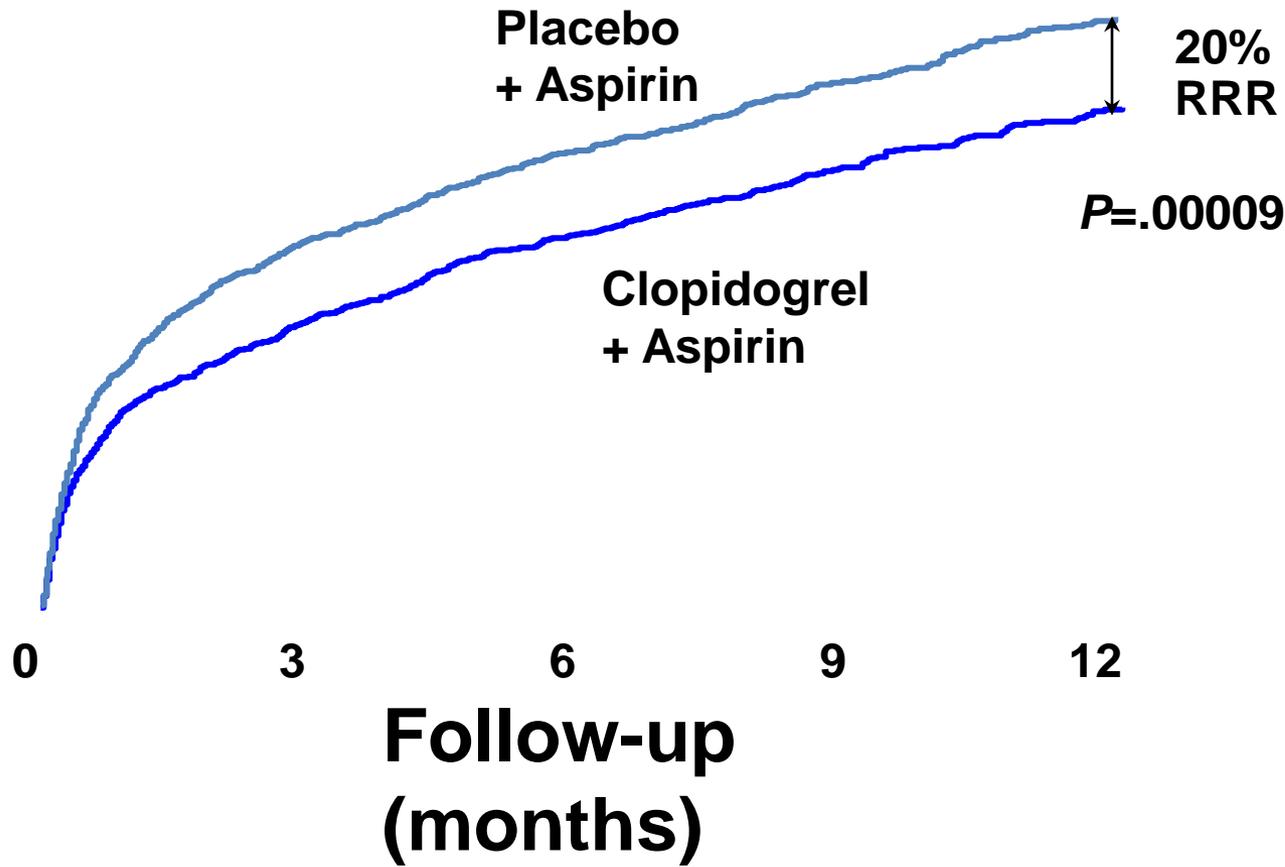
# Treatment of Unstable Angina

Results of a study from the Montreal Heart Institute



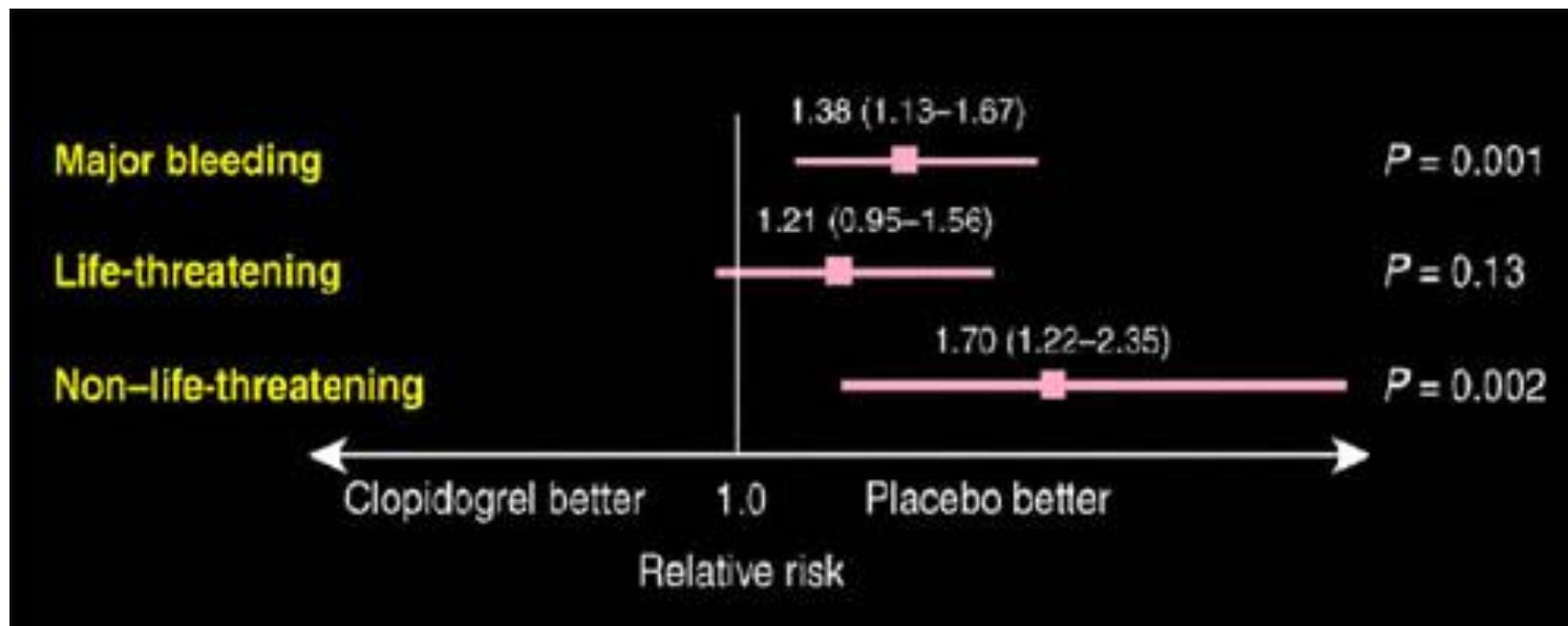
Data from Theroux P, Quimet H, McCans J, et al. Aspirin, heparin, or both to treat acute unstable angina. *N Engl J Med.* 1988;319:1105-1111.

# The Primary Composite End Point in the CURE Trial



Reproduced with permission from Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494-502. Copyright © 2001, Massachusetts Medical Society. All rights reserved.

# CURE Bleeding Complications



Data from Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494-502.

# CURE: Primary End Point in Subgroups

<b>Subgroup</b>	<b>Placebo</b>	<b>Plavix</b>	<b>RR</b>
ST Changes	14.3%	11.5%	0.79
No ST Changes	8.7%	7.0%	0.80
Enzyme Elevation	13.1%	10.7%	0.81
No Enzyme Elevation	10.9%	8.8%	0.79
Post-Randomization Revascularization	13.9%	11.4%	0.81
No Post-Random Revascularization	10.1%	8.1%	0.79

Data from Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494-502.

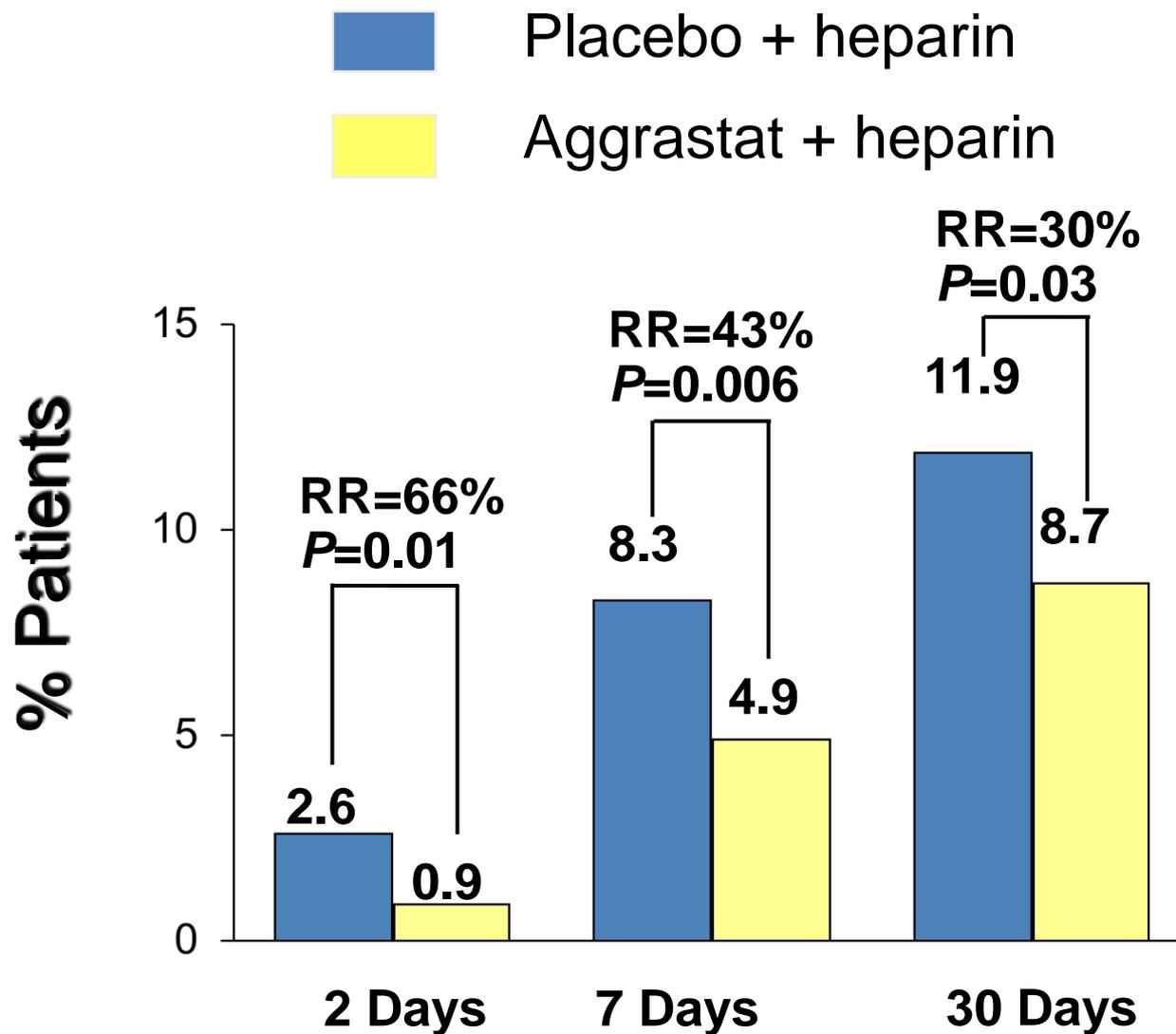
# CURE Secondary End Points



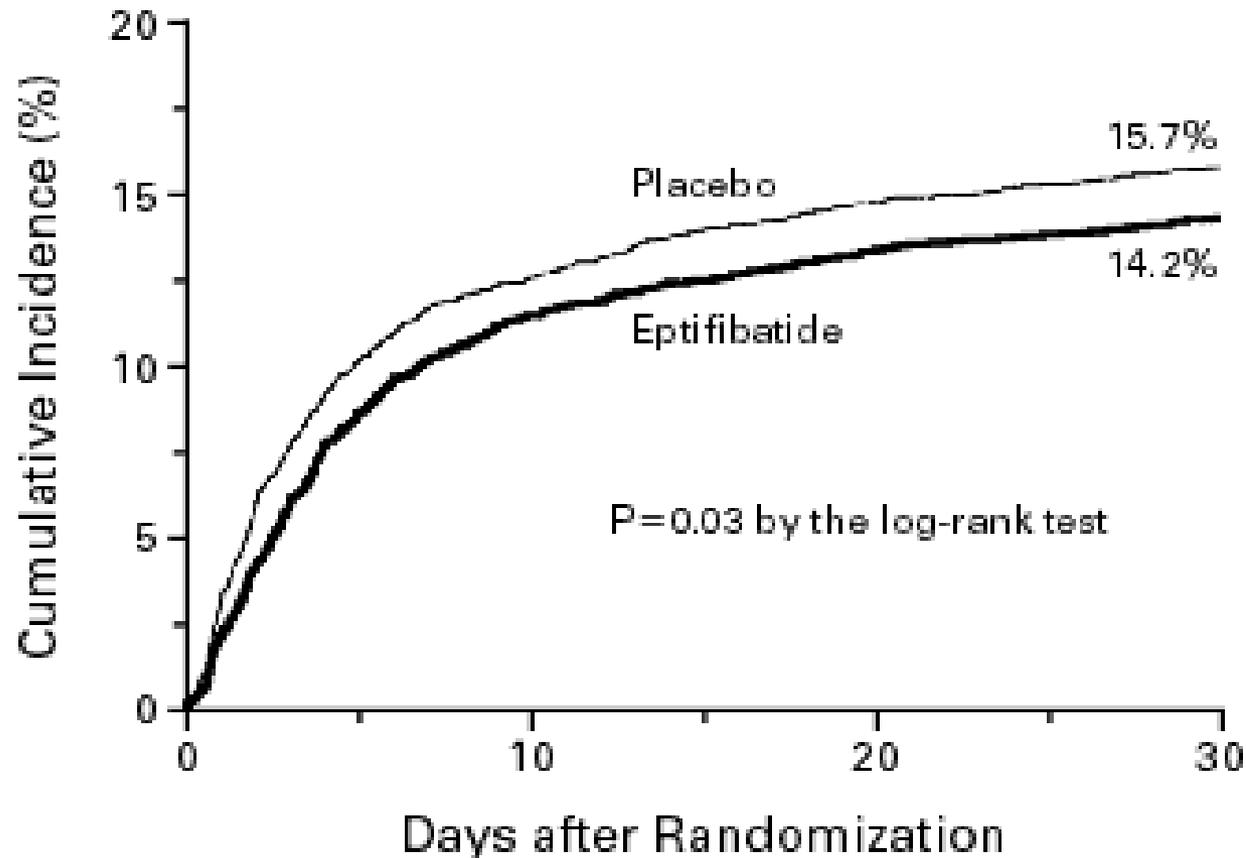
<b>Endpoint</b>	<b>Placebo</b>	<b>Plavix</b>	<b>RR</b>	<b>P Value</b>
CV Death/ MI/CVA	11.7%	9.28%	0.80	0.00005
CV Death/MI CVA/Ref Ischemia	19.02%	16.68%	0.88	0.0004
CV Death	5.4%	5.06%	0.92	NA
MI	6.68%	5.19%	0.77	<0.01
Stroke	1.4%	1.2%	0.85	NA
Refract Ischemia	9.4%	8.8%	0.93	NA
Major Bleeding	2.7%	3.6%	1.34	0.03

Data from Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001;345:494-502.

# PRISM-PLUS: MI/Death Event Rates

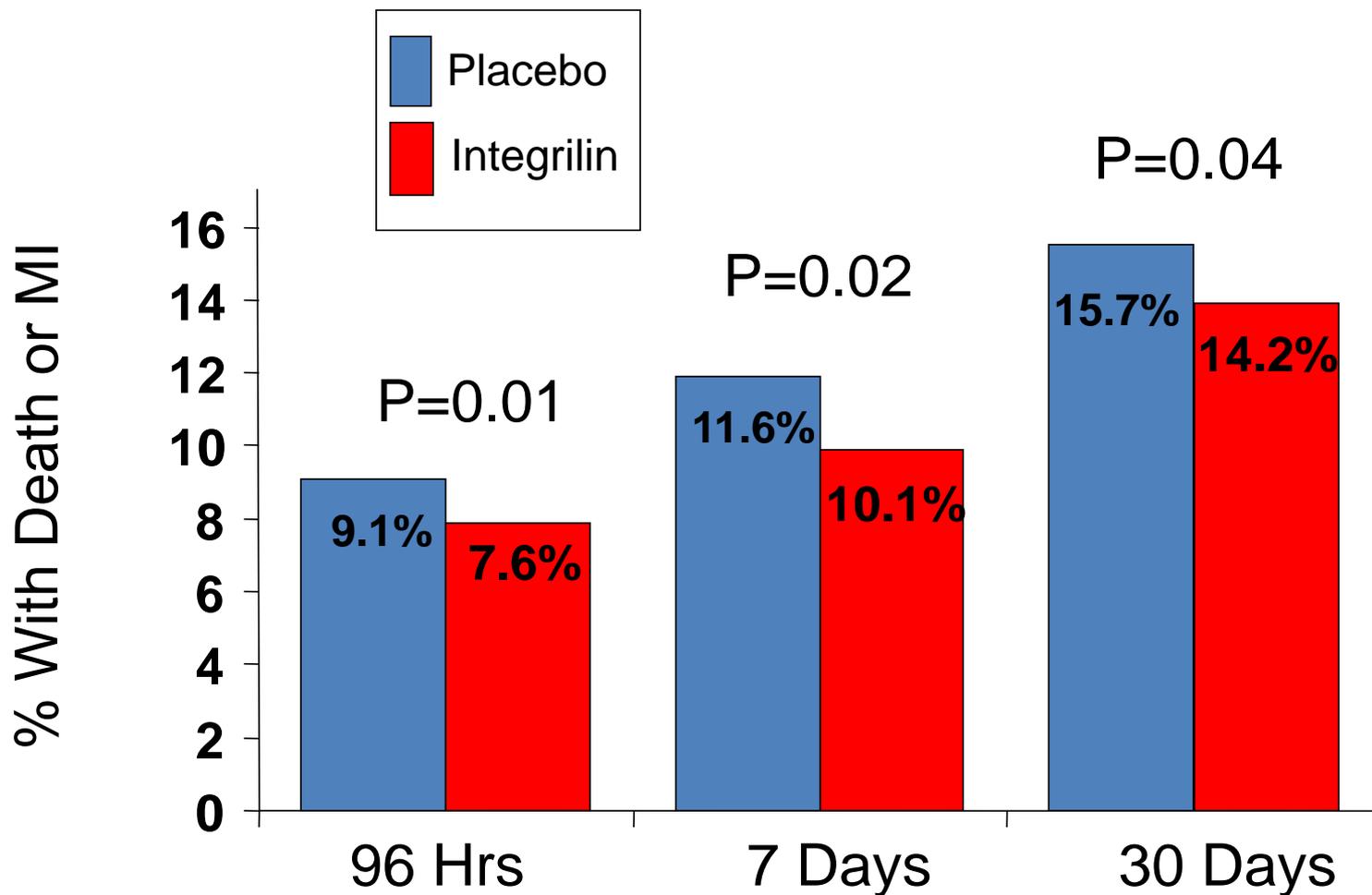


# PURSUIT Primary End Point



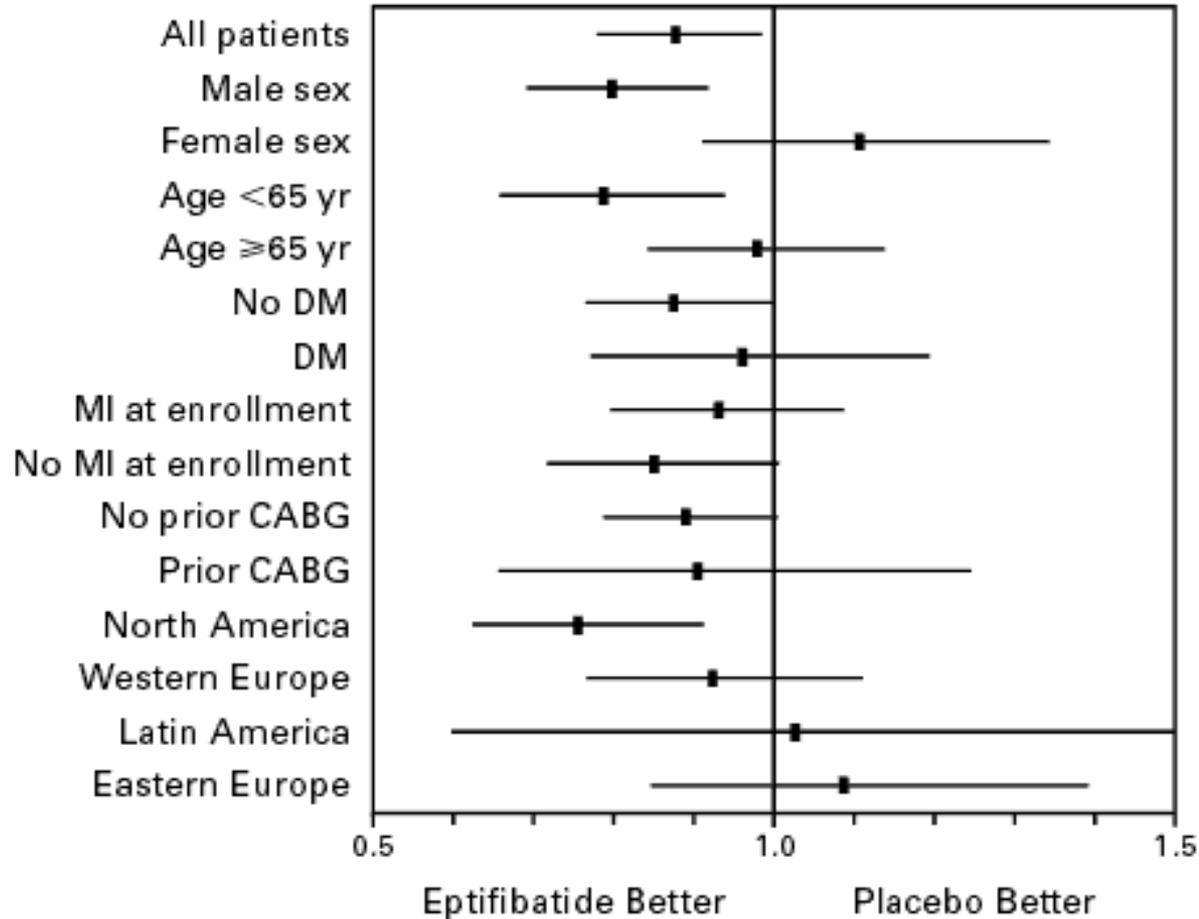
Reproduced with permission from the PURSUIT Trial Investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. Platelet glycoprotein IIb/IIIa in unstable angina: Receptor Suppression Using Integrilin Therapy. *N Engl J Med.* 1998;339:436-443. Copyright © 1998, Massachusetts Medical Society. All rights reserved.

# PURSUIT Primary Composite End Point



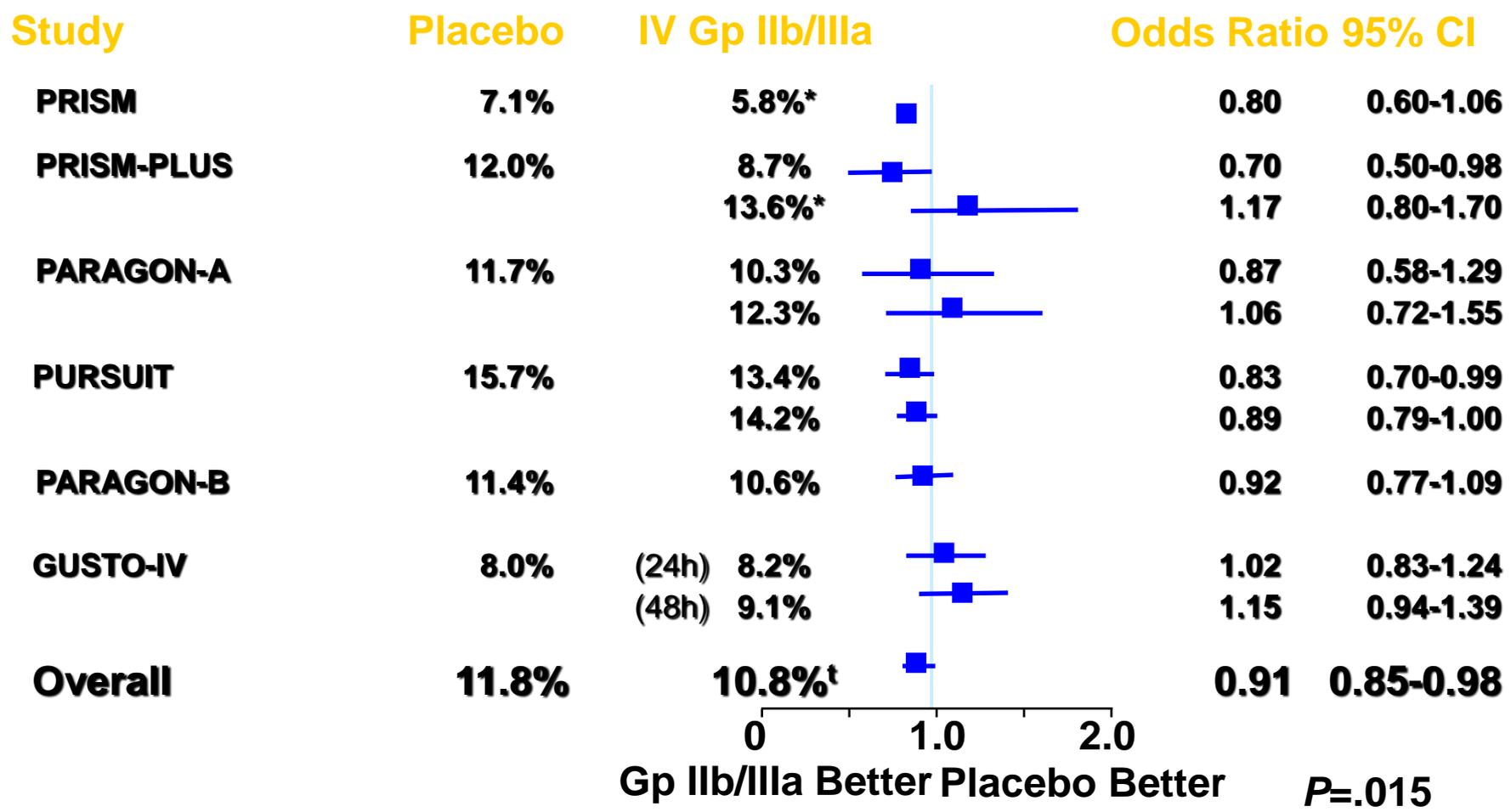
Not powered for statistical analysis

# Subgroup Analyses from the PURSUIT Study



Reproduced with permission from the PURSUIT Trial Investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. Platelet glycoprotein IIb/IIIa in unstable angina: Receptor Suppression Using Integrilin Therapy. *N Engl J Med.* 1998;339:436-443. Copyright © 1998, Massachusetts Medical

# Meta-Analysis of IV Gp IIb/IIIa Inhibitors in NSTEMI-ACS: Death or MI at 30 Days

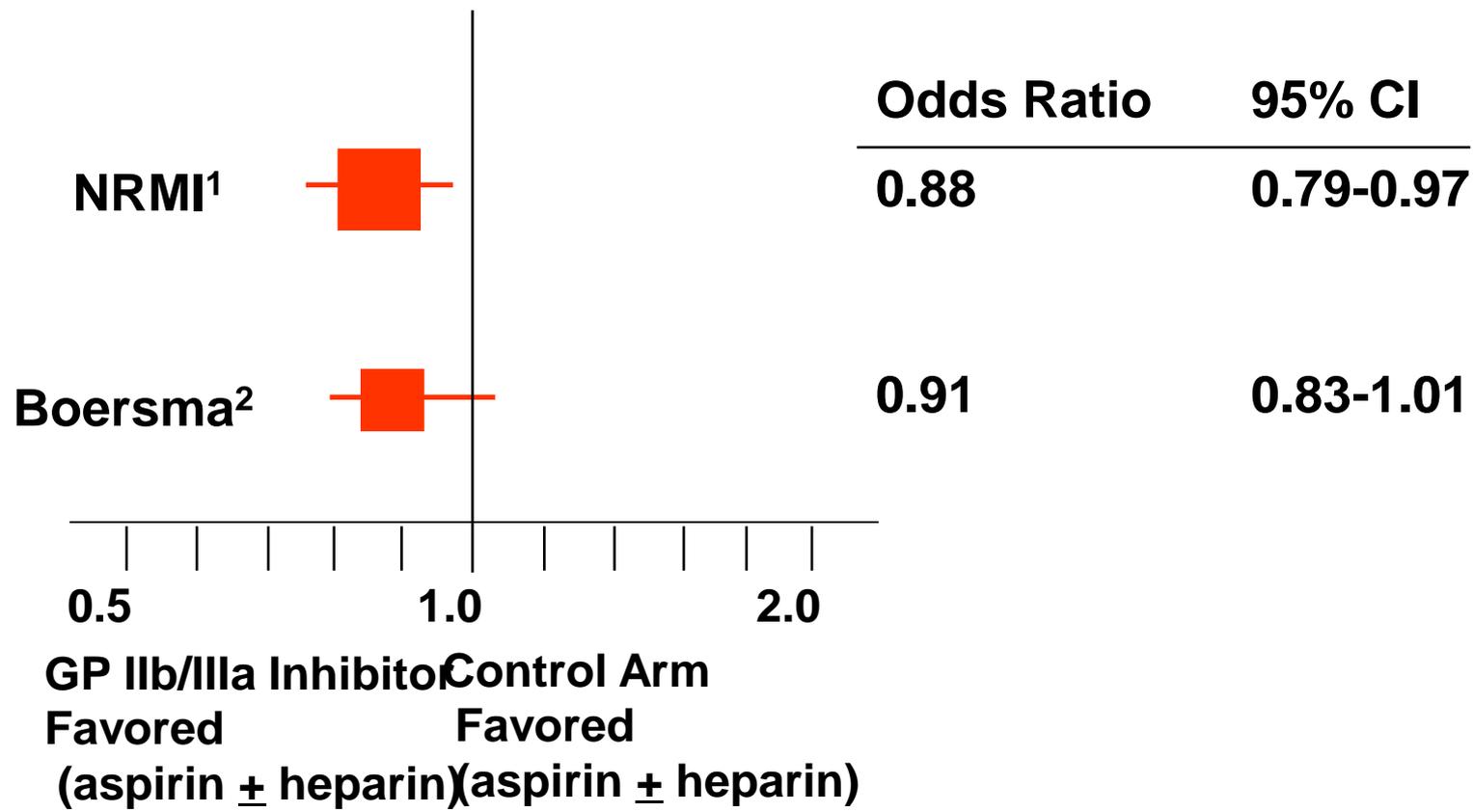


\* Without heparin. † With/without heparin. (l), Low dose; (h), High-dose.  
 Adapted with permission from Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndrome: a meta-analysis of all major randomised clinical trials. *Lancet*. 2002;359:189-198.

# GP IIb/IIIa Inhibitor NSTE-ACS Studies Analysis

## Risk-Adjusted Mortality at 30 Days

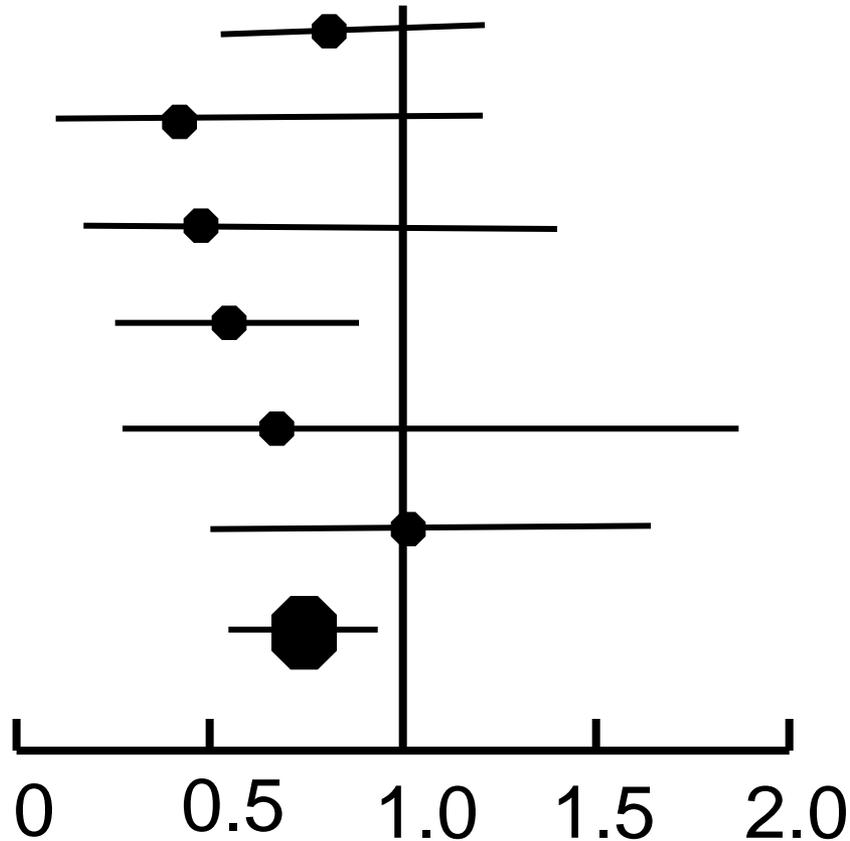
### Odds Ratio for Mortality at 30 Days



Data from (1) Peterson ED, Pollack CV Jr, Roe MT, et al. Early use of glycoprotein IIb/IIIa inhibitors in non-ST-elevation acute myocardial infarction: observations from the National Registry of Myocardial Infarction 4. *J Am Coll Cardiol.* 2003;42:45-53 and (2) Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndrome: a meta-analysis of all major randomised clinical trials. *Lancet.* 2002;359:189-198. Slide reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# GP IIb/IIIa Therapy and Mortality (30 day) in Diabetics with NSTEMI-ACS

PURSUIT  
PRISM  
PRISM-PLUS  
GUSTO IV  
PARAGON A  
PARAGON B  
Pooled



## Mortality:

6.2% vs. 4.6%

OR=0.74

CI=0.59-0.92

P=0.007

Relative Risk of Death  
(versus placebo Rx)

# GP IIb/IIIa Dosing and Administration for Up-Front Therapy in Patients with NSTEMI-ACS



- Dosing:
  - Integrilin: 180 mcg/kg bolus (over 1-2 min), then 2 mcg/kg/min continuous infusion
  - Aggrastat: Initial 0.4 mcg/kg/min for 30 min, then continuous infusion at 0.1 mcg/kg/min
- Always also treat with ASA and some form of heparin (UFH or LMWH)
- Patients most commonly treated 2-4 days
- Follow platelet count qD and D/C for significant fall
- Adjust doses for renal insufficiency:
  - Integrilin: For creatinine 2-4 mg/dL, decrease infusion to 1 mcg/kg/min; avoid if creatinine >4 mg/dL
  - Aggrastat: For CrCl < 30 mL/min, cut all doses in 1/2

# ACC/AHA Recommendations for Antiplatelet Therapy in Patients with NSTEMI-ACS

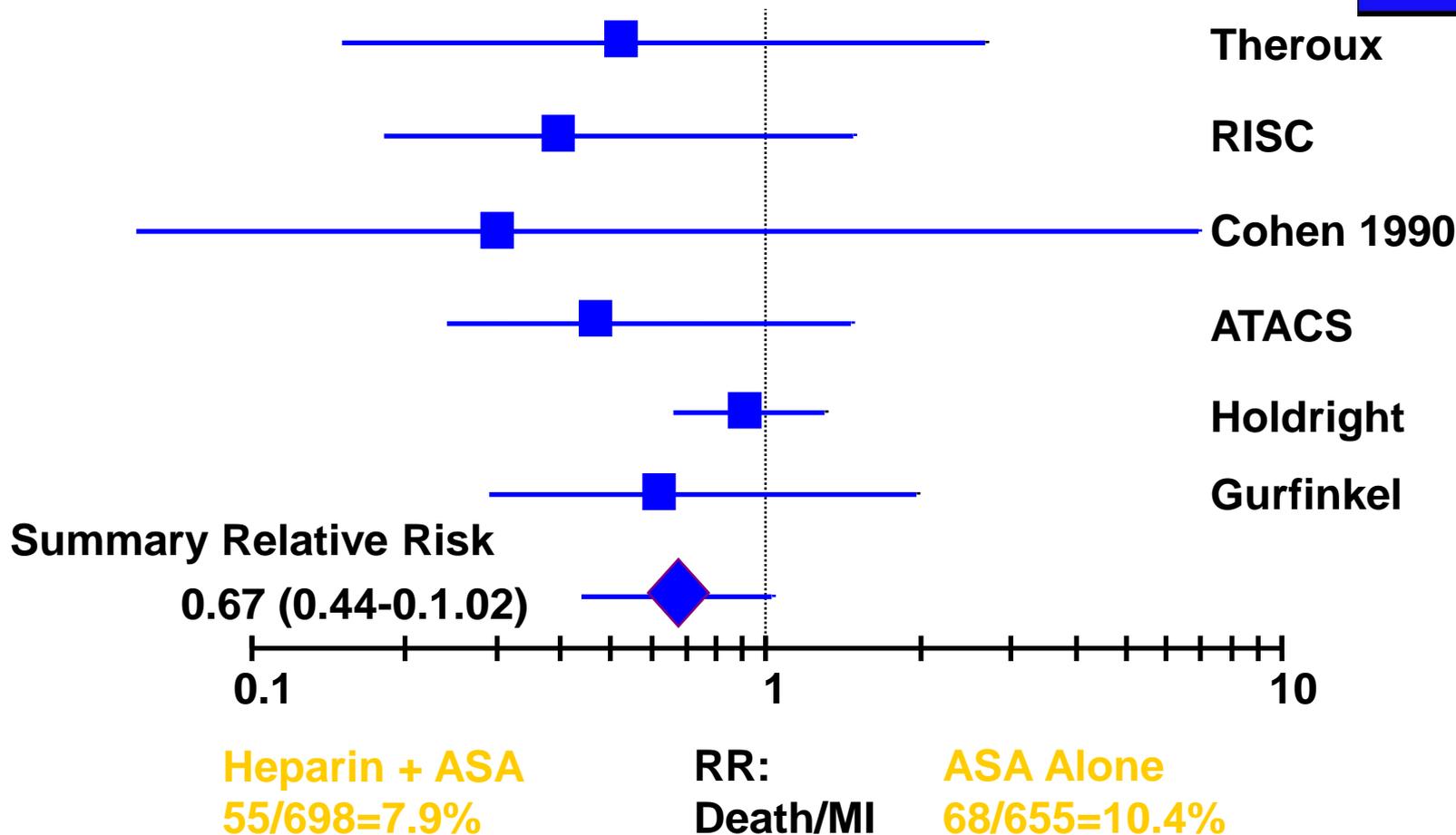
- Class I
  - ASA
  - Clopidogrel if ASA-allergic or intolerant
  - Clopidogrel in addition to ASA if early invasive approach *not* planned
  - Clopidogrel should be withheld for 5-7 days if CABG planned
  - GP IIb/IIIa inhibitor if cardiac cath and PCI planned
- Class IIa
  - GP IIb/IIIa inhibitor in patients with high-risk features if invasive strategy *not* planned
  - GP IIb/IIIa inhibitor in patients *receiving clopidogrel* if cardiac cath and PCI planned
- Class IIb
  - GP IIb/IIIa inhibitor in patients without high-risk features and PCI *not* planned
- Class III
  - Abciximab in patients in whom PCI is *not* planned

# Contraindications to GP IIb/IIIa

- Active or recent bleeding (4-6 weeks)
- Severe hypertension (SBP >180-200 mm Hg; DBP >110 mm Hg)
- Any hemorrhagic CVA (+/- intracranial neoplasm, AVM, or aneurysm)
- Any CVA within 30 days–2 years
- Major surgery or trauma within 4-6 weeks
- Thrombocytopenia ( <100,000/mm<sup>3</sup> )
- Bleeding diathesis/warfarin with elevated INR
- (Doses must be avoided with renal insufficiency or failure)

# Antithrombin Therapy Studies and Recommendations

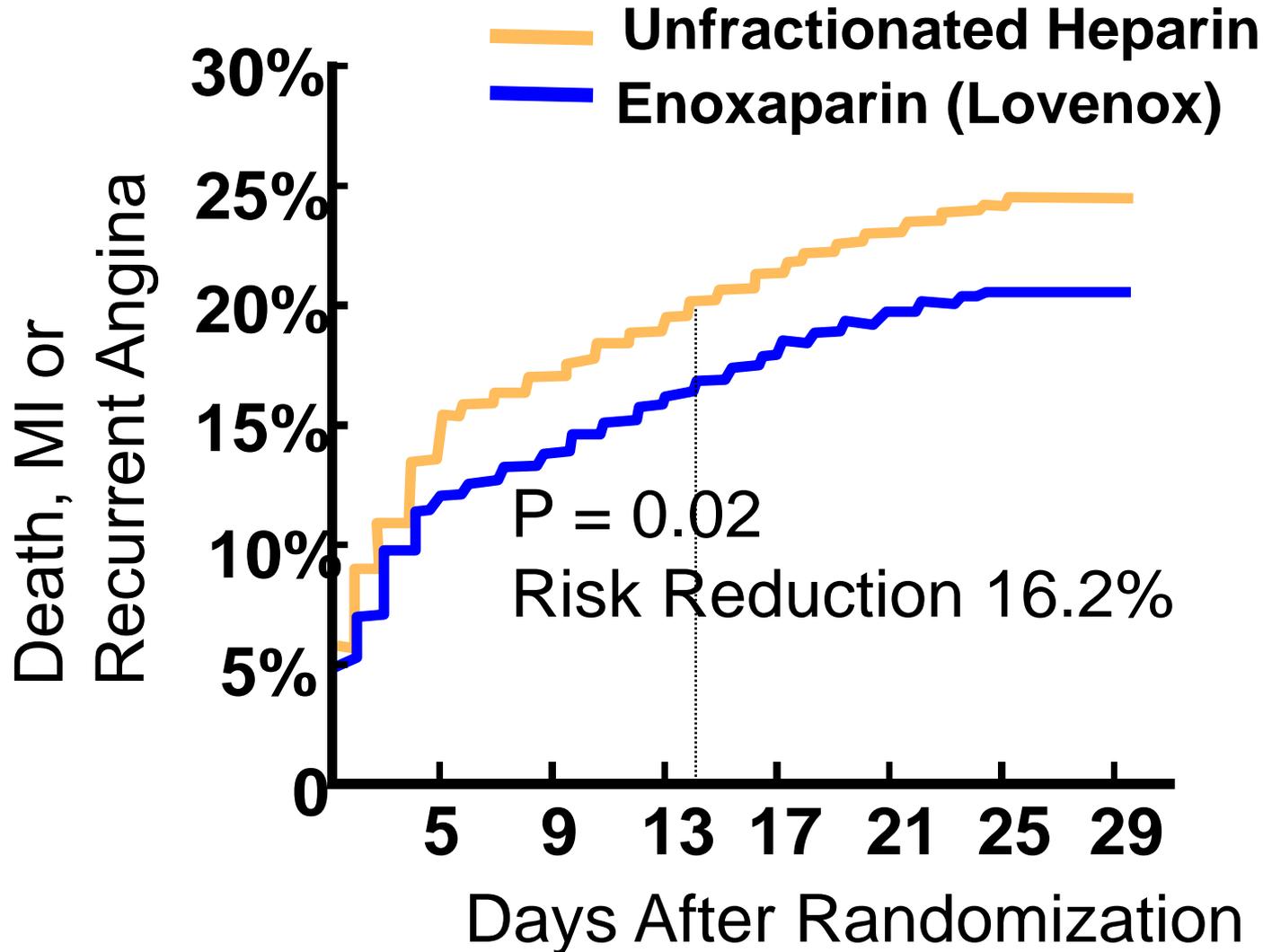
# Comparison of Heparin + ASA vs ASA Alone



ASA indicates acetylsalicylic acid; RISC, Research on InStability in Coronary artery disease; ATACS, Antithrombotic Therapy in Acute Company Syndromes; RR, relative risk; and MI, myocardial infarction.

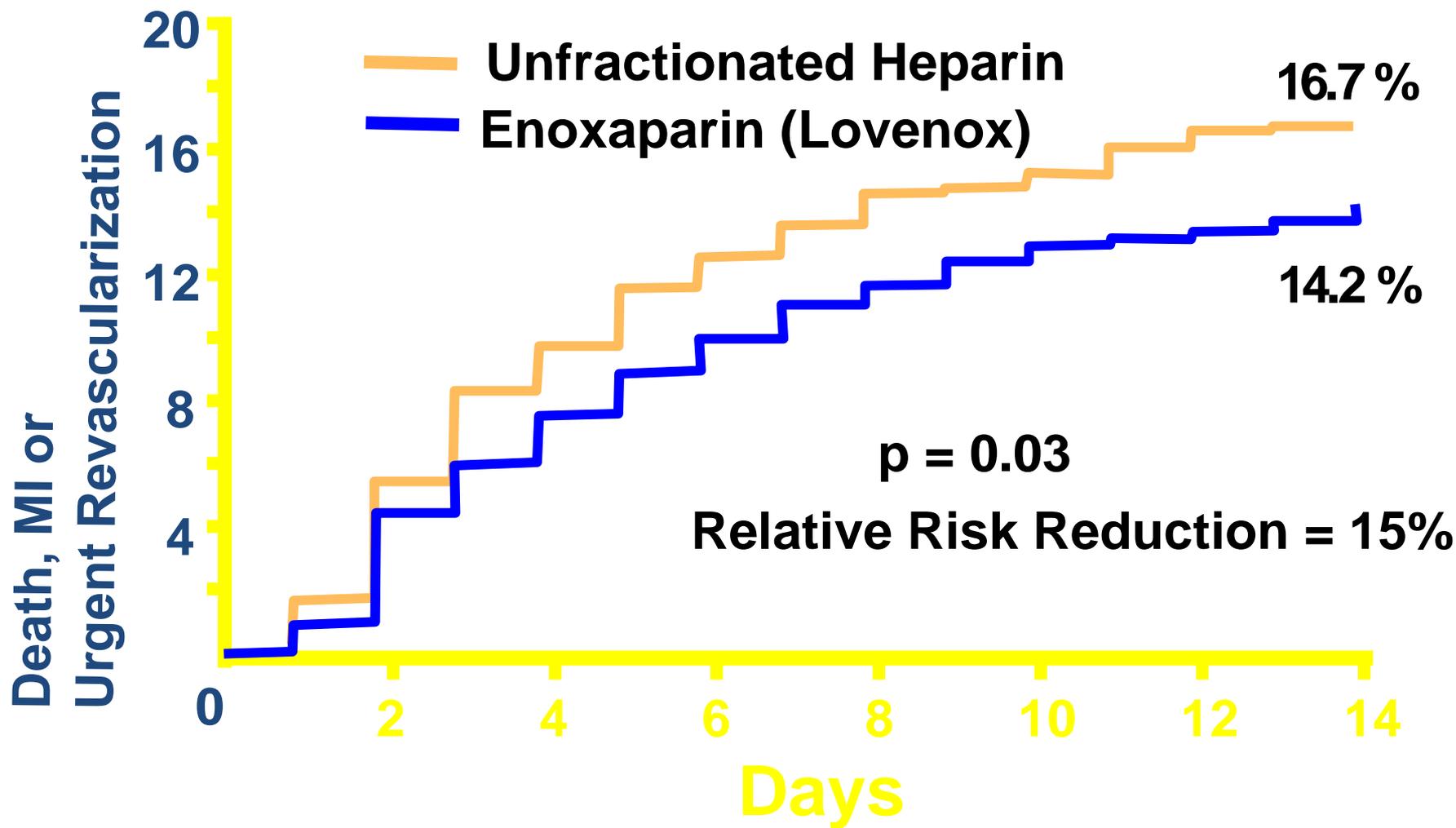
Data from Oler A, Whooley MA, Oler J, et al. Adding heparin to aspirin reduces the incidence of myocardial infarction and death in patients with unstable angina: a meta-analysis. *JAMA*. 1996;276:811-815. Slide reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# ESSENCE Results



Adapted with permission from Cohen M, Demers C, Gurfinkel EP, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for unstable coronary artery disease. Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events Study Group. *N Engl J Med.* 1997;337:447-452. Copyright © 1997, Massachusetts Medical Society. All rights reserved.

# TIMI 11B: Enoxaparin vs. Heparin in NSTE-ACS



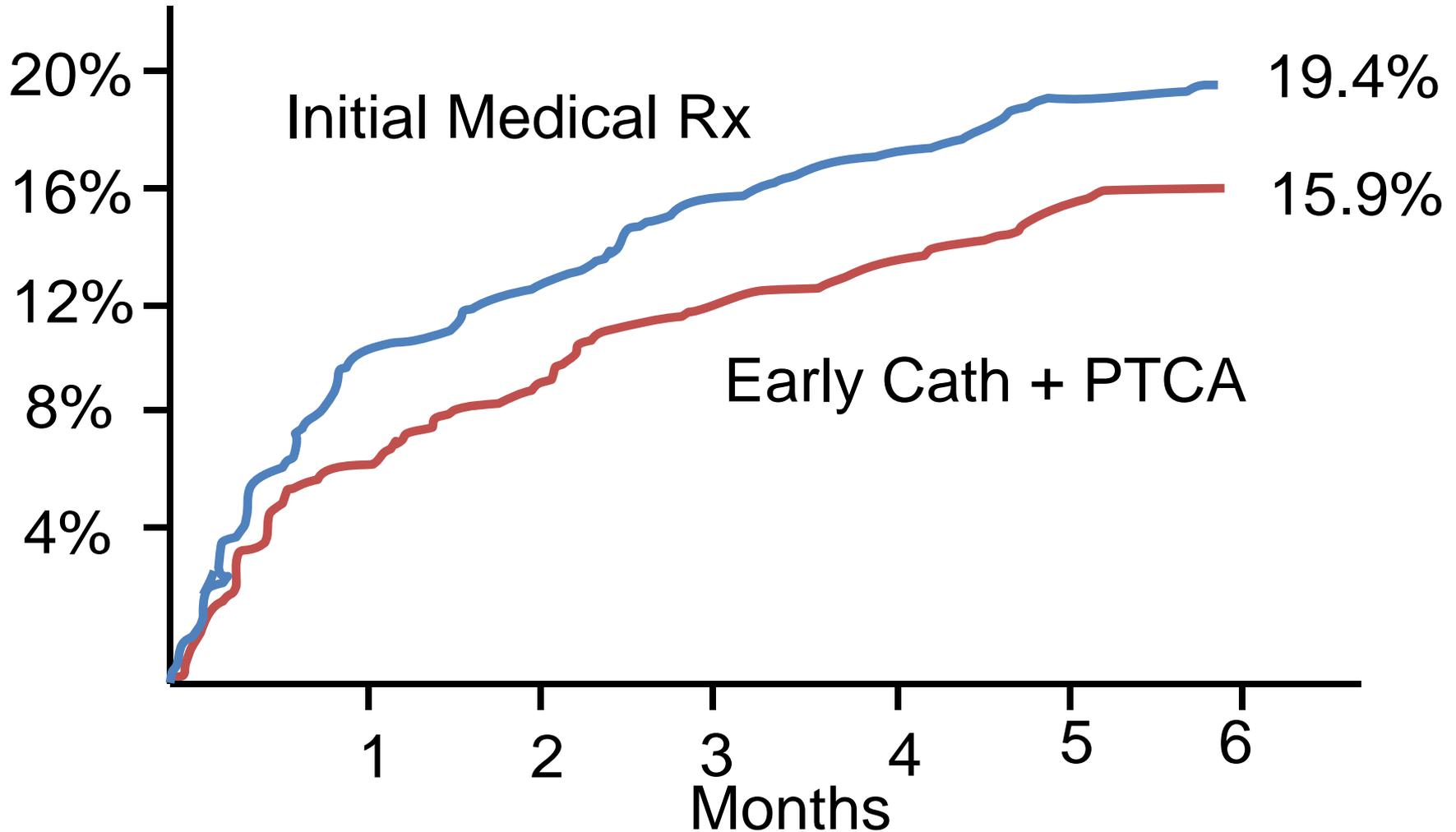
Adapted from Antman EM, et al. *Circulation*. 1999;100:1593-1601.

# Guidelines for the Use of Enoxaparin in Patients with NSTEMI-ACS

- 1 mg/kg SQ q12 hours (actual body weight)
  - An initial 30 mg IV dose can be considered
- Adjust dosing if CrCl <30 cc/min
  - 1 mg/kg SQ q24 hours
- Do not follow PTT; do not adjust based on PTT
- Stop if platelets ↓ by 50% or below 100,000/mm<sup>3</sup>
- If patient to undergo PCI:
  - 0-8 hours since last SQ dose: no additional antithrombin therapy
  - 8-12 hours since last SQ dose: 0.3 mg/kg IV immediately prior to PCI

# Early Invasive Strategy Studies and Recommendations in Patients with NSTE-ACS

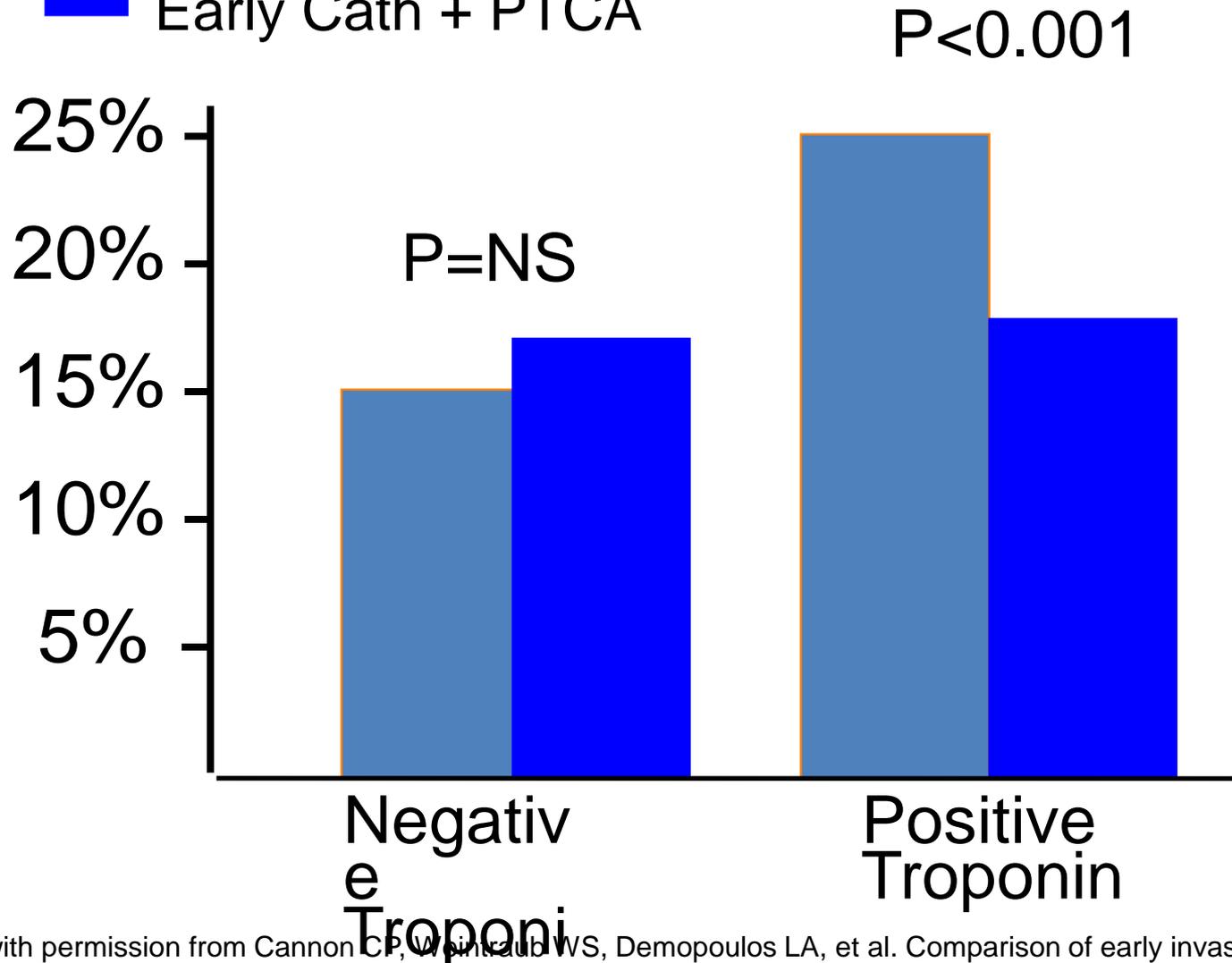
# TACTICS



Adapted with permission from Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med.* 2001;344:1879-1887. Copyright © 2001, Massachusetts Medical Society. All rights reserved.

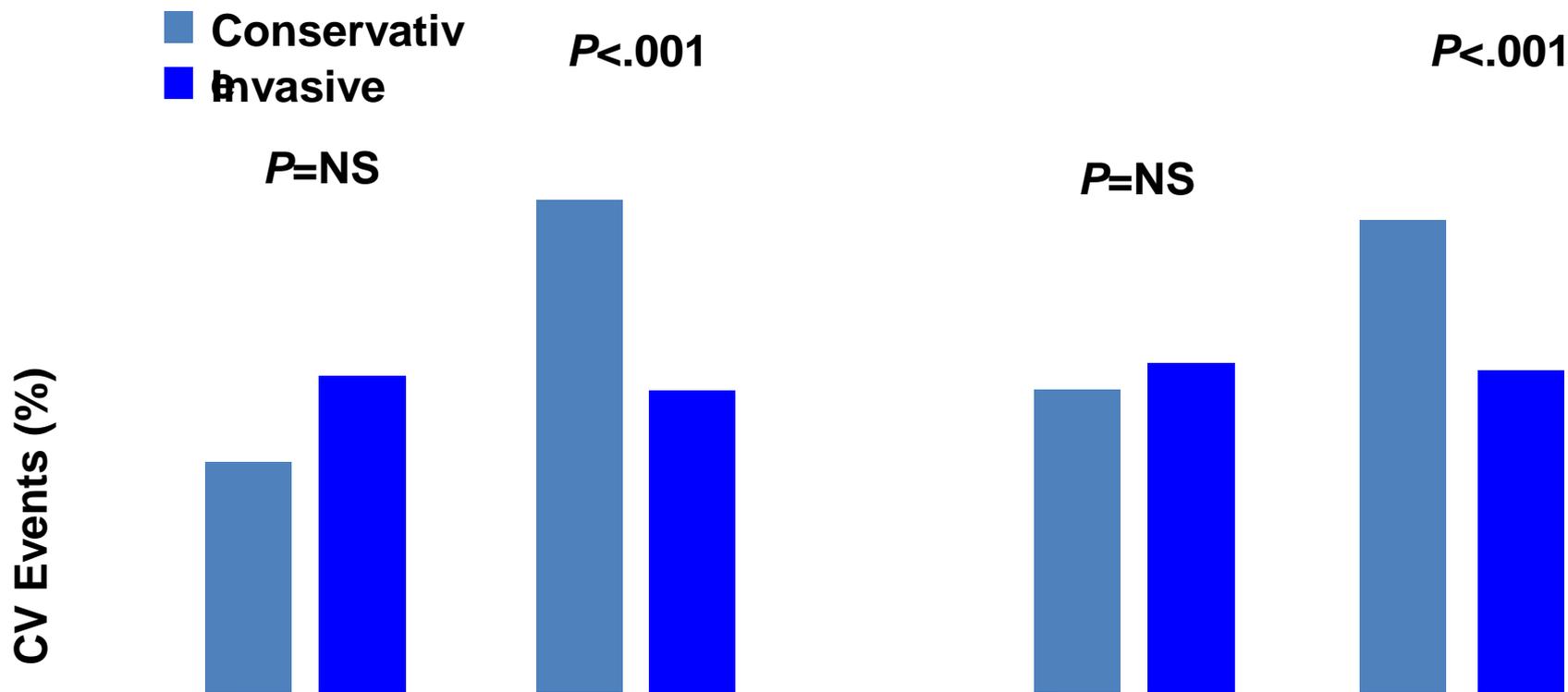
# TACTICS Trial Results Based on Troponin

- Initial Medical Rx
- Early Cath + PTCA



# Benefit of Invasive Strategy by Troponin and ST Changes

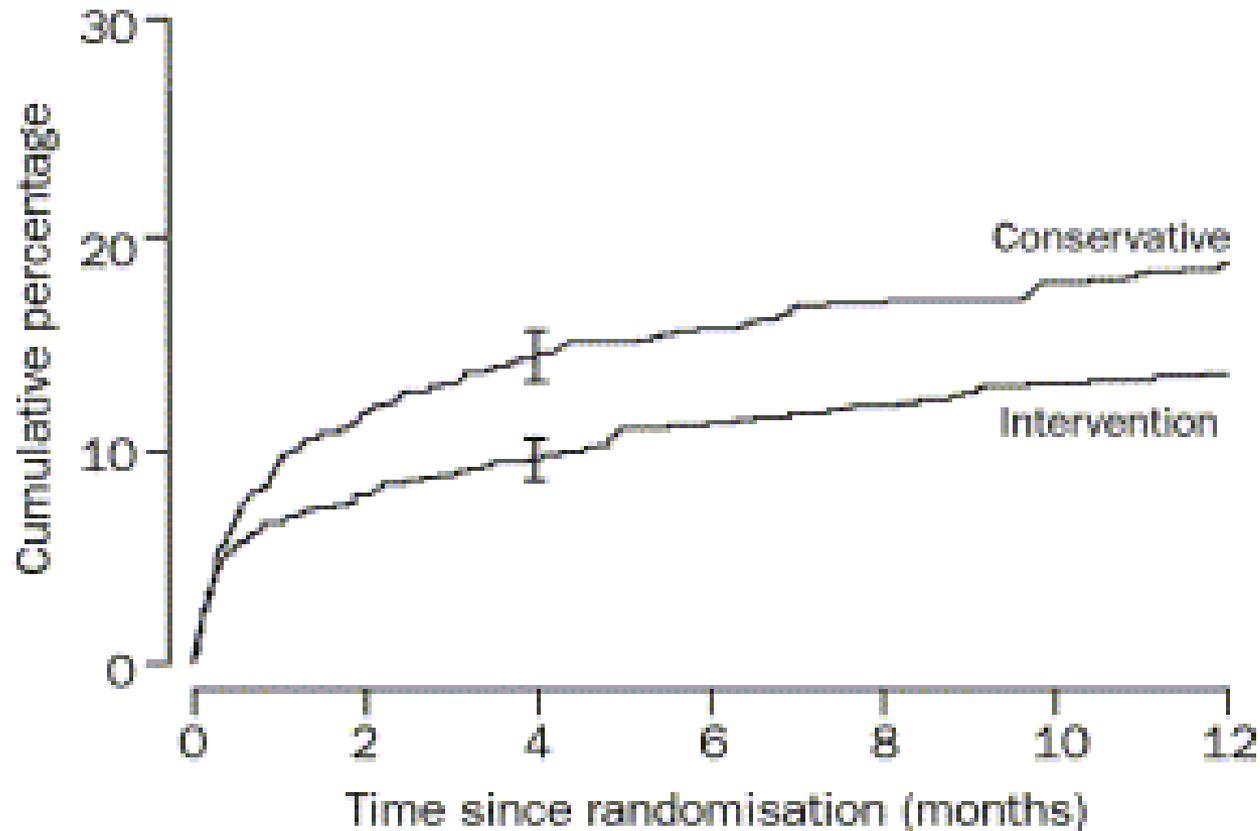
## Death, MI, or Rehospitalization for ACS at 6 Months



TnT indicates troponin T; and ST, ST segment.

Data from (1) Morrow DA, et al. *JAMA*. 2001;286:2405-2412 and (2) Cannon CP, et al. *N Engl J Med*. 2001;344:1879-1887. Slide reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: [www.theheart.org](http://www.theheart.org).

# The Primary Composite Ischemic End Point in RITA-3



## Number at risk

Intervention	895	805	747
Conservative	915	775	713

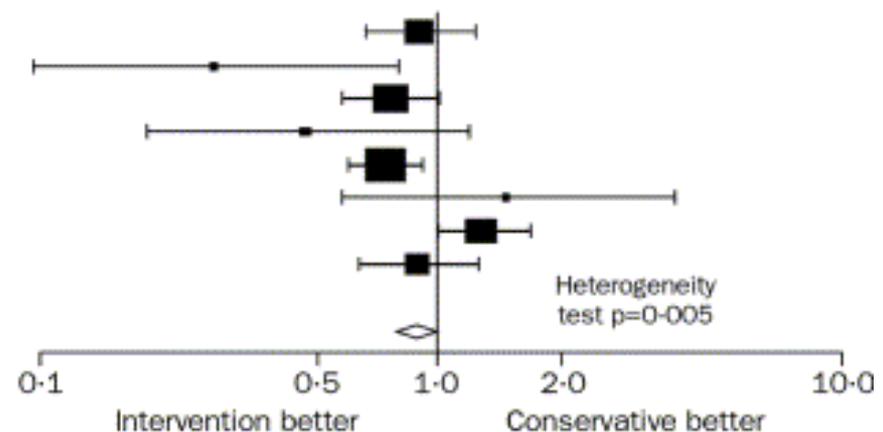
Reproduced with permission from Fox KA, Poole-Wilson PA, Henderson RA, et al. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. *Randomised Intervention Trial of Unstable Angina.*

# Meta-Analysis of Trials of Early Cardiac Cath and Revascularization Versus Initial Medical Therapy Alone in Patients with NSTEMI-ACS

Number of deaths or MIs within 1 year

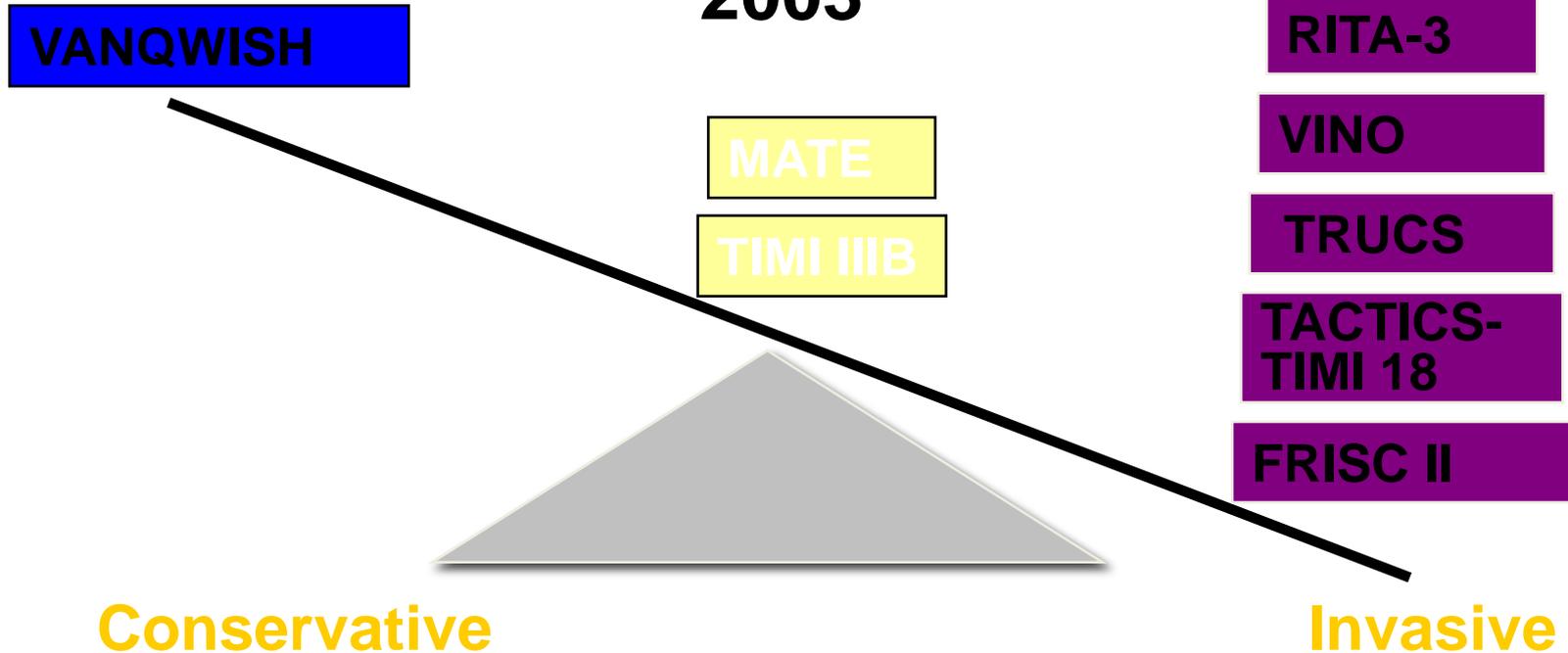
	Intervention	Conservative
RITA 3	68/895 (7.6%)	76/915 (8.3%)
VINO*	4/64 (6.3%)	15/67 (22.4%)
TACTICS-TIMI 18	81/1114 (7.3%)	105/1106 (9.5%)
TRUCS	6/76 (7.6%)	12/72 (16.7%)
FRISC II	127/1219 (10.4%)	174/1234 (14.1%)
MATE	11/111 (9.9%)	6/90 (6.7%)
VANQWISH	111/462 (24.0%)	85/458 (18.6%)
TIMI IIIB	52/484 (10.8%)	62/509 (12.2%)
Combined risk ratio	0.88 (95% CI 0.78-0.99)	

Risk ratio (95% CI)



Reproduced with permission from Fox KA, Poole-Wilson PA, Henderson RA, et al. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Randomised Intervention Trial of unstable Angina. *Lancet*. 2002;360:743-751.

# Invasive vs Conservative Strategy for UA/NSTEMI 2003



UA indicates unstable angina, NSTEMI, non–ST-segment myocardial infarction; ISAR, Intracoronary Stenting and

Antithrombic Regimen Trial; RITA, Randomized Intervention Treatment of Angina; VANQWISH, Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital study; MATE, Medicine vs Angioplasty for Thrombolytic Exclusions trial; TACTICS-TIMI18, Treat Angina with Aggrastat® and Determine Cost of Therapy with Invasive or Conservative Strategy; and FRISC, Fragmin during InStability in Coronary artery disease.

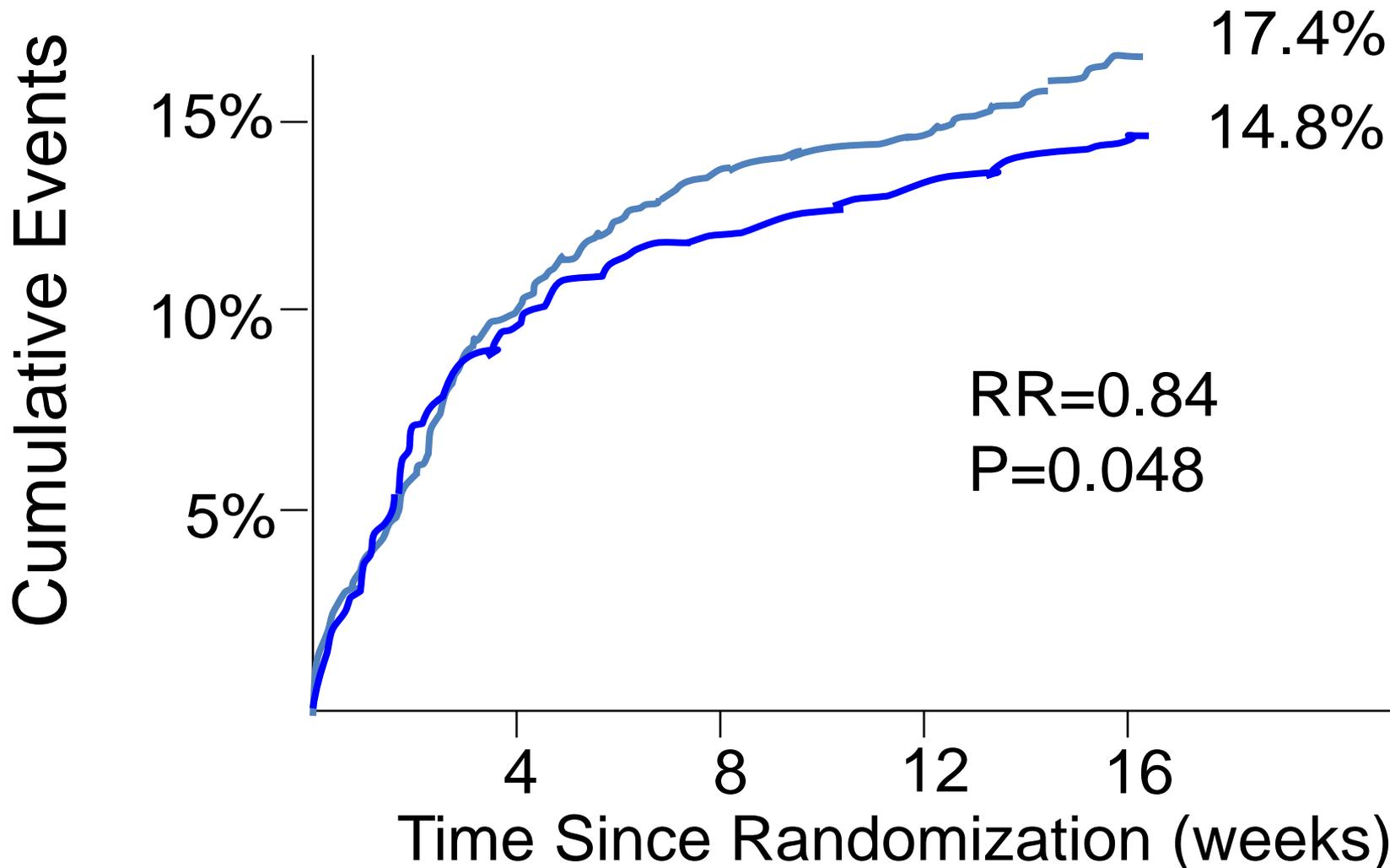
# ACC/AHA Class I Recommendations for Invasive and Medical Strategies in Patients with NSTEMI-ACS

- Class I
  - An early invasive strategy in patients with any high-risk indicators:
    - Recurrent angina/ischemia at rest or with low-level activities
    - Elevated troponin
    - New or presumed new ST-segment depression
    - Recurrent angina/ischemia with CHF Sx and S<sub>3</sub> gallop, pulmonary edema, worsening rales, or new or worsening MR
    - High-risk findings on noninvasive stress testing
    - Depressed LVEF (<40%)
    - Hemodynamic instability
    - Sustained ventricular tachycardia
    - PCI with 6 months or prior CABG
  - In the absence of any of the above high-risk indicators, either an early conservative or an early invasive strategy

# Peri- and Post-Discharge Therapies and Risk Modification

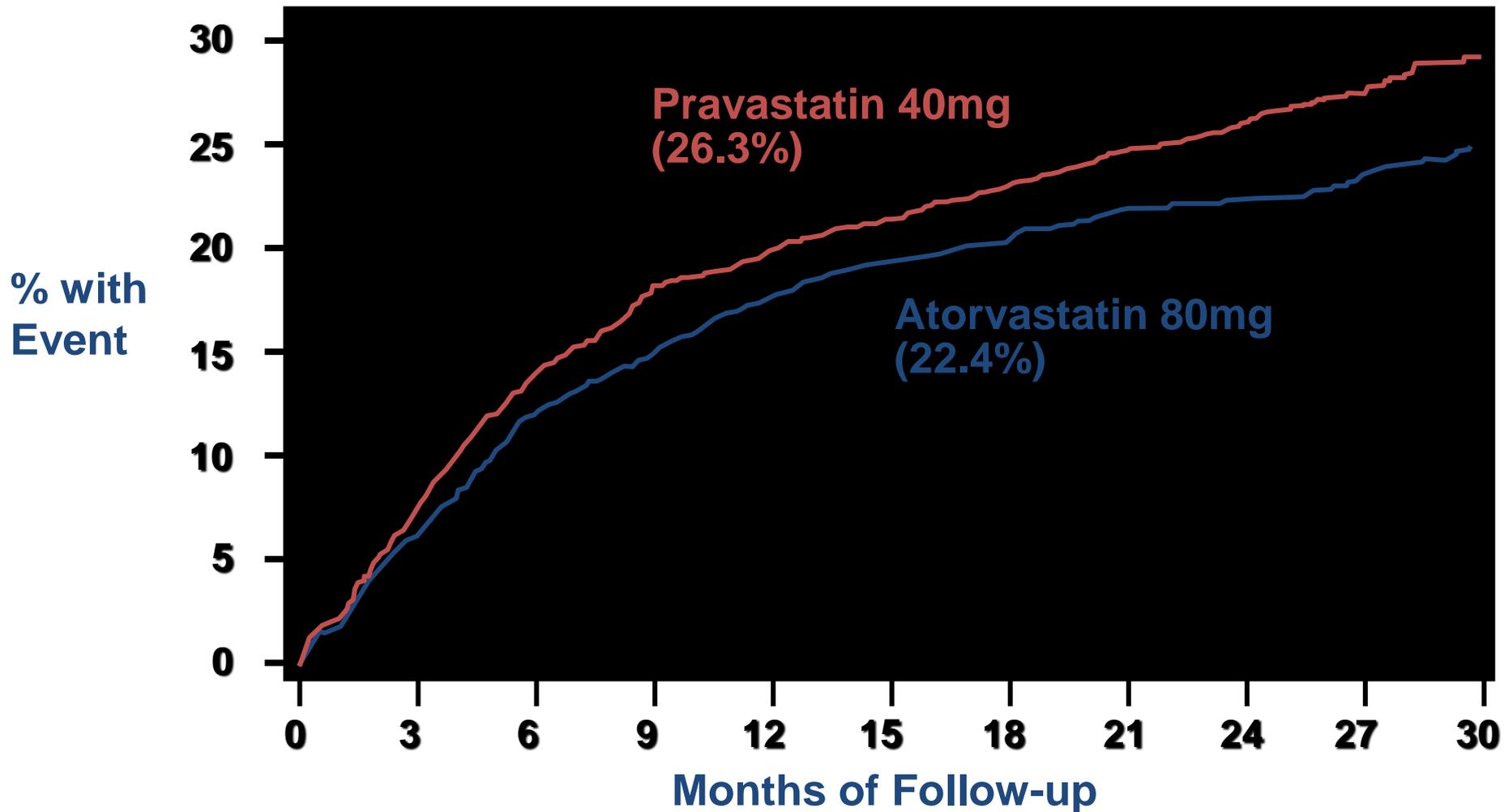
# MIRACL: Acute Statin Rx

— Placebo  
— High-dose statin



Adapted with permission from Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA*. 2001;285:1711-1718. Copyright © 2001, American Medical Association. All rights reserved.

# PROVE-IT TIMI-22 Trial Primary Results



Courtesy of and reproduced with permission from C.P. Cannon.

# ACC/AHA Class I Recommendations for Long-Term Medical Therapy in Patients with NSTEMI-ACS

- Class I
  - Aspirin 75-325 mg qD
  - Clopidogrel 75 mg qD when ASA is not tolerated because of hypersensitivity or GI intolerance
  - Combined ASA + clopidogrel for 9 months after NSTEMI-ACS
  - Beta blockers unless contraindicated
  - Lipid-lower agents and diet if LDL > 100-130 mg/dL
  - ACEI for patients with CHF, LV dysfunction (EF <40%), hypertension, or diabetes

# ACC/AHA Class I Recommendations for Long-Term Risk Factor Modification in Patients with NSTEMI-ACS

- Class I
  - Specific instruction on smoking cessation
  - Specific instruction on optimal weight, diet, and daily exercise
  - Lipid-lowering therapy (statin) for LDL >100-130 mg/dL
  - A fibrate or niacin if HDL <40 mg/dL occurring as an isolated finding or in combination with other lipid abnormalities
  - Hypertension control to a BP of <130/85 mm Hg
  - Tight control of hyperglycemia in diabetics