

# Acute Ischemic Stroke for Hospitalists

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Disclosures: none

# Objectives

1. Outline the management of acute stroke including treatment time points
2. Outline the workup of acute stroke.
3. Describe secondary prevention strategies for acute stroke

# Overview

- **Acute Ischemic Stroke**



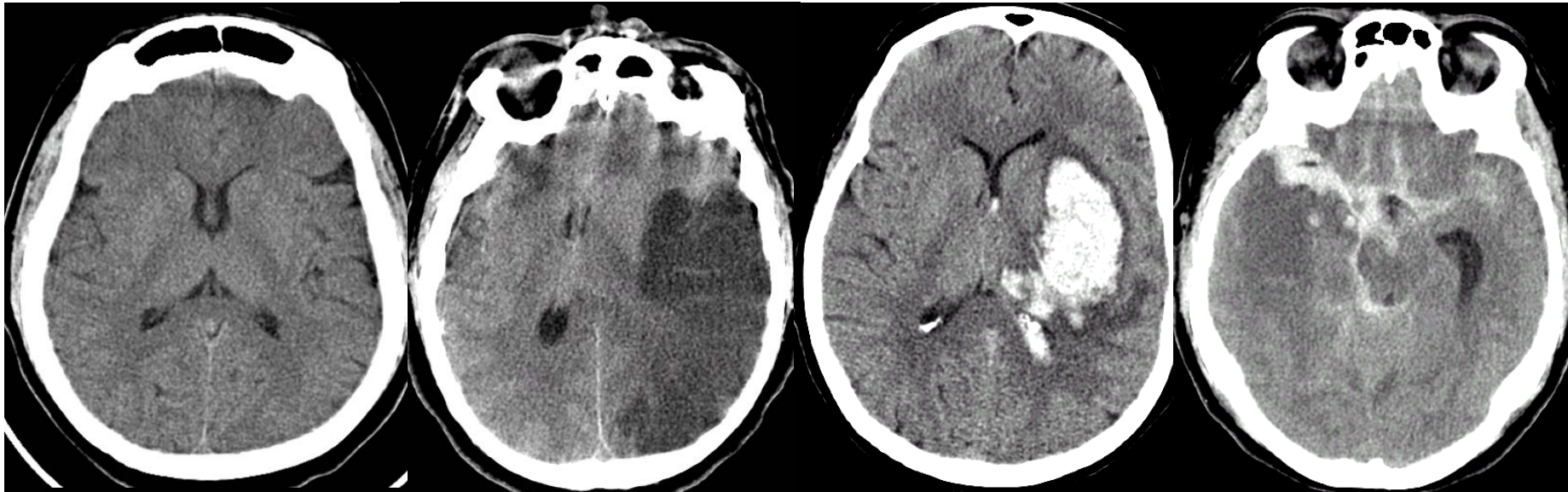
- **Hyperacute therapy**
  - tPA
  - Endovascular therapy
- **Stroke Hospitalization/Workup**
  - Management
  - Workup
- **Secondary Prevention**



- Antiplatelets
- (Afib/DOACs)
- (PFO)

# Stroke Subtypes

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Normal

Ischemic  
Stroke  
87%

Intracerebral  
Hemorrhage  
10%

Subarachnoid  
Hemorrhage  
3%

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# Current Literature: Hyper Acute Therapies for Acute Ischemic Stroke

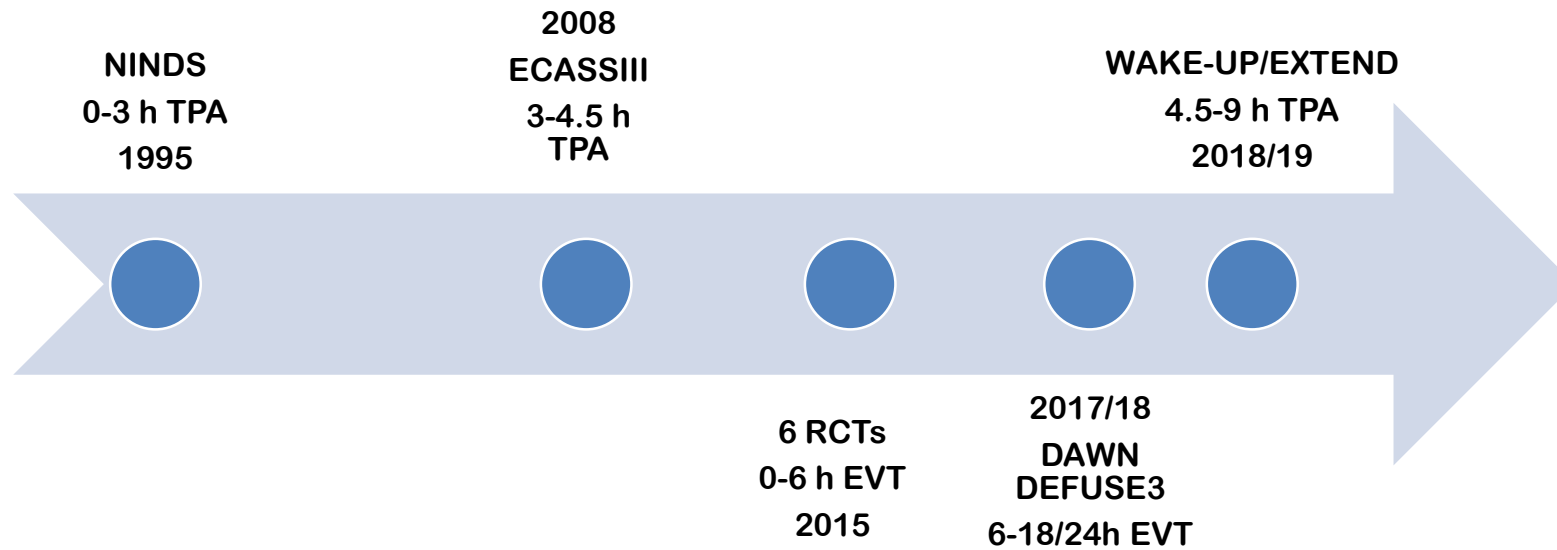
## IV tPA (recombinant tissue-type plasminogen activator)

- **0 – 3 hours:** NINDS trial, 1995
- **3-4.5 hours:** ECASS3, 2007
- **(>4.5 hours** there is some early evidence: WAKE-UP, 2018: EXTEND, 2019)

## Endovascular Mechanical Thrombectomy

- **0 – 6 hours:** MR CLEAN, REVASCAT, SWIFT PRIME, EXTEND-IA, ESCAPE, 2015
- **6-18/24 hours:** DAWN/DEFUSE3, 2017-2018

# Acute Stroke Treatment Timeline of studies



# The New England Journal of Medicine

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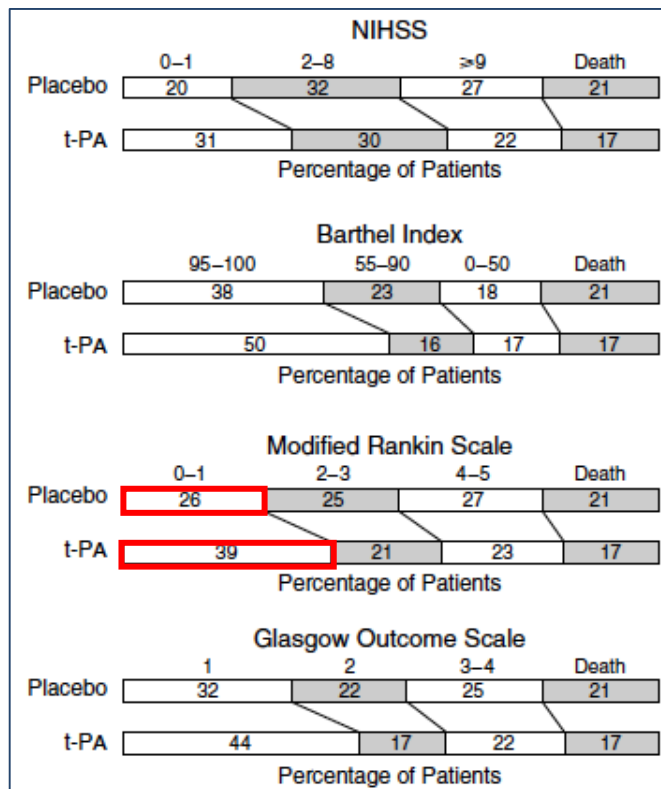
Volume 333

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\*



IV tPA  
NNT = 7  
0-3 h window



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## Modified Rankin Scale (MRS)

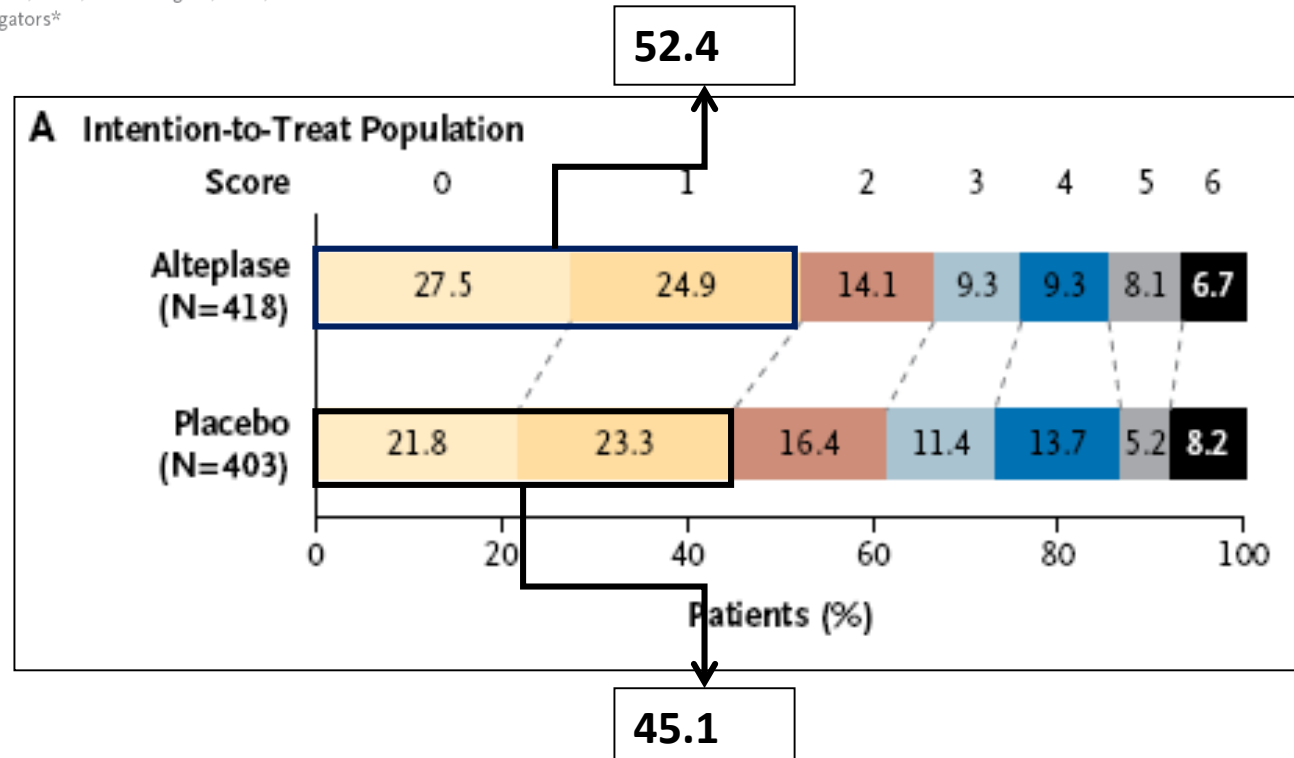
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- 0 No symptoms
  - 1 No significant disability, despite symptoms; able to perform all usual duties and activities
  - 2 Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
  - 3 Moderate disability; requires some help, but able to walk without assistance
  - 4 Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
  - 5 Severe disability; bedridden, incontinent, and requires constant nursing care and attention
  - 6 Death
-

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\*

IV tPA  
NNT=14  
in 3-4.5h window



# The NEW ENGLAND JOURNAL of MEDICINE

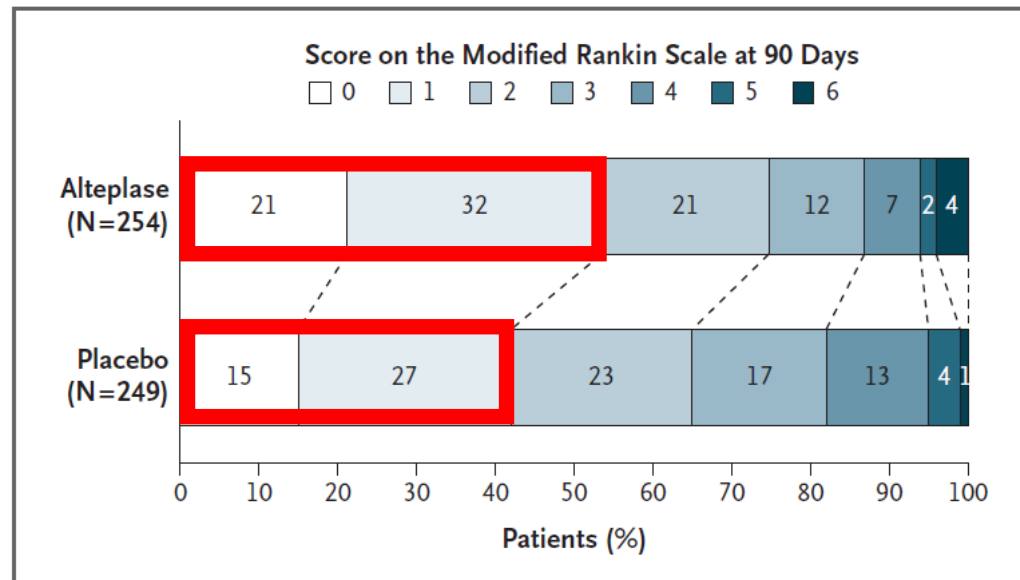
ESTABLISHED IN 1812

AUGUST 16, 2018

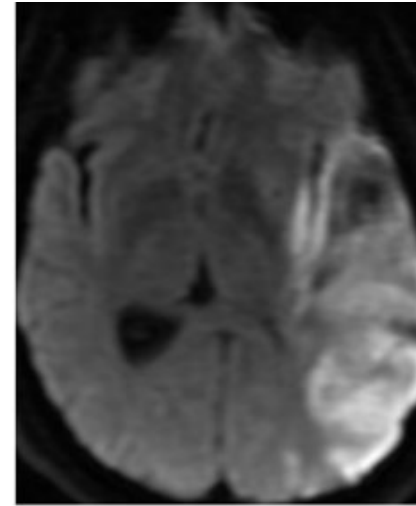
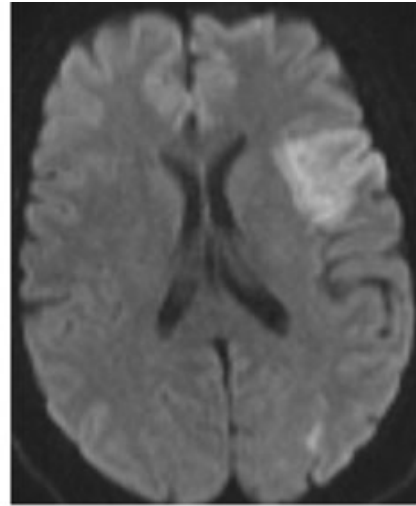
VOL. 379 NO. 7

## MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

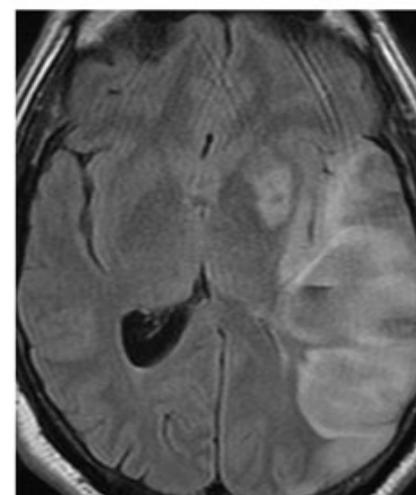
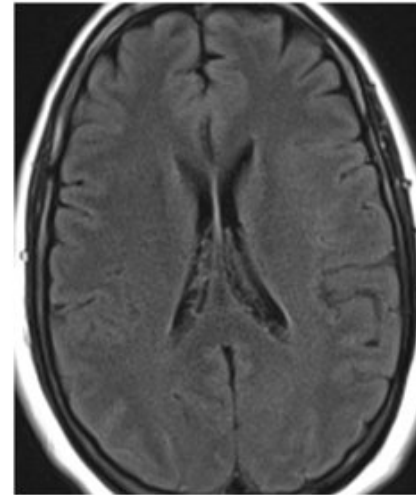
G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators\*



**DWI**



**FLAIR**



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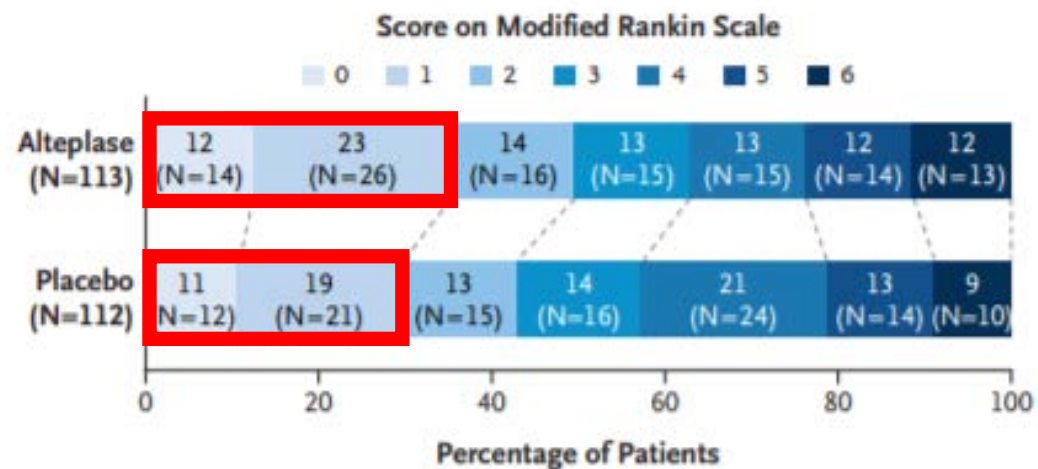
ESTABLISHED IN 1812

MAY 9, 2019

VOL. 380 NO. 19

## Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

H. Ma, B.C.V. Campbell, M.W. Parsons, L. Churilov, C.R. Levi, C. Hsu, T.J. Kleinig, T. Wijeratne, S. Curtze, H.M. Dewey, F. Miteff, C.-H. Tsai, J.-T. Lee, T.G. Phan, N. Mahant, M.-C. Sun, M. Krause, J. Sturm, R. Grimley, C.-H. Chen, C.-J. Hu, A.A. Wong, D. Field, Y. Sun, P.A. Barber, A. Sabet, J. Jannes, J.-S. Jeng, B. Clissold, R. Markus, C.-H. Lin, L.-M. Lien, C.F. Bladin, S. Christensen, N. Yassi, G. Sharma, A. Bivard, P.M. Desmond, B. Yan, P.J. Mitchell, V. Thijs, L. Carey, A. Meretoja, S.M. Davis, and G.A. Donnan, for the EXTEND Investigators\*



# Poll:

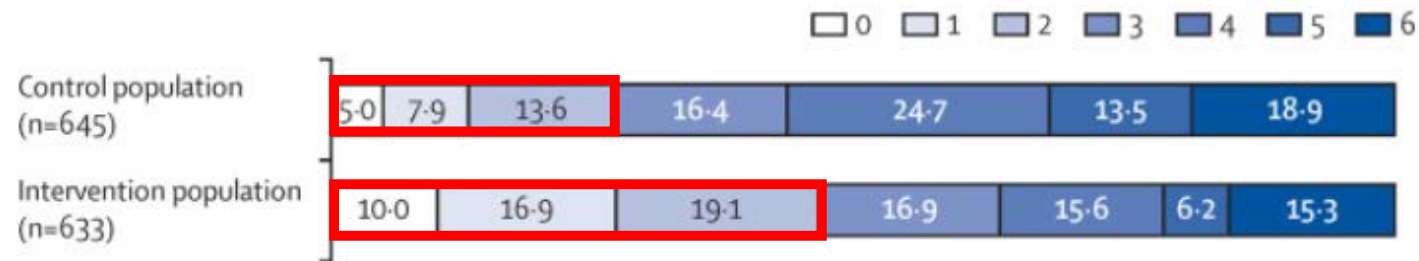
A 75 yo man woke up with left hemiplegia. Last seen normal was 12 hours ago. Noncontrast head CT is normal. CTA shows no large vessel occlusion. Is he a candidate for TPA?

- a. Yes
- b. No
- c. Need more information

## Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

[Prof Mayank Goyal, MD](#) • [Bijoy K Menon, MD](#) • [Wim H van Zwam, MD](#) • [Prof Diederik W J Dippel, MD](#) • [Prof Peter J Mitchell, MBBS](#) • [Prof Andrew M Demchuk, MD](#) • et al. [Show all authors](#)

### A Overall



EVT  
NNT = 2.6  
0-6 h window

(Includes MR CLEAN, REVASCAT, SWIFT-PRIME, EXTEND-IA, ESCAPE)

ORIGINAL ARTICLE

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

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuvan, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators\*

ORIGINAL ARTICLE

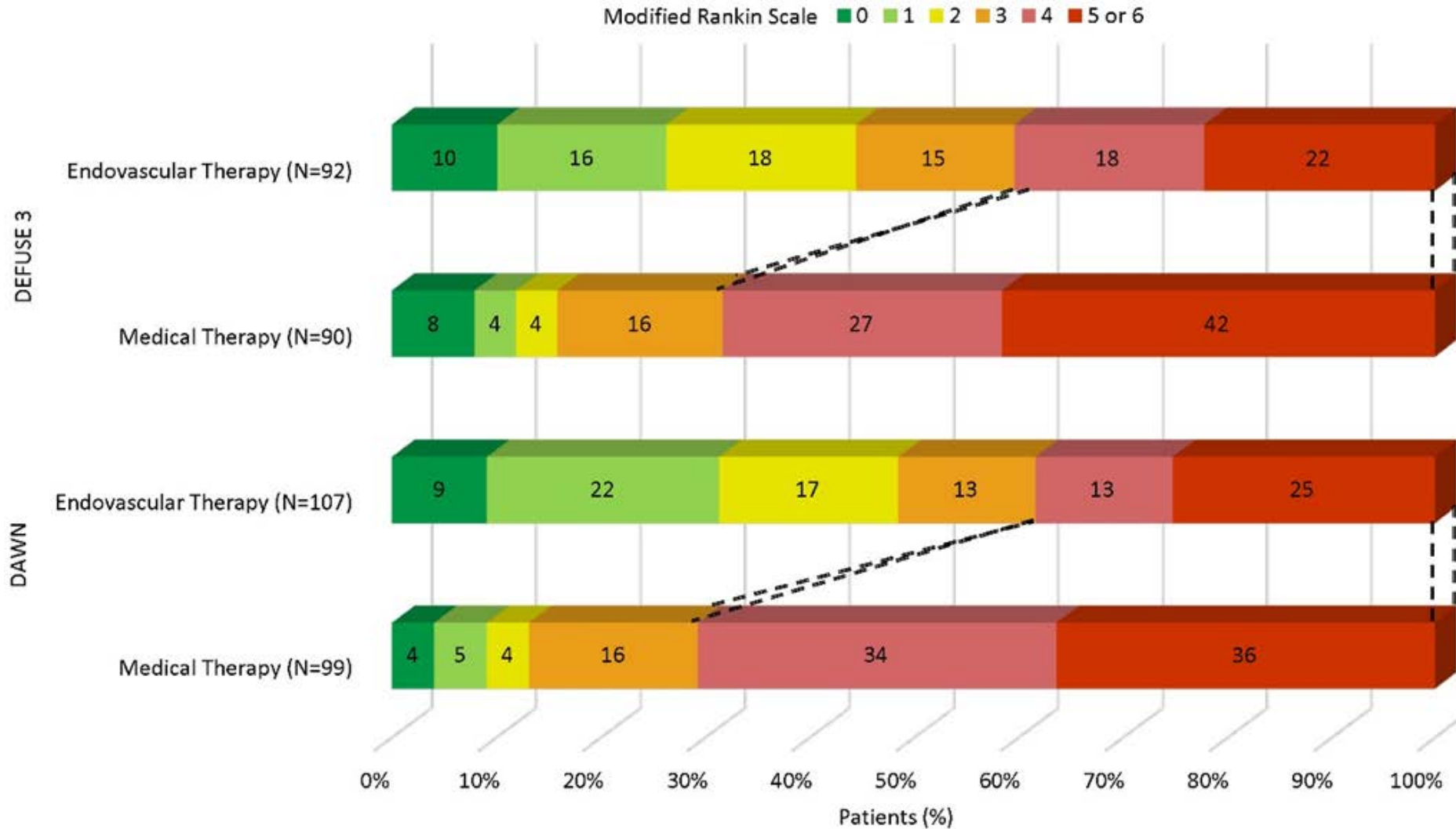
## Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators\*



# DEFUSE 3 and DAWN Trials

NNT = 2.8



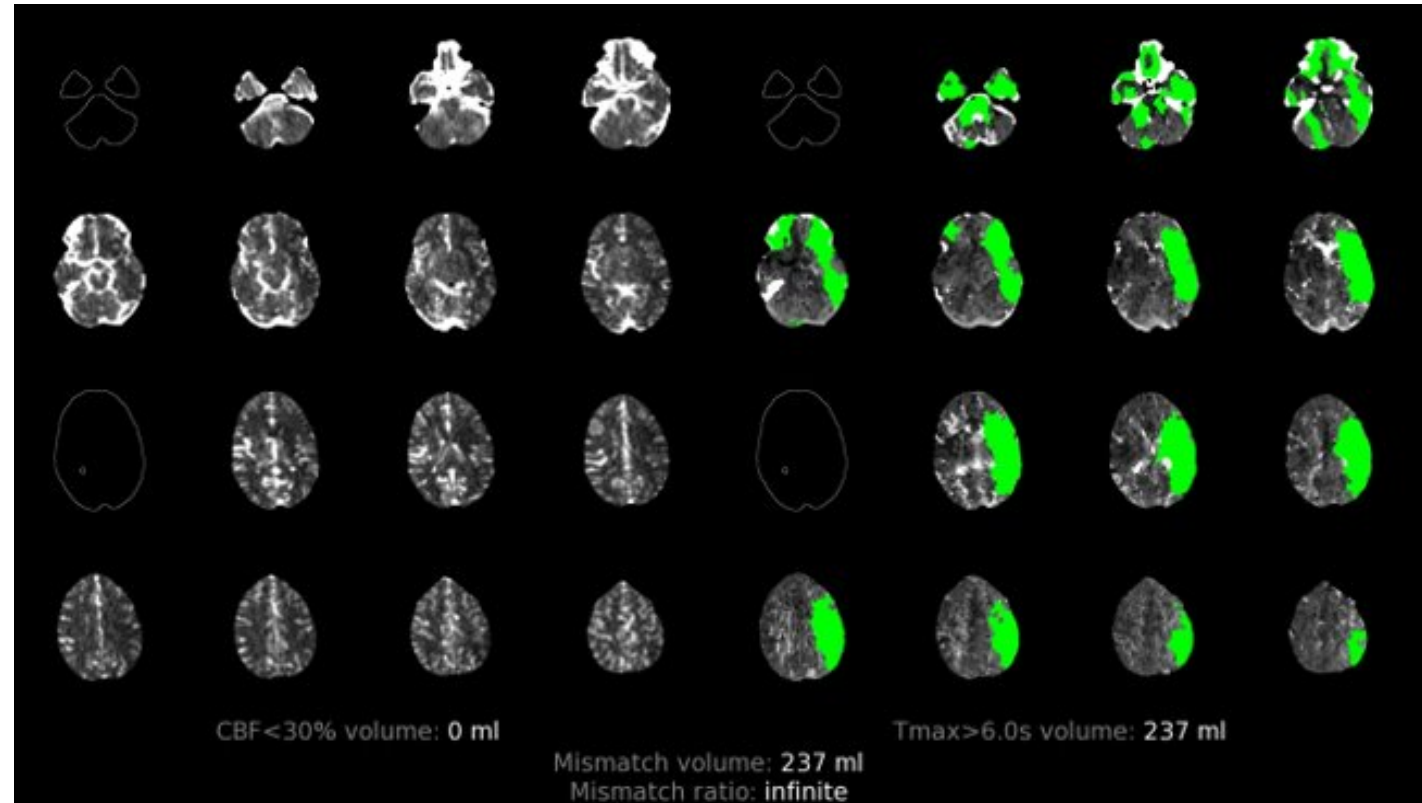
## PERFUSION:

**GREEN:** DELAYED ARRIVAL OF CONTRAST OF MORE THAN 6 SECONDS LIKELY TO PROGRESS TO INFARCTION IF REPERFUSION DOES NOT OCCUR

**PINK:** CEREBRAL BLOOD FLOW OF <30%, LIKELY TO BE IRREVERSIBLY INJURED

**MISMATCH VOLUME:** POTENTIALLY SALVAGEABLE TISSUE

**MISMATCH RATIO**



# Current Literature: Hyper Acute Therapies for Acute Ischemic Stroke

## IV tPA (recombinant tissue-type plasminogen activator)

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## Endovascular Mechanical Thrombectomy

- **0 – 6 hours:** MR CLEAN, REVASCAT, SWIFT PRIME, EXTEND-IA, ESCAPE, 2015 (second-generation stent retriever device for proximal thrombus up to 6 hours after LKW)
- **6-18/24 hours:** DAWN/DEFUSE3, 2017-2018 (select patients with large territory still at risk, benefit from EVT up to 18/24h)

# Poll:

A 40 yo man admitted to a tertiary care hospital with aspiration pneumonia after an overdose develops acute onset of hemiparesis and aphasia witnessed by the nurse. Head CT is normal. CTA shows left M1 occlusion. Last known well 4 hours ago. In addition to permissive hypertension and maintenance of normothermia and normoglycemia what is the best management strategy?

- a. IV tPA
- b. IV tPA and endovascular mechanical thrombectomy
- c. Supportive care only

# Poll:

75 yo woman with DM2, HTN presents with aphasia and R sided weakness, Last known well was 20 hours ago, CTA shows left M1 occlusion, CT perfusion shows a large mismatch, with a small core and large territory at risk for infarct. Is the patient a candidate for mechanical thrombectomy?

- a. Yes
- b. No

# Management and Hospitalization of Stroke Patients

## Management:

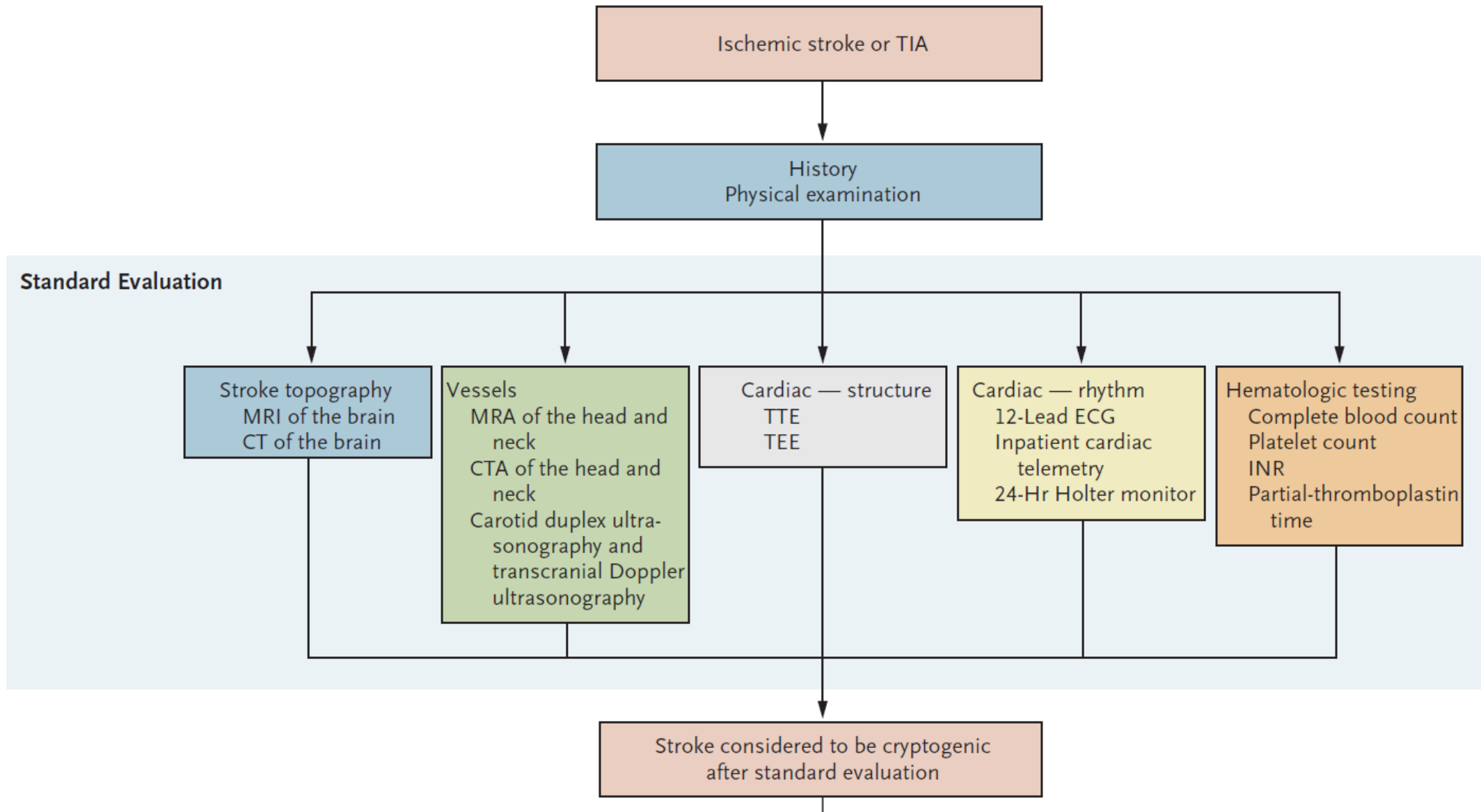
- Permissive HTN
- Normothermia
- Normoglycemia

## Hospitalization:

- Workup for Etiology
- Determine the best secondary prevention (based on etiology)
- Additional testing: 30 day ATM, hypercoag testing

## Workup

- Brain imaging (MRI preferred, HCT if not possible, TIA definition)
- Vessel imaging (CTA vs MRA head/neck, carotid/TCD)
- EKG, telemetry 48 h
- Cardiac Imaging (TTE, +/- bubble study, TEE)
- Stroke labs: fasting lipid panel (goal LDL <70), HgA1C



N Engl J Med 2016;374:2065-74



## Advanced Evaluation

Vessels  
Catheter angioplasty  
Transcranial Doppler  
monitoring for  
emboli  
Vasculitis tests

Cardiac — rhythm  
Prolonged (2–4 wk)  
outpatient cardiac  
telemetry

Hematologic testing  
Arterial hyperco-  
agulability tests  
(all patients)  
Venous hyperco-  
agulability tests  
(if right-to-left shunt)

Stroke considered to be cryptogenic  
after advanced evaluation

## Specialized Evaluation

Genetic testing  
Mitochondrial disease  
CADASIL, Fabry's  
disease, other  
genetic causes

Vessels  
Detailed autoimmune  
evaluation  
CSF examination  
Brain biopsy

Cardiac — structure  
Cardiac CT  
Cardiac MRI

Cardiac — rhythm  
Prolonged (1–3 yr)  
outpatient loop  
recording

Hematologic testing  
Workup for occult  
cancer

N Engl J Med 2016;374:2065-74



## Poll:

A 52 yo man with no prior medications is treated with tPA for a ischemic stroke secondary to large vessel atherosclerosis and is ready for discharge. He was started on aspirin and Plavix during the admission. What antiplatelet agent(s) should he be discharged on?

- a. Aspirin 81 mg daily
- b. Aspirin 325 mg daily
- c. Aspirin 81 mg daily and clopidogrel 75 mg daily indefinitely
- d. Aspirin 81 mg indefinitely and clopidogrel 75 mg for three months
- e. Clopidogrel 75 mg daily indefinitely

## Antiplatelet Agents

- Aspirin 81 mg
- Clopidogrel 75 mg
- Aspirin 25mg + dipyridamole 200 mg BID
- Cilostazol 100 mg BID
- Ticagrelor 90mg BID

# Antiplatelet Failure

Limited data on antiplatelet choice after a stroke or TIA in patients already on aspirin.

Meta analysis in 2017 suggests patients do benefit from either switching agents, or a short course of dual antiplatelet therapy.

HR 0.7 (CI 0.54 – 0.92)

*Stroke*. 2017;48:2610-2613.

## Dual Antiplatelet Therapy

The duration of dual antiplatelet therapy depends on the indication:

- 1) ASA + Plavix for 3 weeks after minor stroke or TIA
- 2) ASA + Plavix for 3 months for large artery atherosclerosis

## CHANCE Trial

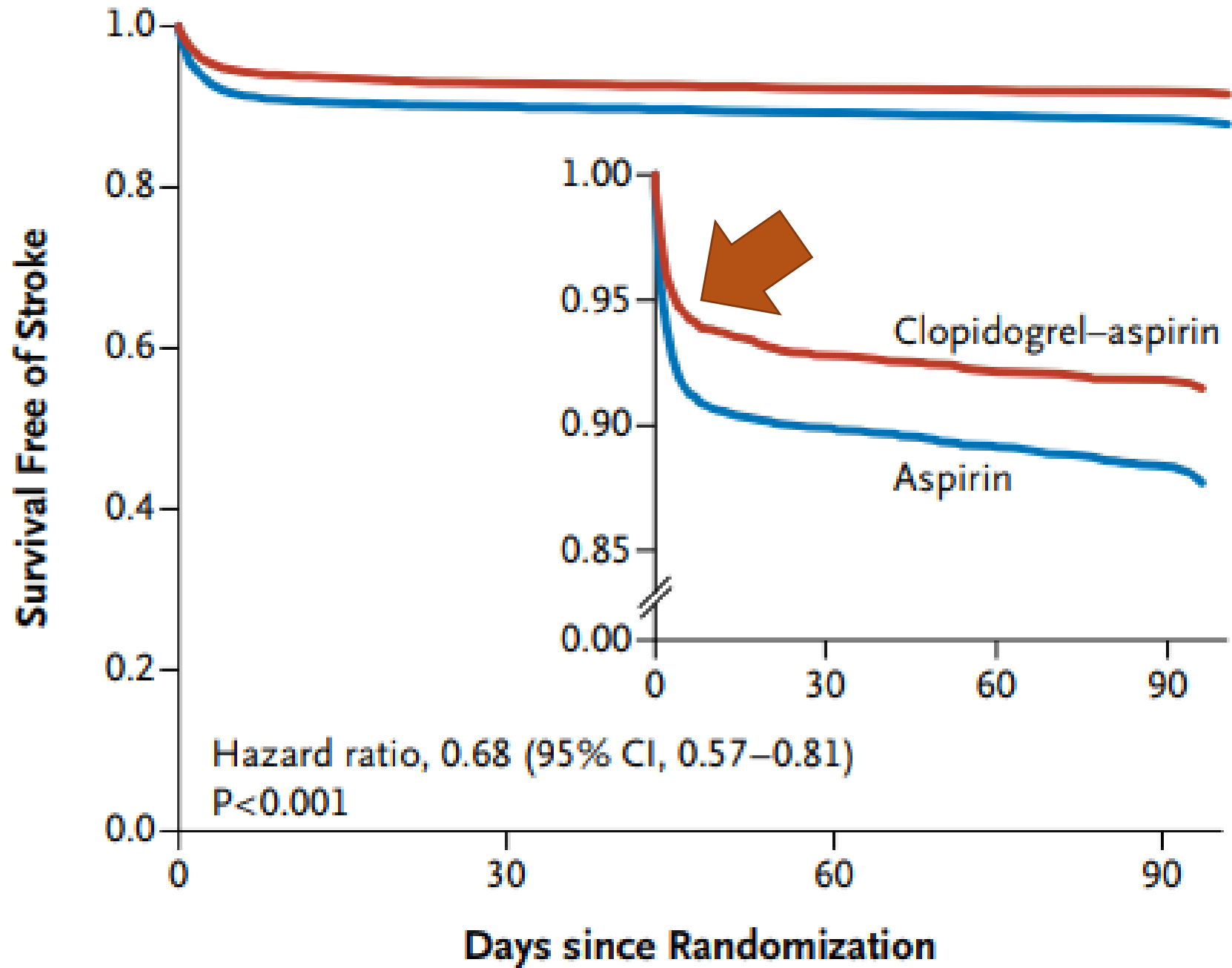
First large, randomized trial of dual antiplatelet therapy after TIA or minor stroke

Plavix for 90 days + plus Aspirin for 21 days vs Aspirin alone

Strokes occurred in 11.7% of the ASA group vs 8.2% in dual therapy (HR 0.68, CI 0.57 – 0.81, P <0.001)

No difference in hemorrhage

But... study done in China. Applicable to US population?



## CHANCE Trial Probability of Survival Free of Stroke.

*N Engl J Med. 2013;369:11-19.*



## POINT Trial

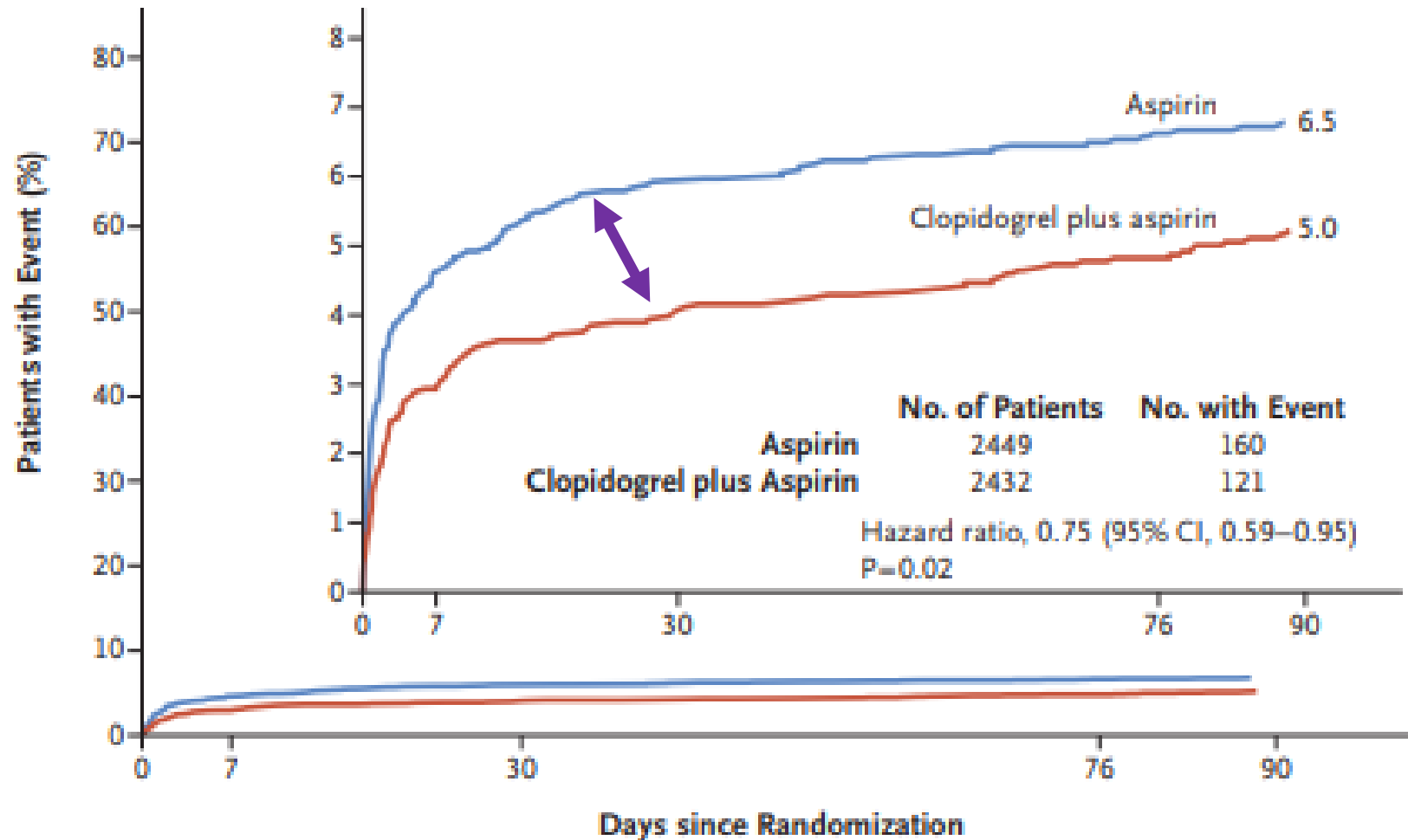
**Aspirin + Plavix for 3 months after minor stroke or TIA reduces early recurrent stroke.**

HR 0.75, CI 0.59 – 0.95, p=0.02

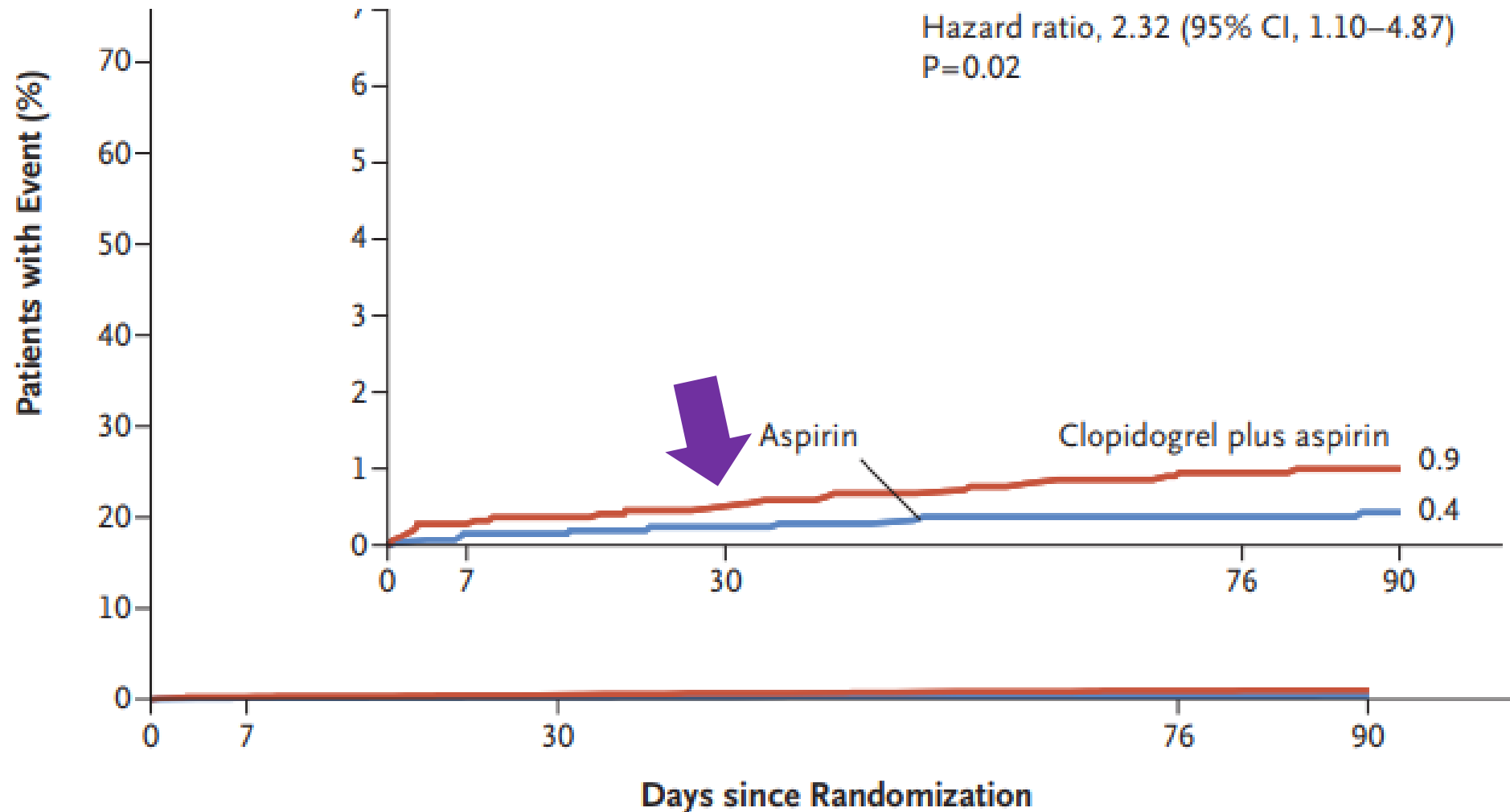
Most recurrent strokes occurred in the first week

Increased risk of bleeding, HR 2.3, but occurred later in the study

# POINT: Aspirin + Plavix for 3 weeks after minor stroke or TIA reduces early recurrent stroke.



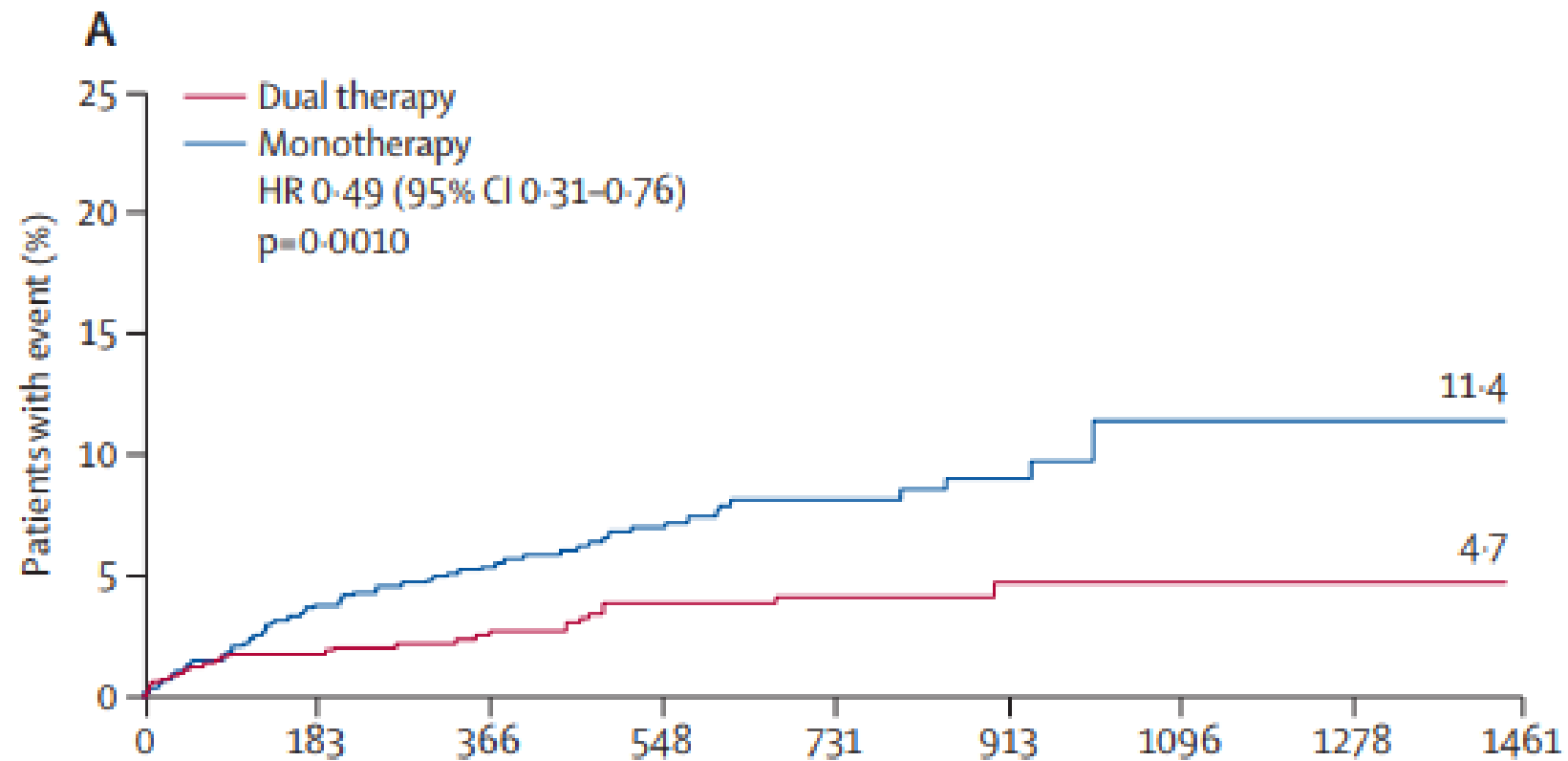
# POINT: Risk of hemorrhage increases after 30 days



# Antiplatelets for Large Artery Atherosclerosis

**SAMMPRIS:** Trial of aggressive medical therapy vs stenting in intracranial atherosclerosis → significantly favored medical therapy

ASA 325 + Clopidogrel 75 x **90 days**, high dose statin, aggressive blood pressure control, diabetic treatment, diet & exercise



Number at risk  
(number censored)

Dual therapy	932 (226)	691 (109)	576 (159)	411 (134)	276 (121)	154 (79)	75 (50)	25 (25)	0 (0)
Monotherapy	947 (150)	764 (124)	628 (193)	426 (138)	283 (129)	152 (70)	79 (57)	22 (22)	0 (0)

## SUMMARY

Dual antiplatelet for 21-30 days for minor stroke or TIA is reasonable

Dual antiplatelet for 90 days for large artery atherosclerosis

Can consider cilostazol if dual antiplatelet necessary for > 90 days

# Additional discussion

Timing of starting anticoagulation

Role of heparin drip

Cardiac monitoring, ATM, ILR

PFO discussion

# References

- *N Engl J Med.* 2016;374:2065-74
- *Lancet Neurol.* 2019 Jun;18(6):539-548.
- *Lancet.* 2014 Jan 25;383(9913):333-41.
- *N Engl J Med.* 2018;379:215-25.
- *N Engl J Med.* 2013;369:11-19.