http://www.metropolitan-hospital.gr/maf-aee.html

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ΑΓΓΕΙΑΚΑ ΕΓΚΕΦΑΛΙΚΑ ΕΠΕΙΣΟΔΙΑ

Καργιώτης Οδυσσέας

Νευρολόγος

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Fellow of the European Board of Neurology

Internationally Certified in Neurosonology

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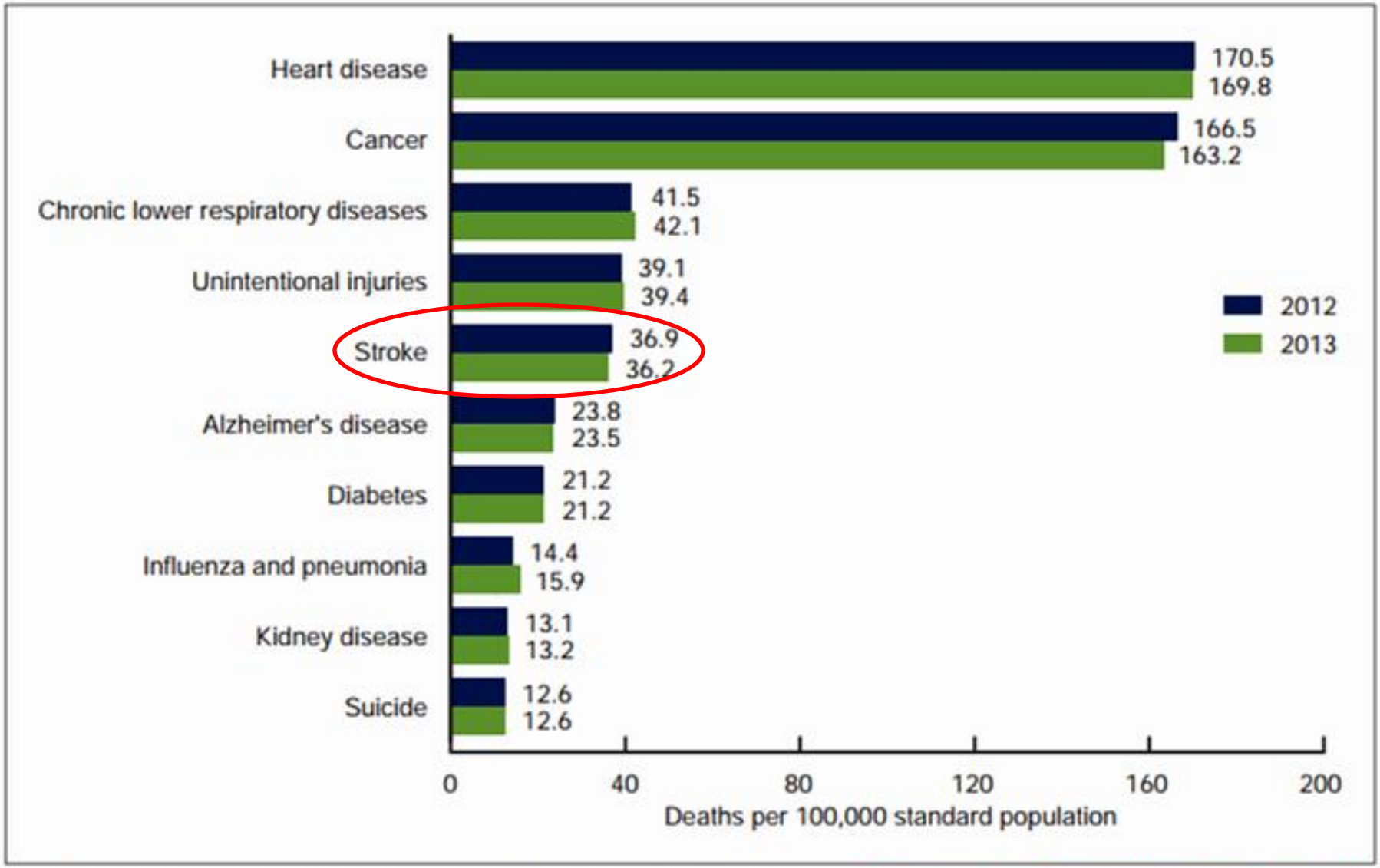
Ορισμός

- Οξεία απώλεια νευρολογικής λειτουργίας λόγω διακοπής της παροχής αίματος σε μια περιοχή του εγκεφάλου.
  - Ισχαιμικά ΑΕΕ
  - Αιμορραγικά ΑΕΕ

Figure 3. Age-adjusted death rates for the 10 leading causes of death: United States, 2012 and 2013



NOTES: Causes of death are ranked according to number of deaths. Access data table for Figure 3 at: http://www.cdc.gov/nchs/data/databriefs/db178_table.pdf#1.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

_stroke.pdf.

Επιδημιολογία

- Η επίπτωση των ΑΕΕ μειώθηκε κατά 40% τις 4 τελευταίες δεκαετίες στις χώρες υψηλού εισοδήματος, αλλά **διπλασιάστηκε** στις χώρες χαμηλού και μεσαίου εισοδήματος.
- **Ωστόσο**, λόγω αύξησης της ηλικίας του πληθυσμού αναμένεται αύξηση των ΑΕΕ στην Ισλανδία, Νορβηγία, Ελβετία από $1,1x10^6$ το 2000 σε $1,5x10^6$ το 2025.
- Disability-adjusted life years lost to stroke θα αυξηθούν από $38x10^6$ το 1990 σε $61x10^6$ το 2020.

•Ferri , et al. J Neurol Neurosurg Psychiatry 2011
•Truelsen, et al. Eur J Neurology 2006
•The Atlas of heart disease and stroke, WHO 2004.
http://www.who.int/cardiovascular_diseases/en/cvd_atlas_15_burden_stroke.pdf

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Από 3η, 4η και μετά 5η αιτία θανάτου…

- Το 2008 το ΑΕΕ υποχώρησε από τρίτη σε **τέταρτη αιτία** θανάτου στις ΗΠΑ και πλέον είναι **πέμπτη**.
- Εν μέρει η υποχώρηση αυτή αντανακλά τα αποτελέσματα μιας δέσμευσης της **American Heart Association/American Stroke Association (AHA/ASA)** προ δεκαετίας να μειώσει τα ΑΕΕ, τη στεφανιαία νόσο και τον καρδιαγγειακό κίνδυνο κατά **25% μέχρι το 2010** (ο στόχος επετεύχθη ήδη το **2009**).
- Οι λόγοι τις επιτυχίας είναι πολυπαραγοντικοί:
  - ✓ **Βελτίωση πρόληψης**
  - ✓ **Βελτίωση αντιμετώπισης τις πρώτες ώρες του οξέος ΑΕΕ**
- Για τη συνέχιση αυτών των ελπιδοφόρων τάσεων, **το κοινό και οι επαγγελματίες υγείας** πρέπει να παραμείνουν σε επιφυλακή με στόχο την περεταίρω βελτίωση της πρόληψης και της αντιμετώπισης των ΑΕΕ.

Και το κόστος…

- Αύξηση κόστους περίθαλψης, απώλειας εργασίας, πρώιμης θνητότητας στους επιζήσαντες με αγγειακό εγκεφαλικό
  - εκτιμώμενο κόστος στις ΗΠΑ το 2010 $73.7 billion
  - εκτιμώμενο κόστος στην Ευρώπη το 2010 €64.1 billion

Lloyd-Jones et al, Circulation, 2010
Gustavsson et al Eur Neurpsychopharmacol, 2011

TABLE 4. 28-Day Case Fatality Rate of Stroke by Type of Stroke and Sex in Arcadia, Greece

	All Strokes		Infarction		Hemorrhage	
Sex/Age, y	Rate	95% CI	Rate	95% CI	Rate	95% CI
Men						
18–54	16.7	NC	14.3	NC	25.0	NC
55–64	13.9	2.6–25.1	7.1	NC	33.3	NC
65–74	16.2	7.8–24.6	10.7	2.6–18.8	29.4	NC
75–84	30.5	21.4–38.9	22.7	12.8–31.1	64.3	39.1–89.3
≥85	38.7	27.6–49.6	36.5	24.6–40.4	50.0	NC
Total	26.3	21.3–31.1	21.3	16.1–26.2	44.0	30.2–57.7
Women						
18–54	22.2	NC	...	...	40.0	NC
55–64	14.3	NC	5.3	NC	37.5	NC
65–74	29.1	17.0–41.0	17.1	5.5–20.5	40.0	NC
75–84	24.4	15.1–32.6	18.9	10.8–26.9	60.0	NC
≥85	37.7	24.6–50.7	30.3	16.5–43.9	80.0	NC
Total	27.1	21.4–32.6	19.3	13.7–24.7	51.8	44.7–81.1
All subjects						
18–54	18.5	NC	11.1	NC	33.3	NC
55–64	14.1	5.5–22.5	6.4	NC	35.7	NC
65–74	21.7	14.5–28.8	13.4	6.6–20.1	31.8	12.3–51.8
75–84	27.3	21.2–33.4	20.7	14.7–26.6	63.2	41.4–84.8
≥85	38.3	24.8–46.7	34.0	24.9–42.9	60.0	35.2–84.7
Total	26.6	22.9–30.2	20.4	16.6–24.0	46.7	35.6–57.8

Values are percentages. NC indicates not calculated, <5 cases.

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α

uthern Greece

K. Tsibouris, MD;
PhD;
os, MD

tion of type of stroke has not been
cidence of stroke by type, and the

d in eastern central Peloponessos,
ll subjects with a first-ever stroke
records, public health centers, and

. The incidence rates (per 100 000)
or men were 5, 31, 113, 240, 662,
, and 2137, respectively. Age- and
jects aged 45 to 84 years was
d in 81% of cases, intracerebral
gures were 85%, 12%, and 3%,
h no differences between men and
ge than for cerebral infarction.
pared with other European studies.
of other industrialized countries.

tality

Το ΑΕΕ στην Ελλάδα

- Μέσο κόστος νοσηλείας 3624.9 €
- Μέσο κόστος αποκατάστασης 5553.3 €

Vasiliadis and Zikic, Neurol Neurochir Pol. 2014

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Παροδικό ΑΕΕ

Table 1. Point Score of ABCD2, ABCD3, and ABCD3-I Scores

	ABCD2 Score	ABCD3 Score	ABCD3-I Score	ABCD3-I(d, c/i) Score	ABCD3-I(c/i) Score
Age ≥60 y	1	1	1	1	1
Blood pressure ≥140/90 mm Hg	1	1	1	1	1
Clinical features					
Speech impairment without weakness	1	1	1	1	1
Unilateral weakness	2	2	2	2	2
Duration, min					
10–59	1	1	1	1	1
≥60	2	2	2	2	2
Diabetes mellitus present	1	1	1	1	1
Dual TIA	NA	2	2	2	2
Imaging					
Ipsilateral ≥50% stenosis of internal carotid artery	NA	NA	2	NA	NA
Ipsilateral ≥50% stenosis of internal carotid artery and/or cerebral major artery	NA	NA	NA	2	2
Acute diffusion-weighted imaging hyperintensity	NA	NA	2	2	NA
Total	0–7	0–9	0–13	0–13	0–11

Dual transient ischemic attack (TIA) was defined as TIA prompting medical attention plus at least one other TIA in the preceding 7 days. (c) indicates carotid stenosis; (d), diffusion-weighted image; (i), intracranial arterial stenosis; and NA, not applicable.

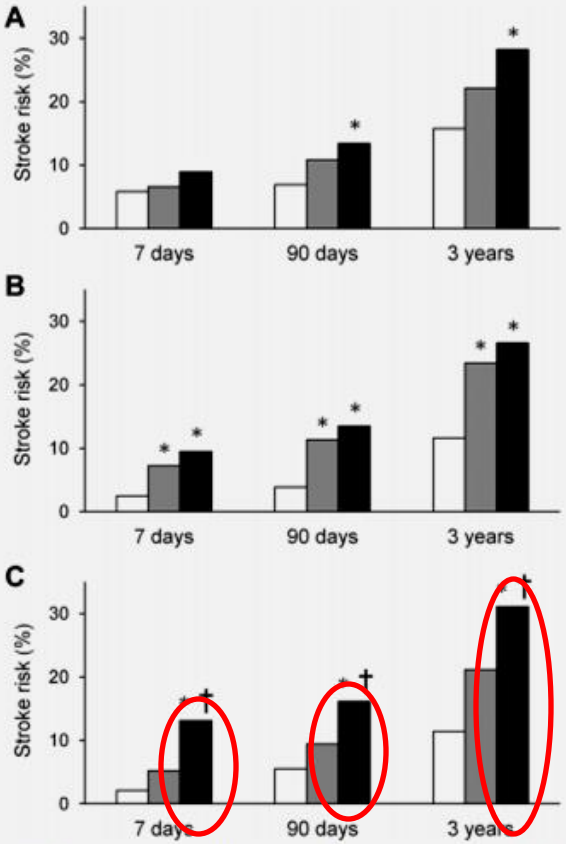

Figure. Stroke incidence after transient ischemic attack (TIA). The incidence of stroke at different time points after TIA is shown according to the risk categories of ABCD2 score (**A**), ABCD3 score (**B**), and ABCD3-I score (**C**). The different columns indicate stroke incidence in low-risk (open column), moderate-risk (shaded column), and high-risk patients (closed column). *P<0.05 vs low-risk patients; †P<0.05 vs moderate-risk patients.

Kiyohara et al, Stroke 2014

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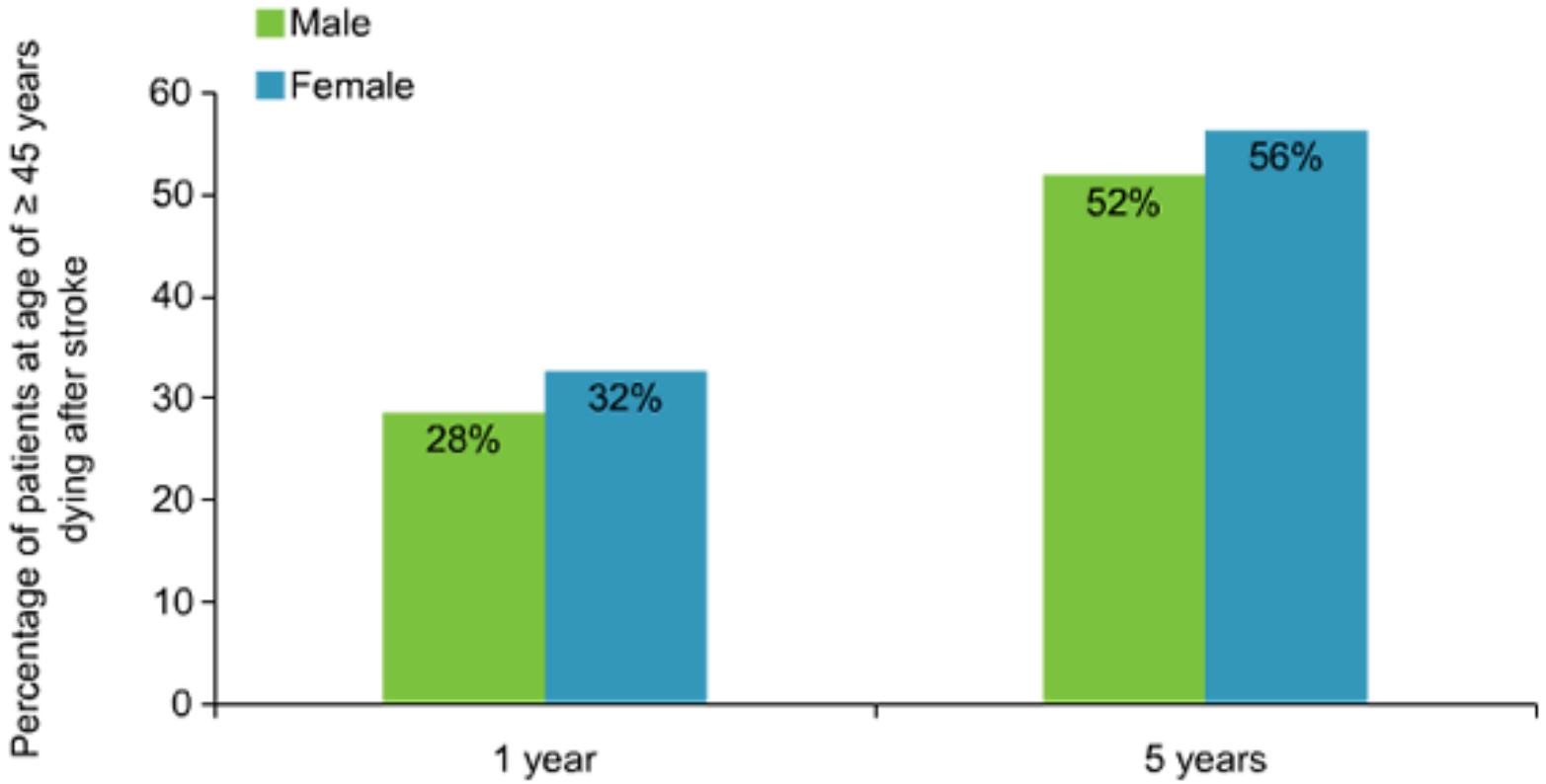
Θνητότητα

Figure 1 : Mortality following a stroke



(Source: Roger VL et al. AHA Heart Disease and Stroke Statistics 2011 update. Circulation 2011;123:e18-e209.)

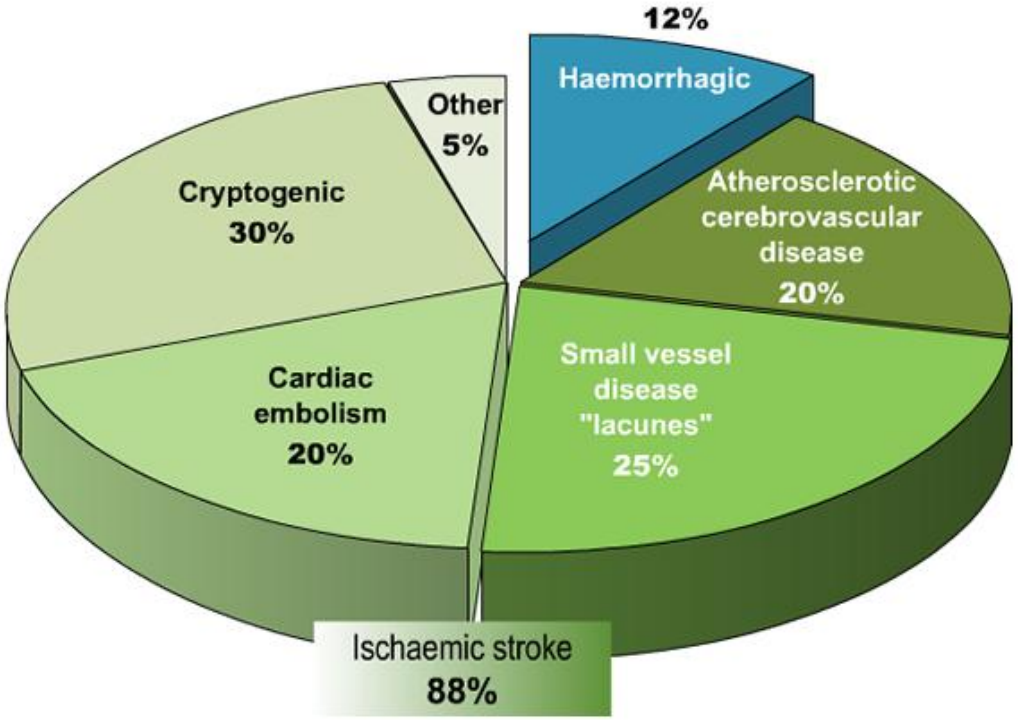
Αιτιολογία

TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

Large-artery atherosclerosis (embolus/thrombosis)*
Cardioembolism (high-risk/medium-risk)*
Small-vessel occlusion (lacune)*
Stroke of other determined etiology*
Stroke of undetermined etiology
a. Two or more causes identified
b. Negative evaluation
c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.
*Possible or probable depending on results of ancillary studies.

Adams et al, Stroke 1993



http://www.strokeforum.com

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Ενημέρωση του κοινού και των επαγγελματιών υγείας

- Τα στοιχεία δείχνουν ότι η αναγνώριση των συμπτωμάτων/σημείων του ΑΕΕ από το κοινό παραμένει φτωχή.
  - 40% των ασθενών με πιθανό ΑΕΕ δεν γνώριζαν τα συμπτώματα και τους παράγοντες κινδύνου (*Lambert Y. Presentation at the ESC in Hamburg, 2011*).
  - 42% των ασθενών με υποψία ΑΕΕ τηλεφώνησαν τον Γεν ιατρό (*Jones et al, Age Ageing 2010*).
- **Εντατική και συνεχής ενημέρωση του κοινού** για τα συμπτώματα/σημεία του ΑΕΕ βελτιώνει την έγκαιρη αναγνώριση του ΑΕΕ.
- California Acute Stroke Pilot Registry (CASPR, Neurology, 2005):
  - ✓ Η θρομβόλυση εντός 3 ωρών θα μπορούσε να αυξηθεί από **4.3% σε 28.6%** εάν όλοι οι ασθενείς έκαναν αμέσως κλήση στο 991

•*Jurkowski et al. New York. Prev Chronic Dis. 2008;5:A41*
•*Mosley et al. Stroke. 2007;38:361–366.*
•*Chiti A et al. Stroke.2007;38:e58–e59.*
•*Kleindorfer et al. Stroke. 2007;38:2864–2868.*

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FAST (face, arm, speech, time) παρόντα στο 88% των ΑΕΕ και των ΠΙΕ

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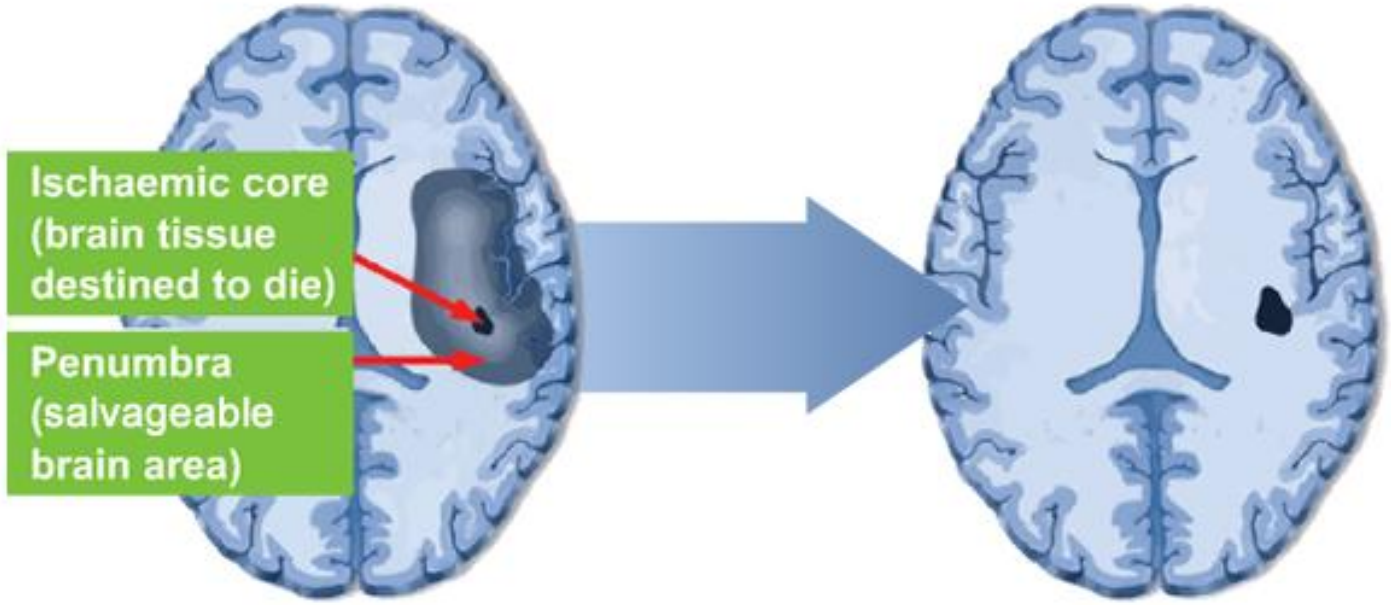
Στόχος…

…να διασωθεί η penubra

Figure 1: Ischaemic penumbra – Potential to reverse neurologic impairment with post-stroke therapy



http://www.strokeforum.com

http://www.metropolitan-hospital.gr/maf-aee.html

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BRAIN STROKE IS A MEDICAL EMERGENCY

If you see any one of these signs **ACT FAST**, call **999** and get immediate medical help

Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

Saver JL, Stroke 2006

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Edward C. Jauch, MD, MS, FAHA, Chair; Jeffrey L. Saver, MD, FAHA, Vice Chair; Harold P. Adams, Jr, MD, FAHA; Askiel Bruno, MD, MS; J.J. (Buddy) Connors, MD; Bart M. Demaerschalk, MD, MSc; Pooja Khatri, MD, MSc, FAHA; Paul W. McMullan, Jr, MD, FAHA; Adnan I. Qureshi, MD, FAHA; Kenneth Rosenfield, MD, FAHA; Phillip A. Scott, MD, FAHA; Debbie R. Summers, RN, MSN, FAHA; David Z. Wang, DO, FAHA; Max Wintermark, MD; Howard Yonas, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology

***Background and Purpose*—**The authors present an overview of the current evidence and management recommendations for evaluation and treatment of adults with acute ischemic stroke. The intended audiences are prehospital care providers, physicians, allied health professionals, and hospital administrators responsible for the care of acute ischemic stroke patients within the first 48 hours from stroke onset. These guidelines supersede the prior 2007 guidelines and 2009 updates.

***Methods*—**Members of the writing committee were appointed by the American Stroke Association Stroke Council's Scientific Statement Oversight Committee, representing various areas of medical expertise. Strict adherence to the American Heart Association conflict of interest policy was maintained throughout the consensus process. Panel members were assigned topics relevant to their areas of expertise, reviewed the stroke literature with emphasis on publications since the prior guidelines, and drafted recommendations in accordance with the American Heart Association Stroke Council's Level of Evidence grading algorithm.

***Results*—**The goal of these guidelines is to limit the morbidity and mortality associated with stroke. The guidelines support the overarching concept of stroke systems of care and detail aspects of stroke care from patient recognition; emergency medical services activation, transport, and triage; through the initial hours in the emergency department and stroke unit. The guideline discusses early stroke evaluation and general medical care, as well as ischemic stroke, specific interventions such as reperfusion strategies, and general physiological optimization for cerebral resuscitation.

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Αρχική αντιμετώπιση επιτόπου..

•Οι διασώστες πρέπει να ξεκινούν την αντιμετώπιση επί τόπου σύμφωνα με τον πίνακα ***(Class I; Level of Evidence B***). Συνιστάται η εφαρμογή ενός πρωτοκόλλου από τους διασώστες.

•Οι ασθενείς πρέπει να μεταφέρονται άμεσα στο πλησιέστερο πιστοποιημένο 'πρωτογενές κέντρο ΑΕΕ' ή 'ολοκληρωμένο κέντρο ΑΕΕ' ή εναλλακτικά σε κέντρο που μπορεί να προσφέρει οξεία θεραπεία ***(Class I; Level of Evidence A)***. Συχνά αυτό απαιτεί αερομεταφορά **ή παράκαμψη νοσοκομείων.**

•Οι διασώστες πρέπει να προβαίνουν **σε προ-νοσοκομειακή ενημέρωση** ***(Class I; Level of Evidence B)***.

Prehospital Evaluation and Management of Potential Stroke Patients	
Recommended	**Not Recommended**
Assess and manage ABCs	Do not initiate interventions for hypertension unless directed by medical command
Initiate cardiac monitoring	
Provide supplemental oxygen to maintain O_2 saturation >94%	
Establish IV access per local protocol	Do not administer excessive IV fluids
Determine blood glucose and treat accordingly	Do not administer dextrose-containing fluids in nonhypoglycemic patients
	Do not administer medications by mouth (maintain NPO)
Determine time of symptom onset or last known normal, and obtain family contact information, preferably a cell phone	
Triage and rapidly transport patient to nearest most appropriate stroke hospital	Do not delay transport for prehospital interventions
Notify hospital of pending stroke patient arrival	

- ABCs indicates airway, breathing, and circulation; IV, intravenous; and NPO, nothing by mouth.

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Κέντρα οξείας αντιμετώπισης ΑΕΕ

- Primary stroke center
  - ✓ Στοιχεία κλειδιά: **ομάδα οξέος ΑΕΕ**, **μονάδα ΑΕΕ**, **διατυπωμένα πρωτόκολλα και ενσωματωμένο σύστημα αντιμετώπισης επείγοντος**
  - ✓ Υποστηρικτικές υπηρεσίες: **computed tomography scans 24 ώρες/7 ημέρες και ταχύς εργαστηριακός έλεγχος**. Διοικητική υποστήριξη, **ιεραρχία** και συνεχιζόμενη εκπαίδευση
- Comprehensive stroke center
  - ✓ CSC ικανά να προσφέρουν **24/7 state-of-the-art φροντίδα** σε όλες τις αγγειακές εγκεφαλικές νόσους.
- Acute Stroke-Ready Hospital
  - ✓ **διατυπωμένα πρωτόκολλα επειγόντων**
  - ✓ Δυνατότητα διακομιδής σε νοσοκομείο με νευροχειρουργική κάλυψη
  - ✓ Υπεύθυνο/διευθυντή της μονάδας που επιβλέπει τις διαδικασίες και τις πολιτικές του ΑΕΕ (κλινικός ή διοικητικός)
  - ✓ Δυνατότητα χορήγησης iv **rtPA**
  - ✓ **computed tomography scans 24 ώρες/7 ημέρες**
  - ✓ Εργαστηριακά **24 ώρες/7 ημέρες**
  - ✓ Διατήρηση λίστας ασθενών

Alberts et al. JAMA 2000 Jun 21;283(23):3102-9.

Κατευθυντήριες οδηγίες

- Συνιστάται η δημιουργία κέντρων ΑΕΕ ***(Class I; Level of Evidence B)***. Η οργάνωσή τους εξαρτάται από τα τοπικά διαθέσιμα μέσα.
- Το ασθενοφόρο **θα πρέπει να παρακάμπτει νοσοκομεία** που δεν έχουν τα μέσα αντιμετώπισης των ΑΕΕ και να μεταβαίνει στο πλησιέστερο νοσοκομείο με δυνατότητα οξείας αντιμετώπισης των ΑΕΕ ***(Class I; Level of Evidence B)***.

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Υποδοχή στα ΤΕΠ

• Οι ασθενείς **με υποψία ΑΕΕ** έχουν την **ίδια προτεραιότητα** με αυτούς με **ΟΕΜ ή σοβαρό τραύμα**, **ανεξάρτητα από τη σοβαρότητα του νευρολογικού** ελλείμματος

•Αρχική εκτίμηση: **airway, breathing, and circulation** (ABCs), εκτίμηση νευρολογικού ελλείμματος (NIHSS).

•**Πρώιμη κινητοποίηση της ομάδας οξέος ΑΕΕ, ενεργοποίηση πρωτοκόλλων.**

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Ενδοφλέβια θρομβόλυση

- NINDS rtPA Stroke Trial (FDA έγκριση το 1996):
  - ✓ 624 ασθενείς με ισχαιμικό ΑΕΕ έλαβαν placebo ή ενδοφλεβίως rtPA (0.9 mg/kg IV, maximum 90 mg) **μέσα σε 3 ώρες από την έναρξη των συμπτωμάτων**: αύξηση πιθανοτήτων θετικής έκβασης (πλήρης ή σχεδόν πλήρης αποκατάσταση στους 3 μήνες, **OR, 1.9**; 95% CI, 1.2–2.9)
  - ✓ Ενδοκράνια αιμορραγία στο **6.4% των ασθενών που έλαβαν rtPA και** 0.6% των ασθενών που έλαβαν placebo
  - ✓ θνητότητα παρόμοια στις δύο ομάδες στους 3 μήνες (17% versus 21%) και στον 1 χρόνο (24% versus 28%)

- ECASS I και ECASS II, ATLANTIS A και ATLANTIS B παρόμοια αποτελέσματα στο παράθυρο ≤3 ώρες

•NEngJ J Med, 1995
•Hacke et al, JAMA, 1995
•Hacke et al, Lancet, 1998
•Clark et al, Stroke , 2000
•Calrk et al, JAMA, 1999

Πρώτη επίσημη έγκριση του tPA στην Ευρώπη

- Το **2002**, η European Medicines Evaluation Agency εγκρίνει την ενδοφλέβια έγχυση rtPA για την αντιμετώπιση του οξέος ισχαιμικού εντός 3 ωρών από την έναρξη των συμπτωμάτων με την προϋπόθεση της εκπόνησης της ECASS III και της εγγραφής των ασθενών στη βάση δεδομένων Safe Implementation of Thrombolysis in Stroke-Monitoring/Observational Study (SITS-MOST).
- SITS-MOST μελέτησε 6483 ασθενείς που αντιμετωπίστηκαν εντός 3 ωρών σε 285 κέντρα σε 14 χώρες παγκόσμιος: **1.7% συμπτωματική αιμορραγία** στις 24 ώρες και **11.3% θνητότητα στους 3 μήνες**, συγκρίσιμα με τις κλινικές μελέτες. (*Wahlgren et al, Lancet, 2007*)

Off-label χρήση

- **Με πάνω από 15 χρόνια εμπειρίας στη θρομβόλυση,** κάποια κέντρα ανέφεραν τα αποτελέσματα της "off-label" θρομβόλυσης.
  - ✓ ηλικιωμένοι (>80 years)
  - ✓ Μικρό έλλειμμα
  - ✓ Ταχέως βελτιούμενα συμπτώματα
  - ✓ Σοβαρή εγχείρηση ή τραύμα τους προηγούμενους 3 μήνες
  - ✓ Από του στόματος αντιπηκτικά
  - ✓ ισχαιμικό ΑΕΕ τους τελευταίους 3 μήνες

- **Τα αποτελέσματα συνολικά ήταν καλύτερα** στους ασθενείς που αντιμετωπίστηκαν με θρομβόλυση σε σχέση με το placebo

- **Η συχνότητα των ενδοκρανιακών αιμορραγιών δεν αυξήθηκε σε αυτούς τους ασθενείς**

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Διεύρυνση θεραπευτικού παραθύρου rtPA iv

- ECASS I, ECASS II, ATLANTIS A, και ATLANTIS B clinical trials μελέτησαν τη χρησιμοποίηση του ενδοφλέβιου rtPA **μέχρι τις 5-6 ώρες**.
- 1847 ασθενείς στο 3- το 6-ωρών χρονικό παράθυρο
- **Μετανάλυση**: όφελος της θεραπείας **στο 3- το 4.5-ωρών παράθυρο**, τόσο στην αύξηση της πιθανότητας άριστου αποτελέσματος όσο και στη συνολική αναπηρία που σχετίζεται με το ΑΕΕ.
- Στο 3- το 4.5-ωρών χρονικό παράθυρο, η παρεγχυματική αιμορραγία μετά τη θρομβόλυση ήταν **5.9% versus 1.7%** του placebo, αλλά **η θνητότητα δεν αυξήθηκε (**13% versus 12%)
- Θετική έκβαση (mrS<3) στους 3 μήνες σε σχέση με το placebo:
  - ✓ rtPA εκκίνηση έγχυσης **3 με 4.5 hours** από την έναρξη των συμπτωμάτων **OR 1.40** (95% CI, 1.05–1.85)

Hache et al, Lancet, 2004

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Διεύρυνση θεραπευτικού παραθύρου rtPA iv: ECASS III trial

- **ECASS III trial:** όφελος του iv rtPA στο 3- to 4.5-ωρών χρονικό παράθυρο
  - ✓ 3.0 με 4.5 ώρες από την έναρξη των συμπτωμάτων τυχαιοποίηση προς intravenous rtPA (n=418) ή placebo (n=403).
  - ✓ Δόση 0.9 mg/kg (maximum of 90 mg), 10% αρχικό bolus, το υπόλοιπο έγχυση εντός 1 ώρας
  - ✓ **Αποκλείστηκαν:** >80 ετών, αρχικό NIHSS score >25, από του στόματος αντιπηκτικά (ακόμα και με INR <1.7), συνδυασμός προηγούμενου ΑΕΕ και ΣΔ
- Αποτελέσματα:
  - ✓ Συμπτωματική **ενδοκρανιακή αιμορραγία** σε 10 ασθενείς που έλαβαν **rtPA (2,4%)** και 1 που έλαβε **placebo (0.2%);** OR, 9.85; 95% CI, 1.26–77.32; *P*=0.008)
  - ✓ **Θνητότητα παρόμοια στις 2 ομάδες**
  - ✓ **Άριστο αποτέλεσμα στις 90 ημέρες** (mRS score 0–1): **rtPA (52.4%)** placebo (**45.2%**; **OR, 1.34**; 95% CI, 1.02–1.76; risk ratio, 1.16; 95% CI, 1.01–1.34;*P*=0.04).
  - ✓ Ή **συνολική θετική έκβαση, 1.28**; 95% CI, 1.00–1.65)

Hacke et al, N Engl J Med, 2008

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IST-3

- (IST-3), μεγαλύτερη τυχαιοποιημένη, placebo-controlled μελέτη του iv rtPA
- 3035 ασθενείς που τυχαιοποιήθηκαν **εντός 6 ωρών** από την έναρξη των συμπτωμάτων
- Κριτήρια επιλογής παρόμοια με προηγούμενες μελέτες του rtPA συν: **χωρίς άνω όριο ηλικίας** και πιο διευρυμένα όρια ΑΠ
- Πρωτογενές καταλυτικό σημείο, an Oxford Handicap Score of 0 to 2 (ζωντανός και ανεξάρτητος) στους 6 μήνες, στο **37%** των ασθενών του rtPA group versus **35%** στο control group **(OR, 1.27**; 95% CI, 1.10–1.47; *P*=0.001).
- Στις 7 ημέρες, θανατηφόρα ή μη ενδοκρανιακή αιμορραγία στο **7% versus 1%** rtPA ή placebo αντίστοιχα
- **Περισσότεροι θάνατοι στις 7 ημέρες στην ομάδα θεραπεία** (11%) από το control group (7%; adjusted OR, 1.60; 95% CI, 1.22–2.08; *P*=0.001), αλλά στους 6 μήνες **27% των ασθενών κατέληξαν και στις 2 ομάδες**

IST-3 collaborative group, Lancet, 2012

http://www.metropolitan-hospital.gr/maf-aee.html

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Inclusion and Exclusion Characteristics of Patients With Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 Hours From Symptom Onset
Inclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit
Onset of symptoms <3 hours before beginning treatment
Aged ≥18 years
Exclusion criteria
Significant head trauma or prior stroke in previous 3 months
Symptoms suggest subarachnoid hemorrhage
Arterial puncture at noncompressible site in previous 7 days
History of previous intracranial hemorrhage
Intracranial neoplasm, arteriovenous malformation, or aneurysm
Recent intracranial or intraspinal surgery
Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)
Active internal bleeding
Acute bleeding diathesis, including but not limited to
Platelet count <100 000/mm³
Heparin received within 48 hours, resulting in abnormally elevated aPTT greate than the upper limit of normal
Current use of anticoagulant with INR >1.7 or PT >15 seconds
Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
Blood glucose concentration <50 mg/dL (2.7 mmol/L)
CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere
Relative exclusion criteria
Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present:
Only minor or rapidly improving stroke symptoms (clearing spontaneously)
Pregnancy
Seizure at onset with postictal residual neurological impairments
Major surgery or serious trauma within previous 14 days
Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
Recent acute myocardial infarction (within previous 3 months)

Additional Inclusion and Exclusion Characteristics of Patients With Acute Ischemic Stroke Who Could Be Treated With IV rtPA Within 3 to 4.5 Hours From Symptom Onset
Inclusion criteria
Diagnosis of ischemic stroke causing measurable neurological deficit
Onset of symptoms within 3 to 4.5 hours before beginning treatment
Relative exclusion criteria
Aged >80 years
Severe stroke (NIHSS>25)
Taking an oral anticoagulant regardless of INR
History of both diabetes and prior ischemic stroke

- INR indicates international normalized ratio; IV, intravenous; NIHSS, National Institutes of Health Stroke Scale; and rtPA, recombinant tissue plasminogen activator.

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Κατευθυντήριες οδηγίες

- Intravenous rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke ***(Class I; Level of Evidence A)***. Physicians should review the criteria (which are modeled on those used in the NINDS Trial) to determine the eligibility of the patient.

- Intravenous rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for administration to eligible patients who can be treated in the time period **of 3 to 4.5 hours** after stroke onset ***(Class I; Level of Evidence B)***. The eligibility criteria for treatment in this time period are similar to those for people treated at earlier time periods within 3 hours, with the following additional **exclusion criteria**: patients **>80 years old**, those taking **oral anticoagulants regardless of INR**, those with a **baseline NIHSS score >25**, those with imaging evidence of ischemic injury involving **more than one third of the MCA territory**, or those with a history of **both stroke and diabetes mellitus**.

Table 1. Contraindications and Warnings

Abbreviation	Definition	Contraindication	Warning
Age/Medical History			
Age >80	Aged over 80	EU-L	EU-G, US-L (>75)
Stroke & Diabetes	History of previous stroke and diabetes mellitus	EU-L	
Hemostasis			
Single Antiplatelets	Use of prior single antiplatelets*		EU-L/G
Dual Antiplatelets	Use of prior dual antiplatelets*		EU-L/G
OAC	Use of prior oral anticoagulation*	EU-L, US-L	
OAC & INR ≤1.7	Oral anticoagulation and INR ≤1.7†	EU-L, US-L	
OAC & INR >1.7	Oral anticoagulation and INR > 1.7†	EU-L, US-L/G	
INR >1.7	International Normalized Ratio > 1.7†	US-L	
APTT >39	Activated partial thromboplastin time >39 seconds without recent use of heparin†		US-L (stop treatment)
Platelets <100	Platelet count <100 giga/L†	EU-L, US-L/G	EU-G
Glucose/BP			
Glucose >400	Glucose level >400 mg/dL, respectively, 22.2 mmol/L†	EU-L	EU-G, US-L
Glucose >180	Glucose level >180 mg/dL, respectively, 10 mmol/L†		EU-G
Glucose <50	Glucose level <50 mg/dL, respectively, 2.8 mmol/L†	EU-L, US-G	EU-G, US-L
BPSYS ≥185	Systolic blood pressure ≥185 mm Hg †	EU-L/G, US-L/G	
BPDIA ≥110	Diastolic blood pressure ≥110 mm Hg †	EU-L/G, US-L/G	
IV Antihypertensives	Use of intravenous antihypertensives on the day of enrolment‡	EU-L	
CT Findings			
Early Changes	Edema, dense middle cerebral artery sign, loss of insular ribbon, lenticular hypodensity, acute infarction, sulcal effacement, or ASPECT-score of 8 or 9§		
Major Early Changes	Mass effect, infarction of >1/3 of the middle cerebral artery territory, midline shift, or ASPECT-score of ≤7§	EU-L, US-G (>1/3)	US-L
ASPECT ≤7	ASPECT-score of ≤7§		
NIHSS			
NIHSS >22	NIHSS of >22†	EU-L (>25)	US-L/G
NIHSS <6	Minor deficit, arbitrarily defined as NIHSS < 6 †	EU-L, US-G	US-L

Frank et al, VISTA collaborators, Stroke 2013

http://www.metropolitan-hospital.gr/maf-aee.html

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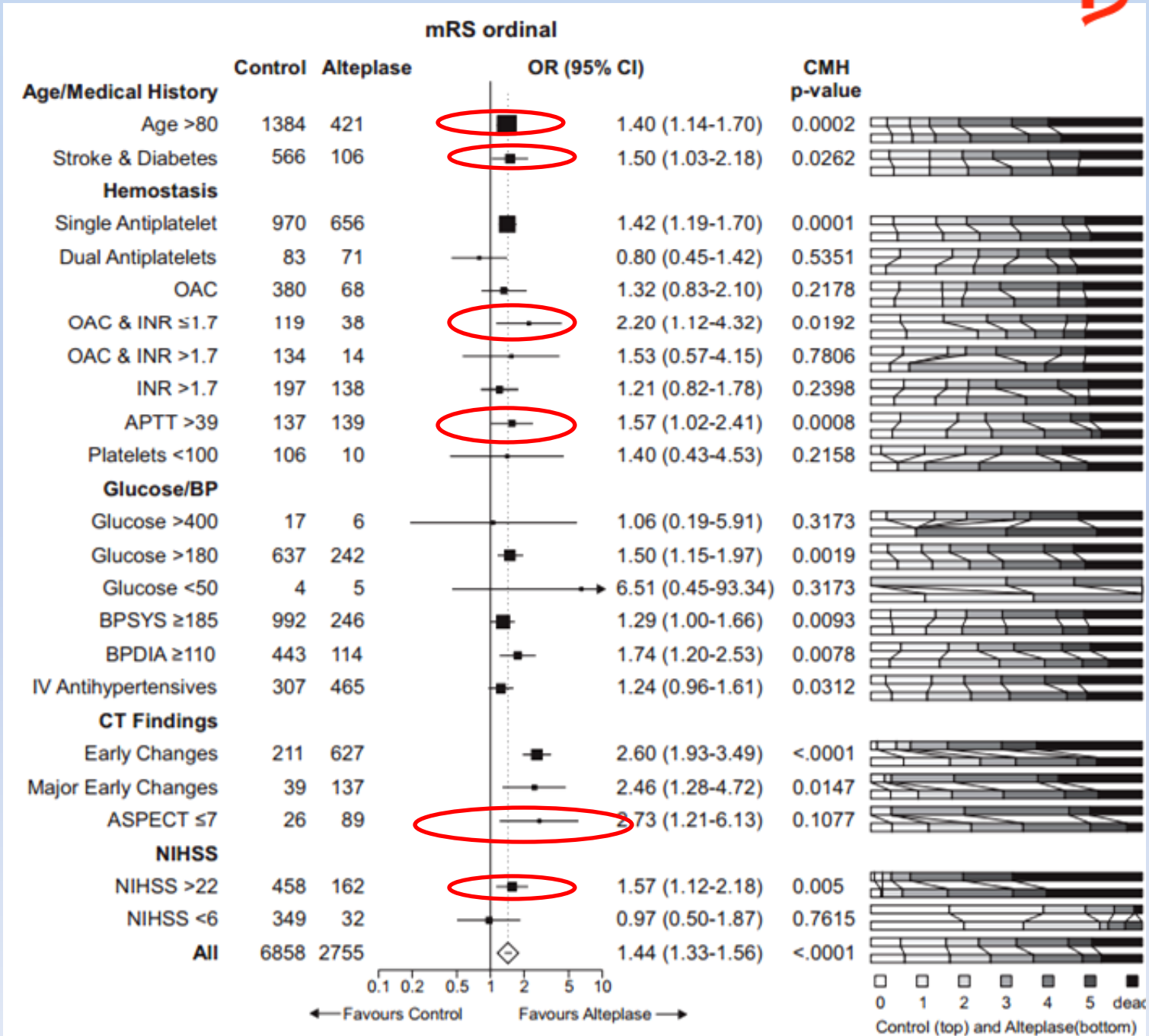


Frank et al, VISTA collaborators, Stroke 2013

Safety and Outcomes of Intravenous Thrombolysis in Stroke Mimics

A 6-Year, Single-Care Center Study and a Pooled Analysis of Reported Series

Georgios Tsivgoulis, MD; Andrei V. Alexandrov, MD; Jason Chang, MD; Vijay K. Sharma, MD; Steven L. Hoover, MD; Annabelle Y. Lao, MD; Wei Liu, MD; Elefterios Stamboulis, MD; Anne W. Alexandrov, PhD; Marc D. Malkoff, MD; James L. Frey, MD

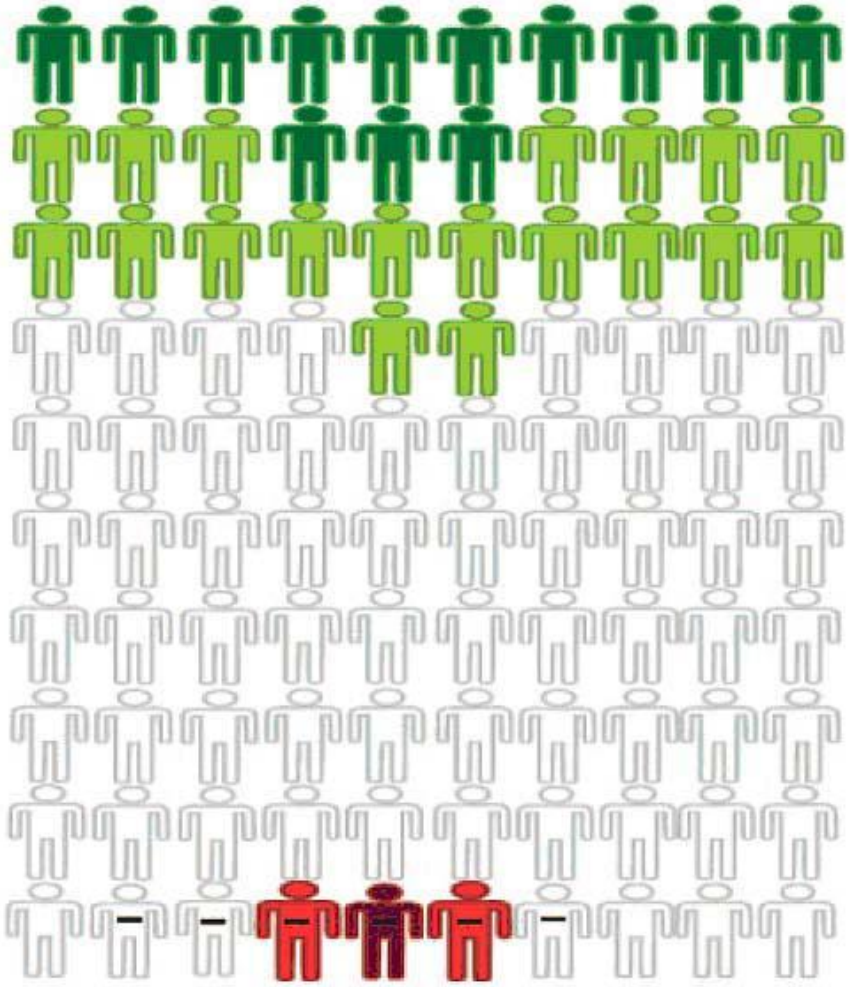
Background and Purpose—Efforts to increase the availability and shorten the time delivery of intravenous thrombolysis in patients with acute ischemic stroke carry the potential for tissue plasminogen activator administration in patients with diseases other than stroke, that is, stroke mimics (SMs). We aimed to determine safety and to describe outcomes of intravenous thrombolysis in SM.

Methods—We retrospectively analyzed stroke registry data of consecutive acute ischemic stroke admissions treated with intravenous thrombolysis over a 6-year-period. The admission National Institutes of Health Stroke Scale score, vascular risk factors, ischemic lesions on brain MRI (routinely performed as part of diagnostic work-up), and discharge modified Rankin Scale scores were documented. Initial stroke diagnosis in the emergency department was compared with final discharge diagnosis. SM diagnosis was based on the absence of ischemic lesions on diffusion-weighted imaging sequences in addition to an alternate discharge diagnosis. Symptomatic intracranial hemorrhage was defined as brain imaging evidence of intracranial hemorrhage with clinical worsening by National Institutes of Health Stroke Scale score increase of ≥4 points.

Results—Intravenous thrombolysis was administered in 539 patients with acute ischemic stroke (55% men; mean age, 66±15 years). Misdiagnosis of acute ischemic stroke was documented in 56 cases (10.4%; 95% CI, 7.9% to 13.3%). Conversion disorder (26.8%), complicated migraine (19.6%), and seizures (19.6%) were the 3 most common final diagnoses in SM. SMs were younger (mean age, 56±13 years) and had milder baseline stroke severity (median National Institutes of Health Stroke Scale, 6; interquartile range, 4) compared with patients with confirmed acute ischemic stroke (mean age, 67±14 years; median National Institutes of Health Stroke Scale, 8; interquartile range, 10; $P<0.001$). There was no case of symptomatic intracranial hemorrhage in SMs (0%; 95% CI, 0% to 5.5%); 96% of SMs were functionally independent at hospital discharge (modified Rankin Scale, 0 to 1).

Conclusions—Our single-center data indicate favorable safety and outcomes of intravenous thrombolysis administered to SM. **(*Stroke*. 2011;42:1771-1774.)**

TPA for Cerebral Ischemia within 3 Hours of Onset-Changes in Outcome Due to Treatment



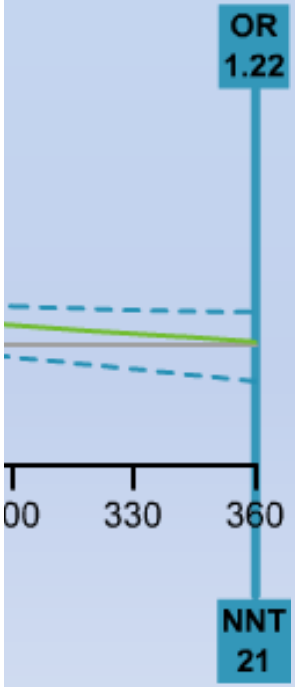
Changes in final outcome as a result of treatment:

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

n!



d an average equivalent of 1

Lees et al, Lancet, 2010

Saver, J. L.&Kalafut, M. (2011). Thrombolytic Therapy in Stroke [Internet]. Medscape. Available from: http://emedicine.medscape.com/article/1160840

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Editorial

Does "Time Is Brain" Also Mean "Time Is Clot"?

Time Dependency of Tissue-Type Plasminogen Activator–Induced Recanalization in Acute Ischemic Stroke

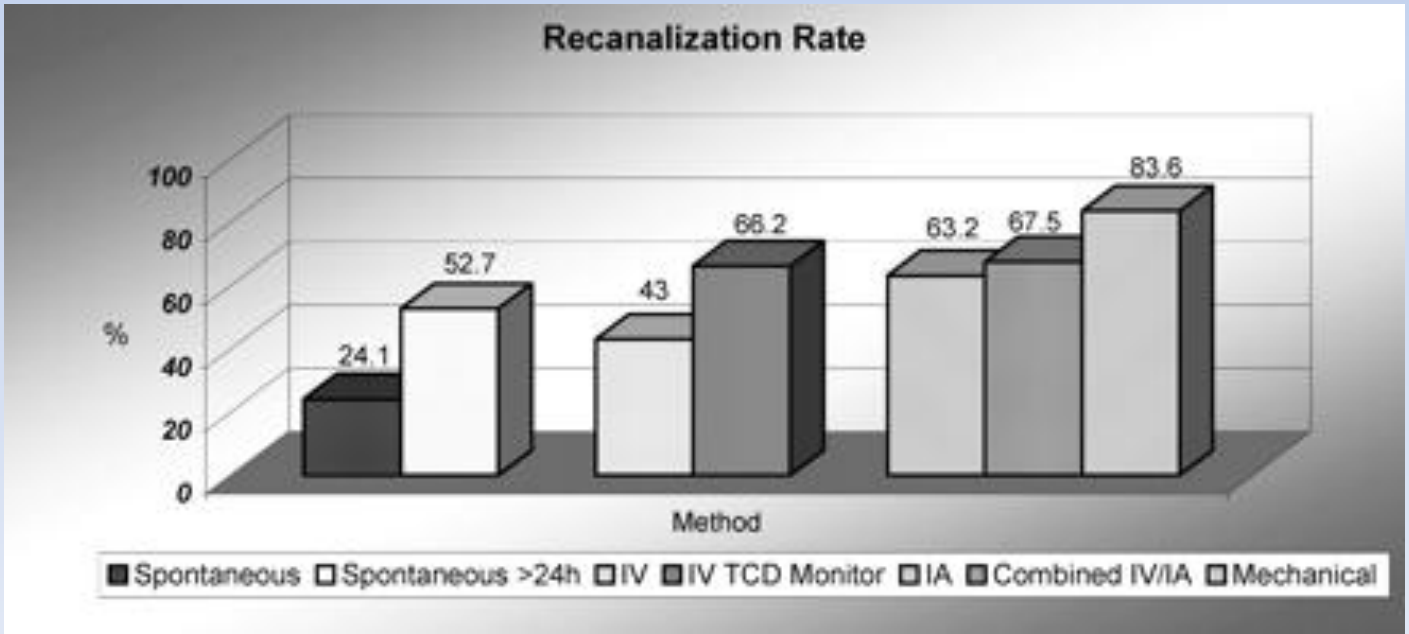
Georgios Tsivgoulis, MD, PhD, MSc, FESO; Andrei V. Alexandrov, MD

able. They also serve as a reminder that the current mantra "Time is Brain" can also mean "Time is Clot" (ie, clot maturation making it more resistive to treatment). Therefore, better, faster, and safer reperfusion therapies[16–18] should be expeditiously tested in ongoing pivotal trials for us to be able to help more patients at centers of all levels of care and in the nick of time.

Stroke, 2014

Επαναιμάτωση

- Ωστόσο με την iv θρομβόλυση τα ποσοστά επαναιμάτωσης παραμένουν σχετικά χαμηλά.
- Αυτόματη (24.1%), **iv θρομβόλυση (46.2%),** iv θρομβόλυση+TCD (66.2%), ενδαρτηριακή θρομβόλυση (63.2%), συνδυασμός iv/ia (67.5%), μηχανική (83.6%).
- 14 και 55% για την έσω καρωτίδα και τη μέση εγκεφαλική αντίστοιχα με iv θρομβόλυση
- Recanalization matters:
  - Καλό λειτουργικό αποτέλεσμα OR 4.43 (95% CI, 3.32 to 5.91)
  - Θνητότητα στους 3 μήνες μειωμένη OR 0.24 (95% CI, 0.16 to 0.35)
  - Παρόμοια συμπτωματική ενδοκρανιακή αιμορραγία OR 1.11 (95% CI, 0.71 to 1.74)



Rha & Shaver, Stroke, 2007

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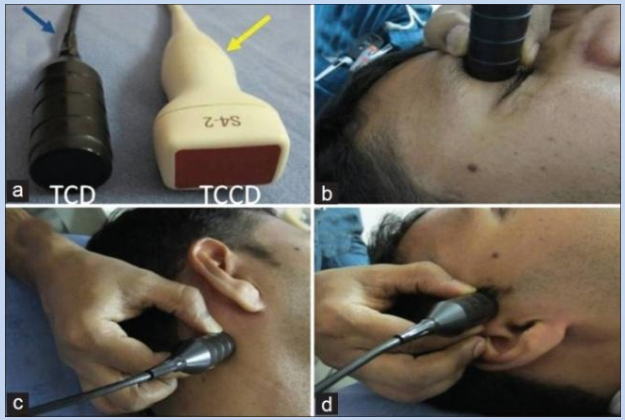
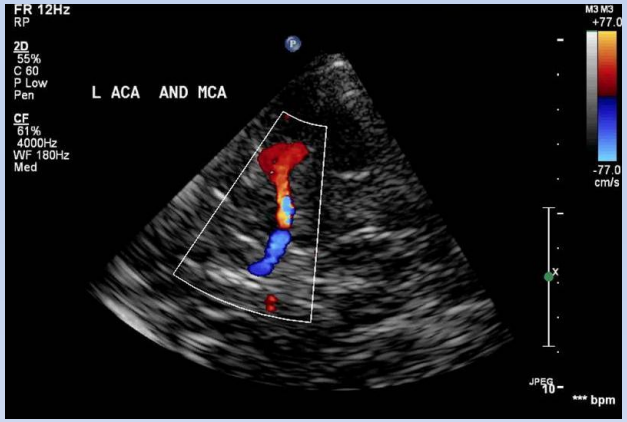
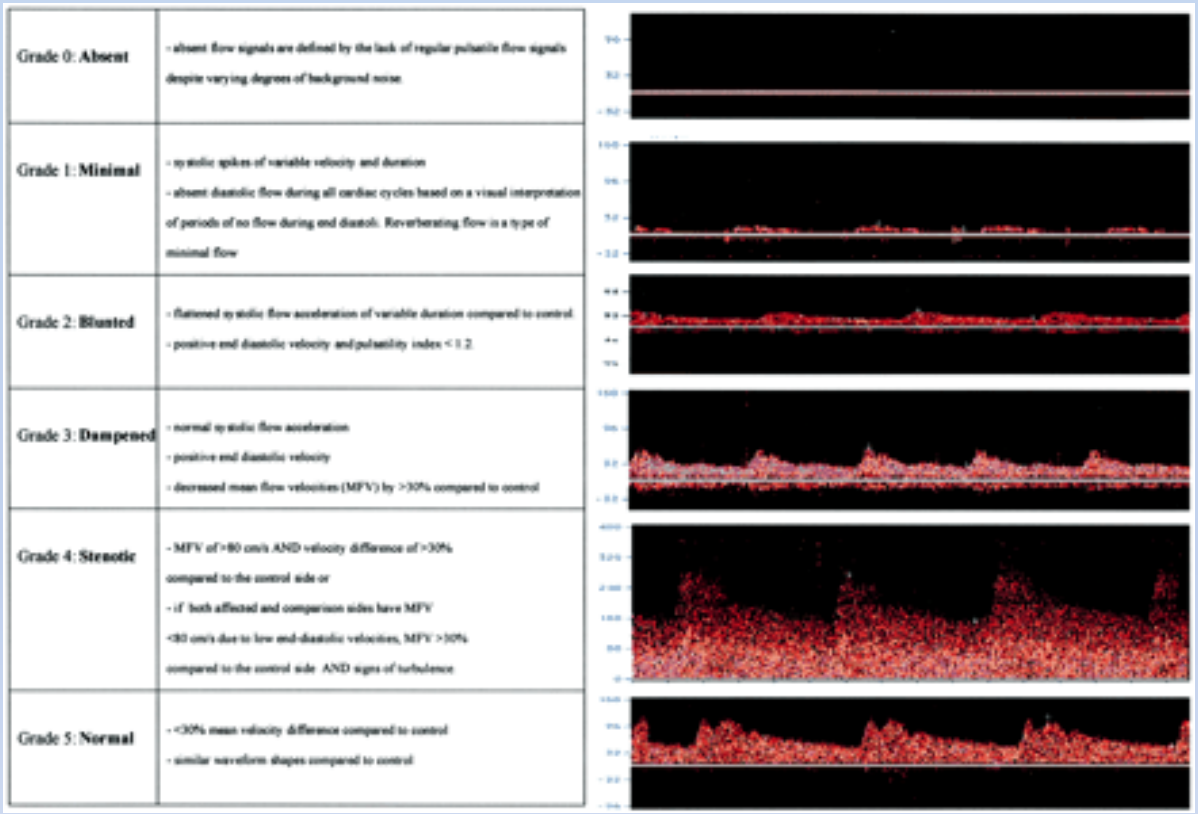
Sonothrombolysis (CLOTBUST trial)







- 126 ασθενείς rtPA μόνο ή rtPA+TCD
- **49% των ασθενών με επαναιμάτωση** εντός 2 ωρών με iv rtPA και TCD **versus 30%** μόνο με iv rtPA (*P*=0.03).
- Ενδοκρανιακή αιμορραγία στο 4.8% και στις δύο ομάδες
- Στους **3 μήνες 42% και 29% αντίστοιχα** modified Rankin score 0-1 (P=0.2)

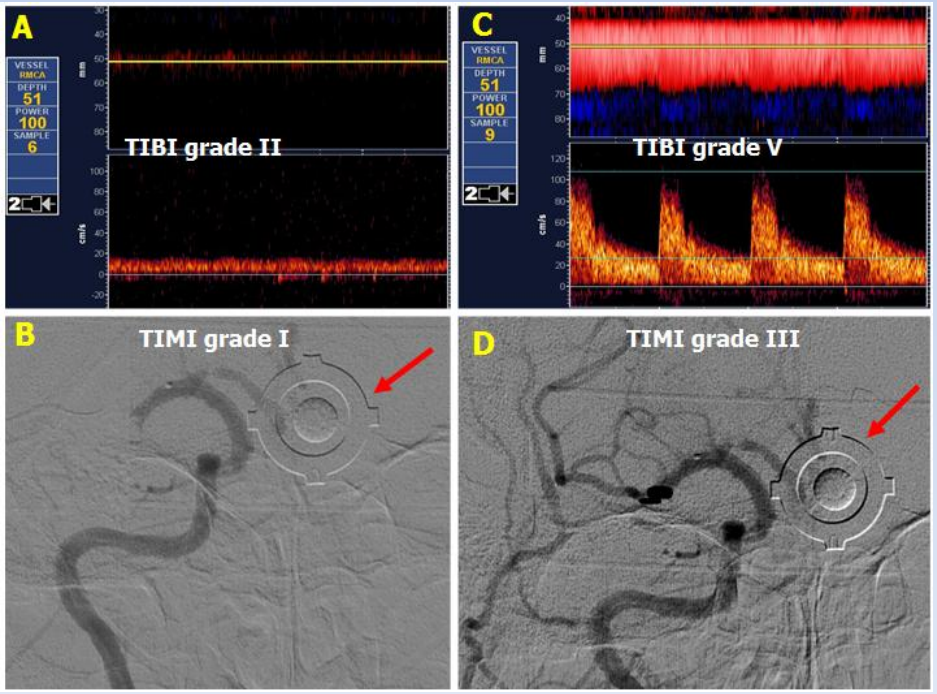
Alexandrov et al, N Engl J Med. 2004

Real-time Validation of Transcranial Doppler Criteria in Assessing Recanalization During Intra-arterial Procedures for Acute Ischemic Stroke

An International, Multicenter Study

Georgios Tsivgoulis, MD; Marc Ribo, MD; Marta Rubiera, MD; Spyros N. Vasdekis, MD; Kristian Barlinn, MD; Dimitrios Athanasiadis, MD; Reza Bavarsad Shahripour, MD; Sotirios Giannopoulos, MD; Elefterios Stamboulis, MD; Mark R. Harrigan, MD; Carlos A. Molina, MD; Andrei V. Alexandrov, MD

Conclusions—At laboratories with high-interrater reliability, TIBI criteria can accurately predict brain recanalization in real time as compared with thrombolysis in myocardial infarction angiographic scores. **(*Stroke*. 2013;44:394-400.)**



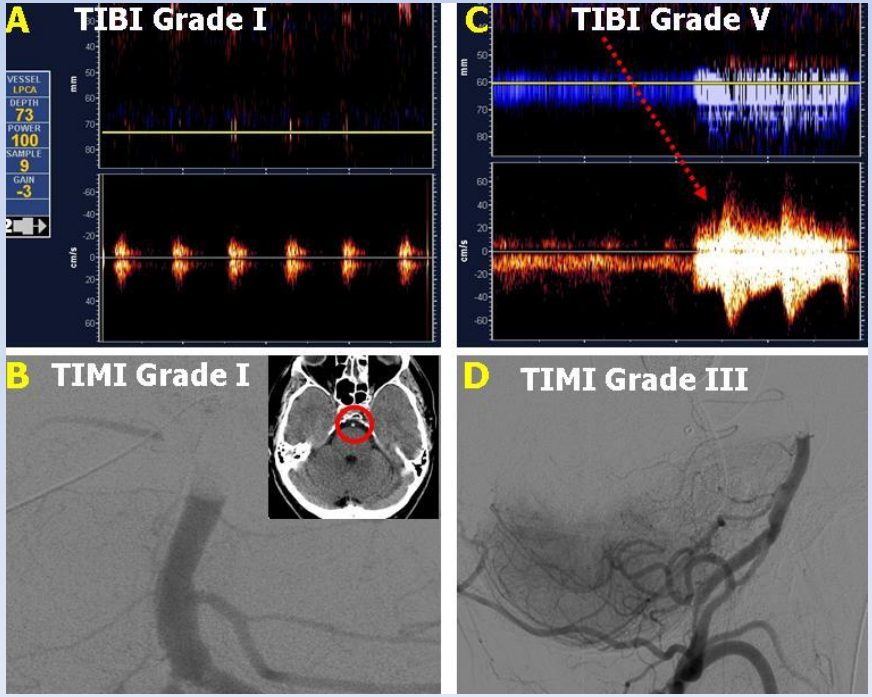
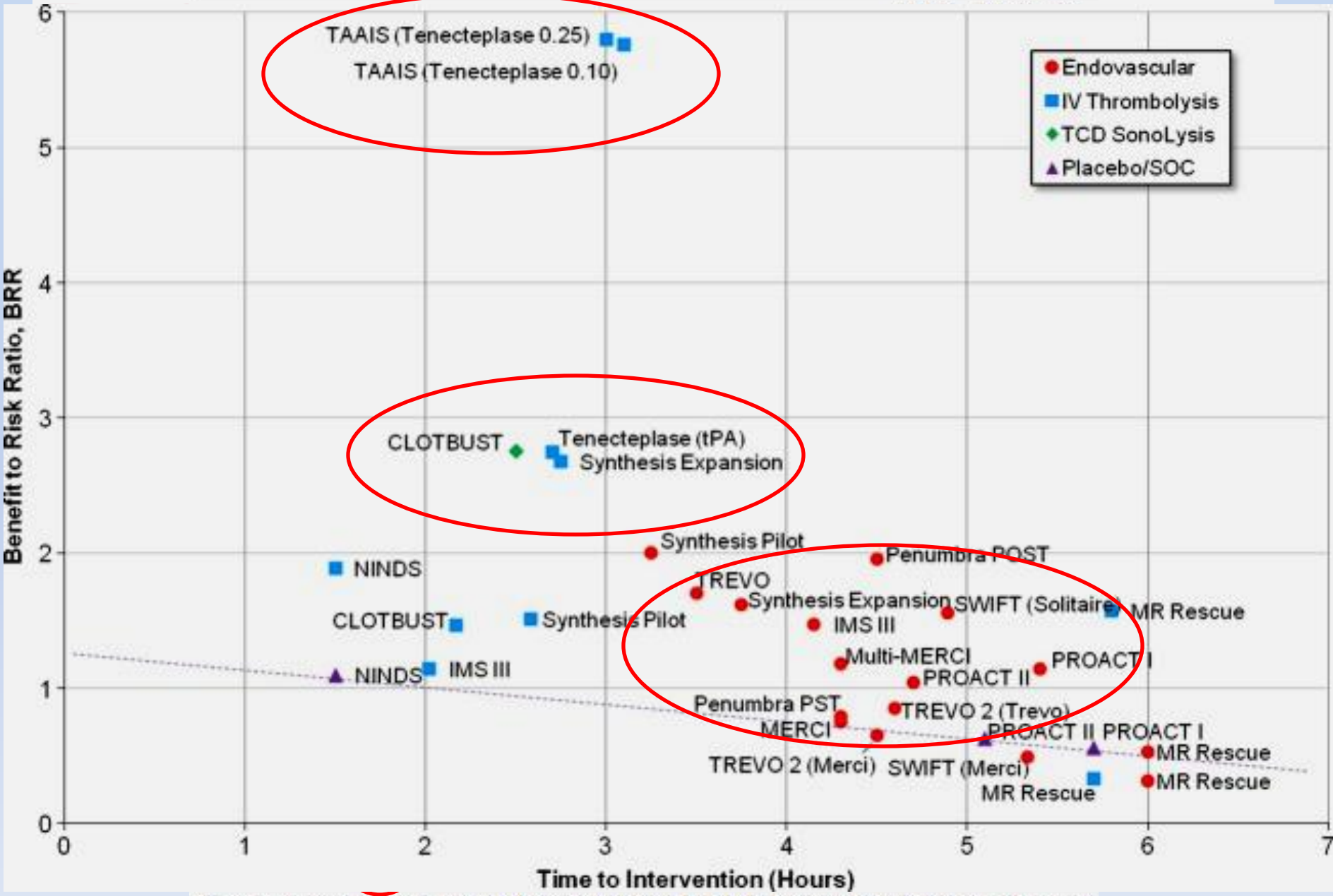


Table 1. Baseline characteristics of included studies.



OTT, onset-to-treatment time; NIHSS, National Institute of Health Stroke Scale; 90d mRS, modified Rankin Scale at 90 days; TCD, transcrania Doppler; IV, intravenous; tPA, alteplase; TNK, tenecteplase; UK, urokinase; SOC, standard of care; IA, intra-arterial; MT, mechanical thrombecto my.

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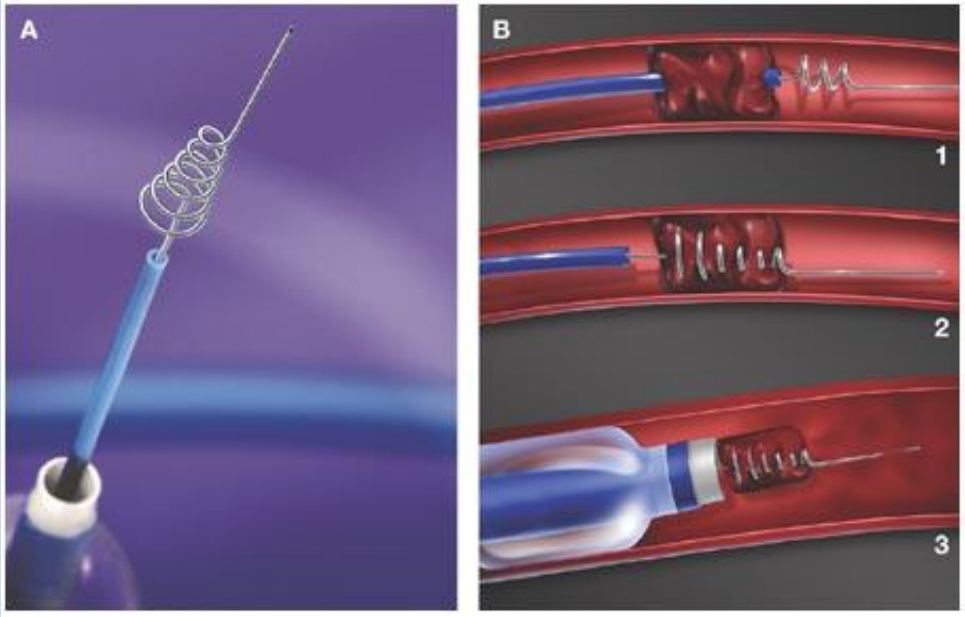
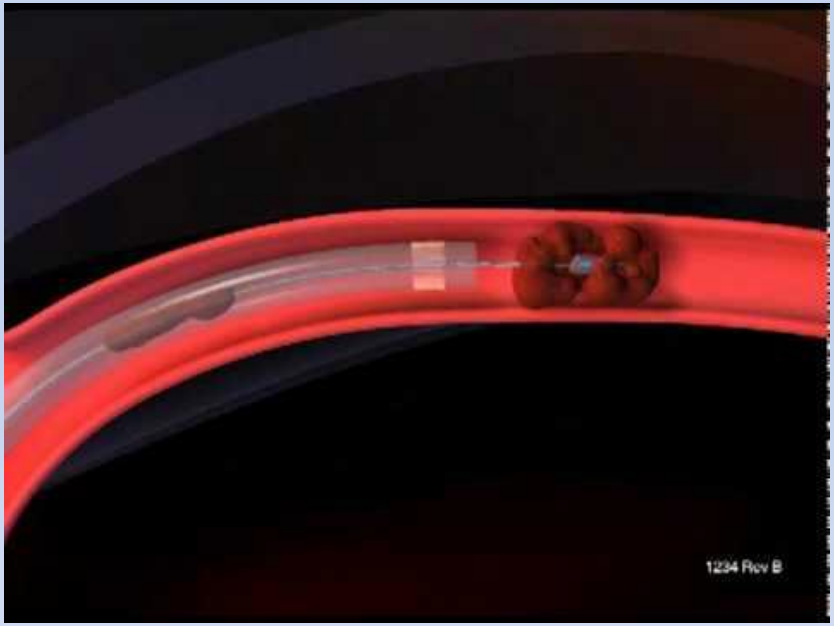
Μηχανική θρομβεκτομή

Πρώτης γενιάς retrievers: Merci and Penumbra





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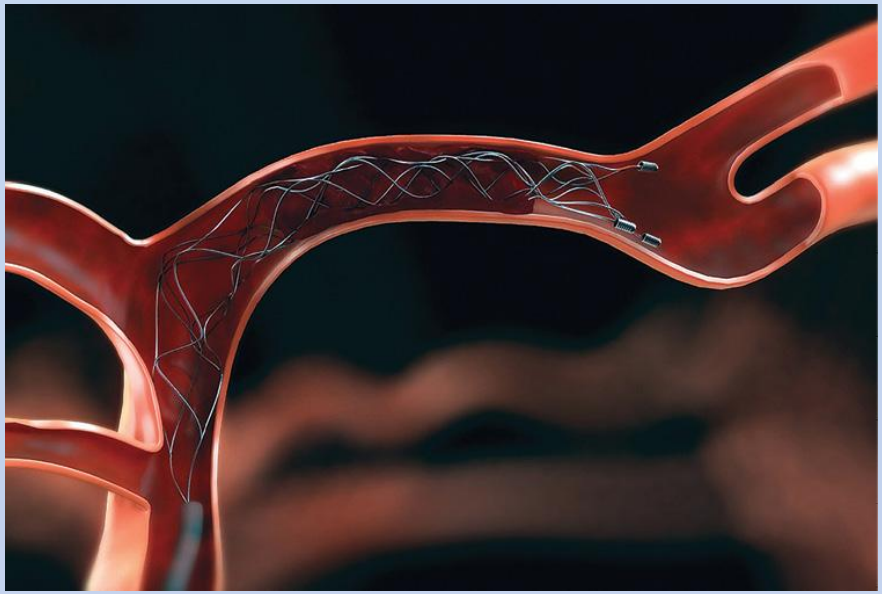
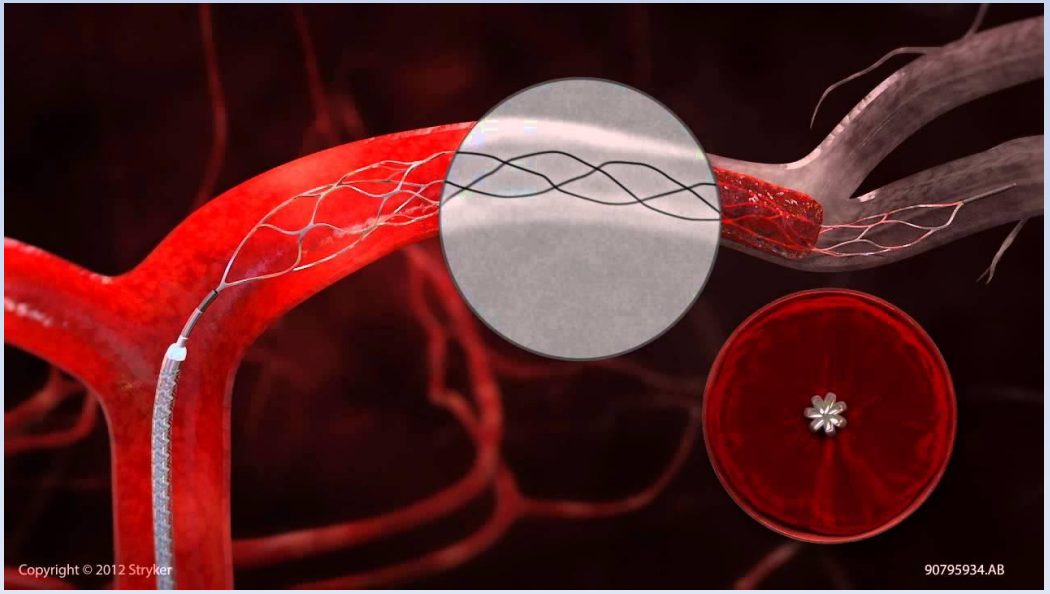
Δεύτερης γενιάς (stent retrievers): Solitaire and Trevo





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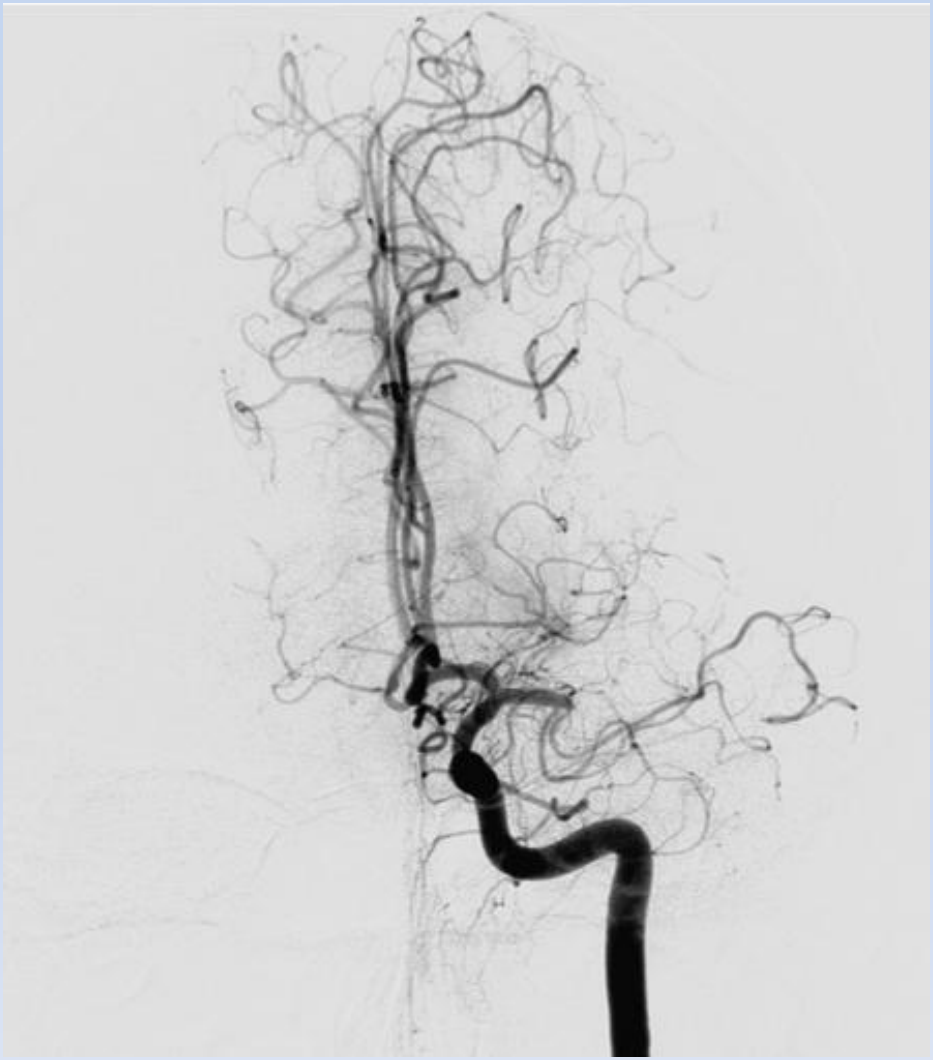
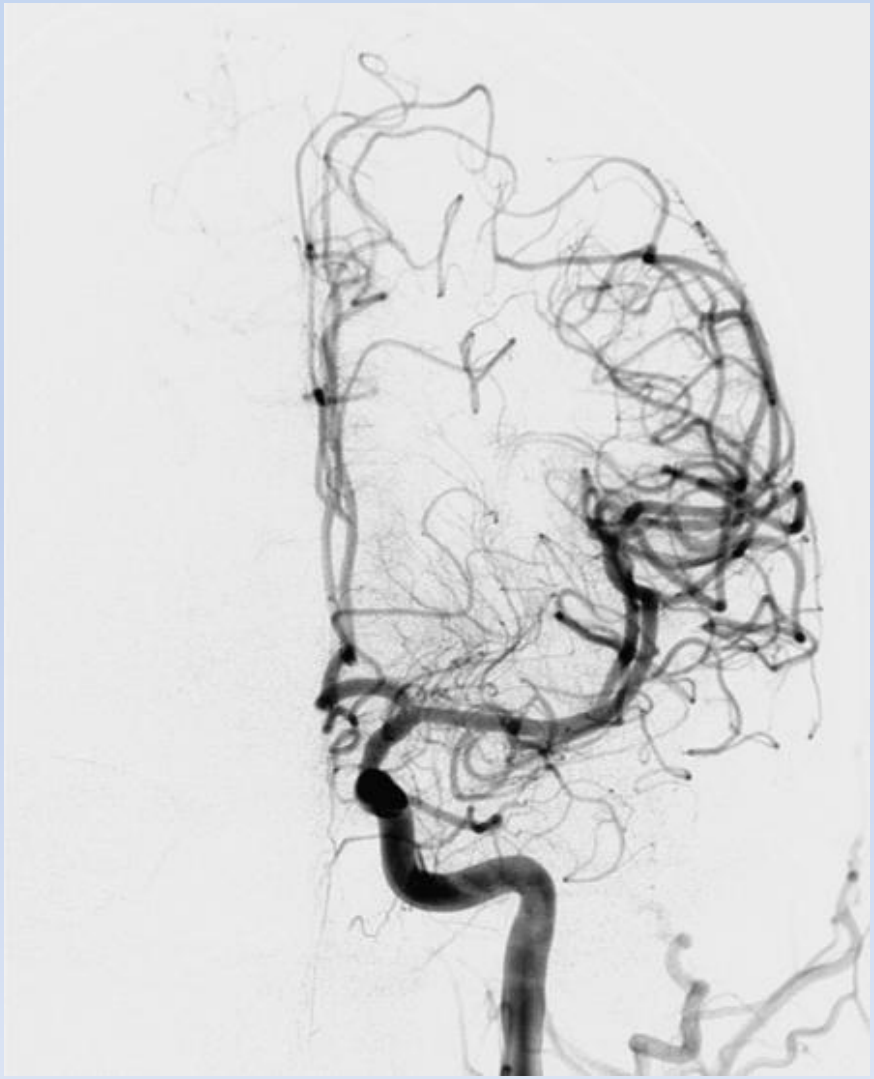
ΠΡΙΝ…



ΚΑΙ ΜΕΤΑ



Castano et al Interv Neuroradiol. 2009

http://www.metropolitan-hospital.gr/maf-aee.html

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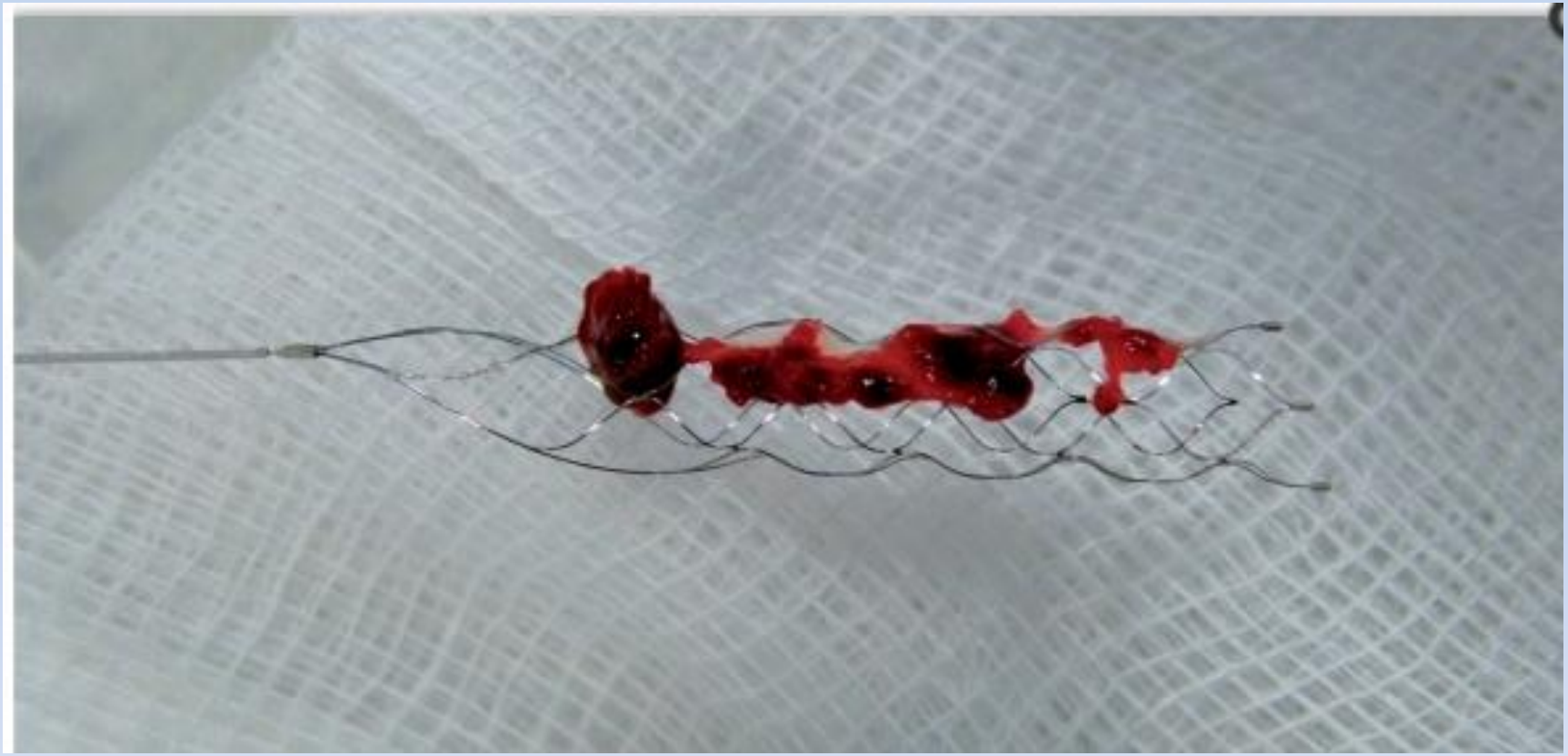
Solitaire



A thrombus retrieved with a single pass of the Solitaire™ AB device

Castano et al Interv Neuroradiol. 2009

Published in final edited form as:
N Engl J Med. 2013 March 7; 368(10): 893–903. doi:10.1056/NEJMoa1214300.

METROPOLITAN HOSPITAL

Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke

Joseph P. Broderick, M.D., Yuko Y. Palesch, Ph.D., Andrew M. Demchuk, M.D., Sharon D. Yeatts, Ph.D., Pooja Khatri, M.D., Michael D. Hill, M.D., Edward C. Jauch, M.D., Tudor G. Jovin, M.D., Bernard Yan, M.D., Frank L. Silver, M.D., Rüdiger von Kummer, M.D., Carlos A. Molina, M.D., Bart M. Demaerschalk, M.D., Ronald Budzik, M.D., Wayne M. Clark, M.D., Osama O. Zaidat, M.D., Tim W. Malisch, M.D., Mayank Goyal, M.D., Wouter J. Schonewille, M.D., Mikael Mazighi, M.D., Ph.D., Stefan T. Engelter, M.D., Craig Anderson, M.D., Ph.D., Judith Spilker, R.N., B.S.N., Janice Carrozzella, R.N., B.A., R.T.(R.), Karla J. Ryckborst, R.N., B.N., L. Scott Janis, Ph.D., Renée H. Martin, Ph.D., Lydia D. Foster, M.S., and Thomas A. Tomsick, M.D. for the Interventional Management of Stroke (IMS) III Investigators

Abstract

BACKGROUND—Endovascular therapy is increasingly used after the administration of intravenous tissue plasminogen activator (t-PA) for patients with moderate-to-severe acute ischemic stroke, but whether a combined approach is more effective than intravenous t-PA alone is uncertain.

METHODS—We randomly assigned eligible patients who had received intravenous t-PA within 3 hours after symptom onset to receive additional endovascular therapy or intravenous t-PA alone, in a 2:1 ratio. The primary outcome measure was a modified Rankin scale score of 2 or less (indicating functional independence) at 90 days (scores range from 0 to 6, with higher scores indicating greater disability).

RESULTS—The study was stopped early because of futility after 656 participants had undergone randomization (434 patients to endovascular therapy and 222 to intravenous t-PA alone). The proportion of participants with a modified Rankin score of 2 or less at 90 days did not differ significantly according to treatment (40.8% with endovascular therapy and 38.7% with intravenous t-PA; absolute adjusted difference, 1.5 percentage points; 95% confidence interval [CI], −6.1 to 9.2, with adjustment for the National Institutes of Health Stroke Scale [NIHSS] score [8–19, indicating moderately severe stroke, or ≥20, indicating severe stroke]), nor were there significant differences for the predefined subgroups of patients with an NIHSS score of 20 or higher (6.8 percentage points; 95% CI, −4.4 to 18.1) and those with a score of 19 or lower (−1.0 percentage point; 95% CI, −10.8 to 8.8). Findings in the endovascular-therapy and intravenous t-PA groups were similar for mortality at 90 days (19.1% and 21.6%, respectively; P = 0.52) and the proportion of patients with symptomatic intracerebral hemorrhage within 30 hours after initiation of t-PA (6.2% and 5.9%, respectively; P = 0.83).

Published in final edited form as:
N Engl J Med. 2013 March 7; 368(10): 904–913. doi:10.1056/NEJMoa1213701.

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Endovascular Treatment for Acute Ischemic Stroke

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Abstract

BACKGROUND—In patients with ischemic stroke, endovascular treatment results in a higher rate of recanalization of the affected cerebral artery than systemic intravenous thrombolytic therapy. However, comparison of the clinical efficacy of the two approaches is needed.

METHODS—We randomly assigned 362 patients with acute ischemic stroke, within 4.5 hours after onset, to endovascular therapy (intraarterial thrombolysis with recombinant tissue plasminogen activator [t-PA], mechanical clot disruption or retrieval, or a combination of these approaches) or intravenous t-PA. Treatments were to be given as soon as possible after randomization. The primary outcome was survival free of disability (defined as a modified Rankin score of 0 or 1 on a scale of 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability despite symptoms, and 6 death) at 3 months.

RESULTS—A total of 181 patients were assigned to receive endovascular therapy, and 181 intravenous t-PA. The median time from stroke onset to the start of treatment was 3.75 hours for endovascular therapy and 2.75 hours for intravenous t-PA (P<0.001). At 3 months, 55 patients in the endovascular-therapy group (30.4%) and 63 in the intravenous t-PA group (34.8%) were alive without disability (odds ratio adjusted for age, sex, stroke severity, and atrial fibrillation status at baseline, 0.71; 95% confidence interval, 0.44 to 1.14; P = 0.16). Fatal or nonfatal symptomatic intracranial hemorrhage within 7 days occurred in 6% of the patients in each group, and there were no significant differences between groups in the rates of other serious adverse events or the case fatality rate.

CONCLUSIONS—The results of this trial in patients with acute ischemic stroke indicate that endovascular therapy is not superior to standard treatment with intravenous t-PA. (Funded by the Italian Medicines Agency, ClinicalTrials.gov number, NCT00640367.)

Intravenous recombinant tissue plasminogen activator (t-PA) is the standard treatment for acute ischemic stroke, but more than half the treated patients do not recover completely or die.[1] Alternative treatments, such as endovascular treatment, have been used for many years. As compared with endovascular treatment, intravenous thrombolysis is associated with a lower probability of recanalization[2–9] (46% of cases with intravenous t-PA vs. >80% with

Published in final edited form as:
N Engl J Med. 2013 March 7; 368(10): 914–923. doi:10.1056/NEJMoa1212793.

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

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Abstract

BACKGROUND—Whether brain imaging can identify patients who are most likely to benefit from therapies for acute ischemic stroke and whether endovascular thrombectomy improves clinical outcomes in such patients remains unclear.

METHODS—In this study, we randomly assigned patients within 8 hours after the onset of large-vessel, anterior-circulation strokes to undergo mechanical embolectomy (Merci Retriever or Penumbra System) or receive standard care. All patients underwent pretreatment computed tomography or magnetic resonance imaging of the brain. Randomization was stratified according to whether the patient had a favorable penumbral pattern (substantial salvageable tissue and small infarct core) or a non-penumbral pattern (large core or small or absent penumbra). We assessed outcomes using the 90-day modified Rankin scale, ranging from 0 (no symptoms) to 6 (dead).

RESULTS—Among 118 eligible patients, the mean age was 65.5 years, the mean time to enrollment was 5.5 hours, and 58% had a favorable penumbral pattern. Revascularization in the embolectomy group was achieved in 67% of the patients. Ninety-day mortality was 21%, and the rate of symptomatic intracranial hemorrhage was 4%; neither rate differed across groups. Among all patients, mean scores on the modified Rankin scale did not differ between embolectomy and standard care (3.9 vs. 3.9, P = 0.99). Embolectomy was not superior to standard care in patients with either a favorable penumbral pattern (mean score, 3.9 vs. 3.4; P = 0.23) or a nonpenumbral pattern (mean score, 4.0 vs. 4.4; P = 0.32). In the primary analysis of scores on the 90-day modified Rankin scale, there was no interaction between the pretreatment imaging pattern and treatment assignment (P = 0.14).

Mechanical Thrombectomy for Emergent Large Vessel Occlusion (ELVO): A Critical Appraisal of Recent RCTs.

METROPOLITAN HOSPITAL

Journal:	*Brain and Behavior*
Manuscript ID:	Draft
Wiley - Manuscript type:	Reviews
Date Submitted by the Author:	n/a
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Search Terms:	cerebrovascular diseases
Abstract:	Background & Purpose: After numerous attempts to prove efficacy for endovascular treatment of ischemic stroke, a series of recent randomized-controlled clinical trials (RCTs) established fast mechanical thrombectomy (MT) as a safe and effective novel treatment for emergent large vessel occlusion (ELVO) in the anterior cerebral circulation. Methods: We reviewed 5 recent RCTs that evaluated the safety and efficacy of MT in ELVO patients and captured available information on recanalization/reperfusion, symptomatic intracranial hemorrhage (sICH), clinical outcome and mortality. MT was performed with stenttrievers (ST), aspiration techniques or a combination of these endovascular approaches. We applied meta-analytical methodology to evaluate the pooled effect of MT on recanalization/reperfusion, sICH, functional independence (modified-Rankin-Scale score of 0-2) and three-month mortality rates in comparison to best medical therapy (BMT). Results: MT was associated with increased likelihood of complete recanalization/reperfusion (RR: 2.22; 95%CI: 1.89-2.62; p<0.00001) and three-month functional independence (RR: 1.72; 95%CI: 1.48-1.99; p<0.00001) without any heterogeneity across trials (I2=0%). The absolute benefit increase of MT for complete recanalization/reperfusion and functional independence was 44 (NNT=2) and 16 (NNT=6) respectively. MT was not associated with increased risk of three-month mortality (15% with MT vs. 19% with BMT) and sICH (4.6% with MT vs. 4.3% with BMT), while small heterogeneity was detected across the included trials (I2<25%). Conclusions: MT is a safe and highly effective treatment for patients with ELVO in the anterior circulation. For every 6 ELVO patients treated with MT three more will achieve complete recanalization at 24 hours following

Table 1

Inclusion criteria across different randomized-controlled clinical trials (RCTs).

RCT	Time window (hours)	Affected Arteries	Lowest NIHSS	Age Limit	Neuroimaging	Lowest ASPECTS
MR CLEAN	<6	TICA, M1, M2, A1, A2	2	-	CT/CTA	-
ESCAPE	<12	TICA, M1	6	-	CT/CTA/CTA Multiphase (for collaterals)	6
EXTEND-IA	<6	TICA, M1, M2	-	-	CT/CTA/CTP (for mismatch)	-
SWIFT PRIME	<6	TICA, M1, M2	8	<80	CT/CTA/MRA/ MRP/CTP (for Infarct core)	6
REVASCAT	<8	TICA, M1	6	<80	CT/CTA (MRA/DSA)	7 (CT) 6 (DWI)

TICA: terminal internal carotid artery, M1, M2 branches of the middle cerebral artery, A1, A2 branches of the anterior cerebral artery, NIHSS: National Institutes of Health Stroke Scale, ASPECTS : Alberta Stroke Program Early CT score, DWI: diffusion weighted imaging.

Table 3.

Complete recanalization rates defined by a modified Thrombolysis in Cerebral Infarction (TICI) score 2b or 3 at the end of mechanical thrombectomy (2nd and 3rd column) and by non-invasive neuroimaging 24-27 hours later (4th and 5th column).

Clinical Trial	MT	BMT	MT	BMT
MR CLEAN	115/196 (59%)	N/A	141/187 (75%)*	68/207 (33%)*
ESCAPE	113/156 (72%)	N/A	N/A	N/A
EXTEND-IA	25/29 (86%)	N/A	33/35 (94%)*	15/35 (43%)*
SWIFT PRIME	73/83 (88%)	N/A	53/64 (83%)**	21/52 (40%)**
REVASCAT	67/102 (66%)	N/A	N/A	N/A

MT: mechanical thrombectomy

BMT: best medical therapy

N/A: non-applicable

* Recanalization shown in brain CTA/MRA at 24 hours. ** Reperfusion shown in brain CT Perfusion/MR perfusion at 27 hours, N/A: not available

Table 4.

Brain infarction volume at 24 hours after treatment measured with CT in MR CLEAN trial and with CT or MRI in SWIFT PRIME and REVASCAT trials.

Clinical Trial	MT (mean, 95% CI)	BMT (mean, 95% CI)	p
MR CLEAN	49ml (22-96)	79ml (34-125)	<0.01
ESCAPE	N/A	N/A	-
EXTEND-IA	N/A	N/A	-
SWIFT PRIME	32ml (0-503)	35ml (0-407)	0.09
REVASCAT	16ml (8-59)	39ml (12-87)	0.02

MT: mechanical thrombectomy

BMT: best medical therapy

Figure 3.

Study or Subgroup	Trombectomy Tx Events	Total	Conventional Tx Events	Total	Weight	Risk Ratio IV, Random, 95% CI
ESCAPE	6	165	4	150	19.3%	1.36 [0.39, 4.74]
EXTEND-IA	0	35	2	35	3.5%	0.20 [0.01, 4.02]
MR CLEAN	18	233	17	267	61.7%	1.21 [0.64, 2.30]
REVASCAT	5	103	2	103	11.8%	2.50 [0.50, 12.59]
SWIFT-PRIME	0	98	3	97	3.7%	0.14 [0.01, 2.70]
Total (95% CI)		**634**		**652**	**100.0%**	**1.17 [0.66, 2.07]**
Total events	29		28			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 4.22$, df = 4 (P = 0.38); $I^2 = 5\%$

Test for overall effect: Z = 0.55 (P = 0.58)

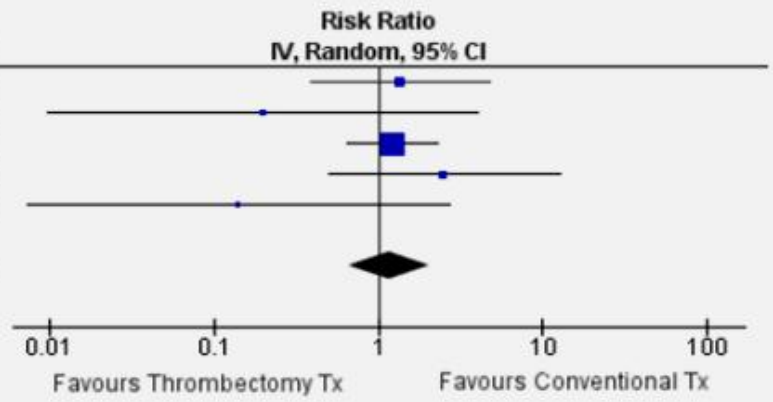
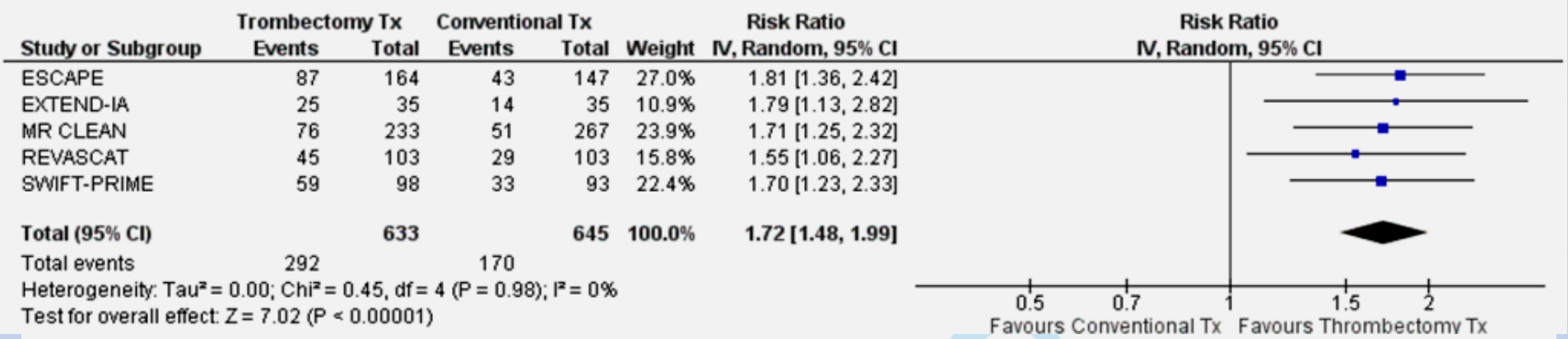


Figure 3.

Association of mechanical thrombectomy (vs. best medical therapy) with the likelihood of symptomatic intracranial hemorrhage (sICH) across different RCTs.

Figure 4.



Study or Subgroup	Trombectomy Tx Events	Total	Conventional Tx Events	Total	Weight	Risk Ratio IV, Random, 95% CI
ESCAPE	87	164	43	147	27.0%	1.81 [1.36, 2.42]
EXTEND-IA	25	35	14	35	10.9%	1.79 [1.13, 2.82]
MR CLEAN	76	233	51	267	23.9%	1.71 [1.25, 2.32]
REVASCAT	45	103	29	103	15.8%	1.55 [1.06, 2.27]
SWIFT-PRIME	59	98	33	93	22.4%	1.70 [1.23, 2.33]
Total (95% CI)		**633**		**645**	**100.0%**	**1.72 [1.48, 1.99]**
Total events	292		170			

Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 4 (P = 0.98); I² = 0%
Test for overall effect: Z = 7.02 (P < 0.00001)

Figure 4.

Association of mechanical thrombectomy (vs. best medical therapy) with the likelihood of functional independence at three months (modified Rankin Scale score of 0-2) across different RCTs.

Figure 5.

Study or Subgroup	Trombectomy Tx Events	Total	Conventional Tx Events	Total	Weight	Risk Ratio IV, Random, 95% CI
ESCAPE	17	164	28	147	21.9%	0.54 [0.31, 0.95]
EXTEND-IA	3	35	7	35	5.4%	0.43 [0.12, 1.52]
MR CLEAN	49	233	59	267	41.3%	0.95 [0.68, 1.33]
REVASCAT	19	103	16	103	19.4%	1.19 [0.65, 2.18]
SWIFT-PRIME	9	98	12	97	12.0%	0.74 [0.33, 1.68]
Total (95% CI)		**633**		**649**	**100.0%**	**0.82 [0.60, 1.11]**
Total events	97		122			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 5.26$, $df = 4$ ($P = 0.26$); $I^2 = 24\%$
Test for overall effect: $Z = 1.29$ ($P = 0.20$)

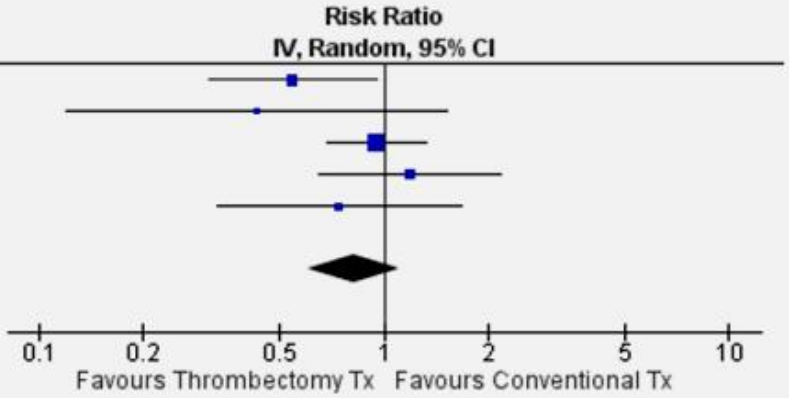


Figure 5.

Association of mechanical thrombectomy (vs. best medical therapy) with the likelihood mortality at three months across different RCTs.

2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons (AANS); Congress of Neurological Surgeons (CNS); AANS/CNS Cerebrovascular Section; American Society of Neuroradiology; and Society of Vascular and Interventional Neurology

William J. Powers, MD, FAHA, Chair; Colin P. Derdeyn, MD, FAHA, Vice Chair; José Biller, MD, FAHA; Christopher S. Coffey, PhD; Brian L. Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Karen C. Johnston, MD, MSc; S. Claiborne Johnston, MD, PhD, FAHA; Alexander A. Khalessi, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; James F. Meschia, MD, FAHA; Bruce Ovbiagele, MD, MSc, MAS, FAHA; Dileep R. Yavagal, MD, MBBS; on behalf of the American Heart Association Stroke Council

Purpose—The aim of this guideline is to provide a focused update of the current recommendations for the endovascular treatment of acute ischemic stroke. When there is overlap, the recommendations made here supersede those of previous guidelines.

Methods—This focused update analyzes results from 8 randomized, clinical trials of endovascular treatment and other relevant data published since 2013. It is not intended to be a complete literature review from the date of the previous guideline publication but rather to include pivotal new evidence that justifies changes in current recommendations. Members of the writing committee were appointed by the American Heart Association/American Stroke Association Stroke Council's Scientific Statement Oversight Committee and the American Heart Association/American Stroke Association Manuscript Oversight Committee. Strict adherence to the American Heart Association conflict of interest policy was maintained throughout the consensus process. Recommendations follow the American Heart Association/American Stroke Association methods of classifying the level of certainty of the treatment effect and the class of evidence. Prerelease review of the draft guideline was performed by 6 expert peer reviewers and by the members of the Stroke Council Scientific Statement Oversight Committee and Stroke Council Leadership Committee.

Table 2. Selected Eligibility Criteria for Recent Randomized, Clinical Trials of Endovascular Treatments for Acute Ischemic Stroke

	Treatment Groups	Eligibility									
Study	Active vs Control	IV r-tPA Eligible	Age, y	Time	Territory	NIHSS Score	Prestroke Function	Anticoagulation/ Coagulopathy	ASPECTS	Vascular Imaging	Other Imaging
SYNTHESIS Expansion	IA drug/any device/ both vs IV r-tPA	Required	18–80	6 h to IAT	Any	≤25	mRS score 0–1	Exclusion criteria	No	No	No
IMS III	2/3 standard-dose IV r-tPA+IA drug/any device/both vs IV r-tPA	Required, ≤3 h	18–82	5 h to IAT	Any	≥10 or 8–9 with occlusion	mRS score 0–2	Exclusion criteria	<4	No	>1/3 MCA excluded
MR RESCUE	Standard (±IV r-tPA)+MERCI or Penumbra vs standard (±IV r-tPA)	Not required	18–85	8 h to IAT Stop by 9 h	Anterior circulation	6–29	mRS score 0–2	Exclusion criteria	No	CTA, MRA	Multimodal CT/MR for stratification
MR CLEAN	Standard (±IV r-tPA)+IA UK, r-tPA, device vs standard (±IV r-tPA)	Not required	>18	6 h to IAT	Anterior circulation	>2	None	Exclusion criteria	No	CTA, MRA, DSA	
ESCAPE	Standard (±IV r-tPA)+stent retriever "recommended" vs standard (±IV r-tPA)	Not required	>18	12 h to randomization	ICA/MCA	>5	Barthel score ≥90	No exclusion criteria	≥6	CTA	Multiphase CTA or CT perfusion for detection of core size and collaterals
SWIFT PRIME	Standard (±IV r-tPA)+stent retriever vs standard (±IV r-tPA)	Required	18–80	6 h to groin	ICA/M1	8–29	mRS score 0–1	Exclusion criteria	≥6	CTA, MRA	CT or MRI mismatch for first 71 ASPECTS ≥6 for remaining 125
EXTEND-IA	Standard (±IV r-tPA)+stent retriever vs standard (±IV r-tPA)	Required	≥18	6 h to groin Complete in 8 h	Anterior circulation	None	mRS score 0–1	Exclusion criteria	No	CTA, MRA	CT/MRI mismatch
REVASCAT	Standard (±IV r-tPA)+stent retriever vs standard (±IV r-tPA)	Not required	18–80 (85)	8 h to groin	ICA/M1	≥6	mRS score 0–1	Exclusion criteria	≥7 (noncontrast CT) ≥6 (MRI-DWI) ≥8 (age	CTA, MRA, DSA	CT perfusion, CTA source, or MRI-DWI required if >4.5 h

Table 3. Selected Patient Characteristics for Recent Randomized, Clinical Trials of Endovascular Treatments for Acute Ischemic Stroke

	Participants (Active/Control)									
Study	n	Age, Mean±SD (IQR), y	NIHSS Score, Median (IQR) [Range]	Territory, %	ASPECTS, Median (IQR)	Device Deployment in Active Group	Onset to IV r-tPA, Mean±SD, Median (IQR), min	Time Onset to Groin Puncture, Mean±SD, Median (IQR), min	TICI Grade 2b/3 Recanalization, %	Time to Reperfusion Mean±SD, Median (IQR), min
SYNTHESIS Expansion	181/181	66±11/67±11	13 (9–17)/13 (9–18)	88/94 anterior		91% IA r-tPA alone 66% Device added 34% 14% stent retriever	165 (140–200)	225 (194–260) to clot		
IMS III	434/222	69/68	17 [7–40]/16 [8–30]	97/97 anterior (clinical)	56.9%/59.0% (8–10)	77% 41% IA r-tPA 38% IA r-tPA+device 21% device only 1.5% stent retriever	122±34/121±34	208±47	41	325±52
MR RESCUE	64/54	66±15	17 (13–21)	ICA 20/13 M1 61/72 M2 19/15		58% MERCI 22% Penumbra 16% both		381±74	27	
MR CLEAN	233/267	66 (55–76)/ 66 (56–76)	17 (14–21) [3–30]/18 (14–22) [4–38]	IC ICA 0.4/1.1 ICA+M1 25.3/28.2 M1 66.1/62.0 M2 7.7/7.9 A1/A2 0.4/0.8	9 (7–10)/ 9 (8–10)	83.7% 81.5% stent retriever IAT 21%	85 (67–110)/ 87 (65–116)	260 (210–313)	59	332 (279–394)
ESCAPE	165/150	71 (60–81)/ 70 (60–81)	16 (13–20)/17 (12–20)	ICA+M1 27.6/26.5 M1/all M2 68.1/71.4 M2 3.7/2.0	9 (8–10)/ 9 (8–10)	91.5% 72.7% stent retriever	110 (80–142)/ 125 (89–183)		72.40	
SWIFT PRIME	98/98	65±13/ 66±11	17 (13–20)/ 17 (13–19)	ICA 18.3/16.0 M1 67/77 M2 14/6	9 (7–10)/ 9 (8–10)	88.8% All stent retriever	110.5 (85–156)/ 117 (80–155)	224 (165–275)	88	
EXTEND-IA	35/35	69±12// 70±12	17 (13–20)/ 13 (9–19)	ICA 31/31 M1 57/51 M2 11/17		77% All stent retriever	127 (93–162)/ 145 (105–180)	210 (166–251)	86	248 (204–277)
REVASCAT	103/103	66±11/ 67±10	17 (14–20)/ 17 (12–19)	ICA 0/1 ICA+M1 26/27 M1 65/64 M2 10/8	7 (6–9)/ 8 (6–9)	95% All stent retriever	118 (90–150)/ 105 (86–138)	269 (201–340)	66	355 (269–430)

ASPECTS indicates Alberta Stroke Program Early CT Score; ESCAPE, Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times; EXTEND-IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial; IA, intra-arterial; IAT, intra-arterial therapy; ICA, internal carotid artery; IMS III, Interventional Management of Stroke Trial III; IQR, interquartile range; IV, intravenous; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke; MR RESCUE, MR and Recanalization of Stroke Clots Using Embolectomy; NIHSS, National Institutes of Health Stroke Scale; r-tPA, recombinant tissue-type plasminogen activator; REVASCAT, Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours; SWIFT PRIME, Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke; and TICI, Thrombolysis in Cerebral Infarction.

Table 4. Selected Clinical Outcomes for Recent Randomized, Clinical Trials of Endovascular Treatments for Acute Ischemic Stroke

		Outcomes												
		Primary End Point			Death (90 d/3 mo)			Symptomatic ICH				mRS 0 to 2 at 90 d		
Study		Active, %	Control, %	Comparison	Active, %	Control, %	Comparison	Time	Active, %	Control, %	Comparison	Active, %	Control, %	Comparison
SYNTHESIS Expansion	mRS 0 to 1 at 3 mo	30.4	34.8	0.71 (0.44 to 1.14)*	14.4	9.9	*P*=0.22	7 d	6	6	*P*=0.53	42.0	46.4	
IMS III	mRS 0 to 2 at 90 d	40.8	38.7	1.5 (–6 to 9)†	19.1	21.6	*P*=0.52	30 h	6.2	5.9	*P*=0.83	40.8	38.7	1.5 (–6 to 9)†
MR RESCUE	Mean mRS	3.9	3.9	*P*=0.99	19	24	*P*=0.75	7 d	5	4	*P*=0.24	19	20	
MR CLEAN	Improvement in mRS at 90 d (shift analysis)			1.67 (1.21 to 2.3)*	21	22		90 d	7.7	6.4		32.6	19.1	2.16 (1.39 to 3.38)*
ESCAPE	improvement mRS at 90 d (shift analysis)			3.1 (2.0 to 4.7)*	10.4	19	0.5 (0.3 to 0.8)§	90 d	3.6	2.7	1.2 (0.3 to 4.6)§	53	29.3	1.7 (1.3 to 2.2)§
SWIFT PRIME	Improvement in mRS at 90 d 5 and 6 combined (shift analysis)			*P*<0.001	9	12	0.74 (0.33 to 1.68)#	27 h	0	3		60	35	1.7 (1.23 to 2.33)#
EXTEND-IA	Median reperfusion at 24 h	100	37	4.7 (2.5 to 9.0)*	9	20	0.45 (0.1 to 2.1)*	36 h	0	6	–6 (–13 to 2)	71	40	4.2 (1.4 to 12)*
	Decrease in NIHSS 8 or NIHSS 0, 1 at 3 d	80	37	6.0 (2.0 to 18.0)*										
REVASCAT	Improvement in mRS at 90 d 5 and 6 combined (shift analysis)			1.7 (1.05 to 2.8)*	18	16	1.2 (0.6 to 2.2)††	90 d	2	2	1.0 (0.1 to7.0)††	43.7	28.2	2.1 (1.1 to 4.0)‖

at the 2015 International Stroke Conference, the MR CLEAN investigators reported a stroke onset–to–reperfusion time of 332 minutes (interquartile range, 279–394 minutes) and demonstrated a marked decline in clinical benefit with time so that the benefit was no longer statistically significant if reperfusion occurred after 6 hours 19 minutes.[16]

http://www.metropolitan-hospital.gr/maf-aee.html

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Recommendations

Endovascular Interventions

1. Patients eligible for intravenous r-tPA should receive intravenous r-tPA even if endovascular treatments are being considered *(Class I; Level of Evidence A)*. (Unchanged from the 2013 guideline)
2. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria *(Class I; Level of Evidence A)*. (New recommendation):
   a. Prestroke mRS score 0 to 1,
   b. Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies,
   c. Causative occlusion of the ICA or proximal MCA (M1),
   d. Age ≥18 years,
   e. NIHSS score of ≥6,
   f. ASPECTS of ≥6, and
   g. Treatment can be initiated (groin puncture) within 6 hours of symptom onset
3. As with intravenous r-tPA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset *(Class I; Level of Evidence B-R)*. (Revised from the 2013 guideline)
4. When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the ICA or proximal MCA (M1) *(Class IIb; Level of Evidence C)*. Additional randomized trial data are needed. (New recommendation)
5. In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable *(Class IIa; Level of Evidence C)*. Inadequate data are available at this time to determine the clinical efficacy of endovascular therapy with stent retrievers for those patients whose contraindications are time based or not time based (eg, prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications). (New recommendation)
6. Although the benefits are uncertain, the use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the M2 or M3 portion of the MCAs, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries *(Class IIb; Level of Evidence C)*. (New recommendation)
7. Endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large-vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group *(Class IIb; Level of Evidence C)*. (New recommendation)
8. Although its benefits are uncertain, the use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the ICA or proximal MCA (M1) *(Class IIb; Level of Evidence B-R)*. Additional randomized trial data are needed. (New recommendation)

hours of symptom onset, but the benefits are not established in this age group *(Class IIb; Level of Evidence C)*. (New recommendation)

8. Although its benefits are uncertain, the use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the ICA or proximal MCA (M1) *(Class IIb; Level of Evidence B-R)*. Additional randomized trial data are needed. (New recommendation)
9. Observing patients after intravenous r-tPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended. *(Class III; Level of Evidence B-R)*. (New recommendation)
10. Use of stent retrievers is indicated in preference to the MERCI device. *(Class I; Level of Evidence A)*. The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances *(Class IIb, Level B-NR)*. (New recommendation)
11. The use of a proximal balloon guide catheter or a large-bore distal-access catheter rather than a cervical guide catheter alone in conjunction with stent retrievers may be beneficial *(Class IIa; Level of Evidence C)*. Future studies should examine which systems provide the highest recanalization rates with the lowest risk for nontarget embolization. (New recommendation)
12. The technical goal of the thrombectomy procedure should be a TICI grade 2b/3 angiographic result to maximize the probability of a good functional clinical outcome *(Class I; Level of Evidence A)*. Use of salvage technical adjuncts, including intra-arterial fibrinolysis, may be reasonable to achieve these angiographic results if completed within 6 hours of symptom onset *(Class IIb; Level of Evidence B-R)*. (New recommendation)
13. Angioplasty and stenting of proximal cervical atherosclerotic stenosis or complete occlusion at the time of thrombectomy may be considered, but the usefulness is unknown *(Class IIb; Level of Evidence C)*. Future randomized studies are needed. (New recommendation)
14. Initial treatment with intra-arterial fibrinolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours' duration caused by occlusions of the MCA *(Class I; Level of Evidence B-R)*. However, these data are derived from clinical trials that no longer reflect current practice, including the use of fibrinolytic drugs that are not available. A clinically beneficial dose of intra-arterial r-tPA is not established, and r-tPA does not have US Food and Drug Administration approval for intra-arterial use. As a consequence,
15. Intra-arterial fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of intravenous r-tPA might be considered, but the consequences are unknown *(Class IIb; Level of Evidence C)*. (Revised from the 2013 guideline)
16. It might be reasonable to favor conscious sedation over general anesthesia during endovascular therapy for acute ischemic stroke. However, the ultimate selection of anesthetic technique during endovascular therapy for acute ischemic stroke should be individualized on the basis of patient risk factors, tolerance of the procedure, and other clinical characteristics. Randomized trial data are needed *(Class IIb; Level of Evidence C)*. (New recommendation)

Imaging

1. Emergency imaging of the brain is recommended before any specific treatment for acute stroke is initiated *(Class I; Level of Evidence A)*. In most instances, nonenhanced CT will provide the necessary information to make decisions about emergency management. (Unchanged from the 2013 guideline)
2. If endovascular therapy is contemplated, a noninvasive intracranial vascular study is strongly recommended during the initial imaging evaluation of the acute stroke patient but should not delay intravenous r-tPA if indicated. For patients who qualify for intravenous r-tPA according to guidelines from professional medical societies, initiating intravenous r-tPA before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible *(Class I; Level of Evidence A)*. (New recommendation)
3. The benefits of additional imaging beyond CT and CTA or MRI and MRA such as CT perfusion or diffusion- and perfusion-weighted imaging for selecting patients for endovascular therapy are unknown *(Class IIb; Level of Evidence C)*. Further randomized, controlled trials may be helpful to determine whether advanced imaging paradigms using CT perfusion, CTA, and MRI perfusion and diffusion imaging, including measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are within 6 hours of symptom onset and have an ASPECTS <6. Further randomized, controlled trials should be done to determine whether advanced imaging paradigms with CT perfusion, MRI perfusion, CTA, and diffusion imaging, including measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are beyond 6 hours from symptom onset. (New recommendation)

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Systems of Stroke Care

1. Patients should be transported rapidly to the closest available certified primary stroke center or comprehensive stroke center or, if no such centers exist, the most appropriate institution that provides emergency stroke care as described in the 2013 guidelines *(Class I; Level of Evidence A)*. In some instances, this may involve air medical transport and hospital bypass. (Unchanged from the 2013 guideline)
2. Regional systems of stroke care should be developed. These should consist of the following:
   a. Healthcare facilities that provide initial emergency care, including administration of intravenous r-tPA, such as primary stroke centers, comprehensive stroke centers, and other facilities, and
   b. Centers capable of performing endovascular stroke treatment with comprehensive periprocedural care, including comprehensive stroke centers and other healthcare facilities, to which rapid transport can be arranged when appropriate *(Class I; Level of Evidence A)*. (Revised from the 2013 guideline)
3. It may be useful for primary stroke centers and other healthcare facilities that provide initial emergency care, including administration of intravenous r-tPA, to develop the capability of performing emergency noninvasive intracranial vascular imaging to most appropriately select patients for transfer for endovascular intervention and to reduce the time to endovascular treatment *(Class IIb; Level of Evidence C)*. (Revised from the 2013 guideline)
4. Endovascular therapy requires the patient to be at an experienced stroke center with rapid access to cerebral angiography and qualified neurointerventionalists. Systems should be designed, executed, and monitored to emphasize expeditious assessment and treatment. Outcomes for all patients should be tracked. Facilities are encouraged to define criteria that can be used to credential individuals who can perform safe and timely intra-arterial revascularization procedures *(Class I; Level of Evidence E)*. (Revised from the 2013 guideline)

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Εξίσου σημαντικές οι μονάδες εγκεφαλικών

- Σημαντικό ρόλο διαδραματίζουν οι μονάδες αγγειακών εγκεφαλικών.
- Μετανάλυση 21 μελετών (3994 ασθενείς)
- Οι μονάδες ΑΕΕ μείωσαν την πιθανότητα:
  - death recorded at final (median one year) follow-up (odds ratio (OR) **0.87**, 95% confidence interval (CI) 0.69 to 0.94; P = 0.005),
  - death or institutionalized care (**OR 0.78**, 95% CI 0.68 to 0.89; P = 0.0003),
  - death or dependency (OR **0.79**, 95% CI 0.68 to 0.90; P = 0.0007).
- Τα αποτελέσματα ήταν ανεξάρτητα από την ηλικία, το φύλο και τη βαρύτητα του ΑΕΕ

Stroke Unit Trialists' Collaboration, Cochrane Database Syst Rev., 2013

Table 2. Combined Outcomes After 12 and 30 Months (Unadjusted)

Death or Institutional Care Outcome	12 Months			30 Months		
	Intervention Group, N=1883	Control Group, N=1085	*P*	Intervention Group, N=1860	Control Group, N=1075	*P*
Dead	428 (22.7)	265 (24.4)		619 (33.3)	376 (35.0)	
Institutional care	177 (9.4)	124 (11.4)		161 (8.7)	109 (10.1)	
At home	1278 (67.9)	696 (64.1)	0.038*	1080 (58.1)	590 (54.9)	0.094*

Implementation of telestroke consultation in conjunction with stroke education and training for healthcare providers can be useful in increasing the use of intravenous rtPA at community hospitals without access to adequate onsite stroke expertise *(Class IIa; Level of Evidence B)*.

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12 months and 95.9% after 30 months for death or institutional care, and 96.5% after 12 months and 95.7% after 30 months for death and dependency. In multivariable regression analysis, there was no significant effect of the TEMPiS intervention for reduced "death or institutional care" at 12 months (OR, 0.89; 95% CI, 0.75–1.07; $P=0.23$) and 30 months (OR, 0.93; 95% CI, 0.78–1.11; $P=0.40$) but a significant reduction of "death and dependency" at 12 months (OR, 0.65; 95% CI, 0.54–0.78; $P<0.01$) and 30 months (OR, 0.82; 95% CI, 0.68–0.98; $P=0.031$).

***Conclusions*—**Implementing a system of specialized stroke wards, continuing education, and telemedicine in community hospitals offers long-term benefit for acute stroke patients. **(*Stroke*. 2009;40:902-908.)**

Key Words: organized stroke care ■ outcome ■ stroke ■ stroke unit ■ telemedicine

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Ευχαριστώ για την προσοχή σας