ΤΑ ΘΡΟΜΒΟΛΥΤΙΚΑ ΦΑΡΜΑΚΑ

-

ΘΡΟΜΒΟΛΥΣΗ

ΒΑΣΙΛΕΙΟΣ ΒΑΖΓΙΟΥΡΑΚΗΣ

ΕΙΔΙΚΟΣ ΚΑΡΔΙΟΛΟΓΟΣ

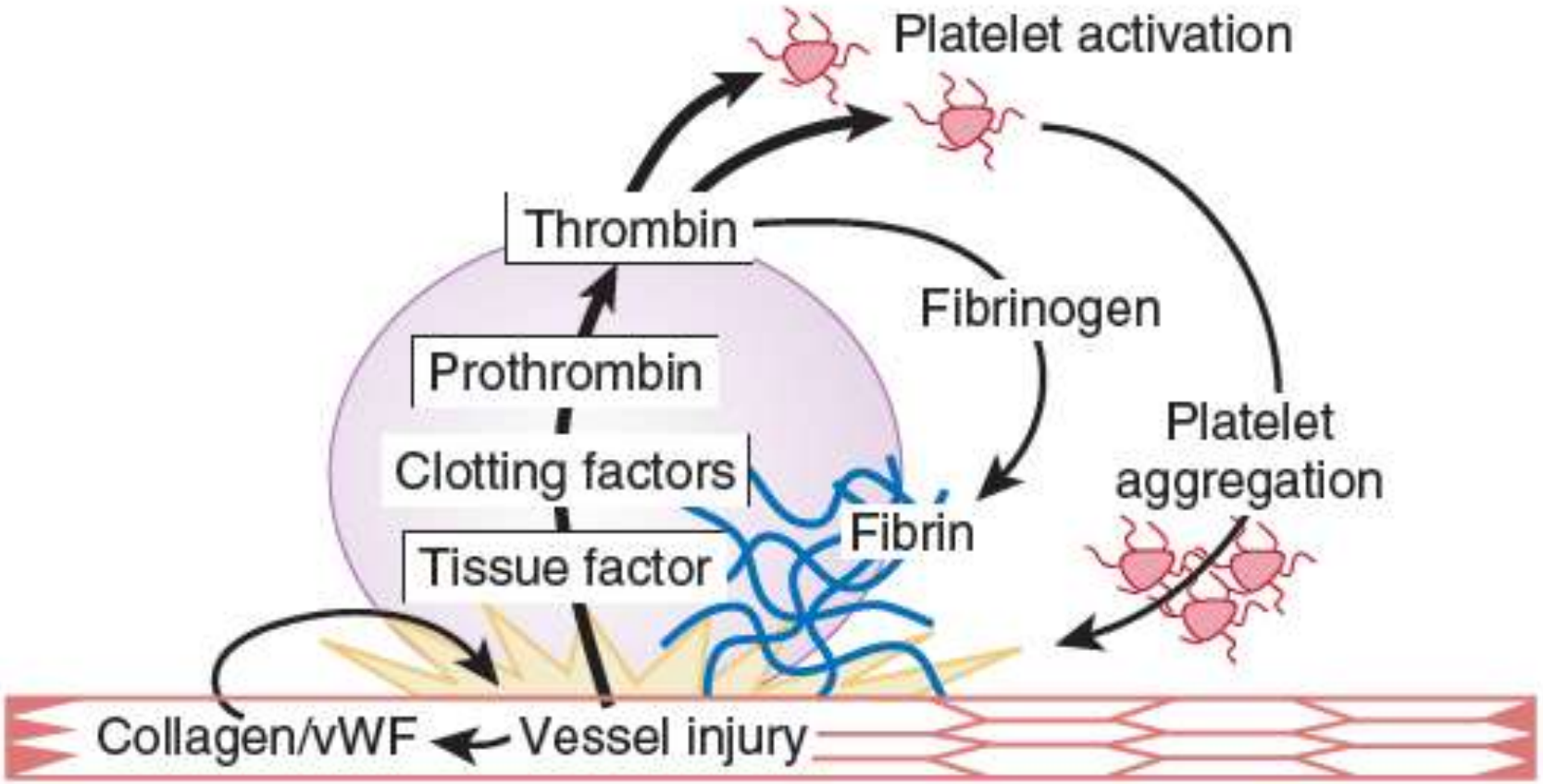
Μ.Ε.Θ. «ΒΕΝΙΖΕΛΕΙΟ» ΝΟΣΟΚΟΜΕΙΟ ΗΡΑΚΛΕΙΟΥ

Αιμόσταση, Θρόμβωση και Ινωδόλυση

- Αιμόσταση: Σημαντικό μέρος της φυσιολογικής ομοιοστατικής απόκρισης του οργανισμού που περιορίζει την αιμορραγία μετά από μικροσκοπική ή μακροσκοπική αγγειακή βλάβη.
- Ινωδόλυση: Φυσικό αντίβαρο της θρόμβωσης που περιορίζει την επέκταση του θρόμβου πέρα του σημείου της βλάβης.

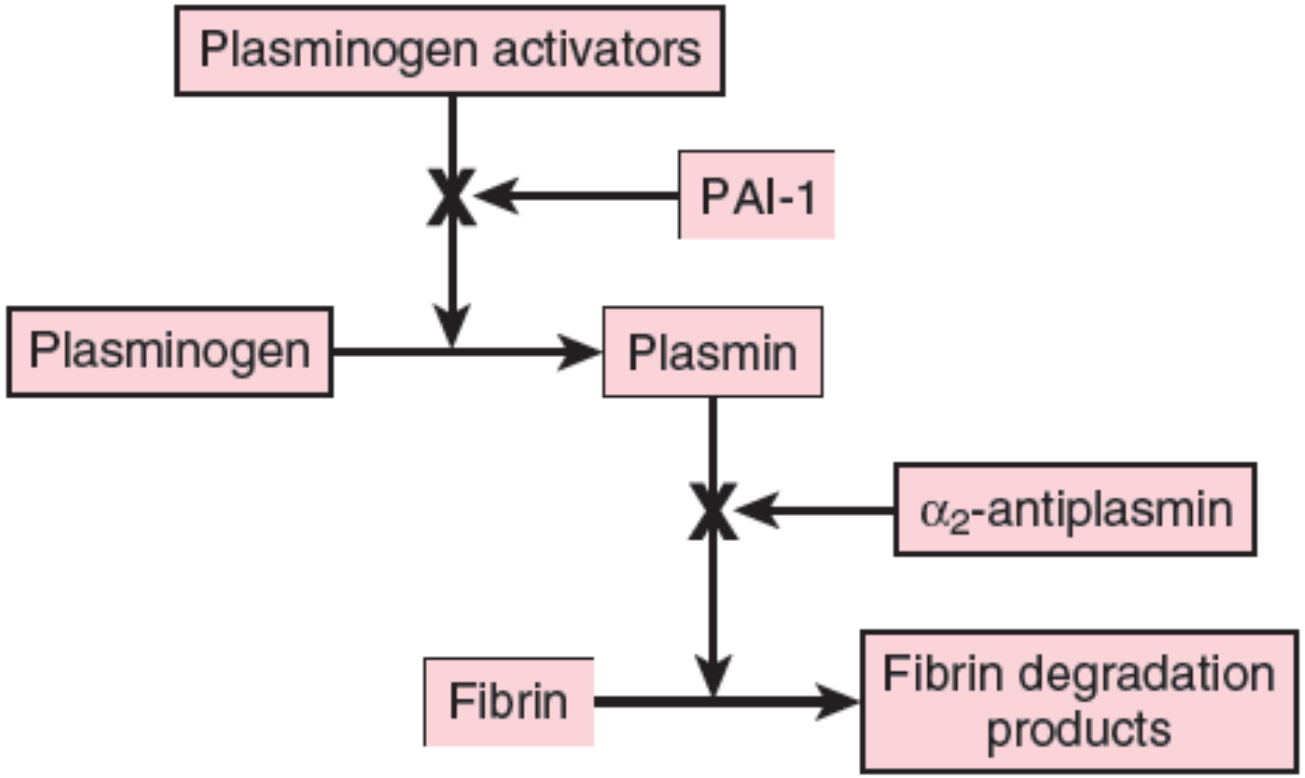
Σε παθολογικές καταστάσεις: **θρόμβωση**-Ο θρόμβος επεκτείνεται πέρα του σημείου της βλάβης και περιορίζει την αιματική ροή σε αγγεία αλλά και καρδιακές βαλβίδες ή άλλες δομές που είναι σημαντικές για τη φυσιολογική αιμοδυναμική λειτουργία.

Συνοπτικά ο μηχανισμός της πήξης



Ο μηχανισμός της πήξης καταλήγει στο σχηματισμό ΘΡΟΜΒΙΝΗΣ που καταλύει τη μετατροπή του ινωδογόνου σε ινώδες.

Συνοπτικά ο μηχανισμός της ινωδόλυσης

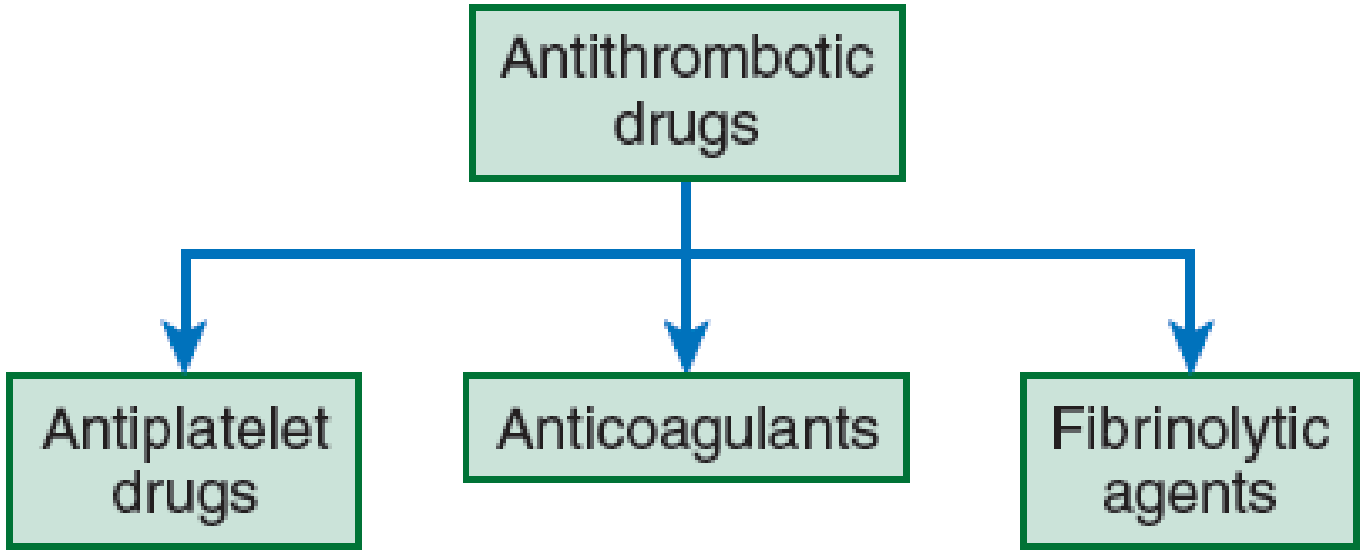


Ο μηχανισμός της ινωδόλυσης καταλήγει στο σχηματισμό ΠΛΑΣΜΙΝΗΣ που αποδομεί το ινώδες.

Κλινικά σημαντικά σύνδρομα θρόμβωσης

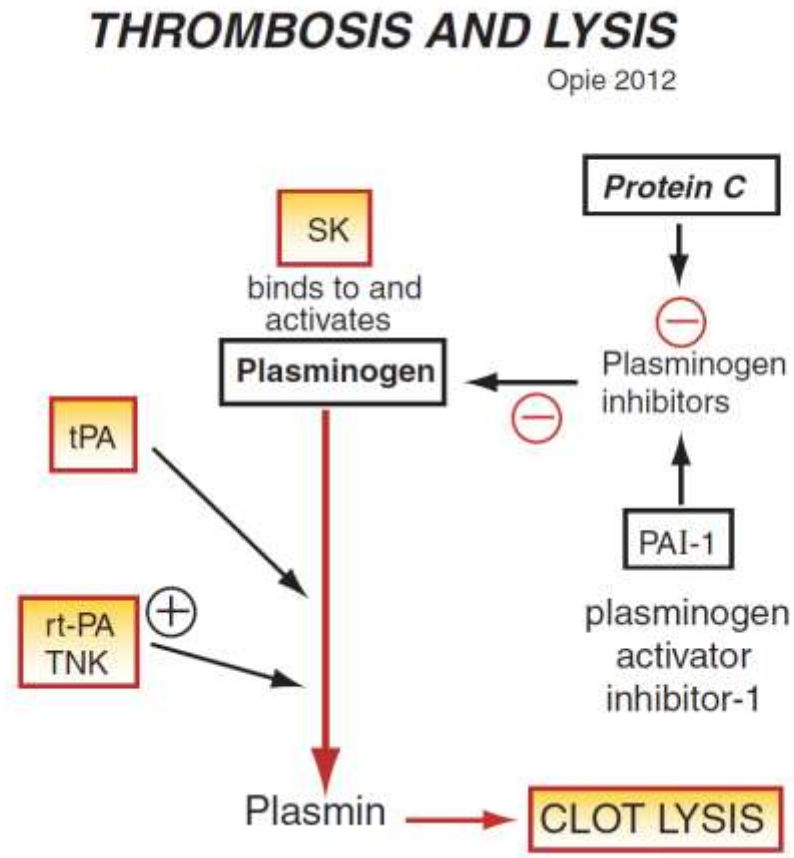
- Οξύ έμφραγμα μυοκαρδίου
- Εν τω βάθει φλεβοθρόμβωση
- Πνευμονική εμβολή
- Οξύ Ισχαιμικό εγκεφαλικό επεισόδιο
- Οξεία περιφερική αρτηριακή απόφραξη
- Απόφραξη εμφυτευμένων ενδαγγειακών καθετήρων

Ταξινόμηση των αντιθρομβωτικών φαρμάκων



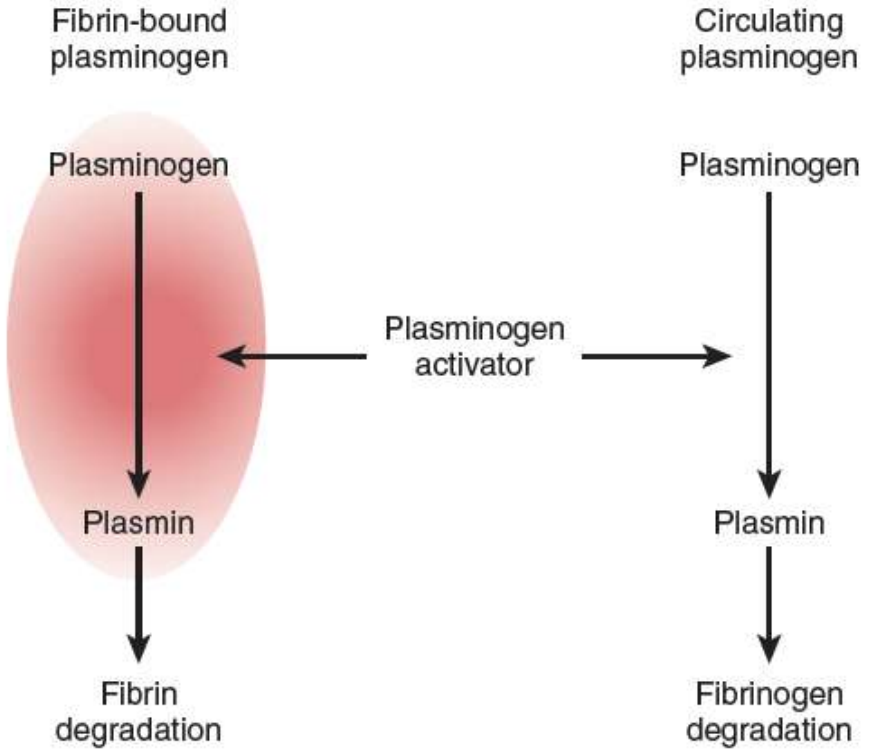
ΘΡΟΜΒΟΛΥΤΙΚΑ ΦΑΡΜΑΚΑ

- Όλα τα ΘΡΟΜΒΟΛΥΤΙΚΑ ΦΑΡΜΑΚΑ έχουν ένα κοινό στόχο: τη δημιουργία ΠΛΑΣΜΙΝΗΣ που ΛΥΝΕΙ το θρόμβο.



- Όλα τα φάρμακα της κατηγορίας αυτής, προσδένονται στο προένζυμο ΠΛΑΣΜΙΝΟΓΟΝΟ και το μετατρέπουν στο ενεργό ένζυμο ΠΛΑΣΜΙΝΗ.
- Η ΠΛΑΣΜΙΝΗ με τη σειρά της προσδένεται στο ΙΝΩΔΟΓΟΝΟ και το ΙΝΩΔΕΣ του θρόμβου και το διασπά, ΛΥΝΟΝΤΑΣ έτσι το θρόμβο.

Διάκριση Θρομβολυτικών φαρμάκων με βάση το σημείο δράσης τους.



- Το πλασμινογόνο βρίσκεται σε δύο μορφές: είτε ελεύθερο στην κυκλοφορία, είτε προσδεμένο στο ινώδες του θρόμβου.
- Τα θρομβολυτικά φάρμακα, ανάλογα με το σημείο πρόσδεσης τους διακρίνονται στα ΕΙΔΙΚΑ του ΙΝΩΔΟΥΣ (πρόσδεση στο ιστικό πλασμινογόνο-λύση του ινώδους) και στα ΜΗ ΕΙΔΙΚΑ (πρόσδεση στο ελεύθερο πλασμινογόνο-λύση του ινωδογόνου).

Οι διαφορές στο σημείο δράσης των θρομβολυτικών φαρμάκων, καθορίζουν και την έκταση των ανεπιθήμητων δράσεων τους: γενικευμένη ινωδόλυση από τα μη-ειδικά, στοχευμένη ινωδόλυση του θρόμβου από τα ειδικά.

Οι δυο κατηγορίες των ΘΡΟΜΒΟΛΥΤΙΚΩΝ ΦΑΡΜΑΚΩΝ

- ΕΙΔΙΚΑ ΤΟΥ ΙΝΩΔΟΥΣ:
  - ΑΛΤΕΠΛΑΣΗ (tPA)-ACTILYSE
  - ΡΕΤΕΠΛΑΣΗ (rPA)-RAPILYSIN
  - ΤΕΝΕΚΤΕΠΛΑΣΗ (TNK-tPA)- METALYSE

- ΜΗ ΕΙΔΙΚΑ ΤΟΥ ΙΝΩΔΟΥΣ
  - ΣΤΡΕΠΤΟΚΙΝΑΣΗ
  - ΟΥΡΟΚΙΝΑΣΗ
  - ΑΝΙΣΤΡΕΠΛΑΣΗ

  Χορηγούνται είτε συστηματικά (ΕΝΔΟΦΛΕΒΙΑ) (π.χ. Έμφραγμα Μυοκαρδίου, Πνευμονική εμβολή, Ισχαιμικό εγκεφαλικό), είτε ΤΟΠΙΚΑ μέσω καθετήρα τοποθετημένου στο σημείο του θρόμβου (π.χ. Περιφερική αρτηριακή θρόμβωση).

Σύγκριση των Εγκεκριμένων Θρομβολυτικών Φαρμάκων

FIBRINOLYTIC AGENT	DOSE	FIBRIN SPECIFICITY*	FIBRINOGEN DEPLETION	ANTIGENIC	PATENCY RATE (90-min TIMI 2 OR 3 FLOW)
Fibrin Specific					
Tenecteplase (TNK)	Single IV weight-based bolus†	++++	Minimal	No	85%
Reteplase (r-PA)	10 units + 10-unit IV boluses given 30 min apart	++	Moderate	No	84%
Alteplase (t-PA)	90-min weight-based infusion‡	++	Mild	No	73-84%
Non–Fibrin Specific					
Streptokinase§	1.5 million units IV given over 30-60 min	No	Marked	Yes¶	60-68%

r-PA, Reteplase plasminogen activator; *t-PA,* tissue plasminogen activator.
*Strength of fibrin specificity: ++++ is stronger; ++ is less strong.
†Bolus of 30 mg for weight less than 60 kg, 35 mg for 60 to 69 kg, 40 mg for 70 to 79 kg, 45 mg for 80 to 89 kg, and 50 mg for 90 kg or greater.
‡Bolus of 15 mg, infusion of 0.75 mg/kg for 30 minutes (maximum, 50 mg), then 0.5 mg/kg (maximum, 35 mg) over the next 60 minutes; the total dose not to exceed 100 mg.
§Streptokinase is no longer marketed in the United States but is available in other countries.
¶Streptokinase is highly antigenic and absolutely contraindicated within 6 months of previous exposure because of the potential for serious allergic reaction.
From O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;61:e78.

Επιλογή Θρομβολυτικού παράγοντα

- Ο ενδεικνυόμενος από τις διεθνείς οδηγίες για την συγκεκριμένη παθολογική κατάσταση που απαιτεί θρομβόλυση (π.χ για την πνευμονική εμβολή, η αλτεπλάση, η στρεπτοκινάση και η ουροκινάση είναι τα μόνα που έχουν ένδειξη).
- Σε ασθενείς που παρουσιάζονται πρώιμα μετά την έναρξη των συμπτωμάτων προτιμάται ένας παράγοντας ειδικός του ινώδους (αλτεπλάση, ρετεπλάση, τενεκτεπλάση).
- Σε ασθενείς χαμηλού κινδύνου (π.χ. νέοι ασθενείς με μικρό, κατώτερο έμφραγμα), μπορεί να χρησιμοποιηθεί η στρεπτοκινάση.
- Τα φάρμακα που απαιτούν μία εφ'απαξ δόση προτιμώνται σε σχέση με τα φάρμακα που απαιτούν πολλαπλές δόσεις, καθώς περιορίζουν την πιθανότητα λάθους κατά τη χορήγηση, έχουν μικρότερο κίνδυνο για μη-εγκεφαλικές αιμορραγίες και μπορούν να χορηγηθούν και πριν τη μετάβαση στο νοσοκομείο.

Θρομβόλυση =Θεραπεία επαναιμάτωσης

ΣΕ ΠΟΙΕΣ ΚΑΤΑΣΤΑΣΕΙΣ???

- Σε οξεία ΑΡΤΗΡΙΑΚΗ ΘΡΟΜΒΩΣΗ και ΑΠΟΦΡΑΞΗ αγγείου

➢Έμφραγμα Μυοκαρδίου με ανάσπαση ST (STEMI)

➢Πνευμονική Εμβολή

➢Ισχαιμικό Εγκεφαλικό Επεισόδιο

ειδικά όταν η ενδεικνυόμενη μηχανική επαναιμάτωση (πρωτογενής αγγειοπλαστική) δεν είναι εφικτή

Θρομβόλυση =Θεραπεία επαναιμάτωσης

Πότε???

- **Όσο το δυνατόν γρηγορότερα από την έναρξη του παθολογικού συμβάντος!!!!**
  - **Η Θρομβόλυση δουλεύει καλύτερα σε πρόσφατα σχηματισμένους θρόμβους.**
  - **Παλαιοί θρόμβοι έχουν εκτεταμένο πολυμερισμό του ινώδους που τους καθιστά ανθεκτικούς στη θρομβόλυση.**
  - **Η ταχύτερη αποκατάσταση της αιματικής ροής, μειώνει τις ισχαιμικές νεκρώσεις, διατηρεί τη βιωσιμότητα του ισχαιμικού ιστού και βελτιώνει την επιβίωση.**
- **Οι διεθνείς οδηγίες προσδιορίζουν ΣΑΦΩΣ τα χρονικά όρια στα οποία πρέπει να γίνεται η θρομβόλυση ώστε να επιτευχθεί το μέγιστο όφελος με τους ελάχιστους κινδύνους!!!!**

ΕΜΦΡΑΓΜΑ ΜΥΟΚΑΡΔΙΟΥ ΜΕ ΑΝΑΣΠΑΣΗ ST

(STEMI)

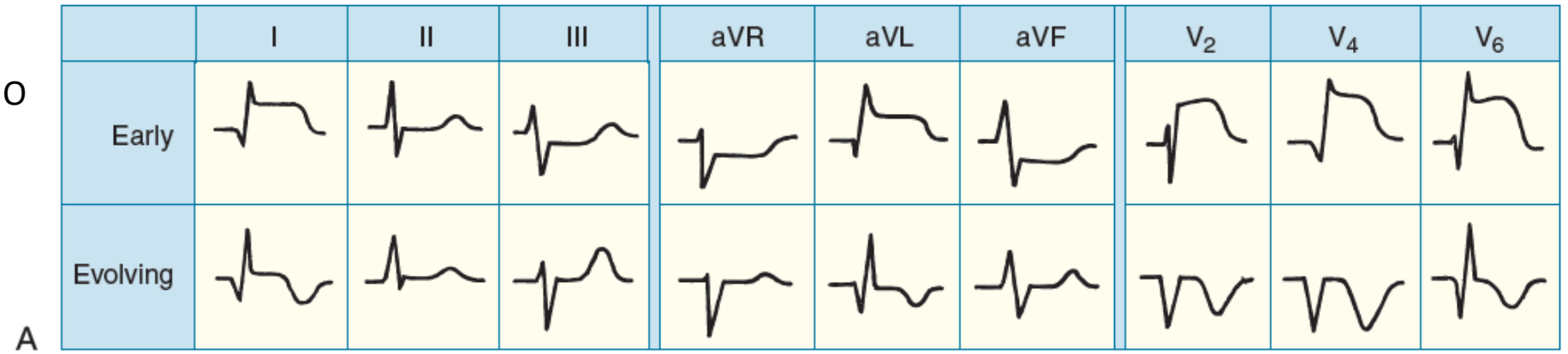
Reperfusion therapy

ESC
European Society of Cardiology

Recommendations	Class	Level
Reperfusion therapy is indicated in all patients with symptoms of ischaemia of ≤12 hours duration and persistent ST-segment elevation.	I	A
A *primary PCI strategy* is recommended over fibrinolysis within indicated time frames.	I	A
If primary PCI cannot be performed timely after STEMI diagnosis, fibrinolytic therapy is recommended within 12 hours of symptom onset in patients without contra-indications.	I	A

ΗΚΓραφική εικόνα STEMI

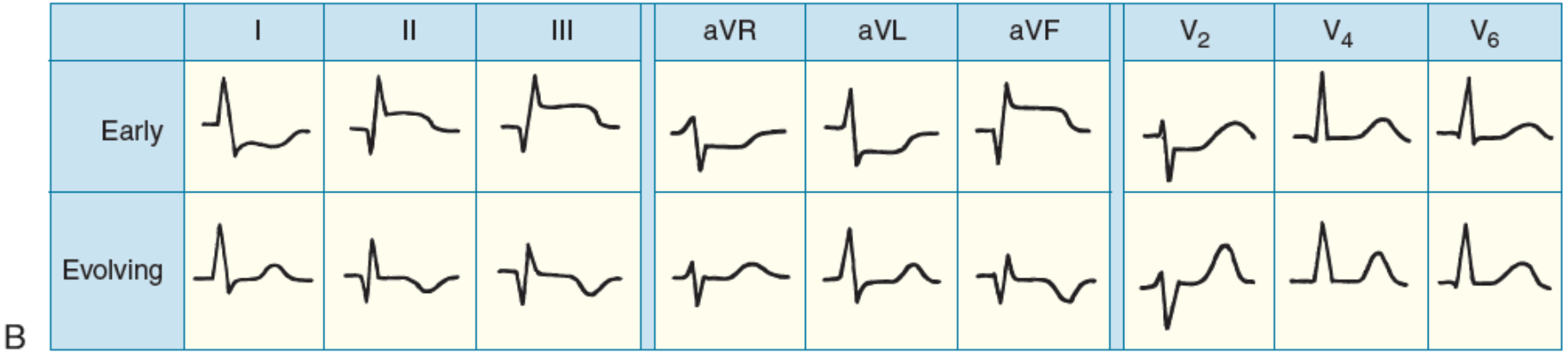
ΠΡΟΣΘΙΟΠΛΑΓΙΟ



A

ECG sequence with inferior Q wave infarction

ΚΑΤΩΤΕΡΟ



B

Fibrinolytic therapy

ESC European Society of Cardiology

Recommendations	Class	Level
When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis, preferably in the prehospital setting.	I	A
A fibrin-specific agent (i.e. tenecteplase, alteplase, reteplase) is recommended.	I	B
A half-dose of tenecteplase should be considered in patients ≥75 years of age.	IIa	B
Antiplatelet co-therapy with fibrinolysis		
Oral or i.v. aspirin is indicated.	I	B
Clopidogrel is indicated in addition to aspirin.	I	A
DAPT (in the form of aspirin plus a $P2Y_{12}$ inhibitor) is indicated for up to 1 year in patients undergoing fibrinolysis and subsequent PCI.	I	C

Fibrinolytic therapy *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Anticoagulation co-therapy with fibrinolysis		
Anticoagulation is recommended in patients treated with lytics until revascularization (if performed) or for the duration of hospital stay up to 8 days. The anticoagulant can be:	I	A
• Enoxaparin i.v. followed by s.c. (preferred over UFH).	I	A
• UFH given as a weight-adjusted i.v. bolus followed by infusion.	I	B
• In patients treated with streptokinase: fondaparinux i.v. bolus followed by an s.c. dose 24 hours later.	IIa	B
Transfer after fibrinolysis		
Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients immediately after fibrinolysis.	I	A

Fibrinolytic therapy *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Interventions following fibrinolysis		
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.	I	A
Rescue PCI is indicated immediately when fibrinolysis has failed (< 50% ST-segment resolution at 60-90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.	I	A
Angiography and PCI of the IRA, if indicated, is recommended between2 and 24 hours after successful fibrinolysis.	I	A
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B

Doses of fibrinolytic agents and antithrombotic co-therapies

ESC European Society of Cardiology

Drug	Initial treatment	Specific contra-indications
Doses of fibrinolytic therapy		
Streptokinase	1.5 million units over 30–60 min i.v.	Previous treatment with streptokinase or anistreplase
Alteplase (tPA)	15 mg i.v. bolus 0.75 mg/kg i.v. over 30 min (up to 50 mg) then 0.5 mg/kg i.v. over 60 min (up to 35 mg)	
Reteplase (rPA)	10 units + 10 units i.v. bolus given 30 min apart	
Tenecteplase (TNK-tPA)	Single i.v. bolus: 30 mg (6000 IU) if <60 kg 35 mg (7000 IU) if 60 to <70 kg 40 mg (8000 IU) if 70 to <80 kg 45 mg (9000 IU) if 80 to <90 kg 50 mg (10000 IU) if ≥90 kg It is recommended to reduce to half-dose in patients ≥75 years of age.	

Contra-indications to fibrinolytic therapy

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Absolute
Previous intracranial haemorrhage or stroke of unknown origin at anytime.
Ischaemic stroke in the preceding 6 months.
Central nervous system damage or neoplasms or arteriovenous malformation.
Recent major trauma/surgery/head injury (within the preceding month).
Gastrointestinal bleeding within the past month.
Known bleeding disorder (excluding menses).
Aortic dissection.
Non-compressible punctures in the past 24 hours (e.g. liver biopsy, lumbar puncture).

Contra-indications to fibrinolytic therapy

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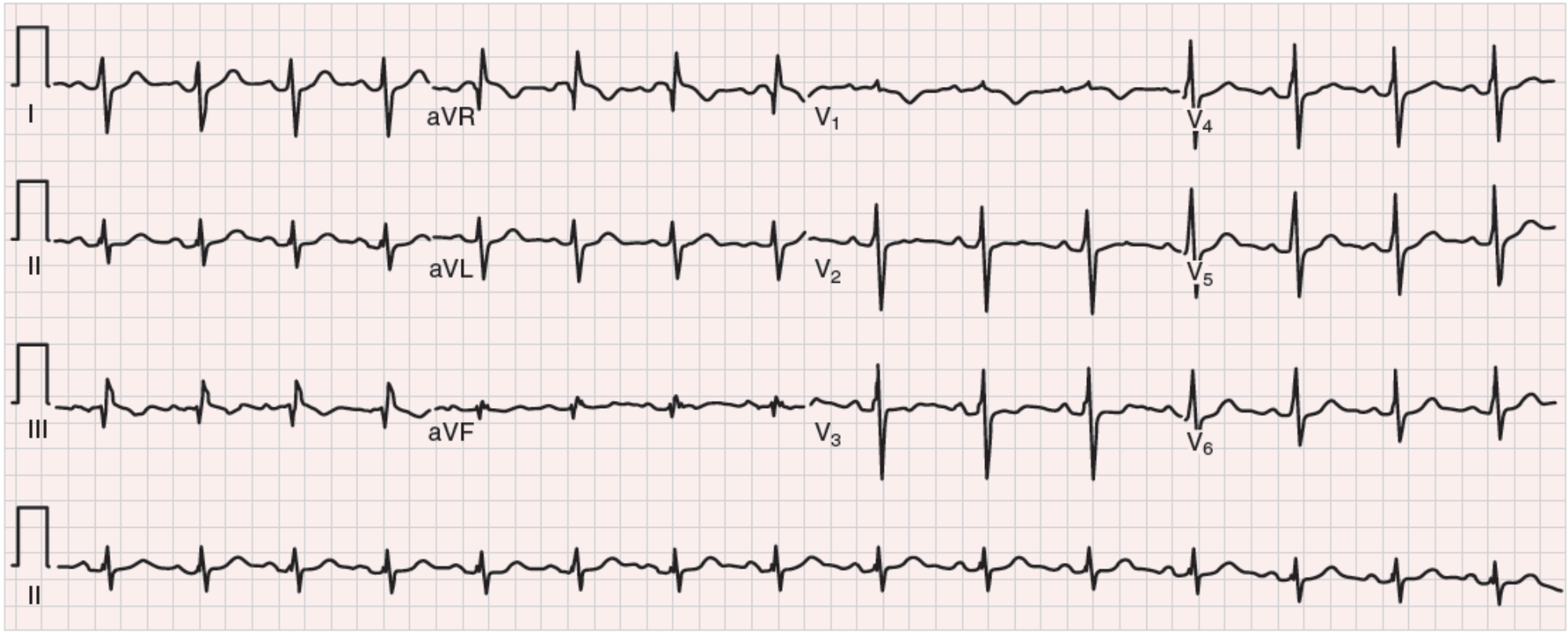
Relative
Transient ischaemic attack in the preceding 6 months.
Oral anticoagulant therapy.
Pregnancy or within 1 week postpartum.
Refractory hypertension (SBP >180 mmHg and/or DBP >110 mmHg).
Advanced liver disease.
Infective endocarditis.
Active peptic ulcer.
Prolonged or traumatic resuscitation.

ΕΝΕΡΓΕΙΕΣ ΜΕΤΑ ΤΗ ΘΡΟΜΒΟΛΥΣΗ

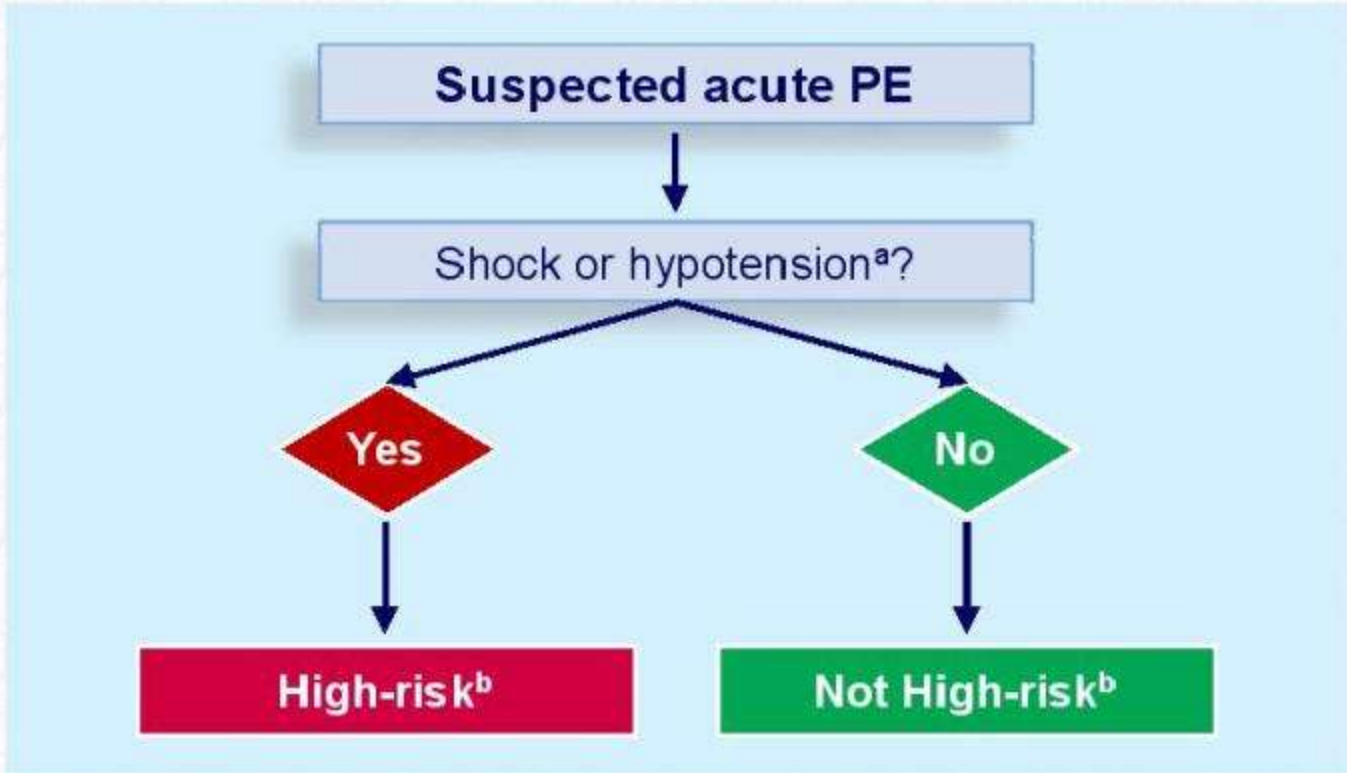
Interventions following fibrinolysis	
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.[124, 235]	I
Rescue PCI is indicated immediately when fibrinolysis has failed (<50% ST-segment resolution at 60–90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.[121,124,236]	I
Angiography and PCI of the IRA, if indicated, is recommended between 2 and 24 h after successful fibrinolysis.[125–128,234]	I
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.[124]	I

ΠΝΕΥΜΟΝΙΚΗ ΕΜΒΟΛΗ (PE)

ΗΚΓ στην ΠΝΕΥΜΟΝΙΚΗ ΕΜΒΟΛΗ



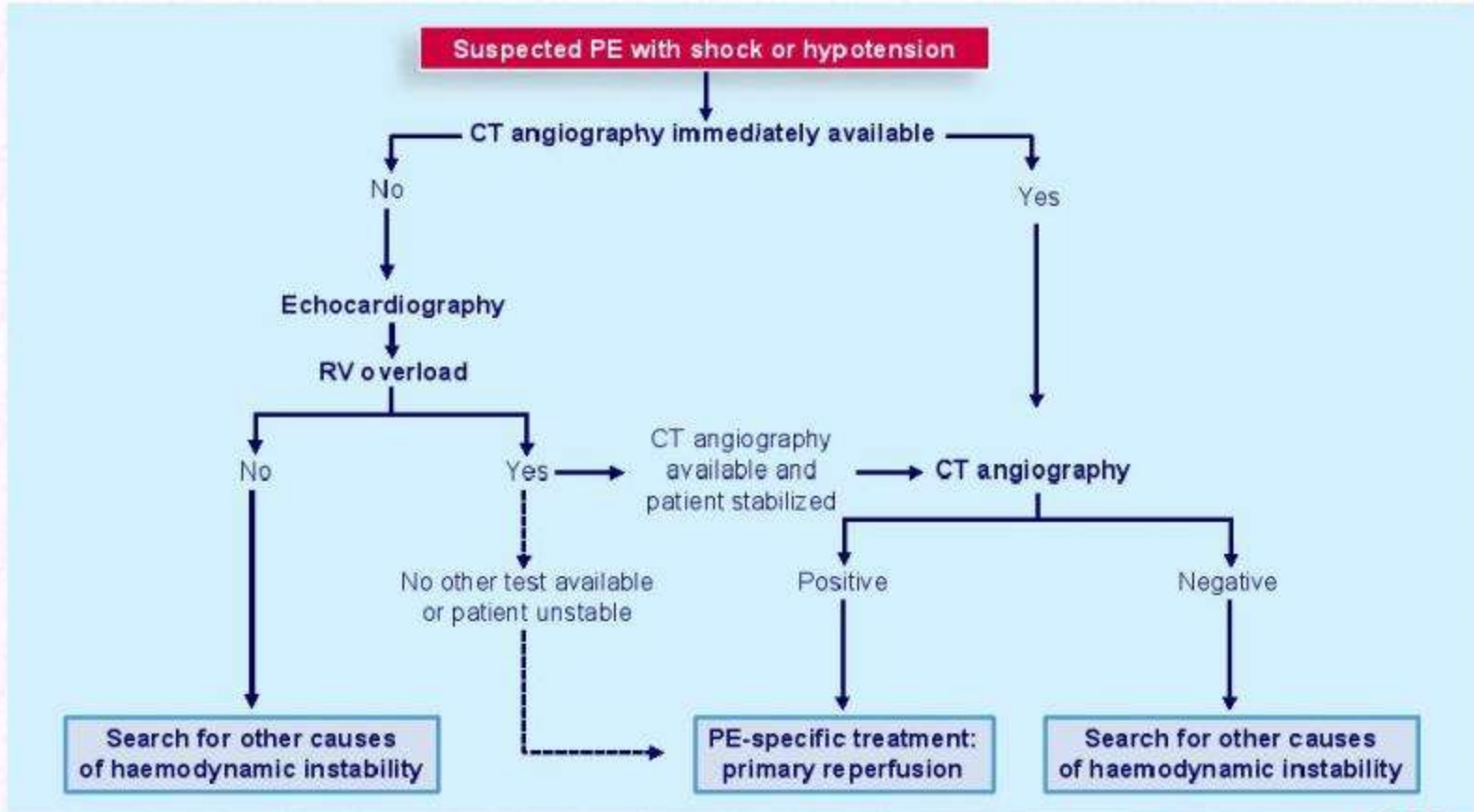
Initial risk stratification of acute PE



[a] Defined as systolic blood pressure <90 mmHg, or a systolic pressure drop by ≥40 mmHg, for >15 minutes, if not caused by new-onset arrhythmia, hypovolaemia, or sepsis.
[b] Based on the estimated PE-related in-hospital or 30-day mortality.

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Diagnostic algorithm: high-risk PE



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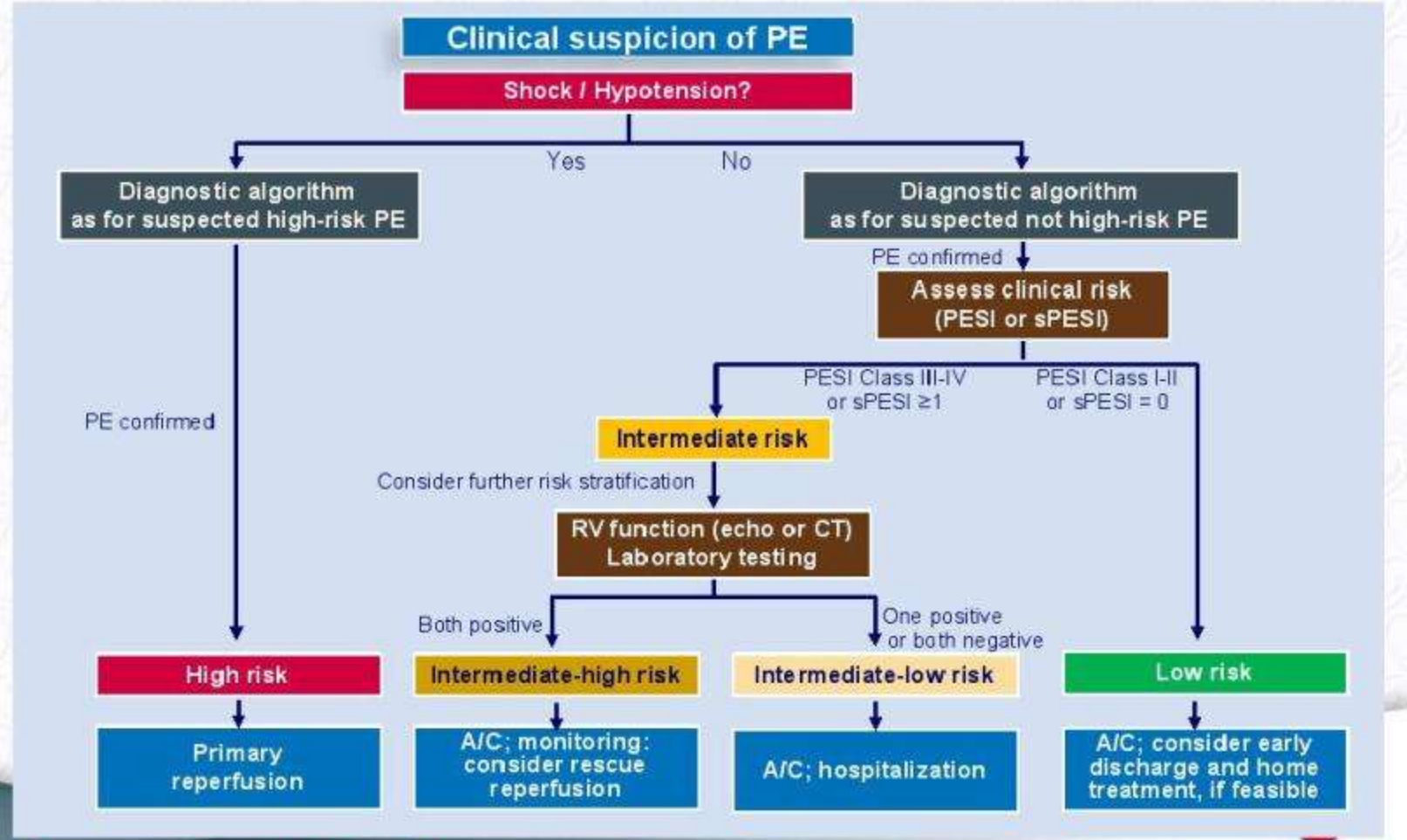
Risk-adjusted management algorithm



www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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Acute phase treatment

Recommendations	Class	Level
PE with shock or hypotension (high risk)		
It is recommended to initiate intravenous anticoagulation with UFH without delay in patients with high-risk PE.	I	C
Thrombolytic therapy is recommended.	I	B
Surgical pulmonary embolectomy is recommended for patients in whom thrombolysis is contraindicated or has failed.	I	C
Percutaneous catheter-directed treatment should be considered as an alternative to surgical pulmonary embolectomy for patients in whom full-dose systemic thrombolysis is contraindicated or has failed.	IIa	C

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Acute phase treatment

Recommendations	Class	Level
PE without shock or hypotension (intermediate or low risk)		
Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients without shock or hypotension.	III	B
Close monitoring is recommended in patients with intermediate-high risk PE to permit early detection of haemodynamic decompensation and timely initiation of rescue reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.	IIb	B

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Thrombolytic treatment of PE

Approved thrombolytic regimens for pulmonary embolism	
Streptokinase	250 000 IU as a loading dose over 30 minutes, followed by 100 000 IU/h over 12-24 hours.
	Accelerated regimen: 1.5 million IU over 2 hours.
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg per hour over 12-24 hours.
	Accelerated regimen: 3 million IU over 2 hours.
rtPA	100 mg over 2 hours; or
	0.6 mg/kg over 15 minutes (maximum dose 50 mg).

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Contraindications to thrombolysis

Absolute contraindications:[a]

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury in the preceding 3 weeks
- Gastrointestinal bleeding within the last month
- Known bleeding risk

Relative contraindications

- Transient ischaemic attack in the preceding 6 months
- Oral anticoagulant therapy
- Pregnancy, or within one week postpartum
- Non-compressible puncture site
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mm Hg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

[a]Absolute contraindications to thrombolysis might become relative in a patient with immediately life-threatening high-risk PE.

ΟΞΥ ΙΣΧΑΙΜΙΚΟ ΕΓΚΕΦΑΛΙΚΟ ΕΠΕΙΣΟΔΙΟ (AIS)

Επείγουσα εκτίμηση του ασθενούς

2.1. Stroke Scales	COR	LOE
1. The use of a stroke severity rating scale, preferably the NIHSS, is recommended.	I	B-NR

Tested Item	Title	Responses and Scores
1A	Level of consciousness	0—Alert
		1—Drowsy
		2—Obtunded
		3—Coma/unresponsive
1B	Orientation questions (2)	0—Answers both correctly
		1—Answers 1 correctly
		2—Answers neither correctly
1C	Response to commands (2)	0—Performs both tasks correctly
		1—Performs 1 task correctly
		2—Performs neither
2	Gaze	0—Normal horizontal movements
		1—Partial gaze palsy
		2—Complete gaze palsy
3	Visual fields	0—No visual field defect
		1—Partial hemianopia
		2—Complete hemianopia
		3—Bilateral hemianopia
4	Facial movement	0—Normal
		1—Minor facial weakness
		2—Partial facial weakness
		3—Complete unilateral palsy
5	Motor function (arm)	0—No drift
	a. Left	1—Drift before 10 s
	b. Right	2—Falls before 10 s
		3—No effort against gravity
		4—No movement
6	Motor function (leg)	0—No drift
	a. Left	1—Drift before 5 s
	b. Right	2—Falls before 5 s
		3—No effort against gravity
		4—No movement
7	Limb ataxia	0—No ataxia
		1—Ataxia in 1 limb
		2—Ataxia in 2 limbs
8	Sensory	0—No sensory loss
		1—Mild sensory loss
		2—Severe sensory loss
9	Language	0—Normal
		1—Mild aphasia
		2—Severe aphasia
		3—Mute or global aphasia
10	Articulation	0—Normal
		1—Mild dysarthria
		2—Severe dysarthria
11	Extinction or inattention	0—Absent
		1—Mild loss (1 sensory modality lost)
		2—Severe loss (2 modalities lost)

Adapted from Lyden et al.[62] Copyright © 1994, American Heart Association, Inc.

Απεικόνιση του εγκεφάλου

1. All patients admitted to hospital with suspected acute stroke should receive brain imaging evaluation on arrival to hospital. In most cases, noncontrast CT (NCCT) will provide the necessary information to make decisions about acute management.	I
2. Systems should be established so that brain imaging studies can be performed within 20 minutes of arrival in the ED in at least 50% of patients who may be candidates for IV alteplase and/or mechanical thrombectomy.	I

Άλλες διαγνωστικές εξετάσεις

2.3. Other Diagnostic Tests	COR
1. Only the assessment of blood glucose must precede the initiation of IV alteplase in all patients.	I
2. Baseline ECG assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I
3. Baseline troponin assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I

Άλλες δοκιμασίες όπως INR, αριθμός αιμοπεταλίων και APTT θεωρούνται απαραίτητες ΜΟΝΟ εάν υπάρχει υποψία διαταραχών πήξης. Εφόσον από το ιστορικό δεν τεκμηριώνεται υποψία διαταραχών, τα αποτελέσματα των παραπάνω εξετάσεων δεν δικαιολογούν πια την καθυστέρηση στην έναρξη της ΘΡΟΜΒΟΛΥΣΗΣ.

ΆΛΛΕΣ ΕΝΕΡΓΕΙΕΣ ΠΡΙΝ ΤΗ ΘΡΟΜΒΟΛΥΣΗ

2. Patients who have elevated BP and are otherwise eligible for treatment with IV alteplase should have their BP carefully lowered so that their systolic BP is <185 mm Hg and their diastolic BP is <110 mm Hg before IV fibrinolytic therapy is initiated.

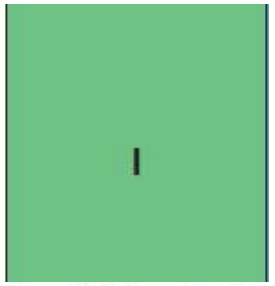

Table 5. Options to Treat Arterial Hypertension in Patients With AIS Who Are Candidates for Acute Reperfusion Therapy*

Class IIb, LOE C-EO
Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:
Labetalol 10–20 mg IV over 1–2 min, may repeat 1 time; or
Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 min, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or
Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h
Other agents (eg, hydralazine, enalaprilat) may also be considered
If BP is not maintained ≤185/110 mm Hg, do not administer alteplase
Management of BP during and after alteplase or other acute reperfusion therapy to maintain BP ≤180/105 mm Hg:
Monitor BP every 15 min for 2 h from the start of alteplase therapy, then every 30 min for 6 h, and then every hour for 16 h
If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:
Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h; or
Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h
If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside

ΘΡΟΜΒΟΛΥΣΗ ΣΤΟ ΙΣΧΑΙΜΙΚΟ ΕΓΚΕΦΑΛΙΚΟ ΕΠΕΙΣΟΔΙΟ

3.5. IV Alteplase	COR
1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 6 to determine patient eligibility.	I
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined in Table 6 determine patient eligibility.	I
BP should be maintained <180/105 mm Hg for at least the first 24 hours after IV alteplase treatment.	I

ΕΝΔΕΙΞΕΙΣ ΕΙΣΑΓΩΓΗΣ ΣΤΟ ΠΡΩΤΟΚΟΛΛΟ ΘΡΟΜΒΟΛΥΣΗΣ

Indications (Class I)	
Within 3 h*	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) is recommended for selected patients who may be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in this table to determine patient eligibility.† (*Class I; LOE A*)
Age	For otherwise medically eligible patients ≥18 y of age, IV alteplase administration within 3 h is equally recommended for patients <80 and >80 y of age.† (*Class I; LOE A*)
Severity	For severe stroke symptoms, IV alteplase is indicated within 3 h from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms.† (*Class I; LOE A*)
	For patients with mild but disabling stroke symptoms, IV alteplase is indicated within 3 h from symptom onset of ischemic stroke. There should be no exclusion for patients with mild but nonetheless disabling stroke symptoms, in the opinion of the treating physician, from treatment with IV alteplase because there is proven clinical benefit for those patients.† (*Class I; LOE B-R*)‡
3–4.5 h*	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) is also recommended for selected patients who can be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined in this table to determine patient eligibility.† (*Class I; LOE B-R*)‡
Age Diabetes mellitus Prior stroke Severity OACs Imaging	IV alteplase treatment in the 3- to 4.5-h time window is recommended for those patients ≤80 y of age, without a history of both diabetes mellitus and prior stroke, NIHSS score ≤25, not taking any OACs, and without imaging evidence of ischemic injury involving more than one third of the MCA territory.† (*Class I; LOE B-R*)‡

ΕΝΔΕΙΞΕΙΣ ΕΙΣΑΓΩΓΗΣ ΣΤΟ ΠΡΩΤΟΚΟΛΛΟ ΘΡΟΜΒΟΛΥΣΗΣ

Urgency	Treatment should be initiated as quickly as possible within the above listed time frames because time to treatment is strongly associated with outcomes.† (*Class I; LOE A*)
BP	IV alteplase is recommended in patients whose BP can be lowered safely (to <185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the BP before starting IV alteplase.† (*Class I; LOE B-NR*)‡
Blood glucose	IV alteplase is recommended in otherwise eligible patients with initial glucose levels >50 mg/dL.† (*Class I; LOE A*)
CT	IV alteplase administration is recommended in the setting of early ischemic changes on NCCT of mild to moderate extent (other than frank hypodensity).† (*Class I; LOE A*)
Prior antiplatelet therapy	IV alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke on the basis of evidence that the benefit of alteplase outweighs a possible small increased risk of sICH.† (*Class I; LOE A*)
	IV alteplase is recommended for patients taking antiplatelet drug combination therapy (eg, aspirin and clopidogrel) before stroke on the basis of evidence that the benefit of alteplase outweighs a probable increased risk of sICH.† (*Class I; LOE B-NR*)‡
End-stage renal disease	In patients with end-stage renal disease on hemodialysis and normal aPTT, IV alteplase is recommended.† (*Class I; LOE C-LD*)‡ However, those with elevated aPTT may have elevated risk for hemorrhagic complications.

ΑΝΤΕΝΔΕΙΞΕΙΣ ΕΙΣΑΓΩΓΗΣ ΣΤΟ ΠΡΩΤΟΚΟΛΛΟ ΘΡΟΜΒΟΛΥΣΗΣ

Time of onset	IV alteplase is not recommended in ischemic stroke patients who have an unclear time and/ or unwitnessed symptom onset and in whom the time last known to be at baseline state is >3 or 4.5 h.† (*Class III: No Benefit; LOE B-NR*)‡§
	IV alteplase is not recommended in ischemic stroke patients who awoke with stroke with time last known to be at baseline state >3 or 4.5 h.† (*Class III: No Benefit; LOE B-NR*)‡§
CT	IV alteplase should not be administered to a patient whose CT reveals an acute intracranial hemorrhage.† (*Class III: Harm; LOE C-EO*)‡§
	There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to alteplase. However, administering IV alteplase to patients whose CT brain imaging exhibits extensive regions of clear hypoattenuation is not recommended. These patients have a poor prognosis despite IV alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury.† (*Class III: No Benefit; LOE* A)§
Ischemic stroke within 3 mo	Use of IV alteplase in patients presenting with AIS who have had a prior ischemic stroke within 3 mo may be harmful.† (*Class III: Harm; LOE B-NR*)‡§
Severe head trauma within 3 mo	In AIS patients with recent severe head trauma (within 3 mo), IV alteplase is contraindicated.† (*Class III: Harm; LOE C-EO*)‡§
	Given the possibility of bleeding complications from the underlying severe head trauma, IV alteplase should not be administered in posttraumatic infarction that occurs during the acute in-hospital phase.† (*Class III: Harm; LOE C-EO*)‡§ (Recommendation wording modified to match Class III stratifications.)
Intracranial/intraspinal surgery within 3 mo	For patients with AIS and a history of intracranial/spinal surgery within the prior 3 mo, IV alteplase is potentially harmful.† (*Class III: Harm; LOE C-EO*)‡§

ΑΝΤΕΝΔΕΙΞΕΙΣ ΕΙΣΑΓΩΓΗΣ ΣΤΟ ΠΡΩΤΟΚΟΛΛΟ ΘΡΟΜΒΟΛΥΣΗΣ

History of intracranial hemorrhage	IV alteplase administration in patients who have a history of intracranial hemorrhage is potentially harmful.† (*Class III: Harm; LOE C-EO*)‡§
Subarachnoid hemorrhage	IV alteplase is contraindicated in patients presenting with symptoms and signs most consistent with an SAH.† (*Class III: Harm; LOE C-EO*)‡§
GI malignancy or GI bleed within 21 d	Patients with a structural GI malignancy or recent bleeding event within 21 d of their stroke event should be considered high risk, and IV alteplase administration is potentially harmful.† (*Class III: Harm; LOE C-EO*)‡§
Coagulopathy	The safety and efficacy of IV alteplase for acute stroke patients with platelets <100 000/mm^3, INR >1.7, aPTT >40 s, or PT >15 s are unknown, and IV alteplase should not be administered.† (*Class III: Harm; LOE C-EO*)‡§ (In patients without history of thrombocytopenia, treatment with IV alteplase can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm^3. In patients without recent use of OACs or heparin, treatment with IV alteplase can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.) (Recommendation wording modified to match Class III stratifications.)
LMWH	IV alteplase should not be administered to patients who have received a treatment dose of LMWH within the previous 24 h.† (*Class III: Harm; LOE B-NR*)‖ (Recommendation wording modified to match Class III stratifications.)
Thrombin inhibitors or factor Xa inhibitors	The use of IV alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful.† (*Class III: Harm; LOE C-EO*)‡§ IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 h (assuming normal renal metabolizing function). (Alteplase could be considered when appropriate laboratory tests such as aPTT, INR, ecarin clotting time, thrombin time, or direct factor Xa activity assays are normal or when the patient has not taken a dose of these ACs for >48 h and renal function is normal.) (Recommendation wording modified to match Class III stratifications.)
Glycoprotein IIb/IIIa receptor inhibitors	Antiplatelet agents that inhibit the glycoprotein IIb/IIIa receptor should not be administered concurrently with IV alteplase outside a clinical trial.† (*Class III: Harm; LOE B-R*)‡§ (Recommendation wording modified to match Class III stratifications.)
Infective endocarditis	For patients with AIS and symptoms consistent with infective endocarditis, treatment with IV alteplase should not be administered because of the increased risk of intracranial hemorrhage.† (*Class III: Harm; LOE C-LD*)‡§ (Recommendation wording modified to match Class III stratifications.)
Aortic arch dissection	IV alteplase in AIS known or suspected to be associated with aortic arch dissection is potentially harmful and should not be administered.† (*Class III: Harm; LOE C-EO*)‡§ (Recommendation wording modified to match Class III stratifications.)
Intra-axial intracranial neoplasm	IV alteplase treatment for patients with AIS who harbor an intra-axial intracranial neoplasm is potentially harmful.† (*Class III: Harm; LOE C-EO*)‡§

ΠΡΩΤΟΚΟΛΛΟ ΘΡΟΜΒΟΛΥΣΗΣ

Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 min, with 10% of the dose given as a bolus over 1 min.
Admit the patient to an intensive care or stroke unit for monitoring.
If the patient develops severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination, discontinue the infusion (if IV alteplase is being administered) and obtain emergency head CT scan.
Measure BP and perform neurological assessments every 15 min during and after IV alteplase infusion for 2 h, then every 30 min for 6 h, then hourly until 24 h after IV alteplase treatment.
Increase the frequency of BP measurements if SBP is >180 mm Hg or if DBP is >105 mm Hg; administer antihypertensive medications to maintain BP at or below these levels (Table 5).
Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them.
Obtain a follow-up CT or MRI scan at 24 h after IV alteplase before starting anticoagulants or antiplatelet agents.

ΕΝΔΟΚΡΑΝΙΑ ΑΙΜΟΡΡΑΓΙΑ ΚΑΤΑ ΤΗ ΘΡΟΜΒΟΛΥΣΗ

Stop alteplase infusion
CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match
Emergent nonenhanced head CT
Cryoprecipitate (includes factor VIII): 10 U infused over 10–30 min (onset in 1 h, peaks in 12 h); administer additional dose for fibrinogen level of <200 mg/dL
Tranexamic acid 1000 mg IV infused over 10 min OR ε-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled (peak onset in 3 h)
Hematology and neurosurgery consultations
Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

ΟΔΗΓΙΕΣ για την ΑΝΑΣΤΡΟΦΗ των ΑΝΤΙΘΡΟΜΒΩΤΙΚΩΝ ΦΑΡΜΑΚΩΝ σε ΕΝΔΟΚΡΑΝΙΑ ΑΙΜΟΡΡΑΓΙΑ

ΘΡΟΜΒΟΛΥΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ -ACTILYSE -METALYSE -RAPILYSIN	ΚΡΥΟΚΑΘΙΖΗΜΑ 10 U I.V Ή ΑΝΤΙ-ΙΝΩΔΟΛΥΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ ΕΠΙ ΑΝΤΕΝΔΕΙΞΗΣ ΤΟΥ ΚΡΥΟΚΑΘΙΖΗΜΑΤΟΣ: ΤΡΑΝΕΞΑΜΙΚΟ ΟΞΥ: 10-15mg/kg I.V. σε 20 min Ή ε-ΑΜΙΝΟΚΑΠΡΟΪΚΟ ΟΞΥ 4-5g I.V.	TRANSAMIN AMICAR	5OOmg/5 ml amp 250mg/ml

Επιπλοκές της Θρομβόλυσης

- **Αιμορραγία**: Σε οποιοδήποτε σημείο του σώματος ΑΛΛΑ η ΕΝΔΟΚΡΑΝΙΑ ΑΙΜΟΡΡΑΓΙΑ είναι η πιο σοβαρή.
  - Εξαρτάται από το φάρμακο που χρησιμοποιήθηκε (υψηλότερα ποσοστά από τα μη-ειδικά του ινώδους φάρμακα) ΑΛΛΑ και από την παρουσία παραγόντων κινδύνου (Υψηλή αρτηριακή πίεση κατά την προσέλευση, μεγάλη ηλικία, χαμηλό σωματικό βάρος, σοβαρή καρδιακή ανεπάρκεια, αιμορραγική διάθεση-νεφρική ή ηπατική ανεπάρκεια).
- **Αλλεργικές αντιδράσεις**: Ειδικά με τη ΣΤΡΕΠΤΟΚΙΝΑΣΗ
- **Εμβολικά επεισόδια**
- **Εγκεφαλικά επεισόδια**

ΣΥΜΠΕΡΑΣΜΑΤΑ

- Η ΘΡΟΜΒΟΛΥΣΗ ΑΠΟΤΕΛΕΙ ΣΗΜΑΝΤΙΚΗ ΘΕΡΑΠΕΥΤΙΚΗ ΜΕΘΟΔΟ ΣΕ ΣΥΓΚΕΚΡΙΜΕΝΕΣ ΚΑΤΑΣΤΑΣΕΙΣ.
- ΠΡΕΠΕΙ ΠΑΝΤΑ ΝΑ ΔΙΕΝΕΡΓΕΙΤΑΙ ΑΠΟ ΚΑΤΑΡΤΙΣΜΕΝΟ ΚΑΙ ΕΜΠΕΙΡΟ ΠΡΟΣΩΠΙΚΟ.
- ΜΠΟΡΕΙ ΝΑ ΣΩΣΕΙ ΖΩΕΣ ΟΤΑΝ ΔΙΕΝΕΡΓΕΙΤΑΙ ΣΩΣΤΑ ΣΥΜΦΩΝΑ ΜΕ ΤΙΣ ΔΙΕΘΝΕΙΣ ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ.