Diagnosis & Management of NSTE-ACS

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Outlines:

- key diagnostic steps for patients with suspected acute coronary syndrome (ACS) to optimize initial triage and early management.
- Describe management strategy for a patient with confirmed unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI)
- Problem based approach discussion

ACS is a clinical diagnosis based on three parameters:

1) Ischemic symptoms e.g. SOB, chest pain
2) ECG findings
3) The presence of myocardial necrosis e.g. imaging, troponins

Introduction

- STEMI
  - persistent ST-segment elevation on a 12-lead ECG,
  - posterior -lead ST-segment elevation
  - or new left bundle branch block (LBBB)
- NSTEMI :
  - In the absence of ST-segment elevation or new LBBB on ECG, evidence of myocardial necrosis, as indicated by an elevation of circulating cardiac biomarkers, is consistent with a diagnosis of NSTEMI.
- Biomarker-negative ACS defines UA

Case 1:

A 66-year-old woman with a 2-day history of intermittent chest pain, presents to the emergency department for evaluation. PHx: hypertension, DM. Her medications include amlodipine, hydrochlorothiazide, and aspirin.

- BP 130/80 mm Hg, HR 80 bpm, and SpO2 99% on room air. Normal cardiovascular examination.
- ECG shows normal sinus rhythm with nonspecific T-wave changes.
- Chest x-ray is normal.
- Laboratory values include two serial troponin I values of <0.01 ng/L, normal electrolytes, D-dimer 130 ng/ml, and normal blood cell count, hba1c 6.7 mmol/L

Which of the following is most appropriate in her care?

A) No further test is needed
B) Invasive coronary angiography
C) Exercise myocardial perfusion
D) V/Q scan
E) Echocardiogram
F) Repeat Troponin

- This patient has chest pain and suspected non-ST-segment elevation acute coronary syndrome.

- Further risk stratification is necessary

Initial Hospital Assessment

TWO Questions

- Diagnosis
- Risk assessment

Diagnosis ?

Likelihood That Signs and Symptoms Represent an Acute Coronary Syndrome Secondary to CAD*

Feature	High Likelihood Any of the following:	Intermediate Likelihood Absence of high-likelihood features and presence of any of the following:	Low Likelihood Absence of high- or intermediate-likelihood features but may have:
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina Known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom Age >70 years Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate likelihood characteristics Recent cocaine use
Examination	Transient MR murmur, hypotension, diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation (≥1 mm) or T-wave inversion in multiple precordial leads	Fixed Q waves ST depression 0.5 - 1 mm or T-wave inversion >0.1 mm	T-wave flattening or inversion <1 mm in leads with dominant waves Normal ECG
Cardiac markers	Elevated cardiac TnI, TnT, or CK-MB	Normal	Normal

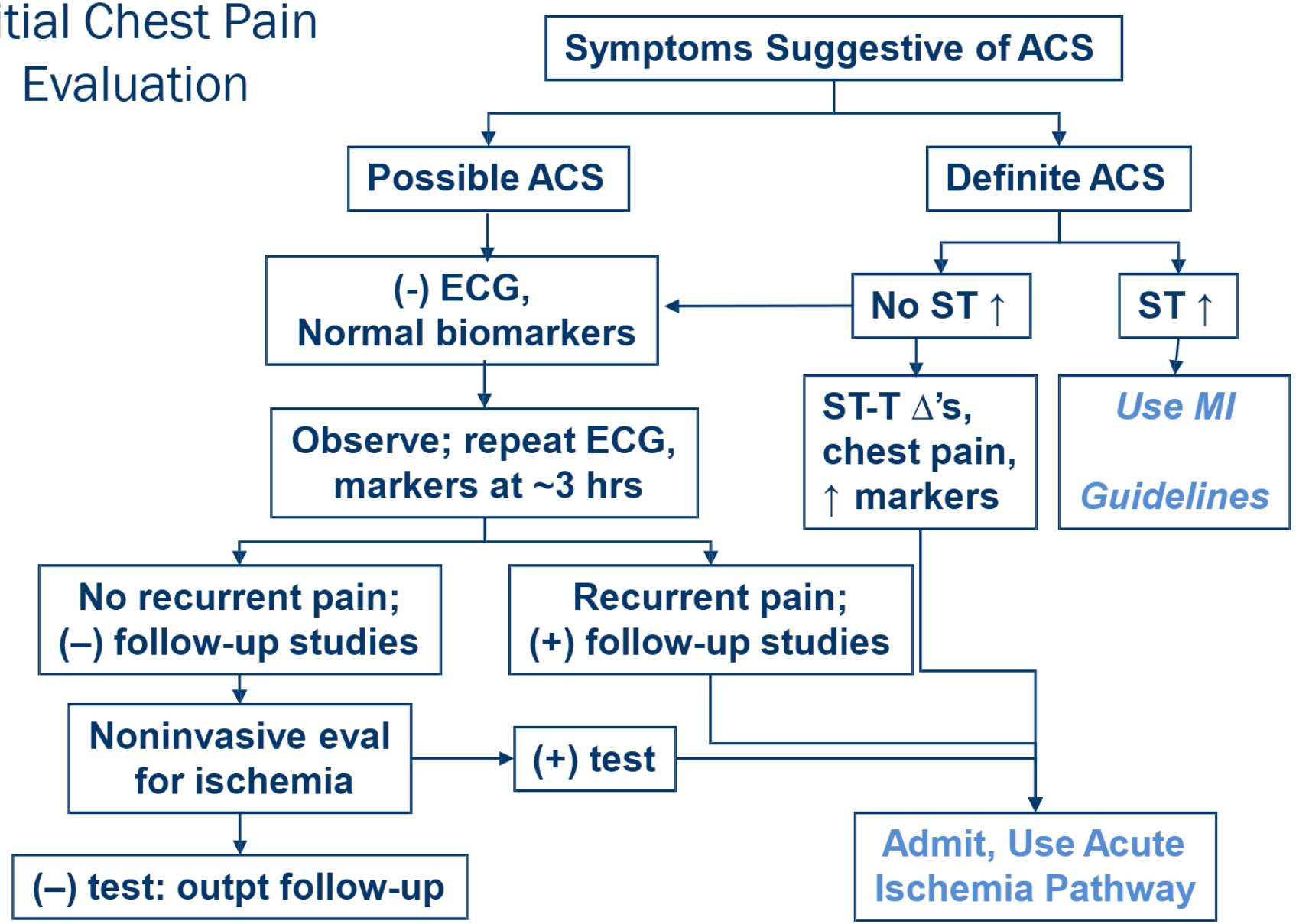
High-sensitivity troponin

- Improve the overall diagnostic accuracy for ACS compared with older assays and, in particular, may accelerate the diagnosis to up to 3 hours from symptom onset

- Stable angina without ACS, the use of a high-sensitivity troponin T assay tested "positive" (i.e., above the 99th percentile) in 11.1% of patients

- Other conditions leading to myocardial necrosis include myocardial trauma, heart failure, stress cardiomyopathy (Takotsubo), pulmonary embolism, myocardial inflammation or infiltration, and drug toxicity.

Initial Chest Pain Evaluation



Definition of Myocardial Infarction

Criteria for Acute Myocardial Infarction

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute MI. Under these conditions any one of the following criteria meets the diagnosis for MI:

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above 99th percentile upper reference limit (URL) and with at least one of the following:
  - Symptoms of ischaemia.
  - New or presumed new significant ST–T changes or new LBBB.
  - Development of pathological Q waves in the ECG.
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
  - Identification of an intracoronary thrombus by angiography or autopsy.

What should we do for low to intermediate likelihood of ACS?

- Noninvasive testing with treadmill ECG
- stress myocardial perfusion imaging (MPI)
- stress echocardiography can be pursued before discharge or within 72 hours of discharge following normal serial ECGs and cardiac troponins.

Can we use CTA ?

Cardiac Computed Tomography Angiogram

- Excellent negative predictive value (>90%)
- An acceptable approach to consider for the exclusion of CAD (Level of Evidence B)
- the positive predictive value is lower (80%)

- ROMICAT II: good negative predictive value for ACS and similar 28-day rates of major adverse cardiovascular events

Cardiovascular Magnetic Resonance

- Delayed-enhancement (DE)-CMR is a highly accurate and well-validated technique to detect myocardial scar and is very sensitive for detecting small or subendocardial infarcts.

Risk assessment ?

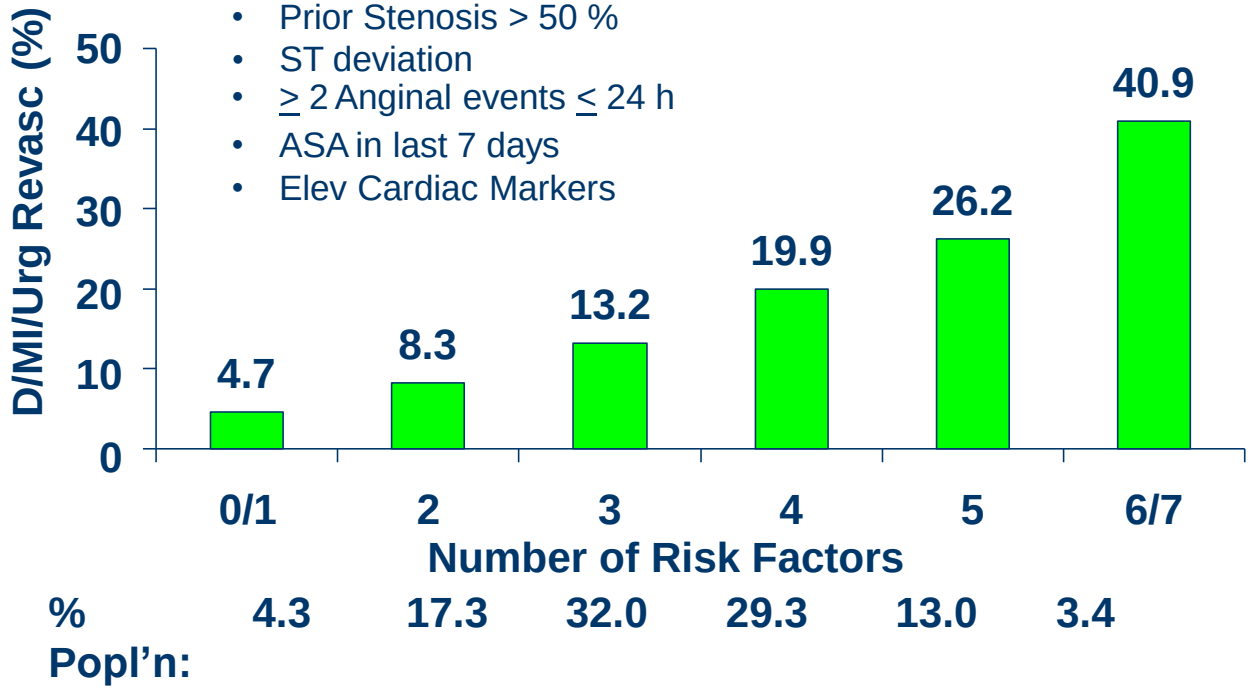
Risk Assessment and Risk Stratification

- Early risk assessment should focus on the clinical exam (history and physical examination), ECG findings, and cardiac markers

- TIMI or GRACE risk scores

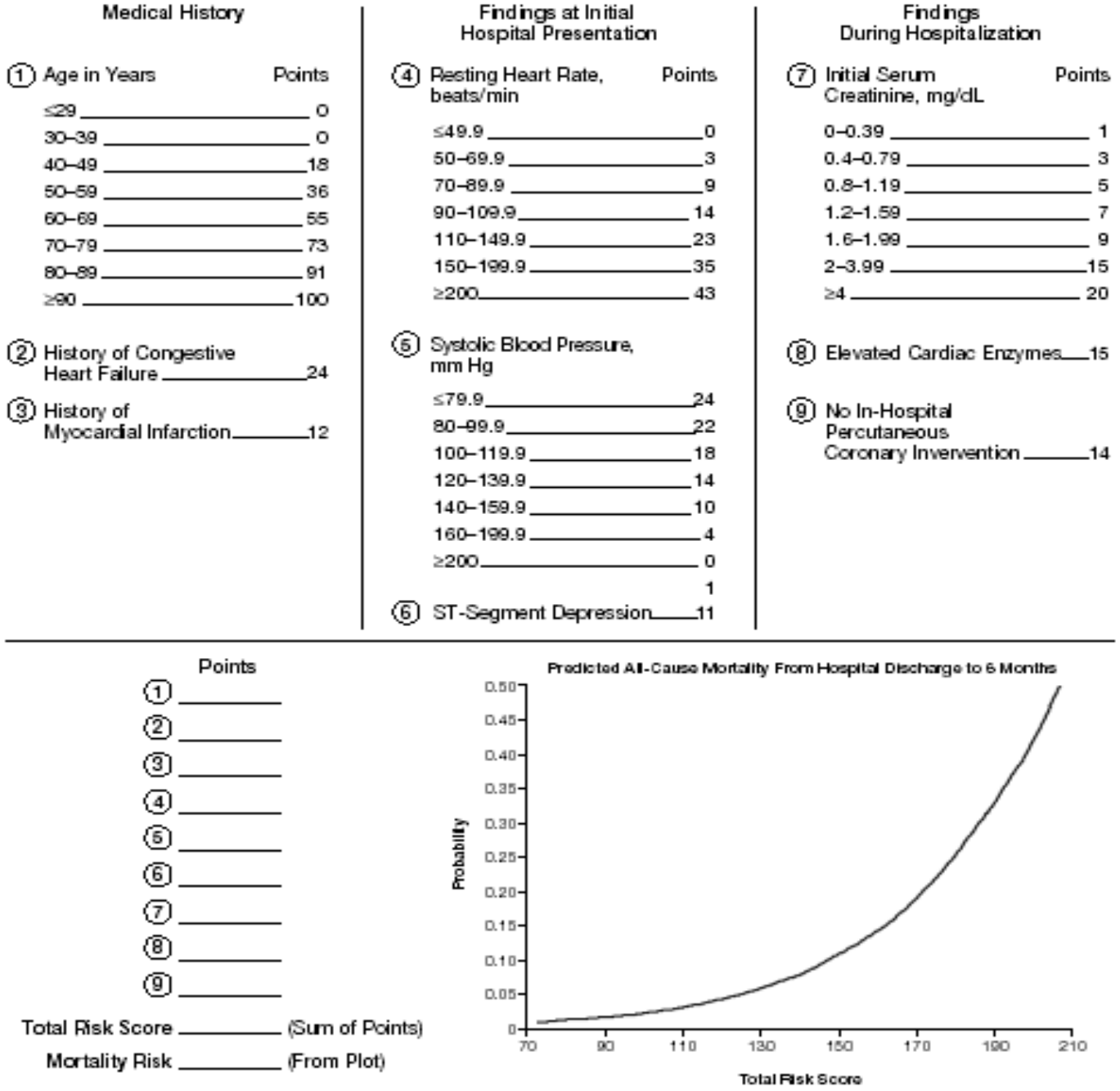
TIMI Risk Score For UA/NSTEMI

- Age ≥ 65 y
- ≥ 3 CAD Risk Factors
- Prior Stenosis > 50 %
- ST deviation
- ≥ 2 Anginal events ≤ 24 h
- ASA in last 7 days
- Elev Cardiac Markers



Antman et al *JAMA 284* : 835, 2000

GRACE Prediction Score for All-Cause Mortality From Discharge to 6 Months



NSTEMI 6-Month Postdischarge Mortality

Risk Category	GRACE Score	Probability of Death
Low	1-88	<3%
Medium	89-118	3-8%
High	119-263	>8%

http://www.outcomes-umassmed.org/grace/grace_risk_table.cfm.

Eagle KA, et al. *JAMA.* 2004;291(22):2727-2733.

Answer is : C: Stress test

- This patient's Thrombolysis in Myocardial Infarction (TIMI) risk score is 2, which gives her a risk of major adverse cardiac events of 8% in the next 14 days.
- Noninvasive stress testing can be used to further risk stratify this patient.
- Resting transthoracic echocardiogram will not provide information about inducible ischemia.
- With a normal D-dimer and low pretest probability of pulmonary embolism, a V/Q scan is not indicated.

Question 2:

- A 69-year-old man with a history of hypertension and stroke was admitted with a non–ST-segment elevation myocardial infarction (NSTEMI). PE: chest lung field, normal heart sound, no murmur, Sp02 95%

- What general measures should not be considered ?
  A. Aspirin
  B. Beta-blocker
  C. Oxygen
  D. ACEI/ARB
  E. Aldactone

General measures

- Oxygen therapy is currently recommended only for patients with
  - Hypoxemia (defined as an oxygen saturation <90%) or
  - respiratory distress

- DETO2X-AMI / AVOID trial
  - increased infarct size in normoxic patients with STEMI treated with the addition of supplemental oxygen

Which of the following general medication you would not consider?

a) IV TNG infusion
b) Concor
c) Adalat
d) Zestril
e) Aldactone
f) Lipitor

Medical Therapy

- *Beta-blockers*
  - inhibition of beta-1 adrenergic receptors in the myocardium, thereby leading to a reduction in cardiac work and myocardial oxygen demand
  - reduces myocardial ischemia, reinfarction, and ventricular arrhythmias, and improves long-term survival.[3]
  - should be initiated within 24 hours (Class I).

C/I: signs of heart failure, a low-output state, high risk for cardiogenic shock (including age >70 years, heart rate >110 bpm, systolic blood pressure <120, or late presentation), significant heart block (PR interval >240 msec, second- or third-degree heart block without a pacemaker), or *active* bronchospasm secondary to asthma or reactive airway disease

- The 2014 AHA/ACC Guideline for the Management of With Non-ST Elevation Acute Coronary Syndromes caution about the early use of intravenous beta-blockers in patients at risk for shock based on the findings from the COMMIT (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) study in patients with STEMI (Class III).[3]

- *Nitrates (class Ib for persistent ischemia, HF, HT)*
  - reduces cardiac preload and wall tension
  - arterial vasodilation may decrease afterload and oxygen demand
  - No survival evidence

Contraindications : hypotension (systolic blood pressure <90 mm Hg or a drop of ≥30 mm Hg from baseline) or recent phosphodiesterase inhibitor use.

- *Calcium channel blockers*
  - mainly limited to symptom control without a clear reduction in acute or long-term mortality
  - immediate-release nifedipine has been shown to be associated with an increased risk of death in patients with CAD and ACS and therefore should be avoided. (3)
  - CCBs are a first-line therapy for variant angina (Prinzmetal's angina)

Analgesia

- Morphine
  - morphine may delay the pharmacodynamic effects of antiplatelet therapy in patients with STEMI, possibly through a delay in intestinal absorption. Class IIb

- *Nonsteroidal anti-inflammatory drugs (Class III)*
  - block endothelial prostacyclin production and can lead to platelet aggregation via thromboxane A2-dependent pathways
  - recurrent cardiovascular events and mortality with NSAID use following ACS

Cholesterol Management

- Statin
  - high-intensity statin therapy
  - may reduce periprocedural MIs when administered prior to PCI and may also reduce contrast-induced nephropathy
- Ezetimibe
- PCSK9 Inhibitors
  - evolocumab and alirocumab

- Renin-Angiotensin-Aldosterone System Inhibitors
  - angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), and aldosterone antagonists,
  - reduce risk of death when patients with LV dysfunction were treated in the early post-MI period in the ISIS-4 (Fourth International Study of Infarct Survival), SAVE (Survival and Ventricular Enlargement) and VALIANT (Valsartan in Acute Myocardial Infarction) trials.

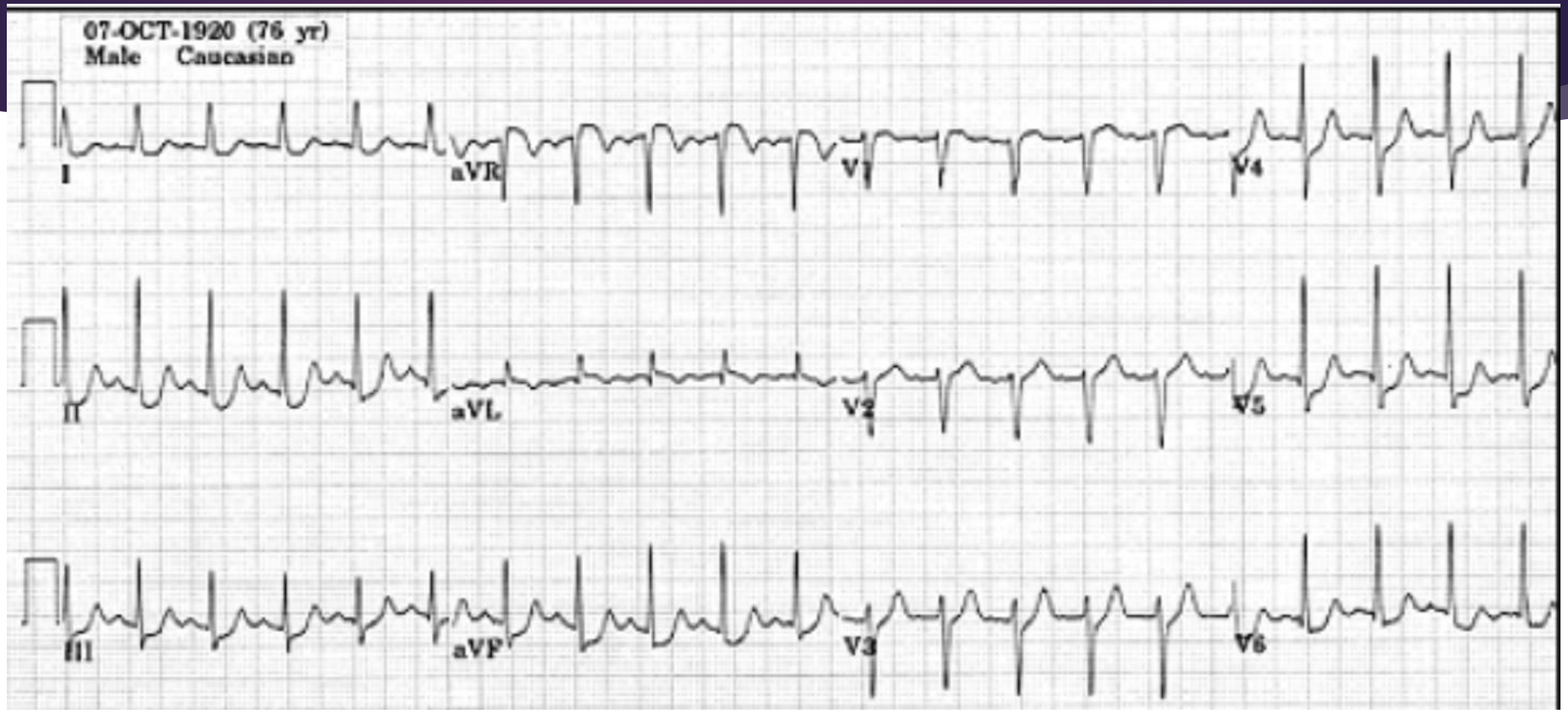
- Aldosterone antagonist (Class IA)
  - Eplerenone
  - an adjunct to ACE inhibitors and beta-blockers in post-MI patients with LV dysfunction and symptomatic heart failure in the EPHESUS

is recommended in patients post–MI without significant renal dysfunction (creatinine >2.5 mg/dL in men or >2.0 mg/dL in women) or hyperkalemia (K >5.0 mEq/L) who are receiving therapeutic doses of ACE inhibitor and beta blocker and have a LVEF 0.40 or less, diabetes mellitus, or HF

- ACE inhibitors or ARBs (class IA)
  - be started or continued in patients with ACS and LV dysfunction and/or those with hypertension, diabetes mellitus, or stable chronic kidney disease (Class I),
  - may be considered in all other patients with cardiac or vascular disease (Class IIa)

Case 3:

- 68/F with hypertension
- No other cardiac history, no DM
- Intermittent chest pain (typical) for 6 hour
- P/E: BP 95/60 mmHg, HR 114 bpm , BW 50kg
- Basal crepitation, Cr 130
- Initial troponin I is 4000 ng/L


07-OCT-1920 (76 yr)
Male Caucasian
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

Which statement is true about initial risk stratification?

A. She has CHF
B. Because her TIMI risk score is 3, she is at intermediate risk
C. The troponin elevation could be due to her renal insufficiency
D. She is at very high risk for poor outcome
E. None of above

Which statement do you most agree with?

A. Because of her age and renal insufficiency, an initial trial of conservative therapy is prudent.
B. Because of her high risk status, an initial invasive approach is preferred
C. She should undergo 48-72 hours of “cooling off” followed by elective cath
D. Any of these strategies is appropriate
E. None of above

Invasive Versus Ischemia-Guided (Conservative) Strategies

Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients With Non–ST-Segment Elevation-Acute Coronary Syndrome

Immediate Invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
	Hemodynamic instability
	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Sustained VT or VF
Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109]) Low-risk Tn-negative female patients
	Patient or clinician preference in the absence of high-risk features
Early Invasive (within 24 h)	None of the above, but GRACE risk score >140 Temporal change in Tn
	New or presumably new ST depression
Delayed invasive (within 25-72 h)	None of the above but diabetes mellitus Renal insufficiency (GFR <60mL/min/1.73m^2)
	Reduced LV systolic funstion (EF <0.40)
	Early postinfarction angina
	PCI within 6 months
	Prior CABG
	GRACE risk score 109 -140; TIMI score ≥2

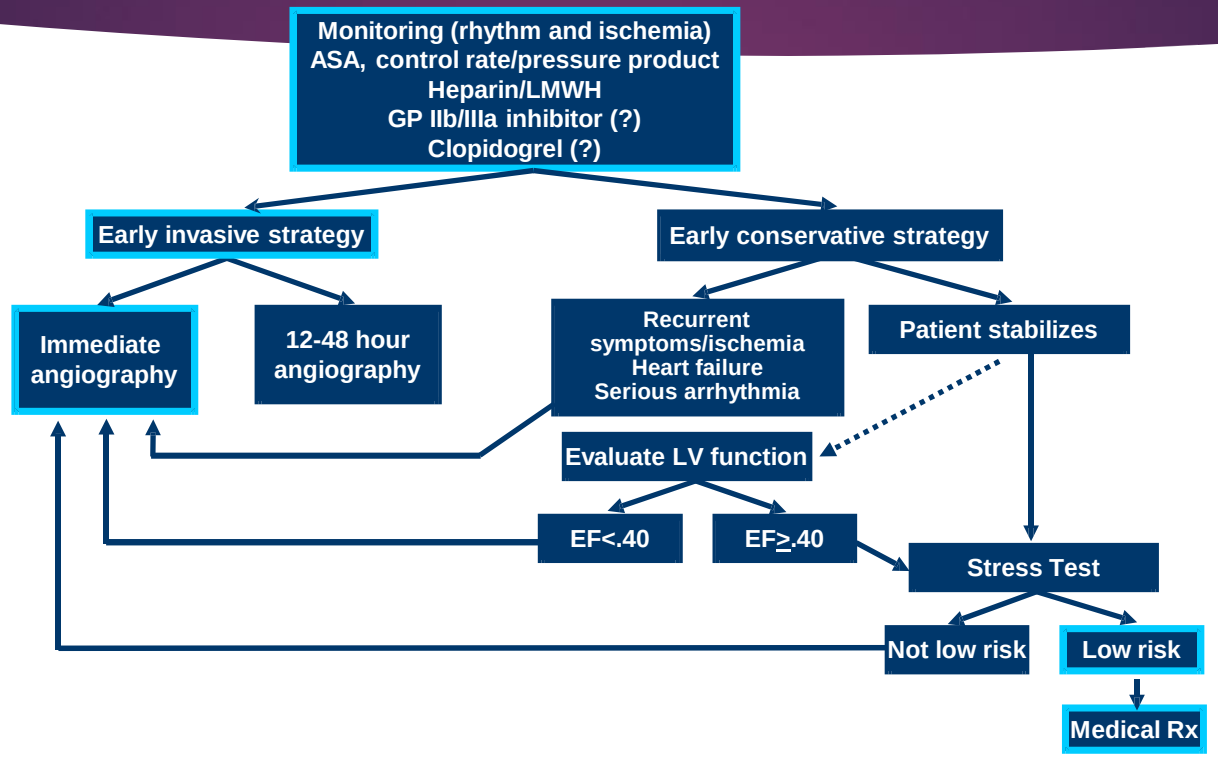
- Routine invasive strategy is generally superior to an ischemia-driven approach.

- In a meta-analysis of randomized trials, a routine invasive strategy resulted in an 18% relative reduction in death or MI, including a significant reduction in MI.

- invasive arm was associated with higher in-hospital mortality (1.8% vs. 1.1%), but a significant reduction in post-discharge mortality (3.8% vs. 4.9%), less severe angina, fewer rehospitalizations, and an improved quality of life.

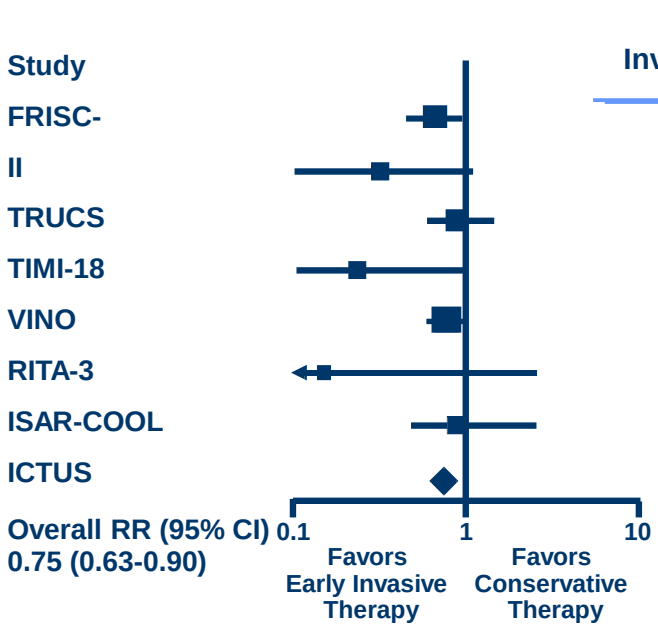
Mehta SR, Cannon CP, Fox KA, et al. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. JAMA 2005;293:2908-17.

UA/NSTEMI HOSPITAL MANAGEMENT



Relative Risk for All-Cause Mortality

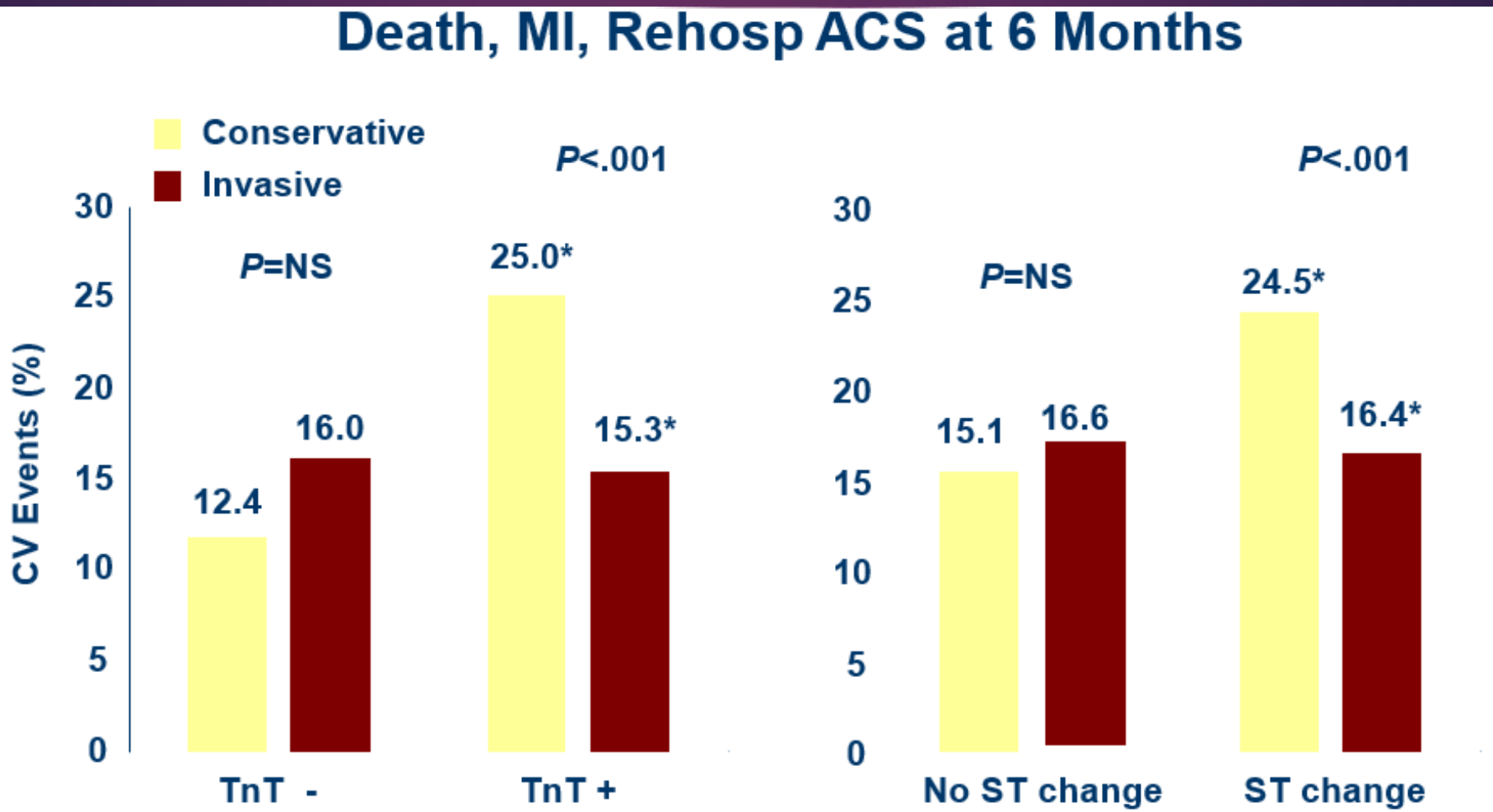
Early Invasive vs Conservative Therapy



	Deaths, n		
	Invasive	Conservative	Follow-up, Months
FRISC-	45	67	24
II	3	9	12
TRUCS	37	39	6
TIMI-18	2	9	6
VINO	102	132	60
RITA-3	0	3	1
ISAR-COOL	15	15	12
ICTUS			

Bavry AA, et al. *J Am Coll Cardiol.* 2006;48:1319-1325.

Benefit of Invasive Strategy by Troponin and ST Changes



Morrow DA. *JAMA*. 2001;286:2405-2412; Cannon CP. *N Engl J Med*. 2001;344:1879-1887.

ACC/AHA UA/NSTEMI Guideline: Invasive versus Conservative Strategy

Preferred Strategy	Patient Characteristics	
Invasive	•Elevated cardiac biomarkers •New ST-segment depression •HF or new or worsening mitral regurgitation •High-risk findings from noninvasive testing • Hemodynamic instability	•Recurrent angina or ischemia at rest • Ventricular tachycardia • PCI within 6 months • Prior CABG •High risk score (e.g., TIMI, GRACE) • LVEF < 40%
Conservative	•Low risk score •Patient/physician preference in absence of high-risk features	

Anderson JL et al., *JACC.* 2007;50(7):1-157.

Early vs. Delayed Invasive Intervention in ACS

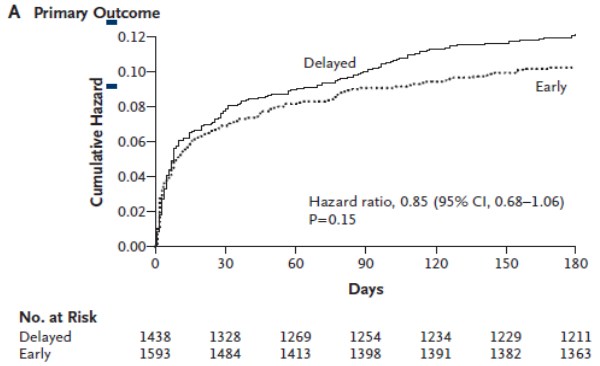
TIMACS trial

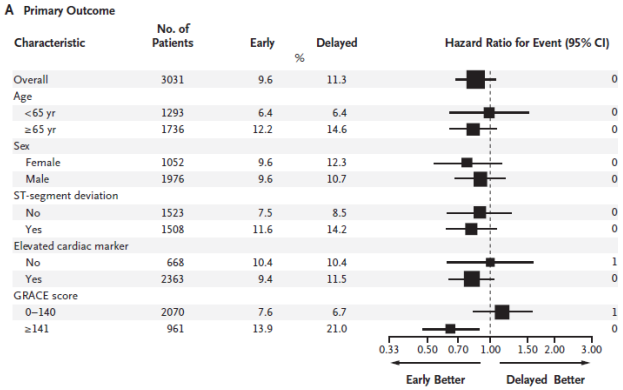
N= 3,031 ACS patients -

1:1 randomization ([routine/early ≤ 24] vs.

[delayed ≥ 36 h] invasive strategy) -

The primary outcome: 6 mo composite of death/MI/CVA





Sharma, et al. N Engl J Med 2009;360:2165.

Plans are made to proceed with coronary angiography in 6 hours. What is the most appropriate initial antiplatelet/antithrombotic strategy?

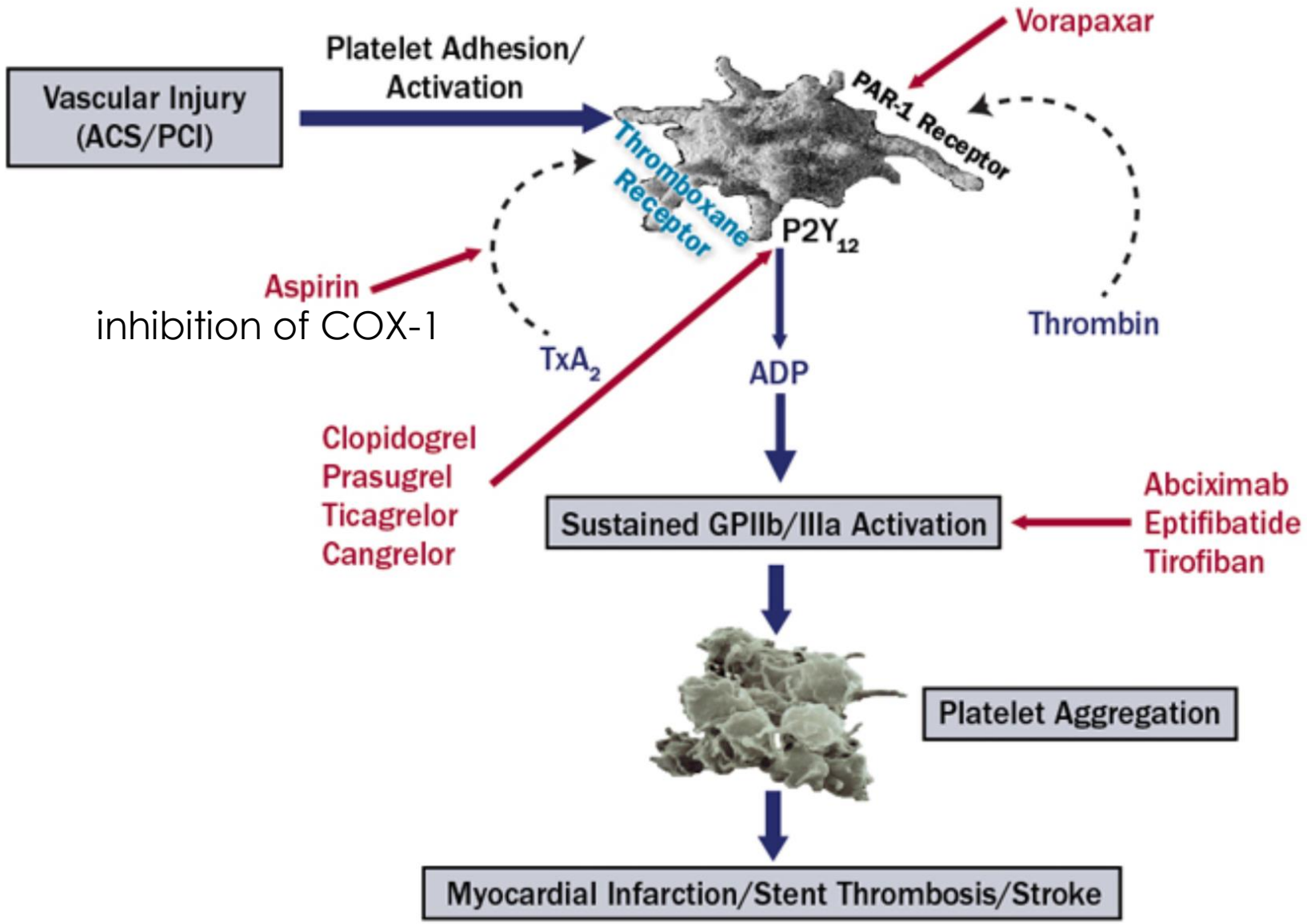
A. Aspirin + bivalirudin
B. Aspirin + prasugrel (60 mg)
C. Aspirin + clopidogrel
D. Aspirin plus subcutaneous enoxaparin
E. Aspirin + ticagrelor

Non-ST Elevation ACS

Antiplatelet Therapy

Anti-Platelet agent

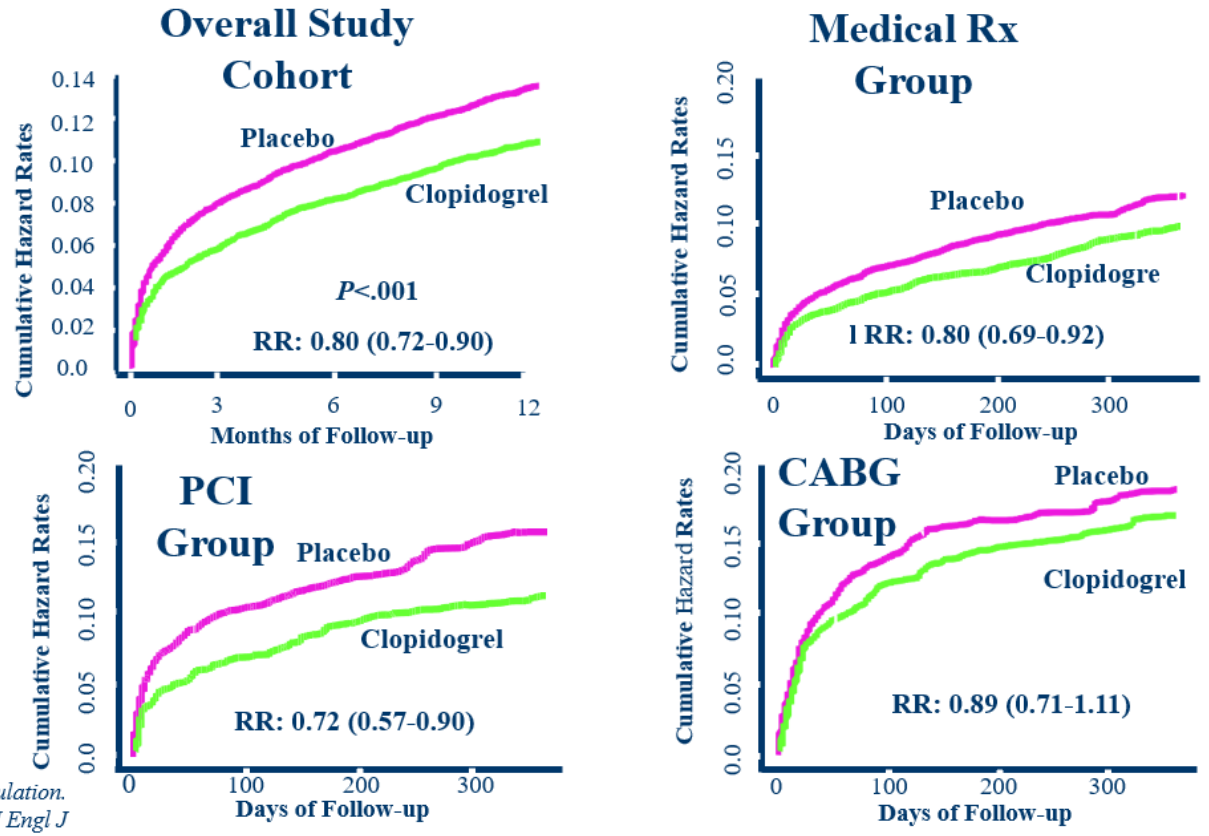
- NSTE ACS is a platelet-centric disease; greater platelet inhibition is associated with reduced ischemic event occurrence
- A great clinical challenge exists to balance the risks of stent thrombosis and ischemic complications versus bleeding
- Bleeding is associated with worse clinical outcomes, and strategies to minimize its occurrence are mandatory in the care of the NSTE-ACS patient


Vascular Injury
(ACS/PCI)
Platelet Adhesion/
Activation
Vorapaxar
PAR-1 Receptor
Thromboxane
Receptor
P2Y12
Aspirin
inhibition of COX-1
TxA2
ADP
Thrombin
Clopidogrel
Prasugrel
Ticagrelor
Cangrelor
Sustained GPIIb/IIIa Activation
Abciximab
Eptifibatide
Tirofiban
Platelet Aggregation
Myocardial Infarction/Stent Thrombosis/Stroke

$P2Y_{12}$ Receptor Blockers

- Because the ADP-$P2Y_{12}$ interaction is pivotal for the amplification of platelet activation and stable platelet aggregation, an early focus of antithrombotic therapy is targeted inhibition of the $P2Y_{12}$ receptor.

CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) study



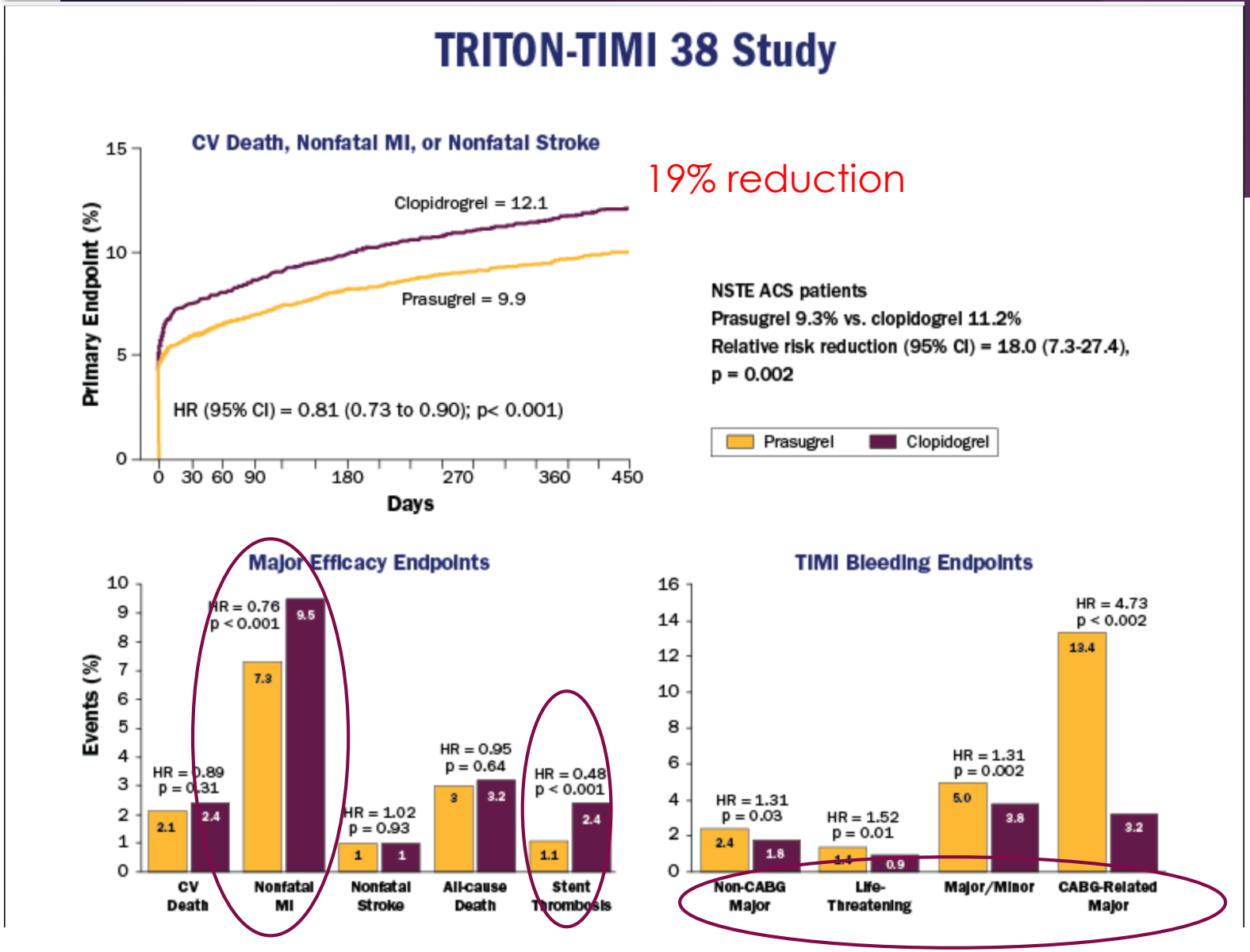
Fox KA, et al. *Circulation.* 2004; Yusuf S, et al. *N Engl J Med.* 2001.

Therapy with clopidogrel (300 mg loading dose followed by 75 mg/day) and aspirin (75-325 mg/day) in patients (n = 12,562) with NSTE ACS was associated with 20% reduction in the primary combined endpoint of 12-month CV mortality, nonfatal MI, and stroke compared with aspirin monotherapy

A significant 34% risk reduction was observed within 24 hours in the clopidogrel group and was maintained throughout the 12 months of the study period.

There was a 1% absolute risk increase (3.7% vs. 2.7%; risk reduction = 1.38%; 95% confidence interval [CI], 1.13-1.67; p = 0.001) in major bleeding and a nonsignificant increase in life-threatening and fatal bleeding.

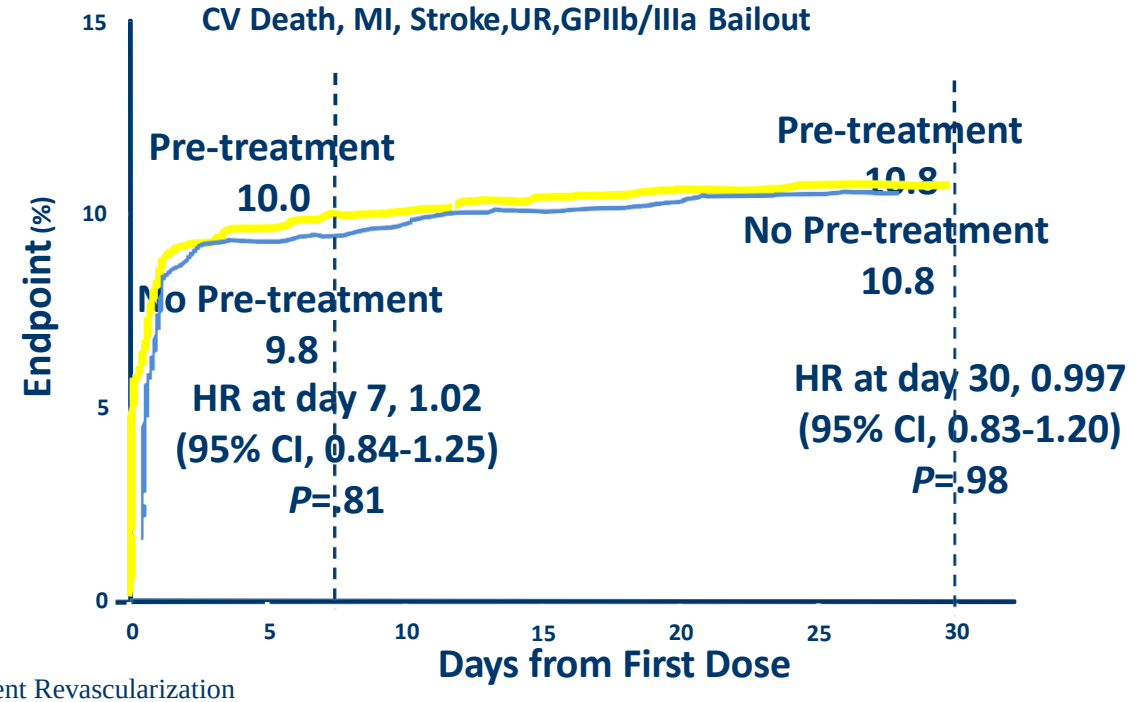
Prasugrel: TRITON-TIMI 38 Trial



A sustained reduction in the primary endpoint with prasugrel therapy compared with clopidogrel therapy (9.3% vs. 11.2%; relative risk reduction = 18.0; 95% CI, 7.3-27.4; p = 0.002) was demonstrated among patients with NSTE ACS.

Wiviott SD, Braunwald E, McCabe CH, et al.

ACCOAST: Primary Efficacy Endpoint

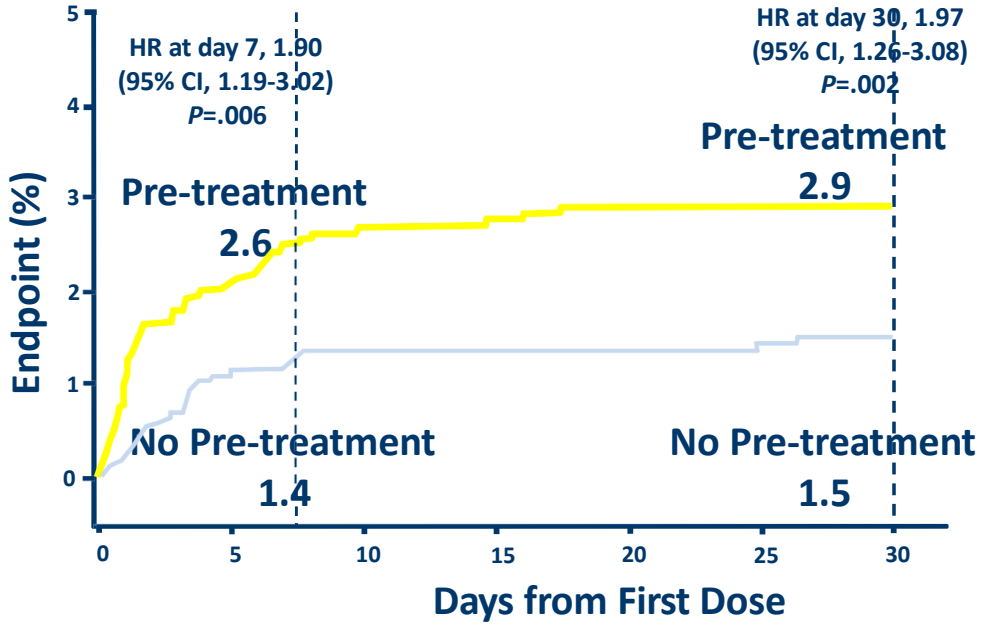


UR=Urgent Revascularization

Montalescot G, et al. *N Engl J Med.* 2013.

In the ACCOAST trial, treatment with prasugrel in NSTEMI before PCI did not reduce ischemic events

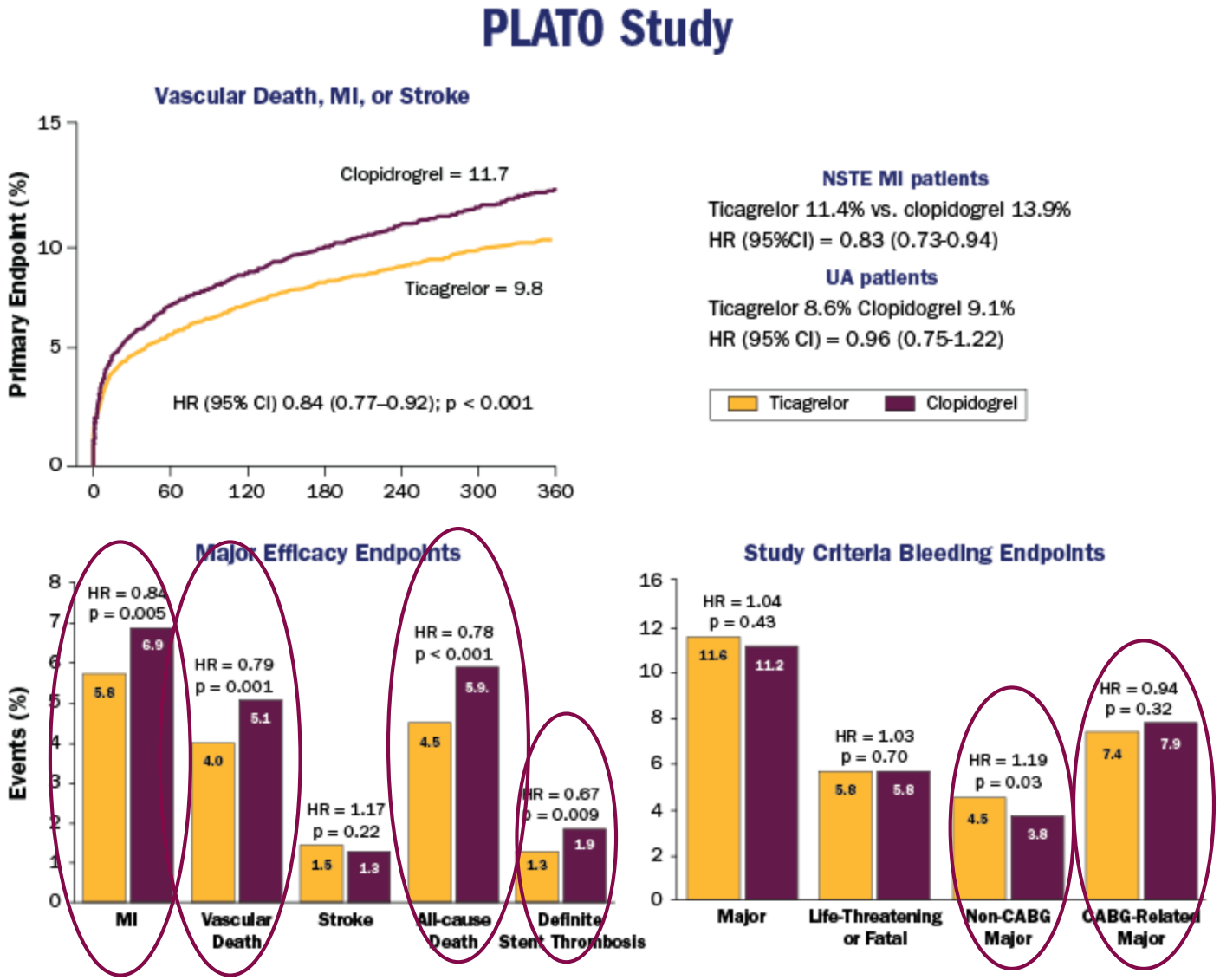
ACCOAST: Primary Safety Endpoint



Montalescot G, et al. *N Engl J Med.* 2013.

In the ACCOAST trial, treatment with prasugrel in NSTEMI before PCI was associated with more bleeding

PLATO (Platelet Inhibition and Patient Outcomes) trial



Ticagrelor therapy was associated with a significant reduction in the primary efficacy endpoint compared with clopidogrel at 30 days (4.8% vs. 5.4%; p = 0.045), and the superiority of ticagrelor was maintained throughout 12 months, with a 16% relative risk reduction (9.8% vs. 11.7%, respectively; p < 0.001). CV death (5.1% clopidogrel; 4.0% ticagrelor; p = 0.001) and MI (6.9% clopidogrel; 5.8% ticagrelor; p = 0.005) but not stroke (1.5% vs. 1.3%, p = 0.22) were significantly reduced by ticagrelor treatment

Summary of anti-platelet agents

Indication	Clopidogrel	Prasugrel	Ticagrelor
Elective PCI	√	No	No
STEMI PPCI	√	√	√
STEMI Lytics	√	No	No
NSTE ACS			
Invasive	√ (600 mg)	√	√
Pre-treat?	√	No	+/-
Conservative	√ (300 mg)	No	√
Triple therapy	√	No	No

GP IIb/IIIa Summary

- Selected use in high risk patients in whom early invasive strategy is planned
  - cath lab initiation (IIa) now preferable to upstream (IIb)
- Avoid in medically treated pts
- Avoid upstream use in low risk pts
- Avoid with bivalirudin
- Beware of relative contraindications!

Non-ST Elevation ACS

Anticoagulant Therapy

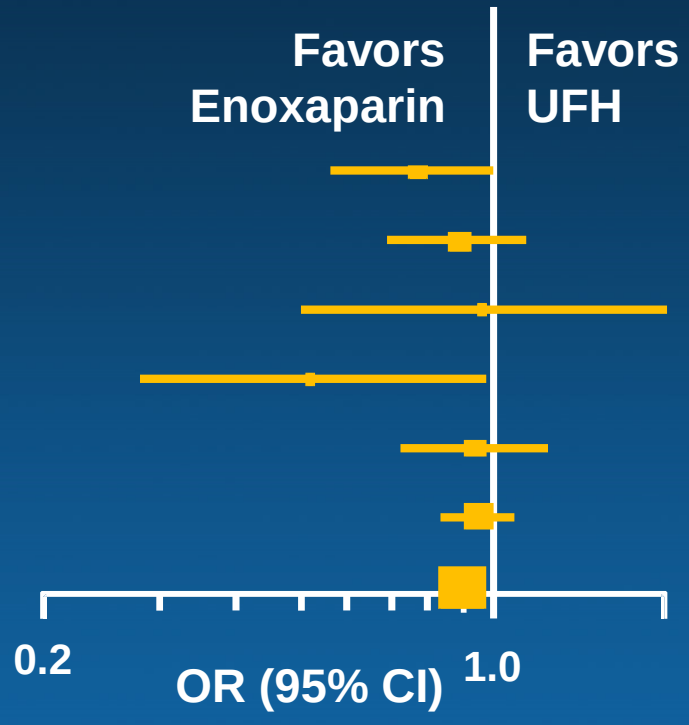
ACC/AHA UA/NSTEMI Guideline: Initial Anticoagulant Algorithm in Invasive and Conservative Strategies

Diagnosis of UA/NSTEMI likely/definite	
Select management strategy	
Invasive strategy Acceptable options: **enoxaparin or UFH (I LOE A) or** **bivalirudin (I LOE B)**	**Conservative strategy Acceptable options:** **enoxaparin or UFH (I LOE A)** **or fondaparinux (I LOE B)** **but** **enoxaparin or fondaparinux are preferable (IIa)**

Anderson JL et al., *JACC.* 2007;50(7):1-157.

Enoxaparin vs Unfractionated Heparin in UA/NSTEMI: A Systematic Overview (N=21,946) Death or MI at 30 Days (ITT*)

Trial	OR (95% CI)
ESSENCE	0.76 (0.58–1.01)
TIMI 11B	0.88 (0.70–1.11)
ACUTE II	0.97 (0.51–1.83)
INTERAC	0.54 (0.30–0.96)
T	0.94 (0.73–1.20)
A to Z	0.96 (0.86–1.07)
SYNERGY	0.91 (0.83–0.99)
Overall	



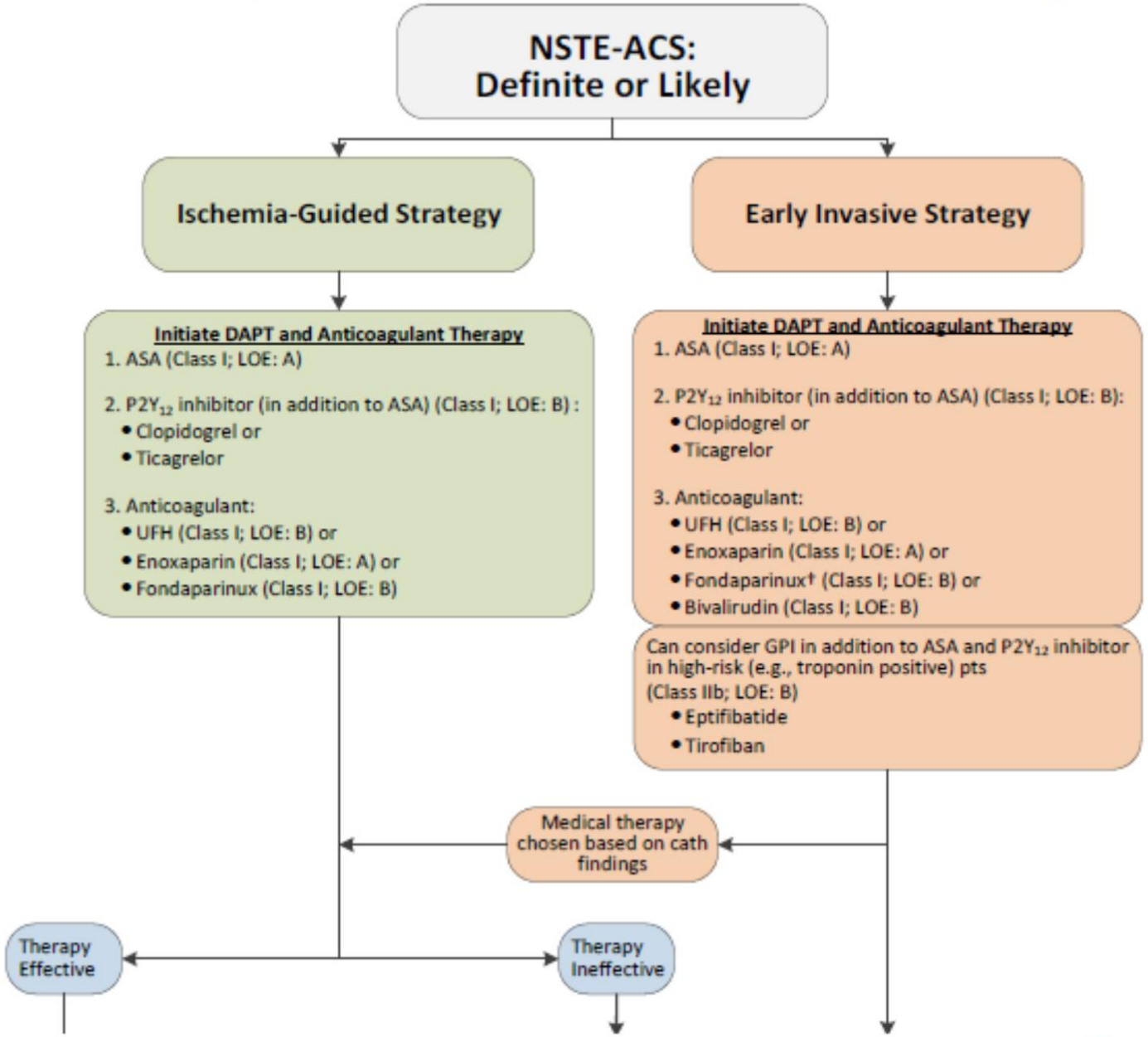
Petersen JL, et al. *JAMA.* 2004;292:89-96.

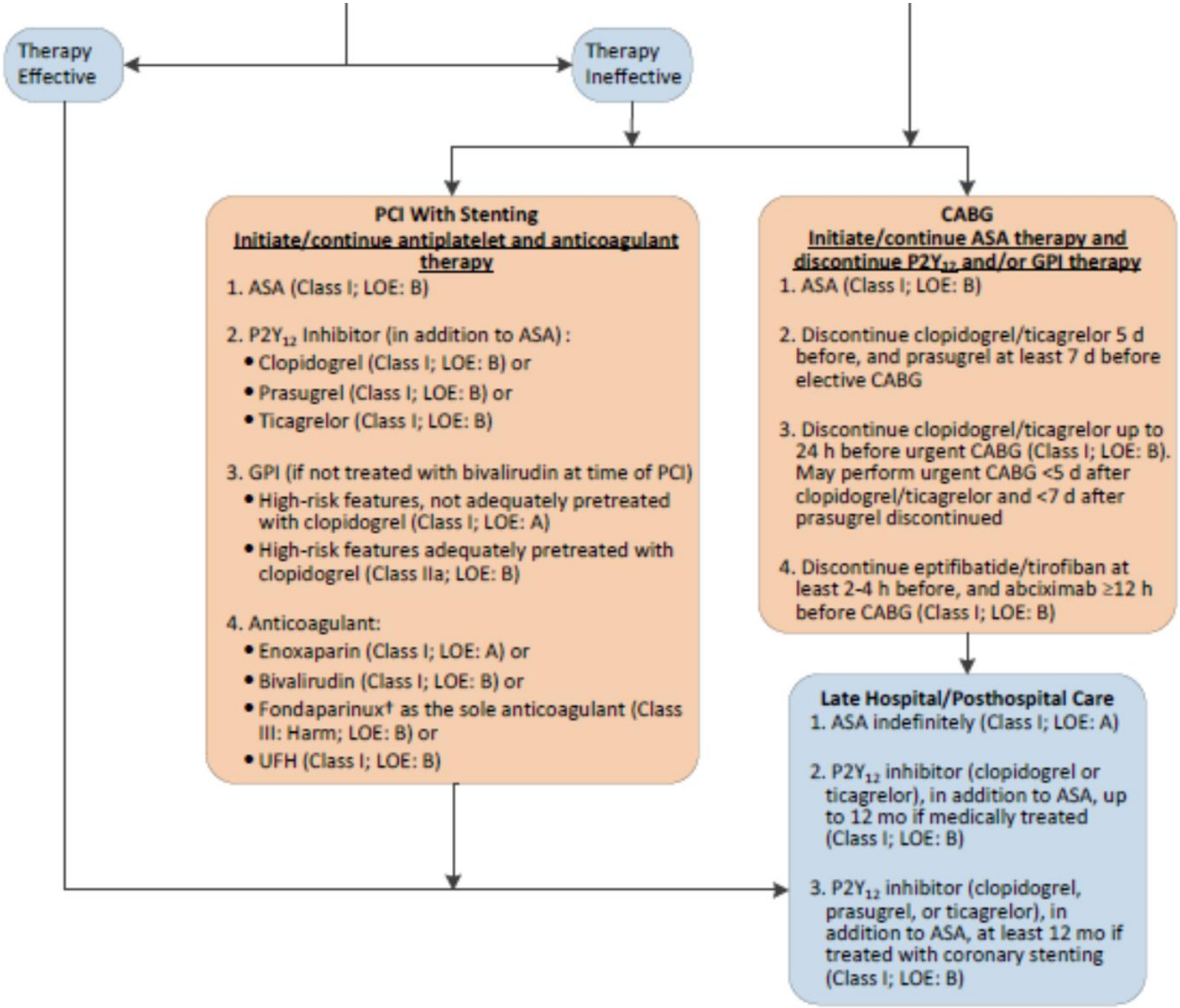
Cangrelor

- Parenterally administered adenosine triphosphate analog with a short half-life (3-6 minutes), with rapid onset/offset of action and dose-dependent and predictable pharmacodynamic effect

- Cangrelor is still awaiting FDA approval as an adjunct to PCI.

Algorithm for Management of Patients With Definite or Likely NSTE-ACS




Therapy Effective
Therapy Ineffective
PCI With Stenting
Initiate/continue antiplatelet and anticoagulant therapy
1. ASA (Class I; LOE: B)
2. P2Y12 Inhibitor (in addition to ASA):
• Clopidogrel (Class I; LOE: B) or
• Prasugrel (Class I; LOE: B) or
• Ticagrelor (Class I; LOE: B)
3. GPI (if not treated with bivalirudin at time of PCI)
• High-risk features, not adequately pretreated with clopidogrel (Class I; LOE: A)
• High-risk features adequately pretreated with clopidogrel (Class IIa; LOE: B)
4. Anticoagulant:
• Enoxaparin (Class I; LOE: A) or
• Bivalirudin (Class I; LOE: B) or
• Fondaparinux† as the sole anticoagulant (Class III: Harm; LOE: B) or
• UFH (Class I; LOE: B)
CABG
Initiate/continue ASA therapy and discontinue P2Y12 and/or GPI therapy
1. ASA (Class I; LOE: B)
2. Discontinue clopidogrel/ticagrelor 5 d before, and prasugrel at least 7 d before elective CABG
3. Discontinue clopidogrel/ticagrelor up to 24 h before urgent CABG (Class I; LOE: B). May perform urgent CABG <5 d after clopidogrel/ticagrelor and <7 d after prasugrel discontinued
4. Discontinue eptifibatide/tirofiban at least 2-4 h before, and abciximab ≥12 h before CABG (Class I; LOE: B)
Late Hospital/Posthospital Care
1. ASA indefinitely (Class I; LOE: A)
2. P2Y12 inhibitor (clopidogrel or ticagrelor), in addition to ASA, up to 12 mo if medically treated (Class I; LOE: B)
3. P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor), in addition to ASA, at least 12 mo if treated with coronary stenting (Class I; LOE: B)

Bonus Question:

A 26/M, Good Past health,

Presents to the emergency department with sudden-onset severe substernal chest pain that began 15 minutes prior to presentation

PE:

His pupils are dilated, heart rate is 105 bpm, and blood pressure is 163/106. He was started on nitroglycerin, but has persistent chest pain.

An electrocardiogram shows ST depressions in leads V_3-V_6.

Which of the following medications would be appropriate to administer?

A. Naloxone
B. Dabigatran
C. Metoprolol
D. Lorazepam
E. Flumazenil

D

- Benzodiazepines with or without nitroglycerin may be used to manage hypertension and tachycardia in patients who present with non-ST elevation acute coronary syndromes (NSTE-ACS) and signs of acute cocaine or methamphetamine intoxication.

- For STE-ACS, lorazepam would be the most reasonable choice of the options listed, although the primary focus would be on emergent coronary angiography and percutaneous coronary intervention, if indicated.

- Beta-blockers should not be administered to patients with ACS with a recent history of cocaine or methamphetamine use who demonstrate signs of acute intoxication due to the risk of potentiating coronary spasm

Thank you