Initial Recognition and Management in the Emergency Department

ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction

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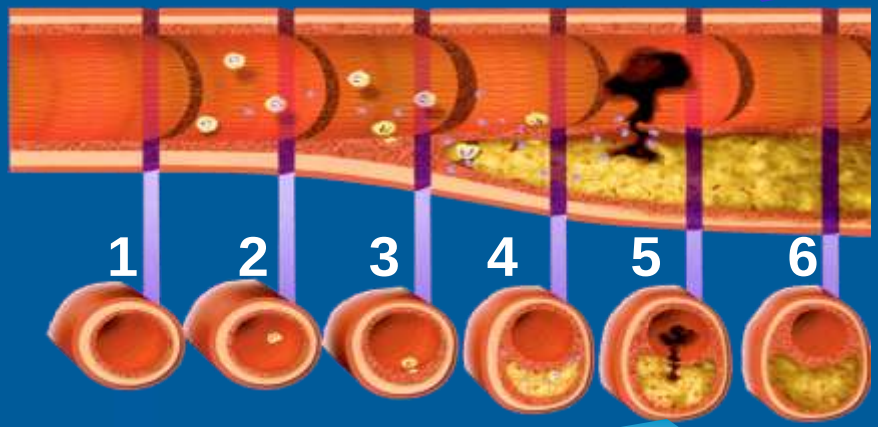
Onset of STEMI
- **Prehospital issues**
- **Initial recognition and management in the Emergency Department (ED)**
- **Reperfusion**

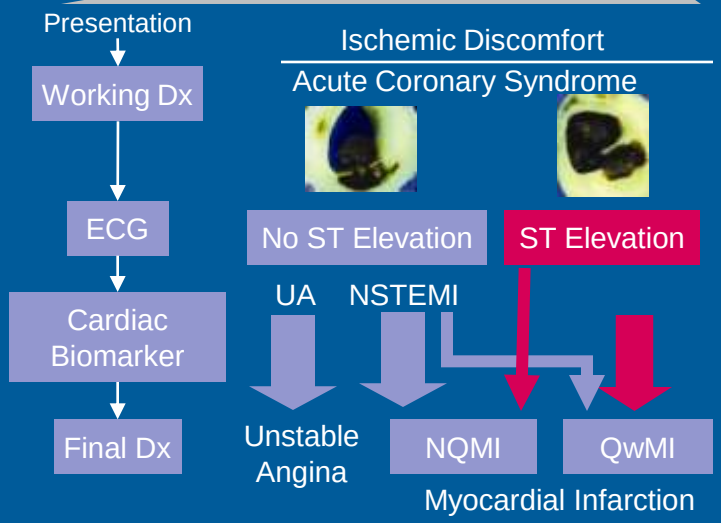
Hospital Management
- **Medications**
- **Arrhythmias**
- **Complications**
- **Preparation for discharge**

Modified from Libby. Circulation 2001;104:365, Hamm et al. The Lancet 2001;358:1533 and Davies. Heart 2000;83:361.

Management Before STEMI

Secondary Prevention/ Long-Term Management





Chronology of the interface between the patient and the clinician through the progression of plaque formation and the onset of complications of STEMI.

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Initial History to Obtain During ST Elevation MI

- Prior ischemia or infarction or revascularization or ischemic evaluation
- Complaints of chest discomfort – characteristics, associated symptoms,
- Risk profile – coronary (age, gender, htn, DM, smoking), dissection (age, FH, bicuspid AoV, pregnancy, htn, trauma)
- Bleeding risk

Symptoms in Acute STEMI

- Chest pain or discomfort, crushing, vise-like, pressure, heartburn
- Retrosternal to jaw, interscapular, neck, arm, epigastrium
- Duration over 30 min, may wax and wane
- Possible relief with belching
- Associated Sx: N&V, sweat, pallor, weakness, fatigue
- Elderly have less chest discomfort

ED Evaluation of Patients With STEMI

Brief Physical Examination in the ED

1. Airway, Breathing, Circulation (ABC)
2. Vital signs, general observation
3. Presence or absence of jugular venous distension
4. Pulmonary auscultation for rales
5. Cardiac auscultation for murmurs and gallops
6. Presence or absence of stroke
7. Presence or absence of pulses
8. Presence or absence of systemic hypoperfusion (cool, clammy, pale, ashen)

Exam in STEMI

- Agitation, anguish, Levine's sign
- Cool clammy skin
- High HR and BP – more Anterior
- Low HR and BP – more Inferior
- Low pulse pressure or low volume pulse – poor SV
- "Ectopic" systolic precordial impulse
- Soft S1, S4, Pdox S2, S3, rales, alternans
- JVD and clear lungs, Kussmaul's Sn
- Murmur of MR or VSD; rub
- AR and poor pulses – dissection

- Neurol exam for CVA, mental status

ED Evaluation of Patients With STEMI

Differential Diagnosis of STEMI: *Life-Threatening*

- Aortic dissection
- Pulmonary embolus
- Perforating ulcer
- Tension pneumothorax
- Boerhaave syndrome (esophageal rupture with mediastinitis)

ED Evaluation of Patients With STEMI

Differential Diagnosis of STEMI: *Other Cardiovascular and Nonischemic*

- Pericarditis
- Atypical angina
- Early repolarization
- Wolff-Parkinson-White syndrome
- Deeply inverted T-waves suggestive of a central nervous system lesion or apical hypertrophic cardiomyopathy
- LV hypertrophy with strain
- Brugada syndrome
- Myocarditis
- Hyperkalemia
- Bundle-branch blocks
- Vasospastic angina
- Hypertrophic cardiomyopathy

ED Evaluation of Patients With STEMI

Differential Diagnosis of STEMI: *Other Noncardiac*

- Gastroesophageal reflux (GERD) and spasm
- Chest-wall pain
- Pleurisy
- Peptic ulcer disease
- Panic attack
- Cervical disc or neuropathic pain
- Biliary or pancreatic pain
- Somatization and psychogenic pain disorder

ECG in STEMI

- ST Elevation identifies patients who benefit from reperfusion therapy
- LBBB or Anterior MI are higher risk*
- STEL of 0.1mV in V1-4 may be false positive – 0.2mV more specific
- Deep ST depression in V1-4 may be “true posterior” – term should be discarded – MRI shows lateral

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Time Course of Infarction - 1

- Hyperacute T waves - peaked positive T waves directed toward infarction, only a few minutes
- ST depression - any time in infarction, doesn't localize, may mean "Non-Q MI", or Non-ST elevation MI – NSTEMI.
- ST elevation - begins in minutes, greatest in 7-12 hr, BEST criterion for urgent intervention (PCI or thrombolysis)

Time Course of Infarction - 2

- Q wave formation - begins at 6-12 hours, usually permanent
- T wave inversion - begins after a day or a few days, lasts often months to years
- ST segment elevation usually resolved by 2 to 8 weeks; afterwards indicates LV aneurysm

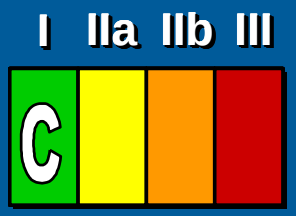
False Positive ECGs

- Early repolarization
- Nondiagnostic ECG
- Pericarditis
- Prior MI
- LBBB
- LVH
- Vasospasm
- Tachycardia
- RBBB
- Pacemaker

- Stress cardiomyopathy
- Myocarditis
- Prior MI
- STEMI due to embolus/spasm
- LBBB
- NSTEMI
- PE

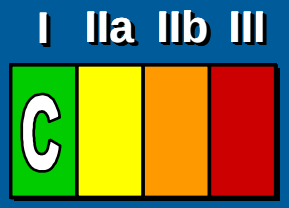
JAMA, December 2007

Electrocardiogram

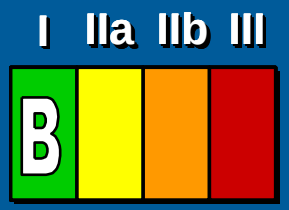


If the initial ECG is not diagnostic of STEMI, serial ECGs or continuous ST-segment monitoring should be performed in the patient who remains symptomatic or if there is high clinical suspicion for STEMI.

Electrocardiogram

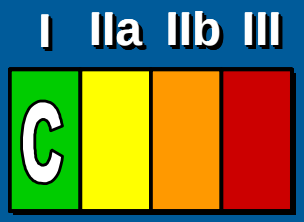


Show 12-lead ECG results to emergency physician within 10 minutes of ED arrival in all patients with chest discomfort (or anginal equivalent) or other symptoms of STEMI.



In patients with inferior STEMI, ECG leads should also be obtained to screen for right ventricular infarction.

Laboratory Examinations



Laboratory examinations should be performed as part of the management of STEMI patients, but should not delay the implementation of reperfusion therapy.

- Serum biomarkers for cardiac damage
- Complete blood count (CBC) with platelets
- International normalized ratio (INR)
- Activated partial thromboplastin time (aPTT)
- Electrolytes and magnesium
- Blood urea nitrogen (BUN)
- Creatinine
- Glucose
- Complete lipid profile

Biomarker Biology

Biomarker	Onset	Peak	Return to Normal
Troponin I	3-12 h	24 h	5-10 d
CK-MB	3-12 h	24 h	2-3 d
Troponin T	3-12 h	12-48 h	5-14 d
Myoglobin	1-4 h	6-7 h	24 h
CKMB tissue isoform	2-6 h	18 h	Unk
CKMM tissue isoform	1-6 h	12 h	38 h

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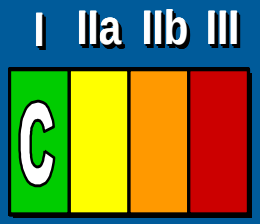
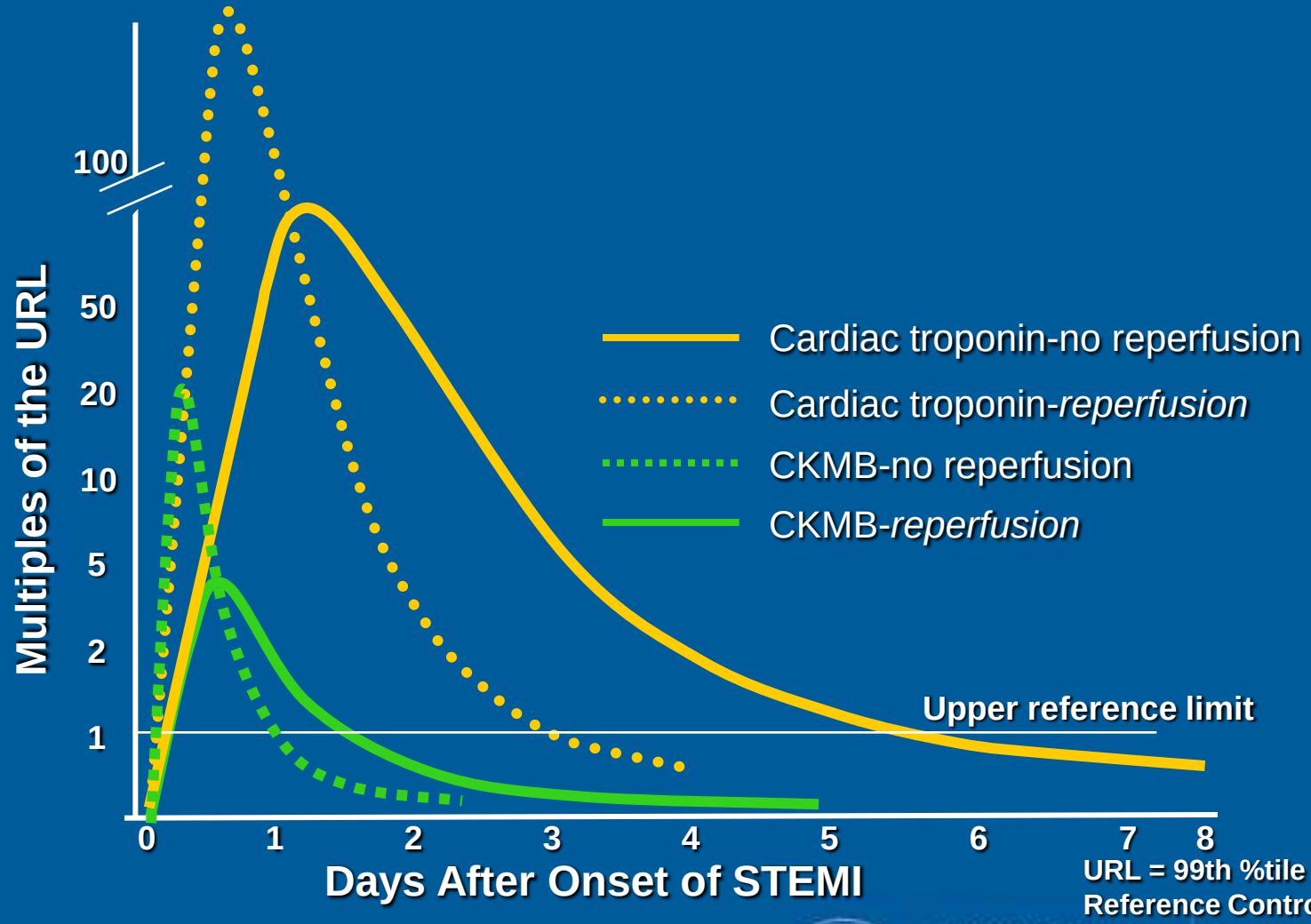
Biomarkers of Cardiac Damage



Cardiac-specific troponins should be used as the optimum biomarkers for the evaluation of patients with STEMI who have coexistent skeletal muscle injury.

For patients with ST elevation on the 12-lead ECG and symptoms of STEMI, reperfusion therapy should be initiated as soon as possible and is not contingent on a biomarker assay.

Cardiac Biomarkers in STEMI



URL = 99th %tile of Reference Control Group

Alpert et al. J Am Coll Cardiol 2000;36:959.
Wu et al. Clin Chem 1999;45:1104.

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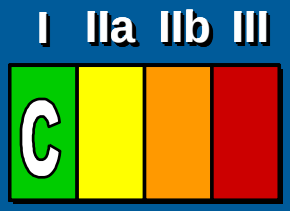
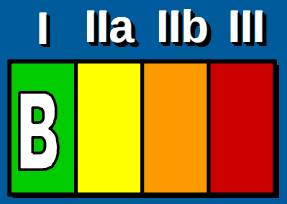
Imaging



Patients with STEMI should have a portable chest X-ray, but this should not delay implementation of reperfusion therapy (unless a potential contraindication is suspected, such as aortic dissection).



Imaging studies such as a high quality portable chest X-ray, transthoracic and/or transesophageal echocardiography, and a contrast chest CT scan or an MRI scan should be used for differentiating STEMI from aortic dissection in patients for whom this distinction is initially unclear.

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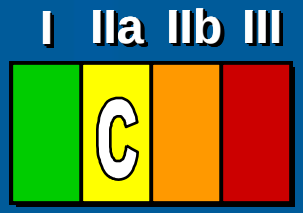
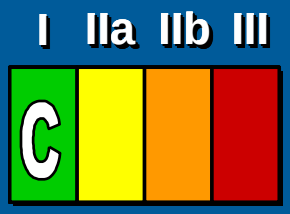
Oxygen

Supplemental oxygen should be administered to patients with arterial oxygen desaturation (SaO_2 < 90%).

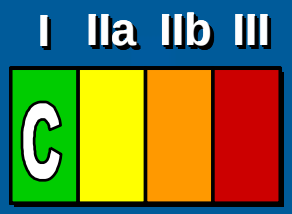


It is reasonable to administer supplemental oxygen to all patients with uncomplicated STEMI during the first 6 hours.

Nitroglycerin



Patients with ongoing ischemic discomfort should receive sublingual NTG (0.4 mg) every 5 minutes for a total of 3 doses, after which an assessment should be made about the need for intravenous NTG.

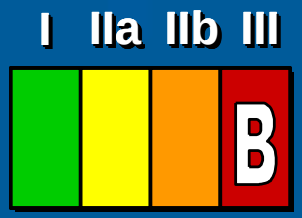


Intravenous NTG is indicated for relief of ongoing ischemic discomfort that responds to nitrate therapy, control of hypertension, or management of pulmonary congestion.

Nitroglycerin

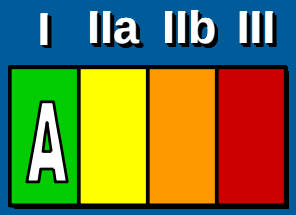
Nitrates should not be administered to patients with:

- systolic pressure < 90 mm Hg or ≥ to 30 mm Hg below baseline
- severe bradycardia (< 50 bpm)
- tachycardia (> 100 bpm) or
- suspected RV infarction.



Nitrates should not be administered to patients who have received a phosphodiesterase inhibitor for erectile dysfunction within the last 24 hours (48 hours for tadalafil).

Aspirin



Aspirin should be chewed by patients who have not taken aspirin before presentation with STEMI. The initial dose should be 162 mg (*Level of Evidence: A*) to 325 mg (*Level of Evidence: C*)

Although some trials have used enteric-coated aspirin for initial dosing, more rapid buccal absorption occurs with non–enteric-coated formulations.

Reperfusion

- Given the current literature, it is not possible to say definitively that a particular reperfusion approach is superior for all pts, in all clinical settings, at all times of day

- The main point is that some type of reperfusion therapy should be selected for all appropriate pts with suspected STEMI

- The appropriate & timely use of some reperfusion therapy is likely more important than the choice of therapy

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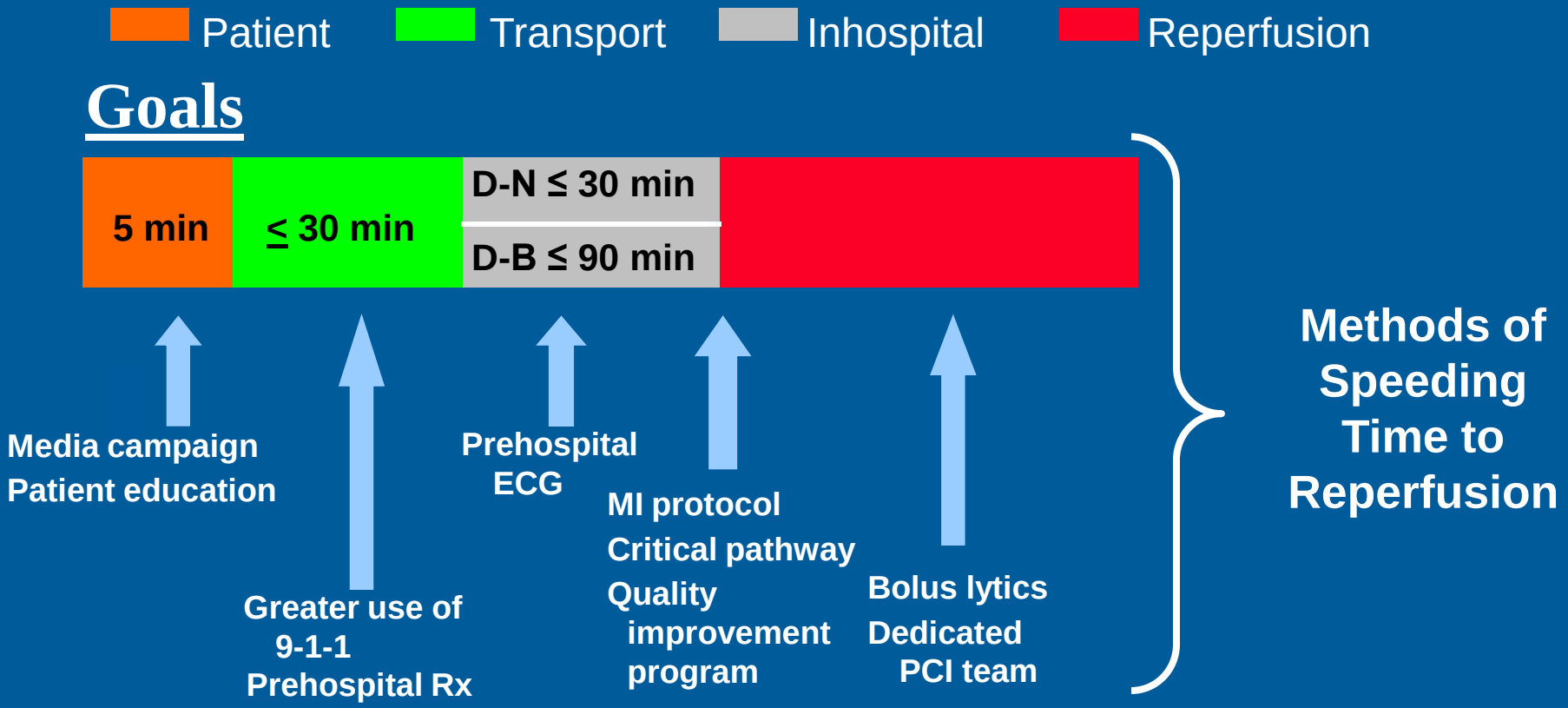
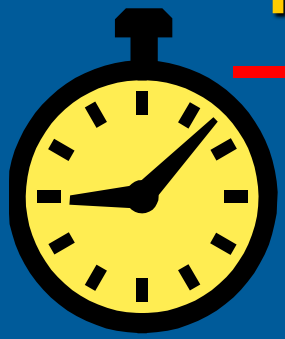
Reperfusion

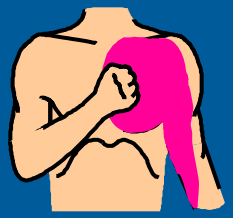
The medical system goal is to facilitate rapid recognition and treatment of patients with STEMI such that **door-to-needle** (or medical contact–to-needle) time for initiation of **fibrinolytic therapy** can be achieved **within 30 minutes** or that **door-to-balloon** (or medical contact–to-balloon) time for **PCI** can be kept **within 90 minutes**.

Reperfusion



Treatment Delayed is Treatment Denied





Symptom Recognition

Call to Medical System

PreHospital

ED

Cath Lab

Increasing Loss of Myocytes

Delay in Initiation of Reperfusion Therapy

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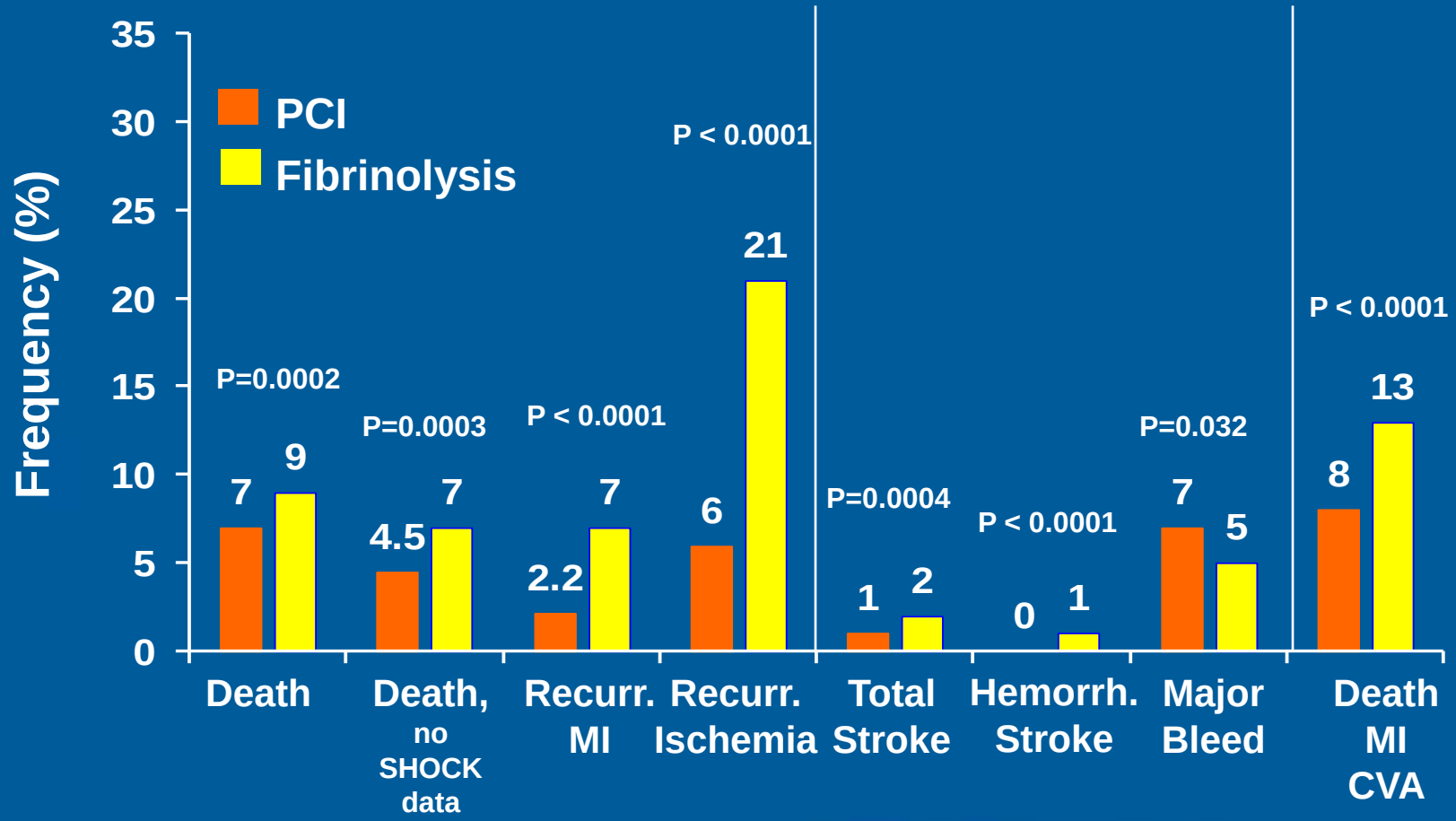
PCI vs Fibrinolysis for STEMI:
Short Term (4-6 wk) Clinical Outcomes



N = 7739, 23 trials

Keeley et al. The Lancet 2003;361:13.

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Overview of PCI vs Lysis: *Issues to Consider*

- Sample Size = 7739
- Data span 10–15 years
- Selection bias of pts enrolled
- 2% mortality benefit with PCI depends on lytic – (not significant vs tPA if SHOCK is excluded)
- Composite endpoint is driven by reMI – potential biases against lytic arms:
  - Hard to diagnose peri-PCI MI
  - UFH used in lytic arms--? Better antithrombins
  - Dependent on use of PCI post-lysis

JACC 2004;44: 671.
Circulation 2004;110: 588.

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Contraindications and Cautions for Fibrinolysis in STEMI

Absolute Contraindications

- Any prior intracranial hemorrhage
- Known structural cerebral vascular lesion (e.g., arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastatic)
- Ischemic stroke within 3 months EXCEPT acute ischemic stroke within 3 hours

NOTE: Age restriction for fibrinolysis has been removed compared with prior guidelines.

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Contraindications and Cautions for Fibrinolysis in STEMI

Absolute Contraindications

- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months

Contraindications and Cautions for Fibrinolysis in STEMI

Relative Contraindications

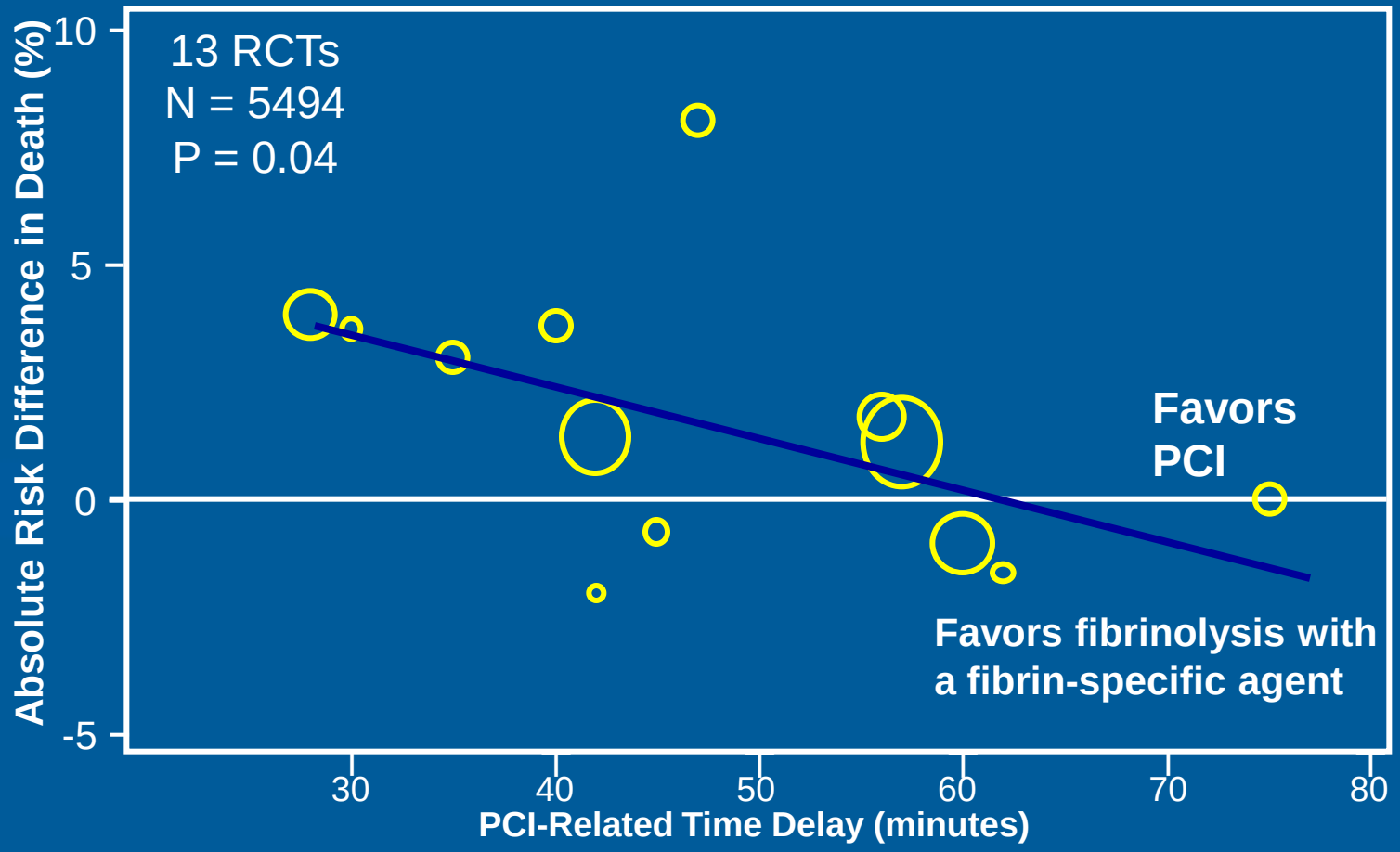
- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (SBP > 180 mm Hg or DBP > 110 mm Hg)
- History of prior ischemic stroke greater than 3 months, dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (> 10 minutes) CPR or major surgery (< 3 weeks)

Contraindications and Cautions for Fibrinolysis in STEMI

Relative Contraindications

- Recent (< 2 to 4 weeks) internal bleeding
- Noncompressible vascular punctures
- For streptokinase/anistreplase: prior exposure (> 5 days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

PCI versus Fibrinolysis with Fibrin-Specific Agents: Is Timing (Almost) Everything?



Nallamothu and Bates. Am J Cardiol 2003;92:824.

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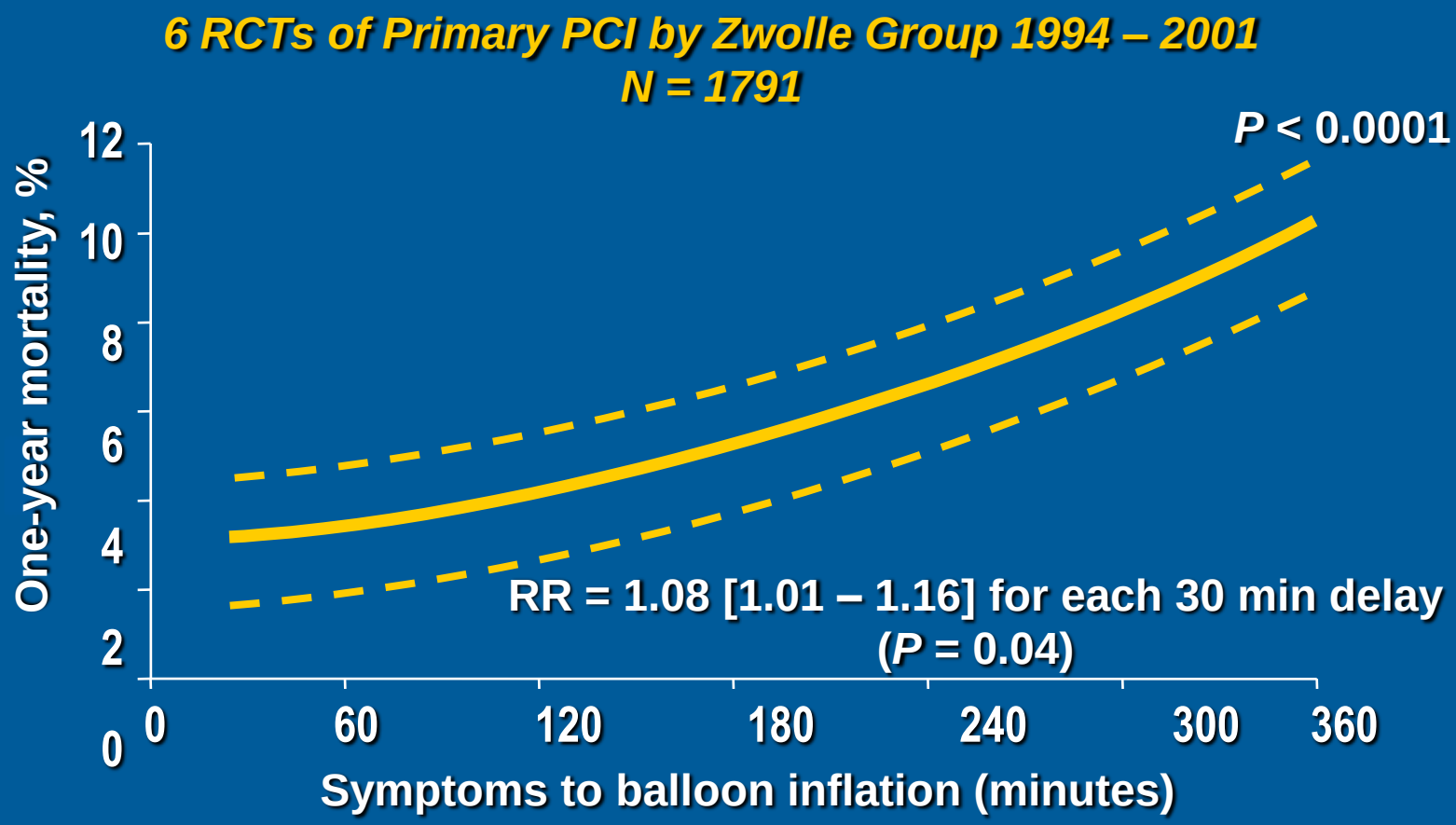
Symptom Onset to Balloon Time and Mortality in Primary PCI for STEMI



DeLuca et al. Circulation 2004;109:1223.

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Reperfusion Options for STEMI Patients

Step One: Assess Time and Risk.

Time Since Symptom Onset

Risk of STEMI

Risk of Fibrinolysis

Time Required for Transport to a Skilled PCI Lab

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Reperfusion Options for STEMI Patients
Step 2: Select Reperfusion Treatment.

If presentation is < 3 hours and there is no delay to an invasive strategy, there is no preference for either strategy.

Fibrinolysis generally preferred

- *Early presentation (≤ 3 hours from symptom onset and delay to invasive strategy)*
- *Invasive strategy not an option*
  - Cath lab occupied or not available
  - Vascular access difficulties
  - No access to skilled PCI lab
- *Delay to invasive strategy*
  - Prolonged transport
  - Door-to-balloon more than 90 minutes
  - > 1 hour vs fibrinolysis (fibrin-specific agent) now

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Reperfusion Options for STEMI Patients
Step 2: Select Reperfusion Treatment.

If presentation is < 3 hours and there is no delay to an invasive strategy, there is no preference for either strategy.

Invasive strategy generally preferred

- *Skilled PCI lab available with surgical backup*
  - Door-to-balloon < 90 minutes
- *High Risk from STEMI*
  - Cardiogenic shock, Killip class ≥ 3
- *Contraindications to fibrinolysis,* including increased risk of bleeding and ICH
- *Late presentation*
  - > 3 hours from symptom onset
- *Diagnosis of STEMI is in doubt*

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PCI vs Lysis: *Additional Data*

- **Mortality advantage of PCI *diminishes*:**
  - **As risk with lytic decreases: PCI = Lysis at 3%**
  - **With increasing delay:**
    - **PCI = Fibrin spec lytic with 60 min delay**
    - **RR = 1.08 for every 30 min from onset of sx**
  - **The earlier patient is seen: PCI = Lysis in < 3 h from sx**
- **Outcomes with PCI are influenced by *time of day* and operator/institution *volume and experience***
- **Trials of transfer for PCI:**
  - **Had very short transport and D-B times**
  - **PCI mortality higher than prehospital lysis in pts treated early (2h)**

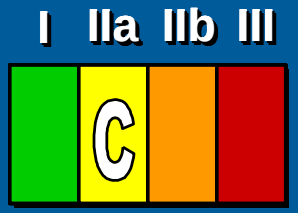
JACC 2004;44: 671
Circ 2004;110: 588

Fibrinolysis

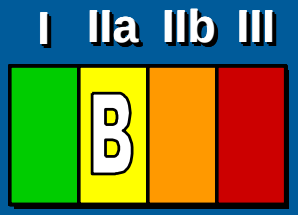
In the absence of contraindications, fibrinolytic therapy **should** be administered to STEMI patients with

symptom onset within the prior 12 hours.

symptom onset within the prior 12 hours and new or presumably new LBBB.



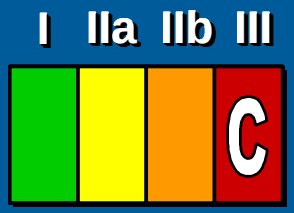
symptom onset within the prior 12 hours and ECG findings consistent with a true posterior MI.



symptom onset in the prior 12 to 24 hours who have continuing ischemic symptoms and ST elevation > 0.1 mV in ≥ 2 contiguous precordial leads or ≥ 2 adjacent limb leads.

Fibrinolysis

Fibrinolytic therapy should **NOT** be administered to



asymptomatic patients whose initial symptoms of STEMI began more than 24 hours earlier.

patients whose 12-lead ECG shows only ST-segment depression, except if a true posterior MI is suspected.

Lytic Agents

Table 15. Comparison of Approved Fibrinolytic Agents

	Streptokinase	Alteplase	Reteplase	Tenecteplase-tPA
Dose	1.5 MU over 30-60 min	Up to 100 mg in 90 min (based on weight)*	10 U × 2 each over 2 min	30-50 mg based on weight (379)†
Bolus administration	No	No	Yes	Yes
Antigenic	Yes	No	No	No
Allergic reactions (hypotension most common)	Yes	No	No	No
Systemic fibrinogen depletion	Marked	Mild	Moderate	Minimal
90-min patency rates, approximate %	50	75	7	75 (380)
TIMI grade 3 flow, %	32	54	60	63
Cost per dose (US $)(381)	$613	$2974	$2750	$2833 for 50 mg

MU = mega units.

*Bolus 15 mg, infusion 0.75 mg/kg times 30 minutes (maximum 50 mg), then 0.5 mg/kg not to exceed 35 mg over the next 60 minutes to an overall maximum of 100 mg.

†Thirty milligrams for weight less than 60 kg; 35 mg for 60-69 kg; 40 mg for 70-79 mg; 45 mg for 80-89 kg; 50 mg for 90 kg or more.

Fibrinolysis

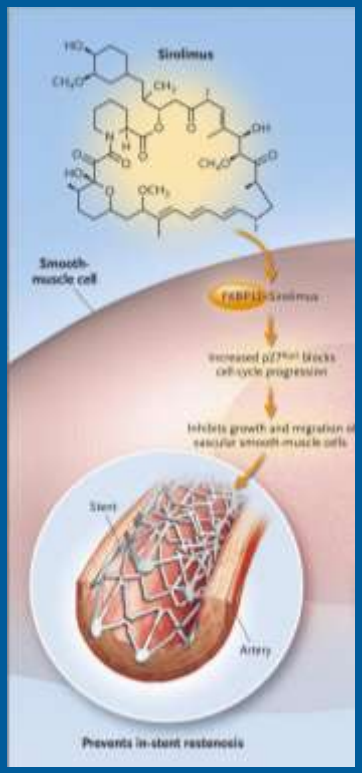
- UHS: “not so much”
- VA: Alteplase
  - >67kg: 15 mg IV bolus then 50 mg/30 min, then 35 mg/60 min
  - <67kg: 15 mg IV bolus then 0.75 mg/kg/30 min, then 0.50 mg/kg/60 min

Evolution of PCI for STEMI

Balloon

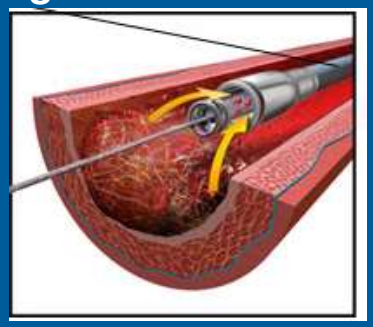
Antiplatelet Rx

Stent

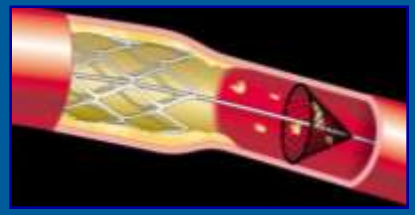


DES

AngioJet



Embolization Protection Device



Thrombus Removal and Distal Embolization Protection Devices

Antman. Circulation 2001;103:2310.

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Primary PCI for STEMI: *General Considerations*

- Patient with STEMI (including posterior MI) or MI with new or presumably new LBBB
- PCI of infarct artery within 12 hours of symptom onset
- Balloon inflation within 90 minutes of presentation
- Skilled personnel available (individual performs > 75 procedures per year)
- Appropriate lab environment (lab performs > 200 PCIs/year of which at least 36 are primary PCI for STEMI)
- Cardiac surgical backup available

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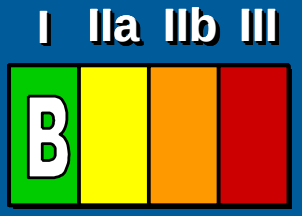
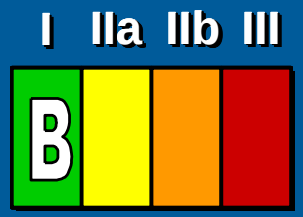
Primary PCI for STEMI: *Specific Considerations*

Medical contact–to-balloon or door-to-balloon should be within 90 minutes.



PCI preferred if > 3 hours from symptom onset.



Primary PCI should be performed in patients with severe congestive heart failure (CHF) and/or pulmonary edema (Killip class 3) and onset of symptoms within 12 hours.

Primary PCI for STEMI: *Specific Considerations*

Primary PCI should be performed in patients less than 75 years old with ST elevation or LBBB who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.

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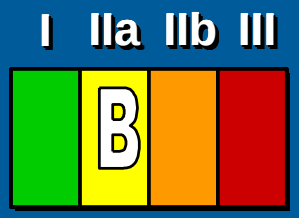
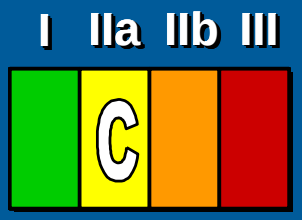
Primary PCI for STEMI: *Specific Considerations*



Primary PCI is reasonable in selected patients 75 years or older with ST elevation or LBBB who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.

Primary PCI for STEMI: *Specific Considerations*



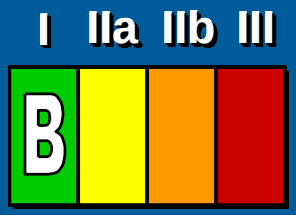
It is reasonable to perform primary PCI for patients with onset of symptoms within the prior 12 to 24 hours and 1 or more of the following:

a. Severe CHF

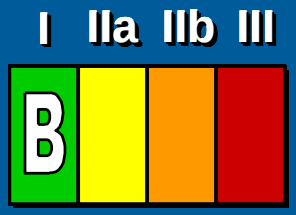
b. Hemodynamic or electrical instability

c. Persistent ischemic symptoms.

Rescue PCI



Rescue PCI should be performed in patients less than 75 years old with ST elevation or LBBB who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.



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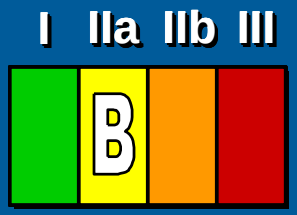
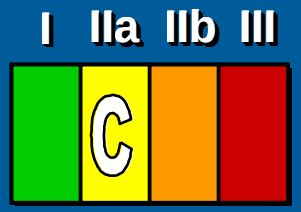
Rescue PCI

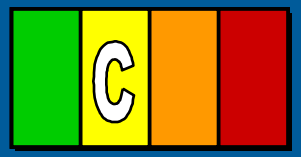


Rescue PCI is reasonable for selected patients 75 years or older with ST elevation or LBBB or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.

It is reasonable to perform rescue PCI for patients with one or more of the following:



a. Hemodynamic or electrical instability



b. Persistent ischemic symptoms.

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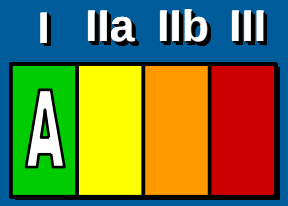
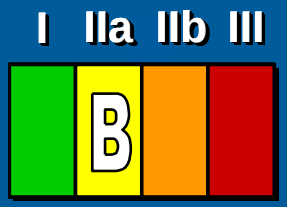
PCI for Cardiogenic Shock



Primary PCI is recommended for patients less than 75 years with ST elevation or LBBB or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.



Primary PCI is reasonable for selected patients 75 years or older with ST elevation or LBBB or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock.

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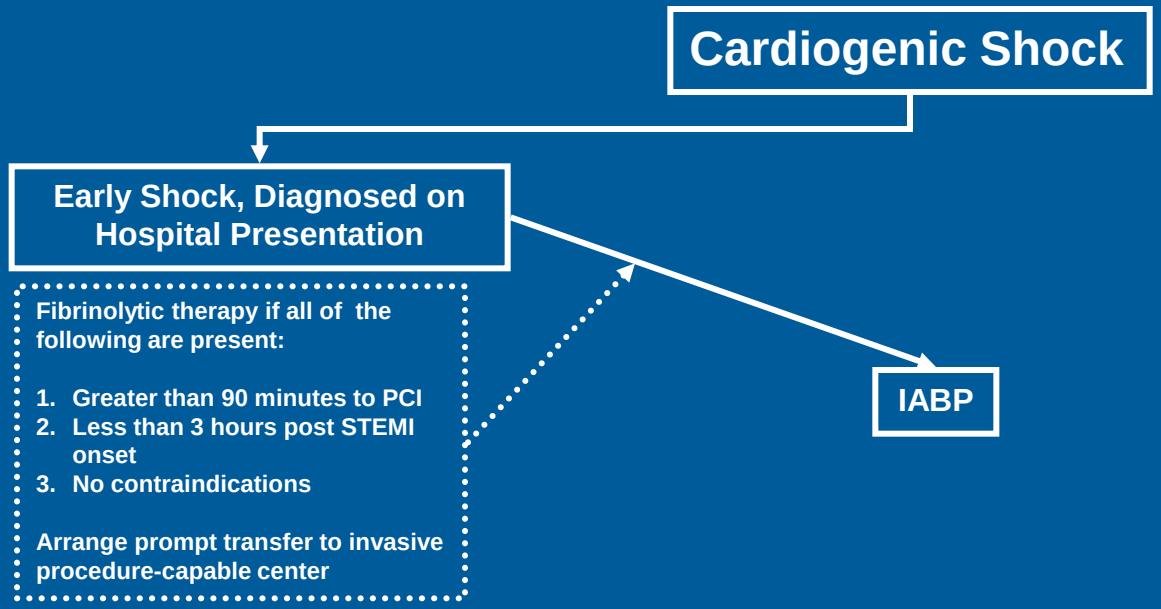
PCI for Cardiogenic Shock



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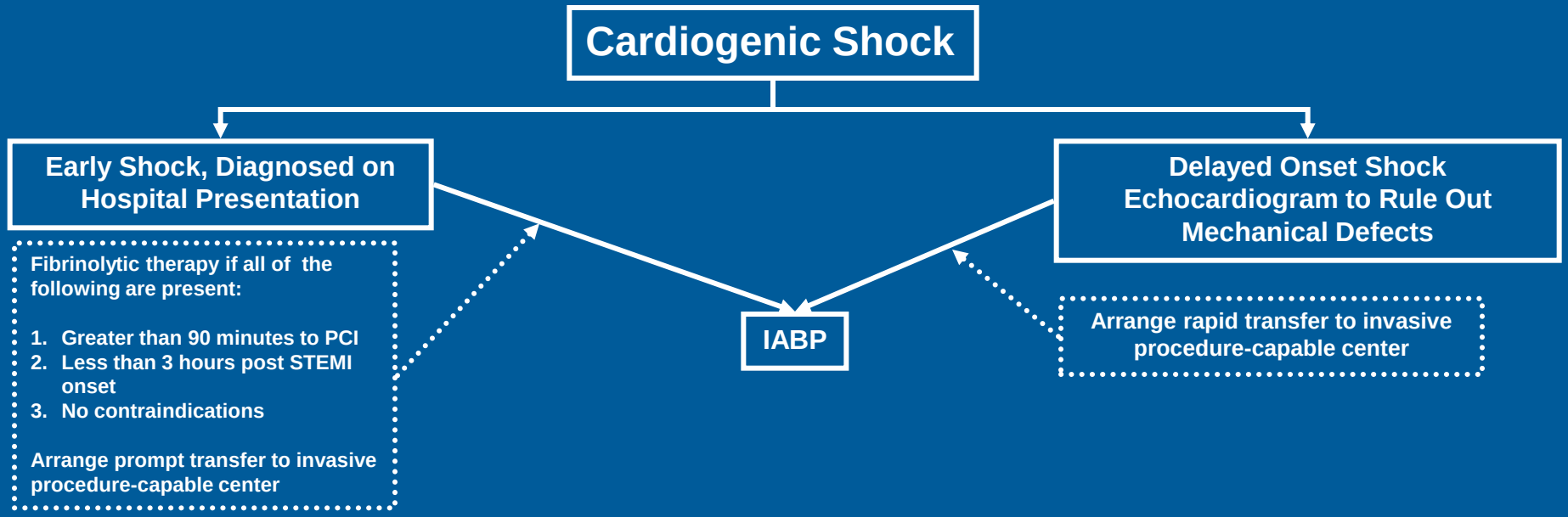
PCI for Cardiogenic Shock



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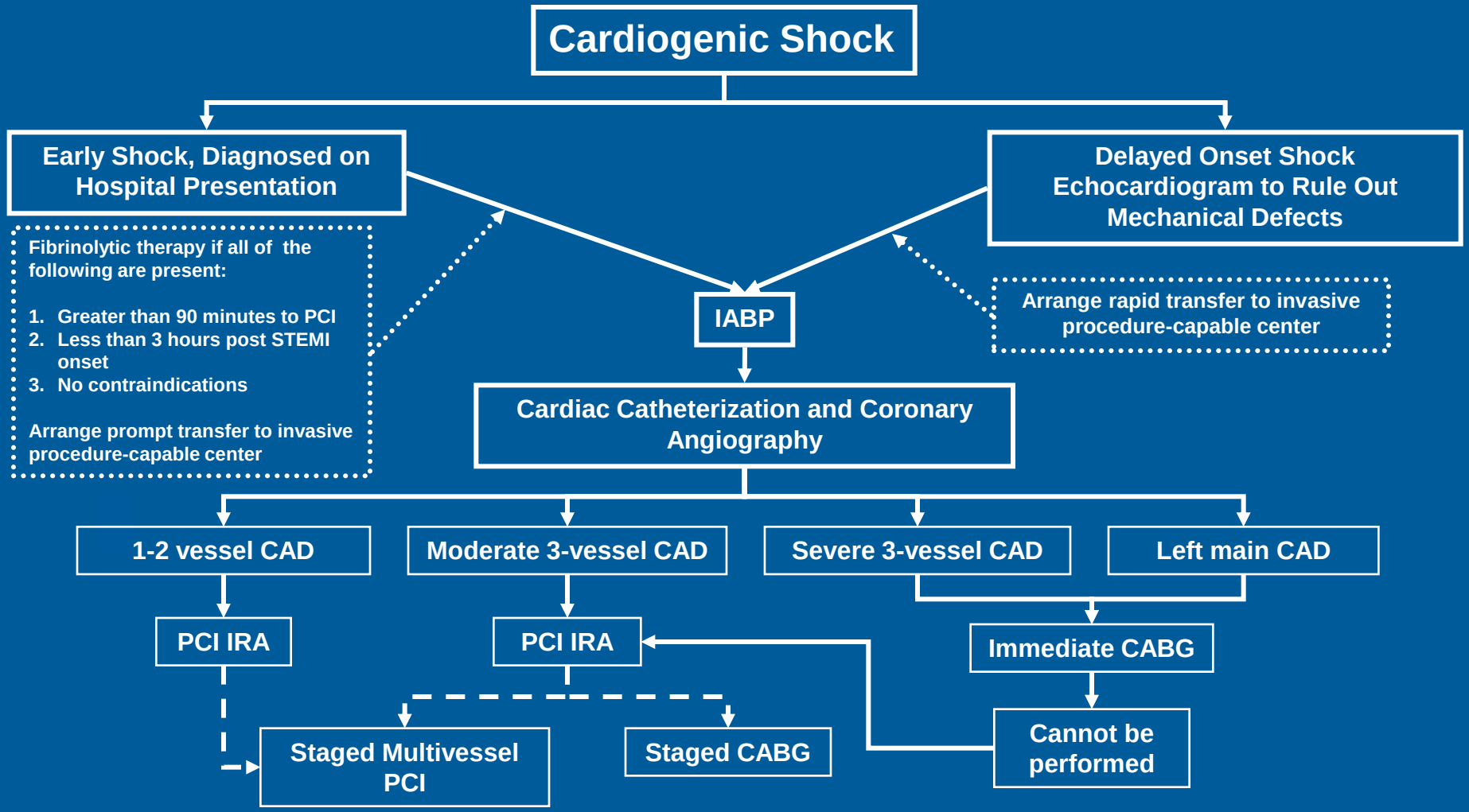
PCI for Cardiogenic Shock



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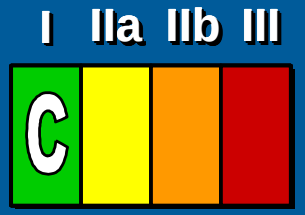
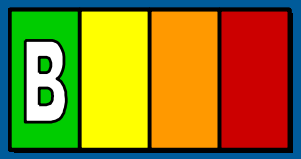
PCI After Fibrinolysis

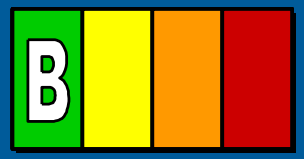
In patients whose anatomy is suitable, PCI should be performed for the following:



- Objective evidence of recurrent MI

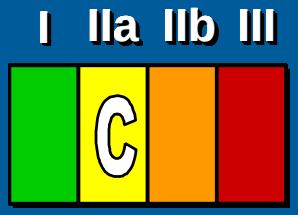


- Moderate or severe spontaneous/provocable myocardial ischemia during recovery from STEMI

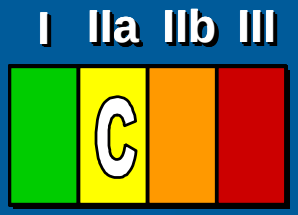


- Cardiogenic shock or hemodynamic instability.

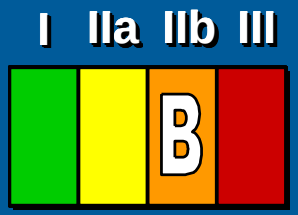
PCI After Fibrinolysis



It is reasonable to perform routine PCI in patients with left ventricular ejection fraction (LVEF) ≤ 0.40, CHF, or serious ventricular arrhythmias.

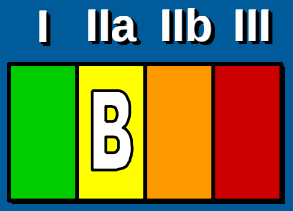


It is reasonable to perform PCI when there is documented clinical heart failure during the acute episode, even though subsequent evaluation shows preserved LV function (LVEF > 0.40).



Routine PCI might be considered as part of an invasive strategy after fibrinolytic therapy.

Assessment of Reperfusion



It is reasonable to monitor the pattern of ST elevation, cardiac rhythm and clinical symptoms over the 60 to 180 minutes after initiation of fibrinolytic therapy.

Noninvasive findings suggestive of reperfusion include:

- Relief of symptoms
- Maintenance and restoration of hemodynamic and/or electrical instability
- Reduction of ≥ 50% of the initial ST-segment elevation pattern on follow-up ECG 60 to 90 minutes after initiation of therapy.

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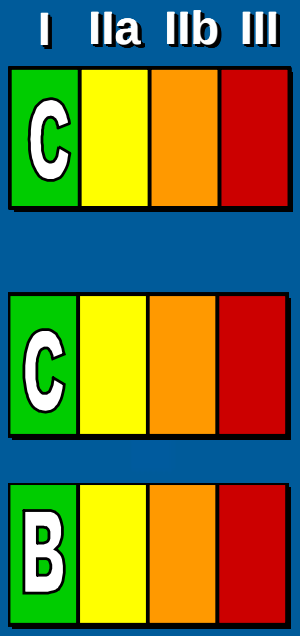
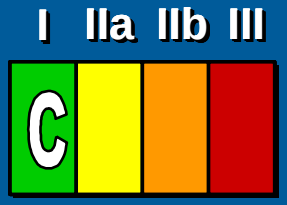
Ancillary Therapy to Reperfusion



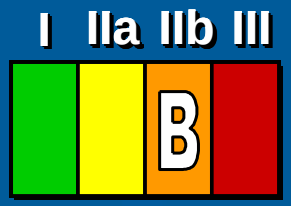
Unfractionated heparin (UFH) should be given intravenously in:

- Patients undergoing PCI or surgical revascularization
- After alteplase, reteplase, tenecteplase
- After streptokinase, anistreplase, urokinase in patients at high risk for systemic emboli.

Ancillary Therapy to Reperfusion



Platelet counts should be monitored daily in patients taking UFH.



Low molecular-weight heparin (LMWH) might be considered an acceptable alternative to UFH in patients less than 75 years who are receiving fibrinolytic therapy in the absence of significant renal dysfunction.

Enoxaparin used with tenecteplase is the most comprehensively studied.

Analgesia

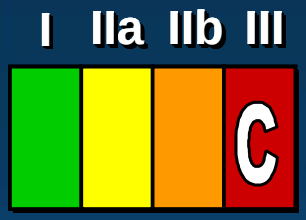
Analgesia

- Morphine remains Class I for STEMI although may increase adverse events in UA/NSTEMI
- NSAID medications increase mortality, reinfarction, and heart failure in proportion to degree of COX-2 selectivity
  - Discontinue on admission for STEMI
  - Do not initiate during acute phase of management

Analgesia

Patients routinely taking nonsteroidal anti-inflammatory drugs (NSAIDs) (except for aspirin), both non-selective as well as COX-2 selective agents, prior to STEMI should have those agents discontinued at the time of presentation with STEMI because of the increased risks of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use.

Analgesia



NSAIDs (except for aspirin), both nonselective as well as COX-2 selective agents, should not be administered during hospitalization for STEMI because of the increased risks of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use.

Beta-Blockers

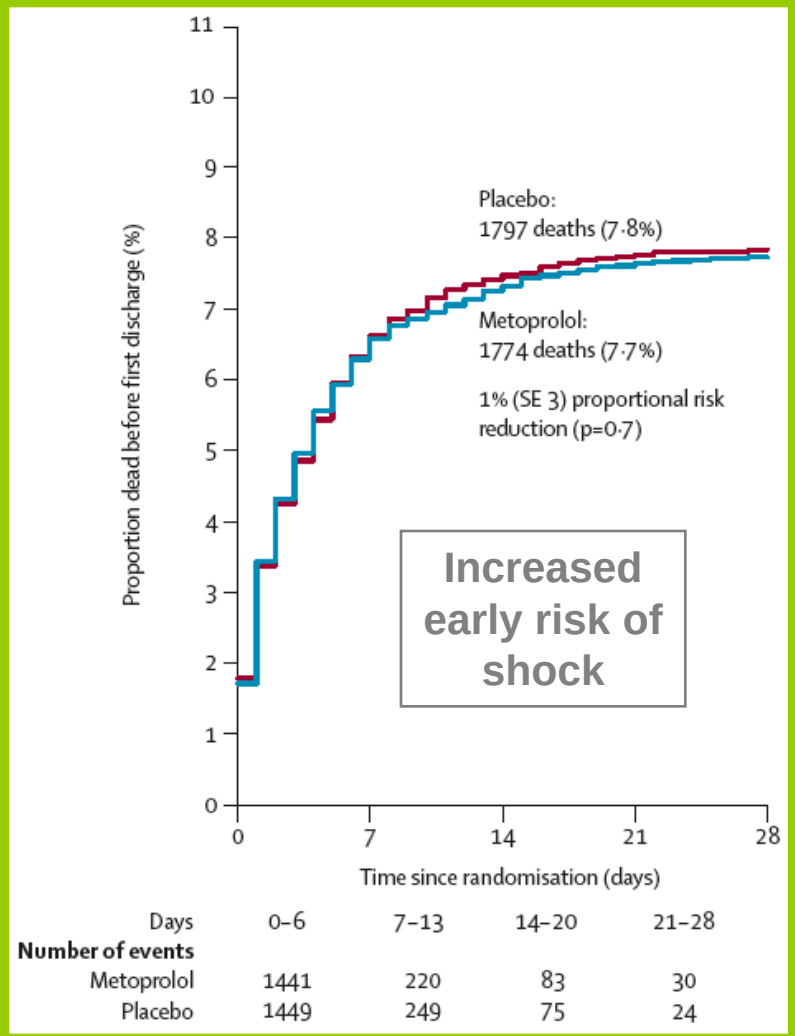
COMMIT: Study design

TREATMENT:	Metoprolol 15 mg iv over 15 mins, then 200 mg oral daily vs matching placebo
INCLUSION:	Suspected acute MI (ST change or LBBB) within 24 h of symptom onset
EXCLUSION:	Shock, systolic BP <100 mmHg, heart rate <50/min or II/III AV block
1° OUTCOMES:	Death & death, re-MI or VF/arrest up to 4 weeks in hospital (or prior discharge)

Mean treatment and follow-up: 16 days

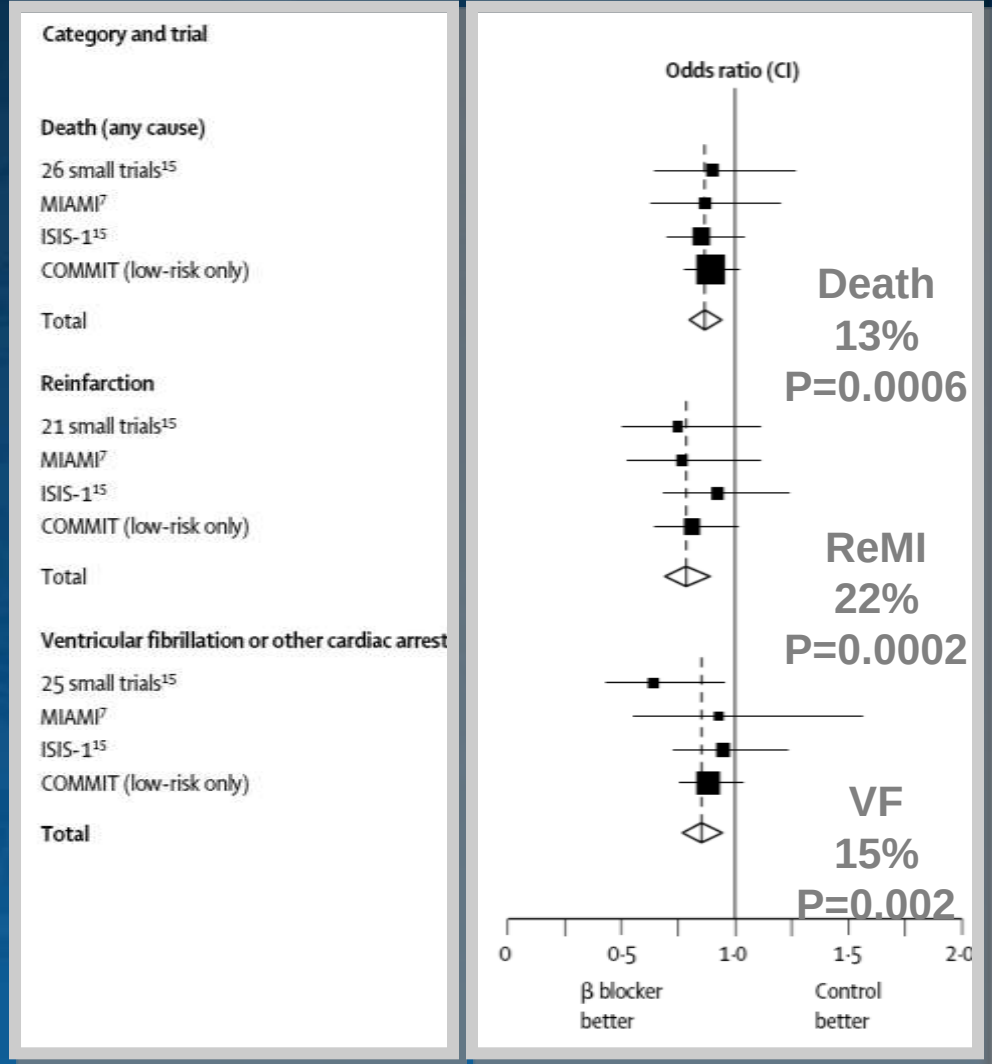
Effects of Metoprolol

COMMIT (N = 45,852)



Days	0–6	7–13	14–20	21–28
Number of events				
Metoprolol	1441	220	83	30
Placebo	1449	249	75	24

Totality of Evidence (N = 52,411)



Risk factors for cardiogenic shock :heart failure, age > 70 , systolic blood pressure < 120, sinus tachycardia > 110 or heart rate < 60, increased time since onset of STEMI symptoms

Lancet. 2005;366:1622.

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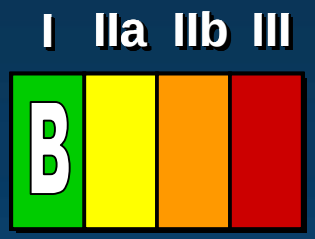
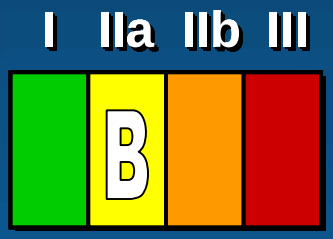
Beta-Blockers



Oral beta-blocker therapy should be initiated in the first 24 hours for patients who do not have any of the following: 1) signs of heart failure, 2) evidence of a low output state, 3) increased risk* for cardiogenic shock, or 4) other relative contraindications to beta blockade (PR interval > 0.24 sec, 2nd- or 3rd-degree heart block, active asthma, or reactive airway disease).



It is reasonable to administer an IV beta blocker at the time of presentation to STEMI patients who are hypertensive and who do not have any of the following: 1) signs of heart failure, 2) evidence of a low output state, 3) increased risk* for cardiogenic shock, or 4) other relative contraindications to beta blockade (PR interval > 0.24 sec, 2nd- or 3rd-degree heart block, active asthma, or reactive airway disease).

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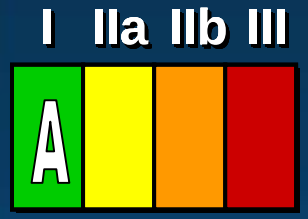
Beta-Blockers

IV beta blockers should not be administered to STEMI patients who have any of the following: 1) signs of heart failure, 2) evidence of a low output state, 3) increased risk* for cardiogenic shock, or 4) other relative contraindications to beta blockade (PR interval > 0.24 sec, 2nd- or 3rd-degree heart block, active asthma, or reactive airway disease).

Primary PCI

Primary PCI



STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 min of first medical contact as a systems goal.

STEMI patients presenting to a hospital without PCI capability, and who cannot be transferred to a PCI center and undergo PCI within 90 min of first medical contact, should be treated with fibrinolytic therapy within 30 min of hospital presentation as a systems goal, unless fibrinolytic therapy is contraindicated.

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Options for Transport of Patients With STEMI and Initial Reperfusion Treatment

Call 9-1-1
Call fast

Onset of symptoms of STEMI → **9-1-1 EMS Dispatch** → **EMS on-scene**

- Encourage 12-lead ECGs.
- Consider prehospital fibrinolytic if capable and EMS-to-needle within 30 min.

EMS Triage Plan

Hospital fibrinolysis: Door-to-Needle within 30 min.

Not PCI capable

Inter-Hospital Transfer

PCI capable

GOALS

5 min.		8 min.	EMS Transport
Patient		**EMS**	

Dispatch
1 min.

Prehospital fibrinolysis
EMS-to-needle within 30 min.

EMS transport
EMS-to-balloon within 90 min.

Patient self-transport
Hospital door-to-balloon within 90 min.

Golden Hour = first 60 min. | **Total ischemic time: within 120 min.**

Antman EM, et al. *J Am Coll Cardiol 2008.* Published ahead of print on December 10, 2007. Available at http://content.onlinejacc.org/cgi/content/full/j.jacc.2007.10.001. Figure 1.

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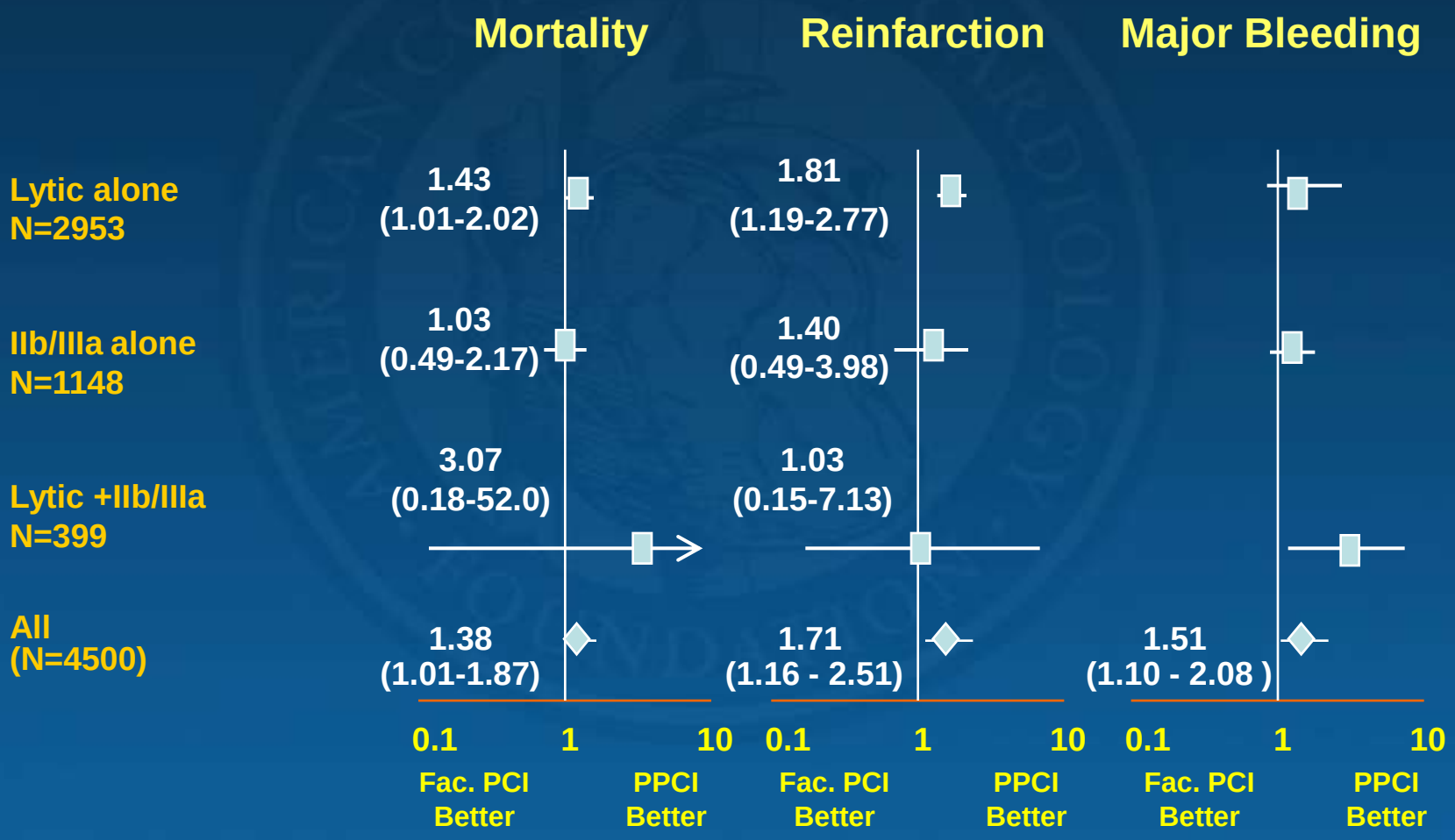
Facilitated PCI

Meta-analysis: Facilitated PCI vs Primary PCI



Keeley E, et al. *Lancet* 2006;367:579.

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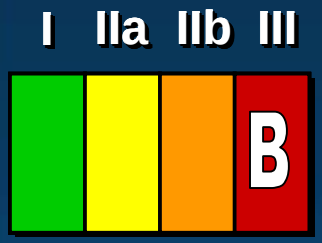
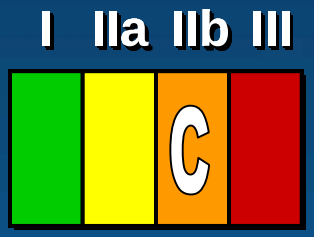
Facilitated PCI



A planned reperfusion strategy using full-dose fibrinolytic therapy followed by immediate PCI is not recommended and may be harmful.



Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present:

a. Patients are at high risk,

b. PCI is not immediately available within 90 minutes, and

c. Bleeding risk is low (younger age, absence of poorly controlled hypertension, normal body weight).

Facilitated PCI

Further Studies Ongoing

- Prehospital fibrinolytic therapy
- Better anticoagulant and antiplatelet therapy
- Use in circumstances of longer delays to PCI

However, based on available data, facilitated PCI offered no clinical benefit, and was associated with harm when full dose fibrinolytics were used.

Rescue and Late PCI

Meta-analysis: Rescue PCI vs Conservative Tx

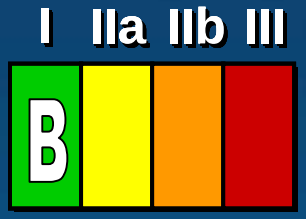
Outcome	Rescue PCI	Conservative Treatment	RR (95% CI)	*P*
Mortality, % (n)	7.3 (454)	10.4 (457)	0.69 (0.46–1.05)	.09
HF, % (n)	12.7 (424)	17.8 (427)	0.73 (0.54–1.00)	.05
Reinfarction, % (n)	6.1 (346)	10.7 (354)	0.58 (0.35–0.97)	.04
Stroke, % (n)	3.4 (297)	0.7 (295)	4.98 (1.10–22.48)	.04
Minor bleeding, % (n)	16.6 (313)	3.6 (307)	4.58 (2.46–8.55)	<.001

In 3 trials, enrolling 700 patients that reported the composite end point of all-cause mortality, reinfarction, and HF, rescue PCI was associated with a significant RR reduction of 28% (RR 0.72; 95% CI, 0.59-0.88; *P*=.001)

Wijeysundera HC, et al. *J Am Coll Cardiol.* 2007;49:422-430.

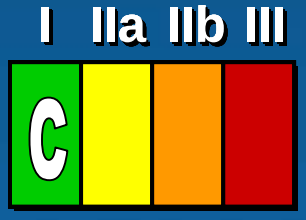
Rescue PCI

A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is recommended in patients who have received fibrinolytic therapy and have:



a. Cardiogenic shock in patients < 75 years who are suitable candidates for revascularization

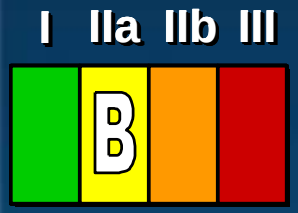
b. Severe congestive heart failure and/or pulmonary edema (Killip class III)



c. Hemodynamically compromising ventricular arrhythmias.

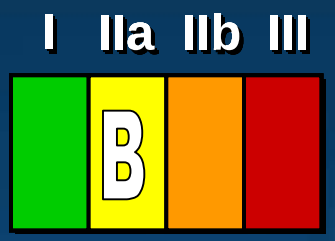
ACC/AHA 2007 STEMI Guidelines Focused Update

Rescue PCI



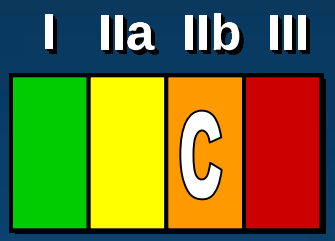
A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is reasonable in patients ≥ 75 years who have received fibrinolytic therapy, and are in cardiogenic shock, provided they are suitable candidates for revascularization.

Rescue PCI



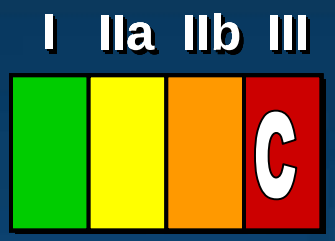
A strategy of coronary angiography with intent to perform rescue PCI is reasonable for patients in whom fibrinolytic therapy has failed (ST-segment elevation < 50% resolved after 90 min following initiation of fibrinolytic therapy in the lead showing the worst initial elevation) and a moderate or large area of myocardium at risk [anterior MI, inferior MI with right ventricular involvement or precordial ST-segment depression].

Rescue PCI



A strategy of coronary angiography with intent to perform PCI in the absence of any of the above Class I or IIa indications might be reasonable in moderate- or high-risk patients, but its benefits and risks are not well established. The benefits of rescue PCI are greater the earlier it is initiated after the onset of ischemic discomfort.

Rescue PCI



A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is not recommended in patients who have received fibrinolytic therapy if further invasive management is contraindicated or the patient or designee do not wish further invasive care.

Occluded Artery Trial (OAT)

Eligibility:

- Confirmed Index MI
- Total IRA occlusion
- 3-28 days (>24 hours)

Exclusion criteria:

- Significant left main or 3 vessel CAD
- Hemodynamic or electrical instability
- Rest or low-threshold angina
- NYHA Class III-IV HF or shock

RESULTS

2166 randomized

1082 PCI + optimal medical therapy
1084 Optimal medical therapy (MED)

Death, MI, CHF Class IV

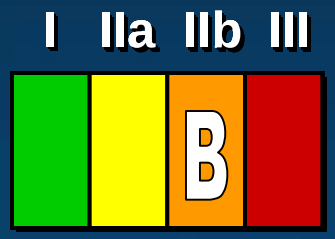
4 year event rate:
17.2% PCI vs 15.6% MED
Hazard Ratio: PCI vs MED=1.16;
95% CI (0.92, 1.45); p=0.20

Fatal and Non fatal MI

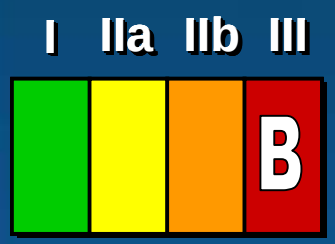
4 year event rate:
7.0% PCI vs 5.3% MED
Hazard Ratio: PCI vs MED=1.36;
95% CI (0.92, 2.00); p=0.13

Hochman JS, et al. *Am Heart J* 2005;150:627-42;
Hochman JS, et al. *N Engl J Med* 2006;355:2395-407.

Late PCI after Fibrinolysis or for Patients Not Undergoing Primary Reperfusion



PCI of a hemodynamically significant stenosis in a patent infarct artery > 24 hours after STEMI may be considered as part of a invasive strategy.



PCI of a totally occluded infarct artery > 24 hours after STEMI is not recommended in asymptomatic patients with 1- or 2-vessel disease if they are hemodynamically and electrically stable and do not have evidence of severe ischemia.

Anticoagulants

Anticoagulant post Lytic

1. Patients undergoing reperfusion with fibrinolytics should receive anticoagulant therapy for a minimum of 48 hours (*Level of Evidence: C*) and preferably for the duration of the index hospitalization, up to 8 days (regimens other than UFH are recommended if anticoagulant therapy is given for more than 48 hours because of the risk of heparin-induced thrombocytopenia with prolonged UFH treatment). (*Level of Evidence: A*)

Anticoagulant regimens with established efficacy include:

a. UFH (initial intravenous bolus 60 U per kg [maximum 4000 U]) followed by an intravenous infusion of 12 U per kg per hour (maximum 1000 U per hour) initially, adjusted to maintain the activated partial thromboplastin time at 1.5 to 2.0 times control (approximately 50 to 70 seconds) (*Level of Evidence: C*). (Note: the available data do not suggest a benefit of prolonging the duration of the infusion of UFH beyond 48 hours in the absence of ongoing indications for anticoagulation; more prolonged infusions of UFH increase the risk of development of heparin-induced thrombocytopenia.)

b. Enoxaparin (provided the serum creatinine is less than 2.5 mg per dL in men and 2.0 mg per dL in women): for patients less than 75 years of age, an initial 30 mg intravenous bolus is given, followed 15 minutes later by subcutaneous injections of 1.0 mg per kg every 12 hours; for patients at least 75 years of age, the initial intravenous bolus is eliminated and the subcutaneous dose is reduced to 0.75 mg per kg every 12 hours. Regardless of age, if the creatinine clearance (using the Cockroft-Gault formula) during the course of treatment is estimated to be less than 30 mL per minute, the subcutaneous regimen is 1.0 mg per kg every 24 hours. Maintenance dosing with enoxaparin should be continued for the duration of the index hospitalization, up to 8 days. (*Level of Evidence: A*)

c. Fondaparinux (provided the serum creatinine is less than 3.0 mg per dL): initial dose 2.5 mg intravenously; subsequently subcutaneous injections of 2.5 mg once daily. Maintenance dosing with fondaparinux should be continued for the duration of the index hospitalization, up to 8 days. (*Level of Evidence: B*)

Anticoagulant post PCI

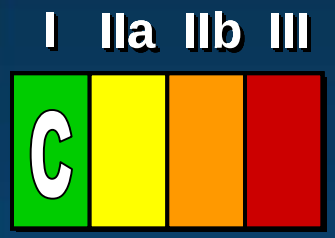
2. For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed:

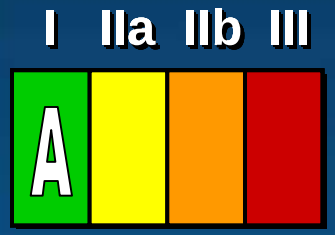
a. For prior treatment with UFH, administer additional boluses of UFH as needed to support the procedure, taking into account whether GP IIb/IIIa receptor antagonists have been administered. *(Level of Evidence: C)* Bivalirudin may also be used in patients treated previously with UFH. *(Level of Evidence: C)*

b. For prior treatment with enoxaparin, if the last subcutaneous dose was administered within the prior 8 hours, no additional enoxaparin should be given; if the last subcutaneous dose was administered at least 8 to 12 hours earlier, an intravenous dose of 0.3 mg per kg of enoxaparin should be given. (*Level of Evidence: B*)

c. For prior treatment with fondaparinux, administer additional intravenous treatment with an anticoagulant possessing anti-IIa activity taking into account whether GP IIb/IIIa receptor antagonists have been administered. (*Level of Evidence: C*)

Anticoagulants





Patients undergoing reperfusion with fibrinolytics should receive anticoagulant therapy for a minimum of 48 hours *(Level of Evidence: C)* and preferably for the duration of the index hospitalization, up to 8 days (regimens other than unfractionated heparin [UFH] are recommended if anticoagulant therapy is given for more than 48 hours because of the risk of heparin-induced thrombocytopenia with prolonged UFH treatment). *(Level of Evidence: A)*

Anticoagulant regimens with established efficacy include:

- UFH *(LOE: C)*
- Enoxaparin *(LOE:A)*
- Fondaparinux *(LOE:B)*

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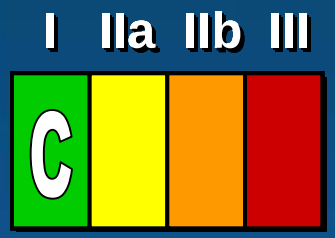
Anticoagulants

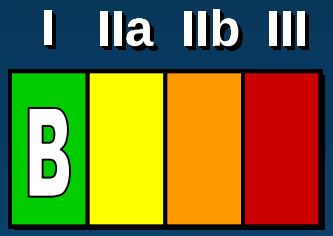


For patients undergoing PCI after having received an anticoagulant regimen, the following dosing recommendations should be followed:

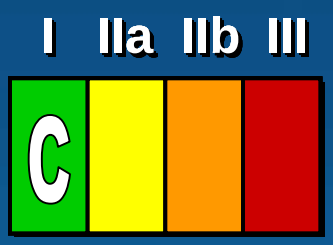
a. For prior treatment with UFH: administer additional boluses of UFH as needed to support the procedure taking into account whether GP IIb/IIIa receptor antagonists have been administered. *(Level of Evidence: C)* Bivalirudin may also be used in patients treated previously with UFH. *(Level of Evidence: C)*

Recommendation continues on the next slide.

Anticoagulants

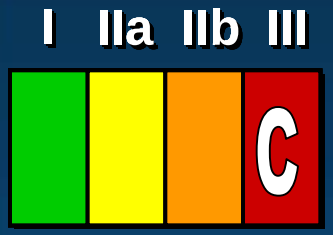


b. For prior treatment with enoxaparin: if the last SC dose was administered within the prior 8 hours, no additional enoxaparin should be given; if the last SC dose was administered at least 8 to 12 hours earlier, an IV dose of 0.3 mg/kg of enoxaparin should be given.



c. For prior treatment with fondaparinux: administer additional intravenous treatment with an anticoagulant possessing anti-IIa activity taking into account whether GP IIb/IIIa receptor antagonists have been administered.

Anticoagulants



Because of the risk of catheter thrombosis, fondaparinux should not be used as the sole anticoagulant to support PCI. An additional anticoagulant with anti-IIa activity should be administered.

Unfractionated Heparin

Advantages

- Immediate anticoagulation
- Multiple sites of action in coagulation cascade
- Long history of successful clinical use
- Readily monitored by aPTT and ACT

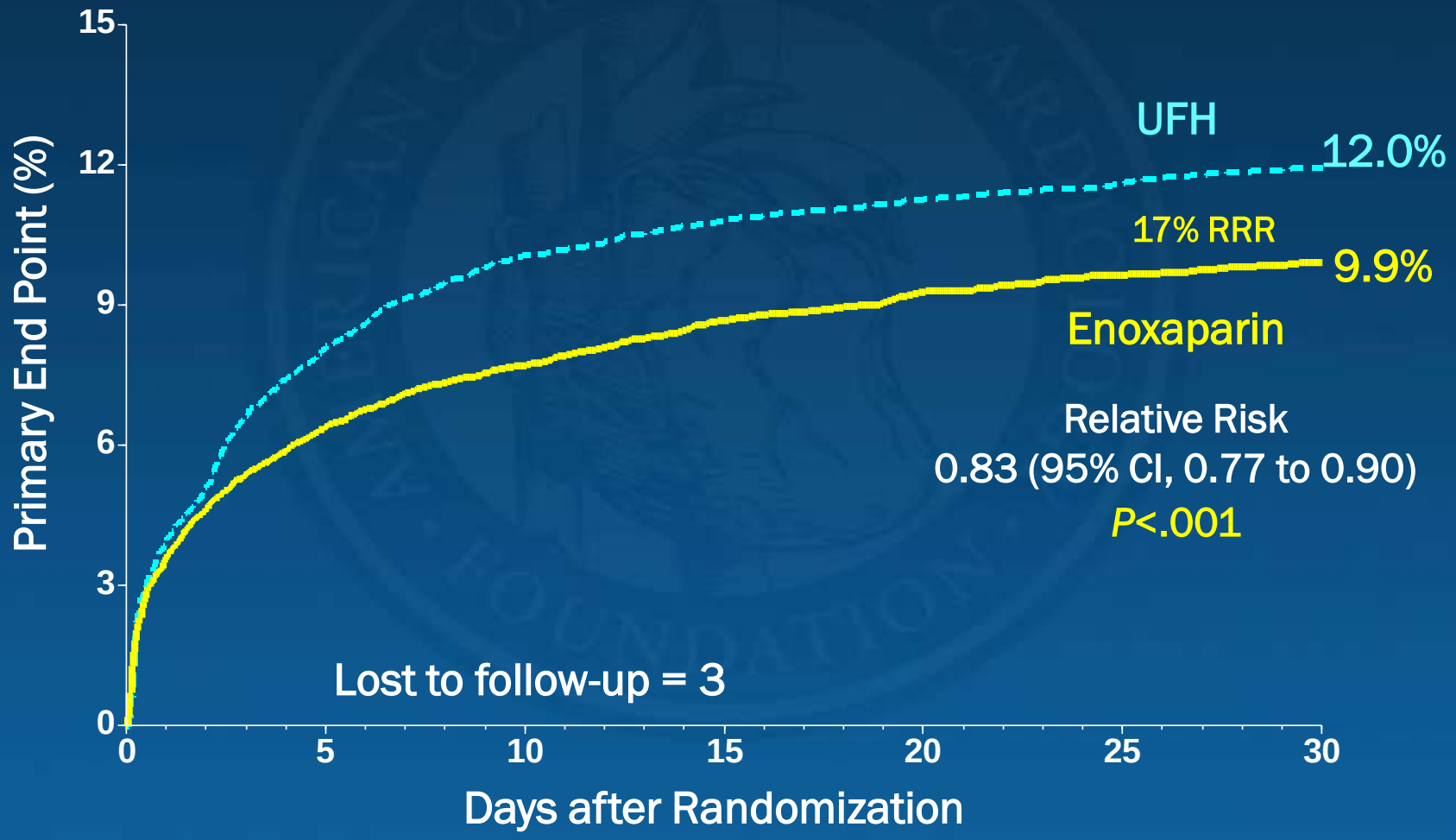
Disadvantages

- Indirect thrombin inhibitor so does not inhibit clot-bound thrombin
- Nonspecific binding to:
  - Serine proteases
  - Endothelial cells

  (can lead to variability in level of anticoagulation)
- Reduced effect in ACS
  - Inhibited by PF-4
- Causes platelet aggregation
- Nonlinear pharmacokinetics
- Risk of HIT

Hirsh J, et al. *Circulation*. 2001;103:2994-3018. aPTT = activated partial thromboplastin time; ACT = activated coagulation time; PF-4 = platelet factor 4; HIT = heparin-induced thrombocytopenia.

ExTRACT-TIMI 25: Primary End Point (ITT) Death or Nonfatal MI



Adapted with permission from Antman EM, et al. *N Engl J Med*. 2006;354:1477-1488.

Low-Molecular-Weight Heparin

Advantages

- Increased anti-Xa to anti-IIa activity → inhibits thrombin generation more effectively
- Induces ↑ release of TFPI vs UFH
- Not neutralized by platelet factor 4
- Less binding to plasma proteins (eg, acute-phase reactant proteins) → more consistent anticoagulation
- Lower rate of HIT vs UFH
- Lower fibrinogen levels
- Easy to administer (SC administration)
- Long history of clinical studies and experience, FDA-approved indications
- Monitoring typically unnecessary

Disadvantages

- Indirect thrombin inhibitor
- Less reversible
- Difficult to monitor (no aPTT or ACT)
- Renally cleared
- Long half-life
- Risk of HIT

Hirsh J, et al. *Circulation*. 2001;103:2994-3018. TFPI = tissue factor pathway inhibitor; UFH = unfractionated heparin; SC = subcutaneous; aPTT = activated partial thromboplastin time; ACT = activated coagulation time.

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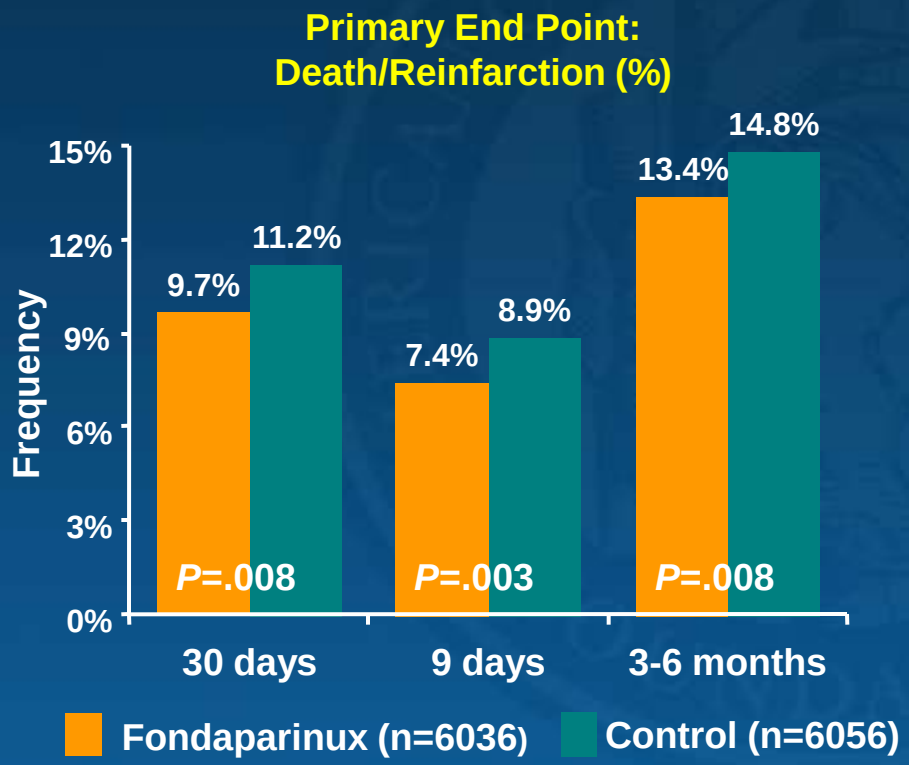
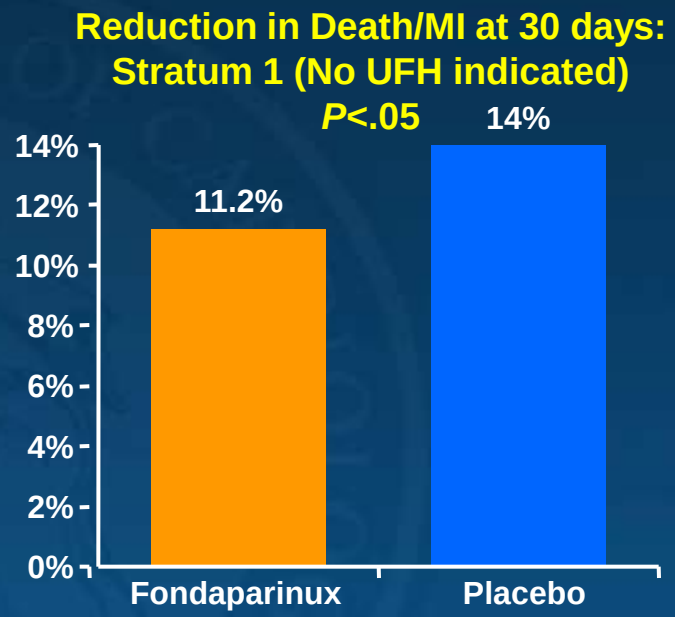
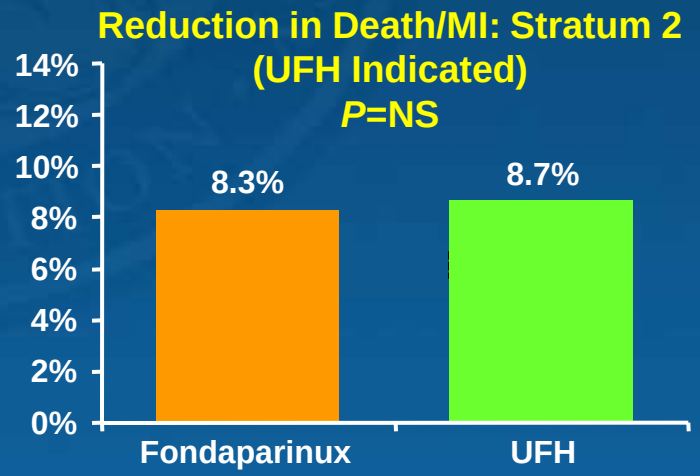
OASIS-6 Trial: Results







Yusuf S, et al. *JAMA*. 2006;295:1519-1530. Adapted with permission from www.clinicaltrialresults.org

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Fondaparinux

Advantages

- SC administration
  - Potential exists for outpatient management
- Once-daily administration
- Predictable anticoagulant response
- Fixed dose
- No antigenicity
- Potentially no need for serologic parameters
- Does not cross the placenta
- HIT antibodies do not cross-react
- Decreased bleeding complications vs UFH or LMWH

Disadvantages

- Difficult to monitor (no aPTT or ACT)
- Long half-life
- Catheter thrombosis during PCI

Simoons ML, et al. *J Am Coll Cardiol*. 2004;43:2183-2190.
Yusuf S, et al. *N Engl J Med.* 2066;354:1464-1476.

Summary of Observations from Trials of Anticoagulants for STEMI

Anticoagulant	Efficacy (through 30 d)	Safety	Use During PCI
Reviparin	Fibrinolysis: probably superior to placebo.* No reperfusion: probably superior to placebo.*	↑ risk of serious bleeds†	No data on reviparin alone during PCI. Additional anticoagulant with anti-IIa activity, such as UFH or bivalirudin, recommended.
Fondaparinux	Fibrinolysis: appears superior to control rx (placebo/UFH). Relative benefit vs placebo and UFH separately cannot be reliably determined from available data.* Primary PCI: when used alone, no advantage over UFH and trend toward worse outcome. No reperfusion: appears superior to control therapy (placebo/UFH). Relative benefit versus placebo and UFH separately cannot be reliably determined from available data.*	Trend toward ↓ risk of serious bleeds†	↑ risk of catheter thrombosis when fondaparinux used alone. Additional anticoagulant with anti-IIa activity, such as UFH or bivalirudin, recommended.
Enoxaparin	Fibrinolysis: appears superior to UFH	↑ risk of serious bleeds†	Enoxaparin can be used to support PCI after fibrinolysis. No additional anticoagulant needed.

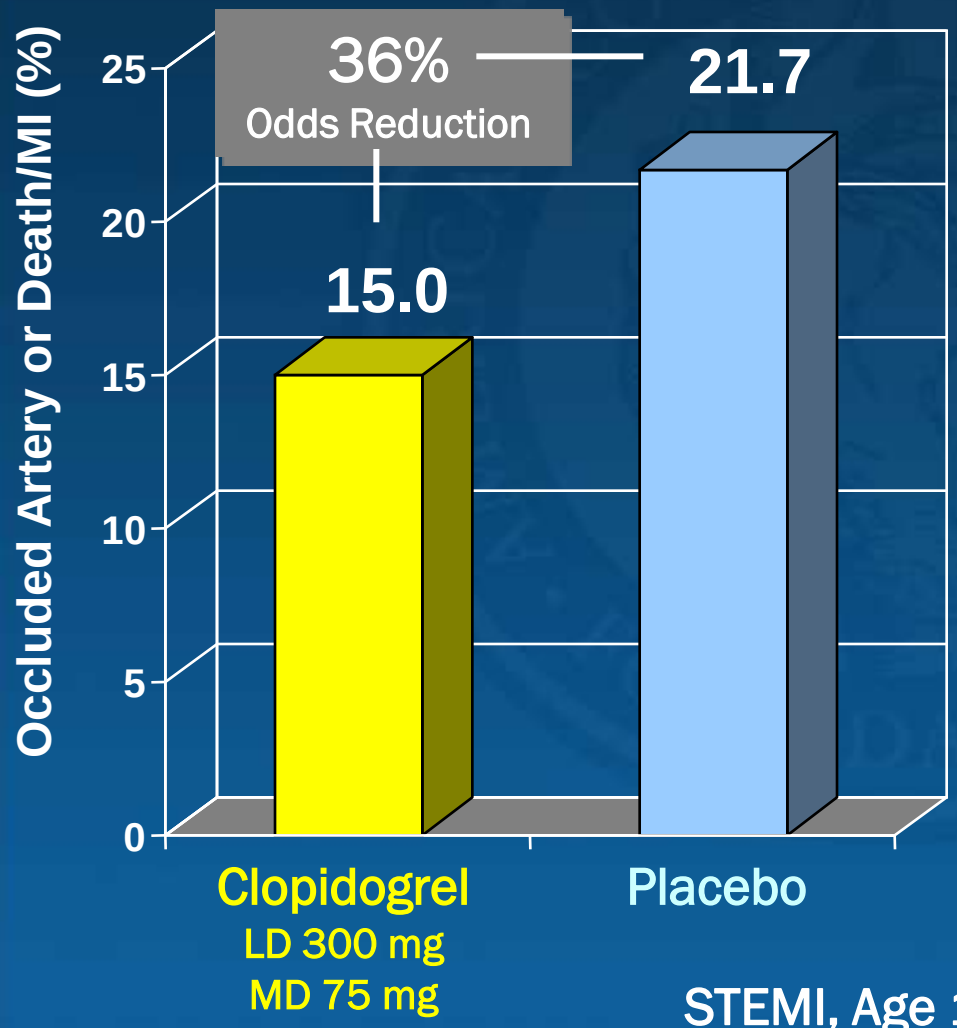
Antman EM, et al. *J Am Coll Cardiol 2008.* Published ahead of print on December 10, 2007. Available at http://content.onlinejacc.org/cgi/content/full/j.jacc.2007.10.001. Table 10.

Aspirin

A daily dose of aspirin (initial dose of 162 to 325 mg orally; maintenance dose of 75 to 162 mg) should be given indefinitely after STEMI to all patients without a true aspirin allergy.

Thienopyridines

CLARITY-TIMI 28 Primary Endpoint:
Occluded Artery (or D/MI thru Angio/HD)

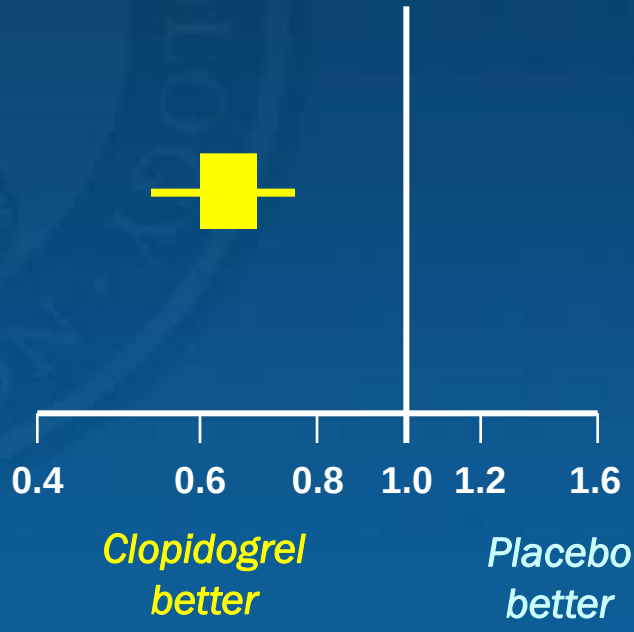


STEMI, Age 18-75

Odds Ratio 0.64

(95% CI 0.53-0.76)

P=0.00000036



Sabatine N Eng J Med 2005;352:1179.

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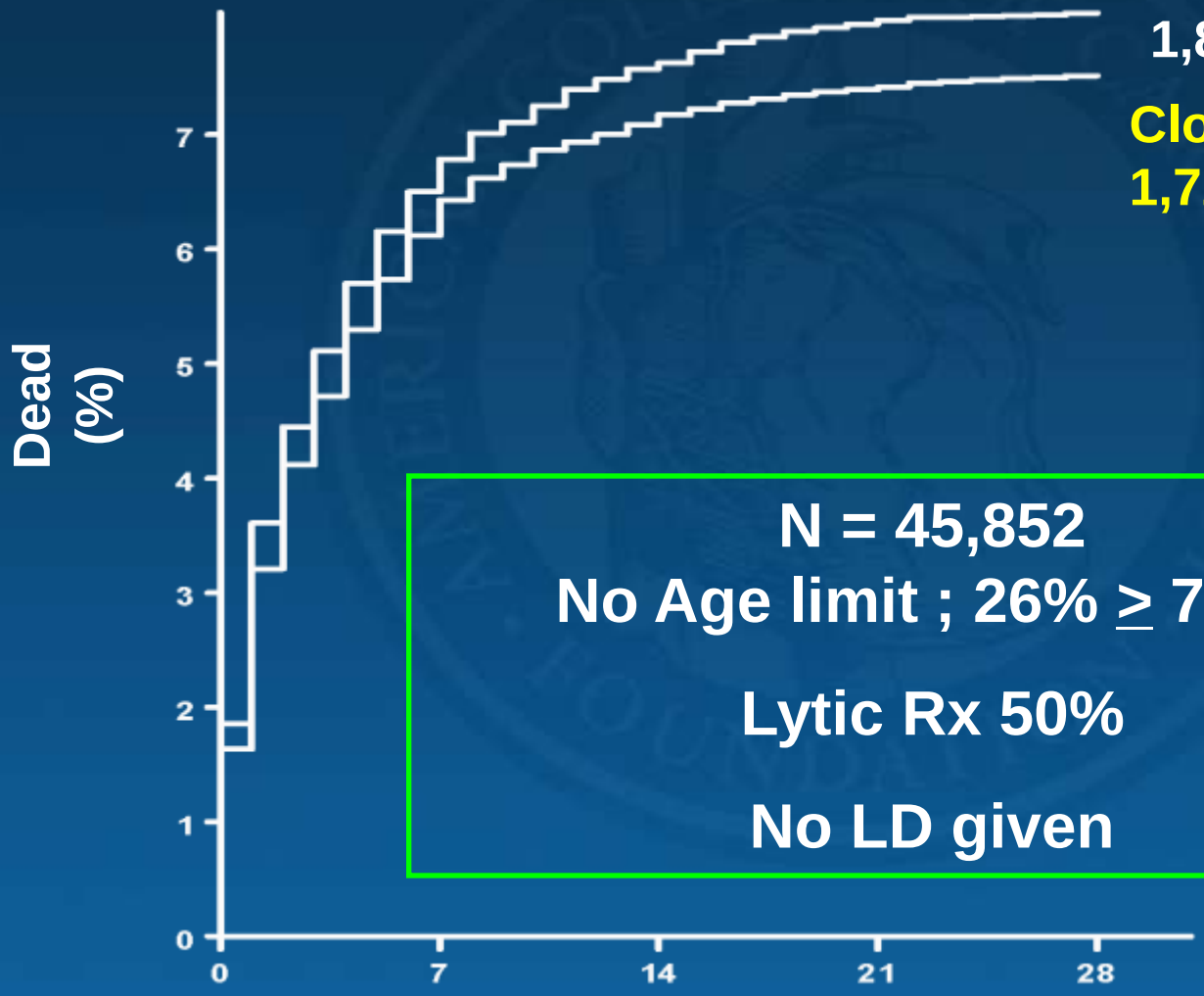
COMMIT: Effect of CLOPIDOGREL on Death In Hospital



Placebo + ASA:
1,846 deaths (8.1%)

Clopidogrel + ASA:
1,728 deaths (7.5%)

0.6% ARD
7% RRR
***P* = 0.03**

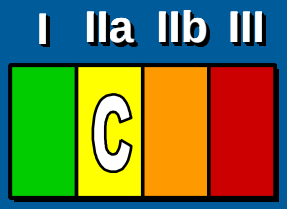
N = 45,852
No Age limit ; 26% ≥ 70 y

Lytic Rx 50%

No LD given

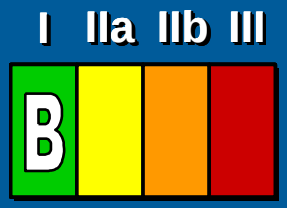
Chen ZM, et al. *Lancet*. 2005;366:1607.

Thienopyridines



Clopidogrel is probably indicated in patients receiving fibrinolytic therapy who are unable to take aspirin because of hypersensitivity or gastrointestinal intolerance.

Thienopyridines



In patients for whom PCI is planned, clopidogrel should be started and continued:

2007 PCI update:

At least 12 months if not high risk for bleeding

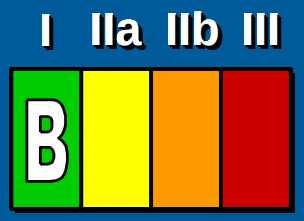
- ≥ 1 month after bare-metal stent
- ≥ 3 months after sirolimus-eluting stent
- ≥ 6 months after paclitaxel-eluting stent
- Up to 12 months in absence of high risk for bleeding.

2007 PCI update: IIb for DES “beyond one year”

AMERICAN COLLEGE of CARDIOLOGY FOUNDATION

American Heart Association. Learn and Live.

Thienopyridines



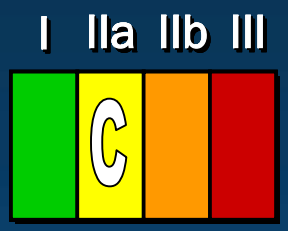
In patients taking clopidogrel in whom CABG is planned, the drug should be withheld for at least 5 days, and preferably for 7 days, unless the urgency for revascularization outweighs the risk of excessive bleeding.

Thienopyridines

Clopidogrel 75 mg per day orally should be added to aspirin in patients with STEMI regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy.

Treatment with clopidogrel should continue for at least 14 days.

Thienopyridines



In patients < 75 years who receive fibrinolytic therapy or who do not receive reperfusion therapy, it is reasonable to administer an oral clopidogrel loading dose of 300 mg. (No data are available to guide decision making regarding an oral loading dose in patients ≥ 75 years of age.)

Long-term maintenance therapy (e.g., 1 year) with clopidogrel (75 mg per day orally) can be useful in STEMI patients regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy.

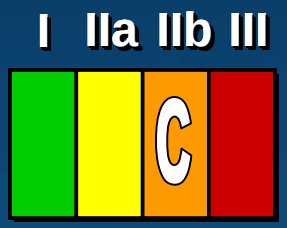
Hospital Care

Anticoagulants

It is reasonable for patients with STEMI who do not undergo reperfusion therapy to be treated with anticoagulant therapy (non-UFH regimen) for the duration of the index hospitalization, up to 8 days.

Convenient strategies that can be used include those with LMWH *(Level of Evidence: C)* or fondaparinux *(Level of Evidence: B)* using the same dosing regimens as for patients who receive fibrinolytic therapy.

Invasive Evaluation



Coronary arteriography may be considered as part of an invasive strategy for risk assessment after fibrinolytic therapy *(Level of Evidence: B)* or for patients not undergoing primary reperfusion. *(Level of Evidence: C)*