

Acute Stroke Management: Innovations

B.Zamani MD

Introduction

- second cause of civil mortality
- Depressing delay in stroke treatment in Iran
- Poverty in richness

case

- 79 yr old lady found hemiplegic in street 4 pm
- Conscious
- Aphasic
- No gaze preference
- Rt hemiplegic
- NIHSS 19

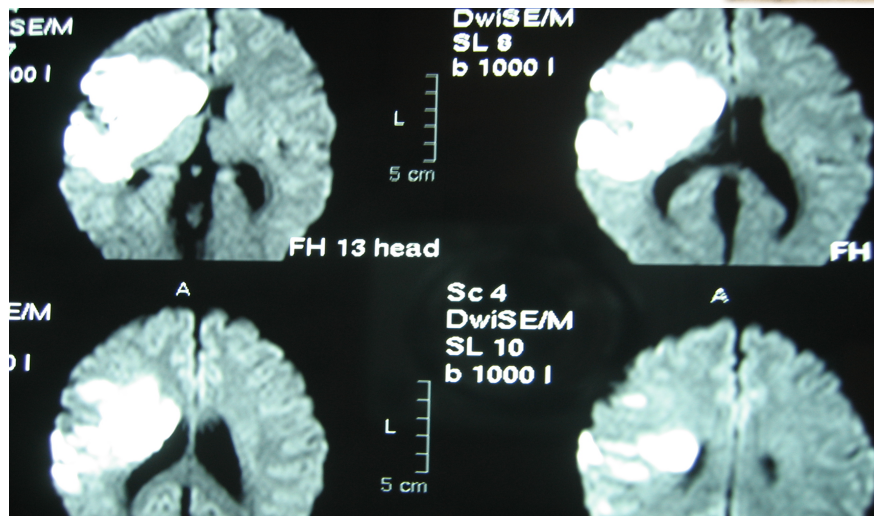
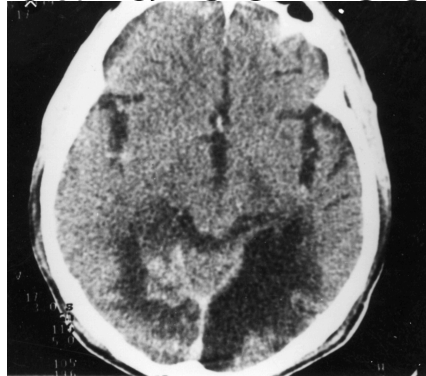
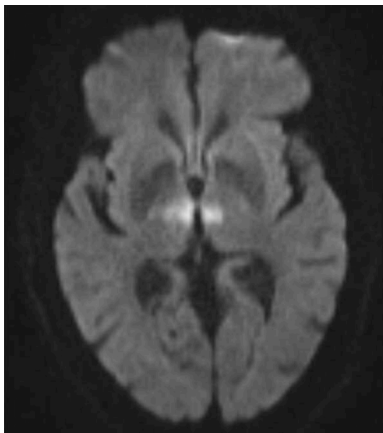
Stroke etiologic classification

- . 1-large vessel atherosclerosis A.intra. B.extr
- . Small vessel disease
- . Cardioemboli
- . Nonatherosclerotic arteriopathy vasculitis
/dissection /FMD

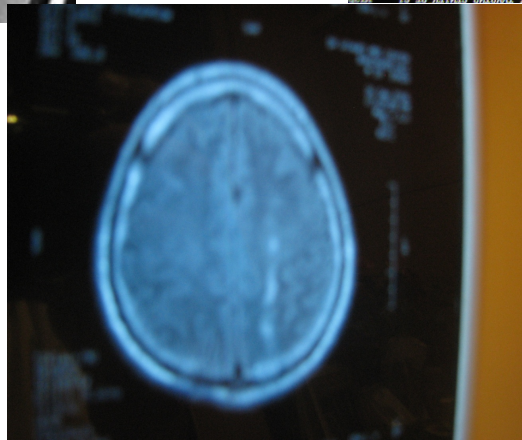
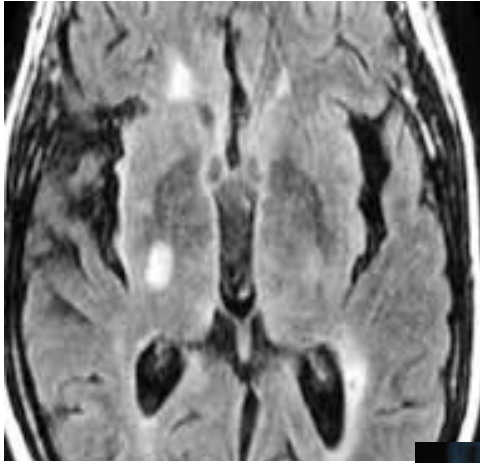
Stroke clinic

- Cardioemboli
- CV disease

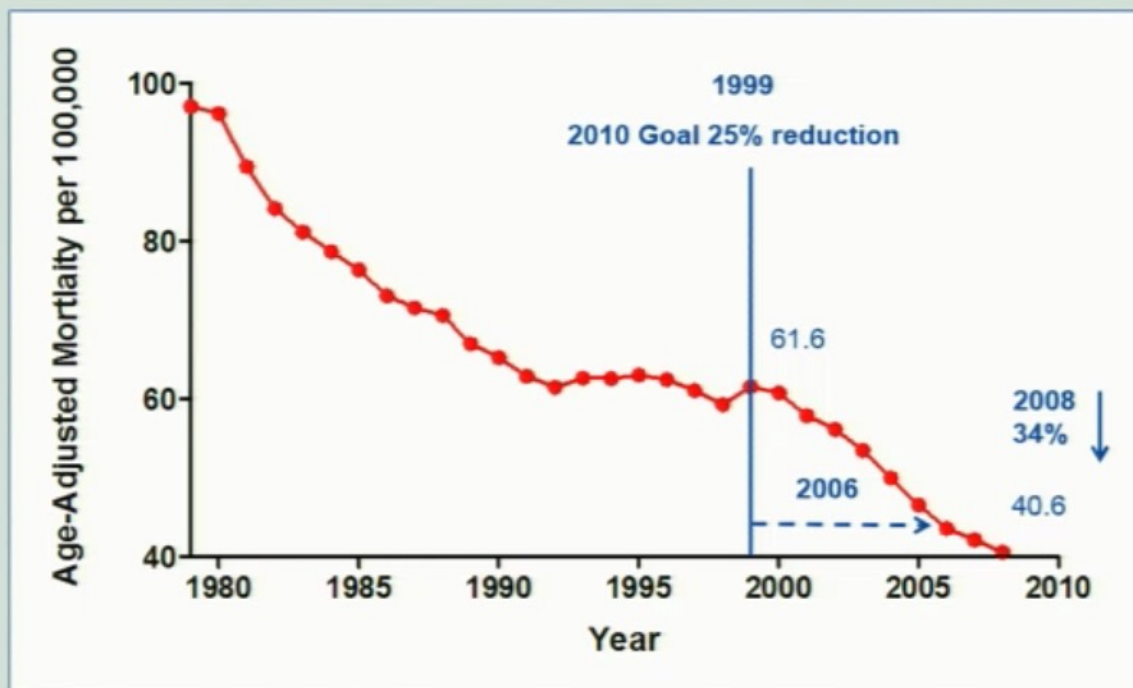
cardioemboli



CV disease

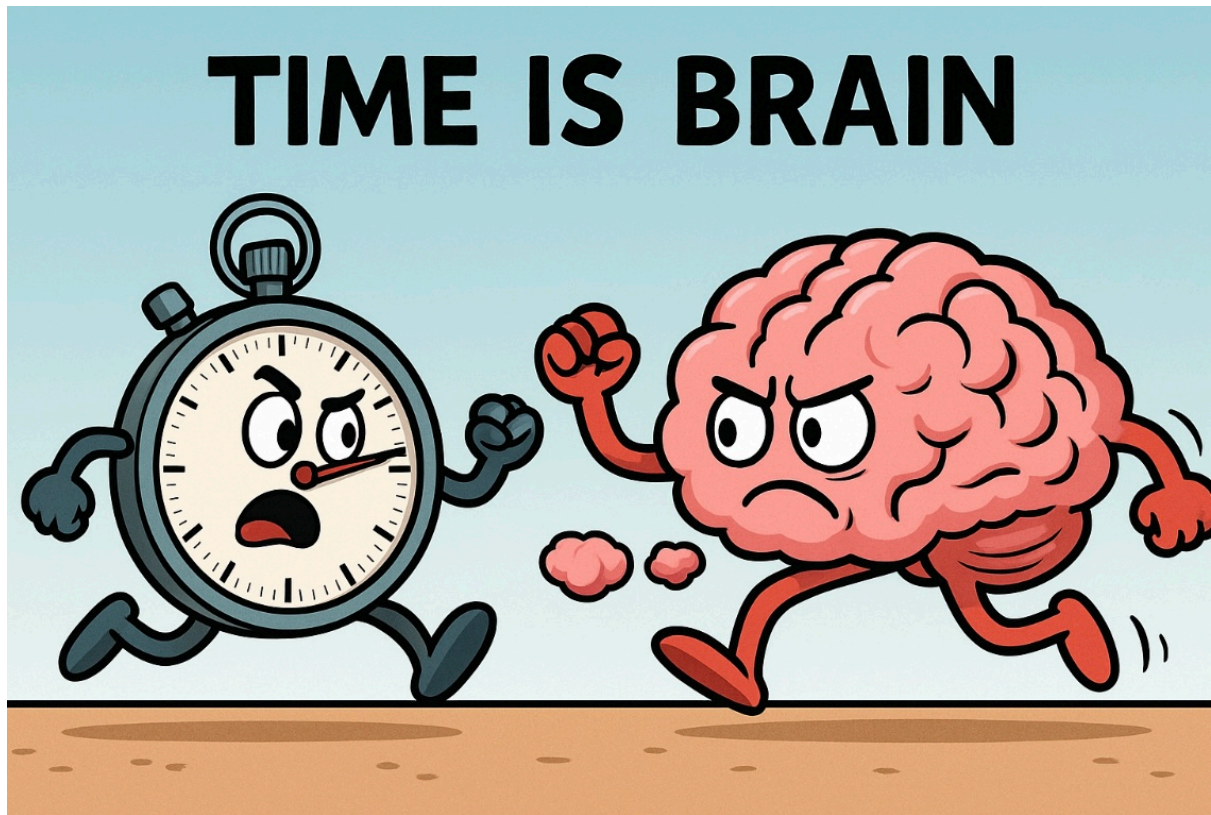


US Stroke Mortality



Data from National Center for Health Statistics US, 2010

. Time is brain



Effects of intravenous thrombolysis in ischemic stroke

No treatment



NINDS placebo arm

tPA 3 to 4.5h from onset



NNT 14

tPA 1 to 1.5h



NNT 4.5

tPA 0 to 1h



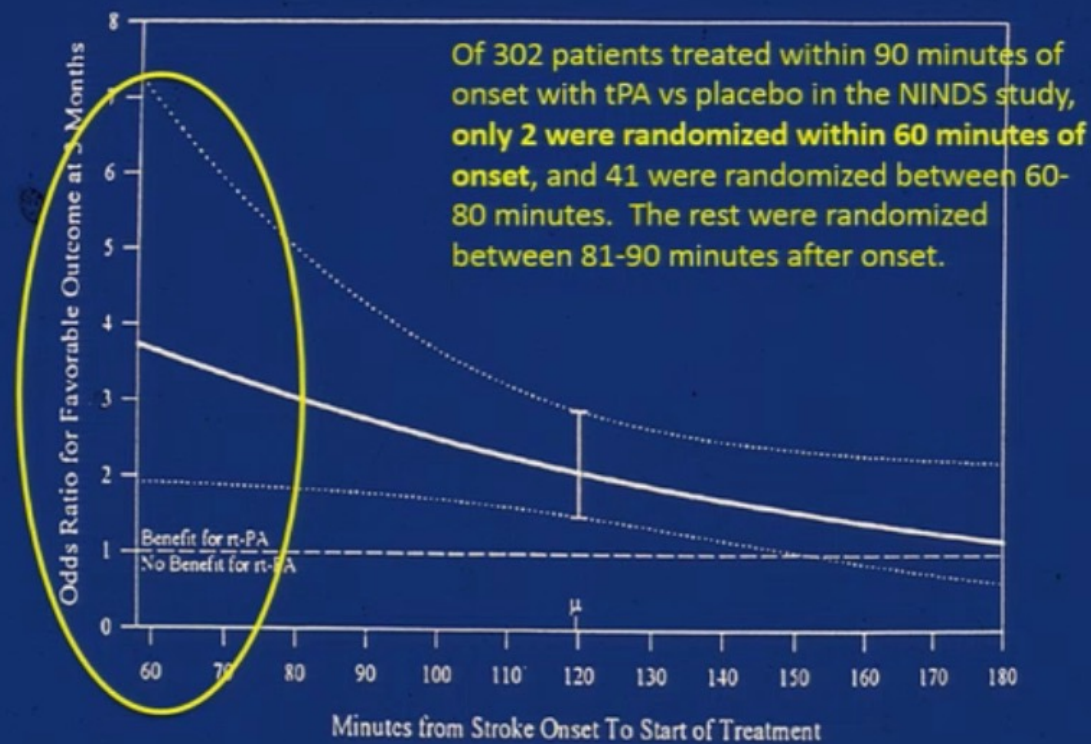
NNT 2?

Pooled analysis of RCTs; Lees et al. Lancet 2016

Extrapolation from registry comparison; Kunz et al. Lancet Neurol. 2016
Circulation 2016

Will ultra early treatment make patients better??

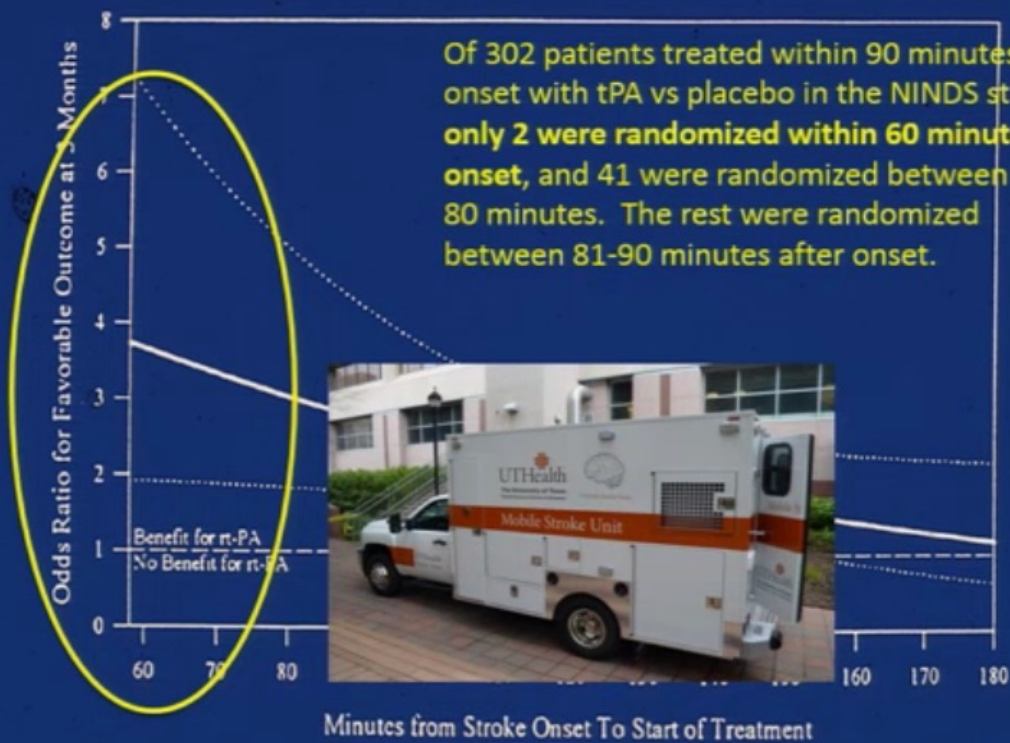
Relation of Time to Treatment to Odds of Ratio of Favorable Outcome



Data From 622 Patients. Odds Ratio of Minimal or No Disability At 3 Months For rt-PA Compared to Placebo-Treated patients. With 95% Confidence Interval (-----). Range of times from 58 to 180 minutes. Mean time to treatment (μ) was 119.7 minutes.

Will ultra early treatment make patients better??

Relation of Time to Treatment to Odds of Ratio of Favorable Outcome



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Pre-Hospital Advances

- Mobile Stroke Units (MSUs):

tPA started en route (BEST-MSU)trial





Marie Curie and her Mobile xray ambulance during World War I



Walter et al, Lancet Neurology, 2012
Randomized Trial of Prehospital vs ED Lytic Initiation



Ebinger et al JAMA 311:2014
31% of patients treated with tPA using a MSU
treated within 60 minutes of onset c/w 4.9%
with standard management

Discharge Home

Treatment 0-60 min

vs

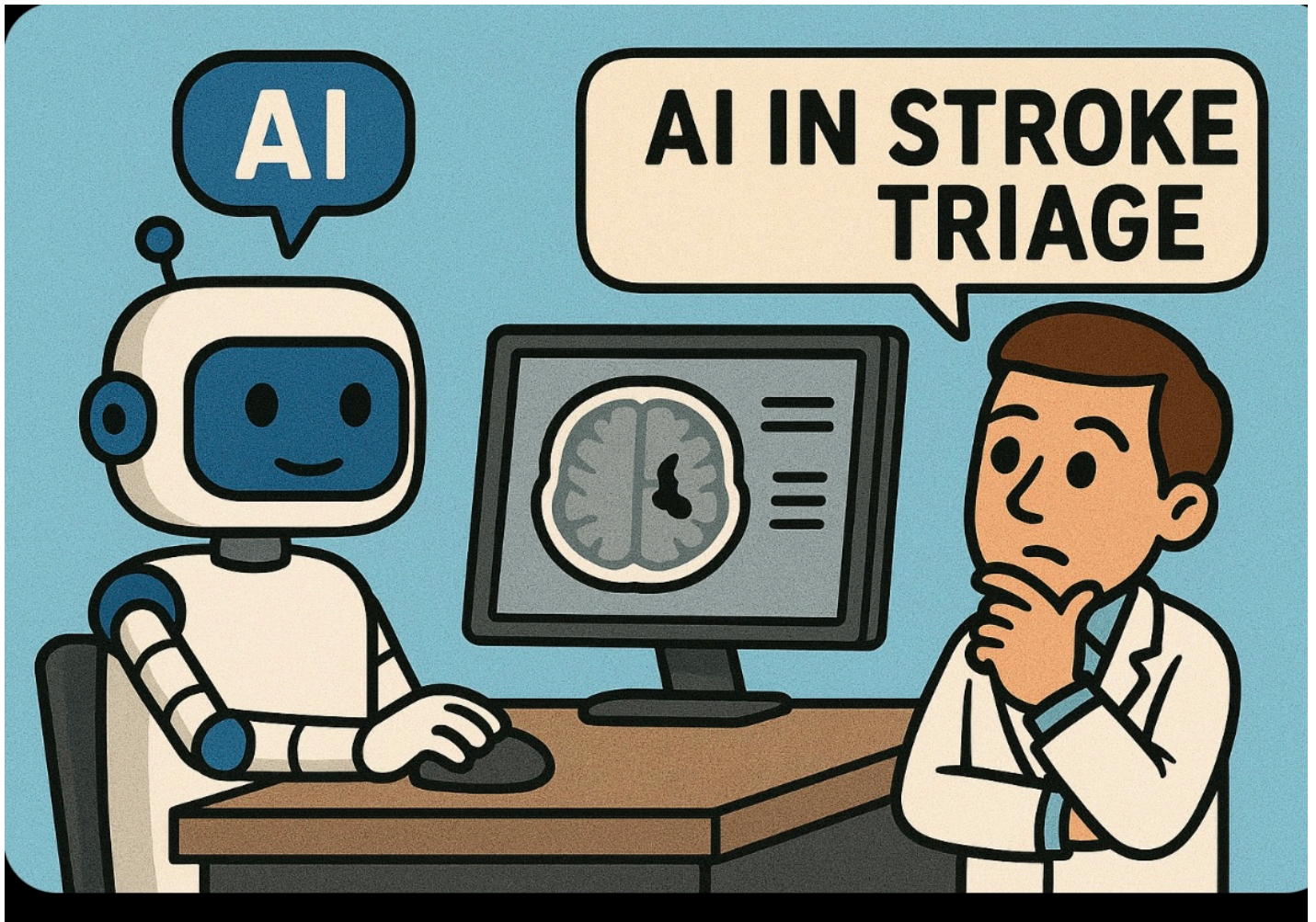
Treatment 60-270 min

OR 1.9



Pre-Hospital Advances

- AI triage tools (Viz.ai, RAPID) improving early detection
- Enhanced EMS protocols and AI-supported dispatch systems



Artificial intelligence to enhance prehospital stroke diagnosis and triage: a perspective



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Artificial intelligence to enhance prehospital

Review

Neurointervention 2025;20(1):4-14.

Print publication date: March 2025

Published online: February 18, 2025

DOI: <https://doi.org/10.5469/neuroint.2025.00052>



Application of Artificial Intelligence in Acute Ischemic Stroke: A Scoping Review

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Received January 23, 2025 Revised February 11, 2025 Accepted February 11, 2025

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Artificial intelligence to enhance prehospital

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Application of Artificial Intelligence in

arXiv:2503.13486 (eess)

Acut

[Submitted on 9 Mar 2025]

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Machine learning for triage of strokes with large vessel occlusion using photoplethysmography biomarkers

Review

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Márton Á. Goda, Helen Badge, Jasmeen Khan, Yosef Solewicz, Moran Davoodi, Rumbidzai Teramayi, Dennis Cordato, Longting Lin, Lauren Christie, Christopher Blair, Gagan Sharma, Mark Parsons, Joachim A. Behar

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'22, Korea Tel:

Received January 23, 2025 Revised February 11, 2025 Accepted February 11, 2025

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In-Hospital Workflow Innovations

- - AI-integrated imaging: ASPECTS, perfusion mismatch
- - One-stop stroke suites: Door-to-groin time reduction
- - TeleStroke programs for rural and remote management

In-Hospital Workflow Innovations

- - AI-integrated imaging: ASPECTS, perfusion mismatch
- - One-stop stroke suites: Door-to-groin time reduction
- - TeleStroke programs for rural and remote management

Example of organized protocol for emergency evaluation of suspected stroke patients Frankfurt

**Stroke „10-for-10“
STANDARD of CARE**

S Stroke syndrome (incl. right, left-sided weakness)

T Time since onset

A Age (≥ 18 years)

N NIHSS (score ≥ 4)

D Diseases (hypertension, atrial fibrillation, previous stroke)

A Anticoagulation & antiplatelets

R Red flags (contraindications for t-PA)

D Do we need more information?

C CT scan (within 60 min of stroke onset)

A Angiography (within 120 min)

R r-tPA (within 4.5 hours)

E Endovascular treatment

of

„10-for-10“ STANDARD of CARE

- Es ist immer Zeit für ein „10-for-10“
- Das ganze Team sollte zuhören.
- Bitte laut und deutlich sprechen.
- Versuche Blickkontakt herzustellen.
- Nur relevante Informationen.
- Rückfragen/Ergänzungen am Schluss.



E Endovascular treatment

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- Rückfragen/Ergänzungen am Schluss.

همیشه وقت برای یک—

“۱۰ برای ۱۰” هست

کل تیم باید گوش بدن—

بلند و روشن صحبت کنید—

در زمان صحبت به چشم—

های یکدیگر نگاه کنید

فقط درباره اطلاعات—

مربوط صحبت کنید

آخر سر وقت برای بحث—

پرسش و پاسخ هست

Different ways to decrease DNT

- Regular meetings for arrangement and feedback



Maneuvers



Ready package



Thrombolysis

Recombinant tissue plasminogen activator rTPA

- . FDA NINS. Up to 3hr
- . Non FDA ECASS. Up to 4.5 hr
- . All ischemic strokes except Very large/improving
/impaired coagulation /refractory hypertension

Acute Anticoagulation

- Acute **anticoagulation** (full-dose UFH, LMWH, and heparinoids) in **unselected** stroke patients has **no net benefit**
 - >23,000 patients in multiple RCTs



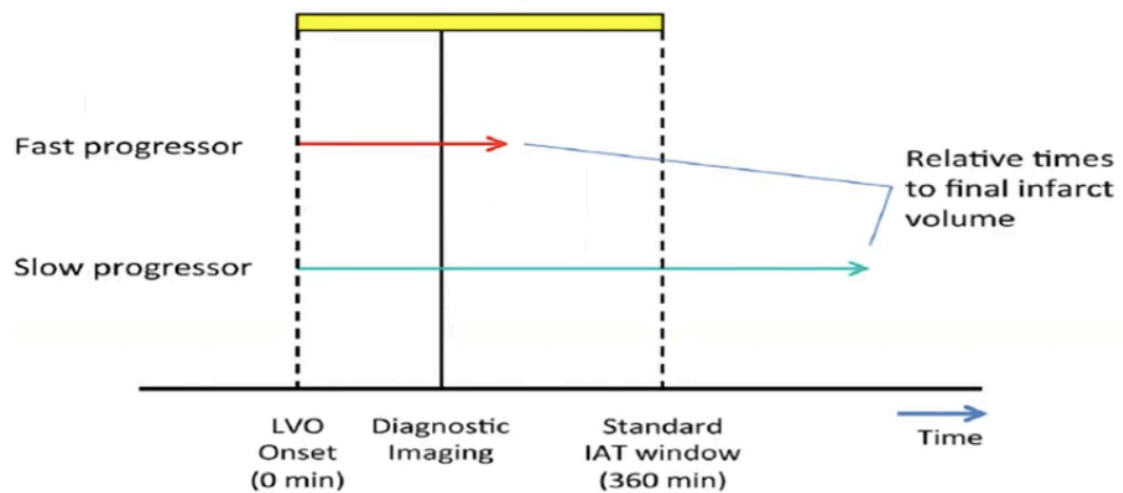
The History of Acute Stroke Care

Paradigm Shifts

- “Time is brain” – Time window
 - NINDS, PROACT II, MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND IA
- “A little more time is also brain” – Late time window
 - ECASS III, HERMES collaborative
- “Perfusion is brain” – Advanced imaging by volume
 - DAWN, DEFUSE 3, WAKE-UP, EXTEND

Paradigm Shift

- Shift in evaluation of patients based on tissue/perfusion window: fast vs. slow progressors

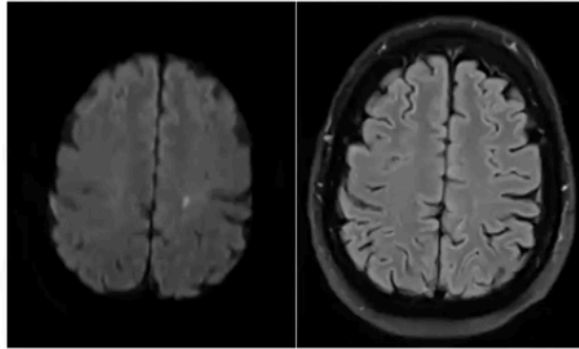


Paradigm Shift: Thrombolysis

	WAKE-UP	EXTEND
NIHSS	<26 (median 6)	4-26 (median 12)
Time	>4.5 hours	4.5-9 hours
Imaging	DWI-FLAIR mismatch: - Positive DWI, <1/3 MCA territory, <1/2 ACA or PCA territory, <100 mL - Negative FLAIR	RAPID (CT or MRI): - Core < 70 mL - Mismatch volume > 10 mL - Mismatch ratio > 1.2
Primary outcome (mRS 0-1 at 90d)	53.3% tPA vs 41.8% placebo (p=0.02)	35.4% tPA vs 29.5% placebo (p=0.04)
Death	4.1% tPA vs 1.2% placebo (p=0.07) at 90d	11.5% tPA vs 8.9% placebo (p=0.67) at 90d 0.02% (5) tPA vs 0.02% (4) placebo at 7d
slCH	2.0% tPA vs 0.4% placebo (p=0.15)	6.2% tPA vs 0.9% placebo (p=0.053)

2019 AHA/ASA Guideline Update

- In patients with wake-up stroke or unknown onset time:
 - If >4.5 hours from last known normal time



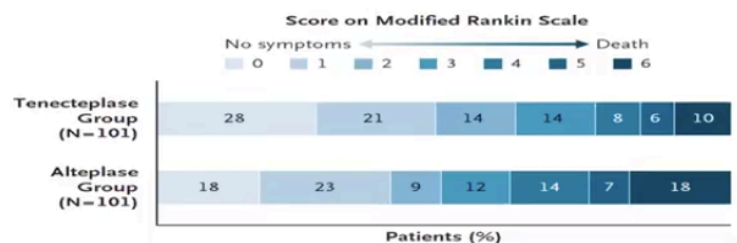
- Use of MRI to identify DWI+ and FLAIR- lesions can select patients who could benefit from IV-tPA within 4.5 hours of stroke symptom discovery

tPA and thrombectomy

- Thrombolysis
 - tPA up to 4.5 hours
 - tPA >4.5 hours with MRI selection
- Thrombectomy
 - Thrombectomy in anterior circulation proximal LVO up to 24 hours in select patients
- Thrombolysis + thrombectomy
 - tPA before thrombectomy up to 4.5 hours

Thrombolysis: TNK

- EXTEND-IA TNK: Tenecteplase 0.25 mg/kg (max dose 25 mg) compared to alteplase prior to endovascular therapy
 - Primary endpoint: Reperfusion of >50% of involved ischemic territory or complete recanalization at time of initial angiogram
 - Achieved in 22% patients with TNK vs 10% with tPA (p=0.002 for noninferiority, p=0.03 for superiority)
 - Secondary endpoint: Better functional outcomes on ordinal shift analysis of 90-day mRS



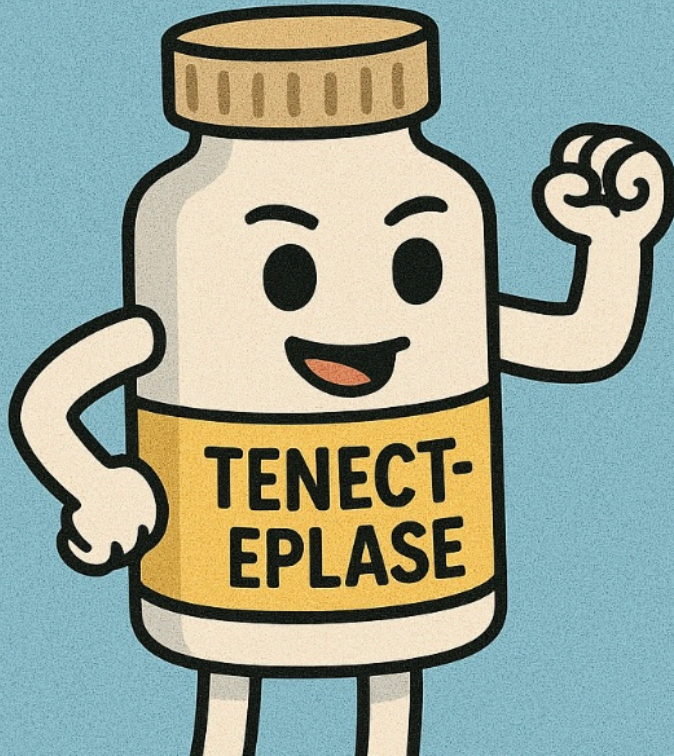
Thrombolysis: TNK

- NOR-TEST (2017): TNK 0.4 mg/kg vs tPA 0.9 mg/kg within 4.5 hours not superior; similar safety profile
 - Most patients noted to have mild stroke and no LVO
- EXTEND-IA TNK
 - Tenecteplase 0.25 mg/kg bolus (max dose 25 mg) compared to alteplase prior to endovascular therapy
- EXTEND-IA TNK Part 2
 - TNK 0.40 mg/kg vs 0.25 mg/kg did not significantly improve reperfusion prior to thrombectomy

IV Thrombolysis: New Developments

- Tenecteplase vs Alteplase:
- Easier administration (bolus)
- Data: EXTEND-IA TNK
- Expanded tPA window in select cases

TENECTEPLASE VS tPA



FDA Approves Tenecteplase for Acute Ischemic Stroke

The approval is based on results of the AcT trial, where tenecteplase was comparable to alteplase for safety and efficacy.

by [Michael O’Riordan](#) | MARCH 03, 2025



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by [Michael O'Riordan](#) | MARCH 03, 2025



April
2025

APPROVED

Stroke



ABSTRACT

| Originally Published 30 January 2025 | 

Abstract 58: Tenecteplase Beyond 4.5 Hours in Acute Ischemic Stroke: A Systematic Review and Meta- analysis of Clinical Trials

Mohammad Aladawi MD Mohammad Abuawwad MD Mohammad

Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy

Authors: Yunnyun Xiong, M.D., Ph.D., Bruce C.V. Campbell, M.B., B.S., Ph.D., Lee H. Schwamm, M.D., Xia Meng, M.D., Ph.D., Aoming Jin, Ph.D., Mark W. Parsons, M.B., B.S., Ph.D., Marc Fisher, M.D., +23, for the TRACE-III Investigators* [Author Info & Affiliations](#)

Published June 14, 2024

N Engl J Med 2024;391:203-212

DOI: 10.1056/NEJMoa2402980 | VOL. 391 NO. 3

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Inclusion and Exclusion Criteria for Tenecteplase (4.5–24 h)

Inclusion Criteria

- Age 18 years or older
- Confirmed AIS, anterior circulation large vessel occlusion
- Last known well 4.5 to 24 hours
- Advanced imaging evidence of salvageable brain tissue (CT perfusion or MRI DWI/FLAIR mismatch)
- Pre-stroke functional independence (mRS 0-1)

Exclusion Criteria

- Hemorrhage on baseline CT/MRI
- Large infarct core on imaging
- NIHSS <6 or very mild symptoms
- Severe comorbidities
- Recent major surgery or trauma within 14 days
- Current anticoagulation
- Platelet count <100,000/ μ L
- SBP $\geq$ 185 mm Hg or DBP >110 mm Hg despite treatment

Tenecteplase in Acute Ischemic Stroke: 4.5–24 Hours

Study	TNK Alone	TNK + Thrombectomy	Imaging Required
TIMELESS	No	Yes	CT perfusion or MRI
TRACE-III	Yes	No	CT perfusion
TWIST	Yes	Rare	Non-contrast CT + NIHSS

Tenecteplase Trials in AIS (4.5-24 Hours)

Trial	Design & Population	Tenecteplase Usage	Thrombectomy	Primary Outcome
TIMELESS	Multicenter, double-blind, randomized, placebo-controlled trial. 455 patients with AIS due to occlusion of middle cerebral artery or internal carotid artery, treated 4.5-24 hours after last known well	Single IV bolus of 0.25 mg/kg (max. 25 mg) Thrombolytic CT perfusion or MRI showing	77.3% underwent endovascular thrombectomy	No significant difference in functional outcomes between TNK and standard care. Symptomatic intracranial hemorrhage rates similar
TRACE-III	Multicenter, open-label, randomized controlled trial. 516 patients presenting 4.5-24 hours after AIS onset due to large-vessel occlusion, without access to thrombectomy	Single IV bolus of 0.25 mg/kg (max. 25 mg) Thrombectomy	Patients did not undergo thrombectomy Non-contrast CT imaging without	No significant difference in functional outcomes between TNK and standard care and similar
TWIST	Randomized, open-label, blinded endpoint trial assessing TNK in wake-up strokes	Non-contrast CT imaging without advanced perfusion imaging	Non-contrast CT imaging without advanced perfusion imaging	No significant difference in functional outcomes similar. rates similar

Until now about 1000 pt had been treated 4/5-24 after stroke

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Thrombectomy

- . All LVO (large vessel occlusion) before 6hour
- . All LVO with mismatch before 24 hours

Endovascular Thrombectomy

- - Extended window (6–24h): DAWN, DEFUSE-3 trials
- - New generation devices: faster revascularization
- - Direct-to-angio protocols for large vessel occlusion

Extended window (6–24h): DAWN, DEFUSE-3 trials



The NEW ENGLAND
JOURNAL of MEDICINE

ORIGINAL ARTICLE

f X in e b

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

Authors: Raul G. Nogueira, M.D., Ashutosh P. Jadhav, M.D., Ph.D., Diogo C. Haussen, M.D., Alain Bonafe, M.D., Ronald F. Budzik, M.D., Parita Bhuvra, M.D., Dileep R. Yavagal, M.D., [+40](#), for the DAWN Trial Investigators* [Author Info & Affiliations](#)

Published November 11, 2017 | N Engl J Med 2018;378:11-21 | DOI: 10.1056/NEJMoa1706442
VOL. 378 NO. 1 | Copyright © 2017



The NEW ENGLAND
JOURNAL of MEDICINE

ORIGINAL ARTICLE

f X in e b

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

Authors: Gregory W. Albers, M.D., Michael P. Marks, M.D., Stephanie Kemp, B.S., Soren Christensen, Ph.D., Jenny P. Tsai, M.D., Santiago Ortega-Gutierrez, M.D., Ryan A. McTaggart, M.D., [+19](#), for the DEFUSE 3 Investigators* [Author Info & Affiliations](#)

Published January 24, 2018 | N Engl J Med 2018;378:708-718 | DOI: 10.1056/NEJMoa1713973
VOL. 378 NO. 8 | Copyright © 2018

1. Large-Bore Aspiration Catheters

- Newer aspiration systems (e.g., Axs Vecta 74, Sofia Plus, React 71/81, Arc™) offer:
 - Higher flow rates and suction power.
 - Improved navigation through tortuous vessels.
- Often used in **ADAPT (A Direct Aspiration First Pass Technique)**.

2. Next-Gen Stent Retrievers

- Tigertriever, Trevo NXT, and EmboTrap III:
 - Offer **adjustable radial force** for tailored clot engagement.
 - Improved flexibility and clot capture on first pass.
 - Some have integrated aspiration compatibility.

3. Combined Techniques ("Solumbra" or CAPTIVE)

- **Stent retriever + aspiration catheter** simultaneously:
 - Improves **first-pass success** and reduces emboli to new territories.
 - Popularized in **PROTECT-PLUS** and **ASTER-2** protocols.

4. Balloon Guide Catheters (BGC)

- Used in ICA to **temporarily arrest flow** during retrieval.
- Reduces distal embolization and increases first-pass efficacy.

5. Robotics & Remote Thrombectomy (Early Stage)

- **CorPath GRX Neuro (Corindus):** robotic-assisted endovascular treatment.
- Aimed at **expanding access** to remote centers.

6. Integrated Stroke Platforms

- Devices that combine **real-time imaging, clot removal, and flow assessment** (e.g., **PhotonGuide** in development).

Direct to Angio Suite for Acute Stroke

Overview

- Paradigm shift bypassing initial imaging to take eligible patients directly to angiography suite for possible thrombectomy
- Aims to reduce time to reperfusion and improve outcomes, particularly in high-volume centers

Clinical Trials

- ANGIOCAT
- RACECAT
- WE-TRUST
- DIRECT ANGIO

Related Concepts

- Mobile stroke units with pre-hospital imaging
- AI-based LVO detection

Post-Acute and Future Innovations

- Neuroprotective agents (e.g., nerinetide)
- AI in functional outcome prediction
- Wearables for rehab and recovery monitoring

Neuroprotective agents (e.g.,
nerinetide)

As of 2025, **no neuroprotective drug** has been **formally approved** for routine clinical use in **acute ischemic stroke**, but several agents are in **late-stage clinical trials** or have shown **promising early results**.

Here's a quick summary:

1. Nerinetide (NA-1)

- A peptide that inhibits excitotoxic cell death pathways.
- Phase 3 trial (**ESCAPE-NA1**) showed **potential benefit in patients not treated with alteplase.**
- Ongoing trial: **ESCAPE-NEXT** – focuses on thrombectomy patients **without prior thrombolytics.**
- Not yet approved, but **closest to clinical use** among neuroprotectants.

2. ApTOLL (Toll-like receptor 4 antagonist)

- Targets inflammation after stroke.
- Early trials (APTIA and APON) showed **good safety profile** and **reduced infarct volume**.
- Currently in phase 2 trials in combination with thrombectomy.

3. Transcranial Laser Therapy (NeuroThera)

- Non-invasive technique being investigated for ischemic stroke.
- Some positive early-phase results, but larger trials are ongoing.

4. Edaravone (Japan/Asia only)

- Approved in **Japan and parts of Asia**.
- A free radical scavenger with mild neuroprotective effects.
- Sometimes used **alongside reperfusion**, but not FDA-approved in US/EU for stroke.

1. Imaging-Based Prognostication

on

- AI analyzes **CT/MRI** to predict:
 - Final infarct volume
 - Core–penumbra mismatch
 - ASPECTS scoring (e.g., e-ASPECTS)
- Enhances early detection of subtle changes

2. Clinical Outcome Prediction

- Integrates data: **NIHSS, age, labs, comorbidities**
- Predicts:
 - 90-day **mRS**
 - **Hemorrhagic transformation**
 - **Mortality risk**

3. Personalized Decision-Making

- Estimates **individualized benefit** from thrombolysis/thrombectomy
 - Supports **extended window** treatment strategies
-

4. Workflow Integration

- AI-driven alerts (e.g., **LVO detection**)
- Real-time support tools (e.g., **Viz.ai**, **RapidAI**)

FUTURE

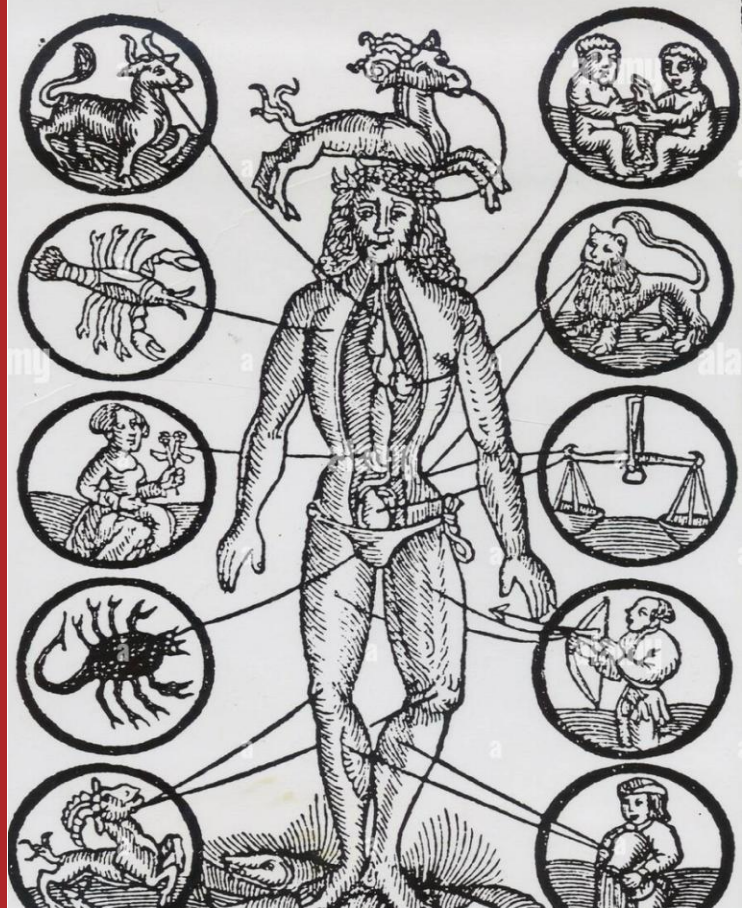
- From time-based to tissue-based decisions
- Precision medicine and equitable stroke care
- Continuous integration of tech into workflows

LEECH THERAPY IN TRADITIONAL MEDICINE

HIRUDOTHERAPY



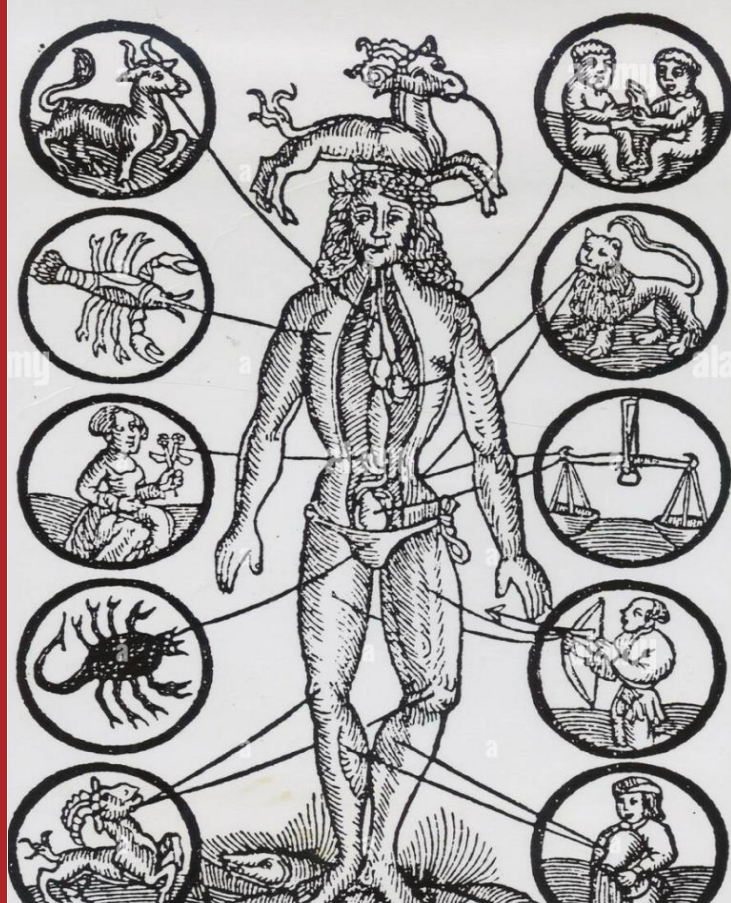
SYED HASAN
MD TANWIR ALAM



LEECH THERAPY IN TRADITIONAL MEDICINE HIRUDOTHERAPY



SYED HASAN
MD TANWIR ALAM



THANK

<http://t.me/elmibz>

کانال مقالات دکتر بابک زمانی در