Stroke Update IVtPA

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Time lost is brain lost!

Stroke 2006

- **Each 59 seconds, an ischemic stroke will have killed 1.9 million brain cells, according to a study published in *Stroke: Journal of the American Heart Association***

Stroke

Stroke Thrombolysis

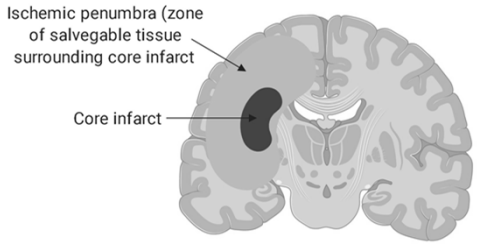
Save a Minute, Save a Day

Atte Meretoja, MD; Mahsa Keshtkaran, MSc; Jeffrey L. Saver, MD; Turgut Tatlisumak, MD; Mark W. Parsons, MD; Markku Kaste, MD; Stephen M. Davis, MD; Geoffrey A. Donnan, MD; Leonid Churilov, PhD

Stroke 2014

- **disability-adjusted life years (DALYs) In each minute saved provided a mean 1.8 days of DALY**
- **patients gain an equivalent of at least a day of healthy life for each minute saved**
- **Save a Minute, Save a Day**

Ischemic penumbra



Acute stroke treatment:
1) Intravenous tissue plasminogen activator (IVtPA)
2) Intra-arterial therapy (IAT), i.e. mechanical thrombectomy

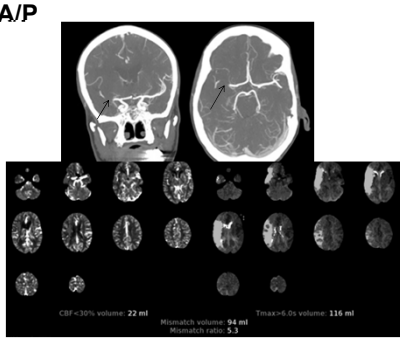
CASE A

- 71 y.o. RH female with a history of history of lung adenocarcinoma s/p LUL lobectomy
- POD 8 lobectomy who at 1am developed witnessed onset of left hemiparesis
- Stroke code was called at 5am
- She had a Chest tube
- Initial NIHSS was 11
- CT brain negative
- BP, labs (coags, BS, etc) WNL

Question: Recommend IVtPA?

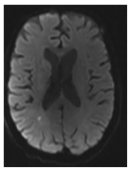
Clinical course

- She received tPA at 529a (4 h 29 min)
- CTA/P



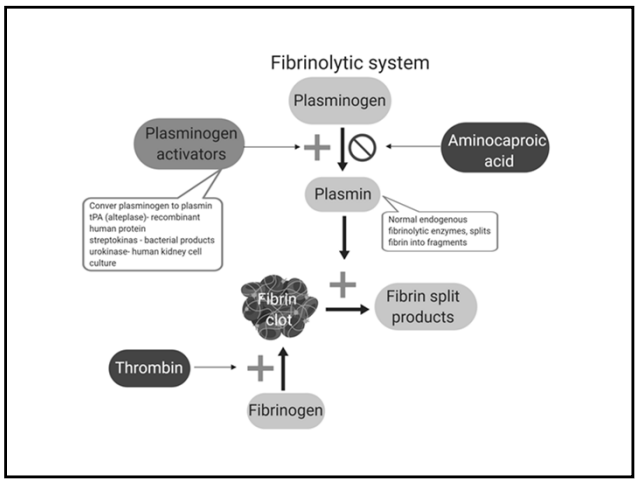
Clinical Course

- Cerebral angiogram negative
- MRI shows small right MCA infarct



- The next day neurological examination showed left hemiparesis, NIHSS-3
- She was transferred to ARF PSD #7
- Follow in stroke clinic at 3 months, mRS-1, NIHSS 0

Thrombolytics



Activase (tPA)

- **produced by recombinant DNA technology**
  - **synthesized using the complementary DNA (cDNA) for natural human tissue-type plasminogen activator obtained from a human melanoma cell line**
  - **purified glycoprotein of 527 amino acids**
- **sterile, white, lyophilized powder for IV administration after reconstitution with sterile Water**
- **supplied in 50 mg and 100 mg vials without vacuum**
- **duration of action 2-10 min**

Intracranial hemorrhage

Incidence of Intracranial Hemorrhage in AMI patients

Dose	Pt #	ICH (%)
100mg, 3 hr	3272	0.4
< 100mg, accelerated	10,396	0.7
150mg	1779	1.3
1-1.4 mg/kg	234	0.4

Dose used in stroke patients

- **IV tPA 0.9 mg/kg total dose (maximum 90 mg)**
  - **10% as bolus over 1 minute**
  - **remaining 90% as infusion over 60 minutes**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Volume 333 DECEMBER 14, 1995 Number 24
TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE
THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

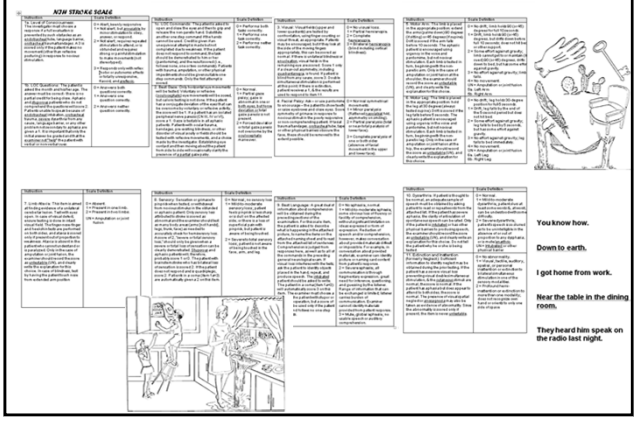
- **Randomized double-blinded, placebo-controlled study**
- **624 pts w/in 3 hr of onset, required pre-tx CT**
- **0.9 mg/kg IV tPA (max 90mg) 10% bolus over 1 m, then remainder over 60 m**
  - **BP < 185/110**

Part I- 291 pts, improve 4 on NIHSS in 24 hr
Part II- 333 pts, clinical outcome at 3 mos
•NIH, Barthel, Modified rankin

NINDs Inclusion Criteria

- Ischemic stroke with a clearly defined time of onset
- deficit measurable on the NIHSS
- base-line CT brain that showed no intracranial hemorrhage

NIHSS



NINDs Exclusion Criteria

- stroke or serious head trauma within the preceding 3 mos
- undergone major surgery within 14 days
- history of intracranial hemorrhage
- SBP >185 mm Hg or DBP >110 mm Hg
- rapidly improving or minor symptoms
- symptoms suggestive of SAH
- GI hemorrhage or urinary tract hemorrhage within 21 days
- arterial puncture at a noncompressible site within 7 days
- seizure at the onset of stroke
- Patients taking anticoagulants or who had received heparin within the 48 hours preceding the onset of stroke and had an elevated aPTT
- prothrombin times > 15 seconds, platelet <100,000 per cubic millimeter, or glucose <50 mg or >400 mg per deciliter
- aggressive treatment required to reduce blood pressure

NINDs

- Part I- Change in NIHSS
  - No significant difference
- Part II- Outcome at 3 months
  - Modified rankin scale (0-6)
    - 0 no symptoms at all
    - 1 no significant disability despite symptoms, able to carry out all usual duties and activities
  - 30% more likely to have minimal disability at 3 mos in tPA group
  - Absolute increase in favorable outcome 11% - 13%

NINDs

- Hemorrhage
  - 6.4% tPA vs 0.6% placebo
- Mortality rate at 3 mo
  - 17% tPA vs 21% placebo
- Interpretation: tPA w/in 3 hr window improves 3 month outcome
- FDA approval 1996

IVtPA trials

1/2 pts (>300) enrolled <90m from onset, post hoc analysis-pt treated early had better outcomes

Study	Pt #	Max dose (mg)	Window (hrs)	Symptomatic ICH % (tpa vs placebo)	Mortality % (tPA vs placebo)
NINDs	624	90 (0.9)	≤3	6.4 vs 0.6	17.4 vs 20.6
ECASS I	620	**100 (1.1)**	≤6	19.8 vs 6.5*	22 vs 15.6
ECASS II	800	90 (0.9)	≤6	8.8 vs 3.4	10.5 vs 10.7
ATLANTIS B	547	90 (0.9)	3-5	7.0 vs 1.1	11.0 vs 6.9

* parenchymal hematoma (symptomatic ICH not reported in ECASS -1)

(1.1mg/kg- max 100mg) higher dose of tPA
17% eliminated due to major protocol violations (most commonly CT early infarct signs)
Major parenchymal hemorrhage was 19.8% (tpa)
No sig difference in BI at 3 months

Initiated in 1991, protocol similar to NINDs In 1993, study changed to 0-5hr due to safety concerns in 5-6 hr group. In 1996 (FDA approved tPA in first 3 hr) modified to 3-5 hr window
Trial terminated 1998 interim analysis suggested that detection of a beneficial effect of tPA was highly unlikely

Reduced does tPA, less protocol violations (9%)
Underpowered, had only 800 pts, needed 2000
No significant difference in pts achieving primary outcome (mRS 0-1 at 90 days) between IV tPA pts (40.3%) & control group (36.6%)

ECASS 3 2008

Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke

Werner Hacke, M.D., Markku Kaste, M.D., Erich Bluhmki, Ph.D., Miroslav Brozman, M.D., Antoni Dávalos, M.D., Donata Guidetti, M.D., Vincent Larrue, M.D., Kennedy R. Lees, M.D., Zakaria Medeghri, M.D., Thomas Machnig, M.D., Dietmar Schneider, M.D., Rüdiger von Kummer, M.D., Nils Wahlgren, M.D., and Danilo Toni, M.D., for the ECASS Investigators*

Extended IVtPA window (3-4.5 h)
Similar to NINDs protocol

ECASS 3

- Enrolled 821
- More patients had a favorable outcome with alteplase than with placebo (52.4% vs. 45.2%; OR, 1.34; 95% CI, 1.02 to 1.76; P = 0.04)
- symptomatic ICH, 2.4% vs. 0.2%; P = 0.008
- Mortality did not differ significantly between the alteplase and placebo groups

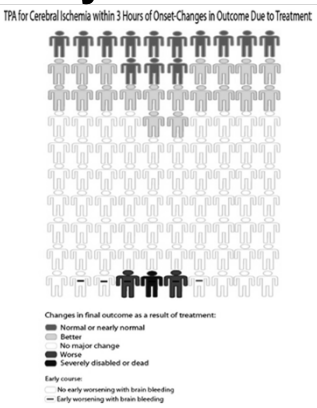
What is considered stroke onset?

- Witnessed onset
- If un-witnessed onset, then considered to be last known normal
- If fell asleep at midnight, awoke at 6 am with neurologic deficits
  - Arrived at ER by 7am
  - Onset of symptoms is considered to be 7 hours ago, not 1 hour

Time of onset = Last known normal

Patient friendly visual

32 patients are better
3 are worse
(1 much worse)
65 are same



Gadhia J et al. Stroke 2010;41:300-306

Source: UCLA Stroke Center (CC BY 4.0)

The evolution of the AHA GUIDELINES

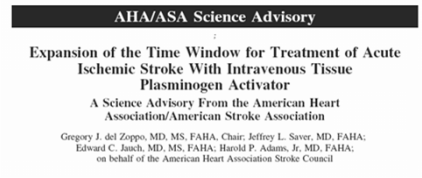
AHA Guidelines 2007

TABLE 11. Characteristics of Patients With Ischemic Stroke Who Could Be Treated With rtPA

Diagnosis of ischemic stroke causing measurable neurological deficit
The neurological signs should not be clearing spontaneously.
The neurological signs should not be minor and isolated.
Caution should be exercised in treating a patient with major deficits.
The symptoms of stroke should not be suggestive of subarachnoid hemorrhage.
Onset of symptoms <3 hours before beginning treatment
No head trauma or prior stroke in previous 3 months
No myocardial infarction in the previous 3 months
No gastrointestinal or urinary tract hemorrhage in previous 21 days
No major surgery in the previous 14 days
No arterial puncture at a noncompressible site in the previous 7 days
No history of previous intracranial hemorrhage
Blood pressure not elevated (systolic <185 mm Hg and diastolic <110 mm Hg
No evidence of active bleeding or acute trauma (fracture) on examination
Not taking an oral anticoagulant or, if anticoagulant being taken, INR ≤1.5
If receiving heparin in previous 48 hours, aPTT must be in normal range.
Platelet count ≥100 000 mm³
Blood glucose concentration ≥50 mg/dL (2.7 mmol/L)
No seizure with postictal residual neurological impairments
CT does not show a multilobar infarction (hypodensity >1/3 cerebral hemisphere).
The patient or family members understand the potential risks and benefits from treatment.

INR indicates international normalized ratio; aPTT, activated partial thromboplastin time.

Extended IVtPA window to 4.5hrs



AHA/ASA Science Advisory

Expansion of the Time Window for Treatment of Acute Ischemic Stroke With Intravenous Tissue Plasminogen Activator

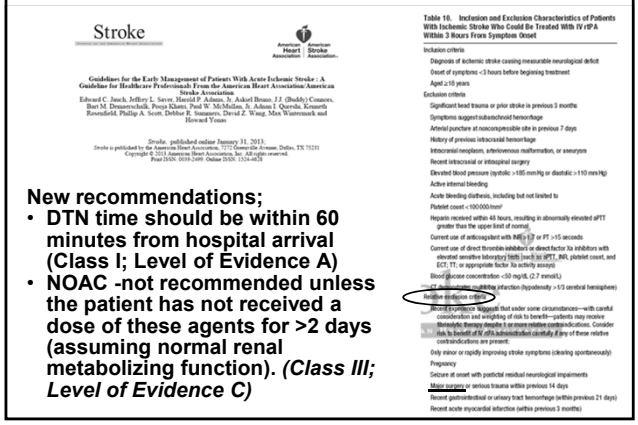
A Science Advisory From the American Heart Association/American Stroke Association

Gregory J. del Zoppo, MD, MS, FAHA, Chair; Jeffrey L. Saver, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Harold P. Adams, Jr, MD, FAHA; on behalf of the American Heart Association Stroke Council

- **rtPA should be administered to eligible patients who can be treated in the time period of 3 to 4.5 hours after stroke *(Class I Recommendation, Level of Evidence B)***

Stroke 2009, 40:2945-2948:

AHA Guidelines 2013



Stroke

Guidelines for the Early Management of Patients With Acute Ischemic Stroke : A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Edward C. Jauch, Jeffrey L. Saver, Harold P. Adams, Jr, Askel Bruno, J.J. (Buddy) Connors, Bart M. Demaerschalk, Pooja Khatri, Paul W. McMullan, Jr, Adnan I. Qureshi, Kenneth Rosenfield, Phillip A. Scott, Debbie R. Summers, David Z. Wang, Max Wintermark and Howard Yonas

Stroke published online January 31, 2013;

Table 10. 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 greater 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 intracranial surgery
- Recent severe head trauma
- 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)

New recommendations;

- **DTN time should be within 60 minutes from hospital arrival (Class I; Level of Evidence A)**
- **NOAC -not recommended unless the patient has not received a dose of these agents for >2 days (assuming normal renal metabolizing function). *(Class III; Level of Evidence C)***

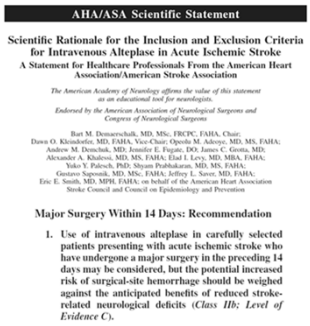
AHA 2015 Guidelines Update IAT

1. **Patients eligible for IVtPA should receive IV-tPA even if IAT is being considered *(Class I; Level of Evidence A).***
2. **Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria *(Class I; Level of Evidence A).***
   a) **prestroke mRS score 0 to 1**
   b) **acute ischemic stroke receiving IV-tPA within 4.5 hours of onset**
   c) **occlusion of the internal carotid artery 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 onset**

AHA 2015 Guidelines Update IAT

3. **As with IV-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)***

AHA 2015 Scientific Statement- IV-tPA



AHA/ASA Scientific Statement

Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke

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

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

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

Bart M. Demaerschalk, MD, MSc, FRCPC, FAHA, Chair; Dawn O. Kleindorfer, MD, FAHA, Vice Chair; Opeolu M. Adeoye, MD, MS, FAHA; Andrew M. Demchuk, MD; Jennifer E. Fugate, DO; James C. Grotta, MD; Alexander A. Khalessi, MD, MS, FAHA; Elad I. Levy, MD, MBA, FAHA; Yuko Y. Palesch, PhD; Shyam Prabhakaran, MD, MS, FAHA; Gustavo Saposnik, MD, MSc, FAHA; Jeffrey L. Saver, MD, FAHA; Eric E. Smith, MD, MPH, FAHA; on behalf of the American Heart Association Stroke Council and Council on Epidemiology and Prevention

Major Surgery Within 14 Days: Recommendation

1. Use of intravenous alteplase in carefully selected patients presenting with acute ischemic stroke who have undergone a major surgery in the preceding 14 days may be considered, but the potential increased risk of surgical-site hemorrhage should be weighed against the anticipated benefits of reduced stroke-related neurological deficits (*Class IIb; Level of Evidence C*).

AHA 2015 Update, consider

- Rapidly improving but still potentially disabled
- Pregnancy
- Major surgery within 14 days (excludes intracranial intraspinal)
- Seizure at onset
- Dural puncture within 7 days
- Psychogenic, malingering, conversion
- Acute MI or Recent MI
- GI bleeding (warning- structural lesion or within 21 days)
- Unruptured cerebral aneurysm (not giant)
- EICs on CT (mod)
- Cervical artery dissection
- Menstruation

AHA 2015, DO NOT recommend

- Hemorrhage on CT
- Prior ICH
- Bleeding diathesis
  - Coumadin INR >1.7
  - NOAC (within 48 hrs)
  - Lovenox (prophylactic and treatment dose) – FIXED IN 2018
- BS < 50 or > 400
- Aortic Arch Dissection
- Endocarditis
- Intra-axial neoplasm (excludes meningioma)

AHA 2018 Guidelines

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

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

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

Correction to: 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Based on recent feedback received from the clinical stroke community related to the article by Powers et al, "2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association," which published ahead of print January 24, 2018, and appeared in the March 2018 issue of the journal (*Stroke*. 2018;49:e46–e110. DOI: 10.1161/STR.0000000000000158), the American Heart Association/American Stroke Association has reviewed the guideline and is preparing clarifications, modifications, and/or updates to several sections in it. Currently, those sections, listed here, have been deleted from the guideline while this clarifying work is in process:

Section 1.3 EMS Systems Recommendation 4
Section 1.4 Hospital Stroke Capabilities Recommendation 1
Section 1.6 Telemedicine Recommendation 3
Section 2.2 Brain Imaging Recommendation 11
Section 3.2 Blood Pressure Recommendation 1
Section 4.3 Blood Pressure Recommendation 2
Section 4.6 Dysphagia Recommendation 1
Section 6.0 All subsections (11)

We continue to support this corrected version of the guideline and its support for clinical decision-making. After review, a revised guideline, with consideration given to the clarifications, modifications, and/or updates of the sections noted above, will be posted over the coming weeks.

New recommendations

- CMBs
- Sickle cell
- Corrected LMWH "treatment dose within 24 hours"
- IAT- expanded to 24 hours window

Medical malpractice

Original Contribution

Systematic Review of Malpractice Litigation in the Diagnosis and Treatment of Acute Stroke

Jack J. Haslett, BSc; Lisa Genadry, BSc candidate; Xiangnan Zhang, MSc; Lindsey A. LaBelle, JD, BA; Joshua Bederson, MD; J. Mocco, MD, MS; Christopher P. Kellner, MD

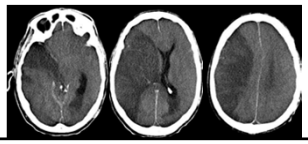
Stroke 2019

- **3 legal databases were used to searched**
- **246 medical malpractice cases related to acute management of ischemic stroke**
  - **71 cases specifically alleged failure to treat with tPA**
  - **1 case related to complications (hemorrhage) after tPA administration, dismissed via summary judgment**
- **litigation related to a failure to give tPA is more common than for cases where tPA was administered**

IV tPA limitations

Katzan. Arch Neur 2004

- **t-PA has had limited impact on overall morbidity and mortality on a national level**
  - **restricted application to < 5% of patients with acute stroke**
  - **strict time window**
    - **delay in presentation the most common reason patients were ineligible for IV thrombolysis**
    - **Only 15% of patients arrived within the 3-hour time window for intravenous IVtPA**
- **Subset of Large vessel occlusions LVO (NIHSS>20) poor recannalization rates**



Incidence and Predictors of Early Recanalization After Intravenous Thrombolysis

A Systematic Review and Meta-Analysis

Pierre Seners, MD*; Guillaume Turc, PhD*; Benjamin Maier, MD; Jean-Louis Mas, MD; Catherine Oppenheim, PhD; Jean-Claude Baron, ScD

Stroke 2016

- **early recanalization (ER; ≤3 hours after start of IV-tPA)**
- **meta-analyses, 26 studies, 2063 patients**
- **overall incidence of partial or complete ER was 33% (95% CI, 27–40), varied according to occlusion site:**
  - **35% (complete ER 21%) for proximal MCA**
  - **13% (complete ER 4%) for ICA**
  - **13% (complete ER 4%) for basilar occlusion**
- **Proximal occlusion and higher NIHSS were the most consistent no-ER predictors**

Thrombectomy for Large Vessel Occlusion (LVO)

Ciarán J. Powers, MD, PhD, FAANS
Associate Professor
Department of Neurological Surgery
Surgical Director, Comprehensive Stroke Center
The Ohio State University Wexner Medical Center

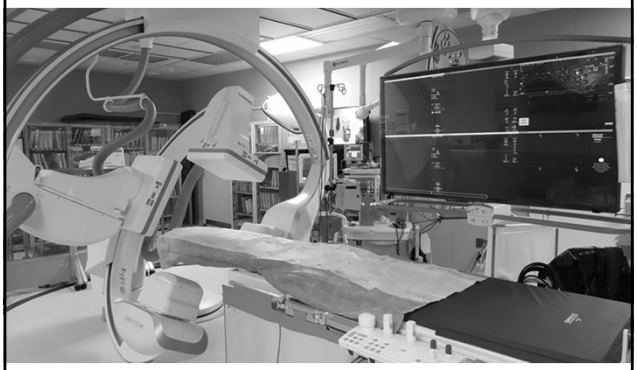
Financial Disclosures

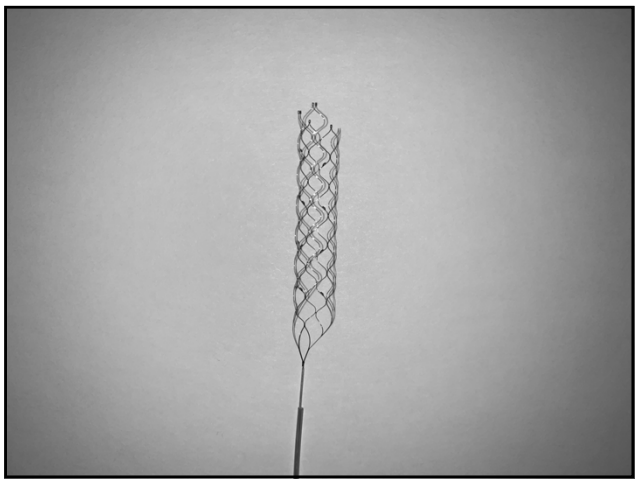
- Clinical Research Support: Medtronic, MicroVention and Stryker Neurovascular
- Fellowship Support: Medtronic

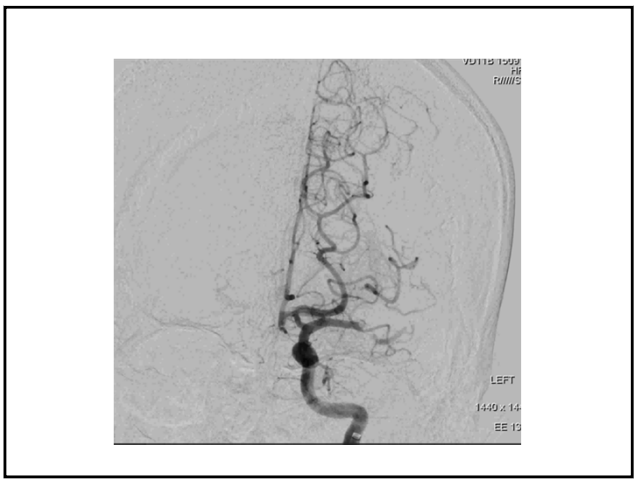
Overview

- Thrombectomy for Large Vessel Occlusion (LVO)
  - MR CLEAN and friends
- Thrombectomy beyond 6 hours
  - DAWN and DEFUSE 3

THROMBECTOMY FOR LVO



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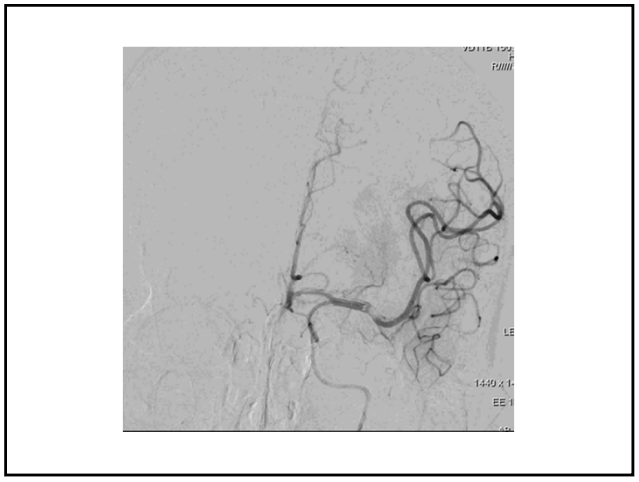

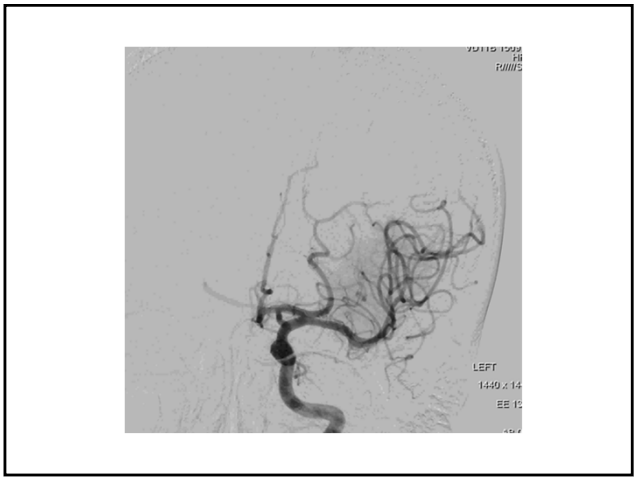
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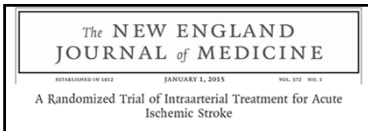
TICI

- Grade 0 = No perfusion.
- Grade 1 = Perfusion past the initial obstruction, but limited distal branch filling with little or slow distal perfusion.
- Grade 2a = Perfusion of less than ½ of the vascular distribution of the occluded artery (e.g., filling and perfusion through 1 M2 division).
- Grade 2b = Perfusion of ½ or greater of the vascular distribution of the occluded artery (e.g., filling and perfusion through 2 or more M2 divisions).
- Grade 3 = Full perfusion will filling of all distal branches.

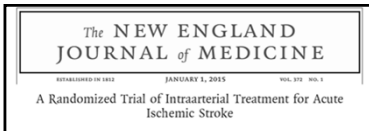
STUDIES SUPPORTING THROMBECTOMY



MR CLEAN

Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands

- Patient population
  - Greater than 18 years with no upper age limit
  - NIHSS greater than or equal to 2
- Imaging
  - Exclude hemorrhagic stroke by CT
  - Occlusion by CTA, MRA or DSA
- Intervention
  - Intra-arterial thrombectomy within 6 hours with or without IV rtPA in patients with intracranial occlusion in anterior circulation artery (ICA, M1, M2, A1 or A2)



MR CLEAN

Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands

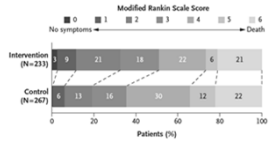
- Primary outcome
  - Modified Rankin scale (mRS) at 90 days
- Secondary outcome
  - NIHSS 24 hours, 5 and 7 days
  - ADL measured by Barthel index
- Imaging outcomes
  - CTA or MRA 24 hours to measure persistence of recanalization
  - CT 5-7 days to measure final infarct volume

Study Stats

- Size: 500 study participants
  - Mean age: 65 years (23 to 96 years)
  - Men: 58.4%
  - 95% of patients in both groups had pre-stroke mRS 2 or better
  - Mean NIHSS: 17
- 267 patients (53.4%) assigned to control
- 233 patients (46.6%) assigned to intervention
  - 196 underwent IA therapy
    - 195 patients underwent mechanical thrombectomy
      - 190 with stent-retriever
    - 88 patients (37.8%) had general anesthesia
    - 30 patients (12.9%) underwent concurrent carotid stent
    - 24 patients (10.3%) received additional IA thrombolytic
    - 1 patient (0.4%) underwent IA tPA only

Results

- Primary
  - Median mRS at 90 days: 3 in Intervention and 4 in Control.
- Secondary
  - mRS 0-3 at 90 days: 51% in Intervention and 35% in Control.
  - Persistent vessel patency: 75% in Intervention and 33% in Control.



	Intervention	Control
mRS 0-1 90 days	27 (12%)	16 (6%)
mRS 0-2 90 days	76 (33%)	51 (19%)
mRS 0-3 90 days	119 (51%)	95 (36%)
NIHSS 24 h median	13 (6-20)	16 (12-21)
NIHSS 5-7 days median	8 (2-17)	14 (7-18)
Persistent vessel patency	141/187 (75.4%)	68/207 (32.9%)
Infarct volume median	49ml (22-96)	79ml (34-125)

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

EXTEND IA

Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial

After MR CLEAN published, study arrested

- Patient population
  - Greater than 18 years with no upper age limit
  - NIHSS no lower limit
  - Pre-stroke mRs less than 2 (functional independence)
- Imaging
  - Exclude hemorrhagic stroke by CT
  - Ischemic core of less than 70 ml with salvageable tissue
  - Occlusion by CTA, MRA or DSA
- Intervention
  - Solitaire thrombectomy started within 6 hours and completed in 8 hours in patients who had received IV rtPA within 4.5 hours of stroke onset with ICA, M1 or M2 occlusion

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

EXTEND IA

Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial

After MR CLEAN published, study arrested

- Primary outcome
  - Reperfusion at 24 hours defined by percent reduction in perfusion-lesion volume between initial and 24-hour CT perfusion studies
  - Early neurological improvement defined by decrease in NIHSS by 8 or more or a score of 0 or 1 3 days after intervention
- Secondary outcome
  - mRs at 90 days
  - Symptomatic hemorrhage
    - SAH
    - Parenchymal hematoma within 36 hours after treatment with increase in NIHSS by 4 or more points
  - Death due to any cause

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

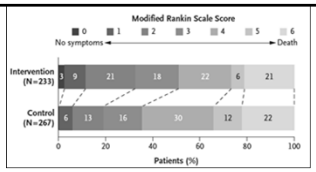
ESCAPE

Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times

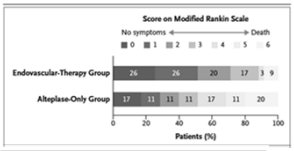
- **Patient population**
  - **Greater than 18 years with no upper age limit**
  - **Functional independence before stroke onset**
- **Imaging**
  - **CT**
    - **Exclude hemorrhagic stroke**
    - **ASPECTS (Alberta Stroke Program Early Computerized Tomography Score), used in ASPECTS to identify patients with small infarct core defined by ASPECT score 6-10**
  - **CTA evaluated for occlusion AND also assess for moderate-to-good vascular collateralization in setting of LVO, which was defined at filling of at least 50% of the MCA pial artery circulation**
- **Intervention**
  - **Intra-arterial thrombectomy within 6 hours with or without IV rtPA in patients with intracranial occlusion in anterior circulation artery (ICA, M1, M2)**
- **Primary outcome**
  - **Modified Rankin scale (mRS) at 90 days)**
- **Secondary outcome**
  - **Early recanalization and reperfusion**
  - **Intracranial hemorrhage**
  - **Angiographic complications**
  - **Neurological disability at 90 days**
  - **Death**
- **Imaging outcomes**

After MR CLEAN published, study arrested

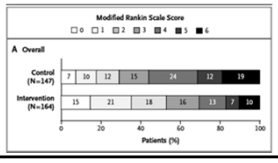
MR CLEAN



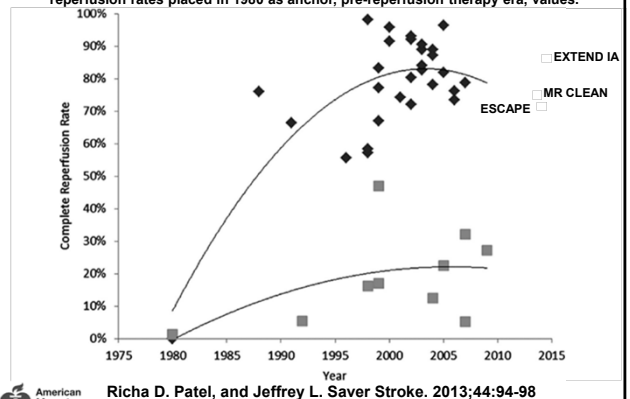
EXTEND IA



ESCAPE



Trends over time in complete reperfusion rates in active arms of coronary (diamond) and cerebral (square) reperfusion trials, without sample size weighting and with spontaneous reperfusion rates placed in 1980 as anchor, pre-reperfusion therapy era, values.



American Heart Association.

Richa D. Patel, and Jeffrey L. Saver Stroke. 2013;44:94-98

THROMBECTOMY BEYOND 6 HOURS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

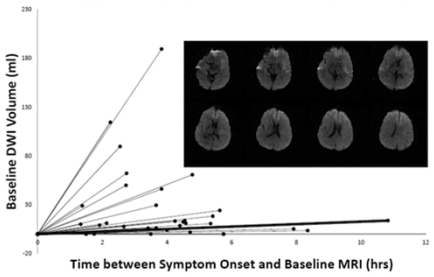
Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

defuse 3

- **Patient population**
  - **Occlusion of intracranial ICA or M1**
  - **Initial infarct size of less than 70 ml AND ratio of the volume of ischemic tissue on perfusion imaging to infarct volume of 1.8 or more**
- **Intervention**
  - **Intra-arterial thrombectomy between 6-16 hrs from LKW**
- **Primary outcome**
  - **Modified Rankin scale (mRS) at 90 days**
- **Secondary outcome**
  - **Functional independence (mRS 0-2) at 90 days**
  - **Infarct volume, lesion growth, reperfusion and recanalization at 24 hours**
  - **Modified TICI score of 2b or 3 for thrombectomy patients**

DEFUSE 2

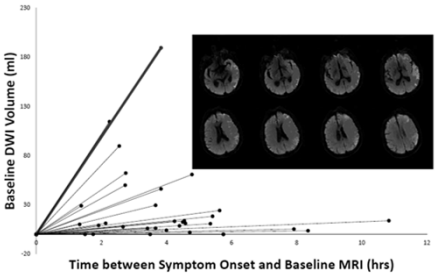
Initial Growth Rate: Known Onset & M1 Occlusion



Wheeler HM, et al. Int J Stroke. 2015

DEFUSE 2

Initial Growth Rate: Known Onset & M1 Occlusion

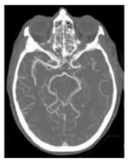


Wheeler HM, et al. Int J Stroke. 2015

Neuroimaging Inclusion Criteria

MRA / CTA reveals

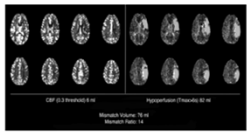
- M1 segment MCA occlusion, or
- ICA occlusion (cervical or intracranial; with or without tandem MCA lesions)



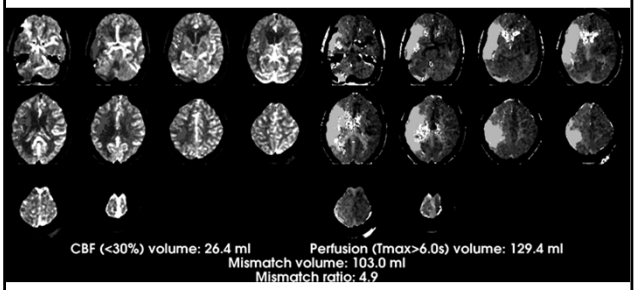
AND

Target Mismatch Profile on CT perfusion or MRI (RAPID)

- Ischemic core volume < 70 mL
  and
- Mismatch ratio > 1.8
  and
- Mismatch volume ≥ 15 mL



RAPID Imaging



Study Stats

- Size: 182 study participants
  - Mean age: 70 years
  - Men: 54%
  - Median NIHSS: 16
- 90 patients assigned to control
- 92 patients assigned to thrombectomy

Results

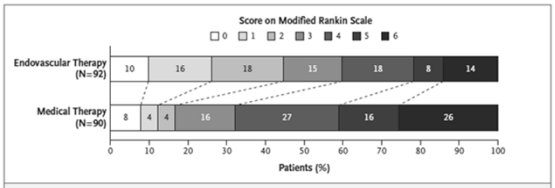


Figure 2. **Scores on the Modified Rankin Scale at 90 Days.**
Patients in the endovascular-therapy group received endovascular therapy plus standard medical therapy. Patients in the medical-therapy group received standard medical therapy alone. Scores on the modified Rankin scale range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, and 6 death. There was a significant difference favoring the endovascular-therapy group over the medical-therapy group in the overall distribution of scores (unadjusted common odds ratio, 2.77; 95% CI, 1.63 to 4.70; P<0.001).

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

DAWN

DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo.

- Patient population
  - Occlusion of intracranial ICA or M1
  - Group A: ≥80 yrs, NIHSS ≥10, infarct ≤20 ml
  - Group B: <80 yrs, NIHSS ≥10, infarct ≤30 ml
  - Group C: <80 yrs, NIHSS ≥20, infarct 30-50 ml
- Imaging
  - Exclude hemorrhagic stroke by CT
  - Occlusion by CTA, MRA or DSA
  - Infarct volume by MRI or CT perfusion
- Intervention
  - Intra-arterial thrombectomy with Trevo device between 6-24 hrs from LKW
- Primary outcome
  - Utility-weighted modified Rankin scale (mRS) at 90 days
  - Functional independence (mRS 0-2) at 90 days
- Secondary outcome
  - Early therapeutic response (decrease of NIHSS ≥10 or NIHSS of 0-1)
  - Death at 90 days
  - TICI 2b-3

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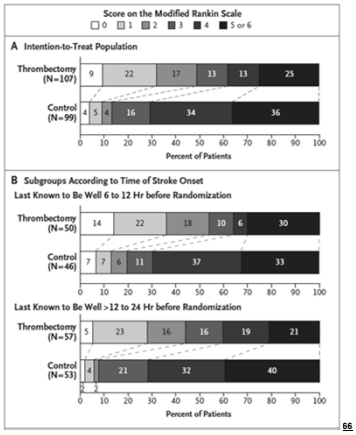
Study Stats

- Size: 206 study participants
  - Mean age: 70 years
  - Age ≥80 yrs: 25%
  - Men: 45%
  - Median NIHSS: 17
- 99 patients assigned to control
- 107 patients assigned to intervention with Trevo device

65



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Summary

- Thrombectomy for Large Vessel Occlusion (LVO)
  - Patients with LVO benefit from thrombectomy up to 24 hours from last known well
  - The window for thrombectomy can be determined by functional imaging