14ème CONGRÈS de la Société de Gérontologie de Bordeaux et du Sud-Ouest
QUAND LES VIEILLES ARTÈRES S'EN MÊLENT
12 & 13 sept. 2024 | PESSAC Institut des Métiers de la Santé
SGBSO SOCIÉTÉ DE GÉRONTOLOGIE DE BORDEAUX ET DU SUD-OUEST

C·H·U Hôpitaux de Bordeaux

université de BORDEAUX

La prise en charge *AIGUË* de l'AVC en 2024

Pr Igor SIBON - CHU Bordeaux

INCIA BORDEAUX neurocampus

cnrs dépasser les frontières

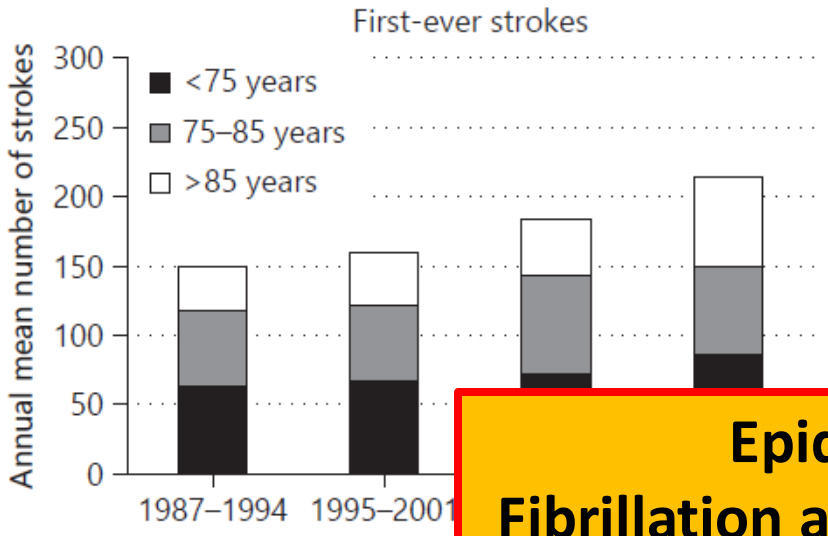
Liens d’intérêt

Relations financières

Consultant Medtronic, Bayer, Boehringer Ingelheim, Servier, Novartis, Bioprojet, Novonordisk

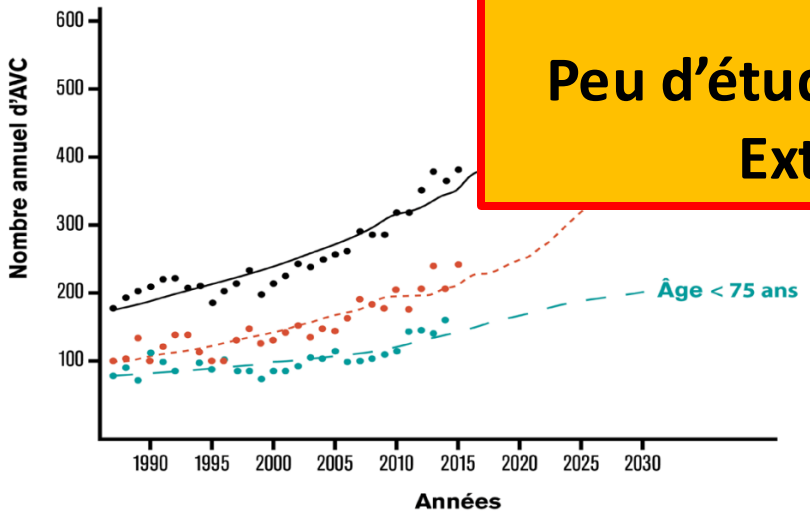
Orateur Boehringer Ingelheim, BMS-Pfizer, Bayer, Astra-Zeneca, Medtronic, Novartis, Novonordisk

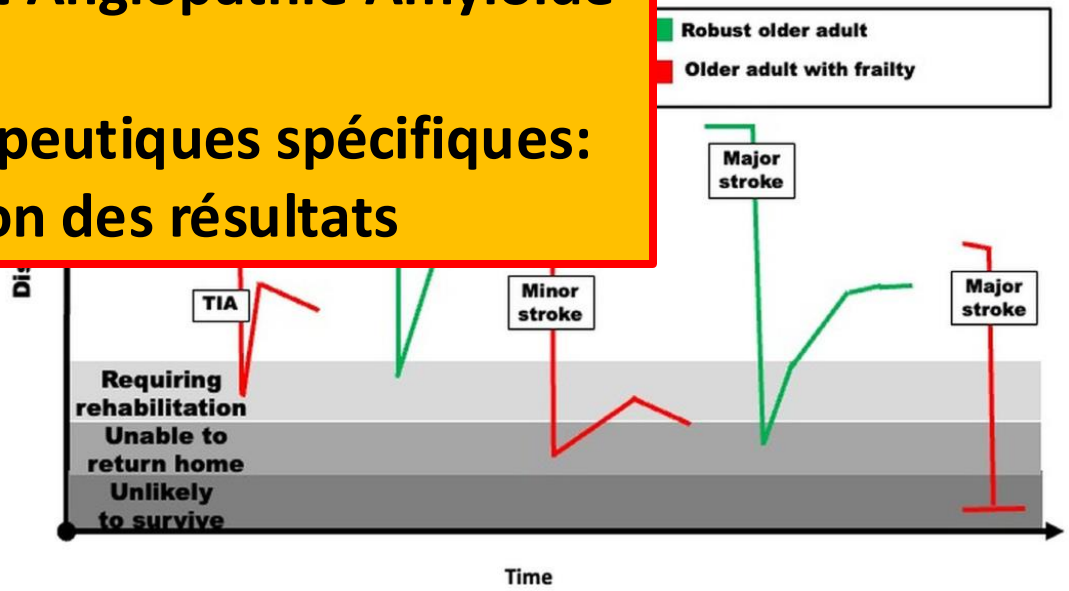
AVC… une pathologie dévastatrice du vieillissement



Epidémiologie spécifique:
Fibrillation atriale et Angiopathie Amyloïde

Peu d'études thérapeutiques spécifiques:
Extrapolation des résultats





Bejot et al., Neuroepidemiol 2019; Naeem F, Quinn T. Pract Neurol 2024

AVC: Conduite à tenir

TIME IS BRAIN

1

Confirmer le diagnostic

Imagerie cérébrale

2

Limiter les lésions cérébrales

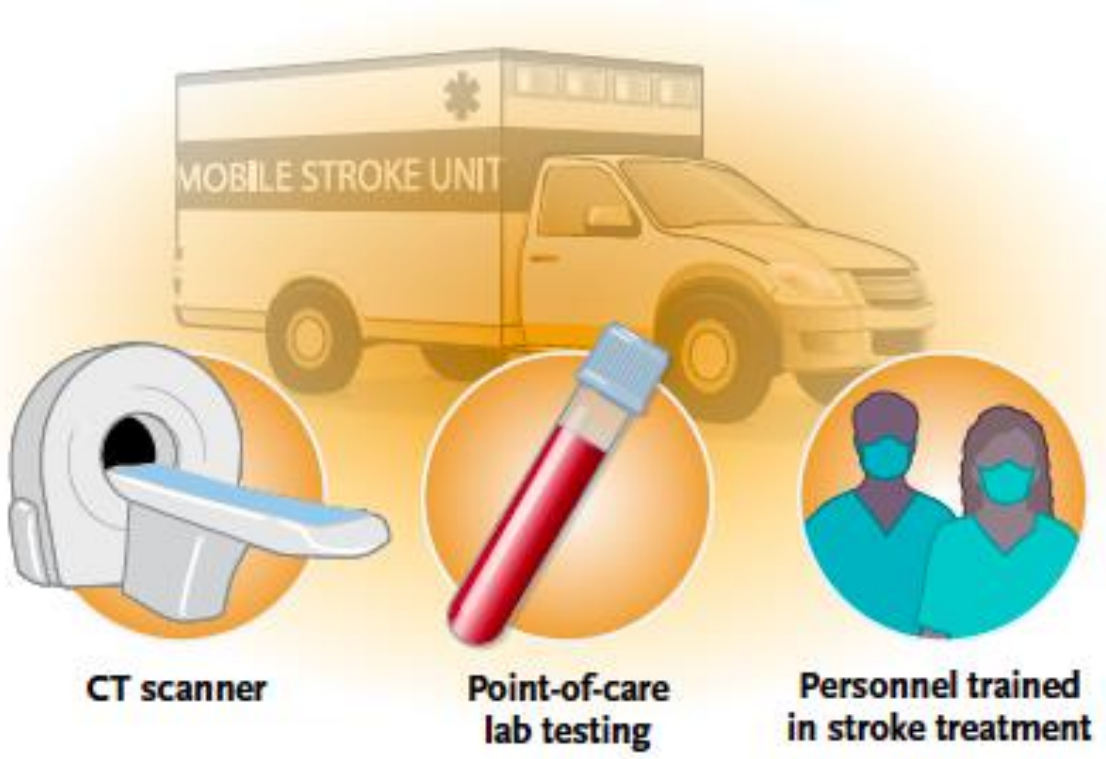
Ischémie

Restaurer la perfusion cérébrale

Hémorragie

Réduire l'expansion de l'hématome

Tout en 1
La Mobile Stroke Unit



Prospective, Multicenter, Controlled Trial of Mobile Stroke Units

Grotta et al., NEJM 2021

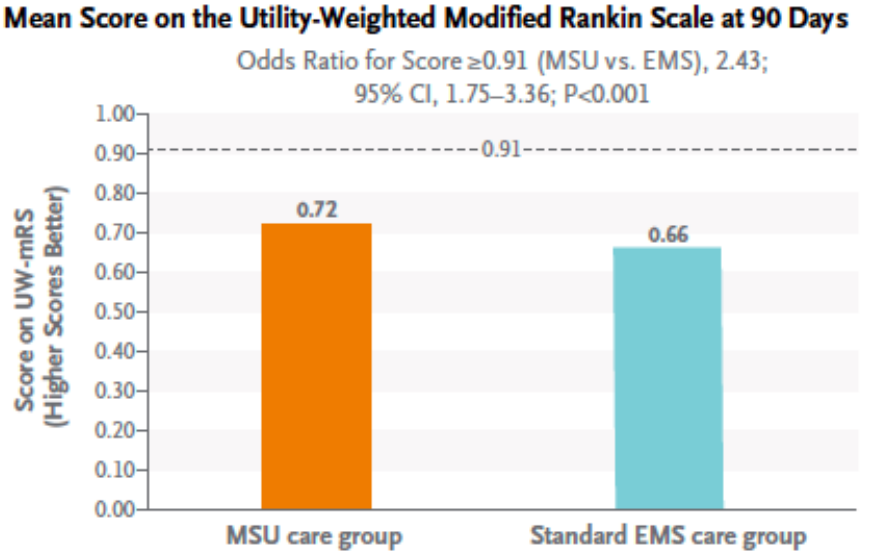
Etude ASPHALT

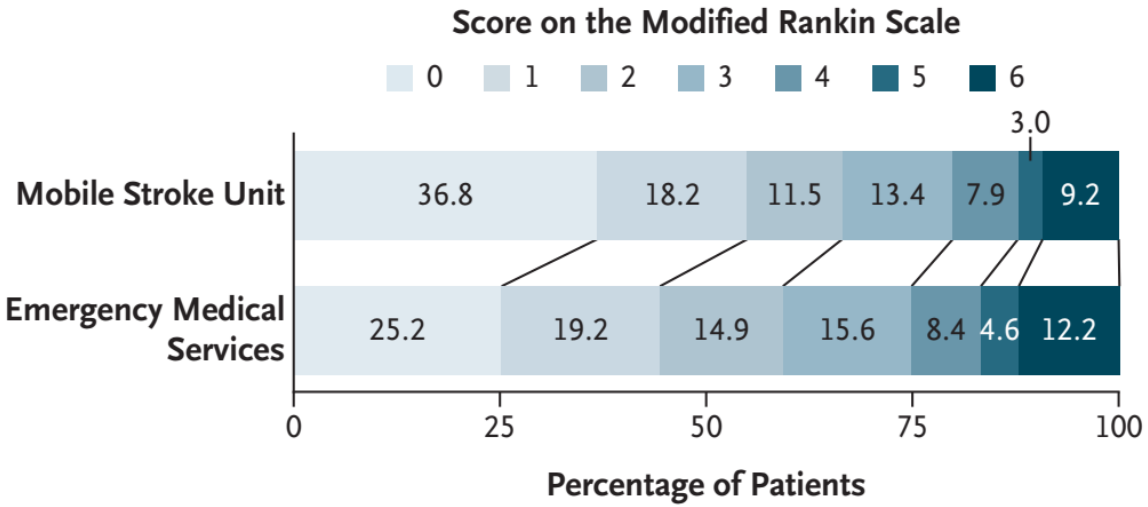
Acute Stroke: Prehospital versus in-HospitAL initiation of Recanalization Therapy

Table 3. Time Metrics in Patients Eligible for t-PA.*

Interval	Mobile Stroke Unit	Emergency Medical Services
	minutes	
Median interval between the time that the patient was last known to be well and t-PA treatment (IQR)	72 (55–105)	108 (84–147)
Median time from 911 alert to t-PA treatment (IQR)	46 (39–55)	78 (66–93)
Median time from ED door to t-PA bolus (IQR)	—	40 (30–51)
Median interval between the time that the patient was last known to be well and the alerting of emergency medical services (IQR)	23 (8–52)	22 (11–60)
Median time from 911 alert to arrival of emergency medical services (IQR)	9 (6–13)	9 (6–13)
Median time from arrival of emergency medical services to ED arrival (IQR)	55 (47–62)	27 (21–33)
Median interval between the time that the patient was last known to be well and endovascular thrombectomy (IQR)	166 (131–202)	163 (134–209)
Median time from 911 alert to endovascular thrombectomy (IQR)	141 (116–171)	132 (114–160)
Median time from ED door to endovascular thrombectomy (IQR)	76 (53–105)	94 (72–124)

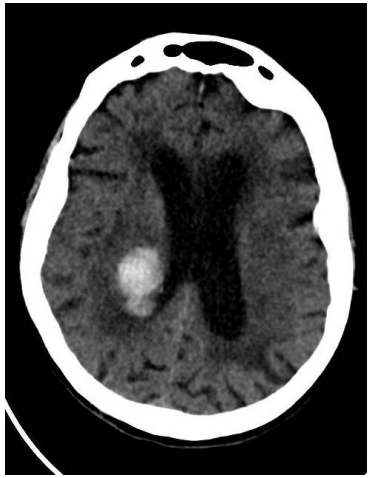
Gain de 36 mn thrombolyse IV
Absence retard thrombectomie
Traitement précoce des hémorragies cérébrales

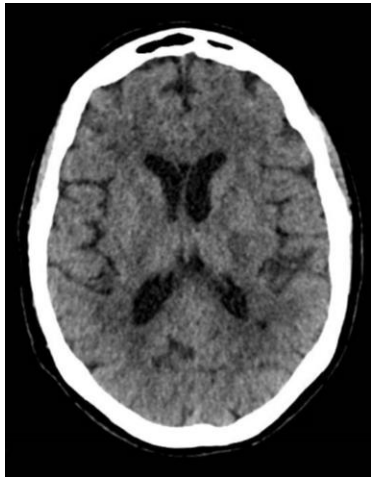


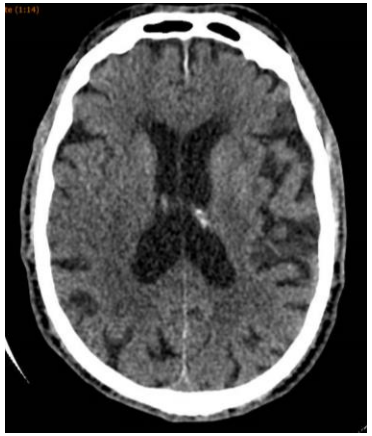


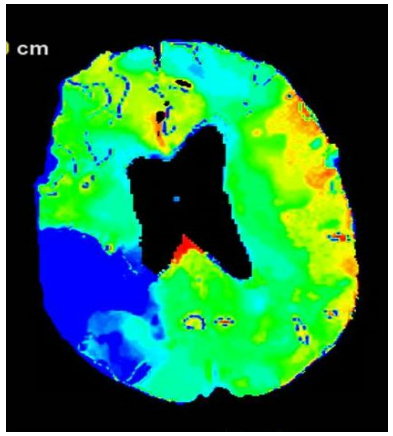
Quelle imagerie cérébrale en 1ère intention ?

TDM







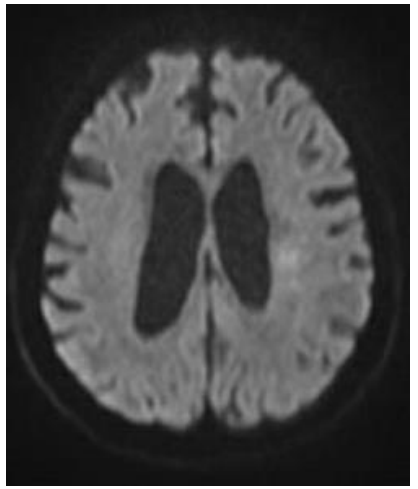


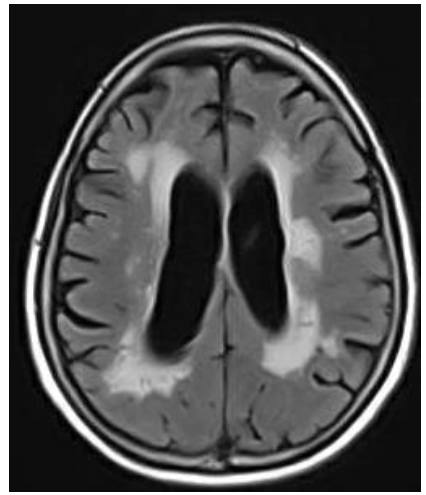
+

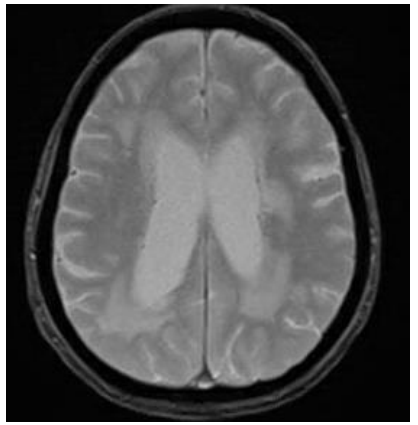
Angiographie

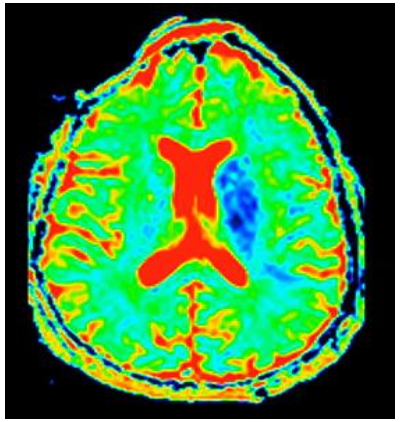
TSA

IRM









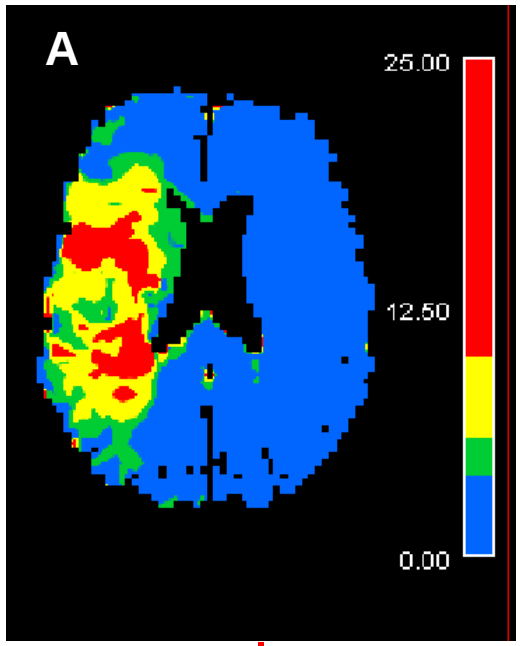
Situation difficile => Imagerie Optimale pour décision thérapeutique adaptée

Imagerie multimodale : viabilité tissulaire *vs* chronomètre

Mismatchs et Thrombus

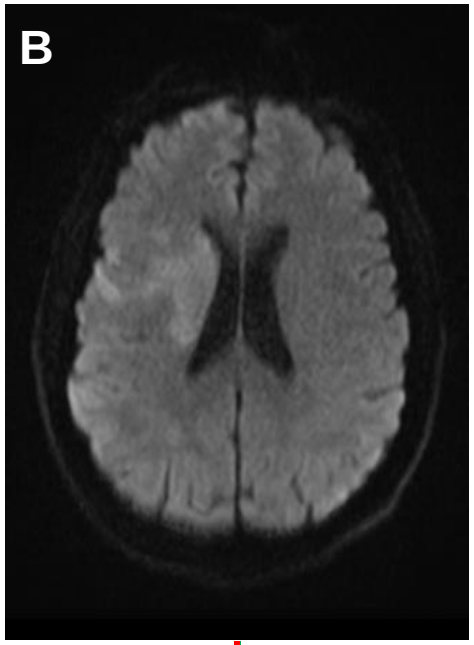
Viabilité tissulaire

PERFUSION

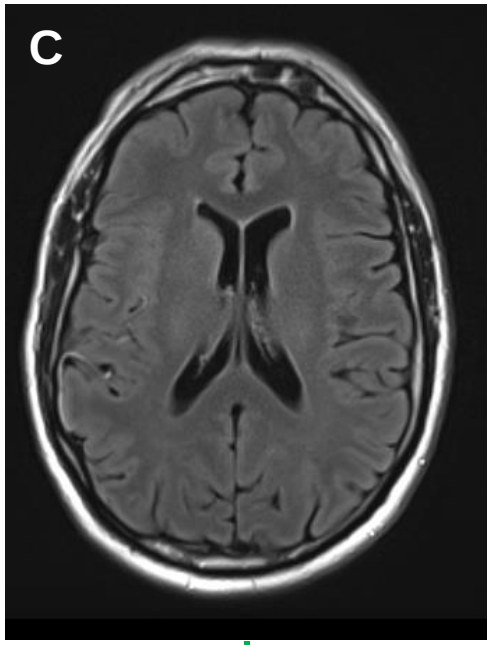


Datation des lésions

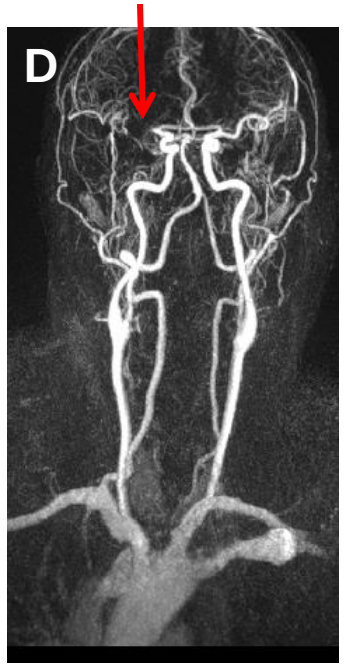
DIFFUSION



FLAIR



Identification du thrombus



Mismatch
Diffusion-Perfusion
Zone de **PENOMBRE**

Mismatch
FLAIR-Diffusion
Délai **< 4h30**

Localisation,
Longueur,
Composition

Régression des symptômes : AIT

TRANSIENT ISCHEMIC ATTACK — PROPOSAL FOR A NEW DEFINITION

Albers GW. et al. NEJM 2002

- *Déficit neurologique focal d'apparition brutale**

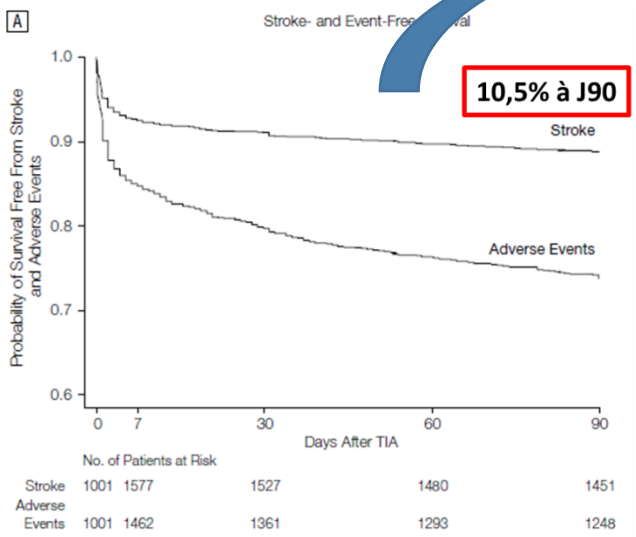
  (moins de 2 min)

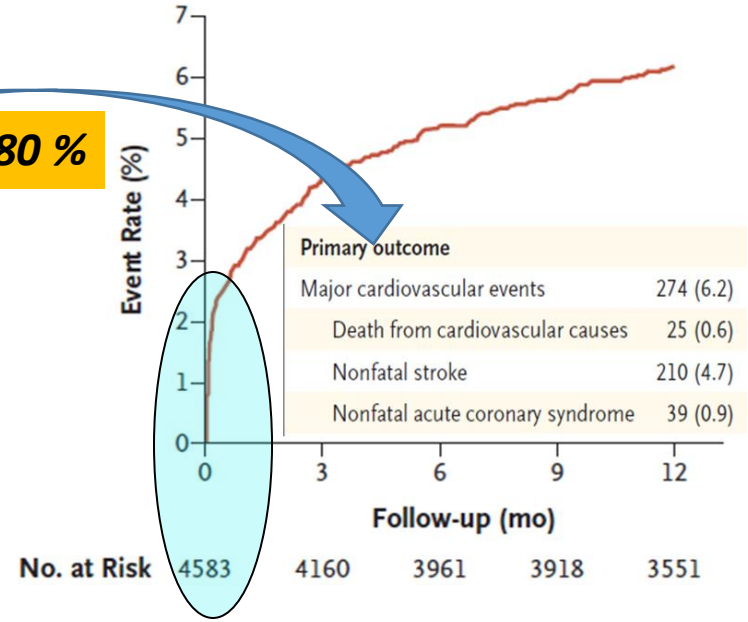
- *Durée ≤ 1h*

  (Typiquement)

- *Imagerie cérébrale normale*

  (CT ou IRM)





Recommendation

In patients suspected of TIA, if a wait of more than 24 hours to planned imaging is foreseen and a delay is judged to increase the risk of further ischaemic events, above the risk of starting antiplatelet medication, we suggest "de novo" antiplatelet monotherapy usage compared to not starting antiplatelet monotherapy.

Quality of evidence: Low ⊕⊕

Strength of recommendation: Weak for intervention ↑?

Lovett JK. et al., Stroke 2003; Amarenco P et al., NEJM 2016; Fonseca AC et al. Eur Stroke J 2021

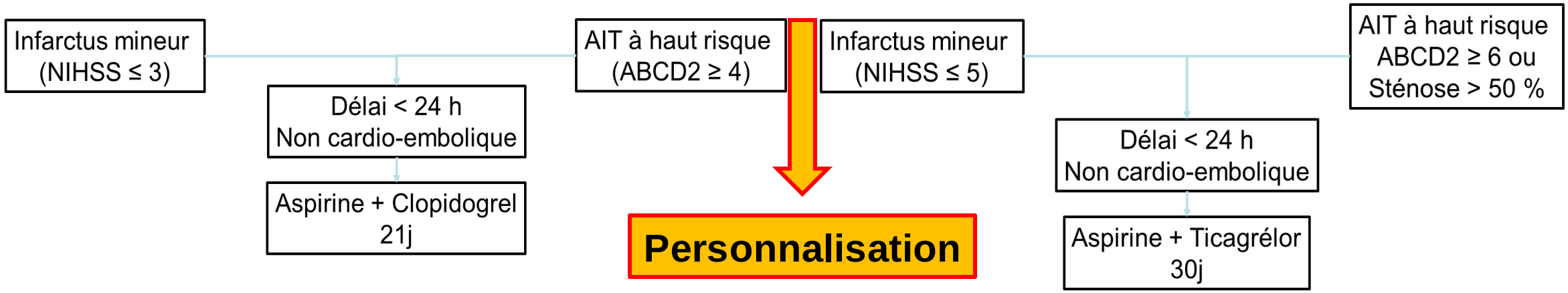
European Stroke Organisation expedited recommendation for the use of short-term dual antiplatelet therapy early after minor stroke and high-risk TIA

Dawson J. et al. Eur Stroke J 2021

Balance bénéfice/risque

Infarctus cérébral : RR 0,7 (0,61-0,81) : 25 évités pour 1000 patients traités (-15/-34)

Hémorragies: RR 1,79 (1,20; 2,69): 19 supplémentaires pour 1000 patients traités (+3/+46)



Administration la plus précoce possible après le début des symptômes

Administration après réalisation d'une imagerie cérébrale

Mécanisme cardio-embolique non suspecté !

Infarctus cérébral invalidant: Thrombolyse intraveineuse => Altéplase

1995

2014

The New England Journal of Medicine

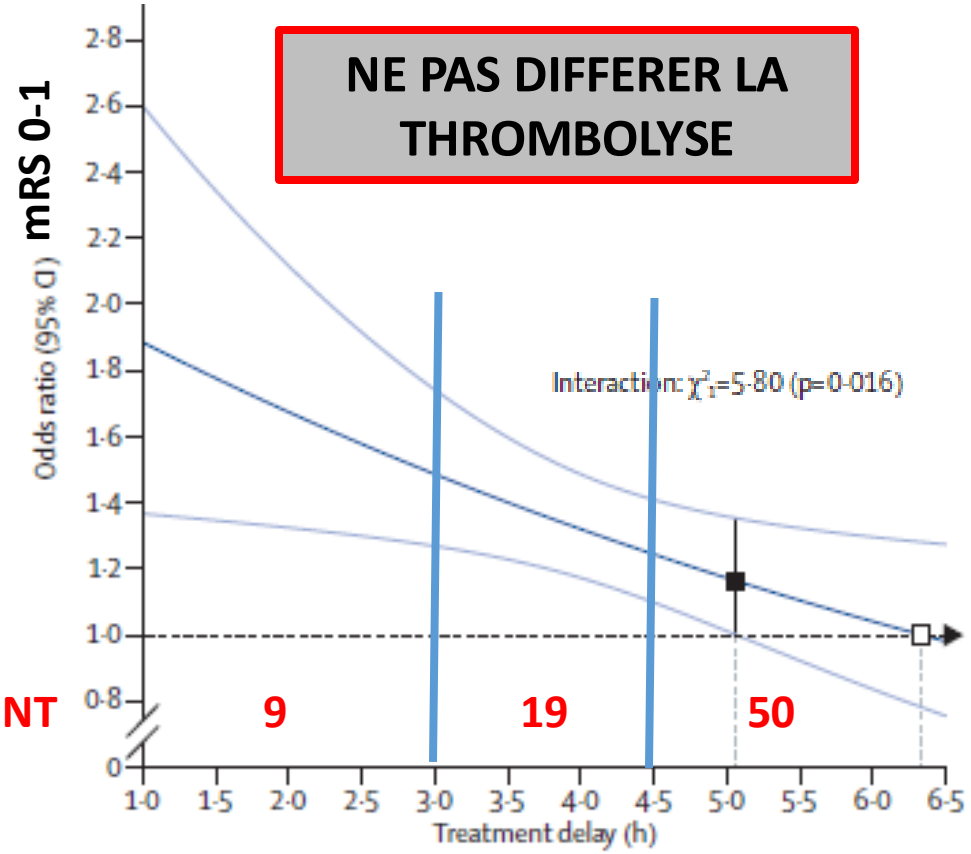
Volume 333 DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

9 études (NINDS, ECASS, ATLANTIS, IST-3)
6756 patients

NE PAS DIFFERER LA THROMBOLYSE



NNT 9 19 50

Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials

	Alteplase (n=3391)	Control (n=3365)	Odds ratio (95% CI)*
Treatment delay			
≤3·0 h	259/787 (32·9%)	176/762 (23·1%)	1·75 (1·35–2·27)
>3·0≤4·5 h	485/1375 (35·3%)	432/1437 (30·1%)	1·26 (1·05–1·51)
>4·5 h	401/1229 (32·6%)	357/1166 (30·6%)	1·15 (0·95–1·40)
Age (years)			
≤80	990/2512 (39·4%)	853/2515 (33·9%)	1·25 (1·10–1·42)
>80	155/879 (17·6%)	112/850 (13·2%)	1·56 (1·17–2·08)
Baseline NIHSS score			
0–4	237/345 (68·7%)	189/321 (58·9%)	1·48 (1·07–2·06)
5–10	611/1281 (47·7%)	538/1252 (43·0%)	1·22 (1·04–1·44)
11–15	198/794 (24·9%)	175/808 (21·7%)	1·24 (0·98–1·58)
16–21	77/662 (11·6%)	55/671 (8·2%)	1·50 (1·03–2·17)
≥22	22/309 (7·1%)	8/313 (2·6%)	3·25 (1·42–7·47)

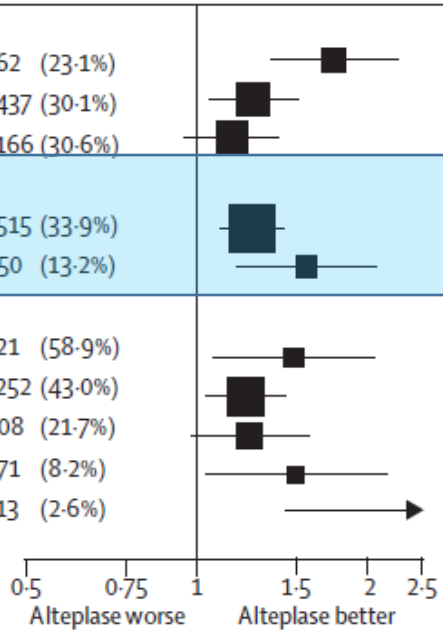
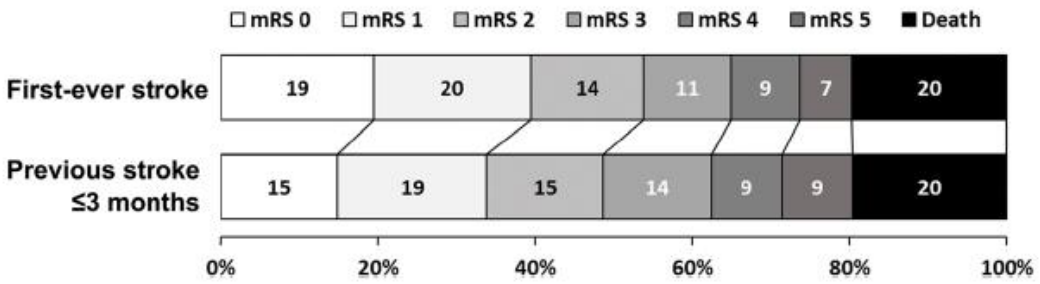


Figure 2: Effect of alteplase on good stroke outcome (mRS 0–1), by treatment delay, age, and stroke severity

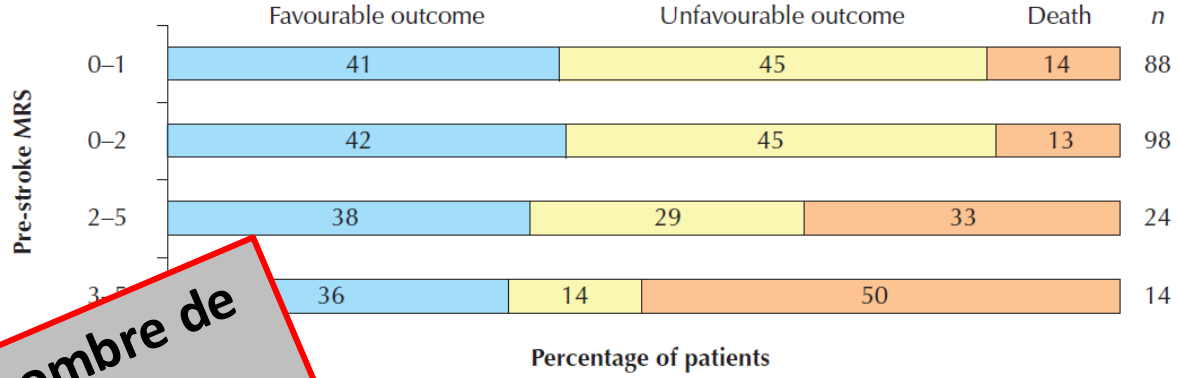
Bénéfice indépendant de l'âge

Recul des limitations d'utilisation…
Inclusion des sujets âgés !

Intravenous Thrombolysis for Stroke Recurring Within 3 Months From the Previous Event



Effects of thrombolysis for acute stroke in patients with pre-existing disability

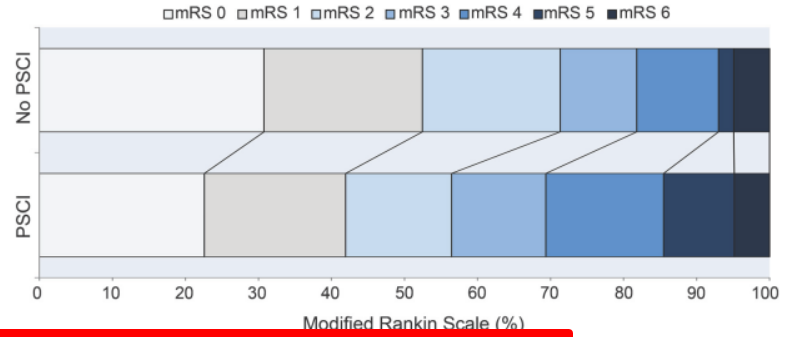


Augmentation du nombre de patients éligibles !!

The Burden of Diabetes and the Chance of a Previous Stroke: Thrombolysis for Recurrent Stroke in Diabetics

in Stroke-Monitoring Study criteria. *Results:* Of the patients, 35 and 33.2% had previous stroke. Of these patients, 14.4% were di pre-vious stroke (index group). The rate of patients with poor functi outcome at discharge, symptomatic intracranial hemorrhage, or mortality did not differ between the index group and patients with either diabetes or previous stroke in 2 × 2 com-parisons. Diabetics with first-ever stroke showed significantly more symptomatic intracranial hemorrhage (9.7%, $P < .001$) than the other groups, poorer functional recovery ($P = .036$), and the highest rate of mortality (12.4%, $P < .001$). Significant

Thrombolytic therapy for stroke in patients with preexisting cognitive impairment



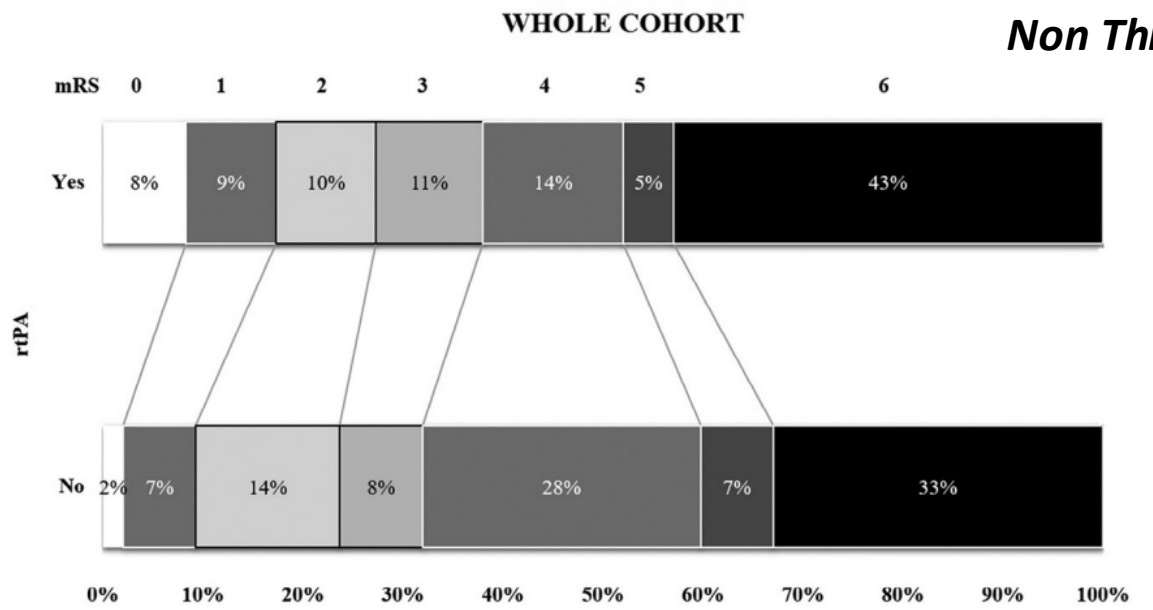
Handicap, Troubles cognitifs, Epilepsie, Antithrombotiques…

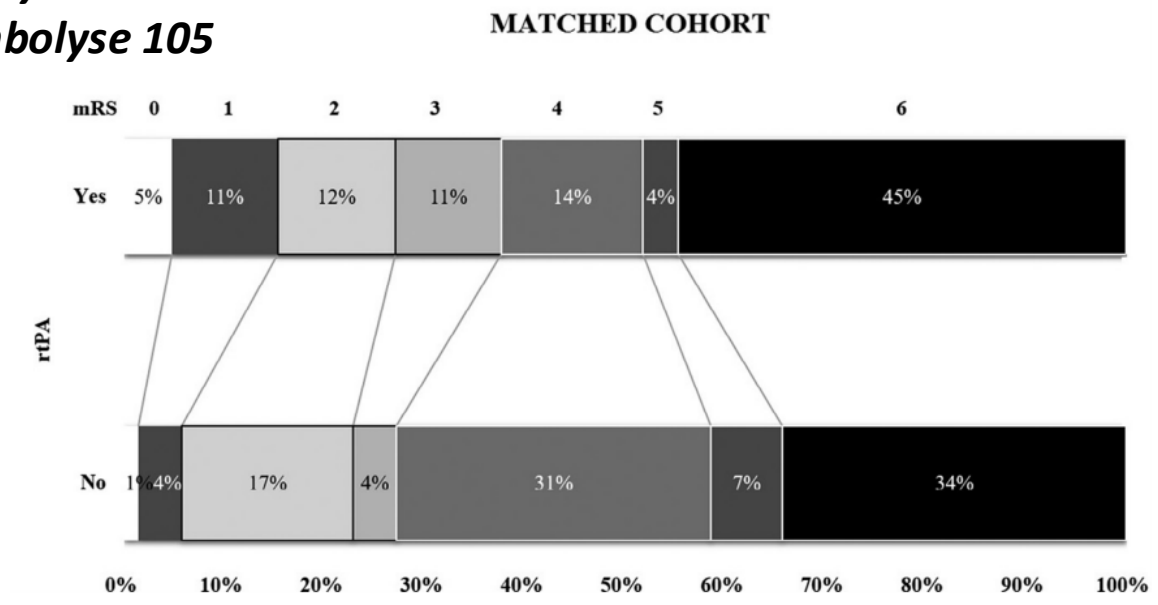
Karlinski et al., Stroke 2015; Filipov et al., 2018; Merkler et al., Stroke 2017; Foell et al., CMAJ 2003

Outcomes of Nonagenarians with Acute Ischemic Stroke Treated with Intravenous Thrombolytics

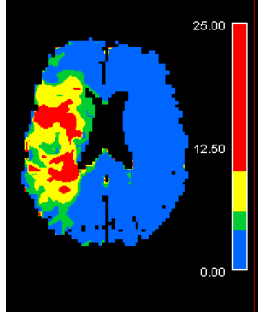
Behrouz et al., JSCVD 2018

N 227
Thrombolyse 122
Non Thrombolyse 105



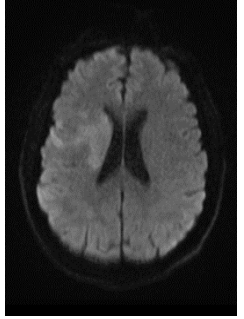


Balance bénéfice / risque hémorragique favorable !



Extending thrombolysis to 4·5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

Campbell et al., Lancet 2019



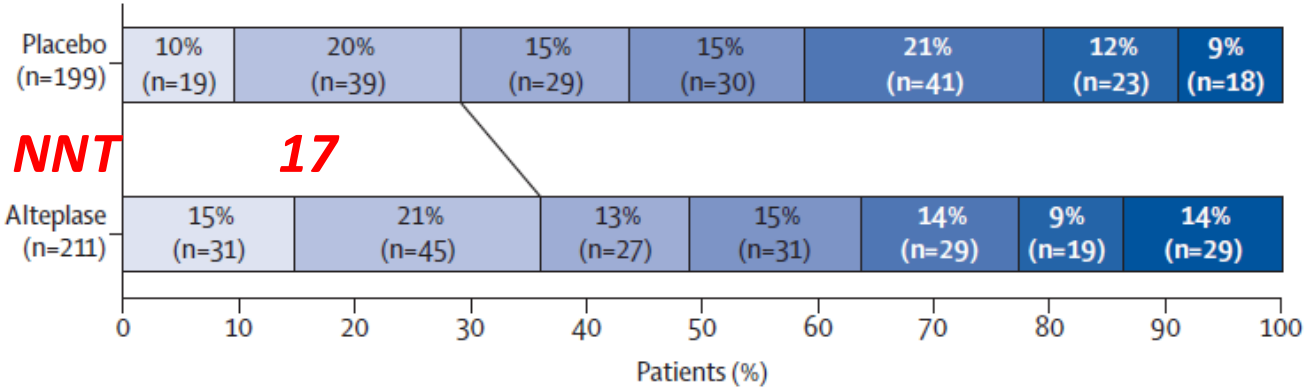
Délai : **4h30-9h00**

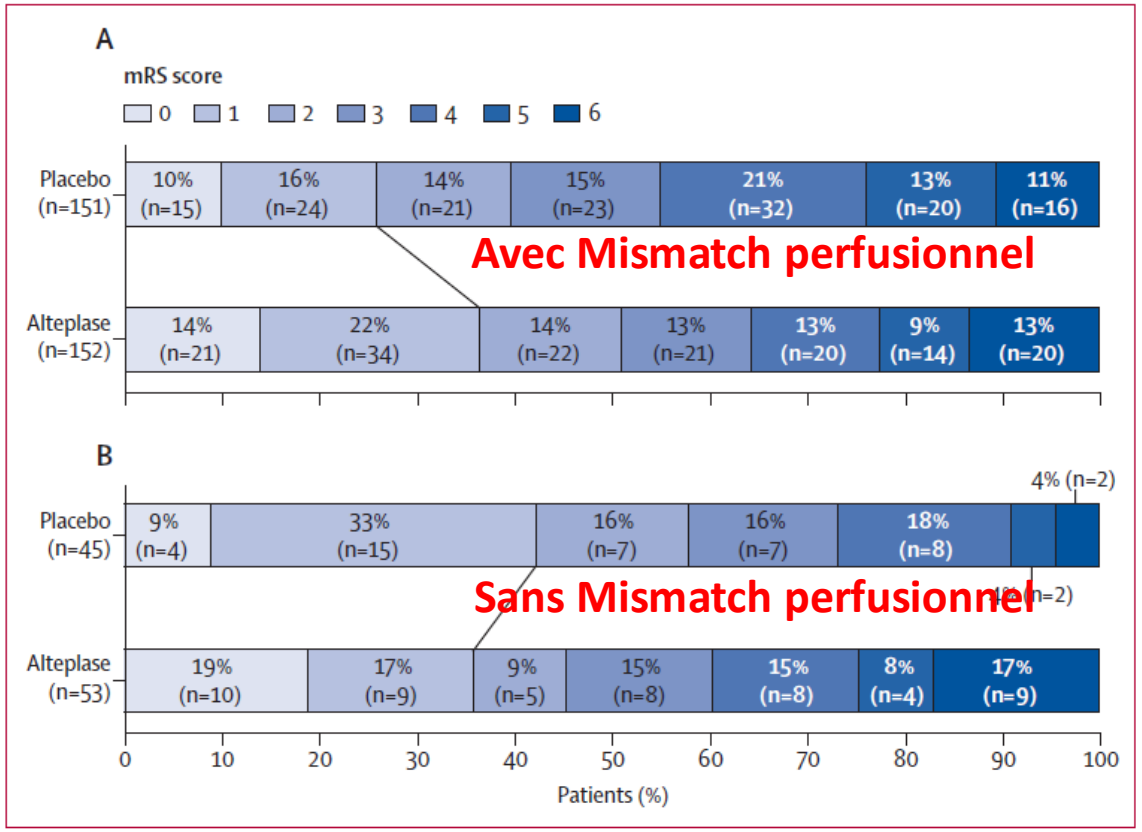
EPITETH // EXTEND // ECASS4/EXTEND
414 patients: 213 Altéplase // 201 Placebo

Analyse imagerie de perfusion

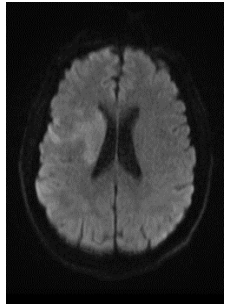
Ratio mismatch **> 1,2**
Volume infarctus **< 70cc**
Différence Infarctus/hypoperfusion **> 10cc**

Logiciel dédié



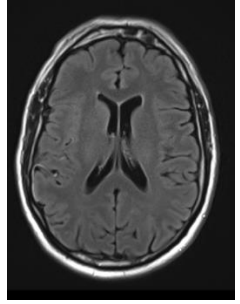


mRs ≤ 2 à 3 mois
NNT = 20



MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

Thomalla et al, NEJM 2018
Wake-up Study



Heure de début indéterminée
Délai depuis constat des symptômes < 4h30

Mismatch FLAIR – Diffusion

Non éligible à la thrombectomie

Altéplase vs Placebo: 800 patients

Objectif principal: mRS 0-1 à j90

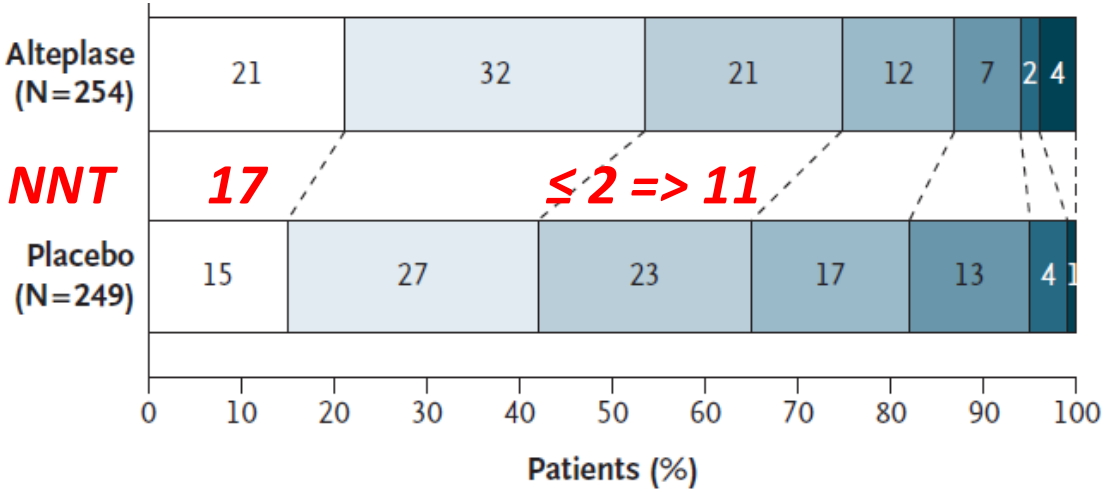


Table 2. Primary and Secondary Efficacy Outcomes (Intention-to-Treat Population).*

Outcome	Alteplase Group (N=254)	Placebo Group (N=249)	Effect Variable	Adjusted Value (95% CI)†	P Value
Primary efficacy end point					
Favorable outcome at 90 days — no./total no. (%)‡	131/246 (53.3)	102/244 (41.8)	Odds ratio	1.61 (1.09 to 2.36)	0.02
Secondary efficacy end points					
Median score on modified Rankin scale at 90 days (IQR)§	1 (1–3)	2 (1–3)	Common odds ratio	1.62 (1.17 to 2.23)	0.003¶
Correlation between treatment response at 90 days and deficit level at baseline — no./total no. (%)‖	72/246 (29.3)	44/244 (18.0)	Odds ratio	1.88 (1.22 to 2.89)	0.004¶
Global Outcome Score at 90 days**			Odds ratio	1.47 (1.07 to 2.04)	0.02¶
Median score on Beck Depression Inventory at 90 days (IQR)††	6.0 (2.0–11.0)	7.0 (2.0–14.0)	Mean difference ($\log_e$)	−0.04 (−0.22 to 0.15)	0.69¶
Total score on EQ-5D at 90 days‡‡	1.9±2.1	2.4±2.4	Mean difference	−0.52 (−0.88 to −0.16)	0.004¶
Score on visual analog scale on EQ-5D at 90 days§§	72.6±19.7)	64.9±23.8	Mean difference	7.64 (3.75 to 11.51)	<0.001¶
Median infarct volume at 22–36 hr (IQR) — ml ¶¶	3.0 (0.8–17.7)	3.3 (1.1–16.6)	Mean difference ($\log_e$)	−0.16 (−0.47 to 0.15)	0.32¶
Secondary					
Symptomatic intracranial hemorrhage					
As defined in SITS-MOST‡	5 (2.0)	1 (0.4)		4.95 (0.57–42.87)	0.15

Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial

Menon et al., Lancet 2022

Alteplase 0,9 mg/kg vs Ténectéplase (0,25 mg/kg)
IC < 4h30
Déficit significatif
Randomisation 1:1

	Tenecteplase group (n=806)	Alteplase group (n=771)
Age, years	74 (63–83)	73 (62–83)
Sex		
Female	382 (47·4%)	373 (48·4%)
Male	424 (52·6%)	398 (51·6%)
Baseline NIHSS score (n=1569)	9 (6–16)	10 (6–17)
Baseline NIHSS score categories		
<8	325/803 (40·5%)	294/766 (38·4%)
8–15	247/803 (30·8%)	256/766 (33·4%)
>15	231/803 (28·8%)	216/766 (28·2%)
Occlusion site on baseline CT angiography (n=1558)*		
Intracranial internal carotid artery	69/801 (8·6%)	66/757 (8·7%)
M1 segment MCA	118/801 (14·7%)	119/757 (15·7%)
M2 segment MCA	174/801 (21·7%)	141/757 (18·6%)
Other distal occlusions†	130/801 (16·2%)	138/757 (18·2%)
Vertebrobasilar arterial system	26/801 (3·2%)	38/757 (5·0%)
Cervical internal carotid artery	17/801 (2·1%)	9/757 (1·2%)
No visible occlusions	267/801 (33·3%)	246/757 (32·5%)
Presence of large vessel occlusion on baseline CT angiography (n=1558)	196/801 (24·5%)	193/757 (25·5%)

Tenecteplase versus alteplase in acute ischaemic cerebrovascular events (TRACE-2): a phase 3, multicentre, open-label, randomised controlled, non-inferiority trial

Wang et al., Lancet 2023

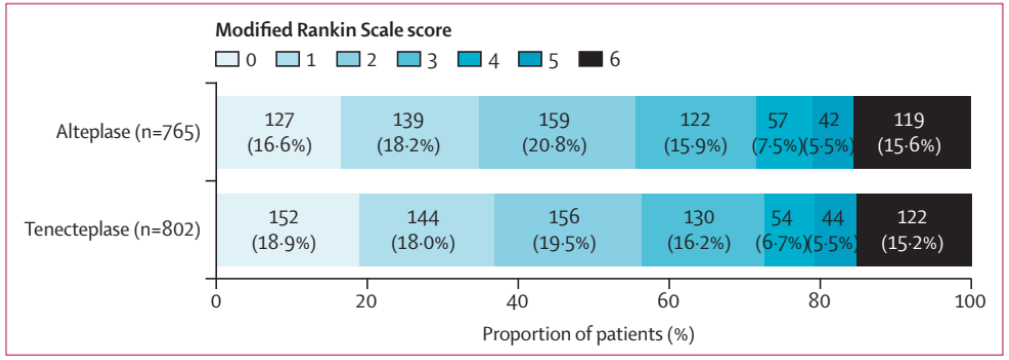
Alteplase 0,9 mg/kg vs Ténectéplase (0,25 mg/kg)
IC < 4h30
Eligibles TLY – inéligibles TM
NIHSS 5-25

	Tenecteplase (n=710)	Alteplase (n=707)
Age, years	67 (58–73)	65 (58–72)
Age		
18–59 years	211 (30%)	218 (31%)
60–79 years	423 (60%)	428 (61%)
≥80 years	76 (11%)	61 (9%)
Sex		
Male	492 (69%)	479 (68%)
Female	218 (31%)	228 (32%)
Ethnicity		
Chinese	710 (100%)	707 (100%)
Weight, kg	65 (59–75)	67 (60–75)
Medical history		
Hypertension	510 (72%)	512 (72%)
Diabetes	172 (24%)	207 (29%)
Hyperlipidaemia	130 (18%)	160 (23%)
Coronary heart disease	167 (24%)	166 (24%)
Arrhythmia	137 (19%)	146 (21%)
Baseline NIHSS score*	7 (5–10)	7 (6–10)

Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial

Menon et al., Lancet 2022

Alteplase 0,9 mg/kg vs Ténectéplase (0,25 mg/kg)
IC < 4h30
Déficit significatif
Randomisation 1:1

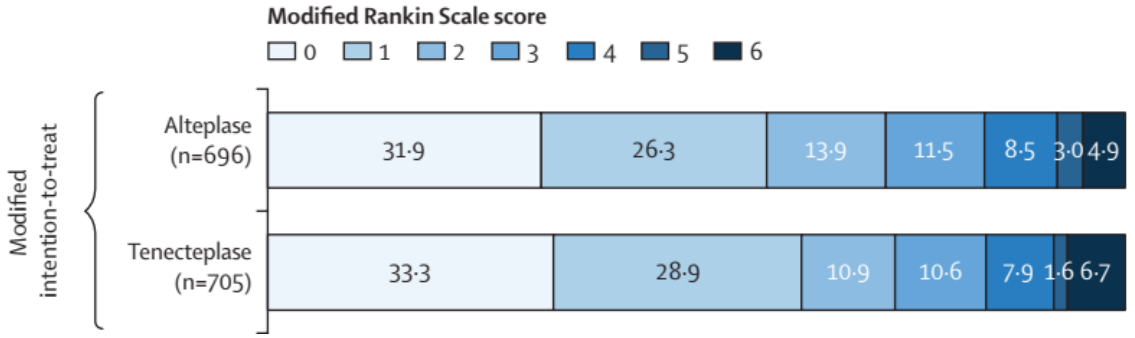


	Tenecteplase group (n=806)	Alteplase group (n=771)	Unadjusted difference in proportion	Adjusted risk ratio*
Primary outcome				
mRS score 0–1 at 90–120 days (n=1567)	296/802 (36·9%)	266/765 (34·8%)	2·1 (–2·6 to 6·9)	..
Secondary outcomes*				
mRS score 0–1 at 90–120 days (n=1567)	296/802 (36·9%)	266/765 (34·8%)	..	1·1 (1·0 to 1·2)
mRS score 0–2 at 90–120 days (n=1567)	452/802 (56·4%)	425/765 (55·6%)	0·8 (–4·1 to 5·7)	1·0 (1·0 to 1·1)
Actual mRS score at 90–120 days (n=1567)	2 (1 to 4)	2 (1 to 4)	..	..
Return to baseline function (n=1454)	219/740 (29·6%)	199/714 (27·9%)	1·7 (–2·9 to 6·4)	1·1 (0·9 to 1·2)

Tenecteplase versus alteplase in acute ischaemic cerebrovascular events (TRACE-2): a phase 3, multicentre, open-label, randomised controlled, non-inferiority trial

Wang et al., Lancet 2023

Alteplase 0,9 mg/kg vs Ténectéplase (0,25 mg/kg)
IC < 4h30
Eligibles TLY – inéligibles TM
NIHSS 5-25



	Tenecteplase (n=711)	Alteplase (n=706)	Effect size (95% CI)*	p value
Symptomatic intracranial haemorrhage within 36 h	15 (2%)	13 (2%)	1·18 (0·56–2·50)	0·72
Symptomatic intracranial haemorrhage within 90 days	17 (2%)	15 (2%)	1·18 (0·59–2·37)	0·74
Parenchymal haematoma 2 intracranial haemorrhage within 36 h	10 (1%)	3 (<1%)	3·73 (0·99–14·13)	0·053
Any intracranial haemorrhage within 90 days	44 (6%)	50 (7%)	0·92 (0·62–1·36)	0·50
Other significant haemorrhage events within 90 days	5 (1%)	5 (1%)	1·05 (0·29–3·90)	0·99
Deaths	46 (7%)	35 (5%)	1·31 (0·86–2·01)	0·22

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

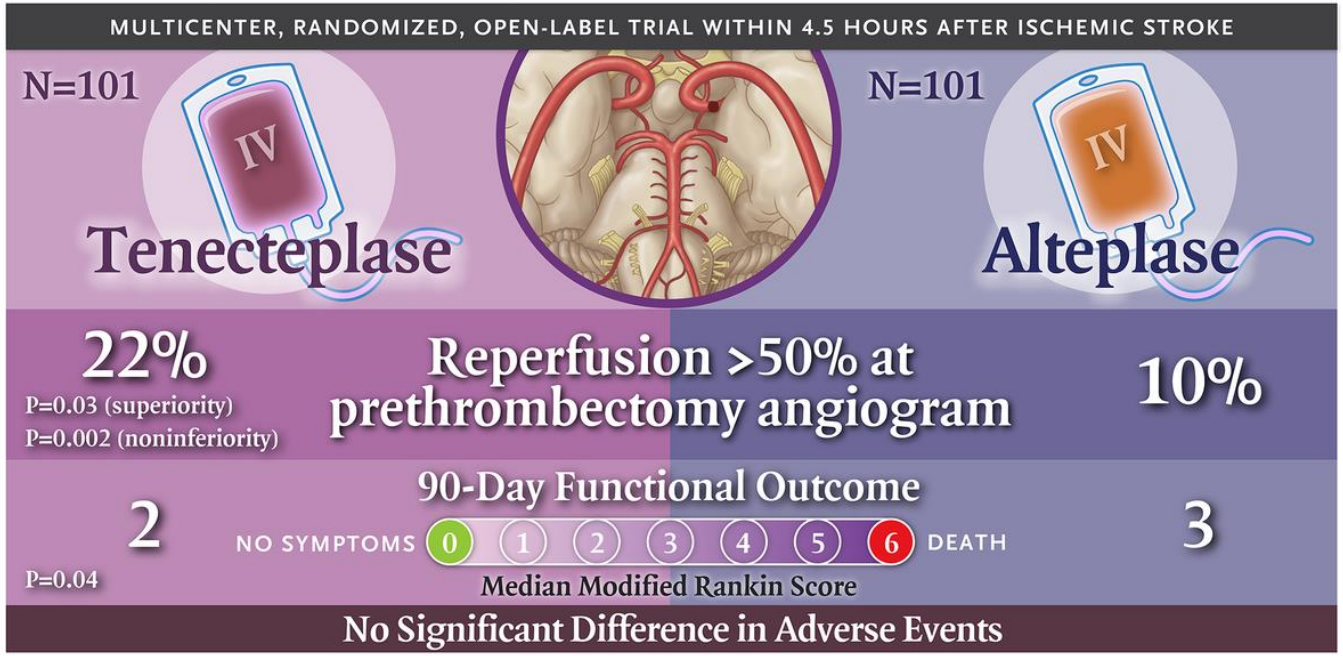
Campbell et al., NEJM 2018

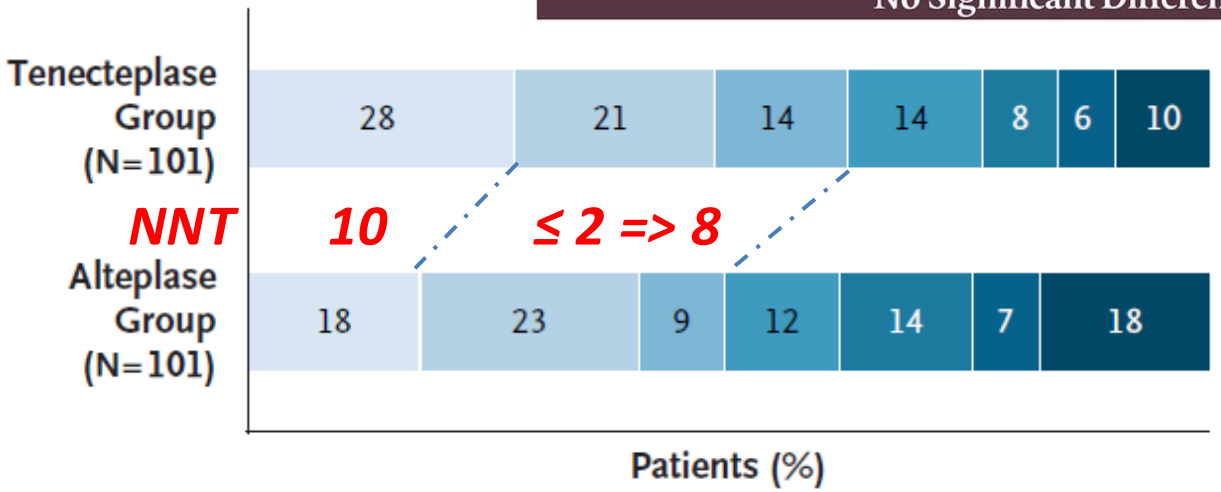
Délai **< 6h**

Occlusion proximale circulation antérieure

202 patients:
Ténecteplase vs Altéplase

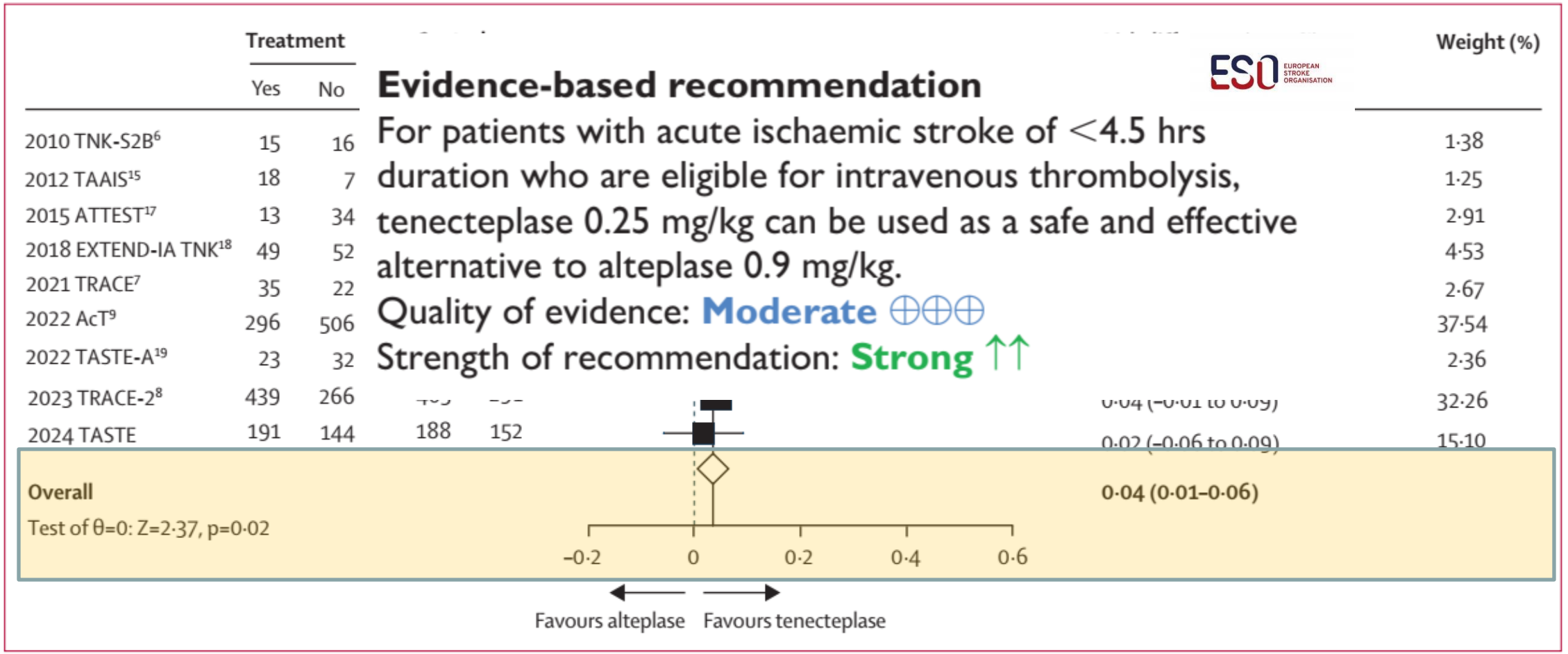
Critères de jugement
Taux de recanalisation pré-thrombectomie
Pronostic fonctionnel





Tenecteplase versus alteplase for thrombolysis in patients selected by use of perfusion imaging within 4·5 h of onset of ischaemic stroke (TASTE): a multicentre, randomised, controlled, phase 3 non-inferiority trial

Parsons et al., Lancet Neurol 2024



Ténectéplase = Alternative thérapeutique

The NEW ENGLAND JOURNAL of MEDICINE

Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours

A PLAIN LANGUAGE SUMMARY

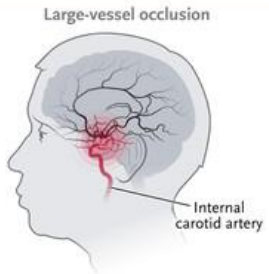
Based on the NEJM publication: Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy by Y. Xiong et al. (published June 14, 2024)

In this trial, researchers investigated the efficacy and safety of intravenous tenecteplase administered 4.5 to 24 hours after the onset of stroke in patients who had had ischemic stroke and did not have access to thrombectomy.

For patients with **large-vessel ischemic stroke** who present within 4.5 hours after onset and do not have access to endovascular thrombectomy, intravenous thrombolytic agents are recommended. However, more than two thirds of patients who have had ischemic stroke present more than 4.5 hours after onset or with an unknown time of onset.

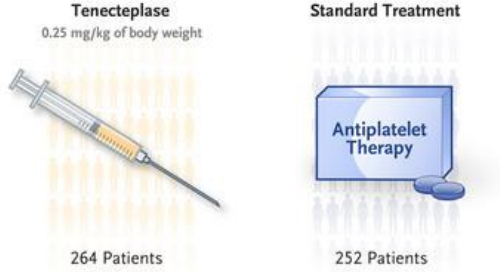
WHY WAS THE TRIAL DONE?

Tenecteplase is an effective thrombolytic agent for eligible patients with stroke who are treated within 4.5 hours after onset. The effect of later administration of tenecteplase in patients without immediate access to thrombectomy is currently unclear.



HOW WAS THE TRIAL CONDUCTED?

516 patients with ischemic stroke due to anterior-circulation large-vessel occlusion who had salvageable tissue 4.5 to 24 hours after the onset of stroke were assigned to receive intravenous tenecteplase (0.25 mg per kilogram of body weight, up to 25 mg) or standard medical treatment. The primary outcome was the absence of disability, which was defined as a score of 0 or 1 on the modified Rankin scale (range, 0 to 6, with higher scores indicating greater disability) at day 90. The key safety outcomes were symptomatic intracranial hemorrhage and death.



PATIENTS

WHO

516 Chinese adults

Median age, 67 years

Men: 68%, Women: 32%

CLINICAL STATUS

Large-vessel occlusion of the middle cerebral artery or internal carotid artery

Treatment initiated 4.5 to 24 hours after stroke onset (i.e., after the patient was last known to be well, including after stroke on awakening and unwitnessed stroke)

With salvageable tissue on perfusion imaging

Without access to endovascular thrombectomy

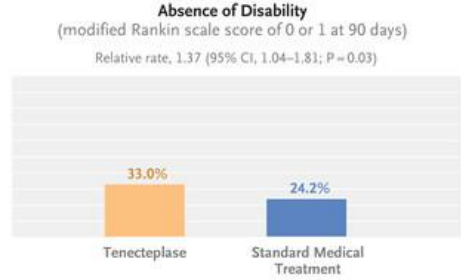
TRIAL DESIGN

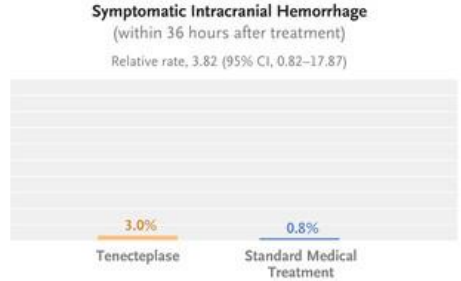
- PHASE 3
- MULTICENTER
- OPEN-LABEL
- BLINDED OUTCOME ASSESSMENT
- RANDOMIZED
- CONTROLLED
- LOCATION: 58 CENTERS IN CHINA

RESULTS

Treatment with tenecteplase resulted in a higher percentage of patients with no disability than standard medical treatment.

The incidence of symptomatic intracranial hemorrhage within 36 hours after treatment appeared to be higher in the tenecteplase group. Mortality at 90 days was similar in the two groups (approximately 13%).





MODIFIED RANKIN SCALE SCORE

The percentage of patients with a modified Rankin scale score of 0 or 1 at 90 days was greater with intravenous tenecteplase than with standard medical treatment.

LIMITATIONS AND REMAINING QUESTIONS

- Treatment was open-label.
- The effect size, although similar to the thrombolytic benefit of tenecteplase within 3 hours after the onset of stroke, was smaller than that of thrombectomy.
- The trial was performed in China, where intracranial atherosclerosis is more prevalent than in Western countries and atrial fibrillation is less prevalent.

CONCLUSIONS

In Chinese patients with ischemic stroke who did not have access to thrombectomy, tenecteplase administered 4.5 to 24 hours after the onset of stroke resulted in a higher percentage of patients with no disability at 90 days than standard medical treatment.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

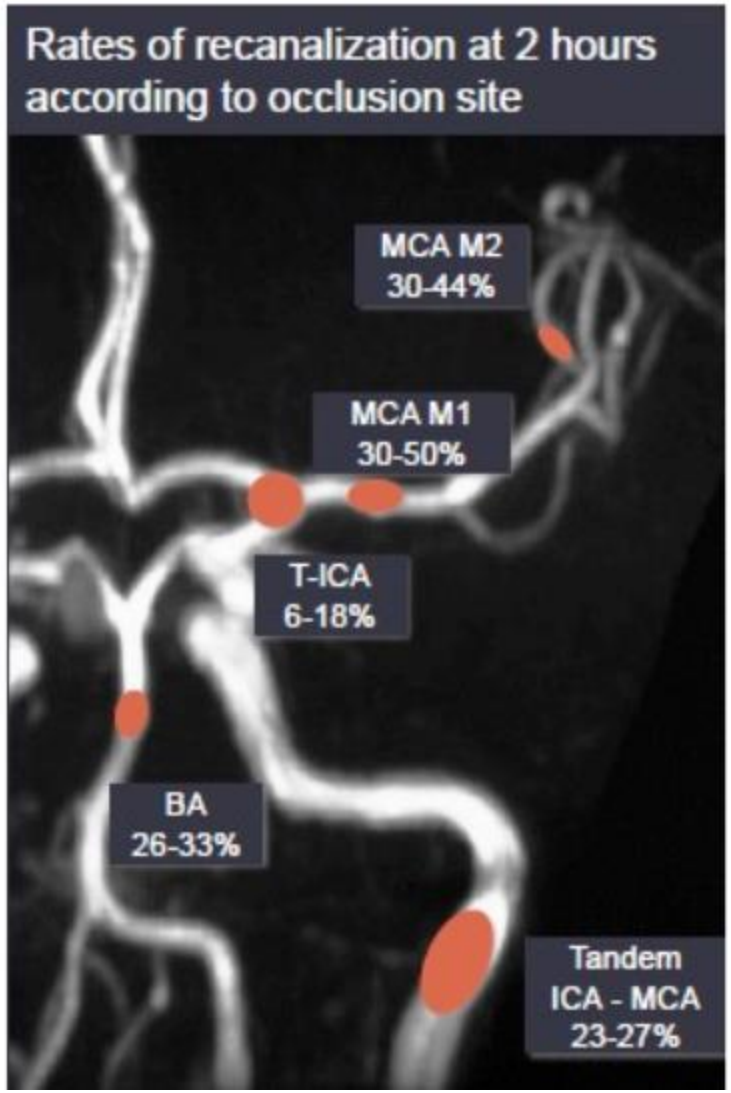
FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT05141305

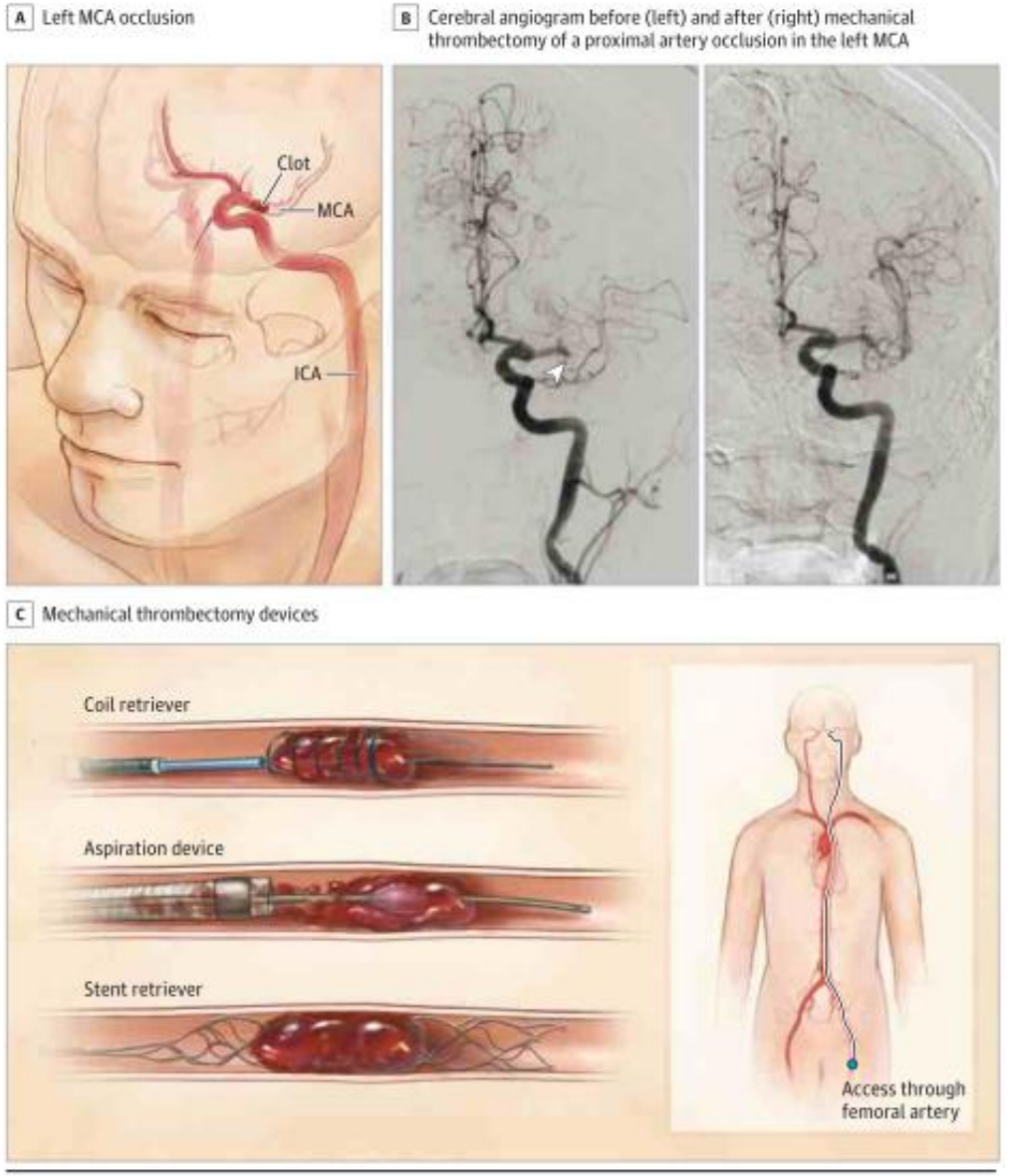
Trial funding: National Natural Science Foundation of China and others

Full citation: Xiong Y, Campbell BCV, Schwamm LH, et al. Tenecteplase for ischemic stroke at 4.5 to 24 hours without thrombectomy. N Engl J Med 2024;391:203-12. DOI: 10.1056/NEJMoa2402980

Réduire les échecs de la thrombolyse



TICI 2b-3 > 80 %



2015

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2015 VOL. 372 NO. 1

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

Berkhemer et et al., NEJM 2015
MR CLEAN

Délai **< 6h**

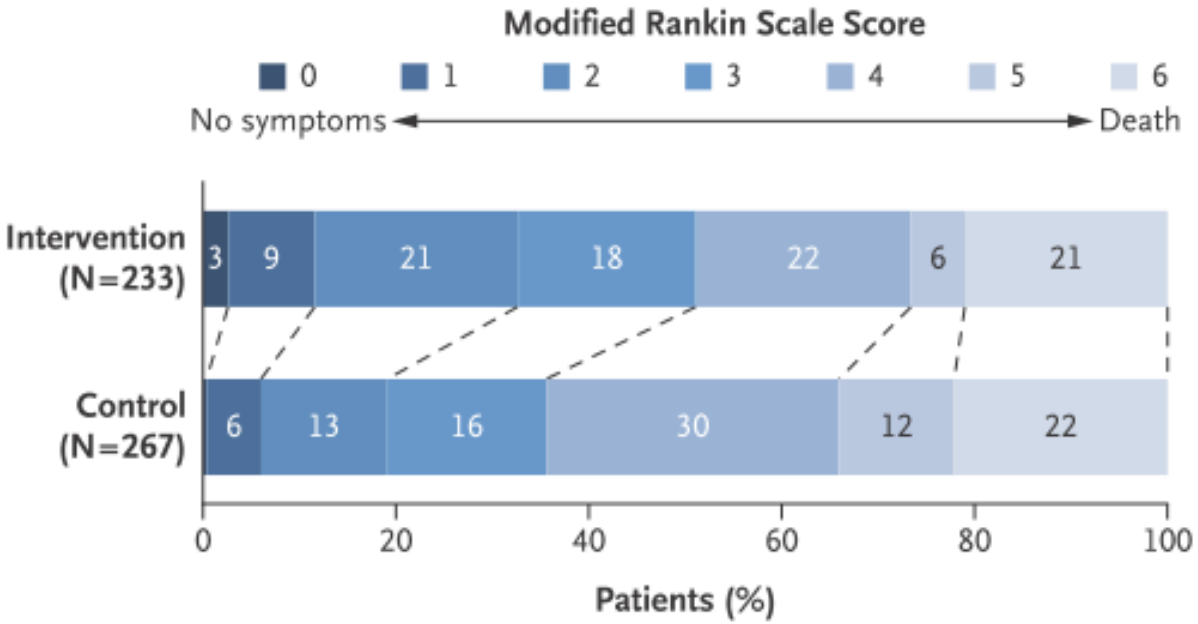
Occlusion proximale circulation antérieure

500 patients:
Meilleur traitement médical vs
Meilleur traitement médical + Thrombectomie mécanique

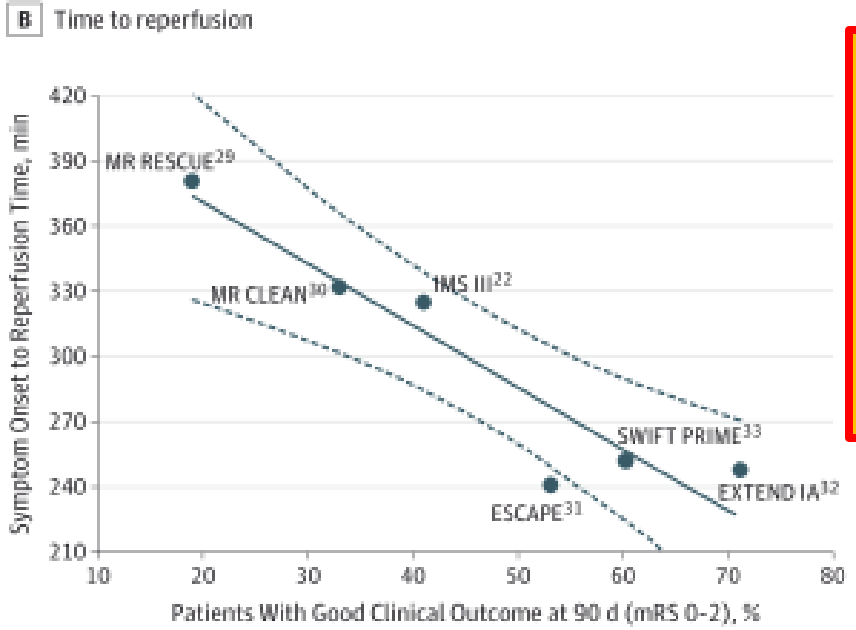
Absence de limite d'âge ou NIHSS
Imagerie Conventionnelle,

Critères de jugement principal
Pronostic fonctionnel

NIHSS moyen à l'admission: 17



mRs ≤ 2 à 3 mois
NNT = 7



Règle 666

≤ 6 heures

NIHSS ≥ 6

ASPECT ≥ 6

Carotidien

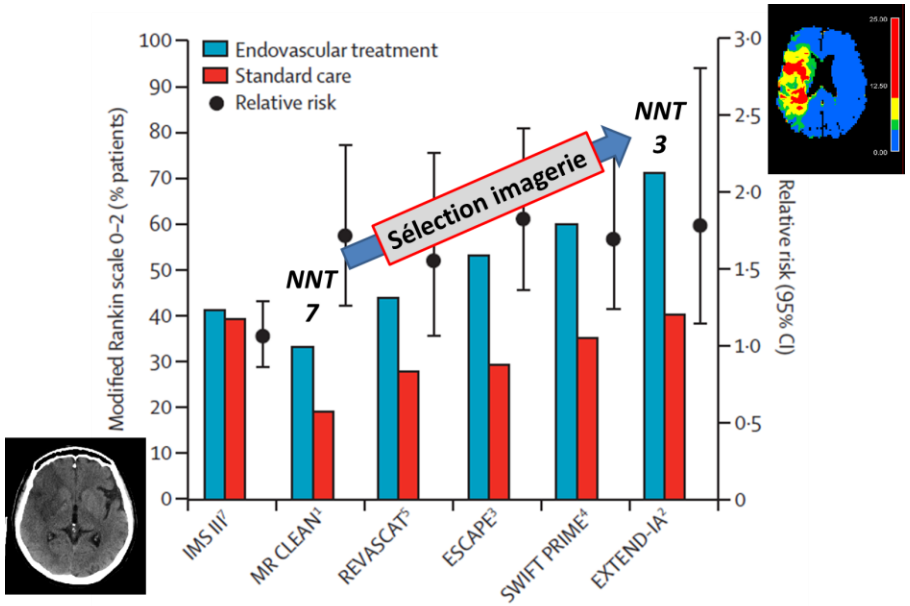
Déterminants de l'efficacité

Recanalisation

Temps

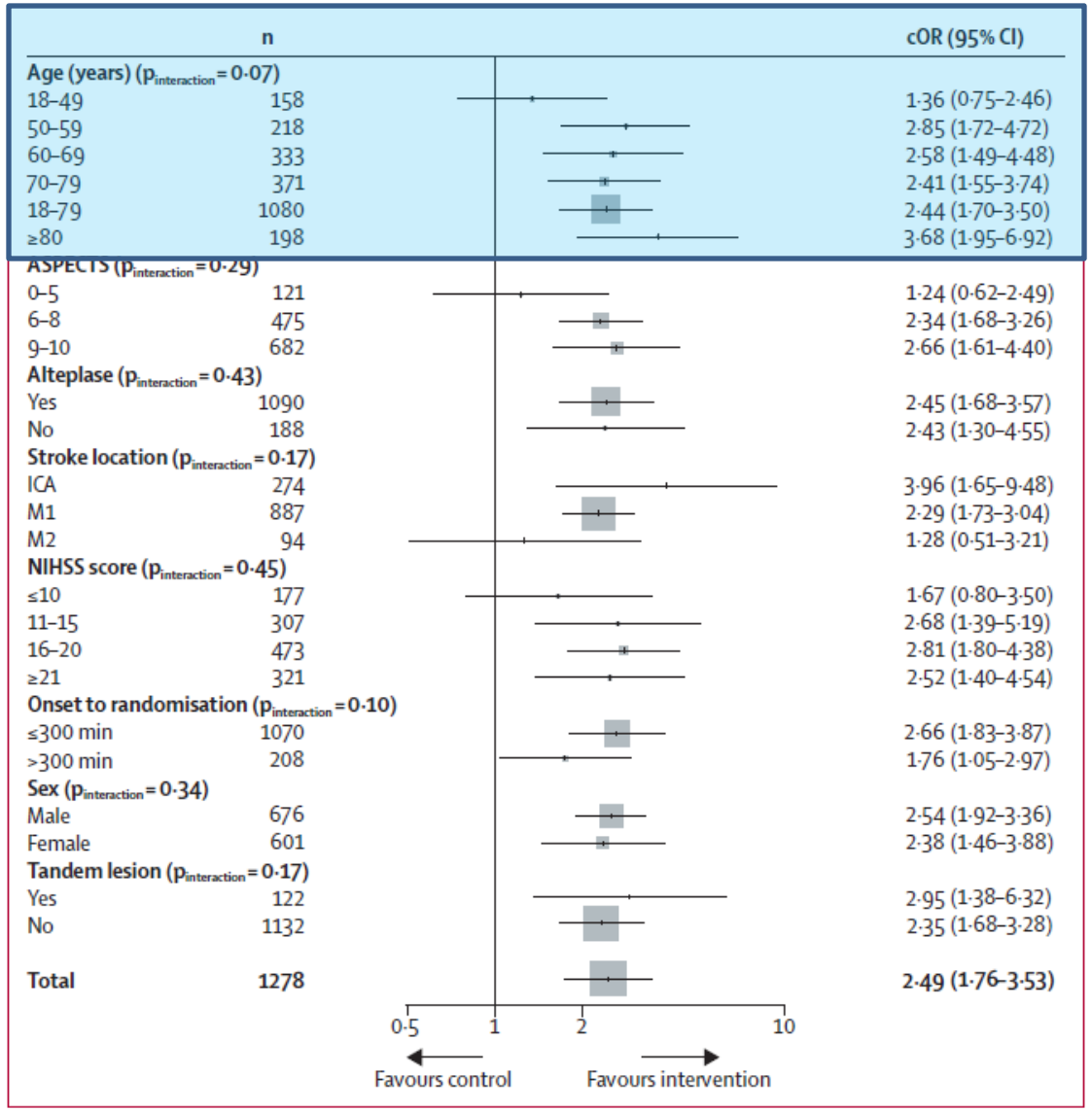
Population

Imagerie

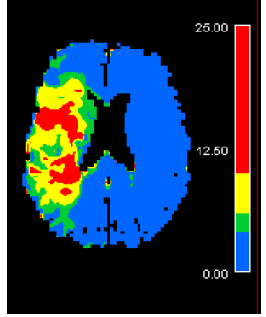


Prabhakaran JAMA 2015

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

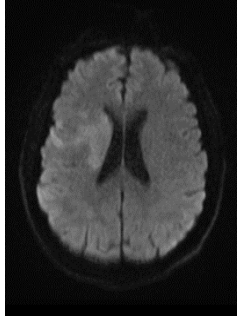


Goyal et al., Lancet 2016



Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (AURORA): a systematic review and individual patient data meta-analysis

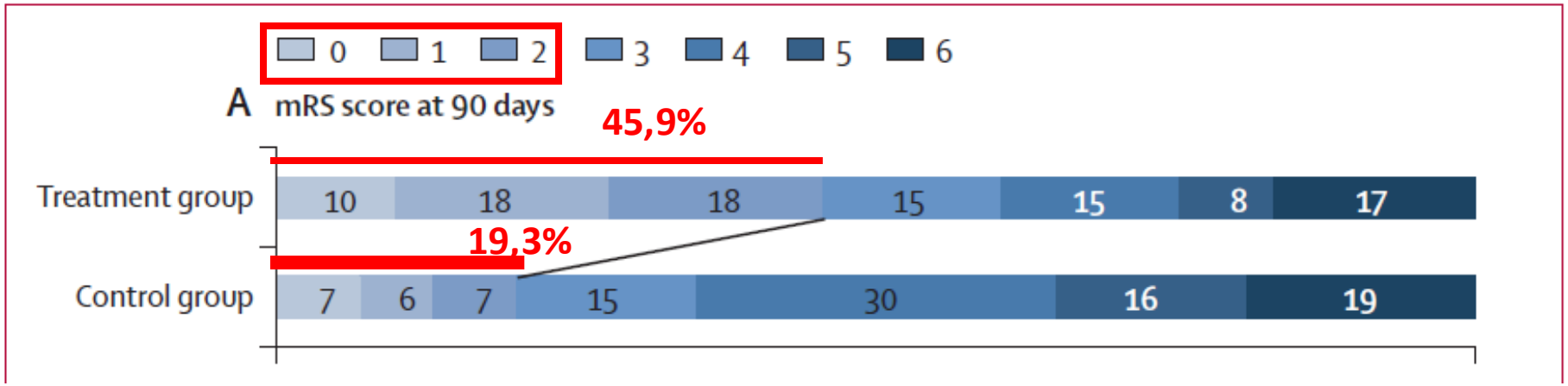
Jovin et al., Lancet 2022



DAWN, DEFUSE 3, ESCAPE, POSITIVE, REVASCAT, RESILIENT

Traitement endovasculaire +/- thrombolyse IV
N = 266

Traitement médical standard
N = 239

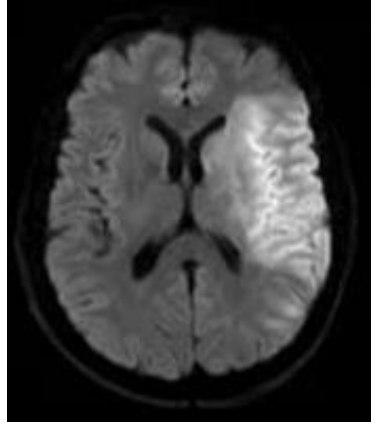


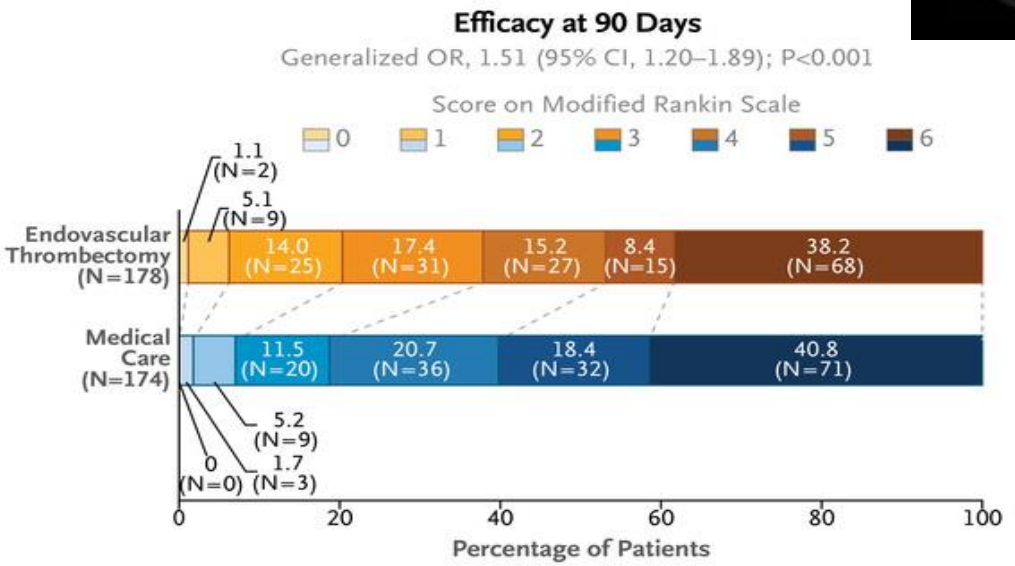
Absence de limite supérieure d'âge…mais mRS 0-1 à l'inclusion

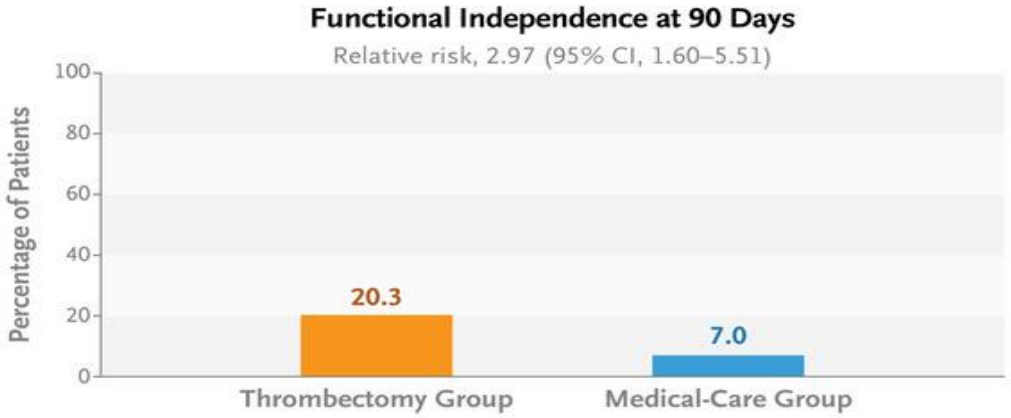
Trial of Endovascular Thrombectomy for Large Ischemic Strokes

Sarraj et al., NEJM 2023 SELECT-2

Infarctus Cérébral < 24h
ASPECT 3-5 ou Volume > 50 cc
18-85 ans; pré-mRS < 2;



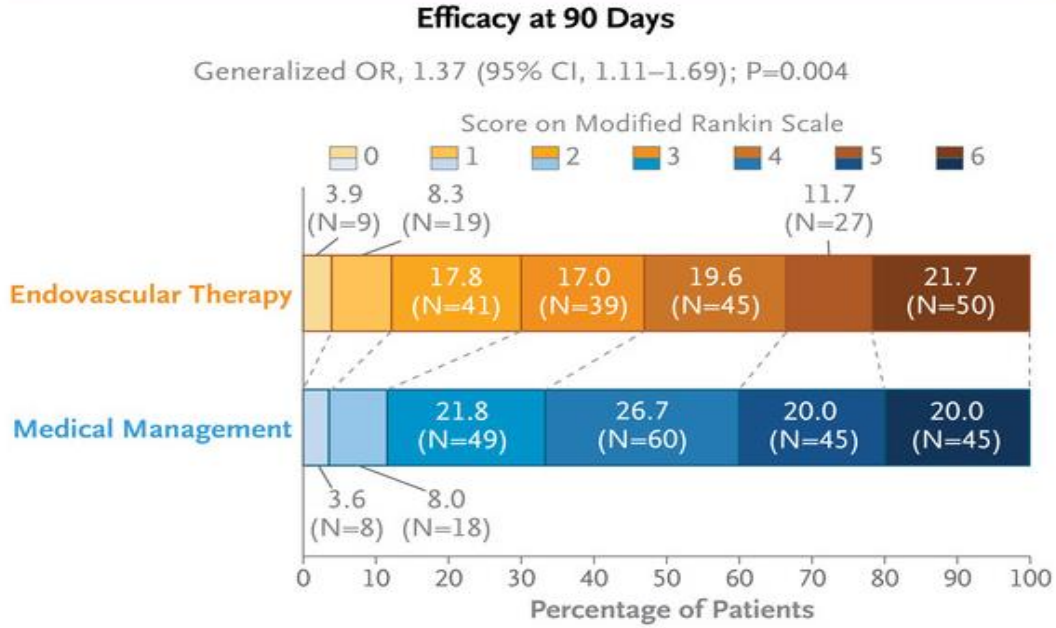




Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct

Huo et al., NEJM 2023 ANGEL-ASPECT

Infarctus Cérébral < 24h
ASPECT 3-5 ou 0-2 + Volume 70-100 cc
18-80 ans; pré-mRS < 2; NIHSS 6-30



Thrombectomy for Stroke with Unrestricted Infarct Size

A PLAIN LANGUAGE SUMMARY

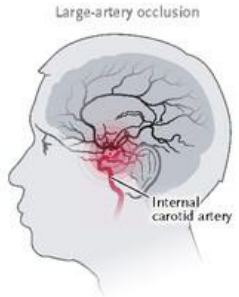
Based on the NEJM publication: Trial of Thrombectomy for Stroke with a Large Infarct of Unrestricted Size by V. Costalat et al. (published May 9, 2024)

In this trial, investigators compared outcomes of thrombectomy plus medical care with outcomes of medical care alone in patients with stroke and a large infarct of unrestricted size.

Large infarcts are defined by an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 0 to 5 on a scale of 0 to 10.

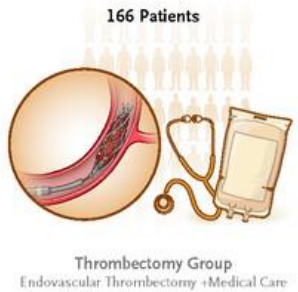
WHY WAS THE TRIAL DONE?

In the initial trials of thrombectomy for stroke with large-artery occlusion in the anterior circulation, patients with the largest infarcts (ASPECTS value, ≤1) were excluded. But because the benefit of thrombectomy did not diminish with larger infarcts in these trials, even patients with the largest infarcts at baseline might benefit.



HOW WAS THE TRIAL CONDUCTED?

333 patients with proximal cerebral vessel occlusion in the anterior circulation and a large infarct (ASPECTS value, ≤5) were assigned to receive either thrombectomy plus medical care or medical care alone. The primary outcome was the score on the modified Rankin scale at 90 days, with higher scores indicating greater disability or death.



PATIENTS

WHO	333 adults
CLINICAL STATUS	At least moderate stroke symptoms
	Able to undergo randomization within 6.5 hours after symptoms began
	Admitted to acute-stroke units or neurologic intensive care units

TRIAL DESIGN

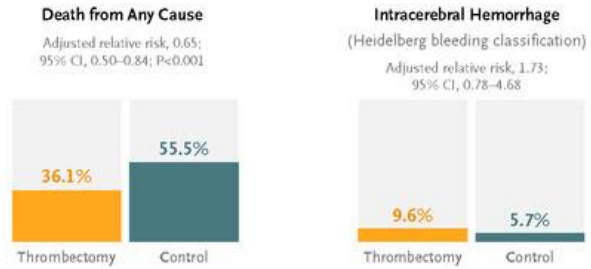
- RANDOMIZED
- PROSPECTIVE
- CONTROLLED
- MULTICENTER
- OPEN-LABEL
- BLINDED OUTCOME EVALUATION

A majority of patients had **a very large infarct** (ASPECTS value, ≤2). Patients with similarly large infarcts were generally excluded from previous trials.

RESULTS

The **modified Rankin scale** score at 90 days favored thrombectomy plus medical care (median score, 4) over medical care alone (median score, 6).

Mortality at 90 days was lower in the thrombectomy group. Thrombectomy led to procedural complications in some patients, and symptomatic intracerebral hemorrhage at 24 hours was more common with thrombectomy than with medical care alone.



Full trial results are available at NEJM.org.

LIMITATIONS AND REMAINING QUESTIONS

- The trial was stopped early because other trials completed in the meantime showed a benefit of thrombectomy in patients with large infarcts of unrestricted size.
- MRI was used for the selection of most patients in the trial, whereas CT is usually used to assess stroke in clinical practice.
- Some patients who were eligible for intravenous thrombolysis therapy did not receive it.

CONCLUSIONS

In patients with stroke with occlusion in the anterior circulation and a large infarct of unrestricted size, thrombectomy plus medical care resulted in better functional outcomes and lower mortality than medical care alone but led to a higher incidence of symptomatic intracerebral hemorrhage.

Links: Full Article | NEJM Quick Take

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT03811769

Funding: Montpellier University Hospital

Full citation: Costalat V, Jovin TG, Albucher JF, et al. Trial of thrombectomy for stroke with a large infarct of unrestricted size. N Engl J Med 2024;390:1677-89. DOI: 10.1056/NEJMoa2314063.

Endovascular vs Medical Management for Late Anterior Large Vessel Occlusion With Prestroke Disability

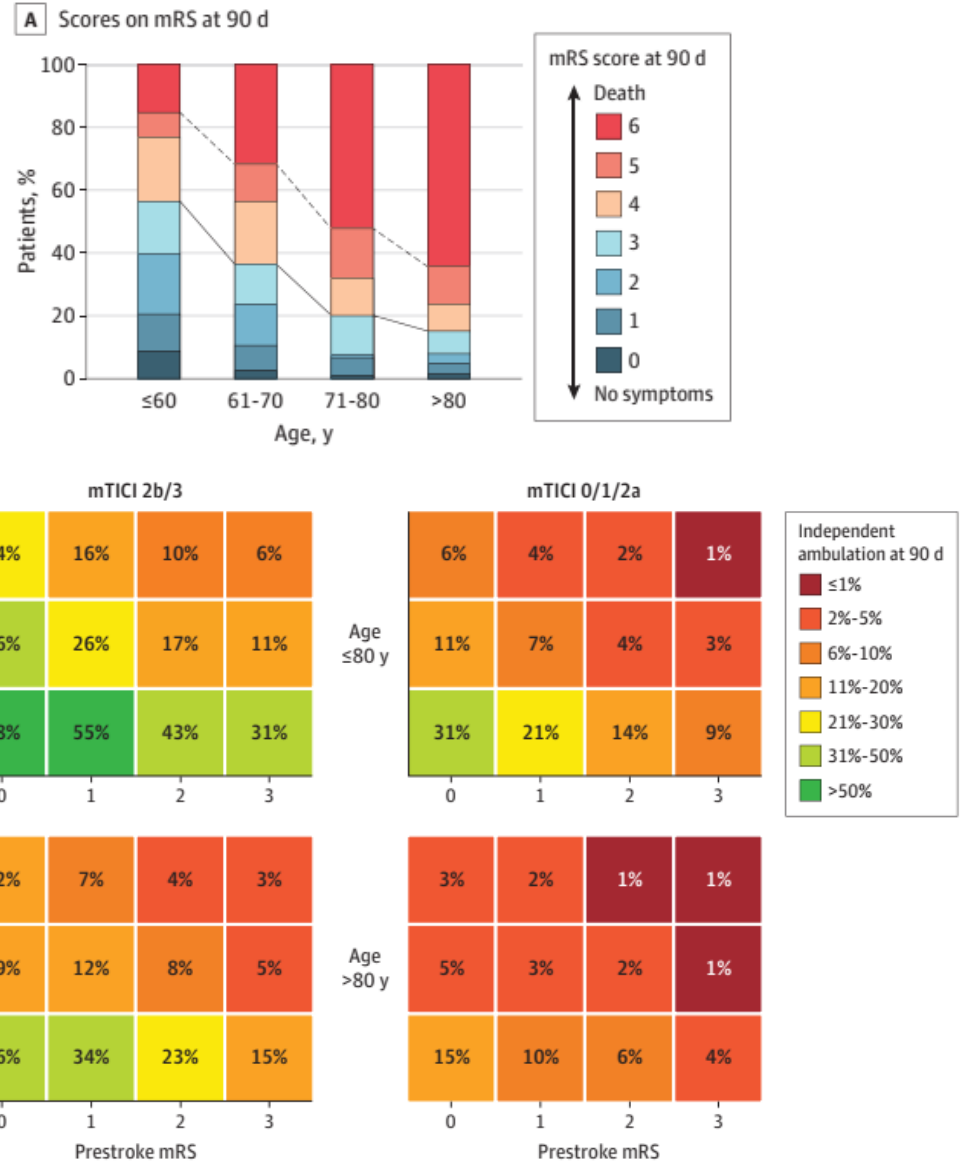
Siegler et al., Neurology 2023

	Multivariable model	
Overall mRS 2–4 (n = 554)		
Medical management	Referent	
Mechanical thrombectomy	3.96 (1.78–8.79)	0.001
Premorbid mRS 2 (n = 276)		
Medical management	Referent	
Mechanical thrombectomy	4.36 (1.01–18.79)	0.048
Premorbid mRS 3 (n = 205)		
Medical management	Referent	
Mechanical thrombectomy	3.80 (1.01–14.24)	0.048
Premorbid mRS 4 (n = 73)		
Medical management	Referent	
Mechanical thrombectomy	4.00 (0.76–21.06)	0.102

Ethique ?

Age and Functional Outcomes in Patients With Large Ischemic Stroke Receiving Endovascular Thrombectomy

Winkelmeier et al., JAMA Network Open 2024



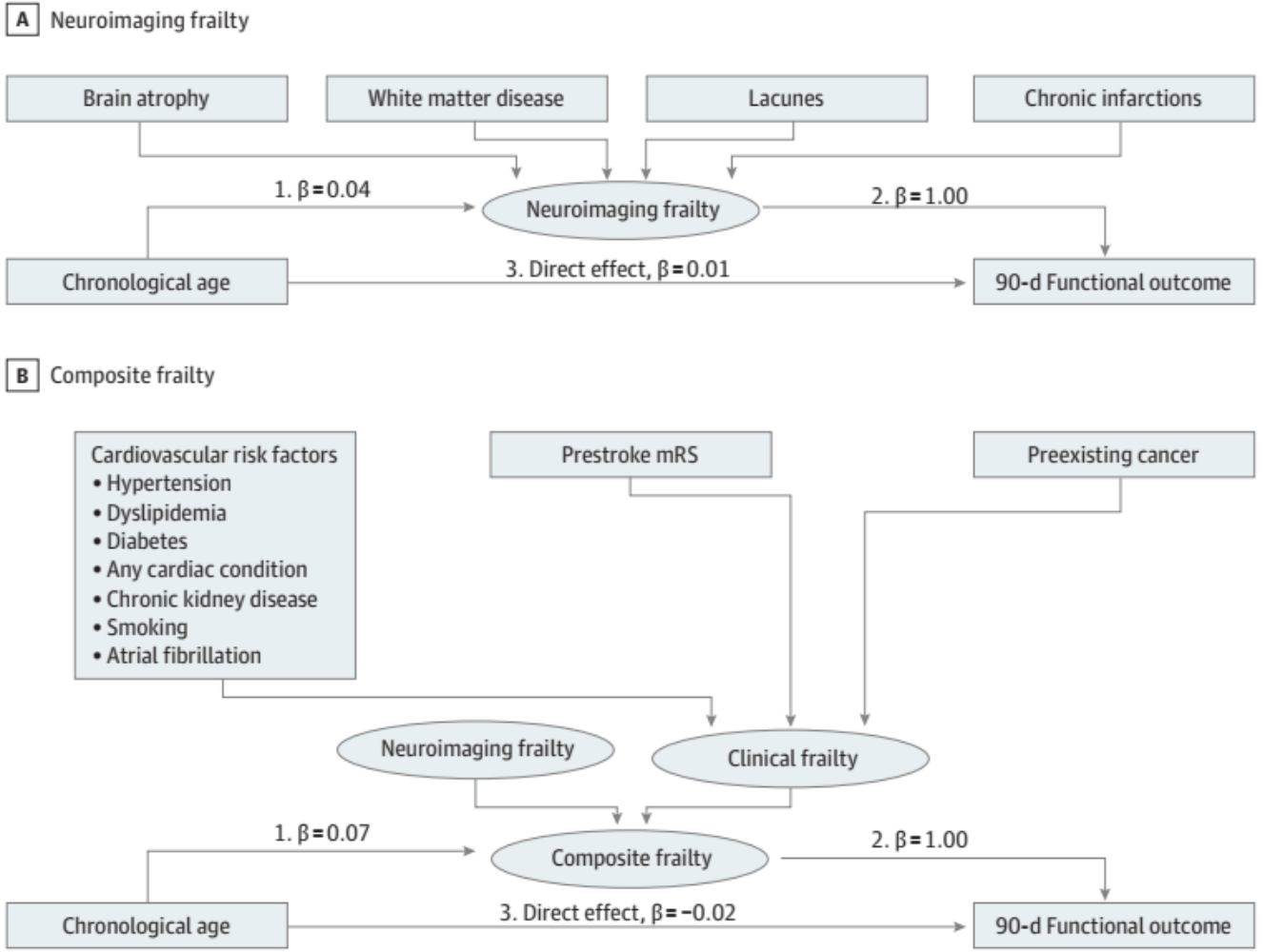
Mediation of Age and Thrombectomy Outcome by Neuroimaging Markers of Frailty in Patients With Stroke

Benali et al., JAMA Network Open 2023

Table 1. Baseline Characteristics

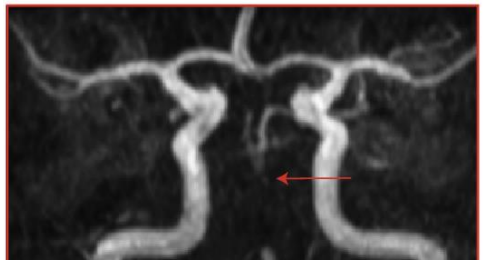
Characteristic	Participants, No. (%) (N = 1102) ≤71 y (n = 555)	>71 y (n = 547)	*P* value
Sex			
Female	238 (42.9)	310 (56.7)	<.001
Male	317 (57.1)	237 (43.3)	
Prestroke mRS score[a]			
0	487 (87.7)	407 (74.4)	<.001
1	51 (9.2)	85 (15.7)	
2	16 (2.9)	50 (9.1)	
3	0	3 (1.0)	
Baseline NIHSS score, median (IQR)[b]	17 (12-21)	17 (13-21)	.06
Comorbidities			
Current smoker	198 (35.7)	34 (6.2)	<.001
Peripheral vascular disease	26 (4.7)	33 (6.1)	.30
Hypertension	321 (57.8)	451 (82.4)	<.001
Hyperlipidemia	221 (39.8)	293 (53.6)	<.001
Diabetes			
Type 1	4 (1.0)	4 (1.0)	.01
Type 2	86 (15.5)	123 (22.5)	
Atrial fibrillation	122 (22.0)	265 (48.4)	<.001
Baseline ASPECTS, median (IQR)[c]	8 (7-8)	8 (7-9)	<.001
Total Fazekas score[d]			
0-1	444 (80.0)	252 (46.1)	<.001
2	63 (11.4)	148 (27.1)	
3-6	48 (8.6)	147 (26.9)	
Global cortical atrophy score[e]			
0	518 (93.3)	300 (54.8)	<.001
1	34 (6.1)	186 (34.0)	
2 or 3	3 (1.0)	61 (11.2)	
CC/IT ratio, median (IQR)	0.10 (0.09-0.13)	0.14 (0.12-0.17)	<.001
Lacunes present	97 (17.5)	175 (32.0)	<.001
≥1 Chronic infarction	57 (10.3)	72 (13.2)	.14
Final infarction volume, median (IQR), mL[f]	27 (9-86)	5 (22-99)	.04
Collaterals			
Good	101 (18.2)	89 (16.3)	.52
Moderate	419 (75.5)	433 (79.2)	
Poor	26 (4.7)	22 (4.0)	
Intracranial occlusion location			
ICA	134 (24.1)	121 (22.1)	.41
M1 branch of middle cerebral artery	395 (71.2)	404 (73.9)	
Intravenous nerinetide treatment	265 (47.7)	284 (51.9)	.17
Intravenous alteplase treatment	345 (62.2)	312 (57.0)	.08

Figure 3. Structural Equation Models Including Different Latent Variables as Possible Mediator



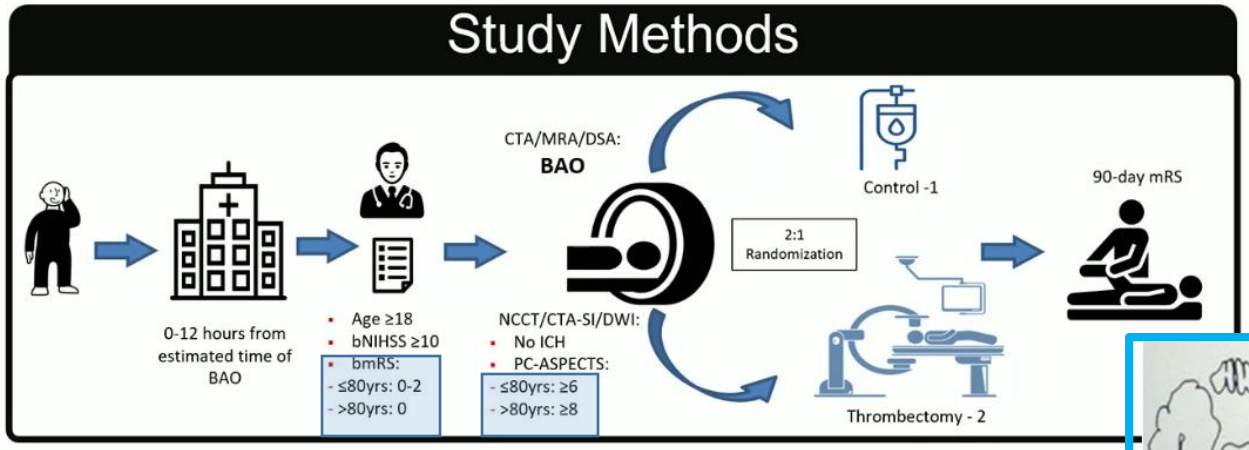
Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion

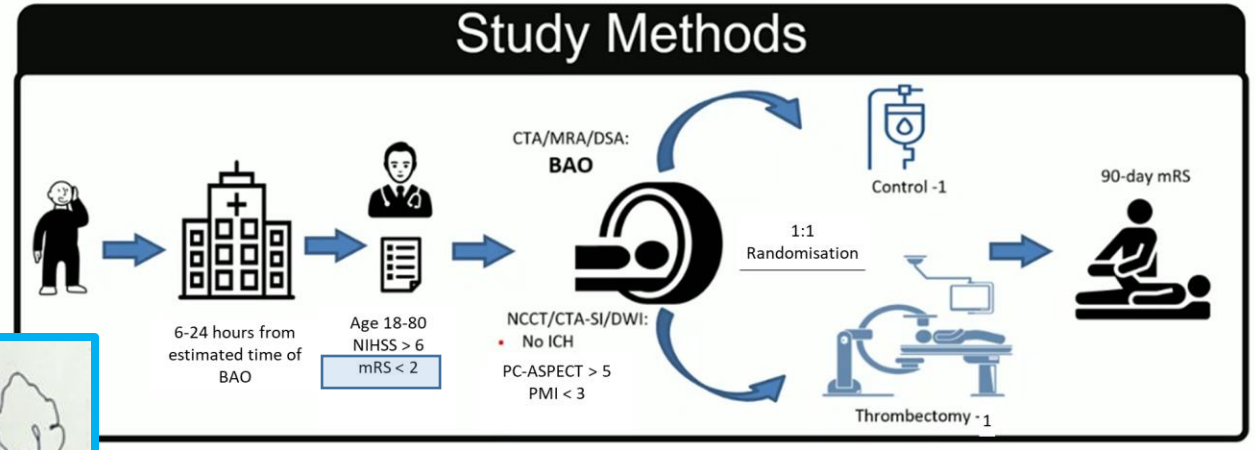
Tao et al –ATTENTION investigators – NEJM 2022



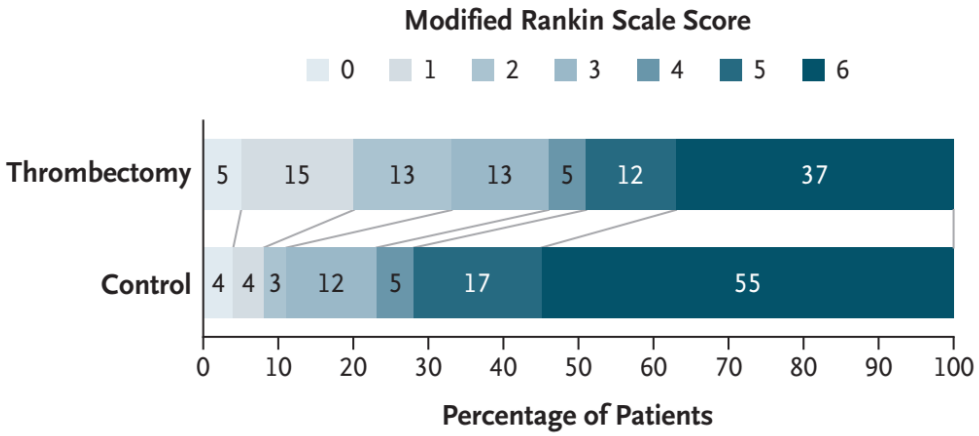
Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion

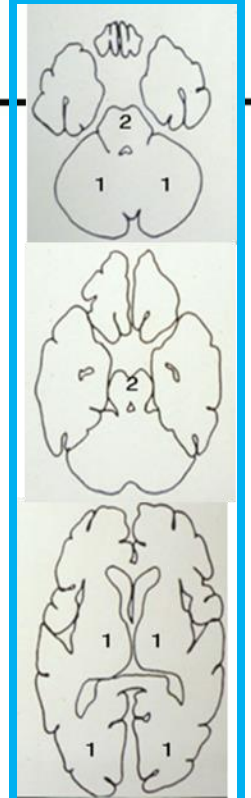
Jovin et al., NEJM 2022



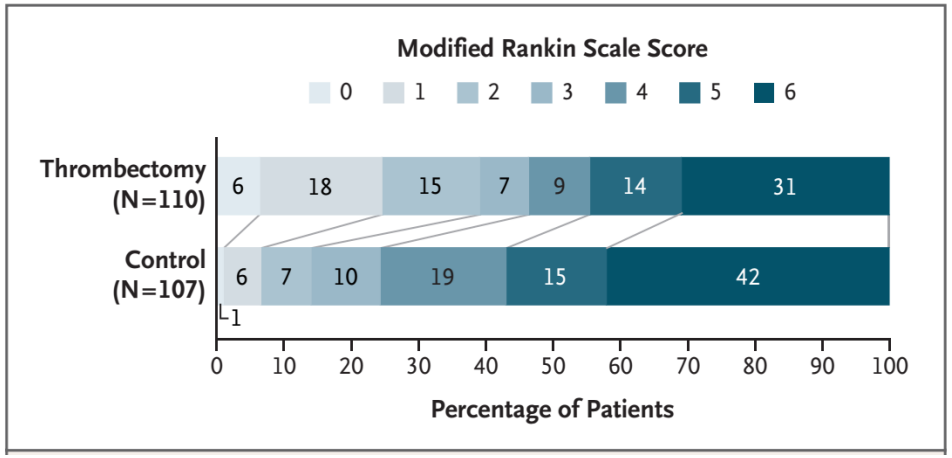


aOR: 2.87 (95% CI, 1.84 to 4.47)



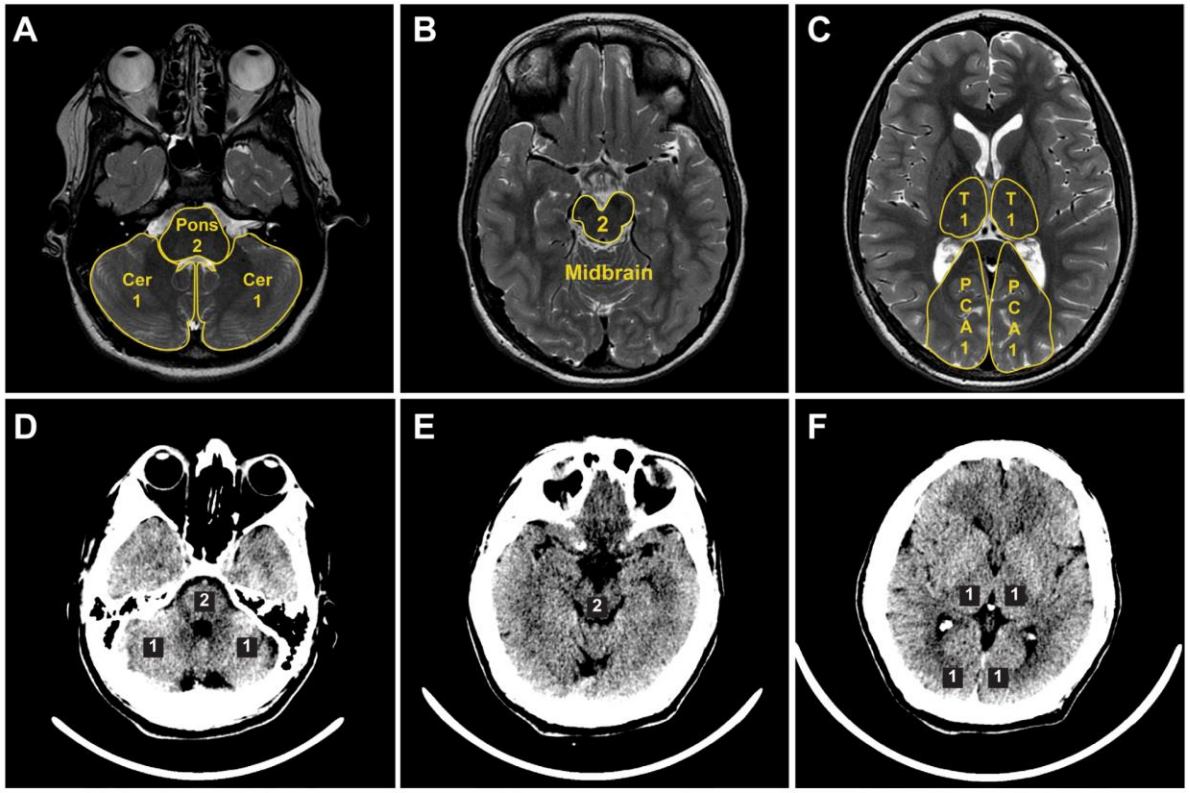


aOR: 2.64 (95% CI, 1.54 to 4.50)



Focused update to guidelines for endovascular therapy for emergent large vessel occlusion: basilar artery occlusion patients

Heit et al., JNIS 2024 // Strbian et al., ESJ 2024



- In patients with acute BAO who meet criteria from the BAOCHE or ATTENTION trials (NIHSS score ≥6, PC-ASPECTS ≥6, CTA with BAO, age 18–89 years), thrombectomy is indicated within 12 hours of last known well (class I, Level B-R).
- In patients with acute BAO who present between 12 and 24 hours from the last known well, NIHSS score ≥6, or PC-ASPECTS ≥6, thrombectomy is reasonable (class IIa, level B-R).
- In patients with acute BAO who present beyond 24 hours from last known well, with NIHSS score ≥6 or PC-ASPECTS ≥6, it may be reasonable to consider thrombectomy on a case by case basis (class IIb, level C-EO).
- In aged <18 years or >89 years presenting with acute BAO, it is reasonable to consider thrombectomy on a case by case basis (class IIb, level C-EO).

Infarctus cérébral par occlusion proximal
< 4h30
=
Place de la Thrombolyse Intraveineuse ?

Augmentation reperfusion précoce

Augmentation reperfusion tardive

Réduction durée procédure

Amélioration microcirculation

Augmentation risque hémorragique

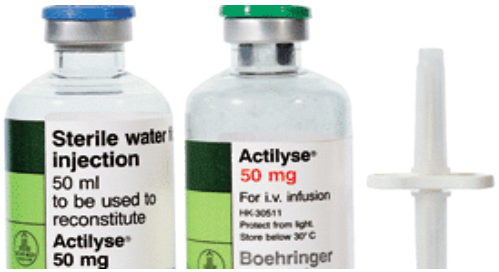
Retarde la thrombectomie

Fragmente le thrombus

Risque d'angioedeme

Coût

+



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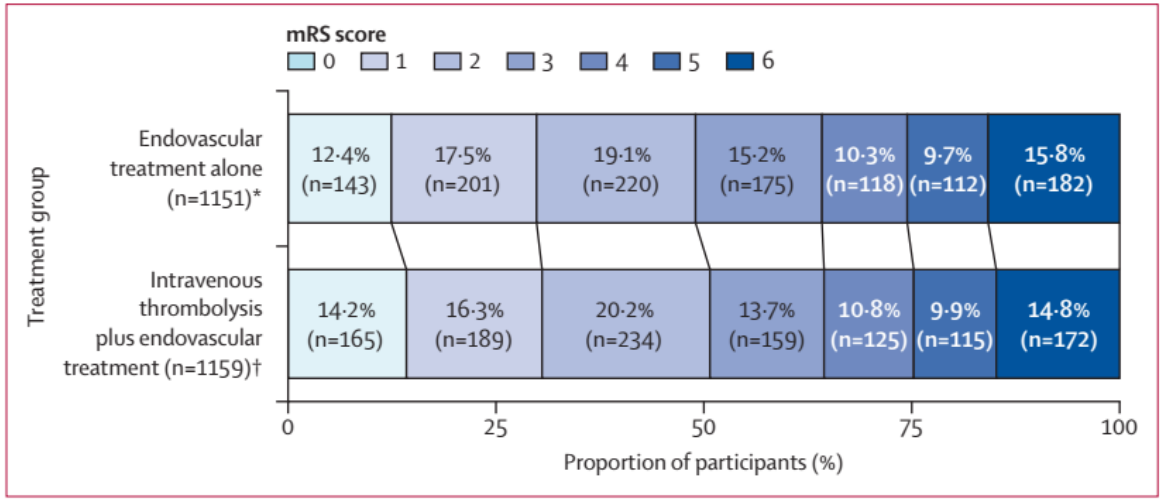
Value of intravenous thrombolysis in endovascular treatment for large-vessel anterior circulation stroke: individual participant data meta-analysis of six randomised trials

Majoie et al., Lancet 2023

6 études Randomisées
1153 patients TM
vs 1160 patients TM+TLY

Etudes de non-infériorité



Adjusted value:
0.89 (95% CI, 0.96 to 1.04); P = 0,14

EUROPEAN STROKE ORGANISATION

For patients directly admitted to a thrombectomy-capable center for an acute ischemic stroke (≤4.5 hours of symptom onset) with anterior circulation large vessel occlusion and who are eligible for both treatments, we recommend intravenous thrombolysis plus mechanical thrombectomy over mechanical thrombectomy alone.

Both treatments should be performed as early as possible after hospital arrival. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis, and intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: **Moderate** ⊕⊕⊕
Strength of recommendation: **Strong** ↑↑

Turc et al., JNIS 2022

Value of intravenous thrombolysis in endovascular treatment for large-vessel anterior circulation stroke: individual participant data meta-analysis of six randomised trials

Majoie et al., Lancet 2023

6 études Randomisées
1153 patients TM
vs 1160 patients TM+TLY

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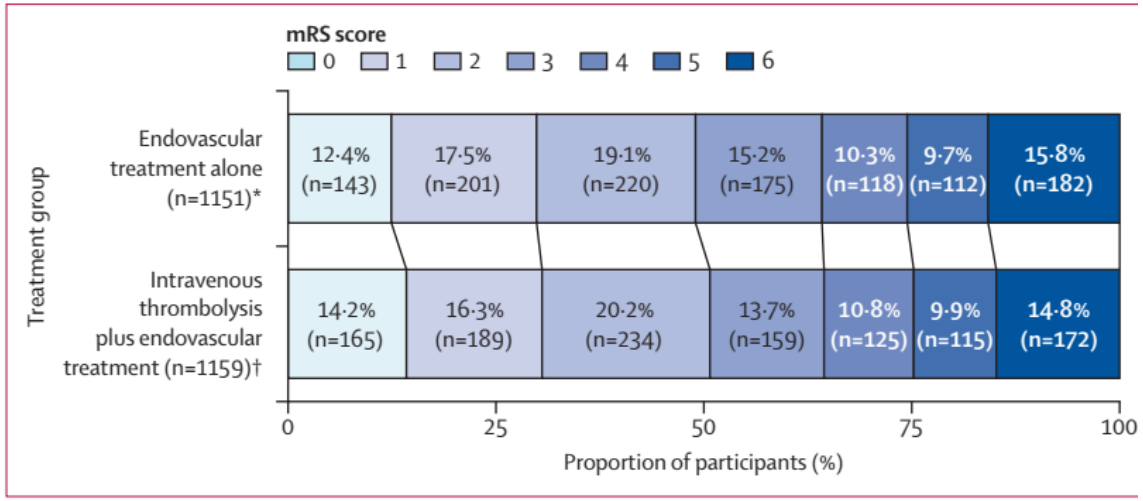
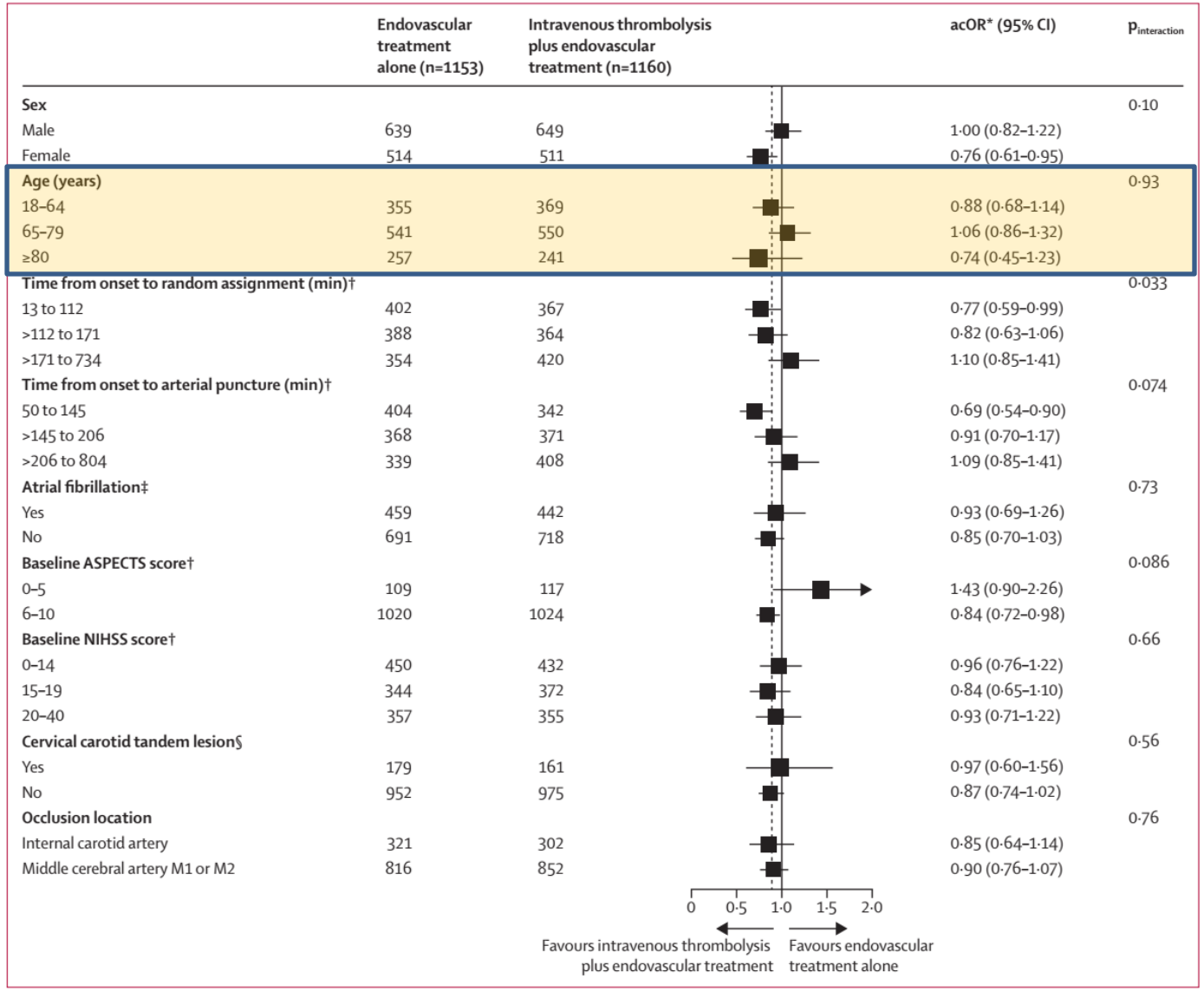
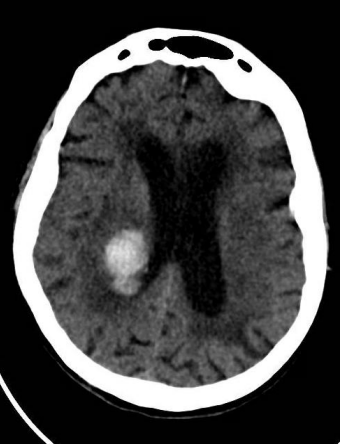


Adjusted value:
0.89 (95% CI, 0.96 to 1.04); P = 0,14





Leading Opinion

International Journal of Stroke WSO

International Journal of Stroke
2024, Vol. 19(5) 482–489

DOI: 10.1177/17474930241250259
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Sage

Treatment for intracerebral hemorrhage: Dawn of a new era

David J Seiffge[1] and Craig S Anderson[2,3]

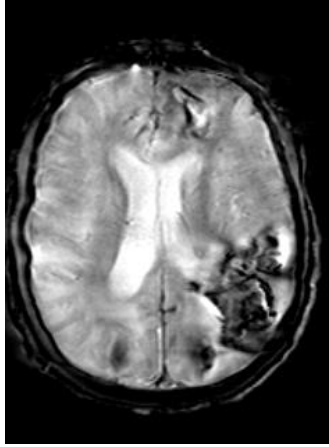
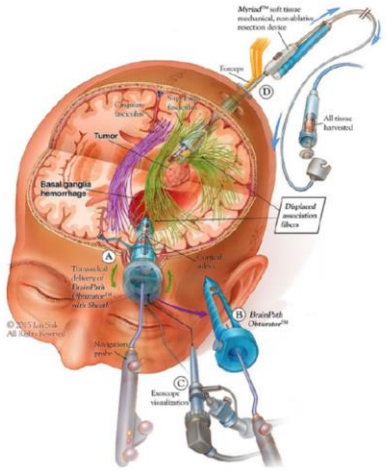


Figure 3. Care bundle approach for hyperacute treatment of intracerebral hemorrhage.[2,3]

Anticoagulant reversal	Blood pressure lowering	Neurosurgery referral	Physiological control
Appropriate reversal agent for therapeutic anticoagulation (i.e. 4-factor prothrombin complex concentrate [PCC], Idarucizumab or Andexanet alfa) within 90 minutes of arrival	**SBP target of 130 to 140mmHg** for patients arriving within 6 hours of onset with an SBP >150mmHg needle-to-target time of <60 minutes	**Referral of suitable patients for neurosurgical evaluation** all patients with good pre-morbid function and any of the following: GCS <9 posterior fossa ICH obstructed 3rd/4th ventricle hematoma volume>30ml "immediate"	**glucose target of 6.1–7.8 mmol/L for patients without Diabetes** (7.8–10.0 mmol/L for patients with diabete) **treatment of pyrexia (**goal body temperature of less than 37.5°C) "within 1 hour"

URGENCE THERAPEUTIQUE

Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage



Pradilla et al., NEJM 2024
ENRICH

- Age 18–80 years
- Pre-randomization head CT demonstrating an acute, spontaneous, primary ICH
- ICH volume between 30 and 80 ml as calculated by the ABC/2 method
- Study intervention can reasonably be initiated within 24 h after the onset of stroke symptoms. If the actual time of onset is unclear, then the onset will be considered the time that the subject was last known to be well
- Glasgow Coma Score GCS 5–14
- Historical Modified Rankin Score 0 or 1

RESEARCH SUMMARY

Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage

Pradilla G et al. DOI: 10.1056/NEJMoa2308440

CLINICAL PROBLEM

Current treatment guidelines for a spontaneous intracerebral hemorrhage (ICH) support surgical evacuation of the hematoma by means of conventional craniotomy only as lifesaving treatment, because randomized trials have not shown improvement in functional outcomes except in selected subgroups. Whether early minimally invasive surgical removal of the hematoma might improve functional outcomes is unknown.

CLINICAL TRIAL

Design: A prospective, multicenter, open-label, adaptive, randomized trial assessed early (within 24 hours) minimally invasive surgical removal of the hematoma as compared with guideline-based medical management in patients with an acute supratentorial ICH.

Intervention: 300 adults presenting within 24 hours after a lobar or anterior basal ganglia ICH with a hematoma volume of 30 to 80 ml were randomly assigned to minimally invasive trans-sulcal parafascicular surgery plus medical management or medical management alone. The primary efficacy end point was the mean score for disability on the utility-weighted modified Rankin scale (UW-mRS) at 180 days (range, 0 to 1, with higher scores indicating better outcomes).

RESULTS

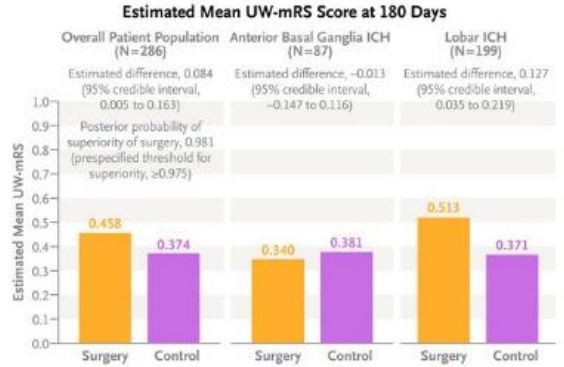
Efficacy: Among evaluable patients, the mean UW-mRS score was better with surgery than with medical management alone. The benefit of surgery appeared to be attributable to intervention for lobar hemorrhages and not for anterior basal ganglia hemorrhages.

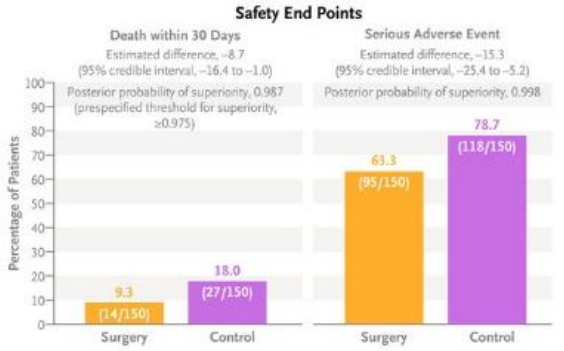
Safety: The percentage of patients who died within 30 days was lower in the surgical group.

LIMITATIONS AND REMAINING QUESTIONS

- The trial excluded patients with hematoma volumes of <30 or >80 ml and those with substantial thalamic or intraventricular extension.
- Recruitment of patients with anterior basal ganglia hemorrhages was halted for futility after relatively few patients had been enrolled, so inferences of potential benefit in these patients are limited.

Links: Full Article | NEJM Quick Take | Editorial





CONCLUSIONS

In patients presenting within 24 hours after an acute supratentorial lobar ICH of 30 to 80 ml, minimally invasive surgical evacuation of the hematoma plus guideline-based medical management improved functional outcomes as compared with medical management alone.

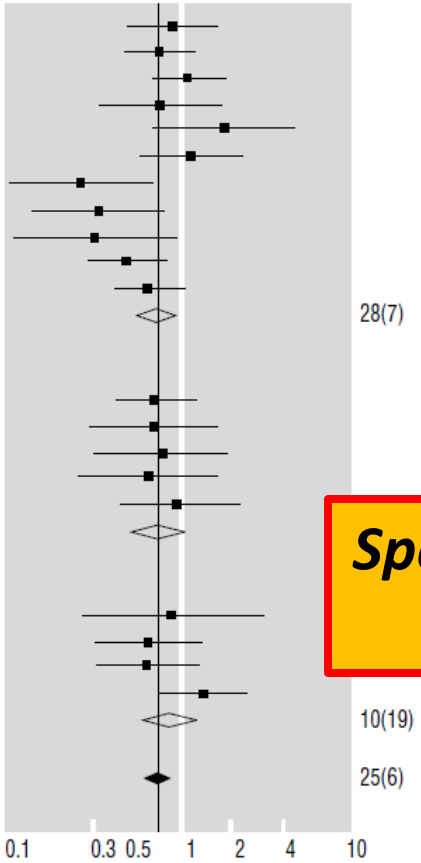
1975

Admission en USINV

Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke

Stroke Unit Trialists' Collaboration *Langhorne et al., BMJ 1997*

Trial	Treatment observed/total	Control observed/total	Observed minus expected	Variance	Odds ratio (95% CI) (Treatment:control)	Odds reduction (SD)
Dedicated stroke unit *v* general medical ward						
Dover[11]	50/98	48/89	-1.36	11.70		
Edinburgh[12]	66/155	78/156	-5.77	19.39		
Goteborg-Ostra[13]	49/215	43/202	1.57	17.95		
Kuopio[17]	22/50	23/45	-1.68	5.97		
Montreal[18]	57/65	52/65	2.50	4.44		
Nottingham[21]	28/98	21/76	0.40	8.71		
Orpington (1995)[23]	18/36	30/37	-5.67	4.17		
Orpington (1993)[22]	9/53	19/48	-5.69	5.10		
Perth[24]	6/29	14/30	-3.83	3.36		
Trondheim[26]	41/110	61/110	-10.00	13.84		
Umea[27]	51/110	105/183	-7.57	17.16		
Subtotal	397/1019	494/1041	-37.10	111.68		28(7)
Mixed assessment/rehabilitation unit *v* general medical ward						
Helsinki[15]	36/121	46/122	-4.83	10.64		
Illinois[16]	22/56	17/35	-2.00	5.35		
New York[19]	15/42	17/40	-1.39	4.94		
Newcastle[20]	18/34	21/33	-1.79	4.14		
Uppsala[28]	40/60	35/52	-0.18	6.22		
Subtotal	131/313	136/282	-10.19	34.26		
Dedicated stroke unit *v* mixed assessment/rehabilitation unit						
Dover[11]	11/18	18/28	-0.35	2.61		
Nottingham[21]	34/78	32/63	-2.51	8.74		
Orpington(1993)[22]	24/71	33/73	-4.10	8.67		
Tampere[25]	43/98	42/113	3.52	12.69		
Subtotal	112/265	125/277	-3.44	32.70		10(19)
Total	640/1597	755/1600	-50.74	178.64		25(6)



mRs ≤ 2 à 3 mois
66% vs 58 %
NNT = 12,5

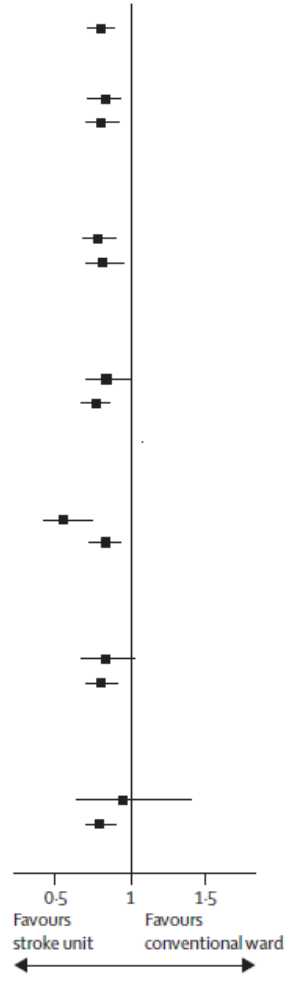
UNV pour TOUS

Spécificités du sujet âgé !
USINV dédiées ?

Stroke-unit care for acute stroke patients: an observational follow-up study *Candelise et al., Lancet 2007*

	Stroke unit n	Stroke unit N	Conventional ward n	Conventional ward N
Overall	2611	4936	4112	6636
Age				
Under 75 years	855	2513	1097	2758
Over 75 years	1756	2423	3033	3878
OR (95%) interaction 1·05 (0·89–1·25)				
Sex				
Women	1390	2346	2358	3441
Men	1221	2590	1754	3195
OR (95%) interaction 0·98 (0·82–1·16)				
Time of admission				
Within 6 h	1113	1926	1631	2526
After 6 h	1498	3009	2481	4110
OR (95%) interaction 0·91 (0·76–1·09)				
Intracranial haemorrhage				
Yes	157	412	575	859
No	2454	4524	3537	5777
OR (95%) interaction 1·56 (1·16–2·10)				
…al fibrillation				
	562	794	976	1280
	2049	4142	3136	5356
…(95%) interaction …3 (0·77–1·24)				
…sciousness				
…onscious	601	675	1191	1303
Conscious	2010	4261	2921	5333
OR (95%) interaction 0·89 (0·64–1·24)				

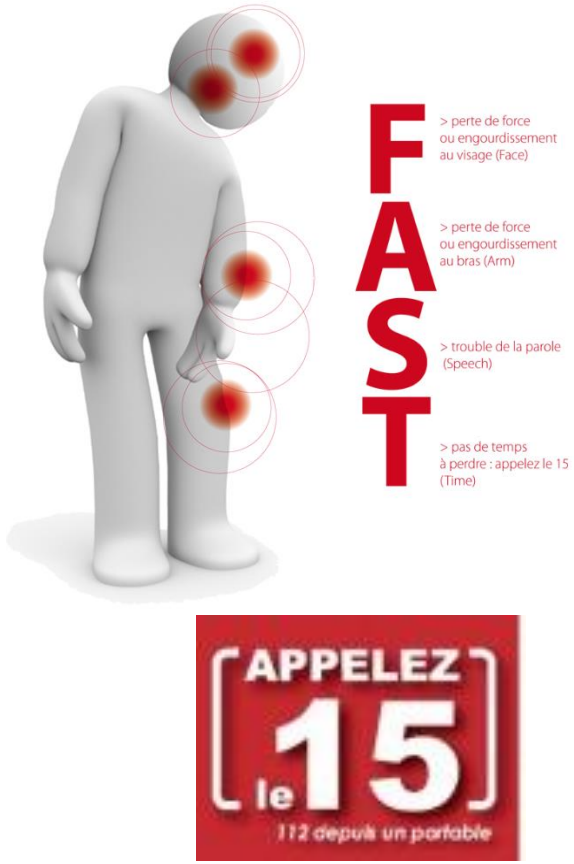
Odds ratio 95% CI



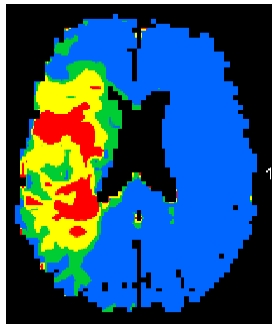
Conclusion

PREVENIR

IDENTIFIER / REAGIR



FILIARISER



UNV dédiée

PERSONNALISER LES PRISES EN CHARGE