Φάρμακα στην επείγουσα καρδιολογία

Οξέα στεφανιαία σύνδρομα
Οξεία Καρδιακή ανεπάρκεια

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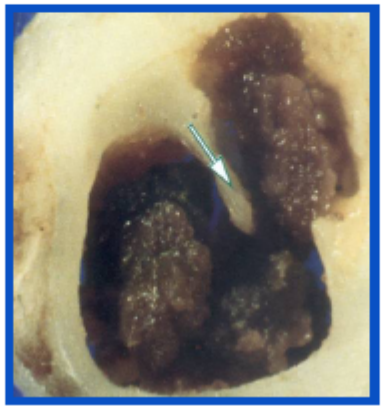
Δ/ντης Γ' Καρδιολογικής,
Ευρωκλινική Αθηνών

ΟΞΕΑ ΣΤΕΦΑΝΙΑΙΑ ΣΥΝΔΡΟΜΑ
ΟΞΕΙΑ ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ:

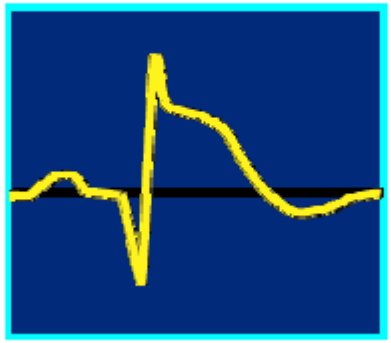
κακός οιωνός…, το "κακό" έρχεται…..

ΟΞΕΑ ΣΤΕΦΑΝΙΑΙΑ ΣΥΝΔΡΟΜΑ

ACS with persistent ST-segment elevation

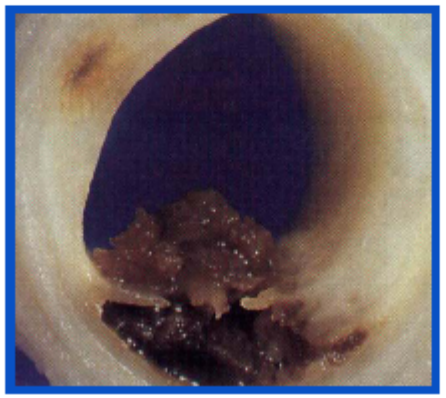


Adapted from Michael Davies

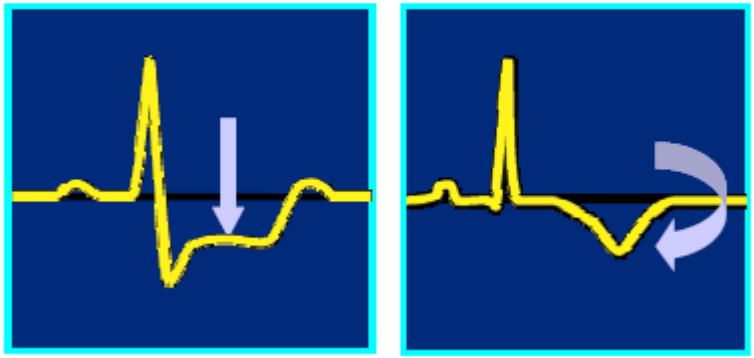


Troponin elevated

ACS without persistent ST-segment elevation



Adapted from Michael Davies



Troponins elevated or not

ΟΞΥ ΣΤΕΦΑΝΙΑΙΟ ΣΥΝΔΡΟΜΟ ΜΕ ΑΝΑΣΠΑΣΗ ΤΟΥ ST

(ΟΞΥ ΕΜΦΡΑΓΜΑ ΜΥΟΚΑΡΔΙΟΥ)

Prehospital Chest Pain Evaluation and Treatment

Class I

Prehospital EMS providers should administer 162 to 325 mg of aspirin (chewed) to chest pain patients suspected of having STEMI unless contraindicated or already taken by the patient. Although some trials have used enteric-coated aspirin for initial dosing, more rapid buccal absorption occurs with non–enteric-coated formulations. *(Level of Evidence: C)*

Class IIa

1. It is reasonable for all 9-1-1 dispatchers to advise patients without a history of aspirin allergy who have symptoms of STEMI to chew aspirin (162 to 325 mg) while awaiting arrival of prehospital EMS providers. Although some trials have used enteric-coated aspirin for initial dosing, more rapid buccal absorption occurs with non–enteric-coated formulations. *(Level of Evidence: C)*
2. It is reasonable that all ACLS providers perform and evaluate 12-lead ECGs routinely on chest pain patients suspected of STEMI. *(Level of Evidence: B)*
3. If the ECG shows evidence of STEMI, it is reasonable that prehospital ACLS providers review a reperfusion "checklist" and relay the ECG and checklist findings to a predetermined medical control facility and/or receiving hospital. *(Level of Evidence: C)*

ACC/AHA GUIDELINES for STEMI

Η εμπειρική θεραπεία ασθενών με STEMI περιλαμβάνει:

M Morphine

O Oxygen

N Nitroglycerin

A Aspirin

6.3.1.3. Analgesia

Class I

Morphine sulfate (2 to 4 mg IV with increments of 2 to 8 mg IV repeated at 5- to 15-minute intervals) is the analgesic of choice for management of pain associated with STEMI. *(Level of Evidence: C)*

- Ο πόνος αυξάνει τη δράση του συμπαθητικού. Η παραγωγή κατεχολαμινών σχετίζεται τόσο με την πλάκα, όσο και με τον θρόμβο. Άρα σημαντική θέση κατέχει η χορήγηση της μορφίνης.
- Η χορηγούμενη δόση εξαρτάται από το βάρος, την ηλικία, την ΑΠ, τη συχνότητα.
- Βοηθά στο ΟΠΟ, μειώνει το άγχος.
- Ανεπιθύμητες ενέργειες: υπόταση, βραδυκαρδία (atropine 0.5-1.5 mg IV), ναυτία και έμετοι.
- Το αντίδοτο είναι η ναλοξόνη, όπου χορηγείται 0,1-0,2mg IV.

Oxygen

Class I

Supplemental oxygen should be administered to patients with arterial oxygen desaturation (SaO_2 less than 90%). *(Level of Evidence: B)*

Class IIa

It is reasonable to administer supplemental oxygen to all patients with uncomplicated STEMI during the first 6 hours. *(Level of Evidence: C)*

Nitroglycerin

Class I

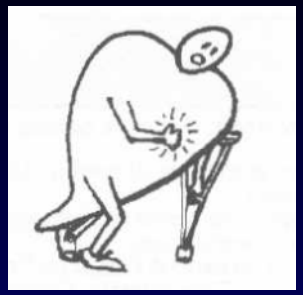
1. Patients with ongoing ischemic discomfort should receive sublingual nitroglycerin (0.4 mg) every 5 minutes for a total of 3 doses, after which an assessment should be made about the need for intravenous nitroglycerin. *(Level of Evidence: C)*
2. Intravenous nitroglycerin is indicated for relief of ongoing ischemic discomfort, control of hypertension, or management of pulmonary congestion. *(Level of Evidence: C)*

Class III

1. Nitrates should not be administered to patients with systolic blood pressure less than 90 mm Hg or greater than or equal to 30 mm Hg below baseline, severe bradycardia (less than 50 beats per minute [bpm]), tachycardia (more than 100 bpm), or suspected RV infarction. *(Level of Evidence: C)*
2. 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). *(Level of Evidence: B)*

ACC/AHA GUIDELINES for STEMI

- Τα νιτρώδη μειώνουν το προφορτίο και το μεταφορτίο, βελτιώνουν τη ροή των στεφανιαίων και διαστέλλουν τα αγγεία.
- Ανακουφίζουν τον ισχαιμικό πόνο.
- Αποφεύγονται σε ασθενείς με: ΣΑΠ<90 mmHg ή πτώση της ΑΠ >30 mmHg από την αρχική, βραδυκαρδία, ταχυκαρδία ή υποψία ΟΕΜ με συμμετοχή της δεξιάς κοιλίας.
- Υπογλωσσίως δίνουμε 0,4 mg.
- Ενδοφλέβια ο ρυθμός είναι 5-10 mcg/min, με αυξήσεις 5-20mcg/min όσο δεν αντενδείκνυται.

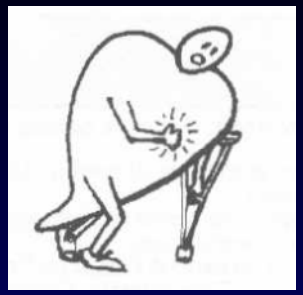


Νιτρώδη

- **Νιτρογλυκερινη**

  διαδερμικά: Μέγιστα Επίπεδα σε 30-60 λεπτά, διάρκεια 1ημέρα,

  υπογλώσσια: Μέγιστα Επίπεδα σε 1-2 λεπτά, διάρκεια 30-60 λεπτά
- **Δινιτρικός Ισορβίτης (pensordil)**



Νιτρώδη

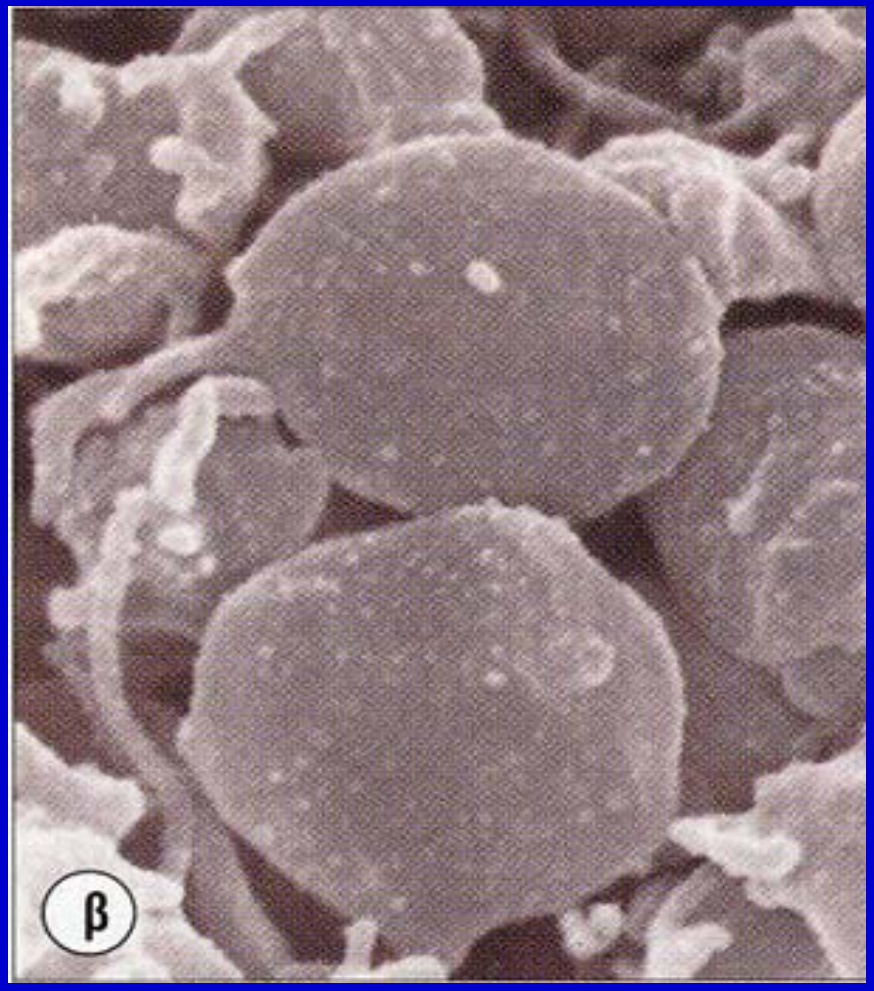
- **Ανοχή**
- **Κίνδυνος ορθοστατικής υπότασης, βραδυκαρδίας, ταχυκαρδίας, εγκεφαλικής ισχαιμίας**

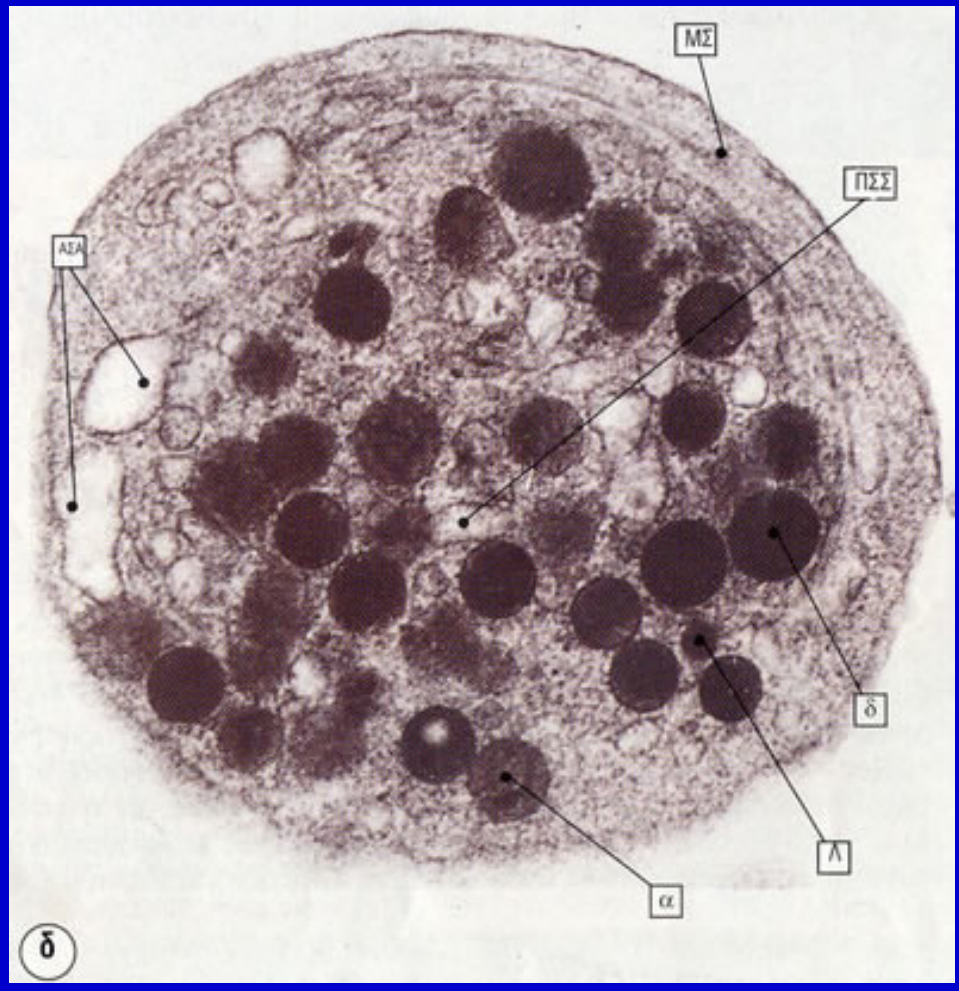
ΝΙΤΡΩΔΗ

Θυμηθείτε το φαινόμενο ανοχής στα νιτρώδη από τη λανθασμένη χρήση τους

ΑΝΤΙΘΡΟΜΒΩΤΙΚΑ ΦΑΡΜΑΚΑ

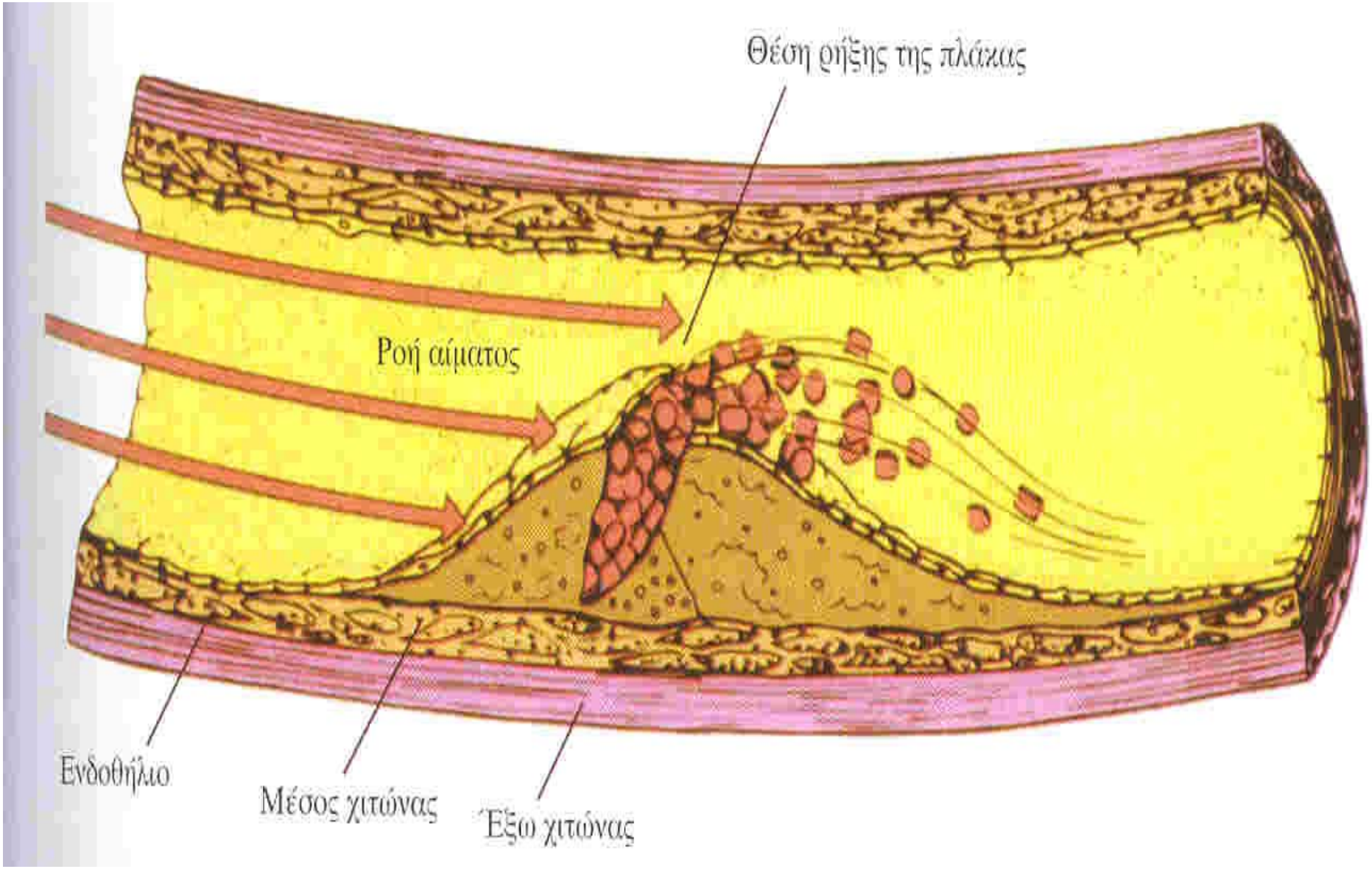
Αιμοπετάλια: ‘εμμορφο απύρηνο συστατικό του αίματος θεματοφύλακας της αιμόστασης αλλά και “πρόβλημα” στα οξέα στεφανιαία σύνδρομα



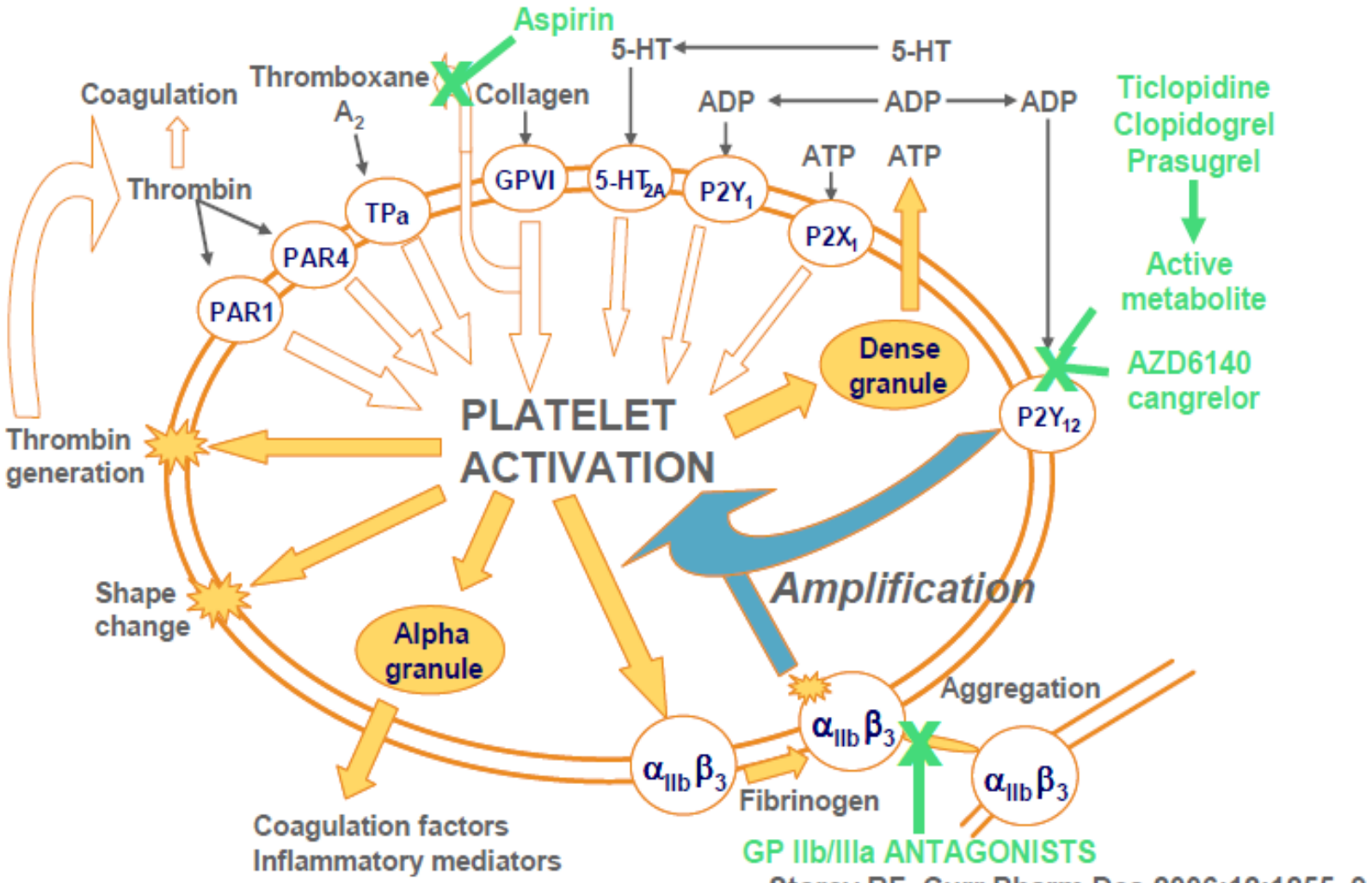


Εικόνες από ηλεκτρονικό μικροσκόπιο

Γιατί χρησιμοποιούμε αντιαιμοπεταλιακά στα οξέα στεφανιαία σύνδρομα

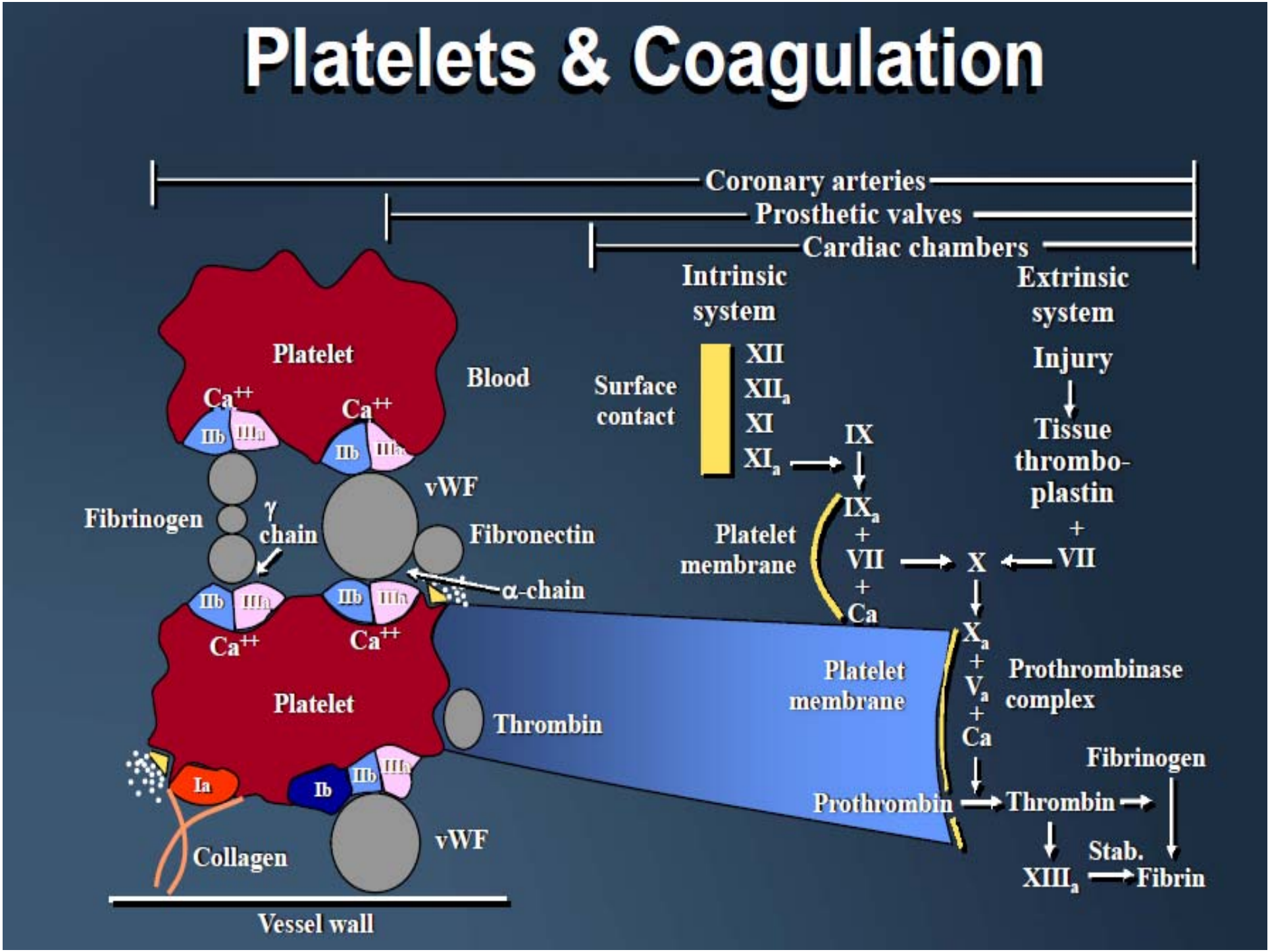


Platelet activation mechanisms

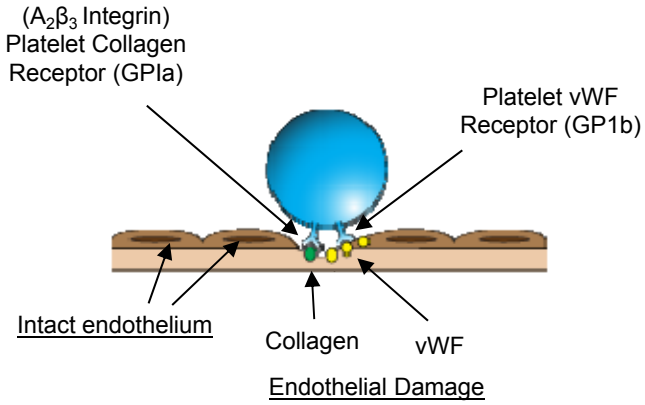


Storey RF. Curr Pharm Des 2006;12:1255–9

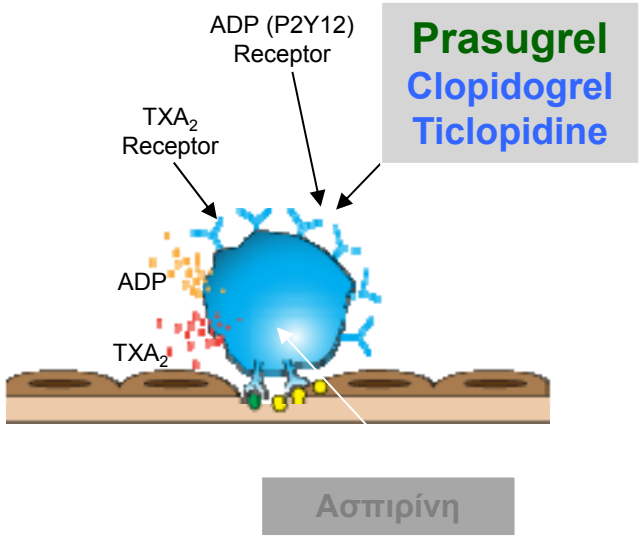
Platelets & Coagulation



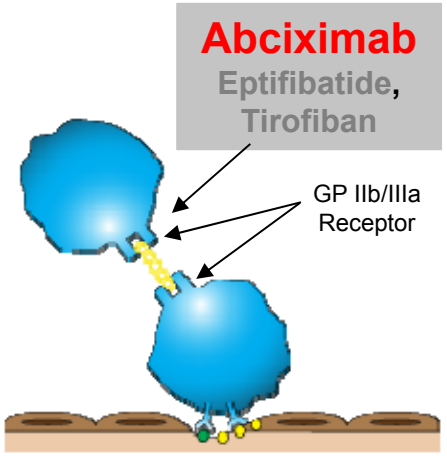
Στοχεύοντας τα αιμοπετάλια



Δεν υπάρχουν αντιαιμοπεταλιακά που στοχεύουν την **Προσκόλληση**



Τα περισσότερα αντιαιμοπεταλιακά στοχεύουν την **Ενεργοποίηση**



Οι αναστ. GP IIb/IIIa δρουν στο "κοινό τελικό βήμα" **Συσσώρευση**

GP = glycoprotein; vWF = von Willebrand factor; ADP = adenosine diphosphate; TX = thromboxane

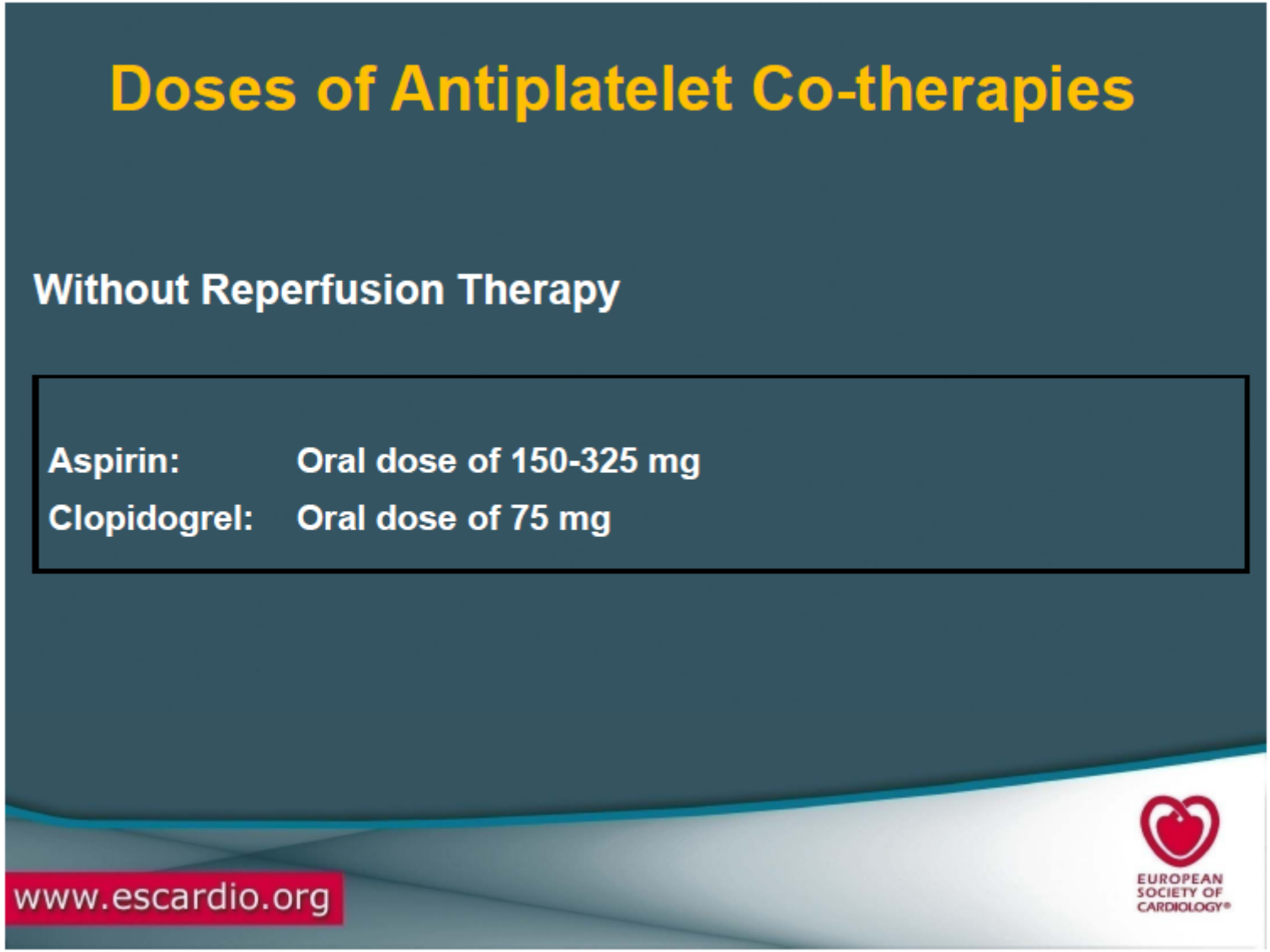
Meadows et al. *Circulation Res*. 2007;100:1261-1275

6.3.1.4. Aspirin

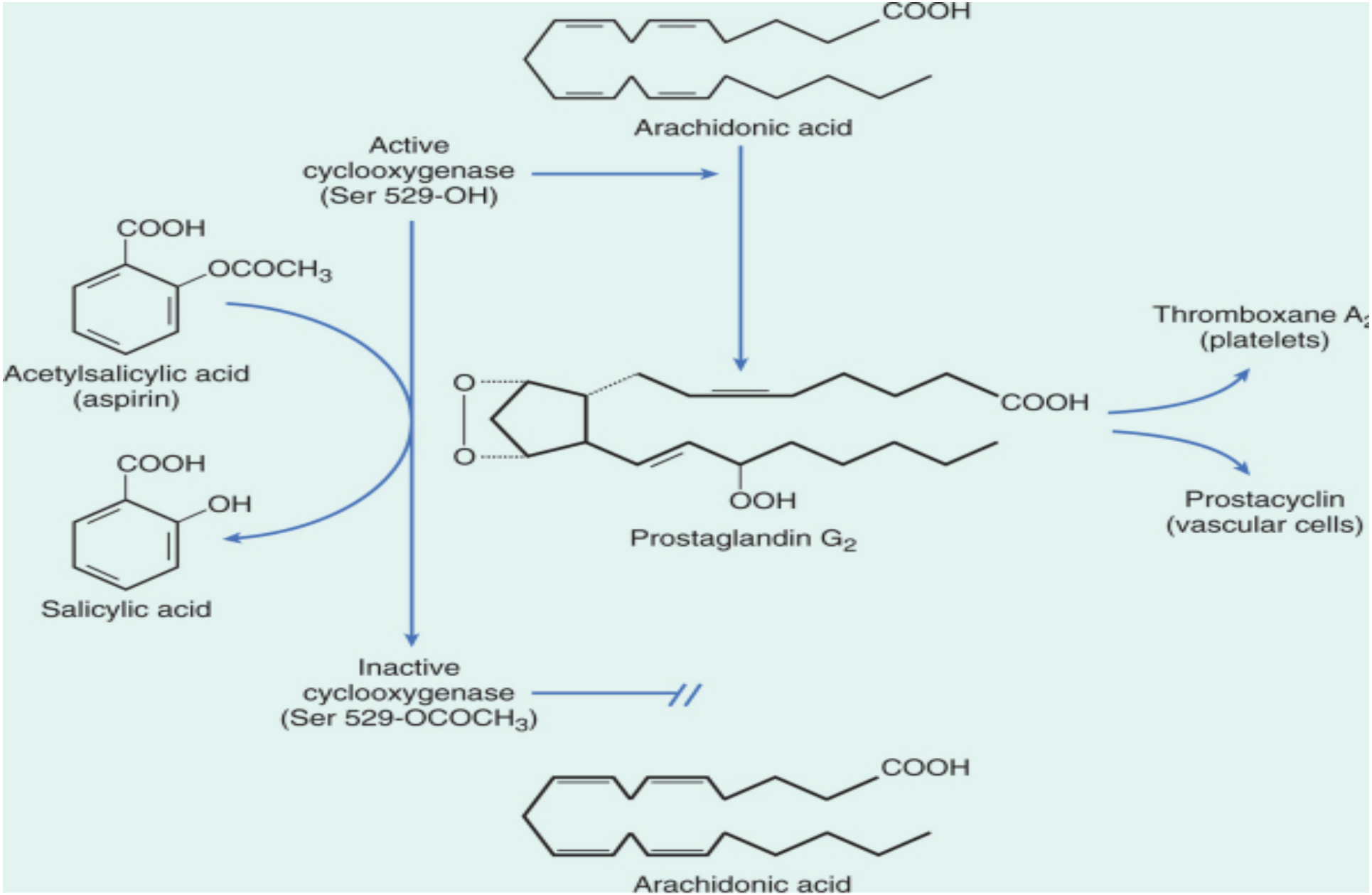
Class I

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 aspirin formulations.

Acute Myocardial Infarction with ST elevation Therapy

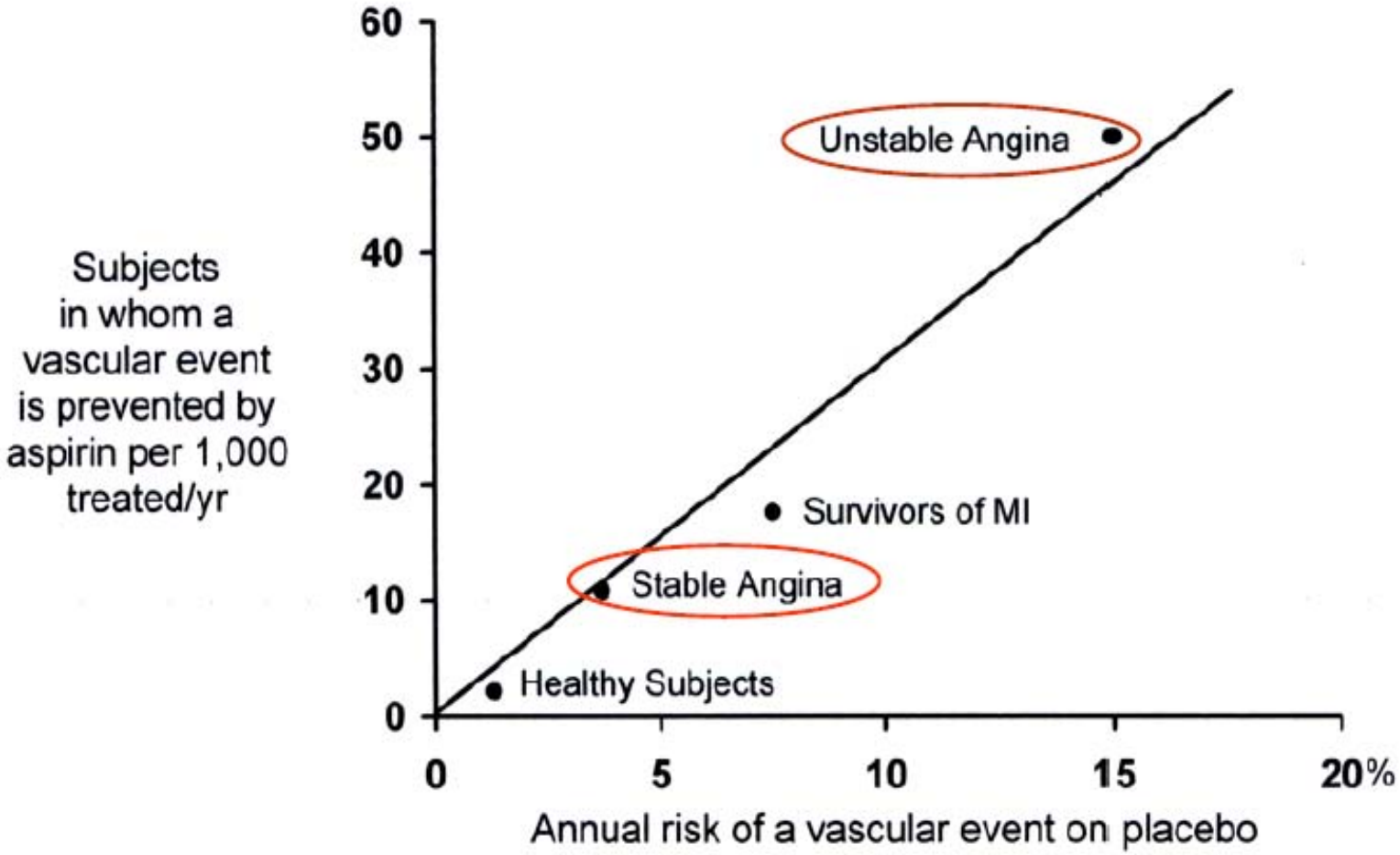


Ασπιρίνη: το μακροβιότερο φάρμακο



Benefits from aspirin therapy

The oldest, the cheapest, very effective…….



ASA efectiveness is related to the degree of thrombus formation activity

ASA in acute coronary syndromes

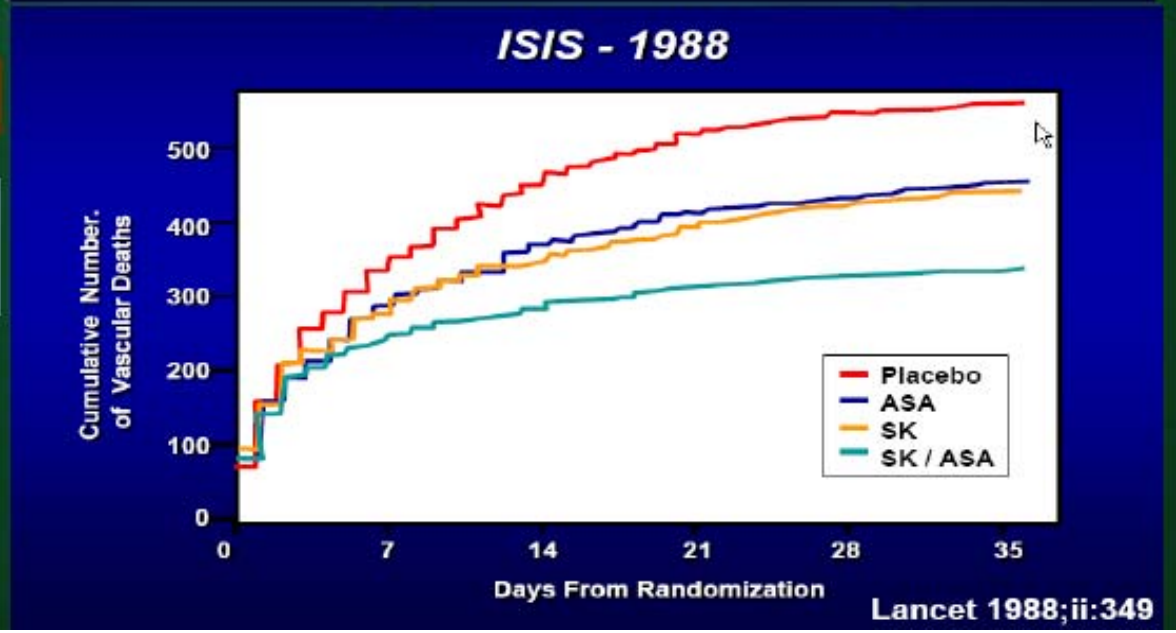
ASA in NSTEMI – death/MI/stroke reduction:in the 4 randomized trials

53%

IA

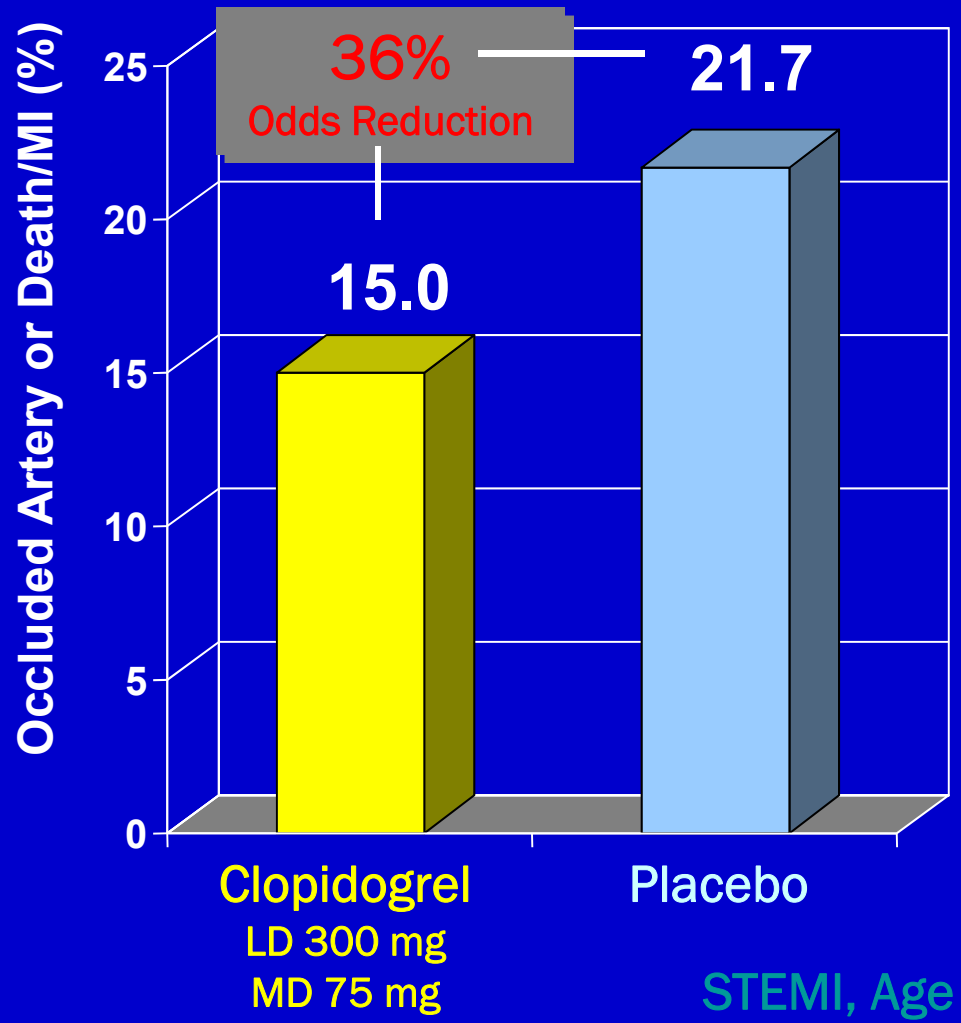
ASA in STEMI

23%



IB

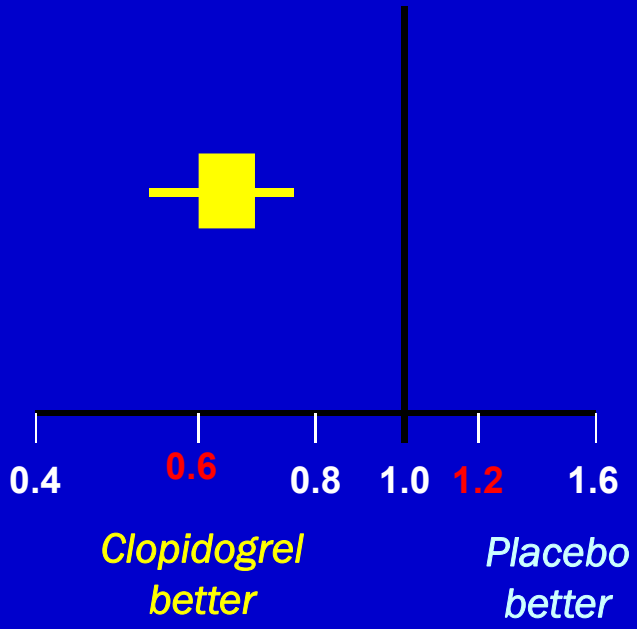
CLARITY-TIMI 28 Primary Endpoint:
Occluded Artery (or D/MI thru Angio/HD)



Odds Ratio 0.64

(95% CI 0.53-0.76)

P=0.00000036



STEMI, Age 18-75

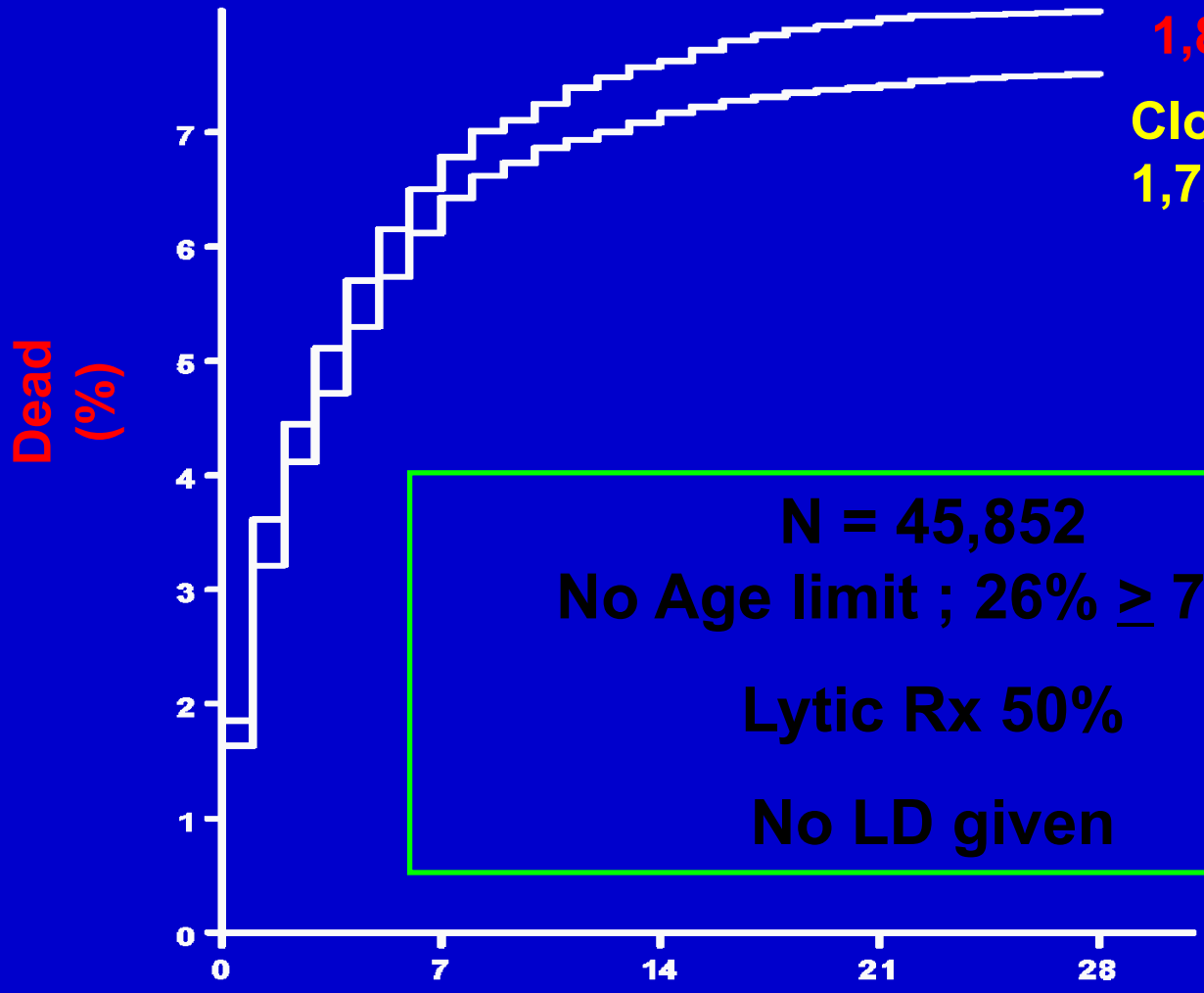
Sabatine N Eng J Med 2005;352:1179.

Clopidogrel in AMI (added to thrombolysis): The CLARITY TIMI 28 Trial

Outcome	Clopidogrel	Placebo	OR (95% CI)	p
CV death/ re-MI/ recurrent ischemia (%)	11.6	14.1	0.80 (0.65-0.97)	0.03
Bleeding (%)	3.4	2.7		0.24

Sabatine MS et al. N Engl J Med 2005

COMMIT: Effect of CLOPIDOGREL on Death In Hospital



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

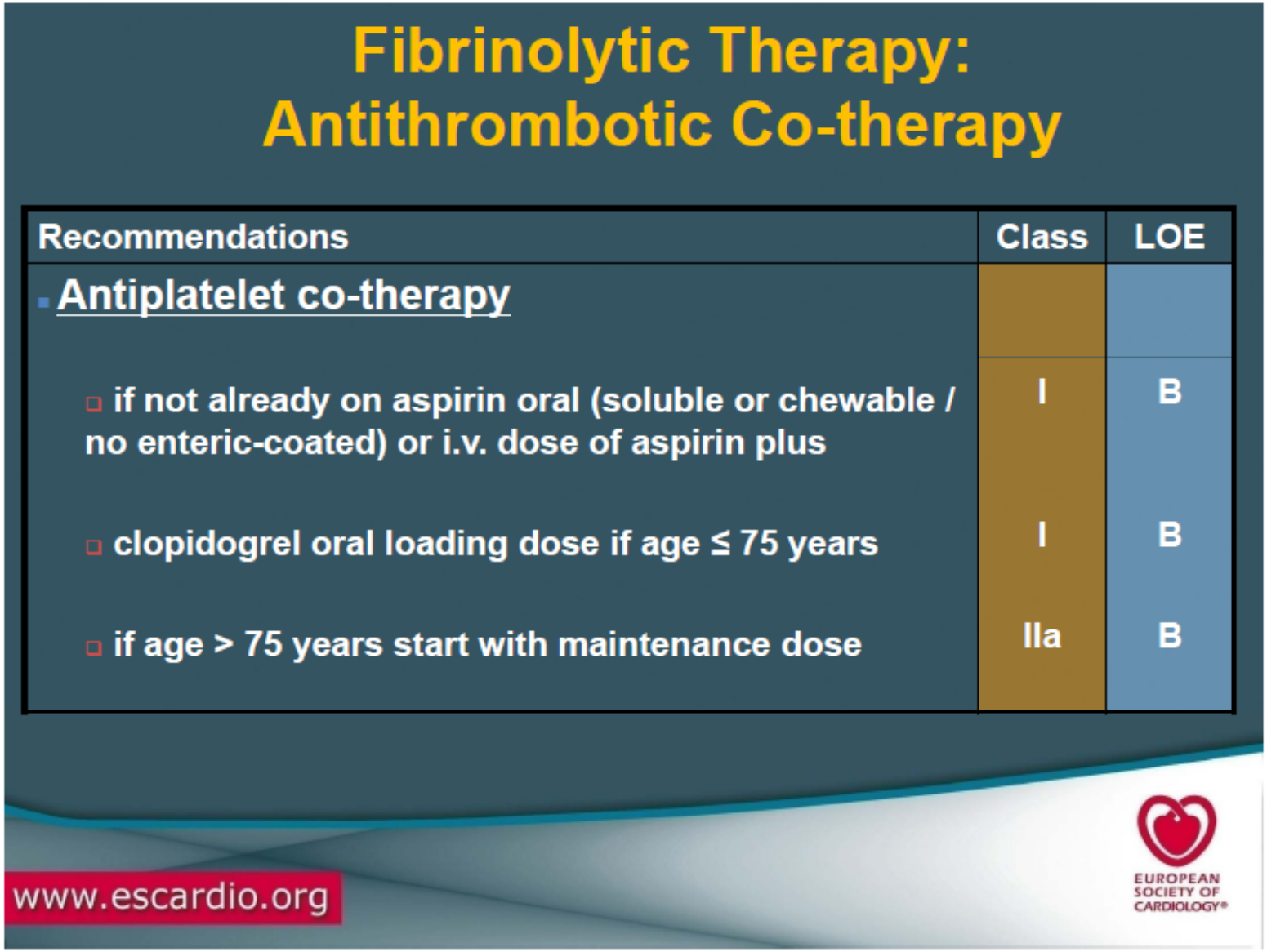
Clopidogrel + ASA:
1,728 deaths (7.5%)

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

N = 45,852
No Age limit ; 26% ≥ 70 y
Lytic Rx 50%
No LD given

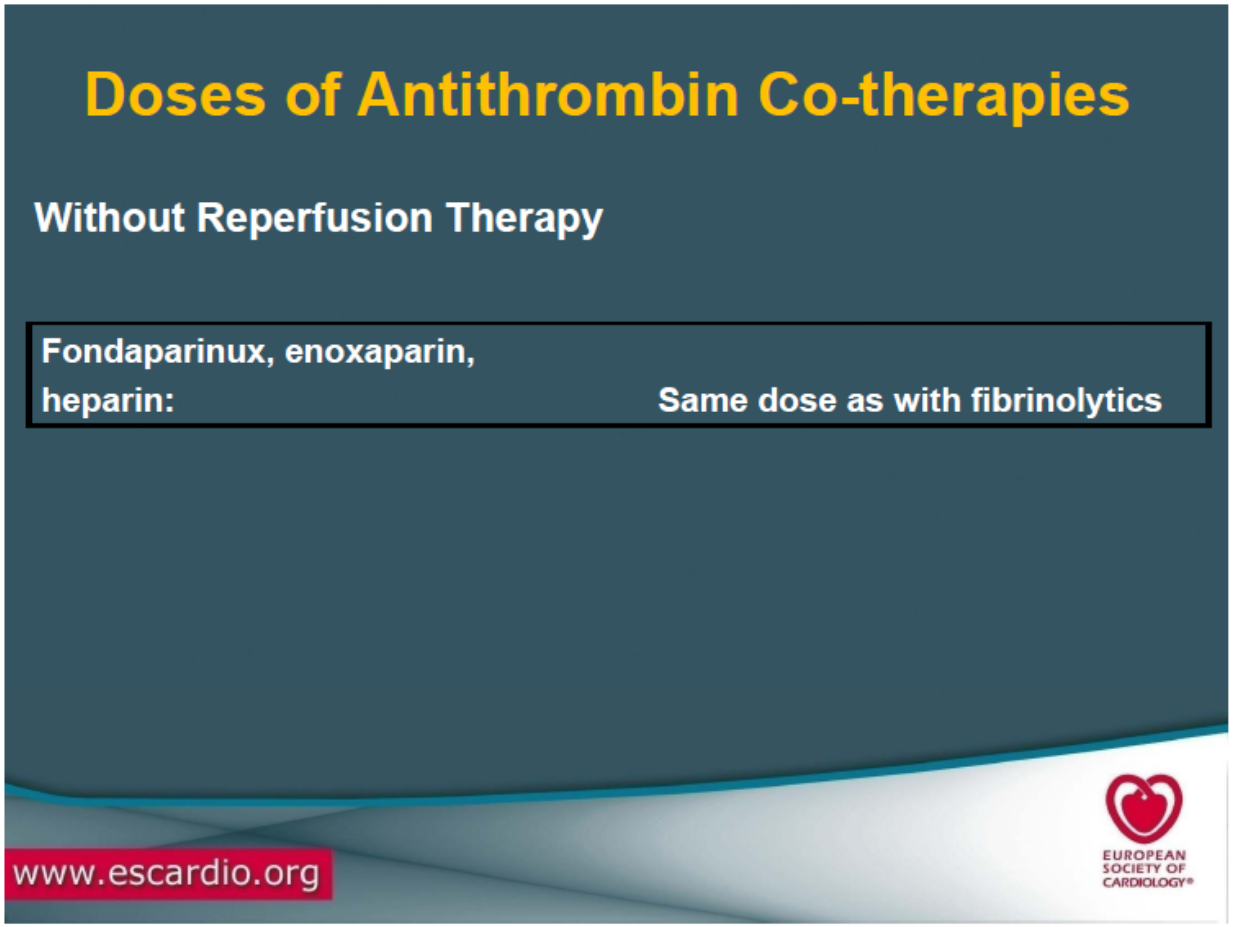
Chen ZM, et al. *Lancet*. 2005;366:1607.

Acute Myocardial Infarction with ST elevation Therapy



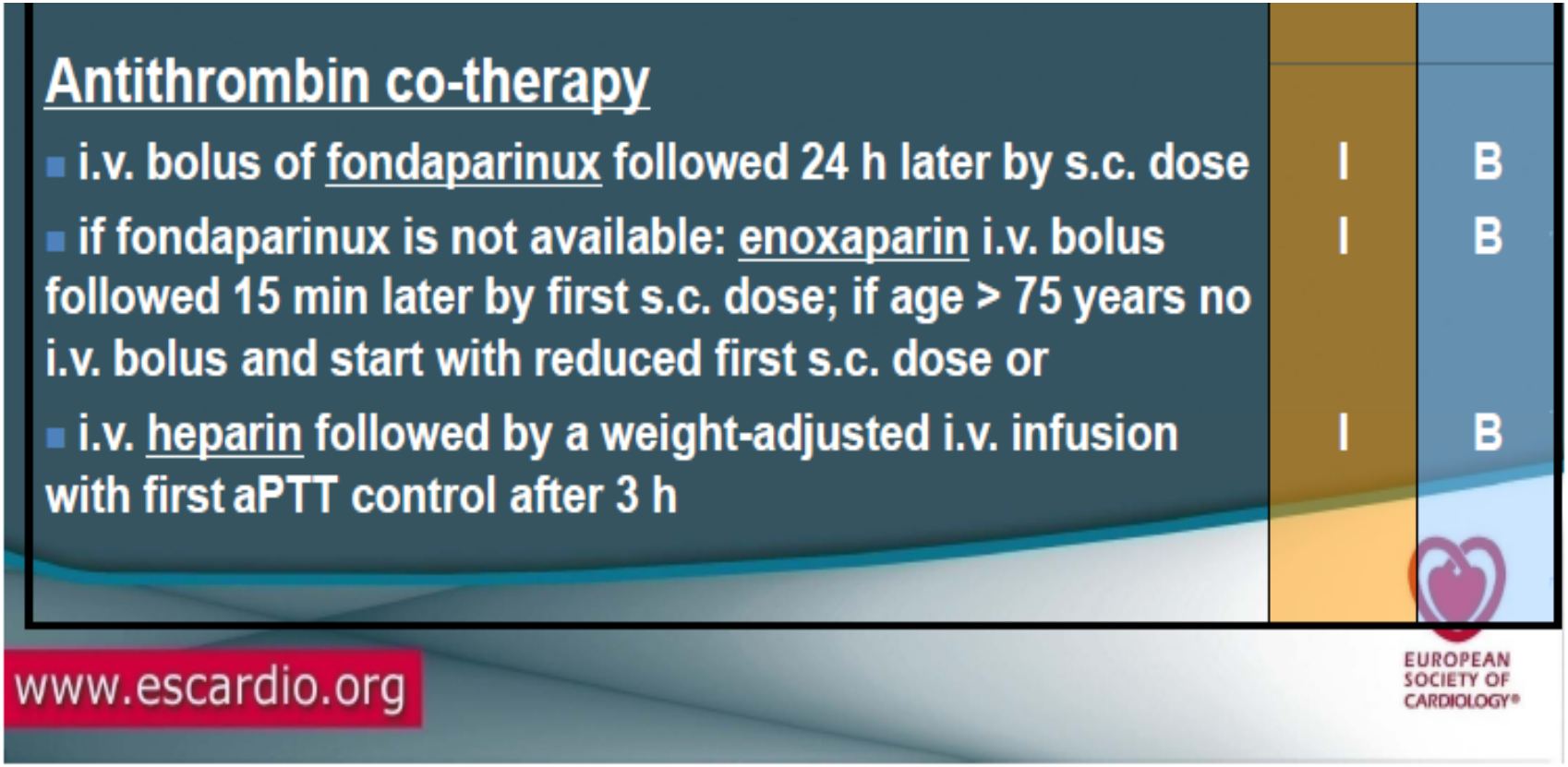
Acute Myocardial Infarction with ST elevation Therapy

Heparins….



Acute Myocardial Infarction with ST elevation Therapy

Heparins….



B- blocker

Class I

Oral beta-blocker therapy should be administered promptly to those patients without a contraindication, irrespective of concomitant fibrinolytic therapy or performance of primary PCI. *(Level of Evidence: A)*

Class IIa

It is reasonable to administer IV beta-blockers promptly to STEMI patients without contraindications, especially if a tachyarrhythmia or hypertension is present. *(Level of Evidence: B)*

Άμεση χορήγηση b-blocker εμφανίζουν μείωση σε:

- **ι) ισχαιμία και επίπτωση των επιπλοκών αυτών που δεν θα λάβουν θρομβόλυση**
- **ιι) ρυθμός επανέφραξης όσων λάβουν θρομβόλυση**
- **ιιι) συχνότητα επικίνδυνων για τη ζωή κοιλιακών ταχυαρρυθμιών.**

Μελέτες

- **ISIS- 1**: Χορήγηση ατενολόλης 5-10mg IV αρχικά και μετά 100 mg p.o → θνητότητα ↓4,3% σε 3,7% (6/1000).
- **MIAMI**: Χορήγηση 15 mg IV μετοπρολόλης, μετά 50 mg p.o για 48 h και 100 mg p.o * 2 /μέρα → θνητότητα ↓4,9% σε 4,3%.
- **TIMI II**:Χορήγηση αλτεπλάσης και μετοπρολόλης 15 mg IV , 50 mg p.o * 2 για 1 μέρα και 100 mg p.o * 2 /μέρα, το νωρίτερο είχε καλύτερα τελικά σημεία από όσους δεν το έλαβαν.
- **CAPRICON** : Αναφέρεται σε ασθενείς μετά ΟΕΜ και δυσλειτουργία της αριστερής κοιλίας.

Contraindications to Beta-Adrenoceptor Blocker Therapy in Acute Myocardial Infarction

- Heart rate < 60 beats/min
- Systolic arterial pressure <100 mm Hg
- Moderate or severe left ventricular failure
- Signs of peripheral hypoperfusion
- PR interval > 0.24 sec
- Second-Third-degree atrioventricular block
- Severe chronic obstructive pulmonary disease
- History of asthma
- Severe peripheral vascular disease
- Insulin-dependent diabetes mellitus

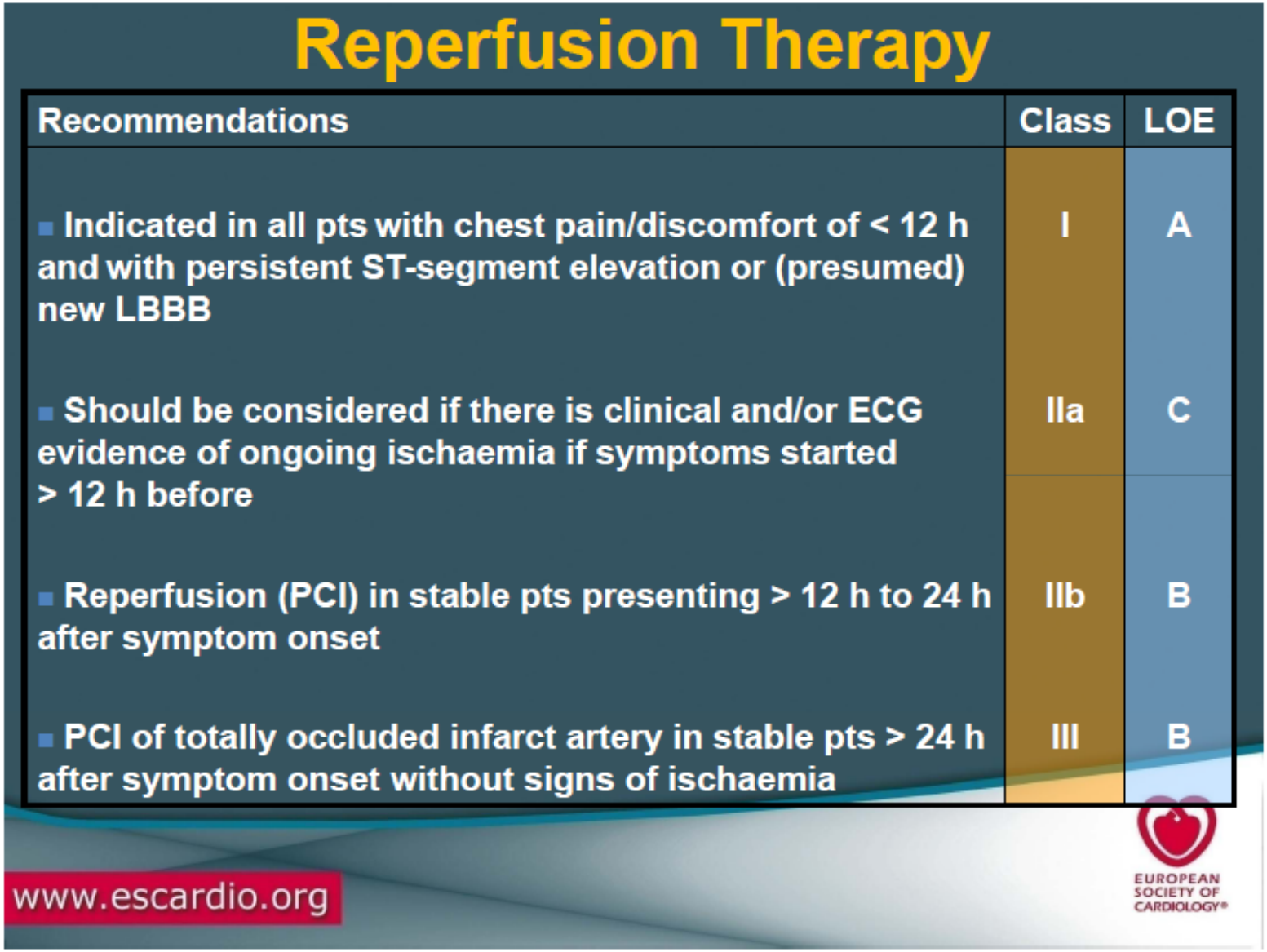
Επαναιμάτωση

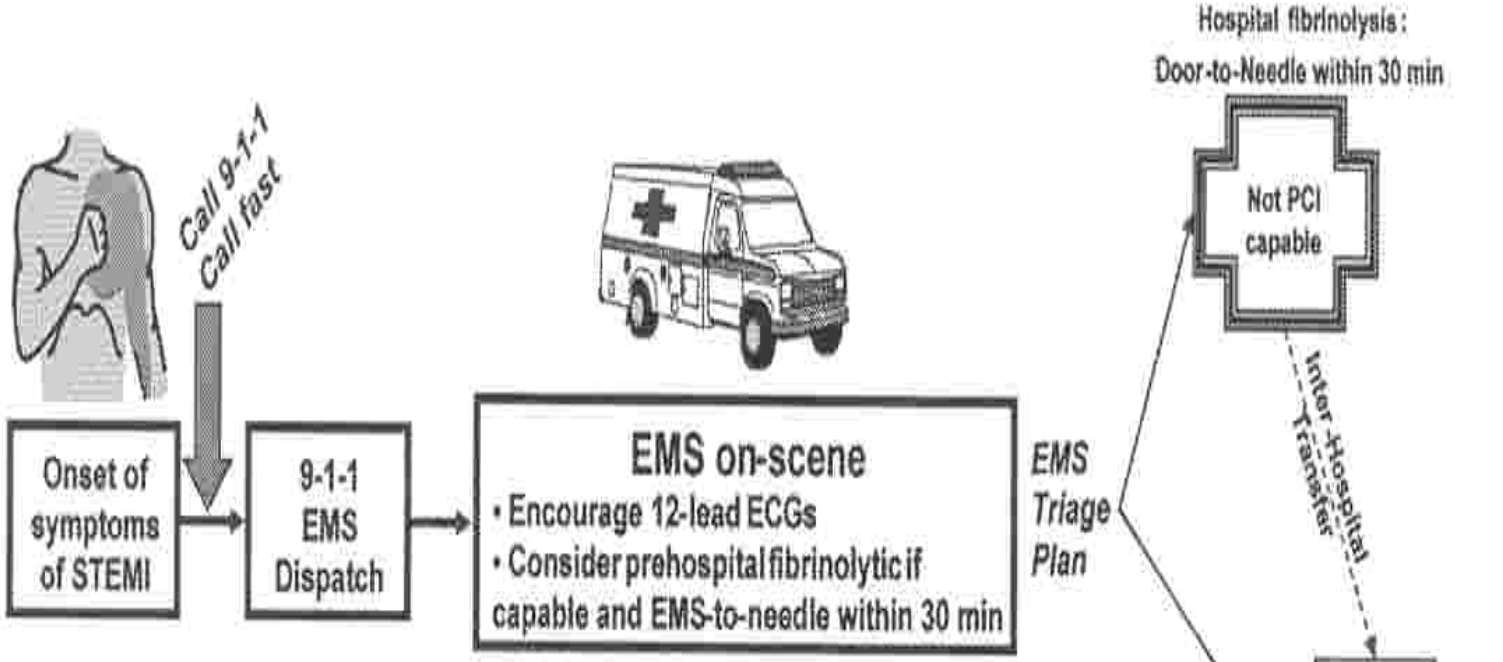
Class I

All STEMI patients should undergo rapid evaluation for reperfusion therapy and have a reperfusion strategy implemented promptly after contact with the medical system. *(Level of Evidence: A)*

ACC/AHA GUIDELINES for STEMI

Acute Myocardial Infarction with ST elevation Therapy





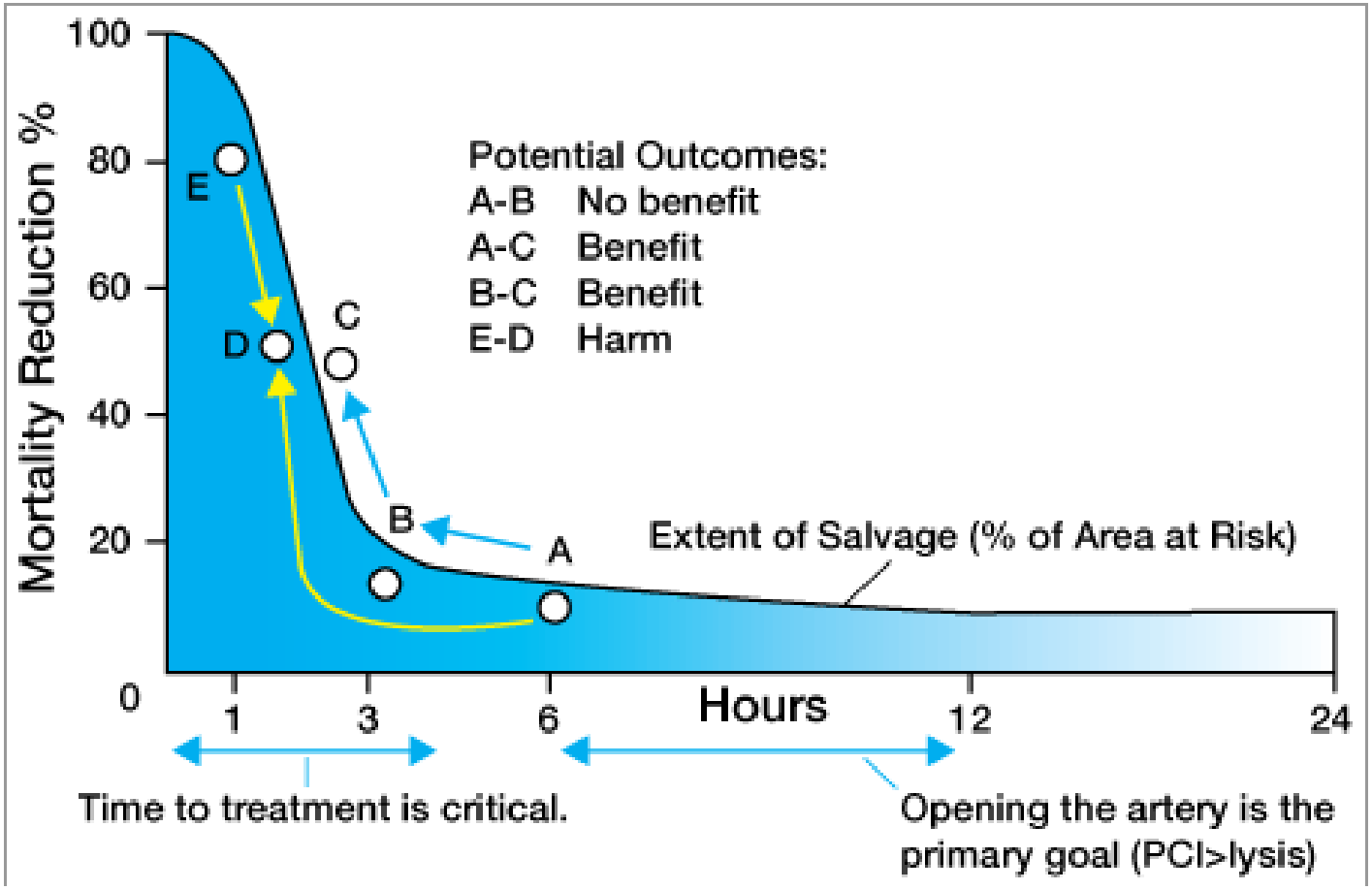
Goals†

Patient	Dispatch	EMS on scene	EMS transport	
5 min after symptom onset	1 min	Within 8 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

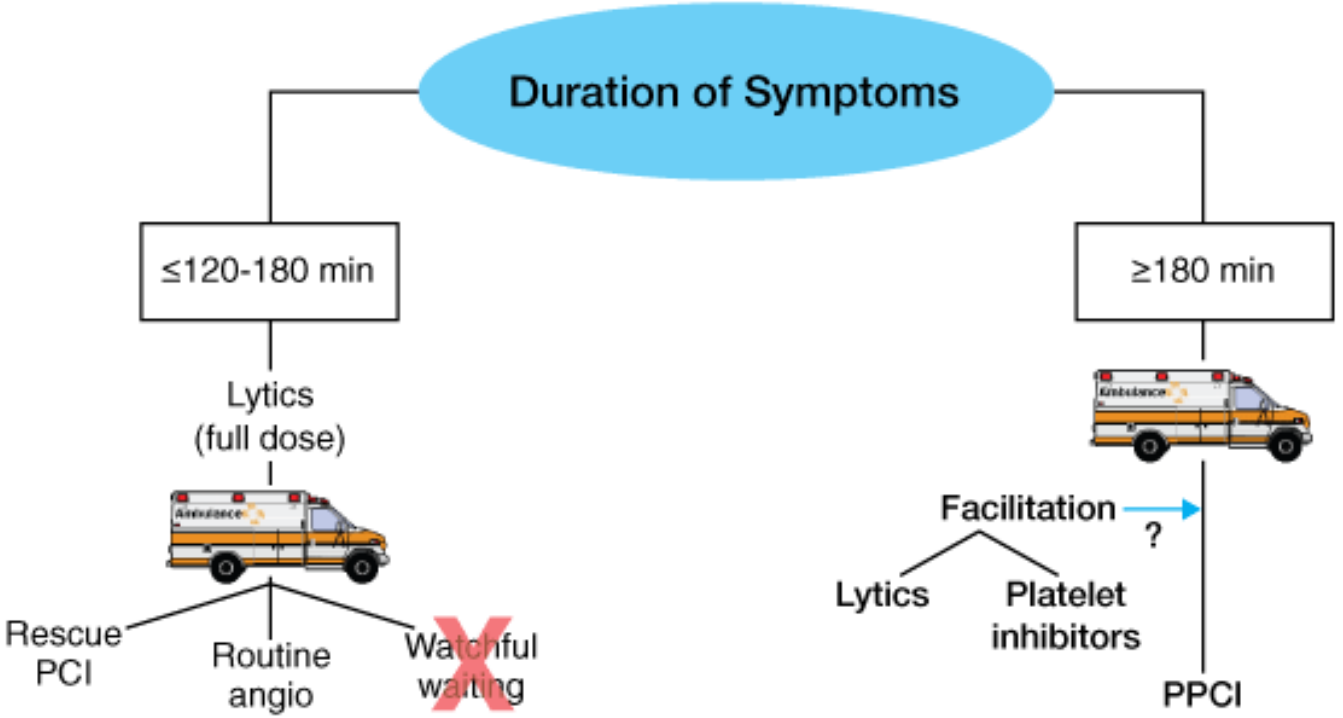
Total ischemic time: Within 120 min*

*Golden Hour = First 60 minutes

Outcome and Reperfusion: a matter of time…

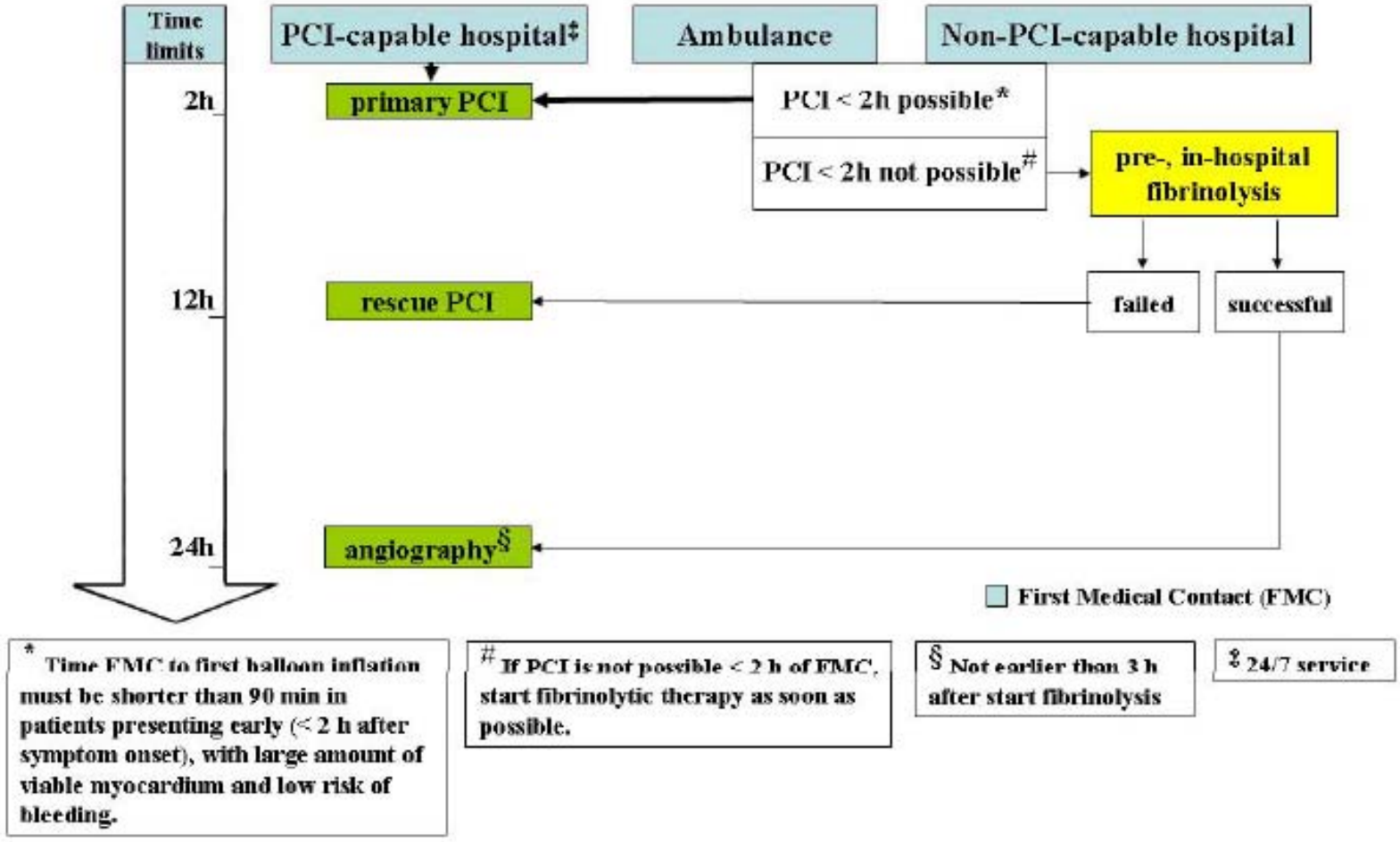


Reperfusion Strategy: a matter of time…



Source: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson
P: *Hurst's The Heart*, 12th Edition: http://www.accessmedicine.com

Acute Myocardial Infarction with ST elevation Therapy



Trials Comparing in-Hospital Thrombolysis with Transfer for Percutaneous Coronary Intervention (PCI) in Patients Presenting <12 Hours from the Onset of Chest Pain

		Death, Reinfarction, Disabling Stroke at 30 Days		
	N	Thrombolysis	Transfer for PCI	P value
PRAGUE-2[133]	850	15.2%	8.4%	<0.003
AIR PAMI[134]	138	13.6%	8.4%	0.33
DANAMI-2[135]	1572	13.7%	8.0%	<0.001

Reperfusion in STEMI:

Time, *time, time*.....

Transport Time ("Incurred Ischemic Time")	Duration from Onset of Symptoms ("Fixed Ischemic Time")	
	0–3 Hours	>3 Hours
0–30 Minutes	PCI + GP IIb/IIIa	PCI + GP IIb/IIIa
30–60 Minutes	Thrombolytic + Clopidogrel	PCI + GP IIb/IIIa
>60 Minutes	Thrombolytic + Clopidogrel	Thrombolytic + Clopidogrel or PCI + GP IIb/IIIa

Acute Myocardial Infarction with ST elevation Therapy

Reperfusion Therapy: Fibrinolytic Therapy

Recommendations	Class	LOE
■ In the absence of contraindications and if primary PCI cannot be performed within the recommended time	I	A
■ A fibrin-specific agent should be given	I	B
■ Pre-hospital initiation of fibrinolytic therapy	IIa	A

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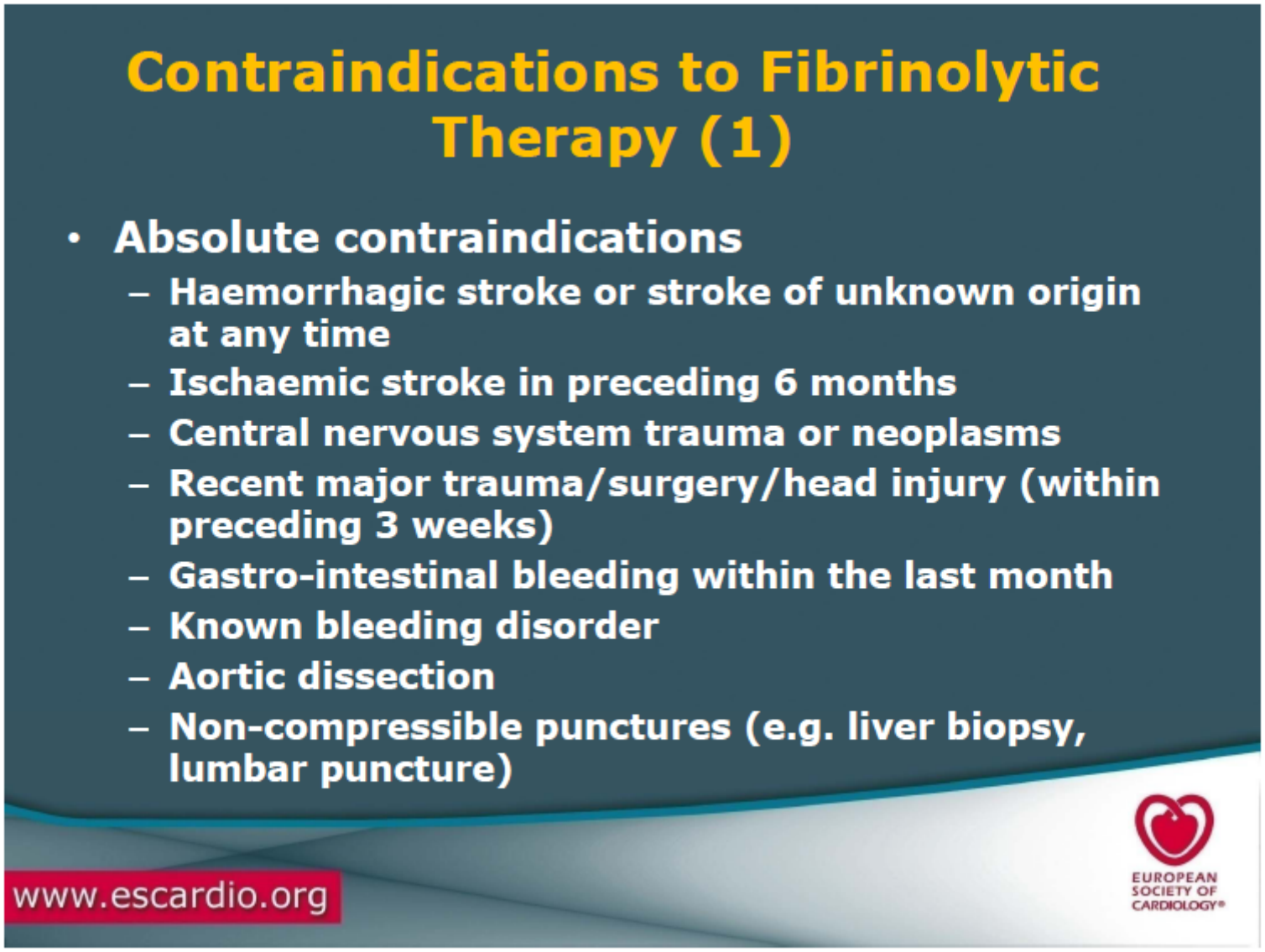
- Όσο πιο γρήγορη η θρομβόλυση τόσο μεγαλύτερη η αποτελεσματικότητα της
- Η μεγαλύτερη μείωση της θνητότητας τις 2 πρώτες ώρες (40-45%)
- Τα νέα θρομβολυτικά με ευκολότερο τρόπο χορήγησης και υψηλή ινωδοεκλεκτικότητα, όπως θα δούμε διευκολύνουν την εφαρμογή της Prehospital θρομβόλυσης

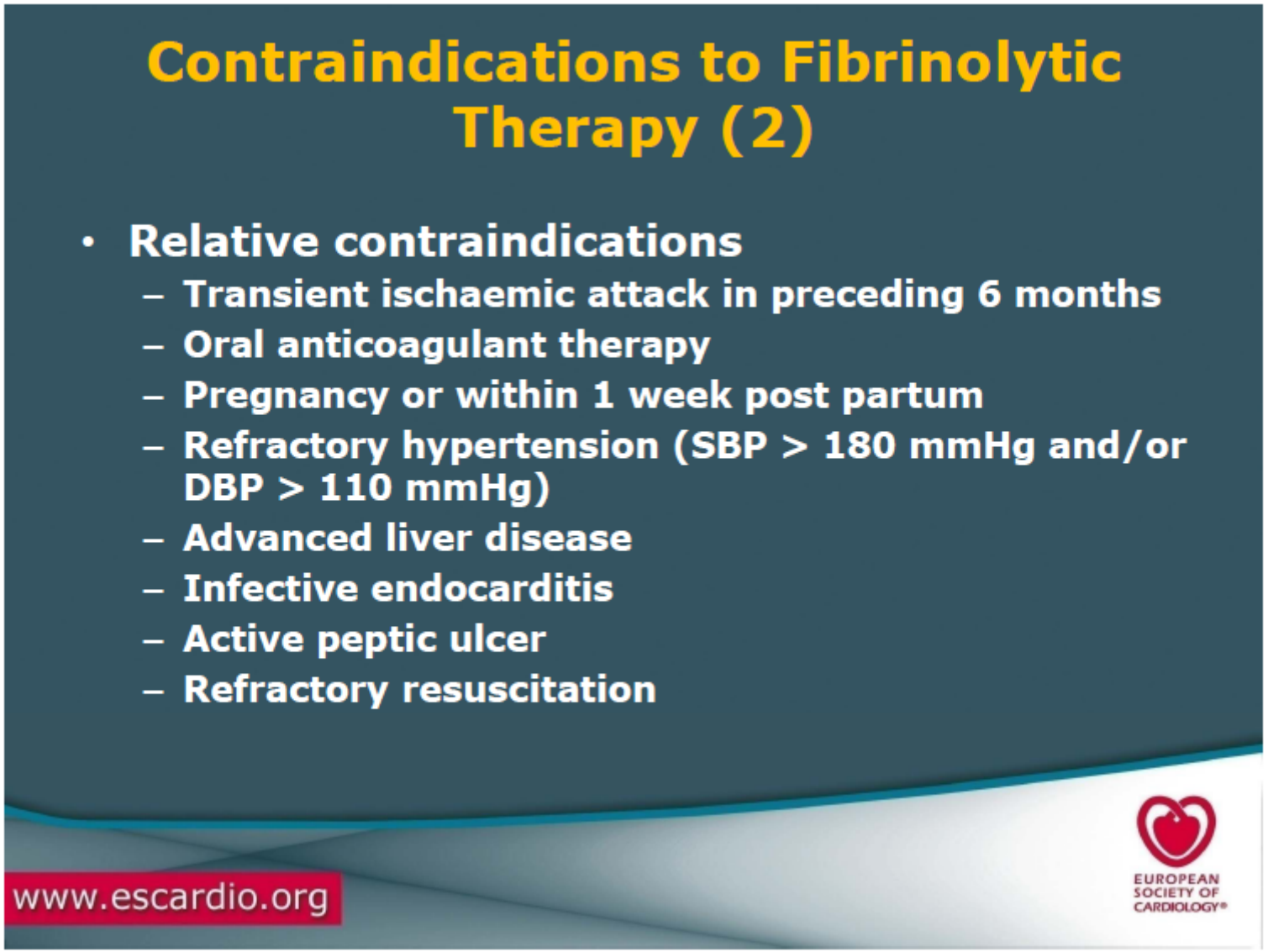
Table 15. Comparison of Approved Fibrinolytic Agents

	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

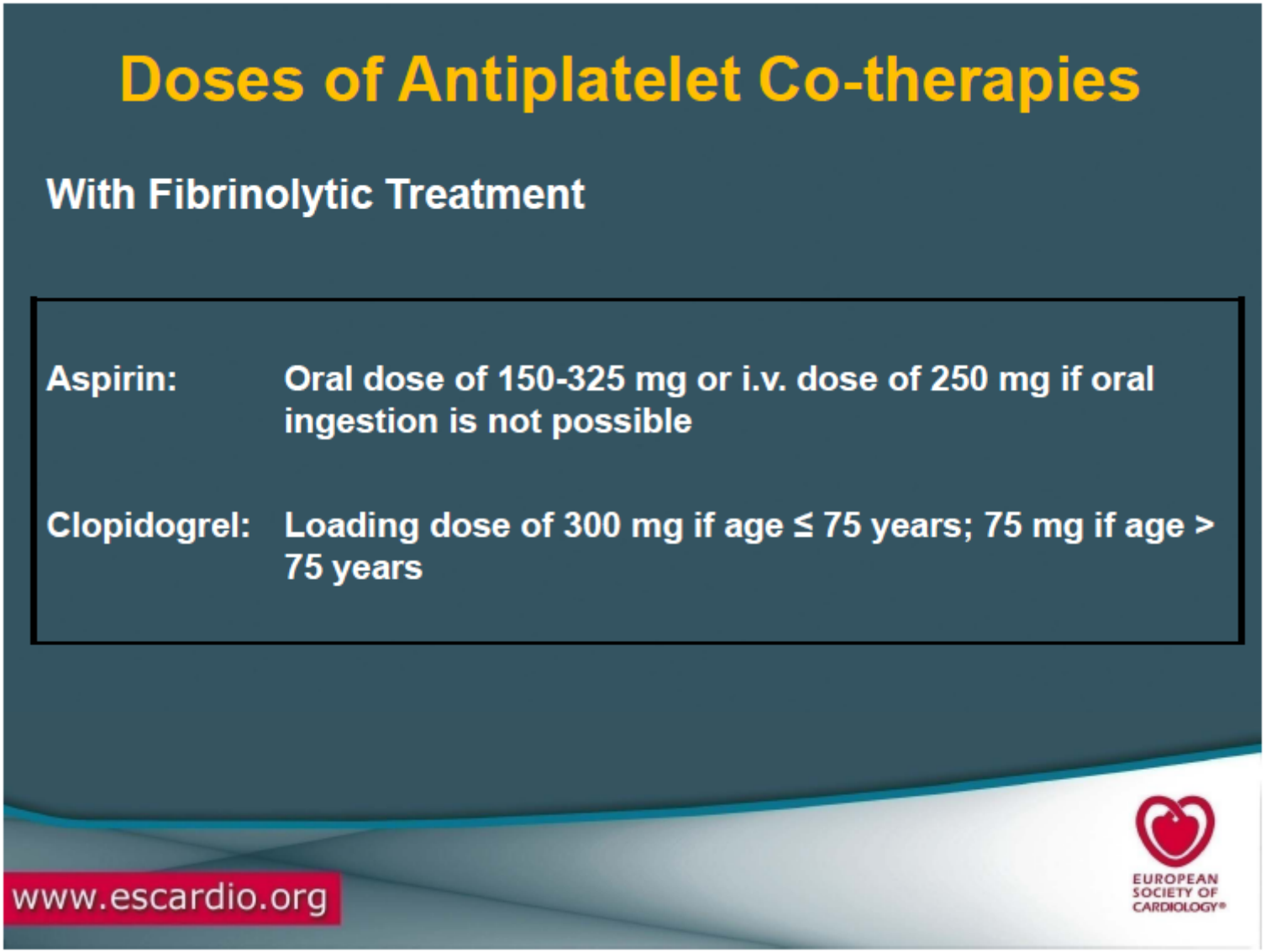
Acute Myocardial Infarction with ST elevation Therapy



Acute Myocardial Infarction with ST elevation Therapy



Acute Myocardial Infarction with ST elevation Therapy



Acute Myocardial Infarction with ST elevation Therapy

Doses of Antithrombin Co-therapies

With Fibrinolytic Treatment

Enoxaparin:	In patients < 75 years and creatinine levels ≤ 2.5 mg/mL or ≤ 221 µmol/L (men) or ≤ 2 mg/ml or 177 µmol/L (women): i.v. bolus of 30 mg followed 15 min later by s.c. dose of 1 mg/kg every 12 h until hospital discharge for a maximum of 8 days. The first two s.c. doses should not exceed 100 mg. In patients > 75 years: no i.v. bolus; start with first s.c. dose of 0.75 mg/kg with a maximum of 75 mg for the first two s.c. doses. In patients with creatinine clearance of < 30 mL/min, regardless of age, the s.c. doses are repeated every 24 h
Heparin:	i.v. bolus of 60 U/kg with a maximum of 4000 U followed by an i.v. infusion of 12 U/kg with a maximum of 1000 U/h for 24 to 48 h. Target aPTT: 50-70 s to be monitored at 3, 6, 12 and 24 h
Fondaparinux:	2.5 mg i.v. bolus followed by a s.c. dose of 2.5 mg once daily up to 8 days or hospital discharge if creatinine ≤ 3 mg/mL or 265 µmol/L

Prehospital Fibrinolysis

Class IIa

Establishment of a prehospital fibrinolysis protocol is reasonable in 1) settings in which physicians are present in the ambulance or 2) well-organized EMS systems with full-time paramedics who have 12-lead ECGs in the field with transmission capability, paramedic initial and ongoing training in ECG interpretation and STEMI treatment, on-line medical command, a medical director with training/experience in STEMI management, and an ongoing continuous quality-improvement program. *(Level of Evidence: B)*

Στη μελέτη CAPTIM τυχαιοποιήθηκαν ασθενείς με έναρξη συμπτωμάτων λιγότερο των 2 ωρών, που έλαβαν προνοσοκομειακή θρομβόλυση και συγκρίθηκαν ως προς την θνητότητα στις 30 μέρες με εκείνους στους οποίους έγινε Primary PCI (2.2% versus 5.7%)

Glycoprotein IIBIIIA inhibitors in preparatory pharmacologic strategy for patients with STEMI prior to primary PCI ?

FINESSE: Study design

Treatment	Pre-PCI treatment with ½ -dose lytic plus abciximab, pre-PCI abciximab alone, and abciximab at time of PCI
Inclusion	Suspected acute MI (ST change or LBBB) within 6 h of symptom onset
Exclusion	Low risk (<60 yo, localized inferior infarct) high risk for bleeding
1° OUTCOMES	Death, VF after 48 hours, shock, CHF within 90 days

Ellis et al. N Eng J Med. 2008;358:2205-2217.

Primary, secondary, and bleeding end points in FINESSE

End point	Primary PCI (%)	Abciximab-facilitated (%)	Combination (abciximab/reteplase)-facilitated (%)	p, combination-facilitated vs primary PCI	p, combination-facilitated vs abciximab-facilitated
Primary end point* at 90 days	10.7	10.5	9.8	NS	NS
>70% ST segment resolution within 60–90 min	31.0	33.1	43.9	0.003	0.01
TIMI major or minor bleeding through discharge or day 7	6.9	10.1	14.5	<0.001	0.008

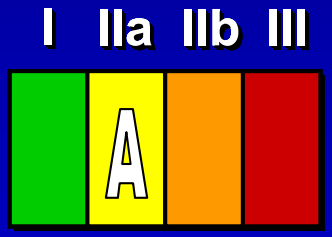
*All-cause mortality; rehospitalization or emergency department treatment for CHF; resuscitated ventricular fibrillation occurring >48 hours after randomization; cardiogenic shock

Ellis et al. N Eng J Med. 2008;358:2205-2217

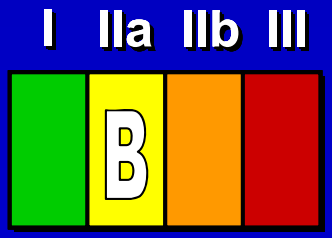
Use of Glycoprotein IIb/IIIa Receptor Antagonists in STEMI

Modified Recommendation

It is reasonable to start treatment with glycoprotein IIb/IIIa receptor antagonists at the time of primary PCI (with or without stenting) in selected patients with STEMI:



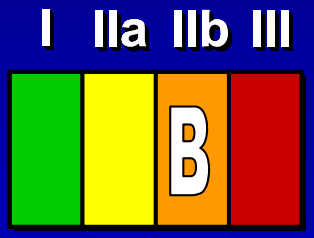
abciximab



tirofiban and eptifibatide

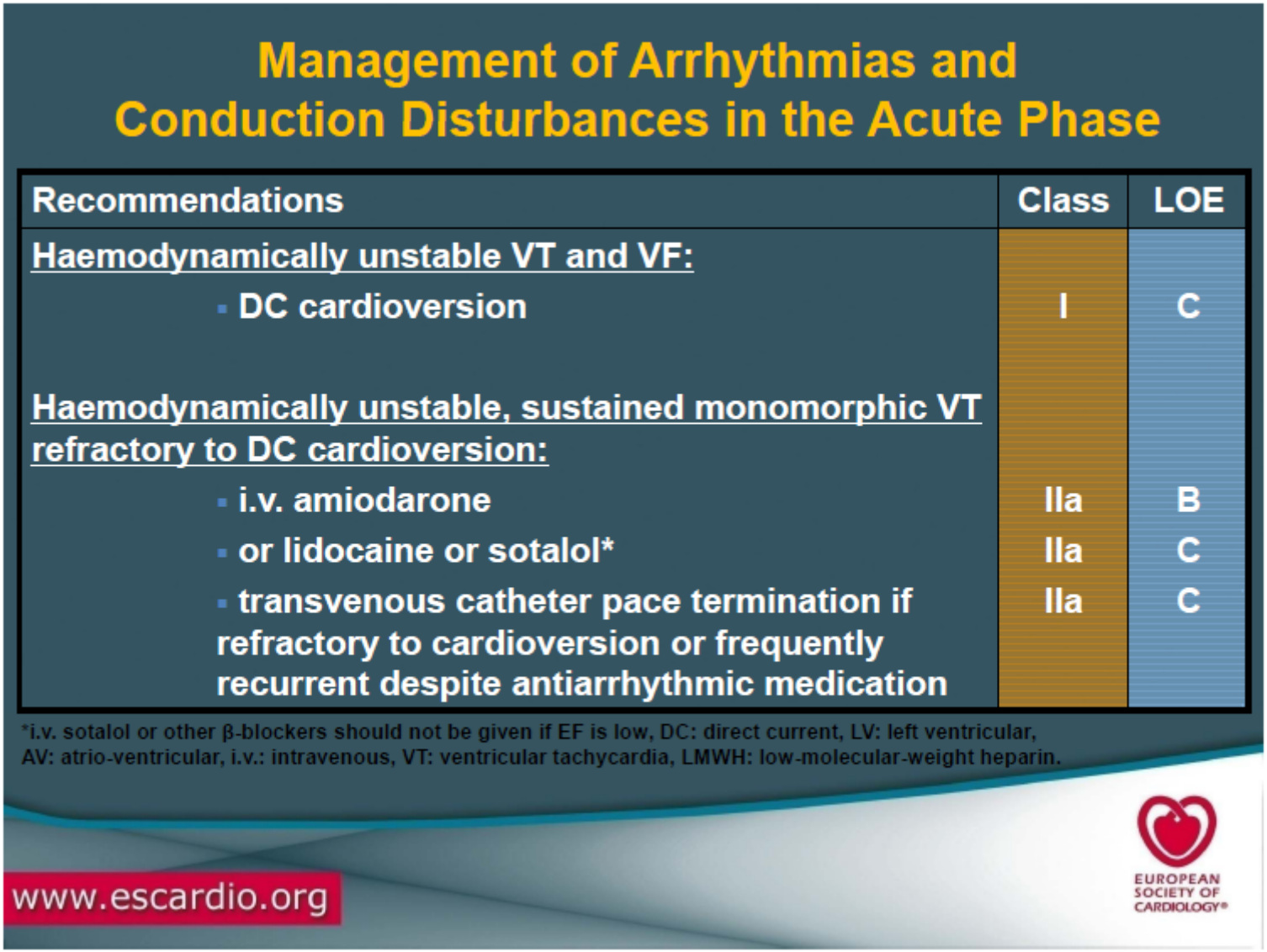
Use of Glycoprotein IIb/IIIa Receptor Antagonists in STEMI

Modified Recommendation



The usefulness of glycoprotein IIb/IIIa receptor antagonists (as part of a preparatory pharmacologic strategy for patients with STEMI prior to arrival in the cardiac catheterization laboratory for angiography and PCI) is uncertain.

Acute Myocardial Infarction with ST elevation Therapy



Management of Arrhythmias and Conduction Disturbances in the Acute Phase

Recommendations	Class	LOE
Haemodynamically unstable VT and VF:		
▪ DC cardioversion	I	C
Haemodynamically unstable, sustained monomorphic VT refractory to DC cardioversion:		
▪ i.v. amiodarone	IIa	B
▪ or lidocaine or sotalol*	IIa	C
▪ transvenous catheter pace termination if refractory to cardioversion or frequently recurrent despite antiarrhythmic medication	IIa	C

*i.v. sotalol or other β-blockers should not be given if EF is low, DC: direct current, LV: left ventricular, AV: atrio-ventricular, i.v.: intravenous, VT: ventricular tachycardia, LMWH: low-molecular-weight heparin.

Acute Myocardial Infarction with ST elevation Therapy

Management of Arrhythmias and Conduction Disturbances in the Acute Phase

Recommendations	Class	LOE
<u>Rate control of atrial fibrillation</u>		
▪ i.v. beta blockers or non-dihydropyridine calcium antagonists (e.g. diltiazem, verapamil)**. If no clinical signs of heart failure, bronchospasm (only for beta blockers), or AV block	I	C
▪ i.v. amiodarone to slow a rapid ventricular response and improve LV function	I	C
▪ i.v. digitalis if severe LV dysfunction and/or heart failure	IIb	C
▪ Electrical cardioversion if severe haemodynamic compromise or intractable ischaemia, or when adequate rate control cannot be achieved with pharmacological agents.	I	C

** These calcium antagonists should be used cautiously or avoided in patients with heart failure because of their negative inotropic effects.

DC: direct current, AV: atrio-ventricular,VT: ventricular tachycardia, LMWH: low-molecular-weight heparin.

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Acute Myocardial Infarction with ST elevation Therapy

Intravenous Doses of Recommended Antiarrhythmic Medications

Drug	Bolus	Maintenance infusion
Amiodarone:	150 mg over 10 min. Supplemental boluses of 150 mg may be given over 10 to 30 min for recurrent arrhythmias, but limited to 6-8 supplemental boluses in any 24-h period	1 mg/min for 6 h and then 0.5 mg/min may be necessary after initial bolus dose
Esmolol: Metoprolol: Atenolol: Propranolol:	500 µg/kg over 1 min, followed by 50 µg/kg/min over 4 min. 2.5 - 5 mg over 2 min; up to 3 doses 5 - 10 mg (1 mg/min) 0.15 mg/kg	60 to 200 µg/kg/min - - - -
Digoxin:	0.25 mg each 2 h, up to 1.5 mg	-
Lidocaine:	0.5 - 0.75 mg/kg	-
Sotalol:	20 - 120 mg over 10 min (0.5 - 1.5 mg/kg). May be repeated after 6 h (maximum 640 mg/24 h).	-
Verapamil:	0.075 - 0.15 mg/kg over 2 min	-
Diltiazem:	0.25 mg/kg over 2 min	-

Acute Myocardial Infarction with ST elevation Therapy

Management of Arrhythmias and Conduction Disturbances in the Acute Phase

Recommendations	Class	LOE
Anticoagulation for atrial fibrillation		
▪ i.v. administration of a therapeutic dose of heparin or a LMWH	I	C
Sinus bradycardia associated with hypotension		
▪ i.v. atropine	I	C
▪ temporary pacing if failed response to atropine	I	C
AV block II (Mobitz 2) or AV block III with bradycardia that causes hypotension or heart failure		
▪ i.v. atropine	I	C
▪ temporary pacing if atropine fails	I	C

DC: direct current, AV: atrio-ventricular, VT: ventricular tachycardia, LMWH: low-molecular-weight heparin.

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Acute Myocardial Infarction with ST elevation Therapy

Intravenous Doses of Recommended Anti-bradycardia Medications

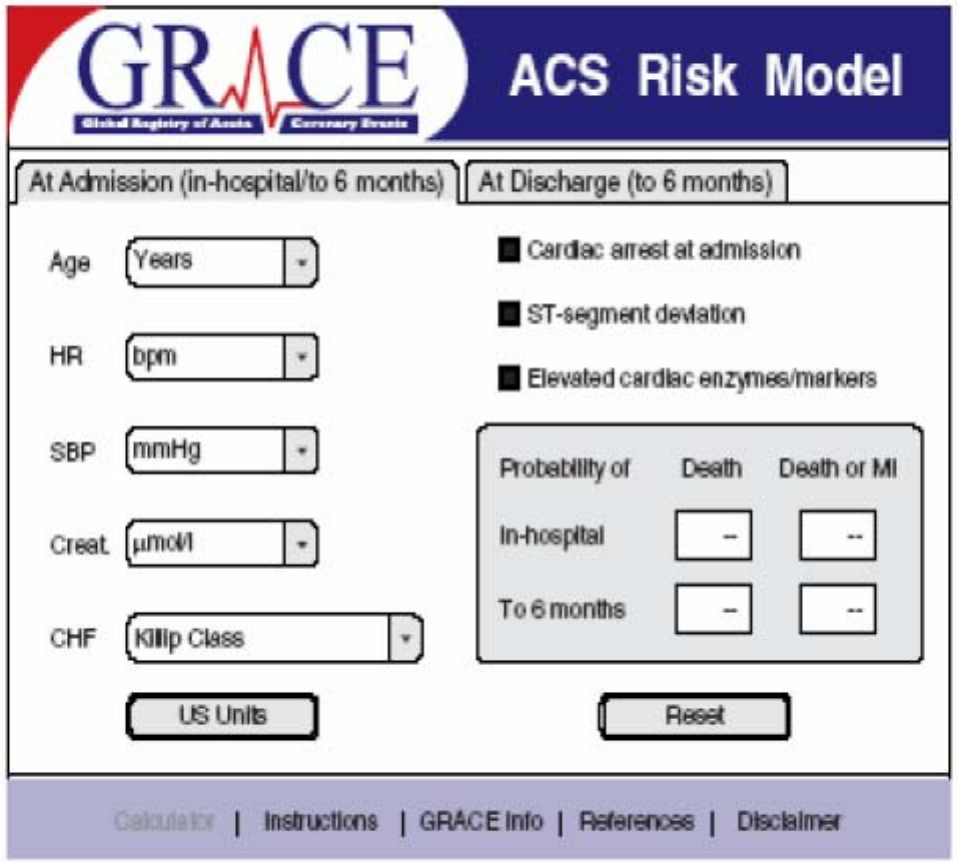
Drug	Bolus	Maintenance infusion
Atropine:	rapid bolus of at least 0.5 mg, repeated up to a total dose of 1.5 – 2.0 mg (0.04 mg/kg)	-
Isoproterenol:	0.05 – 0.1 µg/kg/min, up to 2 µg/kg/min. Dosage adjusted to heart rate and rhythm	-

ΟΞΥ ΣΤΕΦΑΝΙΑΙΟ ΣΥΝΔΡΟΜΟ ΧΩΡΙΣ ΑΝΑΣΠΑΣΗ ΤΟΥ ST

Recommendations for Diagnosis and Risk Stratification (1)

- Diagnosis and short-term risk stratification of NSTE-ACS should be based on a combination of clinical history, symptoms, ECG, biomarkers and risk score results (I-B).

GRACE ACS Risk Model



ESC Guidelines for the Management of NSTE-ACS (28)

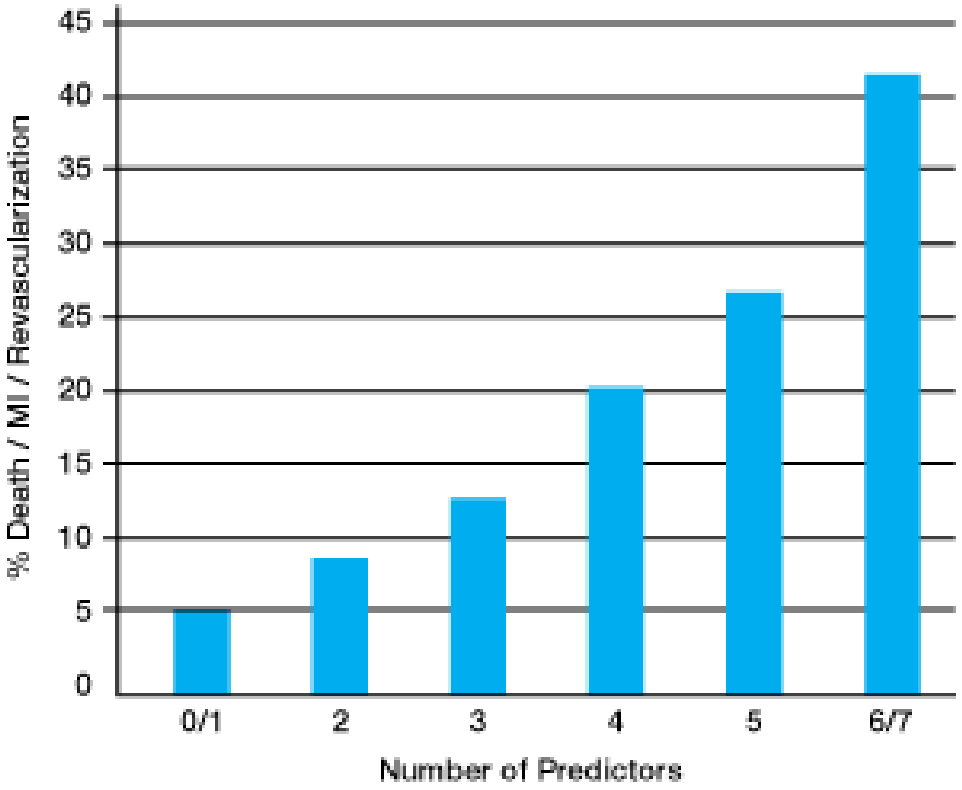
Mortality in hospital and at 6 months in low, intermediate and high risk categories in registry populations according to the GRACE Risk score http://www.outcomes.org/grace

Risk category (tertiles)	GRACE Risk Score	In-hospital deaths (%)
Low	<=108	<1
Intermediate	109-140	1-3
High	>140	>3
Risk category (tertiles)	**GRACE Risk Score**	**Post-discharge to 6 months deaths (%)**
Low	<=88	<3
Intermediate	89-118	3-8
High	>118	>8

TIMI RISC SCORE

Variables

1. Age ≥65 y
2. ≥3 CAD risk factors
   (high cholesterol,
   family history,
   hypertension
   diabetes, smoking)
3. Prior coronary stenosis >50%
4. Aspirin in last 7 days
5. ≥2 anginal events in ≤24 h
6. ST-segment deviation
7. Elevated cardiac markers
   (CK-MB or troponin)



Source: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson
P: *Hurst's The Heart*, 12th Edition: http://www.accessmedicine.com

Therapeutic Options

- Anti-ischaemic agents
- Anti-coagulants
  - UFH or LMWHs
  - Fondaparinux
  - Bivalirudin
- Anti-platelet agents
  - ASA
  - Clopidogrel
  - IIbIIIa Inhibitors
- Revascularisation

Recommendations for Anti-ischaemic Drugs

- Beta-blockers are recommended in the absence of contraindications, particularly in patients with hypertension or tachycardia (I-B).
- Intravenous or oral nitrates are effective for symptom relief in the acute management of anginal episodes (I-C).
- Calcium channel blockers provide symptom relief in patients already receiving nitrates and beta-blockers; they are useful in patients with contraindications to beta-blockade, and in the subgroup of patients with vaso-spastic angina (I-B).
- Nifedipine, or other dihydropyridines, should not be used (III-B), unless combined with beta-blockers (IIa-B)

ESC Guidelines for the Management of NSTE-ACS (36)

What's New with Anti-coagulants

1 - Pharmacological Treatment

- Superior efficacy with equivalent safety of enoxaparin over UFH (Petersen meta-analysis)
- Fondaparinux non-inferior to enoxaparin in OASIS-5
- Fondaparinux reduced bleeding rate by ~ 50% in OASIS-5
- Reduction in bleeding impacts on outcome (significant risk reduction for death, MI and stroke)

2 - Anti-coagulants in the Setting of PCI

- Enoxaparin is not superior to UFH in SYNERGY
- Bivalirudin superior to UFH/LMWH + GPIIb/IIIA inhibitors in ACUITY

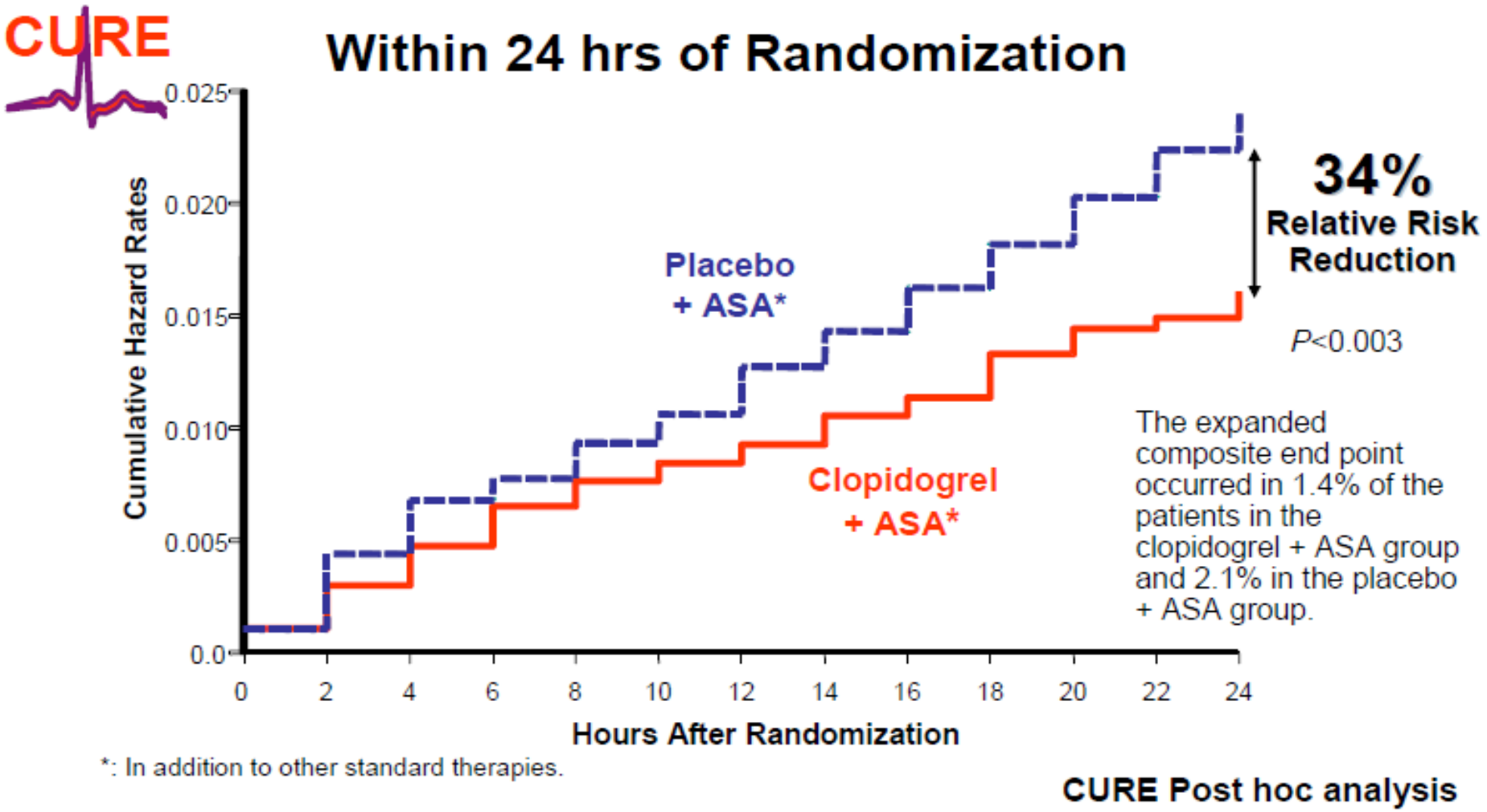
Recommendations for Oral Antiplatelet Drugs (1)

- Aspirin is recommended for all patients presenting with NSTE-ACS without contraindication at an initial loading dose of 160 - 325mg (non-enteric) (I-A), and at a maintenance dose of 75 to 100mg long-term (I-A).

- For all patients, immediate 300mg loading dose of clopidogrel is recommended, followed by 75mg clopidogrel daily (I-A). Clopidogrel should be maintained for 12 months unless there is an excessive risk of bleeding (I-A).

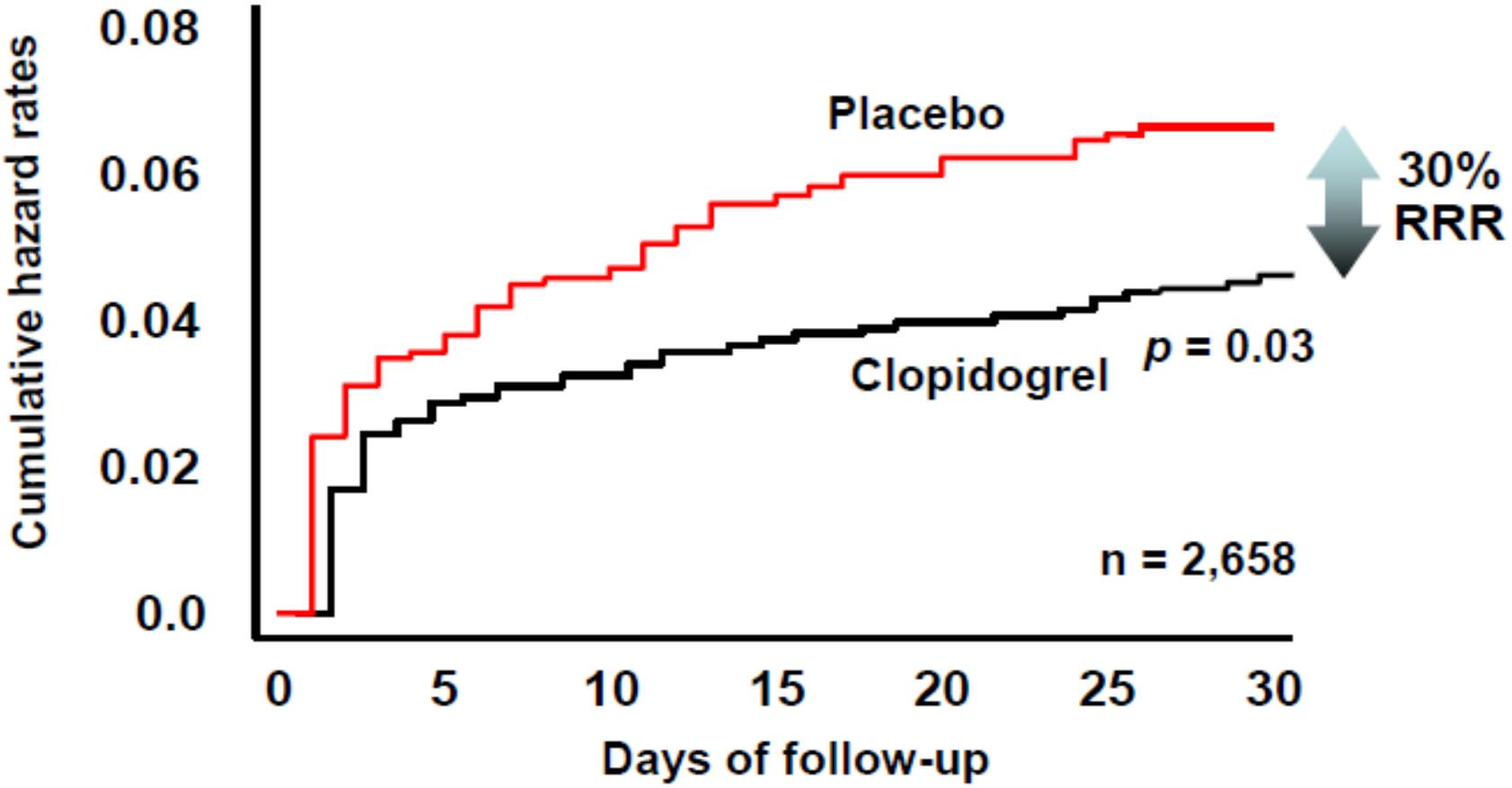
- For all patients with contraindication to aspirin, clopidogrel should be given instead (I-B).

Clopidogrel in unstable angina: The CURE Trial
Death, MI, stroke, severe ischemia 24 hours



Yusuf S et al for the CURE Trial Investigators. *Circulation*. 2003;107:966-972

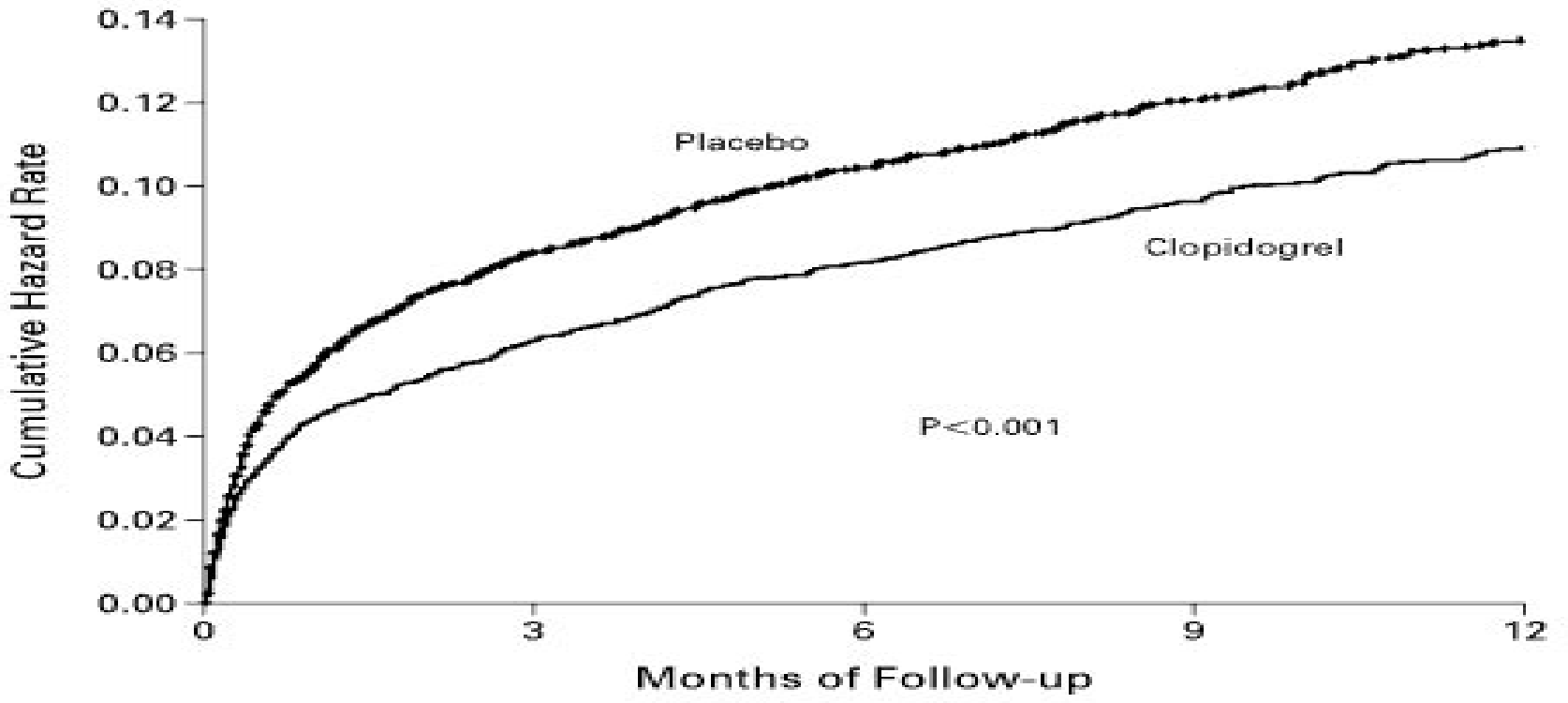
Clopidogrel in unstable angina: The CURE Trial
Death, MI, urgent revascularization 30 days



Pretreatment with clopidogrel (in addition to ASA) in patients with ACS undergoing PCI is beneficial in reducing major ischaemic events up to 30 days after PCI

Mehta SR *et al. Lancet* 2001;358:527–533

Clopidogrel in unstable angina: The CURE Trial
Death, MI, 12 months



No. at Risk					
Placebo	6303	5780	4664	3600	2388
Clopidogrel	6259	5866	4779	3644	2418

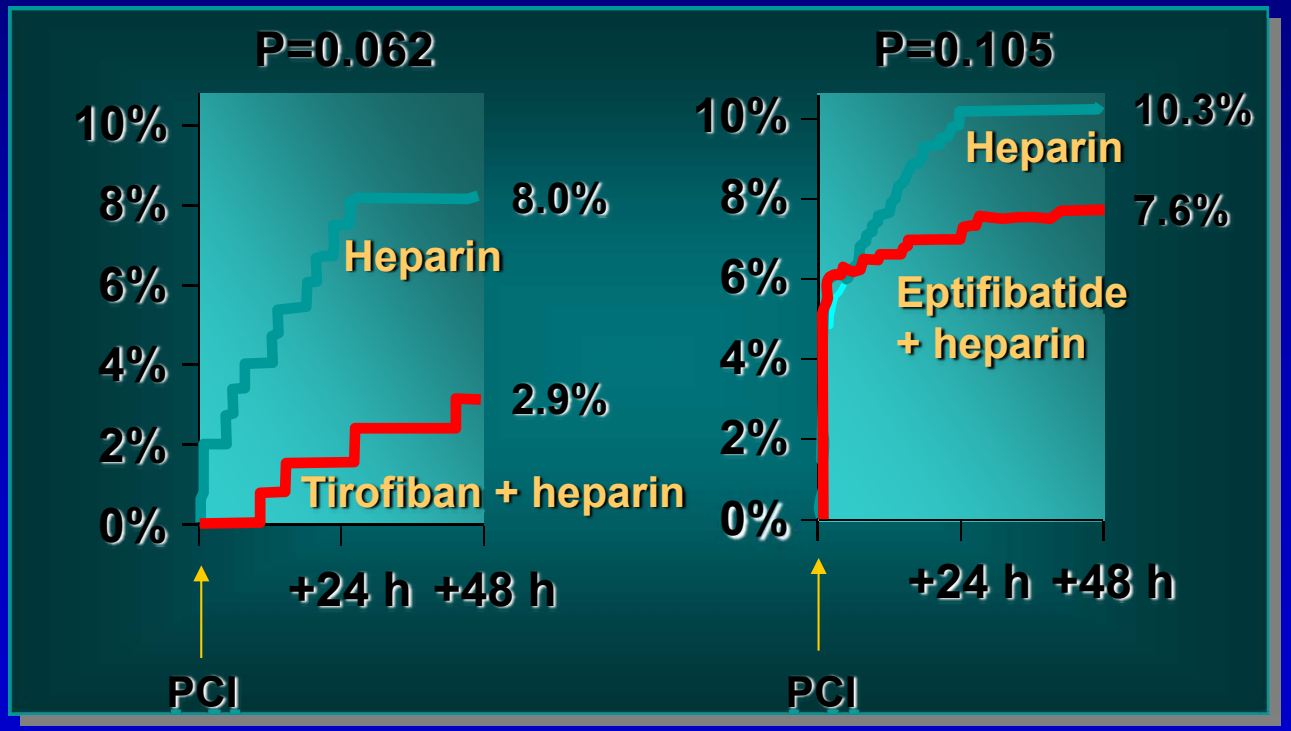
The Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. ***N Engl J Med 2001;345:494-502***

Glycoprotein IIb/IIIa Receptor Antagonists in Non-STEMI

IIb/IIIa inhibitors in NSTEMI/UA: Death/MI conservative strategy

PRISM-PLUS
N=287
Heparin vs.
Tirofiban/heparin

PURSUIT
N=1228
Heparin vs.
Eptifibatide/heparin



PCI in 31%

PCI in 13 %

Recommendations for GP IIb/IIIa Inhibitors (1)

- In patients at intermediate to high risk, particularly patients with elevated troponins, ST-depression, or diabetes, either eptifibatide or tirofiban for initial early treatment are recommended in addition to oral antiplatelet agents (IIa-A).

- The choice of combination of antiplatelet agents and anticoagulants should be made in relation to risk of ischaemic and bleeding events. (I-B)

- Patients who received initial treatment with eptifibatide or tirofiban prior to angiography, should be maintained on the same drug during and after PCI (IIa-B)

ESC Guidelines for the Management of NSTE-ACS (65)

ΟΞΕΙΑ ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ

Acute Heart Failure

- **ACUTE HF** is defined as a rapid onset or change in the signs and symptoms of HF, resulting in the need of urgent therapy
- It may present as new HF or worsening HF in the presence of chronic HF
- It may be associated with worsening symptoms or signs or as a medical emergency such as acute pulmonary oedema
- Multiple cardiovascular and non-cardiovascular morbidities may precipitate AHF

Causes and precipitating factors in Acute Heart Failure

Ischaemic heart disease

- Acute coronary syndromes
- Mechanical complications of acute MI
- Right ventricular infarction

Valvular

- Valve stenosis
- Valvular regurgitation
- Endocarditis
- Aortic dissection

Myopathies

- Postpartum cardiomyopathy
- Acute myocarditis

Hypertension/arrhythmia

- Hypertension
- Acute arrhythmia

Circulatory failure

- Septicaemia
- Thyrotoxicosis
- Anaemia
- Shunts
- Tamponade
- Pulmonary embolism

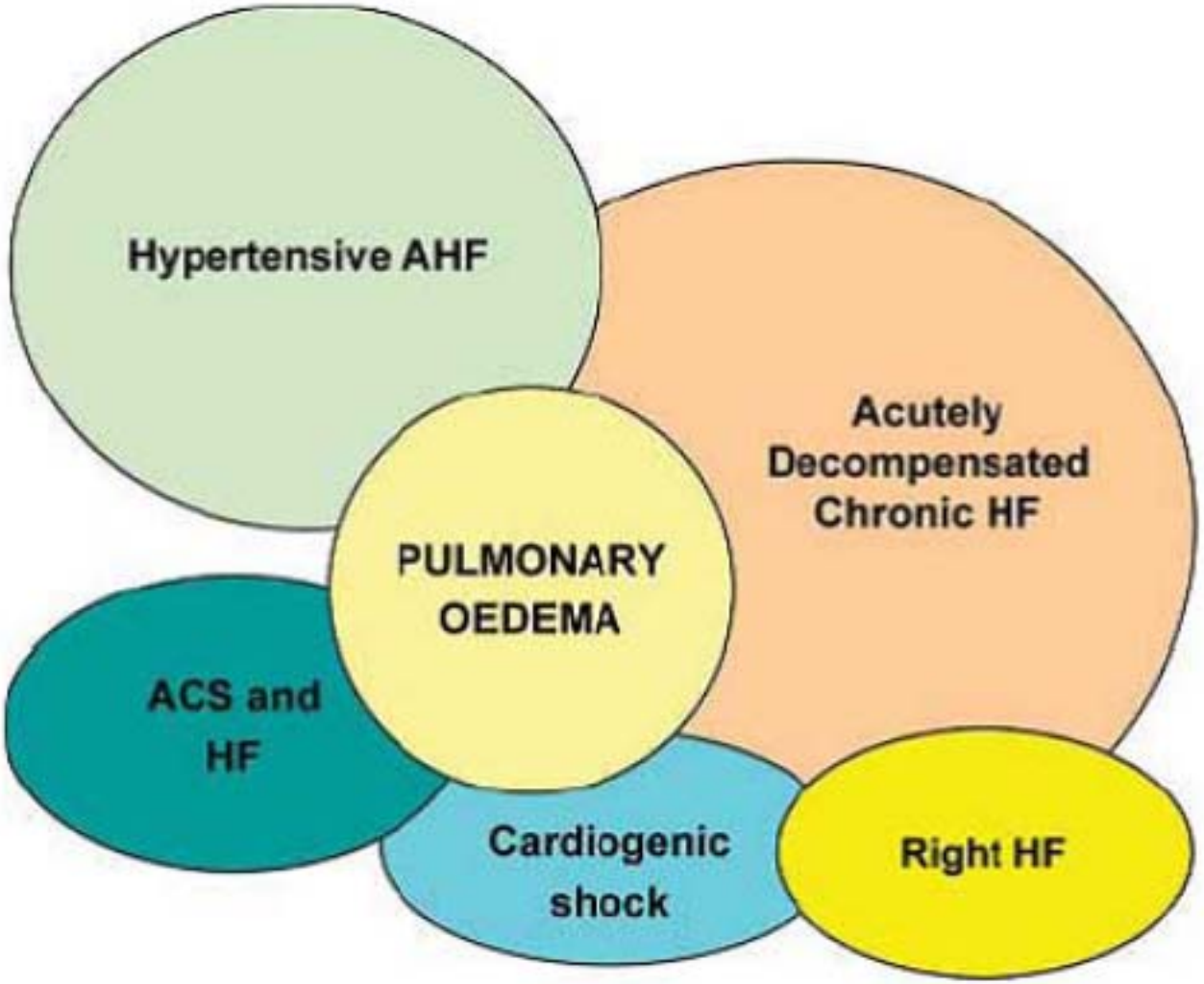
Decompensation of preexisting chronic HF

- Lack of adherence
- Volume overload
- Infections, especially pneumonia
- Cerebrovascular insult
- Surgery
- Renal dysfunction
- Asthma, COPD
- Drug abuse
- Alcohol abuse

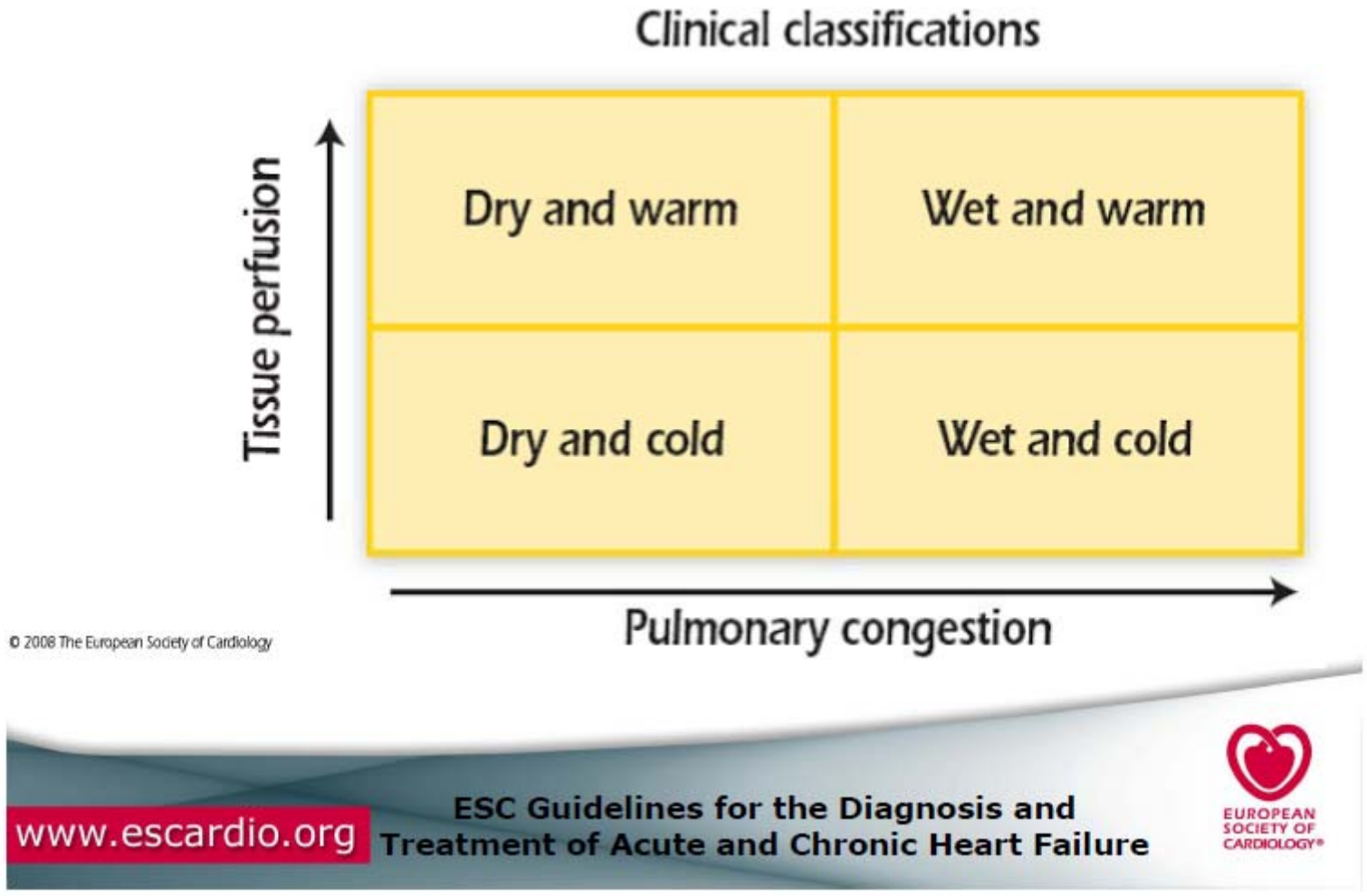
Precipitating factors that may cause acute decompensation in chronic heart failure patients

Dietary indiscretion
Inappropriate reduction in HF medications
Myocardial ischemia, infarction
Arrhythmias (tachycardia or bradycardia)
Infection
Anemia
Initiation of medications that worsen the symptoms of HF Calcium antagonists (verapamil, diltiazem) Beta blockers Nonsteroidal antiinflammatory drugs Thiazolidinediones Antiarrhythmic agents—all Class I agents, sotalol (Class III) Anti-TNF antibodies
Alcohol consumption
Pregnancy
Worsening hypertension
Acute valvular insufficiency

Clinical Classification of Acute Heart Failure



Clinical assessment of pts with acute heart failure



ACUTE HEART FAILURE

Acute heart failure may present in three ways:

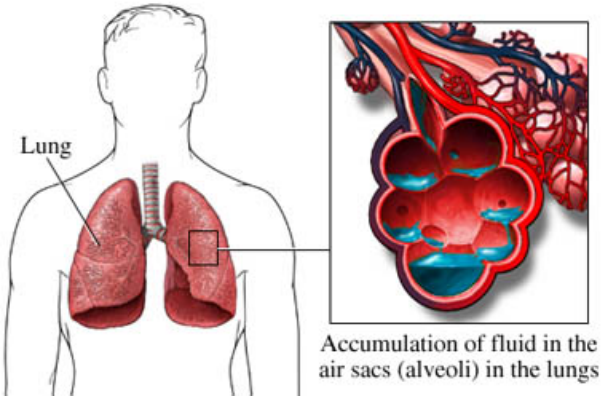
- Acute cardiogenic pulmonary edema..
- Cardiogenic shock..
- Acute decompensation of chronic heart failure..

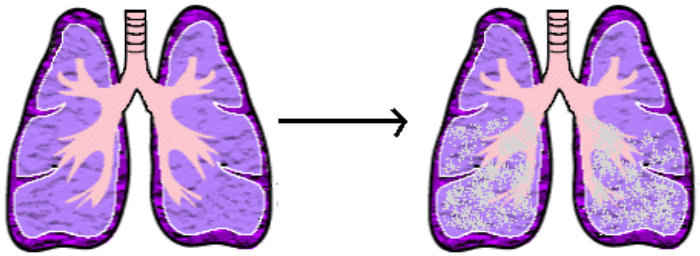
Goals of treatment in acute heart failure

- **Immediate (ED/ICU/CCU)**
  - Improve symptoms
  - Restore oxygenation
  - Improve organ perfusion and haemodynamics
  - Limit cardiac/renal damage
  - Minimize ICU length of stay
- **Intermediate (in hospital)**
  - Stabilize patient and optimize treatment strategy
  - Initiate appropriate (life-saving) pharmacological therapy
  - Consider device therapy in appropriate patients
  - Minimize hospital length of stay
- **Long-term and pre-discharge management**
  - Plan follow-up strategy
  - Educate and initiate appropriate lifestyle adjustments
  - Provide adequate secondary prophylaxis
  - Prevent early readmission
  - Improve quality of life and survival

ACUTE CARDIOGENIC PULMONARY EDEMA

- An increase in the fluid content of the extravascular tissues of the lung is known as pulmonary edema..
- It is a life-threatening emergency characterized by extreme breathlessness..





EMS Management

- Sit upright
- High Flow O_2
- NTG (If SBP > 100)
- Diuretics (furosemide) – use care
- Morphine (base consult)
- Ventilatory Support
  - BVM
  - CPAP
  - intubation/ventilation

MANAGEMENT

1. The patient should be placed in a **sitting position..**
   - This facilitates respiration and reduces venous return..
   - Pulse oximeter should be connected to see oxygen saturation..

2. **High concentration oxygen** by mask, or nasal cannulae to keep PO_2 greater than 60 mmHg.

Non-invasive pressure support ventilation may improve oxygenation and prevent CO_2 retention.

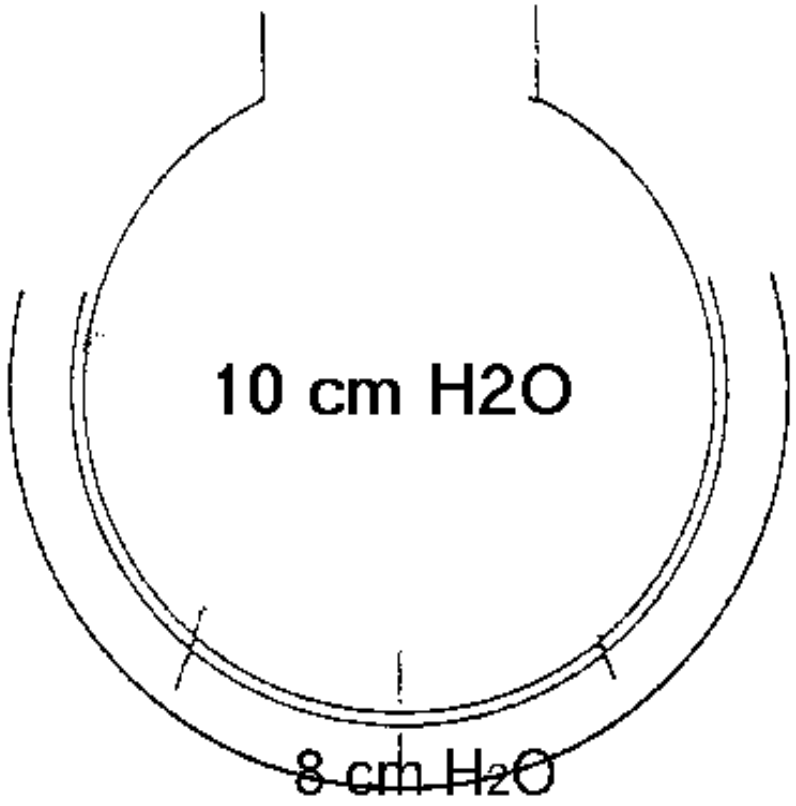
If respiratory distress remain severe, endotracheal intubation and mechanical ventilation may be necessary.

CPAP - Introduction

- CPAP is a non-invasive procedure that is easily applied and can be easily discontinued without untoward patient discomfort.
- CPAP is an established therapeutic modality, recently introduced into the prehospital setting.
- In the primary phase CPAP application in cardiogenic pulmonary edema, thus far, appears to be beneficial to patient outcome.

CPAP Mechanism

- Increases pressure within airway.
- Airways at risk for collapse from excess fluid are stented open.
- Gas exchange is maintained
- Increased work of breathing is minimized



Absolute Contraindications

- Age < 8
- Respiratory or Cardiac Arrest
- Agonal Respirations
- Systolic Blood Pressure < 90
- Pneumothorax
- Major Trauma, esp. head injury with increased ICP or significant chest trauma
- Facial Anomalies (e.g. burns, fractures)
- Vomiting

Relative Contraindications

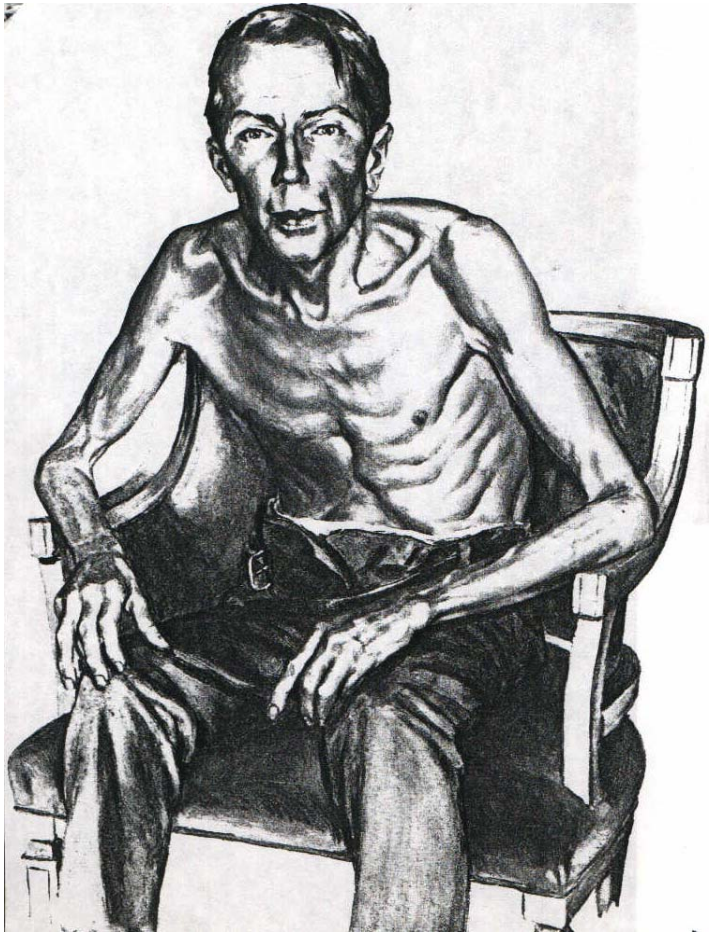
- History of Asthma/COPD
- History of Pulmonary Fibrosis
- Claustrophobia or unable to tolerate mask (after initial 1-2 minutes)

Complications

- Hypotension
- Pneumothorax
- Corneal Drying

Important Points (cont.)

- COPD and Asthmatic patients do *NOT* respond predictably to CPAP.
  - They have a higher risk of complications such as pneumothorax, and thus should *not* be treated in the field with CPAP



CPAP vs. Intubation

- CPAP
  - Non-invasive
  - Easily discontinued
  - Easily adjusted
  - Does not require sedation
  - Comfortable
- Intubation
  - Invasive
  - Usually don’t extubate in field
  - Potential for infection
  - Traumatic

3. **Morphine** (2-5 mg IV) can be repeated every 10-25 minutes until an effect is seen

- **decreases anxiety**
- **increases venous capacitance**
- **lower left atrial pressure (i.e. decreasing pre-load)**
- **improve the breathlessness..**

N.B. Morphine must be avoided if the systolic B.P. is < 90 mmHg.

4. **Diuretics**

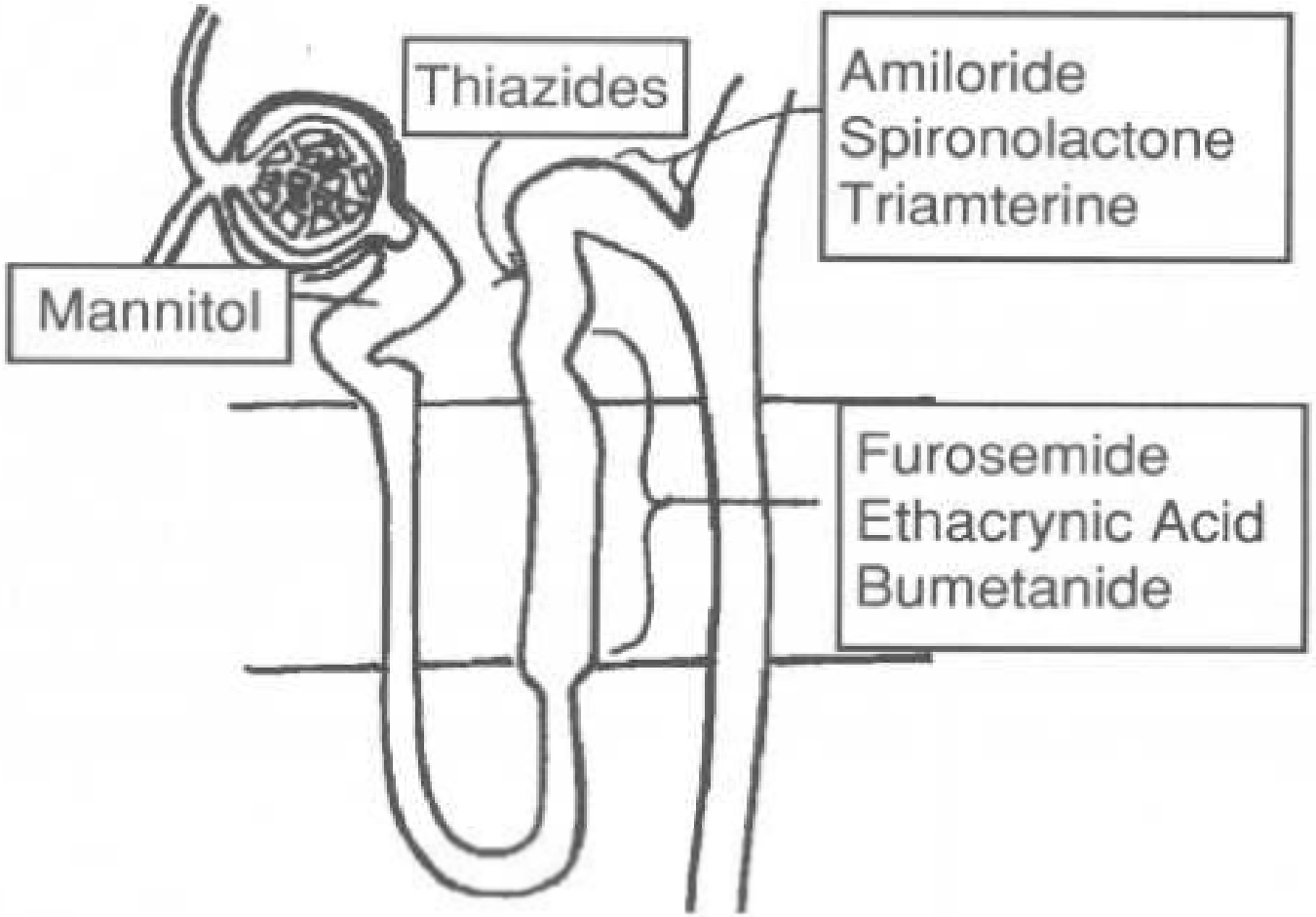
Inj. Lasix >> immediate vasodilatation, decreases pulmonary congestion within minutes, **well before its diuretic action begins.**

(an initial dose of 20-80 mg IV and can be increase based on response, to a maximum of 200mg in subsequent doses).

5. **Vasodilators**

e.g. nitroglycerine >> relief by reducing the preload.

ΔΙΟΥΡΗΤΙΚΑ: *τόπος δράσης*



ΔΙΟΥΡΗΤΙΚΑ: μηχανισμοί

- Αυξάνουν την νεφρική απέκκριση νατρίου (νατριουρητικά) ή αποβαλλόμενα τα ίδια (ωσμωτικώς δρώντα) συμπαρασύρουν ύδωρ αυξάνοντας έτσι τη διούρηση.
- Χορηγούνται για να μειωθεί ο βαθμός ενυδάτωσης τον οργανισμού και κατ᾽ επέκταση ο όγκος παλμού.
- Κλασσικά φάρμακα για την υπέρταση και την καρδιακή ανεπάρκεια

ΔΙΟΥΡΗΤΙΚΑ: ανεπιθύμητες ενέργειες

- **Ανεπιθύμητη ενέργεια των ανταγωνιστών της αλδοστερόνης και των προστατευτικών της απώλειας καλίου διουρητικών είναι η υπερκαλιαιμία, ενώ των καλιουρητικών η υποκαλιαιμία.**
- **Κοινή ανεπιθύμητη ενέργεια και των δύο κατηγοριών είναι η υπονατριαιμία.**
- **Όλων των διουρητικών πιθανή ανεπιθύμητη ενέργεια είναι η αφυδάτωση, ιδιαιτέρως όταν συνυπάρχουν και άλλοι παράγοντες, όπως π.χ. πυρετός, διάρροια και ιδίως σε ηλικιωμένα άτομα τους θερινούς μήνες.**
- **Η φουροσεμίδη ενδέχεται να μειώσει το ασβέστιο τον ορού, ενώ οι θειαζίδες να το αυξήσουν.**

Indications and Dosing of diuretics in acute heart failure

Fluid retention	Diuretic	Daily Dose (mg)	Comments
Moderate	furosemide or bumetanide or torasemide	20 - 40 0.5 - 1 10 - 20	Oral or i.v. according to clinical symptoms Titrate dose according to clinical response - Monitor K, Na, creatinine, blood pressure
Severe	furosemide furosemide infusion bumetanide torasemide	40 - 100 (5 - 40 mg/h) 1 - 4 20 - 100	i.v. Increase dose. better than very high bolus doses oral or i.v. oral
Refractory to loop diuretic	add hydrochlorothiazide or metolazone or spironolactone	50 - 100 2.5 - 10 25 - 50	Combination better than very high dose of loop diuretics MTZ more potent if creatinine clr < 30ml/min Spironolactone best choice if no renal failure and normal or low serum potassium
With alkalosis	acetazolamide	0.5 mg	i.v.
Refractory to loop diuretics and thiazides	add dopamine (renal vasodilation) or dobutamine		Consider ultrafiltration or haemodialysis if coexisting renal failure Hyponatraemia

Diuretics Dosage

Diuretics	Initial dose (mg)		Usual daily dose (mg)	
Loop diuretics*				
▪ furosemide	20 - 40		40 - 240	
▪ bumetanide	0.5 - 1.0		1 - 5	
▪ torasemide	5 - 10		10 - 20	
Thiazides**				
▪ bendroflumethiazide	2.5		2.5 - 10	
▪ hydrochlorothiazide	25		12.5 - 100	
▪ metolazone	2.5		2.5 - 10	
▪ indapamide	2.5		2.5 - 5	
Potassium-sparing diuretics***				
	+ ACEI/ARB	– ACEI/ARB	+ ACEI/ARB	– ACEI/ARB
▪ spironolactone/ eplerenone	12.5 - 25	50	50	100 - 200
▪ amiloride	2.5	5	20	40
▪ triamterene	25	50	100	200

Indications and Dosing of vasodilators in acute heart failure

Vasodilator	Indication	Dosing	Main side-effects	Other
Nitroglycerine	Pulmonary congestion/oedema BP >90 mmHg	Start 10–20 μg/min, increase up to 200 μg/min	Hypotension, headache	Tolerance on continuous use
Isosorbide dinitrate	Pulmonary congestion/oedema BP >90 mmHg	Start with 1 mg/h, increase up to 10 μg/h	Hypotension, headache	Tolerance on continuous use
Nitroprusside	Hypertensive HF congestion/ oedema BP >90 mmHg	Start with 0.3 μg/kg/min and increase up to 5 μg/kg/min	Hypotension, isocyanate toxicity	Light sensitive
Nesiritide*	Pulmonary congestion/oedema BP >90 mmHg	Bolus 2 μg/kg + infusion 0.015–0.03 μg/kg/min	Hypotension	

6. **Nebulization with salbutamol**

Nebulization with aerolin may be required because bronchospasm may occur in response to pulmonary edema..

7. **Inotropic agents**

Required in low output states particularly when hypotension is present. Dobutamin improves cardiac contraction in severe heart failure.

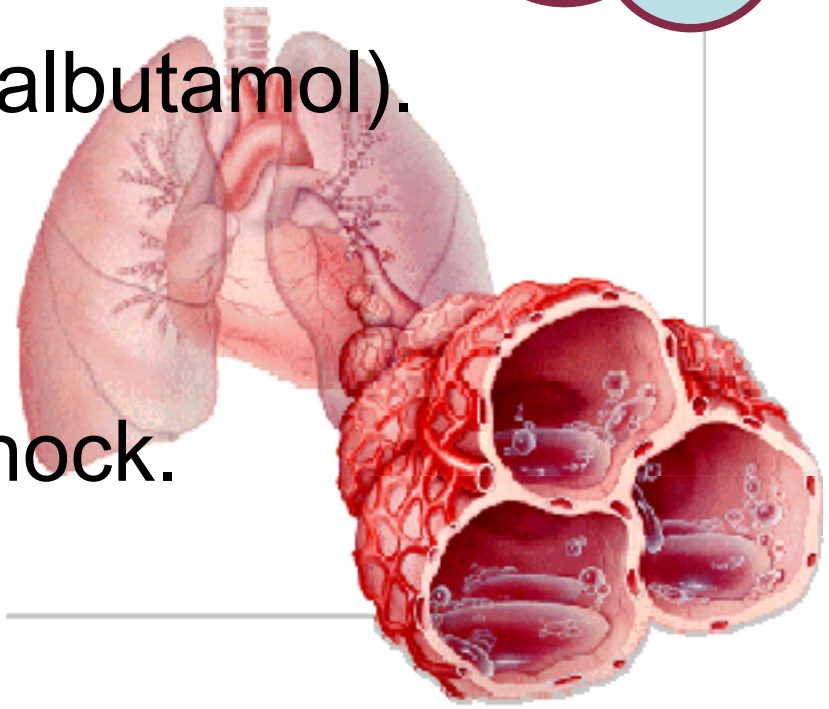
Dosing of inotropes in acute heart failure

	Bolus	Infusion rate
Dobutamine	No	2 to 20 µg/kg/min (ß+)
Dopamine	No	< 3 µg/kg/min: renal effect (δ+) 3 - 5 µg/kg/min: inotropic (ß+) > 5 µg/kg/min: (ß+), vasopressor (α+)
Milrinone	25 - 75 µg/kg over 10 - 20 min	0.375 - 0.75 µg/kg/min
Enoximone	0.25 - 0.75 mg/kg	1.25 - 7.5 µg/kg/min
Levosimendan*	12 µg/kg over 10 min (optional)**	0.1 µg/kg/min which can be decreased to 0.05 or increased to 0.2 µg/kg/min
Norepinephrine	No	0,2 - 1,0 µg/kg/min
Epinephrine	Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3 - 5 min	0.05 - 0.5 µg/kg/min

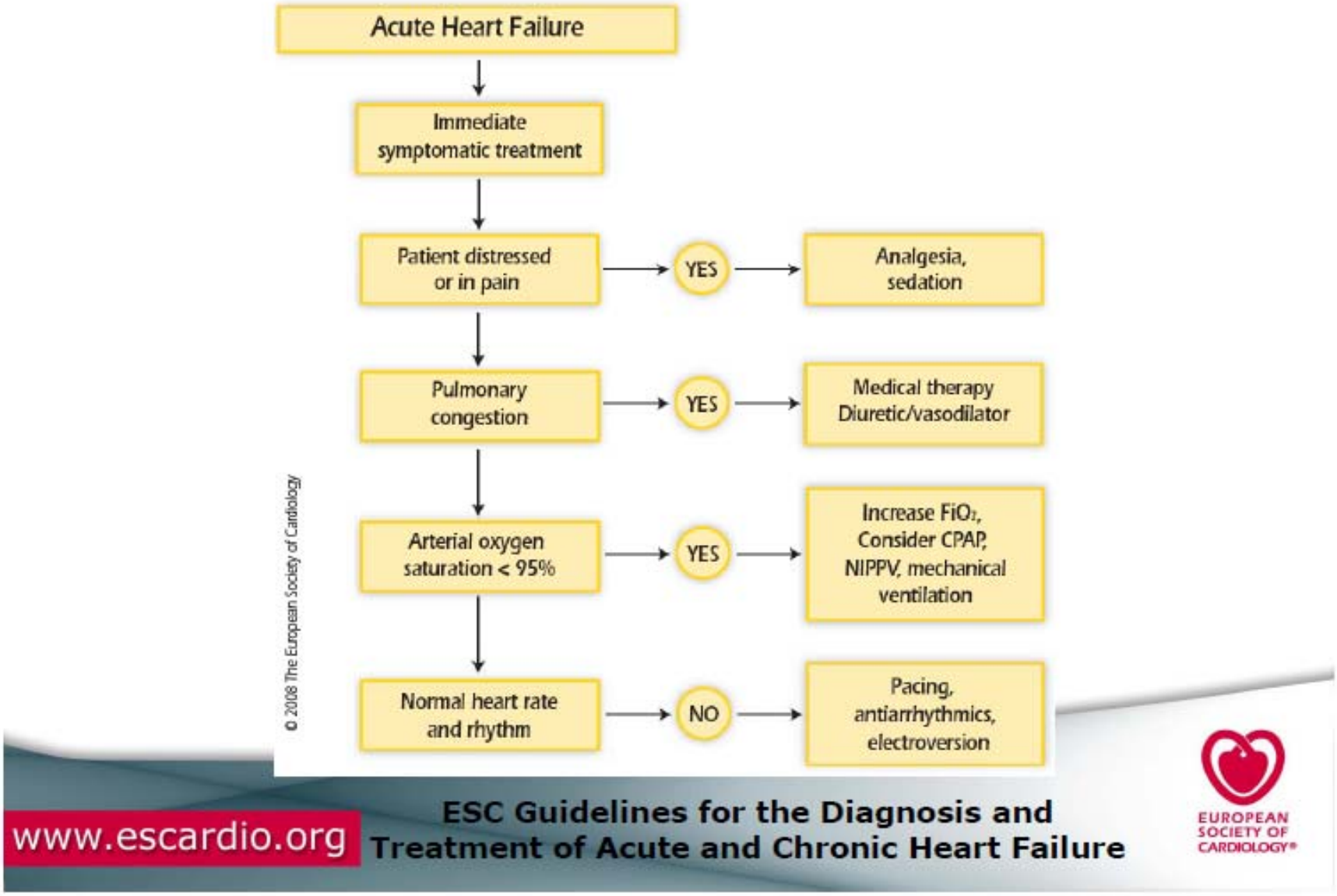
* This agent also has vasodilator properties.

** In hypotensive patients. (SBP < 100 mmHg) initiation of therapy without a bolus is recommended.

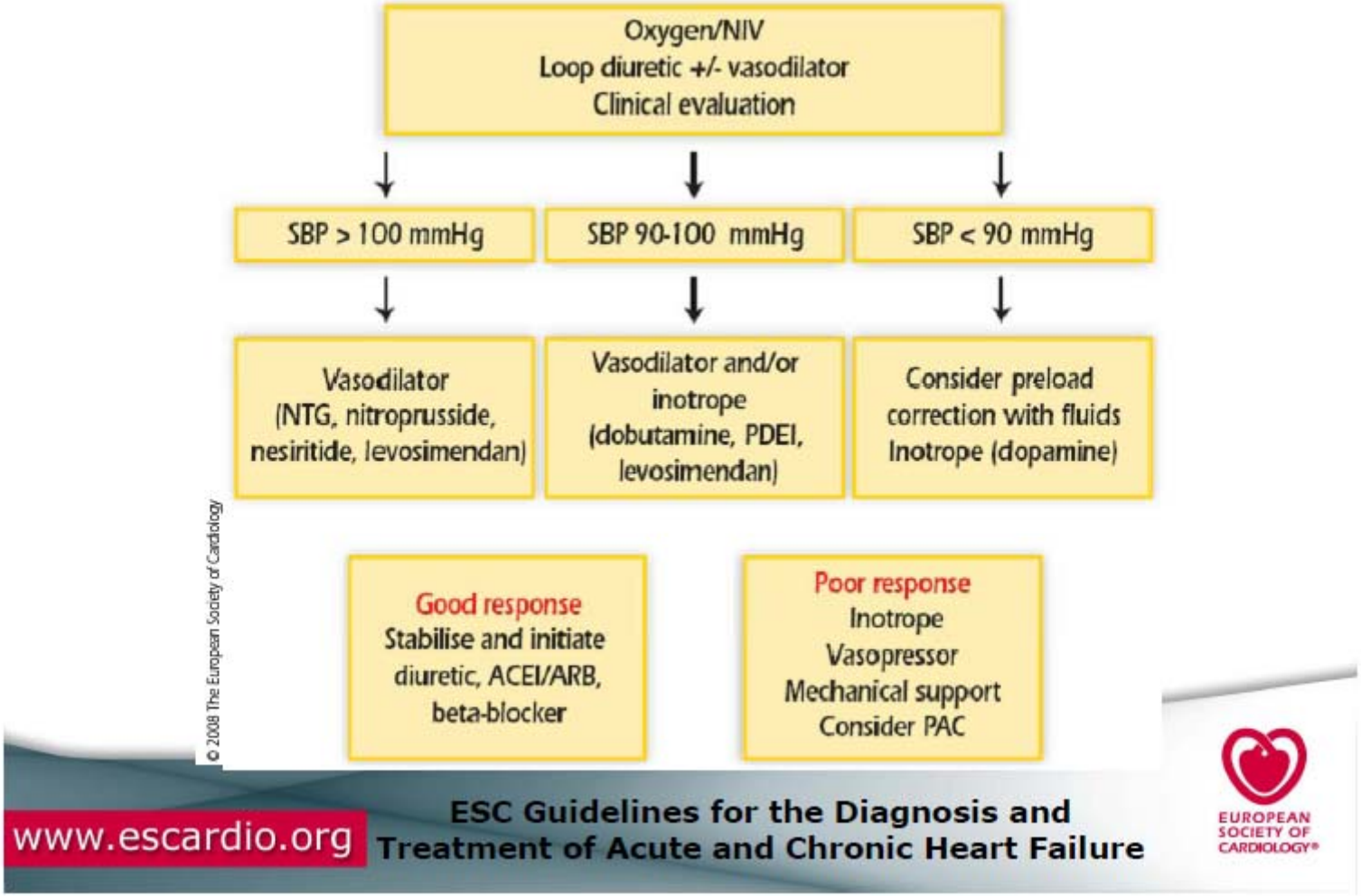
- U →→ upright sitting position.
- N →→ Nitroglycerine.
- L →→ Lasix.
- O →→ Oxygen.
- A →→ Albuterol (salbutamol).
- D →→ Dobutamin.
- M →→ Morphine.
- E →→ Electrical shock.



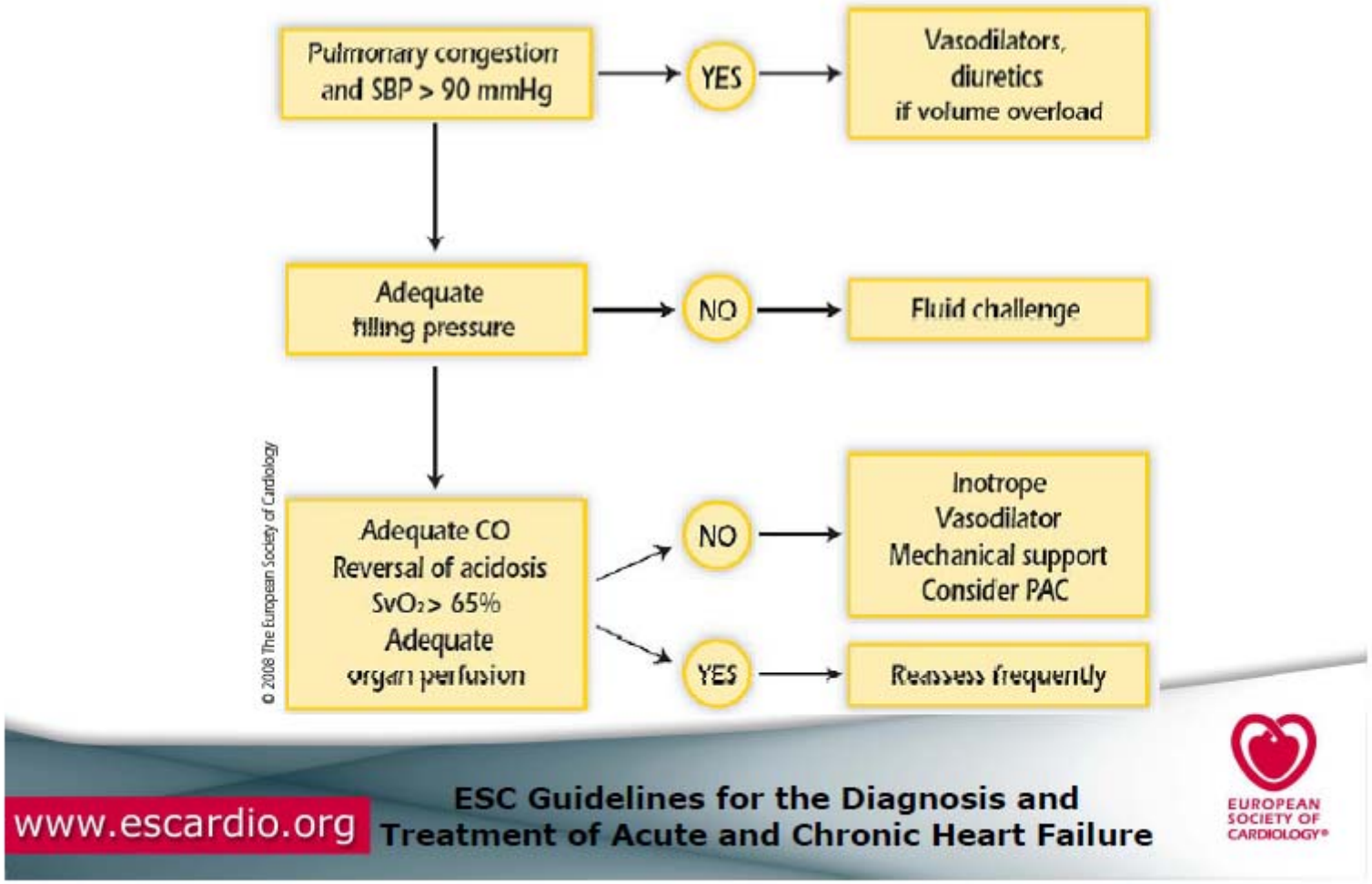
Initial treatment algorithm in Acute Heart Failure



Treatment Strategy in acute heart failure according to systolic blood pressure



Treatment Strategy in acute heart failure according to LV filling pressure



CARDIOGENIC SHOCK

- Cardiogenic shock (pump failure) is an extreme type of cardiac failure with a high mortality of approximately 90%.

- Shock is a severe failure of tissue perfusion, characterized by hypotension, a low cardiac output and signs of poor tissue perfusion such as oligourea, hypotension, cold extremities.

MANAGEMENT

- **In Coronary Care Unit,** if possible.

- **General measures:**

Complete rest.

Continuous 60% oxygen administration.

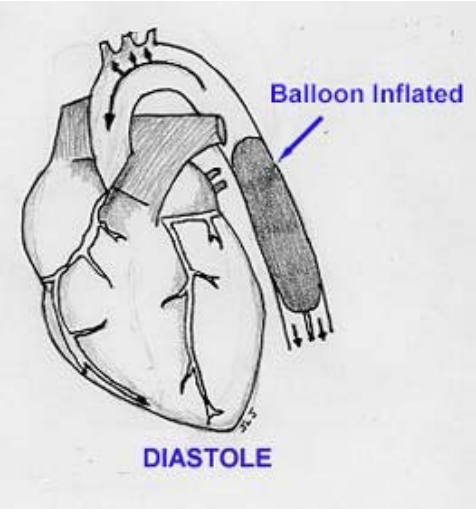
Pain and anxiety relief.

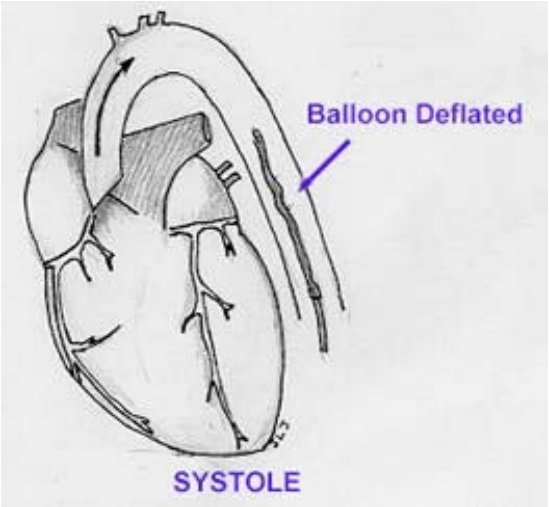
- **Inotropic support**

Dopamine and dobutamine, noradrenaline.

- **Intra-aortic balloon pump**

Mechanical device that assists the left ventricle.





- **Revascularization** by angioplasty or bypass surgery.

  Definitive therapy.

- **Thrombolysis**

  Less successful but it should be given if a patient is not a candidate of angioplasty or bypass surgery or if immediate revascularization is not available.

Acute Myocardial Infarction with ST elevation Therapy

Treatment of Pump Failure and Cardiogenic Shock (I)

Recommendations	Class	LOE
<u>Treatment of mild heart failure (Killip class II)</u>		
▪ O_2	I	C
▪ Loop diuretics: i.e. furosemide: 20–40 mg i.v. repeated at 1–4 hourly intervals if necessary	I	C
▪ nitrates: if no hypotension	I	C
▪ ACE-inhibitor in the absence of hypotension, hypovolaemia or renal failure	I	A
▪ angiotensin receptor blocker (valsartan) if ACE-inhibitor is not tolerated	I	B

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Acute Myocardial Infarction with ST elevation Therapy

Treatment of Pump Failure and Cardiogenic Shock (II)

Recommendations	Class	LOE
<u>Treatment of severe heart failure (Killip class III)</u>		
▪ O_2	I	C
▪ ventilatory support according to blood gasses	I	C
▪ furosemide: cfr. supra	I	C
▪ nitrates if no hypotension	I	C
▪ inotropic agents: dopamine	IIb	C
and/or dobutamine	IIa	B
▪ haemodynamic assessment with balloon floating catheter	IIb	B
▪ early revascularization	I	C

Acute Myocardial Infarction with ST elevation Therapy

Treatment of Pump Failure and Cardiogenic Shock (III)

Recommendations	Class	LOE
Treatment of shock (Killip class IV)		
▪ O_2	I	C
▪ mechanical ventilatory support according to blood gases	I	C
▪ haemodynamic assessment with balloon floating catheter	IIb	C
▪ inotropic agents: dopamine	IIb	B
and dobutamine	IIa	C
▪ intra-aortic balloon pump	I	C
▪ LV assist devices	IIa	C
▪ early revascularization	I	B

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”A clinical response to treatment directed at HF alone is not sufficient for the diagnosis, but is helpful when the diagnosis remains unclear after appropriate diagnostic investigations”

- Clinicians responsible for managing patients with HF must frequently make treatment decisions without adequate evidence or consensus expert opinion

Peter Bruggel 1527-69, « Hunters of the winter »