5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 11

Current treatment in neurology (Level 1)

Stroke: acute treatment and prevention

Urs Fischer
Bern, Switzerland

Email: urs.fischer@insel.ch

Stroke: acute treatment and prevention

Urs Fischer
University of Bern, Switzerland

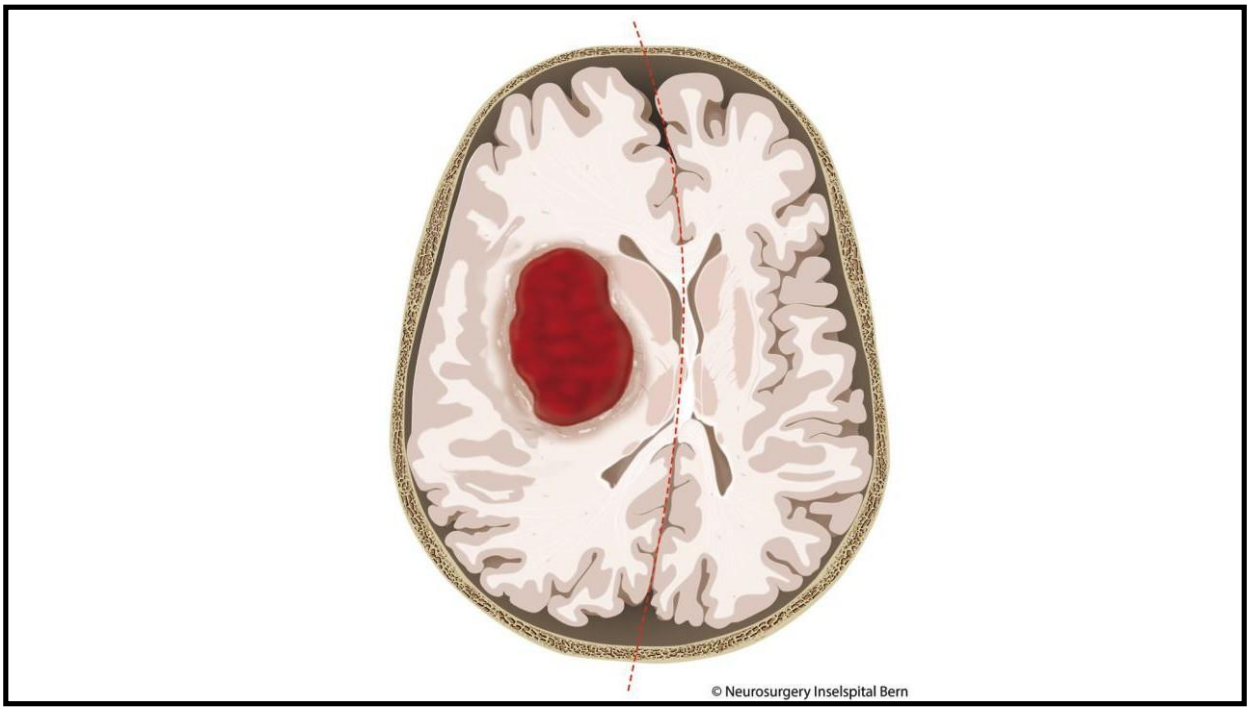
UNIVERSITÄT BERN

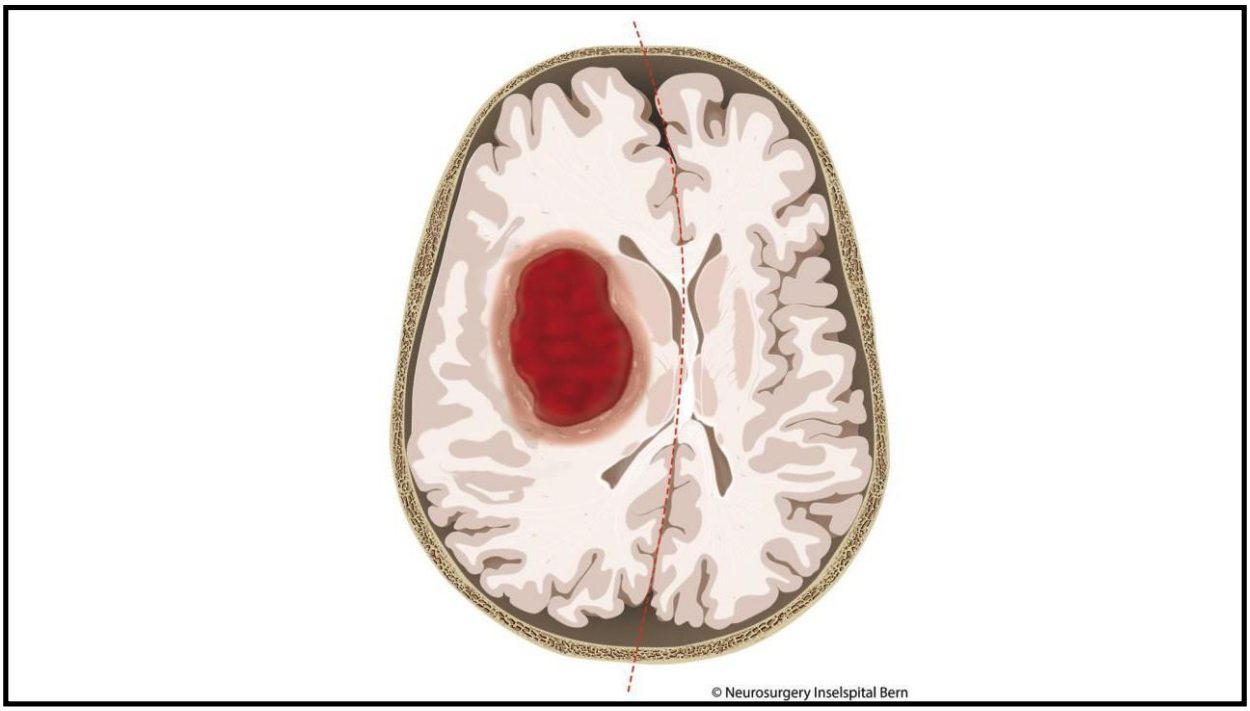
NEUROZENTRUM
Neurocentre | Neurocentro
Inselspital Universitätsspital Bern
Universitäre Psychiatrische Dienste Bern

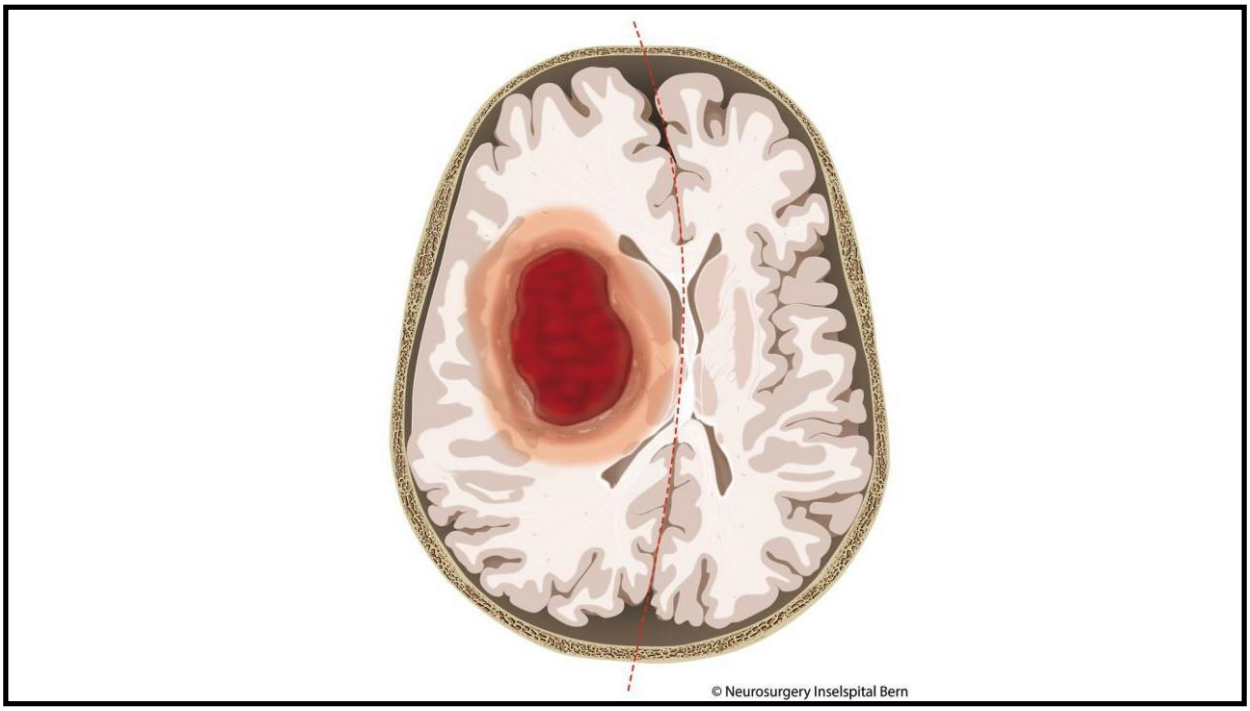
Neurochirurgie
Neurologie
Neuropädiatrie
Neuroradiologie
Psychiatrie

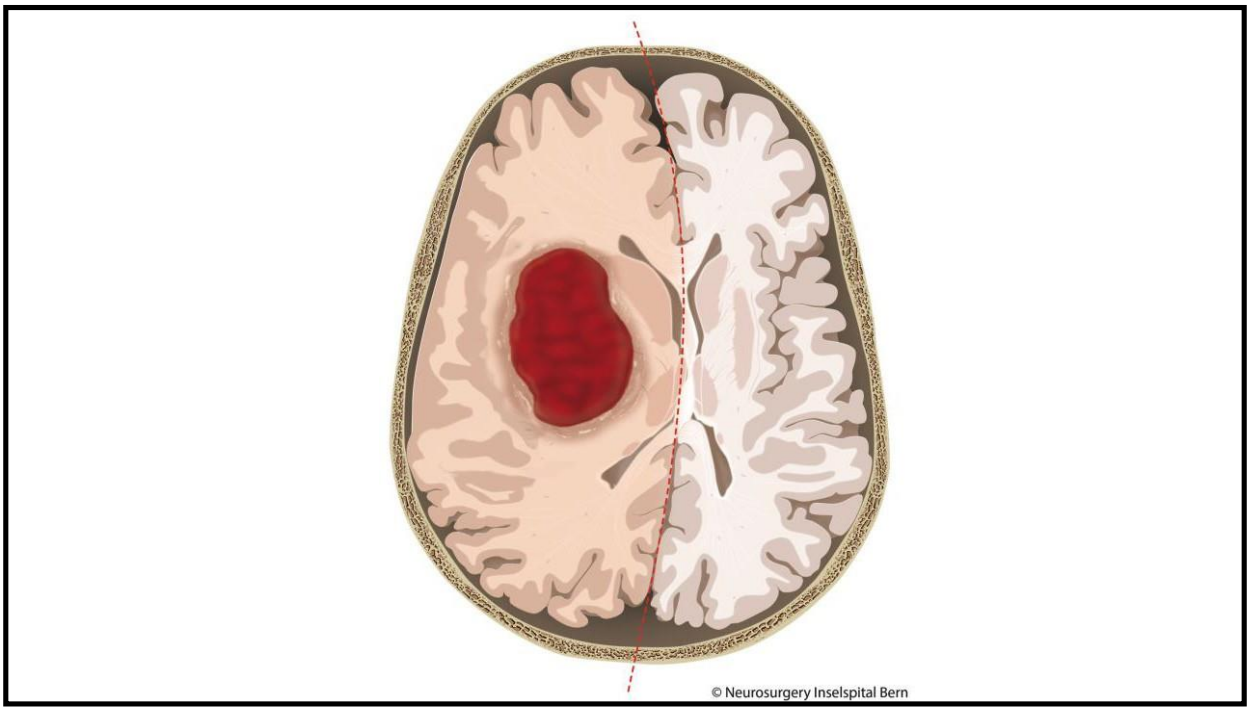
Disclosures

- Principal investigator ELAN trial
- Co-Principal investigator SWITCH trial
- Co-Principal investigator SWIFT DIRECT trial
- Consultant for Covidien/Medtronic and Stryker
- Research support: SNSF, SHF, Medtronic

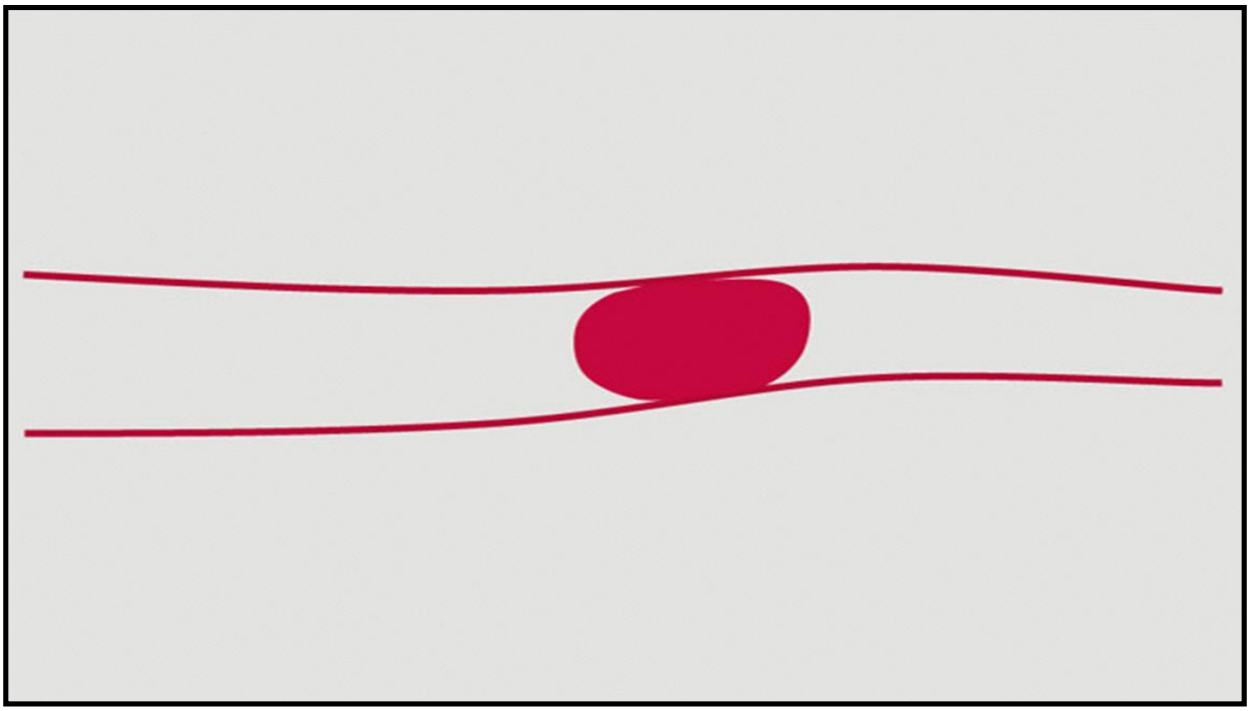

© Neurosurgery Inselspital Bern


© Neurosurgery Inselspital Bern


© Neurosurgery Inselspital Bern


© Neurosurgery Inselspital Bern

Acute ischaemic stroke treatment



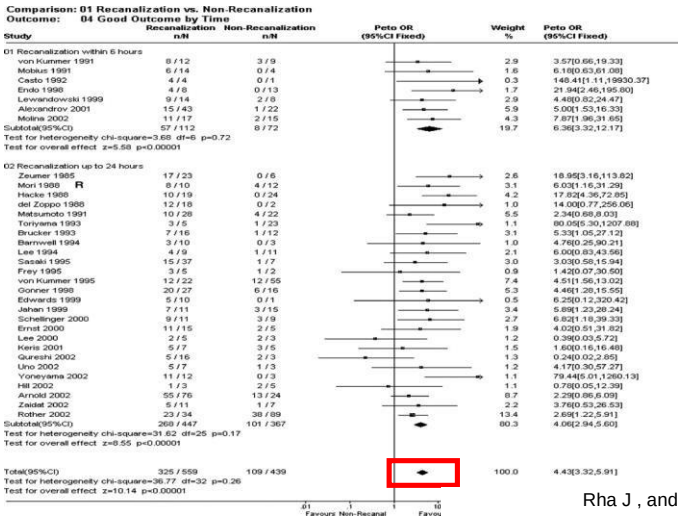
Predictors of good outcome in 623 patients with “anterior circulation stroke”

Multivariate analysis

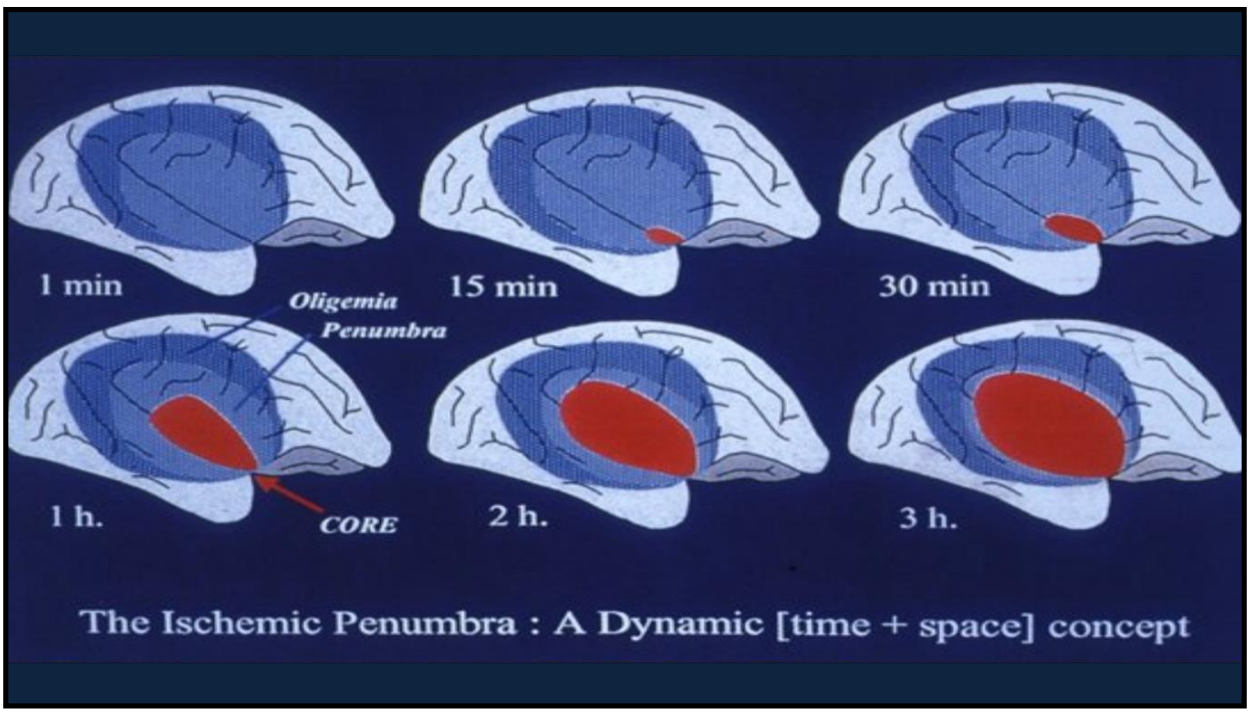
Predictors	p	OR	CI
Recanalisation	<0·0001	4·13	2·55-6·69
Hypercholesterolemia	0·002	1·94	1·28-2·93
Collaterals	0·002	1·59	1·19-2·11
Diabetes	0·002	0·38	0·21-0·71
NIHSS	<0·0001	0·88	0·84-0·92
Age	<0·0001	0·96	0·95-0·98
Prior antithrombotic therapy	0·036	0·62	0·39-0·97

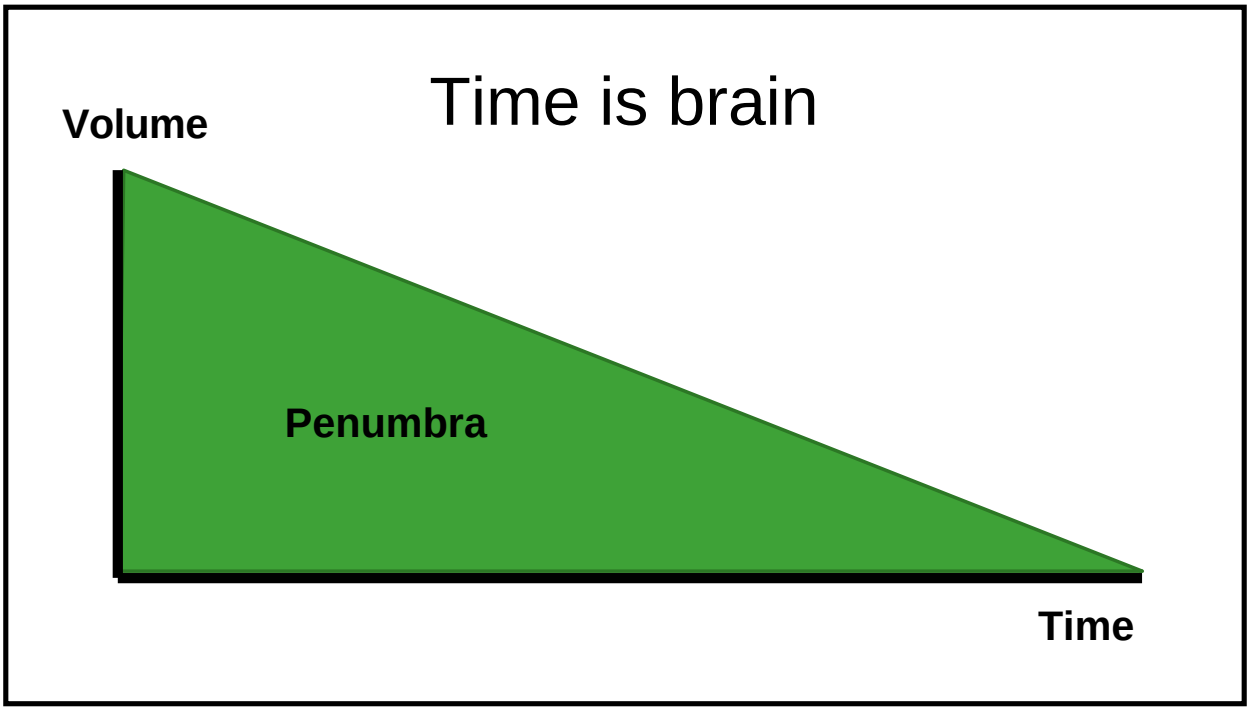
A. Galimanis et al, Stroke. 2012;43:1052-1057

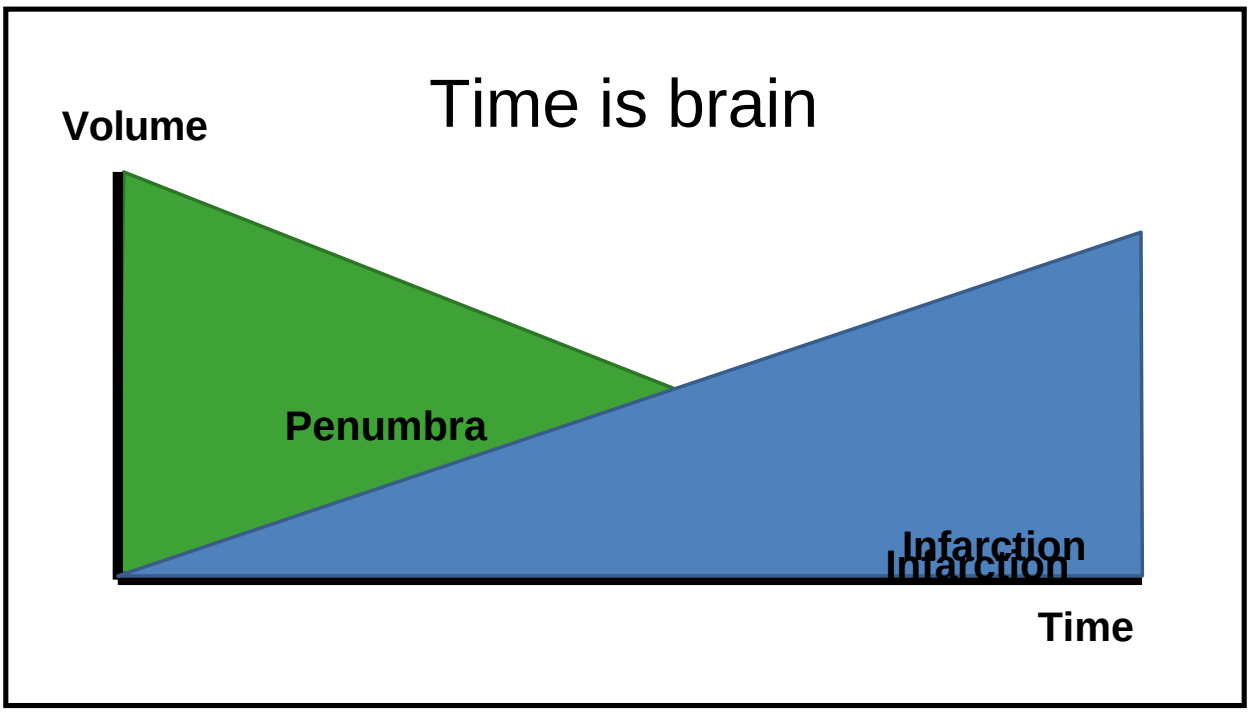
Outcome at 3 months in recanalised and non-recanalised patients



Rha J , and Saver J L Stroke 2007;38:967-973


1 min
15 min
30 min
Oligemia
Penumbra
1 h.
CORE
2 h.
3 h.
The Ischemic Penumbra : A Dynamic [time + space] concept


Time is brain
Volume
Penumbra
Time


Time is brain
Volume
Penumbra
Infarction
Time

Time Is Brain—Quantified
Jeffrey L. Saver

Stroke 2006, 37:263-266: originally published online December 8, 2005

1.9 million neurons / min

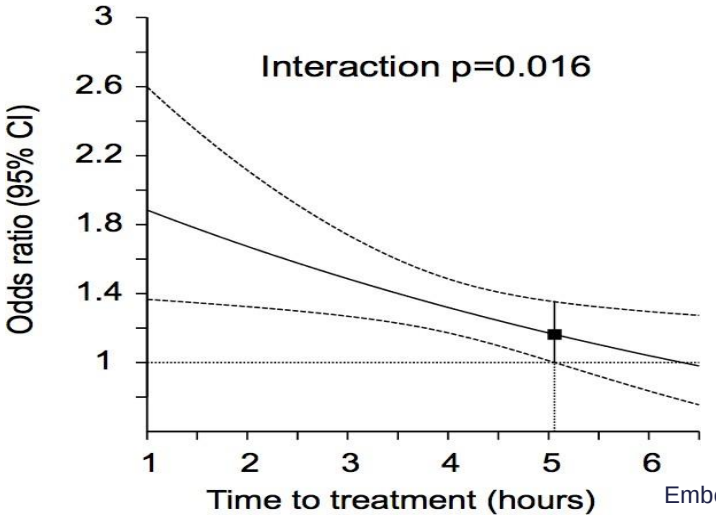
Bernese Stroke Clock App

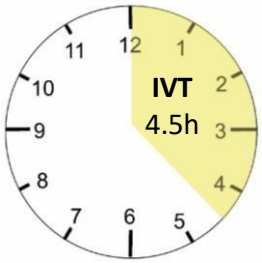
Available on the App Store

Available on the Android App Store

Effect on mRS 0-1 by treatment delay

(ECASS, ATLANTIS, NINDS,EPITHET, IST-3)

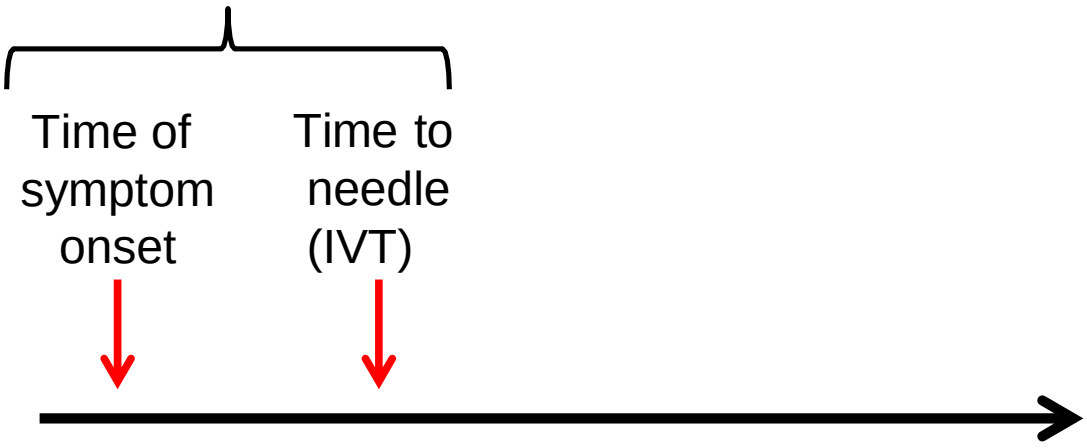




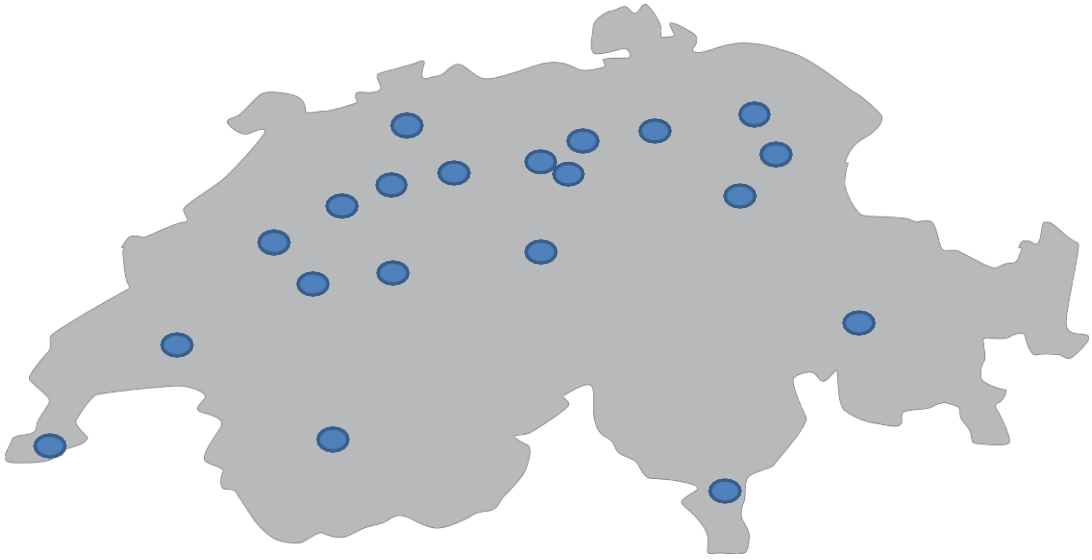
Emberson et al. Lancet 2014

Acute stroke treatment

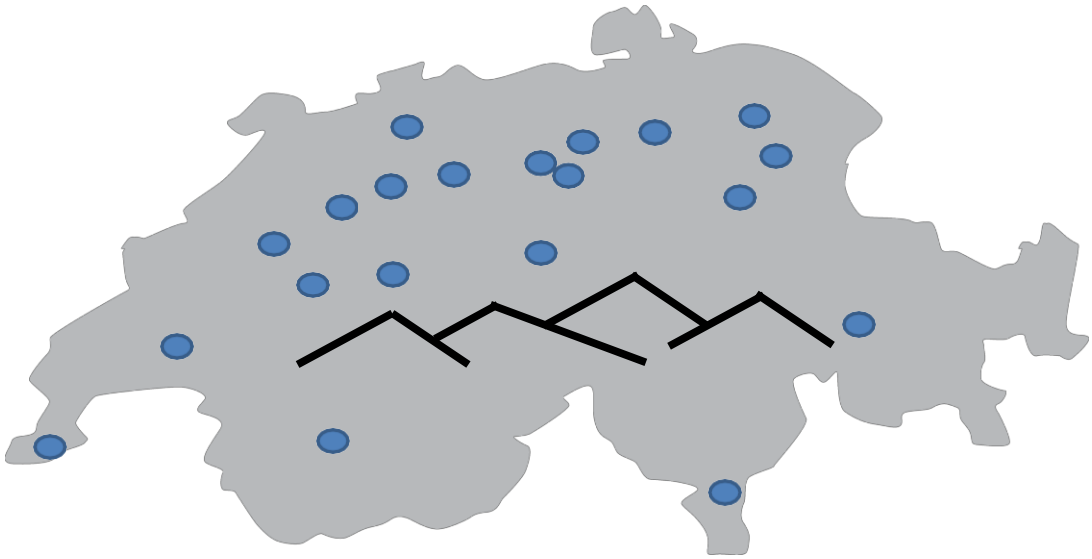
Shorten time to needle!



Stroke Units in CH



Stroke Units in CH



Endovascular stroke treatment


The NEW ENGLAND JOURNAL of MEDICINE

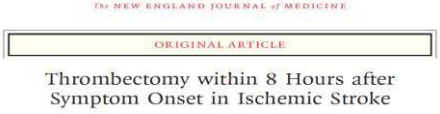
ORIGINAL ARTICLE

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke


The NEW ENGLAND JOURNAL of MEDICINE

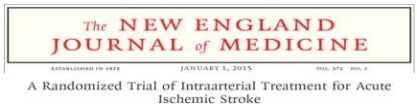
ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

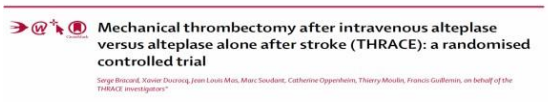

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

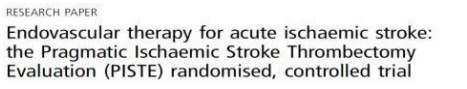
Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection


The NEW ENGLAND JOURNAL of MEDICINE

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke


Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial

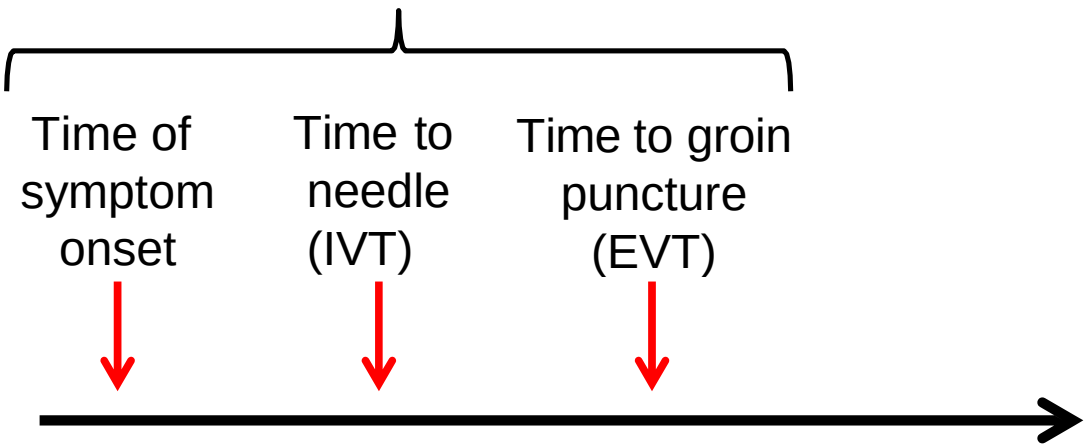

Aspiration Thrombectomy After Intravenous Alteplase Versus Intravenous Alteplase Alone


RESEARCH PAPER

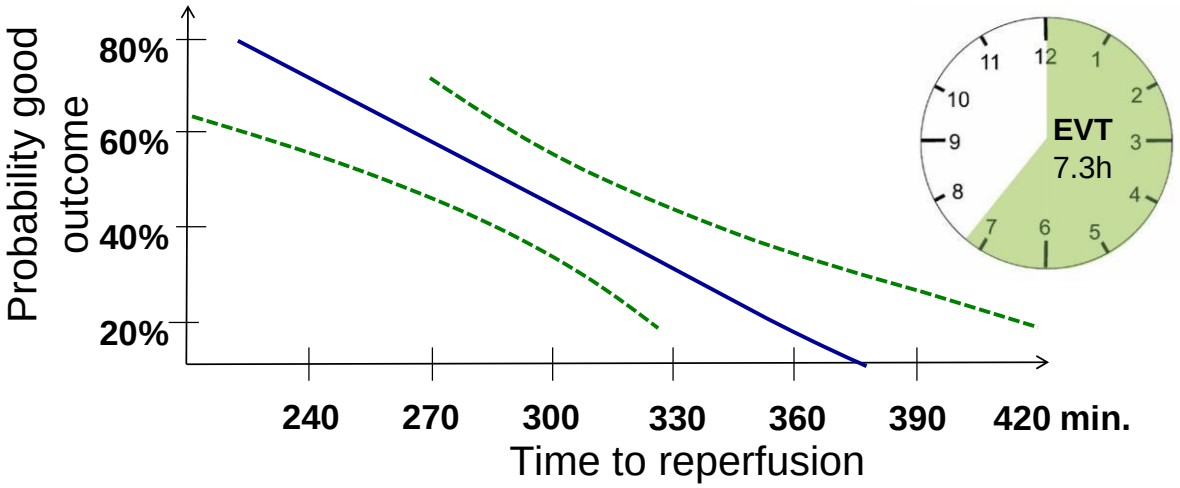
Endovascular therapy for acute ischaemic stroke: the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial

Acute stroke treatment

Shorten time to puncture!



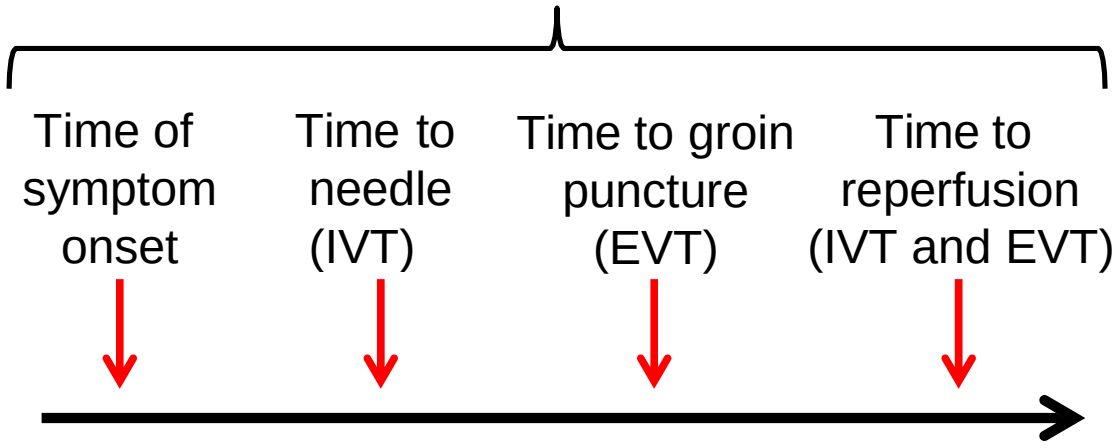
Benefit of endovascular reperfusion



Prabhakaran JAMA 2015; Khatri Lancet Neurology 2014; Mazhigi Circulation 2013

Acute stroke treatment

Shorten time to reperfusion!

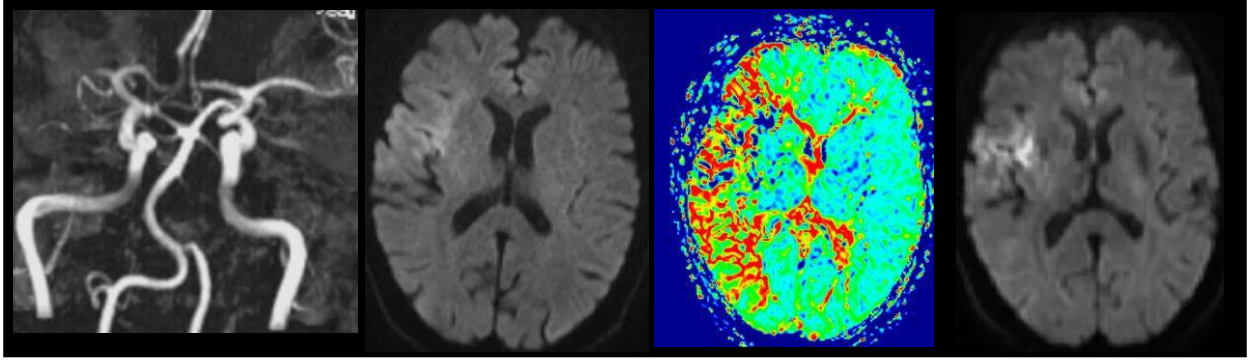


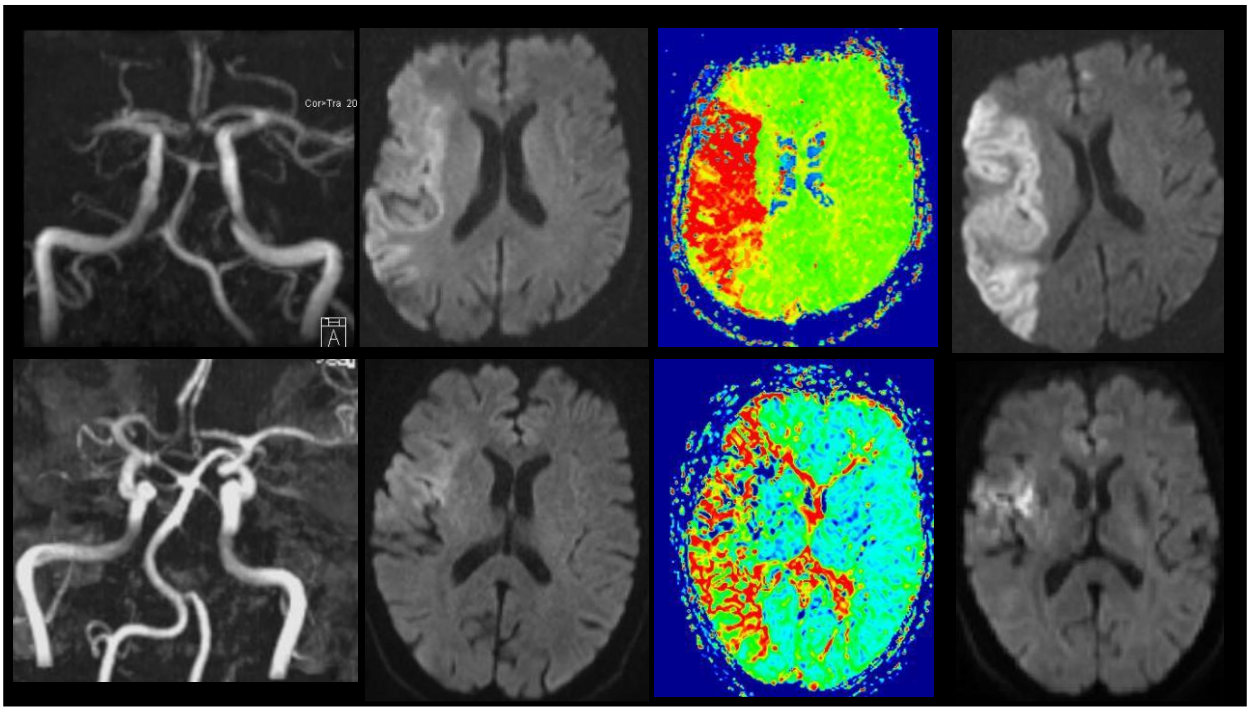
Aim: to recanalise occluded vessels as good and as fast as possible

Treatment effect:

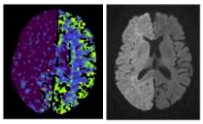
same for all patients?

M1 occlusion 2 hours after onset



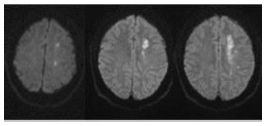


Variablity in infarct growth



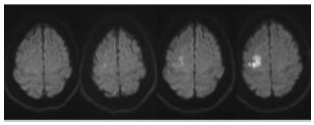
2h

>460 billion neurons/min



2h 5h 11h

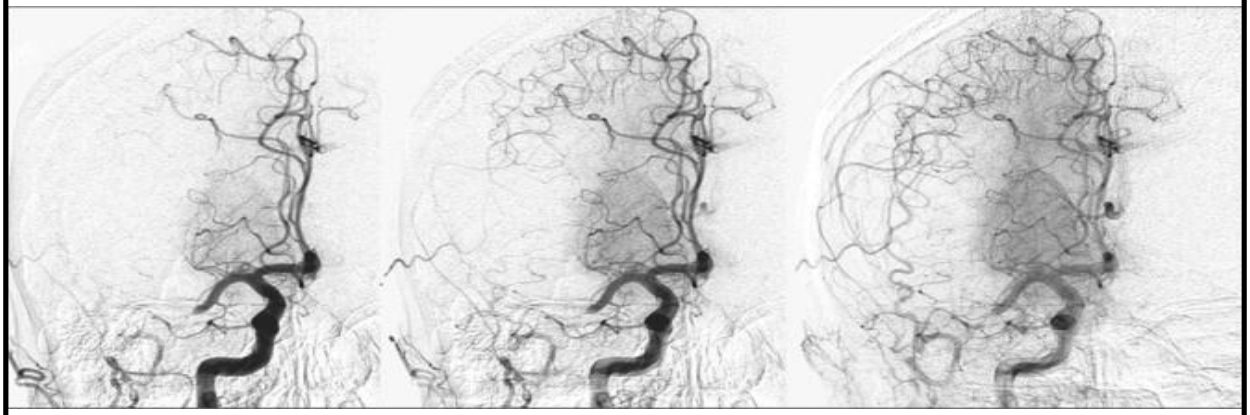
650.000 neurons/min



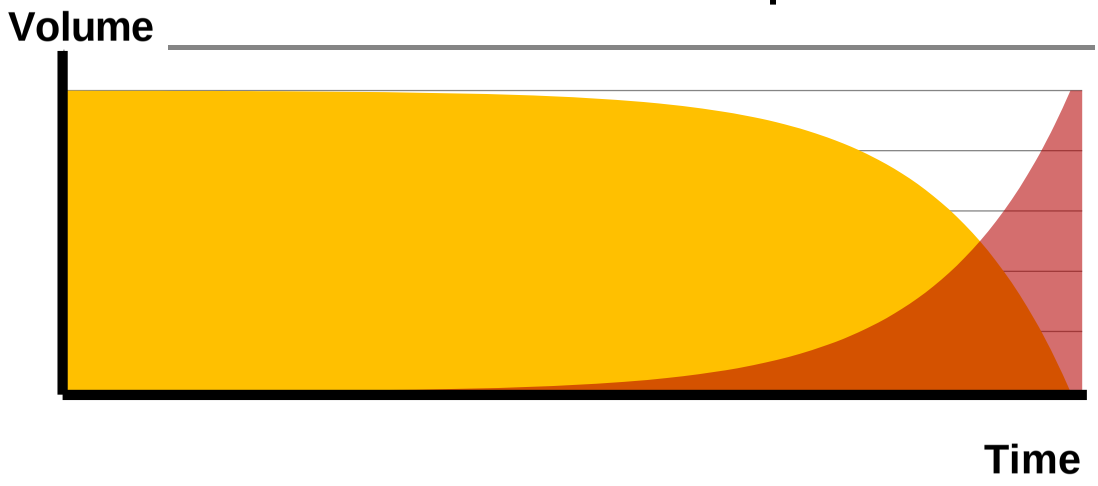
1d 7d 12d 17d

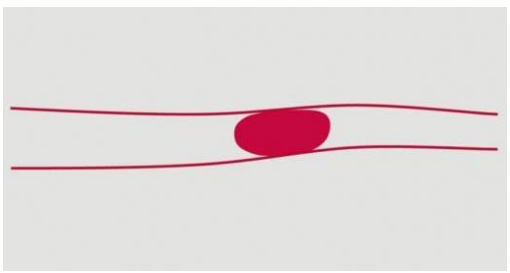
9000 neurons/min

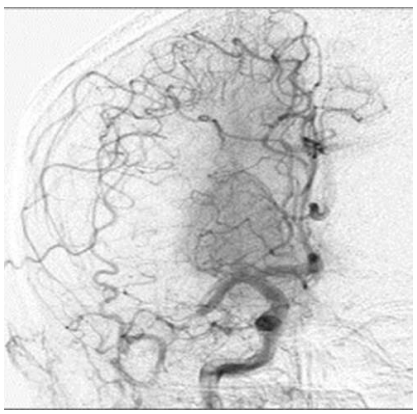
Impact of the collaterals



Time is brain, but collaterals set the pace!







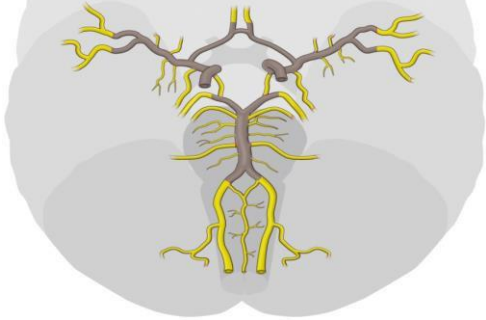
Precision medicine!

Personalised medicine!

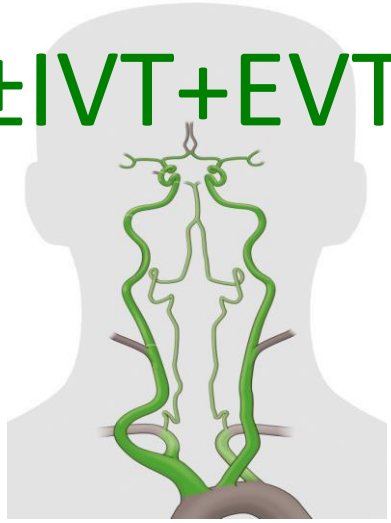
Reperfusion in stroke: current status

Best candidates for…

IVT



±IVT+EVT



What is new?

The New England
Journal of Medicine

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*

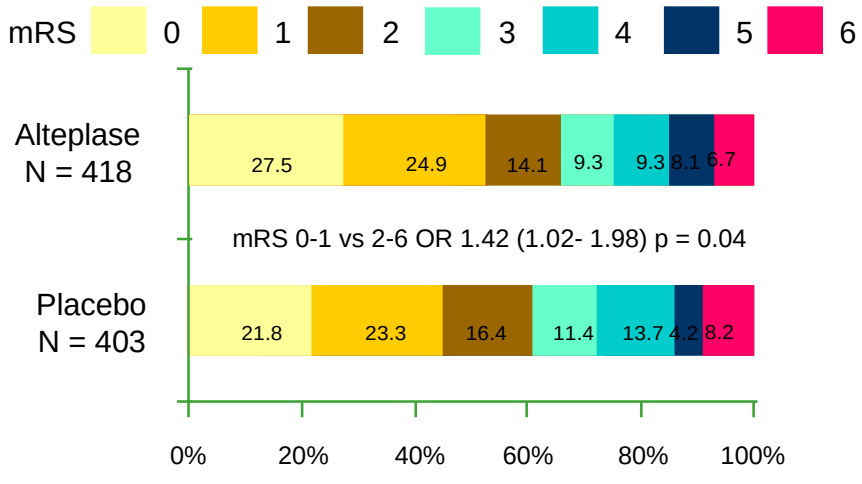
Abstract *Background.* Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke.

Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over base-line values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part 2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS.

Results. In part 1, there was no significant difference between the group given t-PA and that given placebo in the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hemorrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given t-PA but only 0.6 percent of patients given placebo ($P<0.001$). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group ($P=0.30$).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intravenous t-PA within three hours of the onset of ischemic stroke improved clinical outcome at three months. (N Engl J Med 1995;333:1581-7.)

ECASS III 3-4.5 hours



W. Hacke et al, NEJM 2008; 359:1317-29

IVT is the standard treatment for all AIS patients within 4.5h without contraindications

Contraindications for IVT:

- minor neurological deficit or symptoms rapidly improving …
- severe stroke as assessed clinically (e.g. NIHSS>25) …
- seizure at onset of stroke …
- patients with any history of prior stroke and concomitant diabetes
- prior stroke within the last 3 months
- platelet count of below 100,000/mm3
- systolic blood pressure > 185 or diastolic BP > 110 mm Hg, or aggressive management (intravenous pharmacotherapy) necessary to reduce BP to these limits
- blood glucose < 50 or > 400 mg/dl.
- (Actilyse is not indicated for the treatment of acute stroke in adults over 80 years of age)
- …

Contraindications for IVT:

- minor neurological deficit or symptoms rapidly improving …
- severe stroke as assessed clinically (e.g. NIHSS>25) …
- seizure at onset of stroke …
- patients with any history of prior stroke and concomitant diabetes
- prior stroke within the last 3 months
- platelet count of below 100,000/mm3
- systolic blood pressure > 185 or diastolic BP > 110 mm Hg, or aggressive management (intravenous pharmacotherapy) necessary to reduce BP to these limits
- blood glucose < 50 or > 400 mg/dl.
- (Actilyse is not indicated for the treatment of acute stroke in adults over 80 years of age)
- …

IVT for minor strokes

PRISMS

JAMA | Original Investigation

Effect of Alteplase vs Aspirin on Functional Outcome for Patients With Acute Ischemic Stroke and Minor Nondisabling Neurologic Deficits
The PRISMS Randomized Clinical Trial

Pooja Khatri, MD, MSc; Dawn O. Kleindorfer, MD; Thomas Devlin, MD; Robert N. Sawyer Jr, MD; Matthew Starr, MD; Jennifer Mejilla, DO; Joseph Broderick, MD; Anjan Chatterjee, MD; Edward C. Jauch, MD, MS; Steven R. Levine, MD; Jose G. Romano, MD; Jeffrey L. Saver, MD; Achala Vagal, MD, MS; Barbara Purdon, PhD; Jenny Devenport, PhD; Andrey Pavlov, PhD; Sharon D. Yeatts, PhD; for the PRISMS Investigators

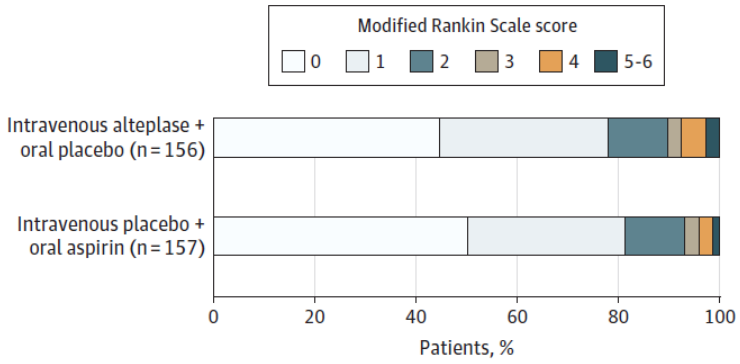
JAMA. 2018;320(2):156-166. doi:10.1001/jama.2018.8496

OBJECTIVE To evaluate the efficacy and safety of alteplase in patients with NIHSS scores of 0 to 5 whose deficits are not clearly disabling.

RESULTS Among 313 patients enrolled at 53 stroke networks (mean age, 62 [SD, 13] years; 144 [46%] women; median NIHSS score, 2 [interquartile range {IQR}, 1-3]; median time to treatment, 2.7 hours [IQR, 2.1-2.9]), 281 (89.8%) completed the trial. At 90 days, 122 patients (78.2%) in the alteplase group vs 128 (81.5%) in the aspirin group achieved a favorable outcome (adjusted risk difference, −1.1%; 95% CI, −9.4% to 7.3%). Five alteplase-treated patients (3.2%) vs 0 aspirin-treated patients had sICH (risk difference, 3.3%; 95% CI, 0.8%-7.4%).

CONCLUSIONS AND RELEVANCE Among patients with minor nondisabling acute ischemic stroke, treatment with alteplase vs aspirin did not increase the likelihood of favorable functional outcome at 90 days. However, the very early study termination precludes any definitive conclusions, and additional research may be warranted.

Figure 2. Modified Rankin Scale Score Distributions at 90 Days by Treatment Group



These distributions, which were used for the primary outcome analysis, included imputation for missing 90-day scores.

IVT for wake-up strokes?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

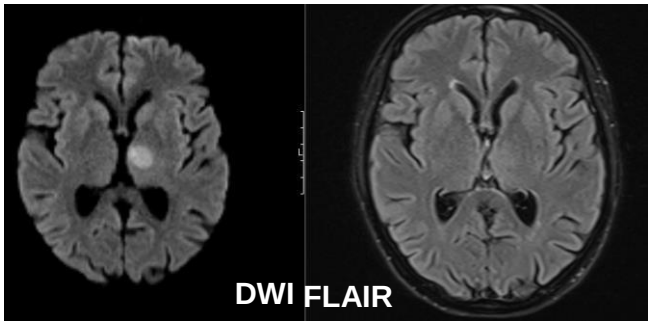
MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

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*

This article was published on May 16, 2018, at NEJM.org.

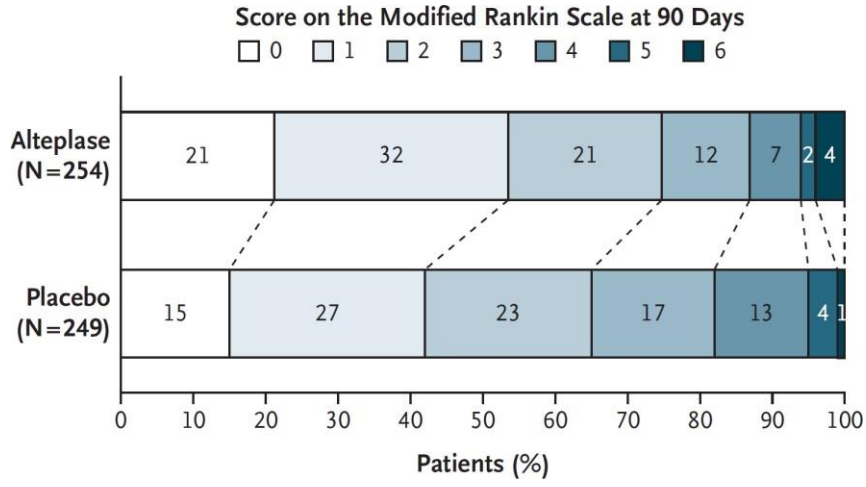
WAKE-UP Trial

- 18-80 years
- Wake-up stroke or unknown time of symptom onset, NIHSS < 25
- «Time since last seen well» > 4.5h
- No large vessel occlusion
- MRI Diffusions-FLAIR mismatch



Thomalla NEJM 2018

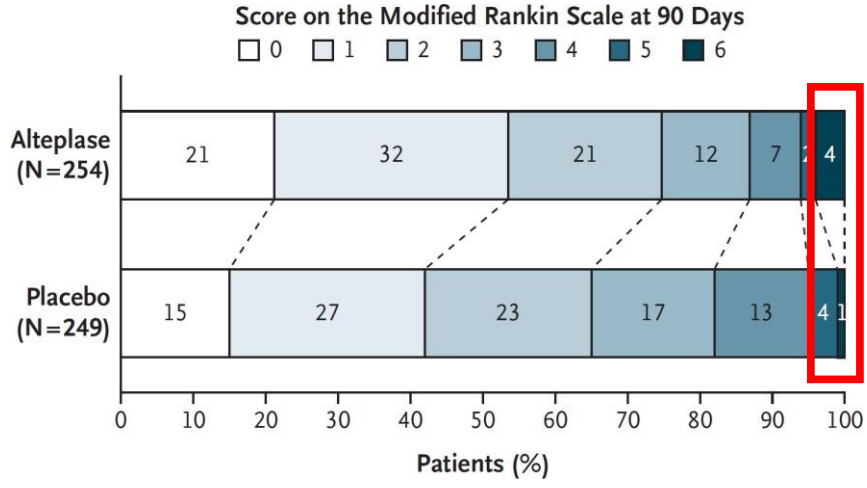
WAKE-UP Trial



NNT: 8.7

Thomalla NEJM 2018

WAKE-UP Trial



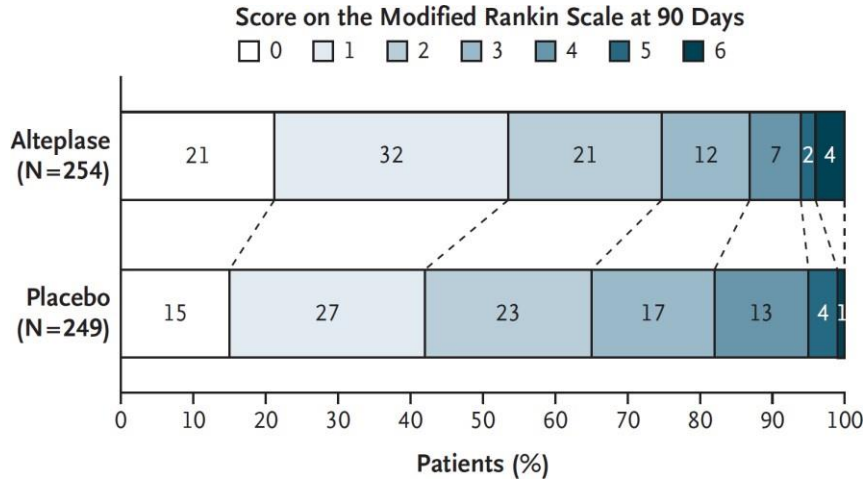
Death

4.1%

1.2%

Thomalla NEJM 2018

WAKE-UP Trial



sICH

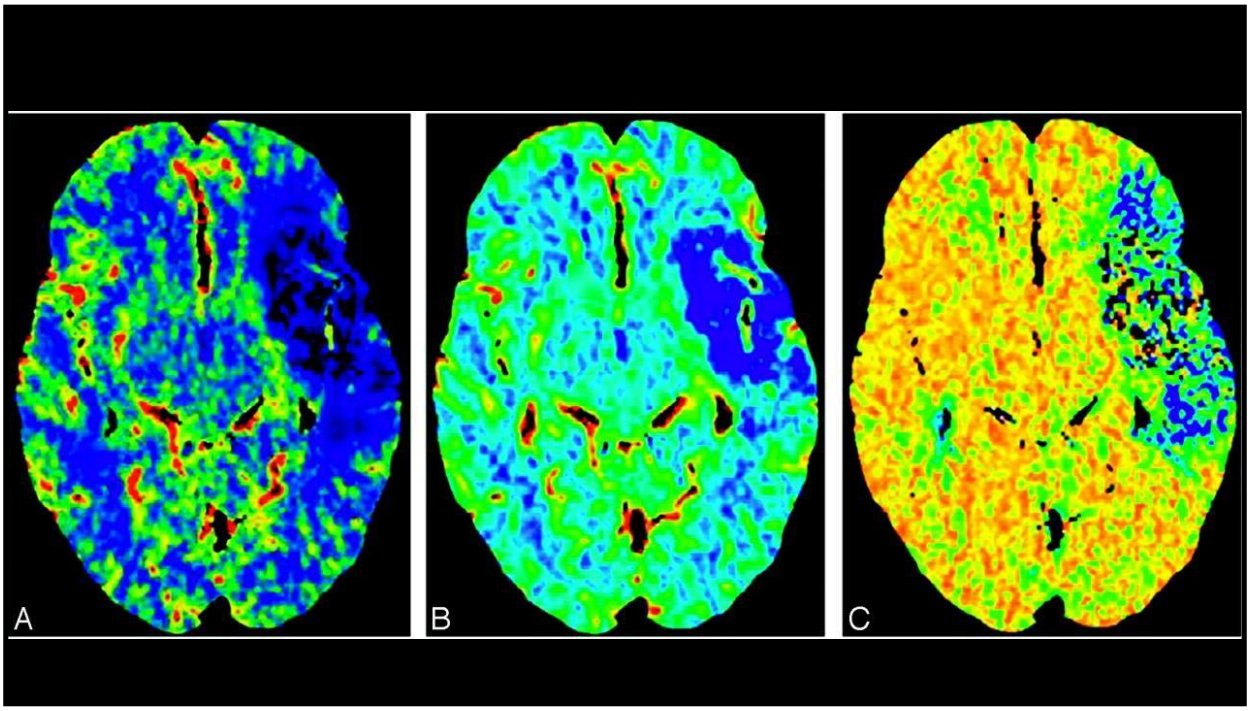
2.0%

0.4%

NNH: 27.8

Thomalla NEJM 2018

Is IVT also safe and efficous 4.5 - 9 hours after symptom onset?



The NEW ENGLAND JOURNAL of MEDICINE

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*

BACKGROUND

The time to initiate intravenous thrombolysis for acute ischemic stroke is generally limited to within 4.5 hours after the onset of symptoms. Some trials have suggested that the treatment window may be extended in patients who are shown to have ischemic but not yet infarcted brain tissue on imaging.

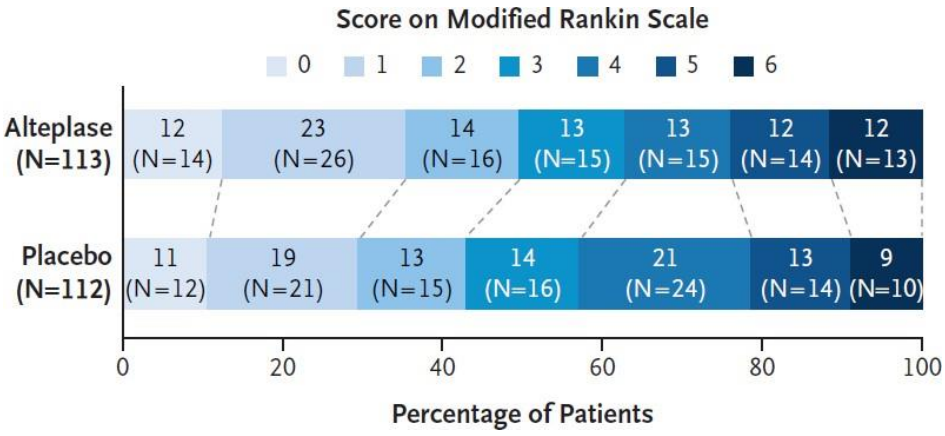
METHODS

We conducted a multicenter, randomized, placebo-controlled trial involving patients with ischemic stroke who had hypoperfused but salvageable regions of brain detected on automated perfusion imaging. The patients were randomly assigned to receive intravenous alteplase or placebo between 4.5 and 9.0 hours after the onset of stroke or on awakening with stroke (if within 9 hours from the midpoint of sleep). The primary outcome was a score of 0 or 1 on the modified Rankin scale, on which scores range from 0 (no symptoms) to 6 (death), at 90 days. The risk ratio for the primary outcome was adjusted for age and clinical severity at baseline.

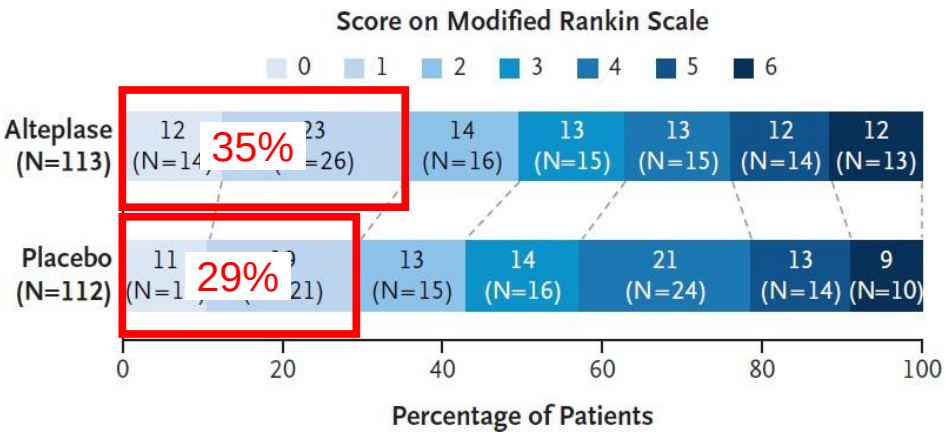
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Alteplase (N=113)	Placebo (N=112)
Age — yr	73.7±11.7	71.0±12.7
Male sex — no. (%)	59 (52.2)	66 (58.9)
Median NIHSS score (IQR)†	12.0 (8.0–17.0)	10.0 (6.0–16.5)
Clinical history of atrial fibrillation — no. (%)	46 (40.7)	36 (32.1)
Geographic region — no. (%)		
Australia, New Zealand, and Finland	90 (79.6)	88 (78.6)
Taiwan	23 (20.4)	24 (21.4)
Time from stroke onset to randomization — no. (%)		
>4.5 to 6.0 hr	12 (10.6)	11 (9.8)
>6.0 to 9.0 hr	28 (24.8)	28 (25.0)
Awoke with stroke symptoms‡	73 (64.6)	73 (65.2)
Median time from stroke onset to hospital arrival (IQR) — min	308 (227–362)	293 (230–357)
Median time from stroke onset to initiation of intravenous therapy (IQR) — min	432 (374–488)	450 (374–500)
Median time from hospital arrival to initiation of intravenous therapy (IQR) — min	124 (81–179)	127 (87–171)
Imaging result		
Large-vessel occlusion — no.(%)§	78 (69.0)	81 (72.3)
Median volume of irreversibly injured ischemic-core tissue at initial imaging (IQR) — ml¶	4.6 (0–23.2)	2.4 (0–19.5)
Median perfusion-lesion volume at initial imaging (IQR) — ml‖	74.3 (40.1–134.0)	78 (47.7–111.8)

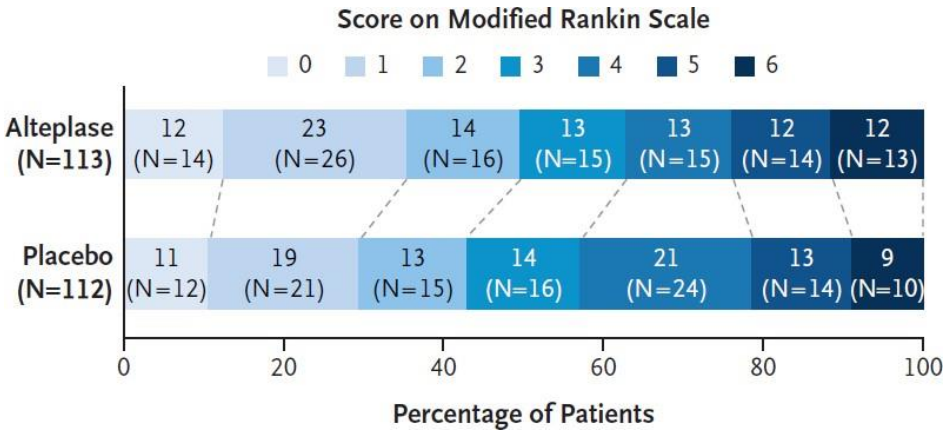
EXTEND



EXTEND



EXTEND



sICH

6.2%

0.9%

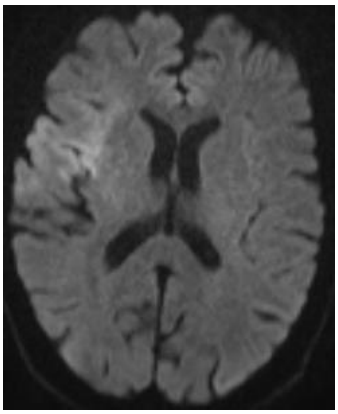
EXTEND

CONCLUSIONS

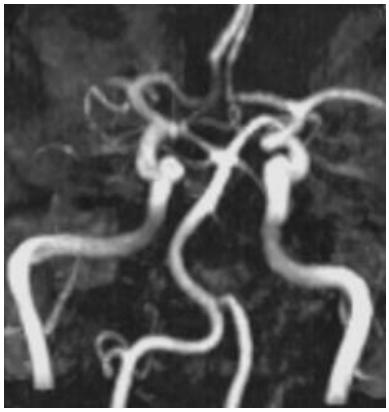
Among the patients in this trial who had ischemic stroke and salvageable brain tissue, the use of alteplase between 4.5 and 9.0 hours after stroke onset or at the time the patient awoke with stroke symptoms resulted in a higher percentage of patients with no or minor neurologic deficits than the use of placebo. There were more cases of symptomatic cerebral hemorrhage in the alteplase group than in the placebo group. (Funded by the Australian National Health and Medical Research Council and others; EXTEND ClinicalTrials.gov numbers, NCT00887328 and NCT01580839.)

Imaging

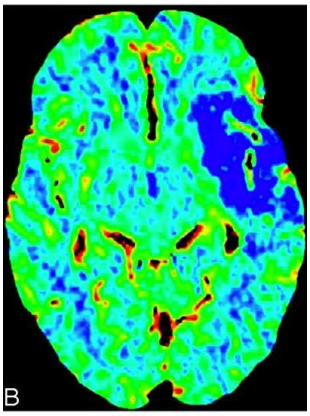
Rule out haemorrhage



Site of vessel occlusion



Salvagable tissue?

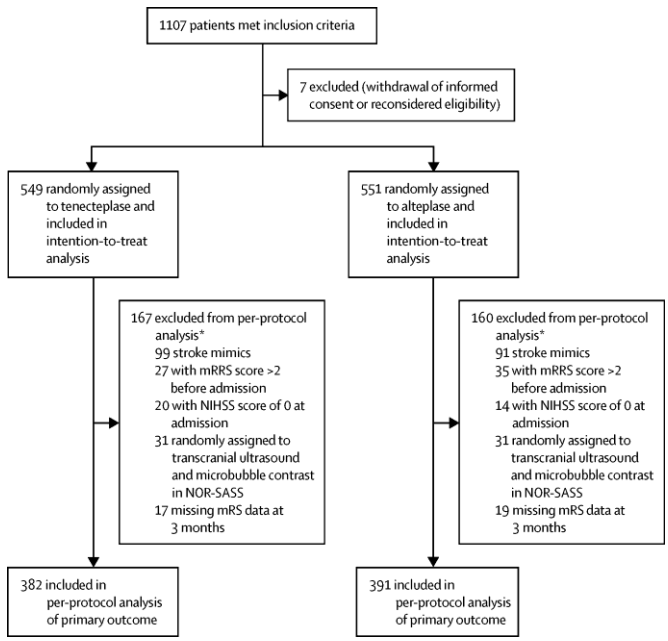


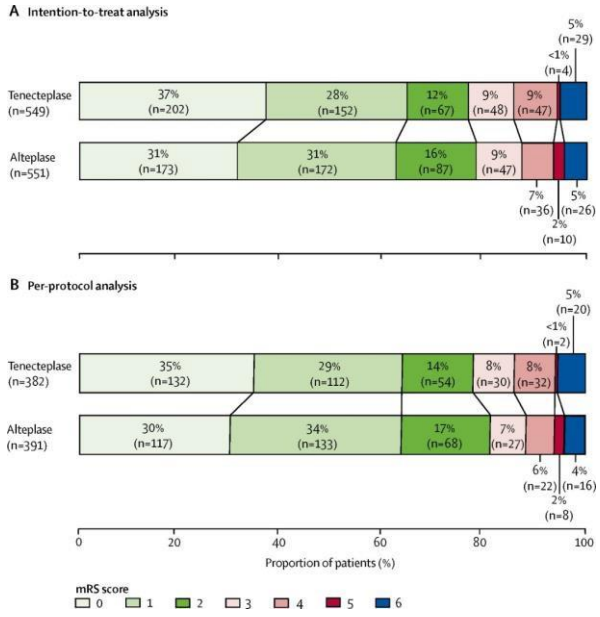
Alteplase or Tenecteplase?

Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial

Dr Nicola Logallo, PhD, Vojtech Novotny, MD, Jörg Assmus, PhD, Christopher E Kvistad, PhD, Lars Alteheld, MD, Ole Morten Rønning, PhD, Bente Thommessen, PhD, Karl-Friedrich Amthor, MD, Hege Ihle-Hansen, PhD, Prof Martin Kurz, PhD, Håkon Tobro, MD, Kamaljit Kaur, MD, Magdalena Stankiewicz, MD, Maria Carlsson, MD, Åse Morsund, MD, Titto Idicula, PhD, Anne Hege Aamodt, PhD, Christian Lund, PhD, Prof Halvor Næss, PhD, Ulrike Waje-Andreassen, PhD, Prof Lars Thomassen, PhD

The Lancet Neurology
Volume 16, Issue 10, Pages 781-788 (October 2017)
DOI: 10.1016/S1474-4422(17)30253-3





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 26, 2018 VOL. 378 NO. 17

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collecutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis, for the EXTEND-IA TNK Investigators*

ABSTRACT

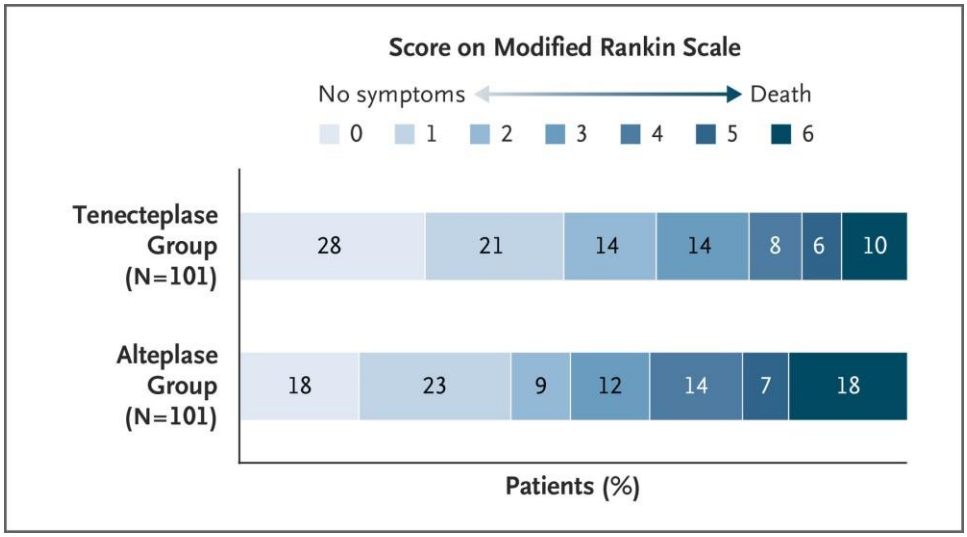
BACKGROUND

Intravenous infusion of alteplase is used for thrombolysis before endovascular thrombectomy for ischemic stroke. Tenecteplase, which is more fibrin-specific and has longer activity than alteplase, is given as a bolus and may increase the incidence of vascular reperfusion.

METHODS

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Campbell at the Department of Neurology, Royal Melbourne Hospital, 300 Grattan St, Parkville, VIC 3050, Australia, or at

EXTEND-IA TNK Trial



Campbell NEJM 2018

Endovascular stroke treatment

2014 / 2015

MR CLEAN

ESCAPE

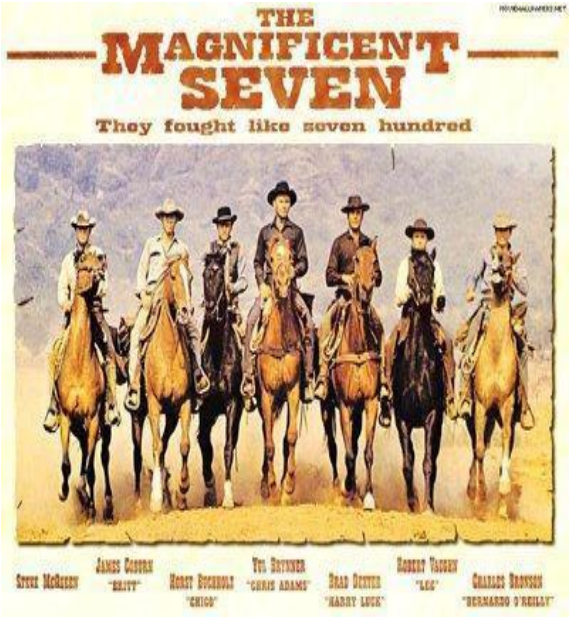
EXTEND-IA

SWIFT PRIME

REVASCAT

THRACE

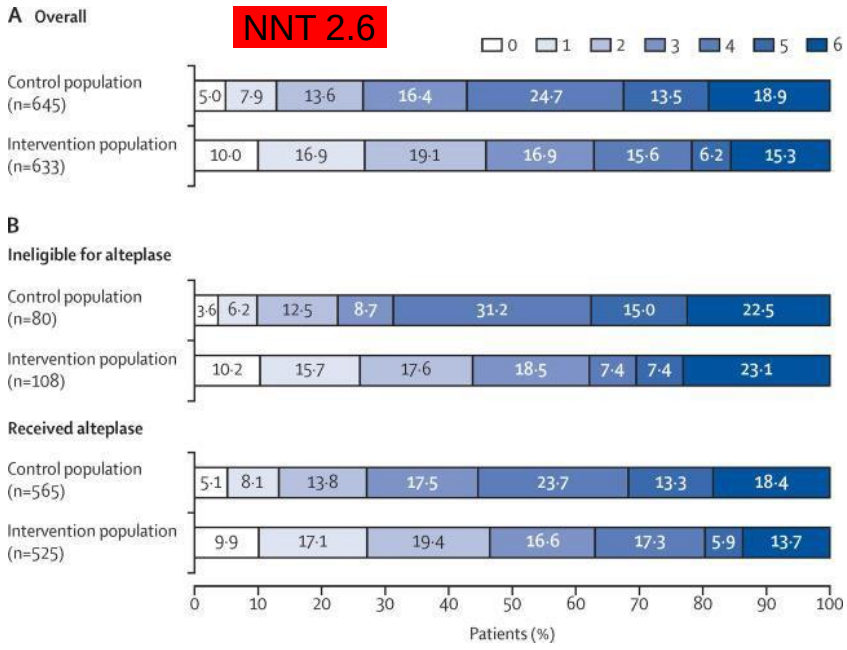
THERAPY



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

Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Peter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majoie, Aad van der Lugt, Maria A de Miquel, Geoffrey A Donnan, Yvo B W E M Roos, Alain Bonafe, Reza Jahan, Hans-Christoph Diener, Lucie A van den Berg, Elad I Levy, Olvert A Berkhemer, Vitor M Pereira, Jeremy Rempel, Mònica Millán, Stephen M Davis, Daniel Roy, John Thornton, Luis San Román, Marc Ribó, Debbie Beumer, Bruce Stouch, Scott Brown, Bruce C V Campbell, Robert J van Oostenbrugge, Jeffrey L Saver, Michael D Hill, Tudor G Jovin, for the HERMES collaborators

www.thelancet.com **Published online February 18, 2016 http://dx.doi.org/10.1016/S0140-6736(16)00163-X**



The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Solitaire
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Solitaire
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Solitaire
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Stent retriever
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Stent retriever
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Stent retriever
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Stent retriever
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Stent retriever
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Stent retriever
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Stent retriever
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Stent retriever
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Stent retriever
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Stent retriever
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Stent retriever
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Stent retriever
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

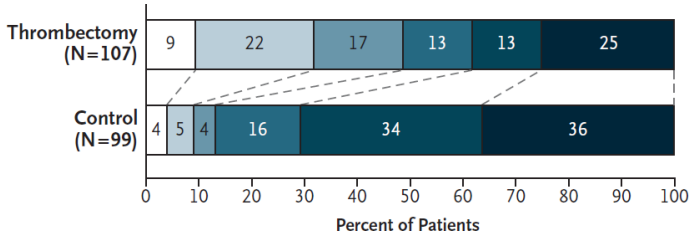
The maginificent seven

	Treatment	IVT	Time	Age	NIHSS	Vessel	Imaging criteria	Device
MR CLEAN	BMT vs. EVT ± IVT	87%	< 6 h	>18 years	≥2	ICA, M1/2, A1/2		EVT (81%)
ESCAPE	BMT vs. EVT ± IVT	73%	< 12 h	unlimited	>5	ICA, M1/2	ASPECT 5	EVT (86%)
REVASCAT	BMT vs. EVT ± IVT	68%	< 8 h	18-85 years	≥6	ICA, M1	ASPECT >6	Stent retriever
EXTEND-IA	IVT vs IVT+EVT	100%	< 6 h	>18 years		ICA, M1/2	Core <70ml, mismatch	Stent retriever
SWIFT PRIME	IVT vs IVT+EVT	100%	< 6 h	18-85 years	8-29	ICA, M1	ASPECTS ≥6	Stent retriever
THRACE	IVT vs IVT+EVT	100%	< 4.5 h	18-80 years	10-25	ICA, M1, BA		EVT
THERAPY	IVT vs IVT+EVT	100%	< 4.5 Sh	18-85 years	≥8	>8mm	<1/3 MCA territory	Penumbra

EVT after 6 hours?

DAWN trial

ICA/M1 occlusion
6-24h after symptom onset
Mismatch clinical deficit – infarct core (i.e.. >10 und <21ml)

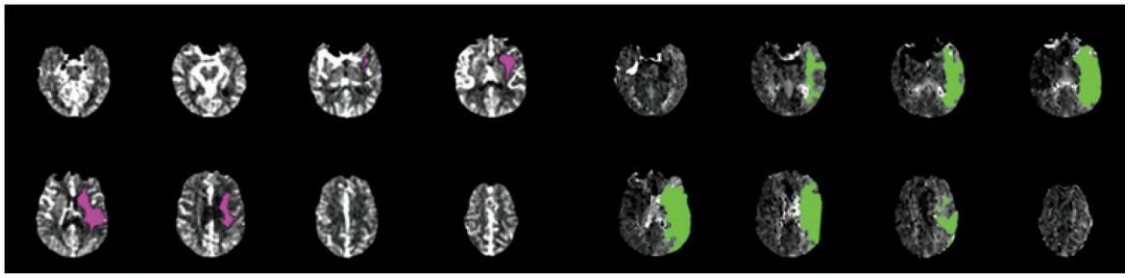


NNT 2.8 for functional independence (mRS 0-2)

Nogueira NEJM 2018

DEFUSE 3 trial

ICA/M1 occlusion
6-16h after symptom onset
Infarct core <15ml, Penumbra >70ml



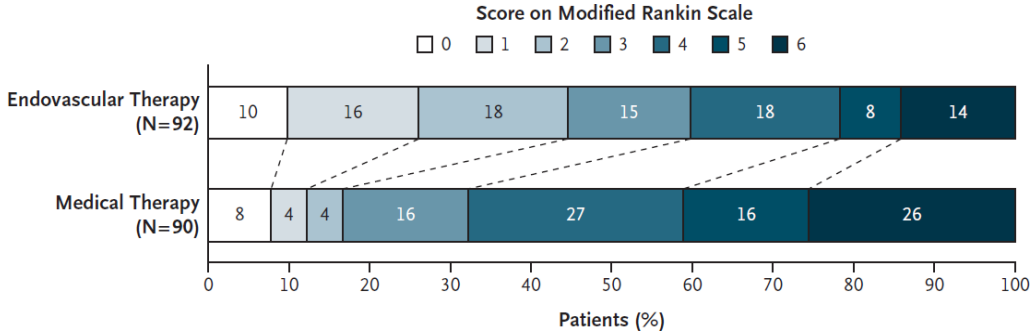
Volume of Ischemic Core, 23 ml

Volume of Perfusion Lesion, 128 ml

Albers NEJM 2018

DEFUSE 3 trial

ICA/M1 occlusion
6-16h after symptom onset
Infarct core <15ml, Penumbra >70ml

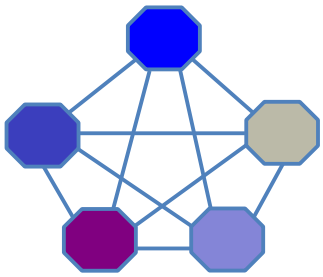


Albers NEJM 2018

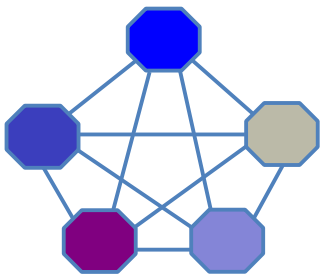
Unanswered questions

- LVO and low NIHSS (IN EXTREMIS, Endo Low, etc.)
- LVO and low ASPECTS (IN EXTREMIS, TENSION, etc.)
- Basilar artery occlusion (BASICS)
- Bridging (SWIFT DIRECT, MR CLEAN noIV, safe DIRECT, etc)
- Distal occlusions (M2/M3)
- Dissections
- Anesthesia (SIESTA, SEGA, AMETIS, GASS, etc.)
- Etc.

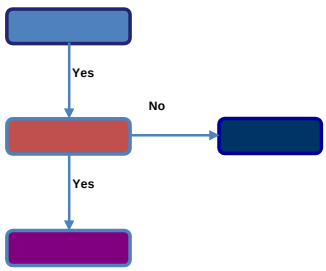
Organisation of stroke care



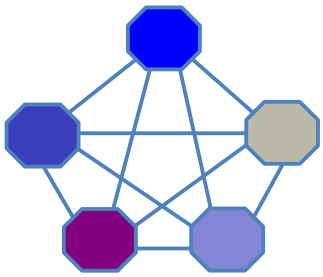
Networks



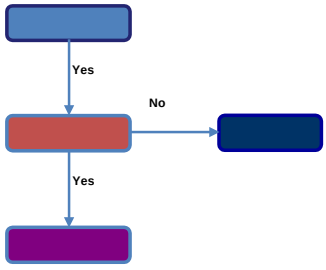
Networks



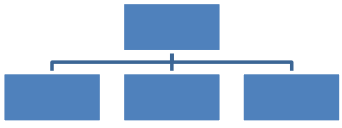
Pathways



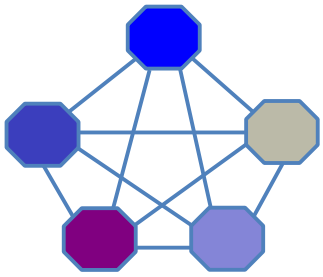
Networks



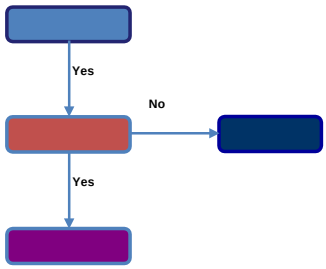
Pathways



Structures



Networks



Pathways

Structures

Communication

Aim of stroke treatment 2019

- To treat patients as soon and effective as possible
- Patients **with** LVO should be immediately transfered to an endovascular stroke center
- Patients **without** LVO should be transfered to the nearest thrombolysing stroke unit

Drip and ship or mothership ?

Review

International Journal of Stroke WSO

International Journal of Stroke
2019, Vol. 14(1) 12–22

DOI: 10.1177/1747493018806157
journals.sagepub.com/home/wso
SAGE

Systematic review of organizational models for intra-arterial treatment of acute ischemic stroke

Alfonso Ciccone[1], Eivind Berge[2] and Urs Fischer[3]

Abstract

Background: Intra-arterial treatment of acute ischemic stroke requires changes to acute stroke services since most hospitals do not have on-site intra-arterial treatment facilities.

Aim: To identify models for delivery of intra-arterial treatment and to compare process performance and clinical and radiological outcomes of the different models.

Methods: We systematically searched the literature and contacted experts in the field. We performed a qualitative synthesis to identify models, and a quantitative review and meta-analysis of clinical and radiological outcomes under different organizational models.

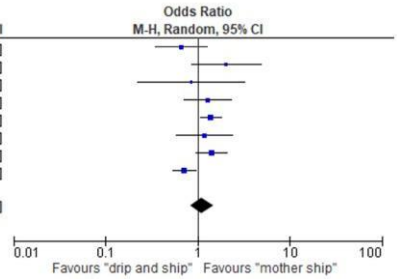
Summary of review: The searches retrieved 148 publications, of which 27 were used for the identification and description of models, and 9 for the comparison of the different models. We identified four main models: the mother-ship, drip-and ship, mobile interventionist, and mobile stroke unit models. There were no randomized-controlled

Favourable functional outcome

(B)

Study or Subgroup	Mother ship model Events	Total	Drip and ship model Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Gerschenfeld 2017	30	59	61	100	10.8%	0.66 [0.35, 1.27]
SWIFT-PRIME 2015	44	67	15	31	7.6%	2.04 [0.86, 4.85]
Hiyama 2016	5	12	15	33	3.9%	0.86 [0.23, 3.26]
Park 2016	119	438	16	71	11.8%	1.28 [0.71, 2.33]
Froehler 2017	299	498	212	408	19.9%	1.39 [1.07, 1.81]
Rinaldo 2017	23	62	26	78	10.0%	1.18 [0.59, 2.37]
Weber 2016	88	200	82	230	16.7%	1.42 [0.96, 2.09]
Peréz de la Ossa 2016	396	662	205	303	19.3%	0.71 [0.53, 0.95]
Total (95% CI)		**1998**		**1254**	**100.0%**	**1.11 [0.83, 1.48]**
Total events	1004		632			

Heterogeneity: Tau² = 0.09; Chi² = 18.25, df = 7 (P = 0.01); I² = 62%
Test for overall effect: Z = 0.73 (P = 0.47)



Ciccone, Berge, Fischer, IJS

Ischemic Stroke

REVIEW

Mothership versus drip and ship for thrombectomy in patients who had an acute stroke: a systematic review and meta-analysis

Mohammad Ismail,[1] Xavier Armoiry,[2,3] Noam Tau,[4] François Zhu,[5] Udi Sadeh-Gonik,[6] Michel Piotin,[7] Raphael Blanc,[7] Mikaël Mazighi,[7] Serge Bracard,[5,8] René Anxionnat,[5,8] Emmanuelle Schmitt,[5] Gioia Mione,[9] Lisa Humbertjean,[9] Jean-Christophe Lacour,[9] Sébastien Richard,[9,10] Charlotte Barbier,[1] Bertrand Lapergue,[11] Benjamin Gory[5,8]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/neurintsurg-2018-014249).

For numbered affiliations see end of article.

ABSTRACT

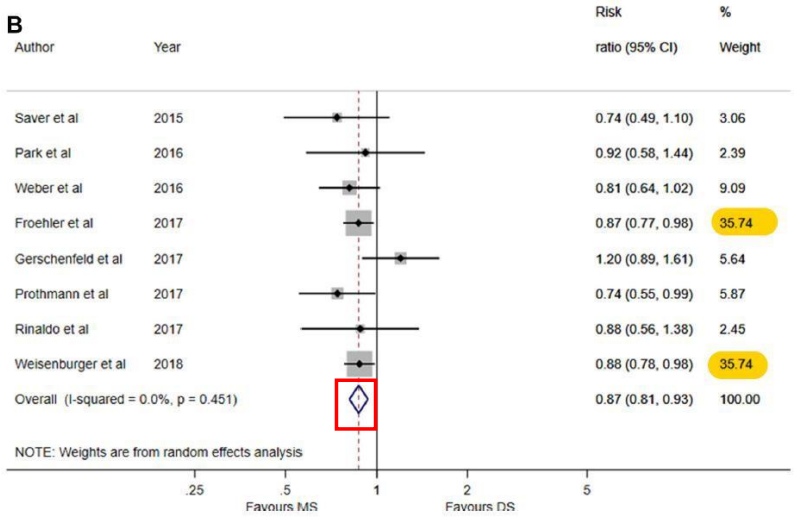
Background The effectiveness of mechanical thrombectomy (MT) in acute ischemic stroke due to large vessel occlusion is time-dependent. While only stroke centers with endovascular capabilities perform MT, many patients who had a stroke initially present to the closest primary stroke centers capable of

INTRODUCTION

Several randomized trials have demonstrated the clinical benefit of adding mechanical thrombectomy (MT) to standard medical therapy, compared with standard medical therapy alone, in the treatment of patients who have an acute ischemic stroke with large vessel occlusion (LVO) of the anterior circula

J NeuroIntervent Surg: first published as 10.1136/neurintsurg-201

Favourable functional outcome



Randomized controlled trial!

Stroke Center

Stroke Unit

RACECAT

Randomized controlled trial!

Stroke Center

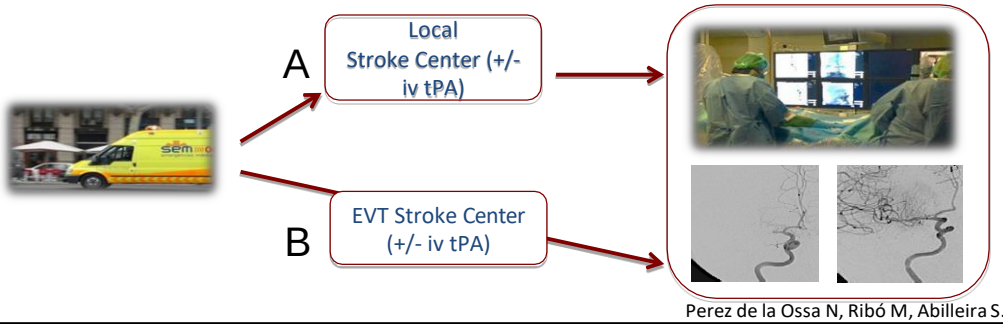
Stroke Unit

RACECAT

RACECAT (*NCT02795962*)

A Trial Comparing TRAnsfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients with Suspected Large Vessel Occlusion in the Catalan Territory.

- Prospective, multicenter, academic trial (unrestricted grant from Medtronic)
- Cluster randomized, controlled (pre-established temporal sequence)
- Acute stroke patients with suspected acute large vessel occlusion identified by EMS
- Two strategies will be compared:



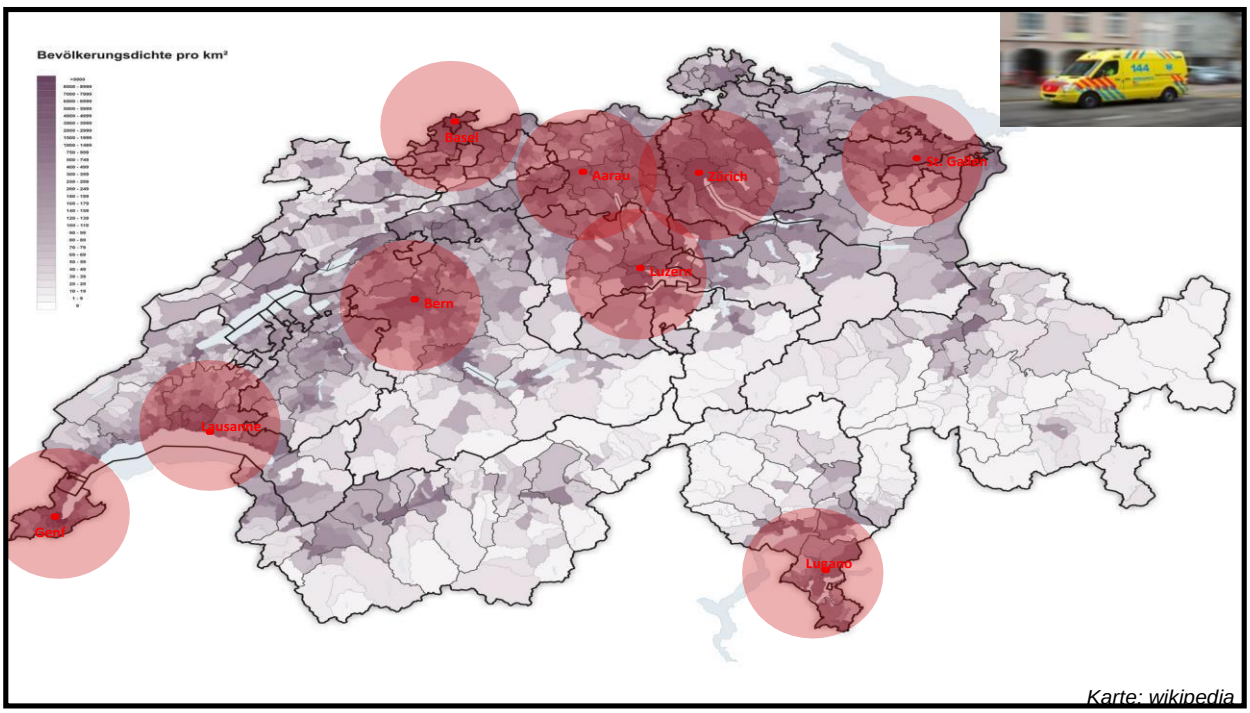
97

Perez de la Ossa N, Ribó M, Abilleira S. 2016

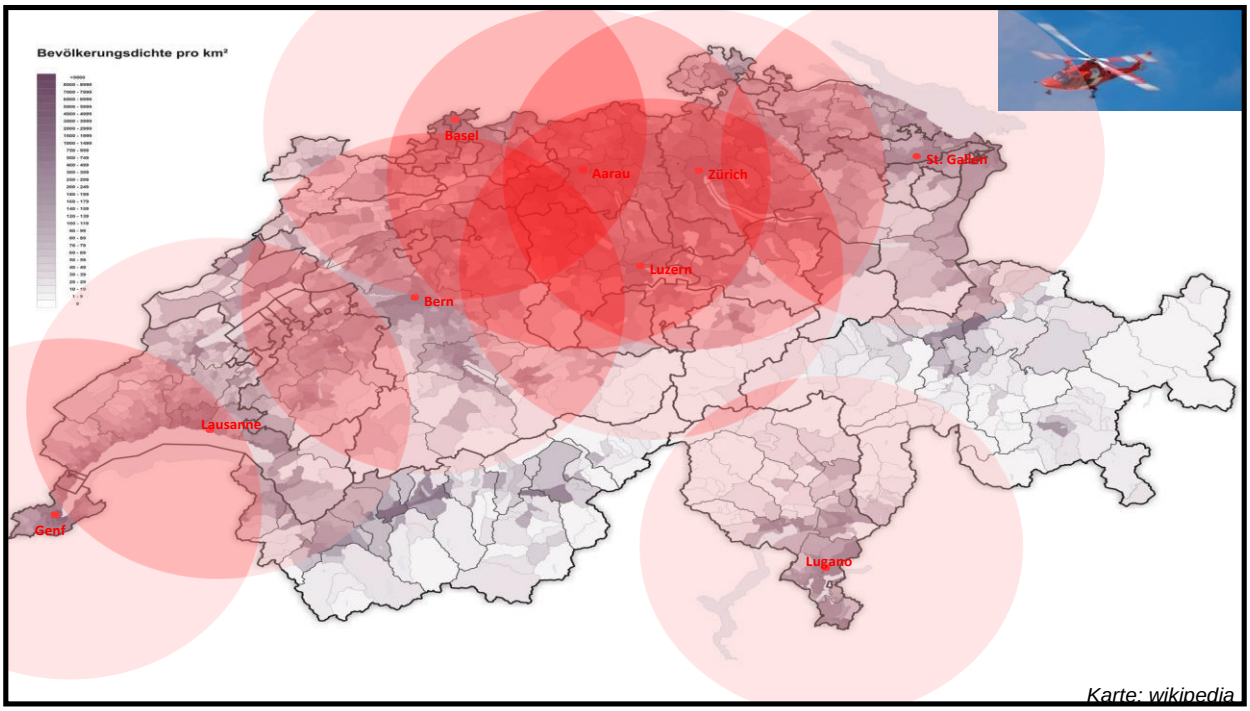
What to do in the absence of evidence ?

Ideal candidates for direct transport

- High suspicion of LVO
- Time from symptom onset >4h and <24 hours
- Contraindications for IVT
  - Unknown time of symptom onset
  - Wake-up and siesta stroke
  - (N)OAC therapy
  - Prior surgery
  - Etc.

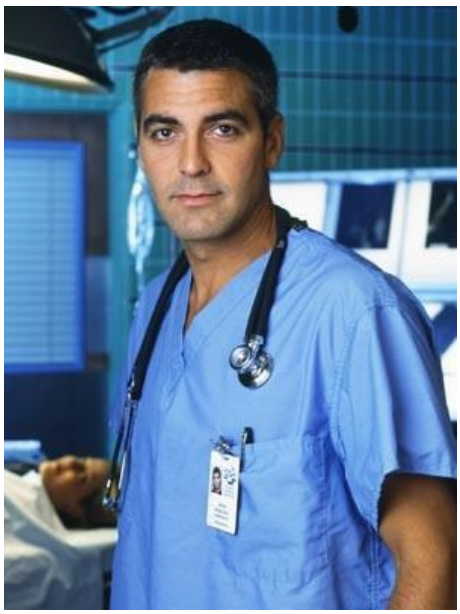


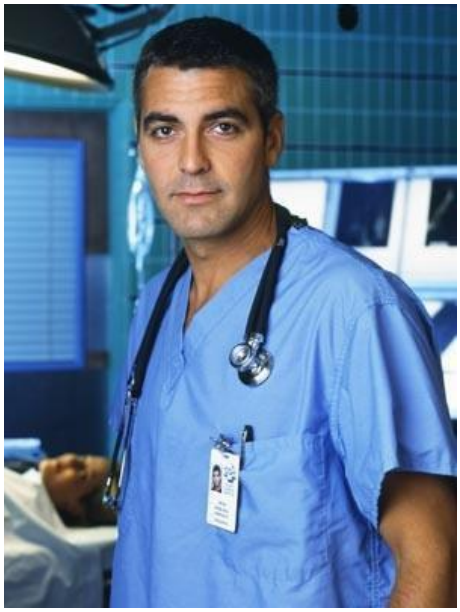
Karte: wikipedia



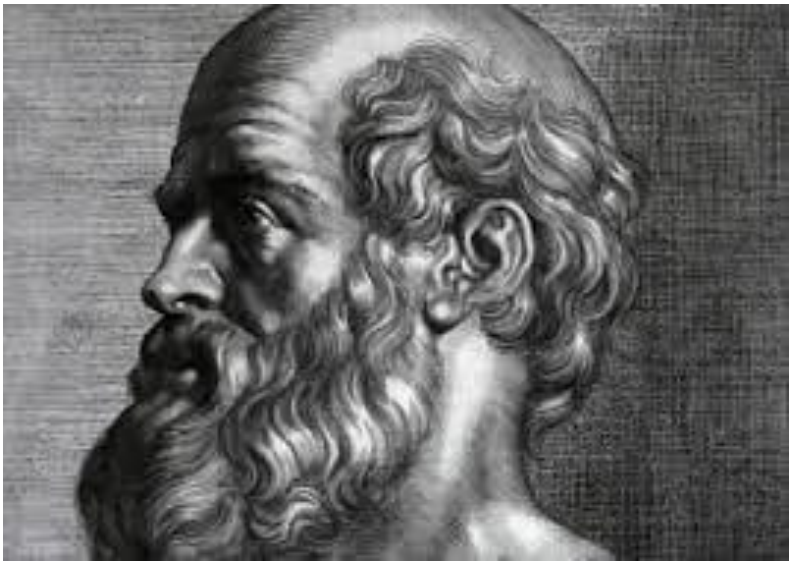
Karte: wikipedia

Secondary prevention





“Prevention is better than cure”



Hippokrates

Stroke can
be prevented!

Primary
prevention

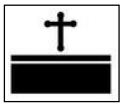
Modifiable risk factors responsible for disability-adjusted life-years

Globally

- Blood pressure
- Smoking
- BMI
- Childhood undernutrition
- Fasting plasma glucose
- Alcohol use
- Houshold air pollution
- Unsafe water
- Unsafe sex
- Fruit

Developed countries

- Blood pressure
- BMI
- Smoking
- Alcohol use
- Fasting plasma glucose
- Total cholesterol
- Glomerular filtration
- Sodium
- Physical activity
- Fruits

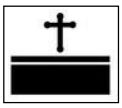


GBD 2013 Risk Factors Collaborators, Lancet 2015

Modifiable risk factors responsible for stroke

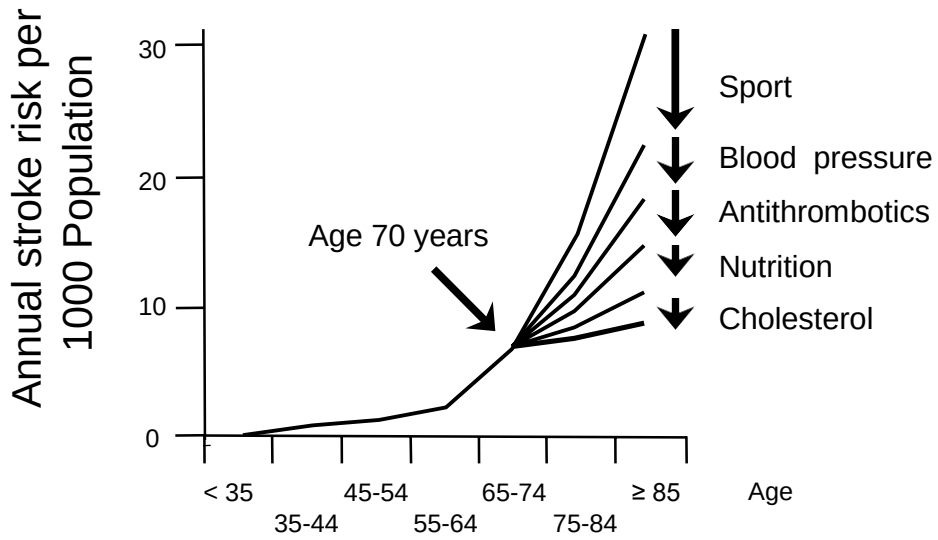
In each region of the world, these 10 modifiable risk factors explain 90% of strokes :

- Hypertension
- Current smoking
- Waist-hip-ratio
- Physical inactivity
- Unhealthy diet (incl. Sodium)
- Alcohol intake
- Lipids (apolipoproteins B/A1)
- Diabetes / ↑HbA1c / ↑ FPG
- Psychosocial factors
- Cardiac causes (incl. AF)



INTERSTROKE / O'Donnell Lancet 2010 and 2016

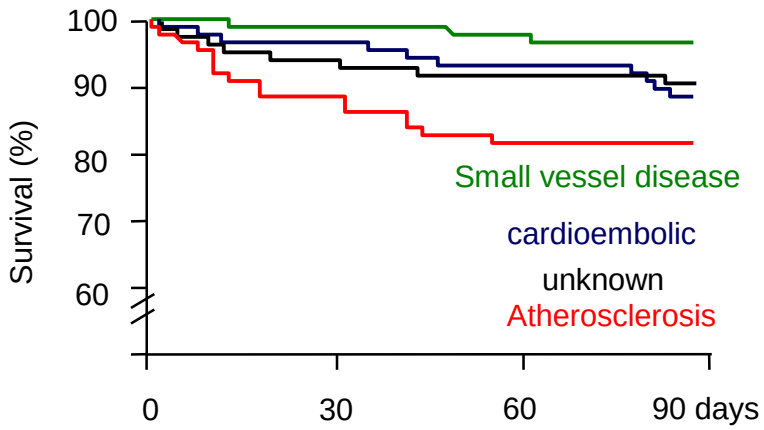
What can we achieve?



Secondary prevention

Recurrence risk is dependent of underlying aetiology

Oxford Vascular Study, Lovett et al. Neurology 2004; 62: 569-574



Antithrombotics and anticoagulation

Antiplatelet or anticoagulation
after ischemic stroke/TIA ?

- Antiplatelets
  - Atherosclerosis (including intracranial stenosis)
  - Lacunar stroke (microangiopathic)
  - Undetermined origin
- Anticoagulation
  - Cardiac cause and high recurrence risk
  - Cardiac cause, with low/intermediate risk but recurrent embolic events

AHA/Sacco Stroke 2007; ESO 2008

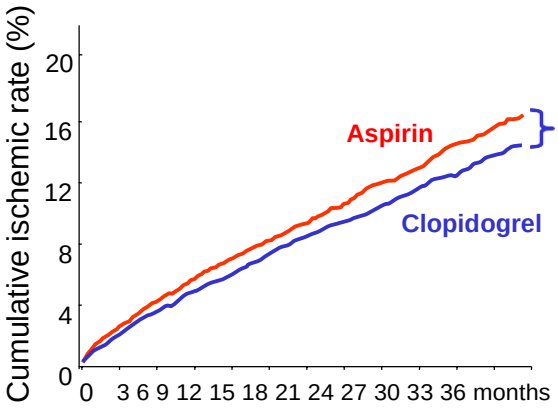
Antiplatelets: which, how long?

Aspirin after acute stroke or TIA

- Aspirin load 325-500mg, then 100mg/d
  - Avoid if thrombolysis
- If Aspirin allergy : consider clopidogrel load 300 mg
  - Then 75mg/d
- Consider combination of clopidogrel & Aspirin
  - For limited duration in high risk recurrence risk (see later)

Based on : IST, CAST, CAPRIE, EARLY, MATCH, CHANCE, POINT

Clopidogrel vs. aspirin in vascular patients
CAPRIE (N=19'185)



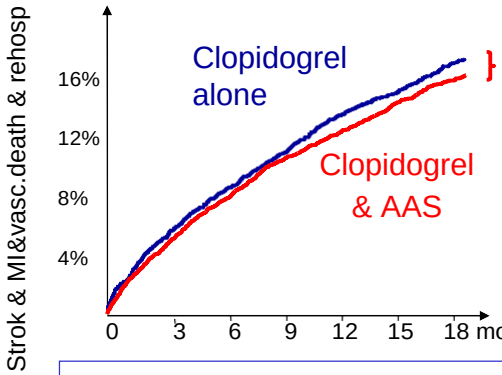
↓ 8.7%* overall

↓ 5.2% stroke (ns)
↓ 12.0%* stroke (meta)

↓ Bleedings

ASA vs. placebo: Antithrombotic Trialists Collaboration, BMJ 2002 and Algra JNNP 1996 and 1999;
ASA vs clopidogrel: CAPRIE Steering Committee, Lancet 1996
Meta-analysis thiopyridines: Hankey Stroke 2000

Long-term combination clopidogrel & aspirin
after stroke / TIA : MATCH (N=7'599)



No difference in ischaemic event (- 6.4%)

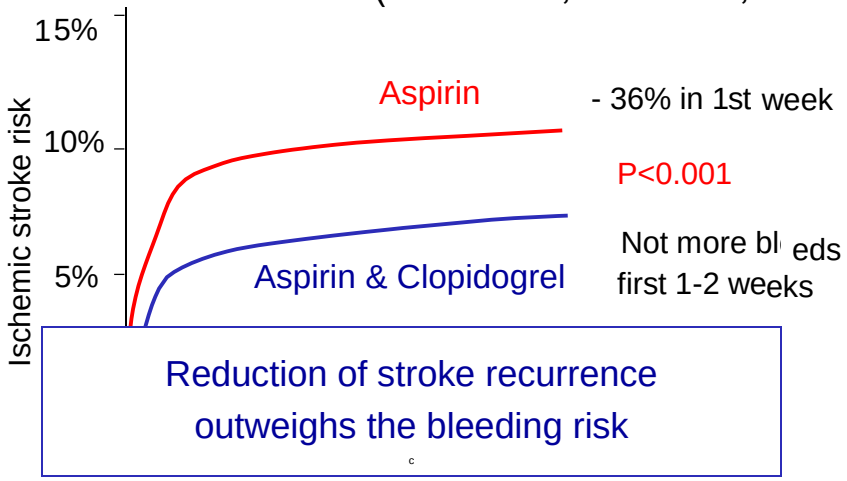
Significantly more hemorrhages with combination

Combination ASA + clopidogrel: **not** indicated for **longterm** prevention of stroke after stroke

MATCH: Diener Lancet 2004;
Similar results in SPS-3/Benavente, NEJM 2013, and CHARISMA: Bhatt NEJM 2006

Early aggressive antiplatelets

after non-cardio stroke (CHANCE, N=5'170, China)

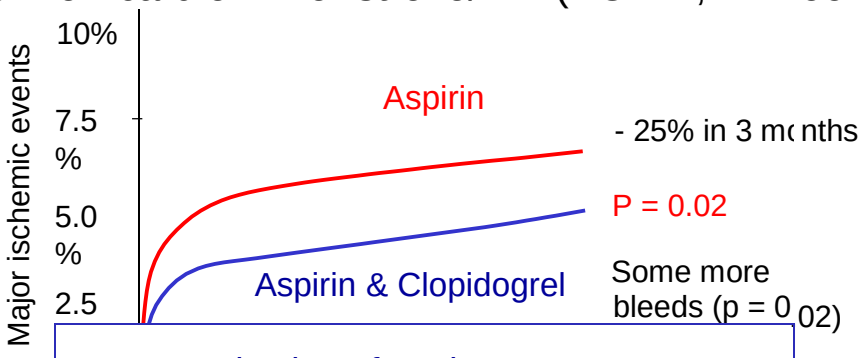


Reduction of stroke recurrence outweighs the bleeding risk

CHANCE/Pan Neurology 2017

Early aggressive antiplatelets

after non-cardio minor stroke/TIA (POINT, N=4'881)

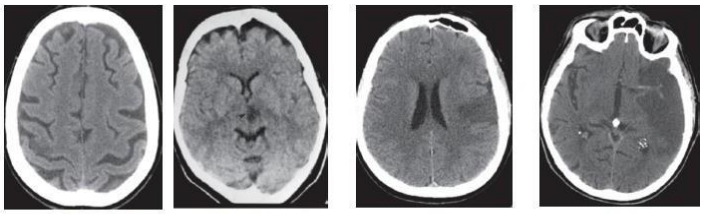


Reduction of stroke recurrence outweighs the bleeding risk

POINT/Johnston NEJM 2018

Anticoagulation after AIS and AF: when to start?

+



small cortical | small posterior | medium | large

minor moderate major ELAN EARLY LATE

Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillatioN (ELAN):

an international, multicentre, randomised-controlled, two-arm, assessor-blinded trial

PI: Urs Fischer

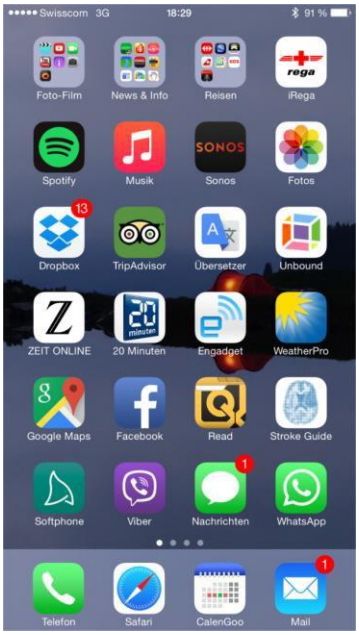
INSELSPITAL UNIVERSITÄTSSPITAL BERN HÔPITAL UNIVERSITAIRE DE BERNE | NEUROZENTRUM Neurocentre · Neurocentro | FNSNF Swiss National Science Foundation | Swiss Heart Foundation Fighting against Heart Disease and Stroke | ELAN

minor moderate major ELAN

Stroke Guide

Available on the App Store

Available on the Android App Store



6 Swiss secrets

how to prevent strokes

6 Swiss secrets

how to prevent strokes

Lots of sport

Lee Stroke 2003

Relax with friends

Henderson Stroke 2013

Black chocholate

Buitrago-Lopez BMJ 2011

Vegetables & fruits

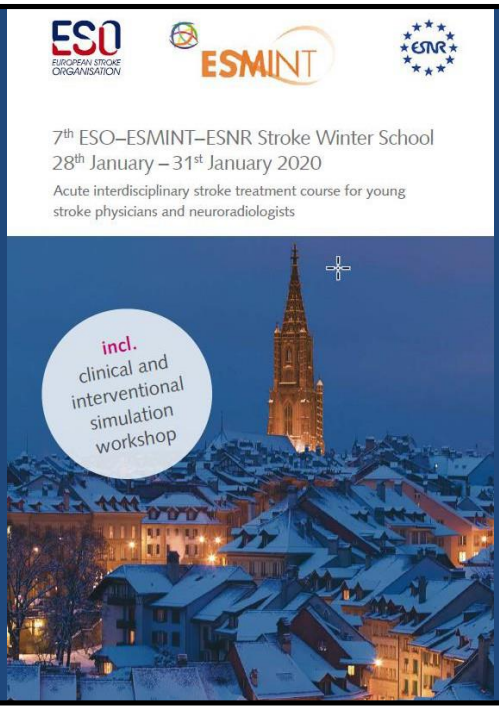
He Lancet 2006

Low-fat dairies

Larsson Stroke 2012/ Dehghan Lancet 2018

3-5 cups/day

Ding Circulation 2013




ESO-WSO CONFERENCE
Jointly Organised by the European Stroke Organisation &
the World Stroke Organization
ESO
EUROPEAN STROKE ORGANISATION
World Stroke Organization
A United Voice for Stroke
VIENNA
12-15 MAY 2020
PRE-CONFERENCE DAY 12 MAY
www.eso-wso-conference.org