2024 MID-ATLANTIC CONFERENCE

12th ANNUAL CURRENT CONCEPTS IN VASCULAR THERAPIES

2024

Carotid Occlusions

What Do We Do Now?

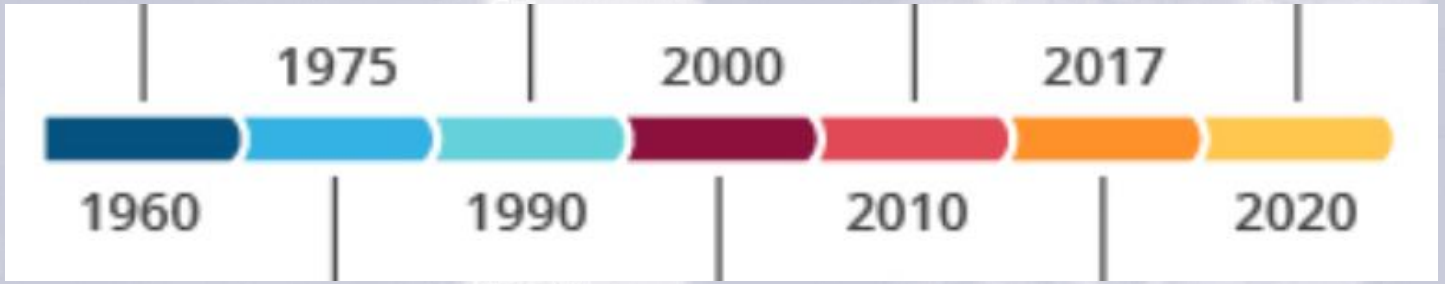
Todd W Gensler MD FACS

April 19, 2024

CAROTID OCCLUSIONS

- Natural History

- Therapies over Time
  - Acute
  - Chronic



- Current Recommendations

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NAT'L HISTORY ICA OCCLUSION

- 15-45% pts have complete Circle of Willis
- 40-69% PRESENT W/ SIGNIFICANT DEFICIT
- PTS CAN HAVE DELAYED CVA AFTER ICA OCCLUSION

Delayed stroke following carotid occlusion

Seth Finklestein, M.D., George M. Kleinman, M. D., Richard Cuneo, M.D., and J. Richard Baringer, M. D. | AUTHORS INFO & AFFILIATION

January 1980 issue • 30 (1) 84 • https://doi.org/10.1212/WNL.30.1.84

BAD

OPINION | VOLUME 140, ISSUE 2, P181-191, AUGUST 1980

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PDF [1 MB]

An overview of the stroke problem in the carotid territory

Allan D. Callow, MD • Show footnotes

DOI: https://doi.org/10.1016/0002-9610(80)90002-1

AJS The American Journal of Surgery®

- 1044 pts w/ ICA Occlusion- CTS
  - 25% had new stroke over 44 months
  - Other studies→new stroke 23%/yr

June 21, 1976

Joint Study of Extracranial Arterial Occlusion

X. Internal Carotid Artery Occlusion

William S. Fields, MD; Noreen A. Lemak, MD

Author Affiliations

JAMA. 1976;235(25):2734-2738. doi:10.1001/jama.1976.03260510028020

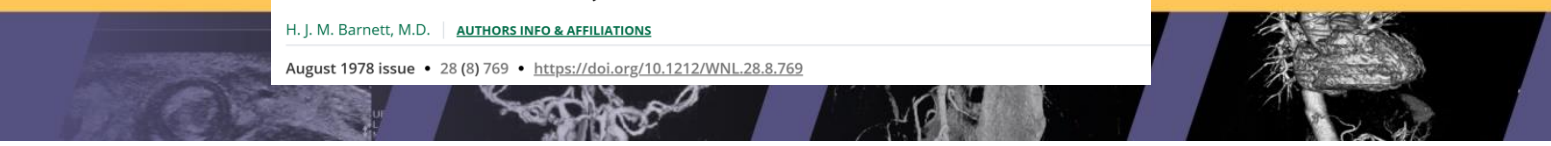
ARTICLES | August 1, 1978

Delayed cerebral ischemic episodes distal to occlusion of major cerebral arteries

H. J. M. Barnett, M.D. | AUTHORS INFO & AFFILIATIONS

August 1978 issue • 28 (8) 769 • https://doi.org/10.1212/WNL.28.8.769

Neurology®



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Sept 22, 1969

Joint Study of Ext
IV. A Review of Su

William F. Blaisdell, MD; Roy H. Clauss, MD

» Author Affiliations

JAMA. 1969;209(12):1889-1895. doi:10.10(

Intracranial Hemorrhage Following Surgical Revasc cute Stroke

Edwin J. W

ew More +

Page Range
Volume/Iss
DOI link: h

OF
URGERY
ANS SINCE 1944

- Blaisdell—42% morta
- Wylie—55%
- Meyer—16-55%

Ann Surg. 1986 Jan; 203(1): 82–89.
doi: 10.1097/00000658-198601000-00014

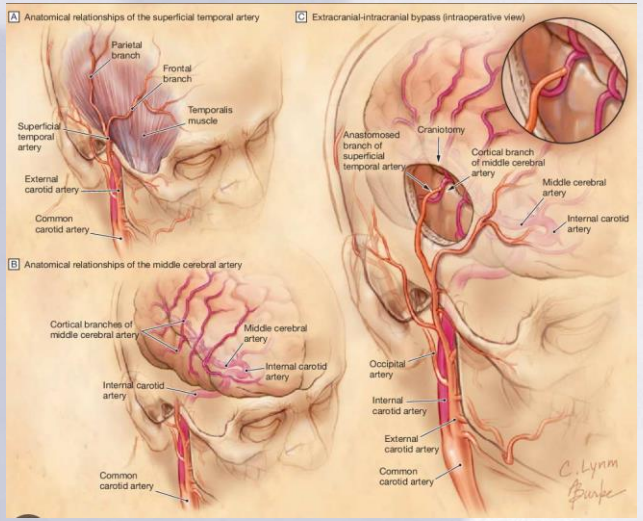
PMCID: PMC1251043
PMID: 3942424

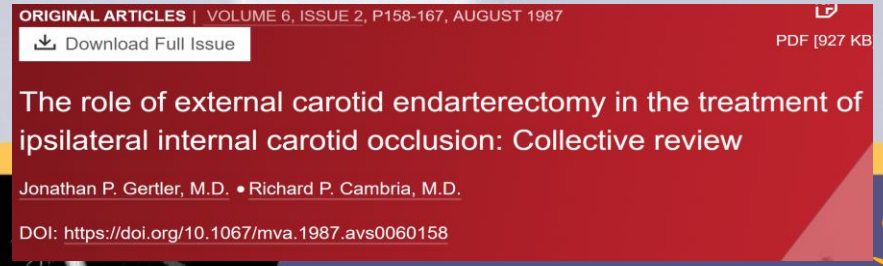
Emergency carotid endarterectomy for patients with acute carotid occlusion and profound neurological deficits.

F B Meyer, T M Sundt, Jr, D G Piepgras, B A Sandok, and G Forbes

CHRONIC CAROTID OCCLUSION—80'S

- EC-IC Bypass
  - Yasargill—1969
  - EC-IC BYPASS STUDY
- Carotid Endarterectomy (std)
  - NO BENEFIT
- ECA Endarterectomy
  - LIMITED ROLE





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Failure of Extracranial–Intracranial Arterial Bypass to Reduce the Risk of Ischemic Stroke — Results of an International Randomized Trial

Author: The EC/IC Bypass Study Group * Author Info & Affiliations

Published November 7, 1985 | N Engl J Med 1985;313:1191-1200 | DOI: 10.1056/NEJM198511073131904
VOL. 313 NO. 19

- Symptomatic ICA/MCA disease (stenosis or occlusion)
- 714--best medical care
- 663—BMC + EC-IC bypass
- Avg F/U 55.8 months.

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DEFINITIONS

- SYMPTOMATIC DISEASE
  - MILD CVA OR TIA w/in 3 months
- ANATOMIC CONSIDERATIONS
  - stenosis or occlusion of the trunk or major branches before the bifurcation or trifurcation of the MCA
  - stenosis of the ICA at or above the C-2 vertebral body
  - occlusion of the ICA
- MEDICAL THERAPY
  - ASA 325mg QID
  - Anti-hypertensives

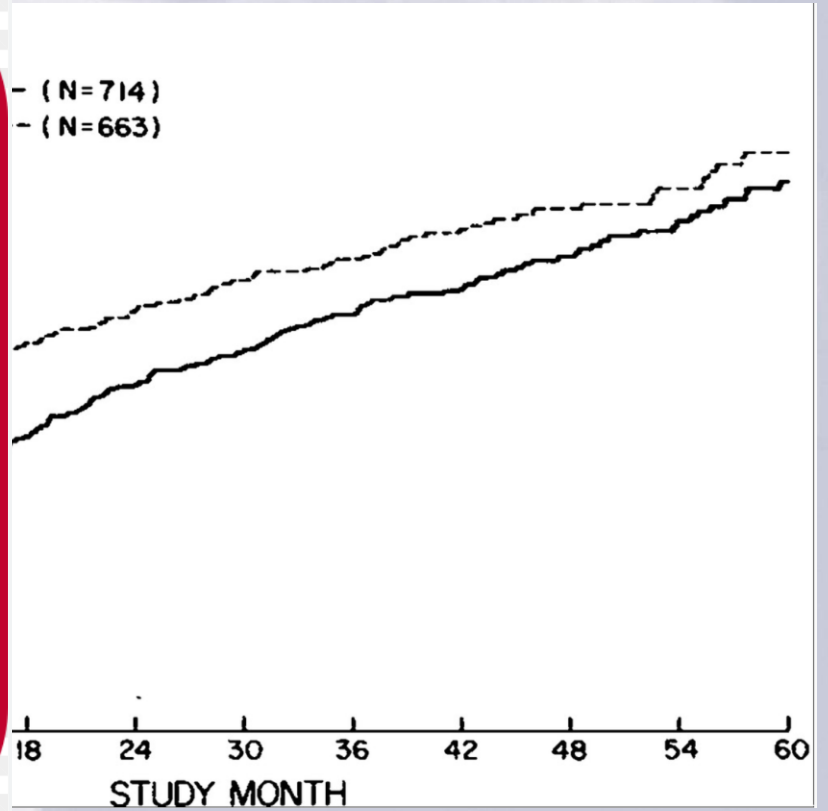
Table 1. Entry Characteristics of 1377 Study Participants.

Characteristics	Treatment Group	
	Medical	Surgical
No. of patients		
Age (mean yr)		
Sex (%)		
Male		
Female		
Randomization diagnosis (%)		
Transient ischemic attack		
Minor stroke		
Other medical problems (%)		
Hypertension		
Diabetes		
Angina pectoris		
Prior myocardial infarction		
Intermittent claudication		
Medications at entry (%)		
Platelet antiaggregants		
Antihypertensive agents		
Blood pressure at entry (mean mm Hg)		
Systolic		
Diastolic		
Most distal angiographic lesion (%)*		
Middle cerebral artery		
Stenosis		
Occlusion		
Internal carotid artery		
Stenosis (above C-2)	16.7	15.4
Occlusion, no symptoms†	38.7	37.0
Occlusion, recurrent symptoms	20.6	21.1

*Refers to the most distal angiographic lesion for which the patient was randomized, ignoring the proximal part of tandem lesions.

†No symptoms were experienced between angiographic demonstration of the occlusion and randomization.

ALL STROKES—FATAL AND NON-FATAL



MAJOR STROKE @ 30 D

SURGERY—4.5% BMT—1.3%

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ECA ENDARTERECTOMY/BYPASS COLLATERAL PATHWAYS

Facial→periorb plexus→ophthalmic

Int Maxillary→Middle Meningeal→
Leptomingeal coll→ACA

Occipital→persist hypoglossal→PCA

ICA<-->BASILAR

Persistent Hypoglossal Art

Persistent Trigeminal Art

ORIGINAL ARTICLES | VOLUME 6, ISSUE 2, P158-167, AUGUST 1987
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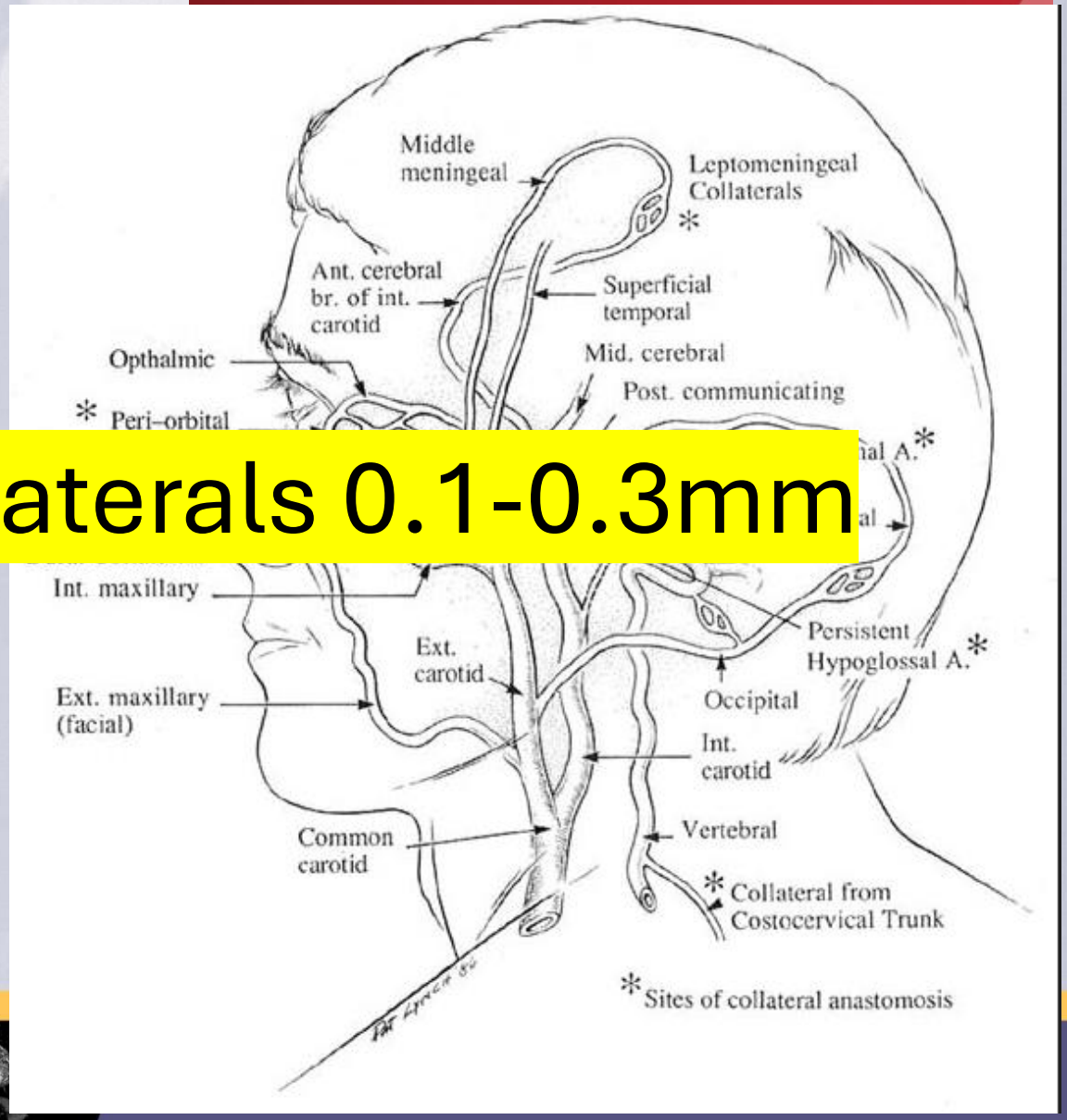
The role of external carotid endarterectomy in the treatment of ipsilateral internal carotid occlusion: Collective review

Size of Collaterals 0.1-0.3mm



ECA ENDARTERECTOMY/BYPASS

ORIGINAL ARTICLES | VOLUME 6, ISSUE 2, P158-167, AUGUST 1987
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The role of external carotid endarterectomy in the treatment of ipsilateral internal carotid occlusion: Collective review

Jonathan P. Gertler, M.D. • Richard P. Cambria, M.D.

DOI: https://doi.org/10.1067/mva.1987.avs0060158

- Neurologic symptoms in the setting of ICA occlusion
  - EMBOLIC events through the external carotid artery (ECA)
    - CAROTID STUMP syndrome
  - HEMODYNAMIC insuff 2° inadeq collaterals
  - Propagation of clot intracranially
- ECA RECONSTRUCTION can ADDRESS
  - Emboli
  - Hemodynamic insufficiency

ECA ENDARTERECTOMY/BYPASS

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The role of external carotid endarterectomy in the treatment of ipsilateral internal carotid occlusion: Collective review

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DOI: https://doi.org/10.1067/mva.1987.avs0060158

- 218 cases for analysis
  - 195 endart
  - 23 bypass
- Results
  - 83% resolution of sxs
  - Add'l 7% w/ marked improvement
  - Periop mortality—3%
  - Neuro complx—5%

ECA ENDARTERECTOMY/BYPASS BEST RESULTS

ORIGINAL ARTICLES | VOLUME 6, ISSUE 2, P158-167, AUGUST 1987
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The role of external carotid endarterectomy in the treatment of ipsilateral internal carotid occlusion: Collective review

Jonathan P. Gertler, M.D. • Richard P. Cambria, M.D.

DOI: https://doi.org/10.1067/mva.1987.avs0060158

- PERFORMED FOR HEMISPHERIC or RETINAL SXS
  - As opposed to non-specific sxs or previous stroke
- NO CONTRALAT CAROTID DZ
  - Vertebrobasilar disease has no deleterious effect
- PERFORMED LATER IN THE STUDY

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ECA ENDARTERECTOMY/BYPASS
BEST RESULTS

ORIGINAL ARTICLES | VOLUME 6, ISSUE 2, P158-167, AUGUST 1987
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  - As opposed to non-specific sxs or previous stroke
- NO CONT
  - Vertebrobasilar disease has no deleterious effect
- PERFORMED LATER IN THE STUDY

LIMITED ROLE

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ICA OCCLUSION—90'S

- tPA protocols
- CEA still being attempted
  - Conflicting reports

ICA Occlusion—90's

Details Related Ref

Pilot randomized trial of tissue plasminogen activator in acute ischemic stroke. The TPA Bridging Study Group.

E C HaleyJr, T G Brott, G L Sheppard, W Barsan, J Broderick, J R Marler, G L Kongable, J Spilker, S Massey and C A Hansen

Originally published 1 Jul 1993 | https://doi.org/10.1161/01.STR.24.7.1000 | Stroke. 1993;24:1000–1004

Stroke

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Acute Extracranial ICA Occlusion

Acute carotid artery occlusion—operative or conservative management

Bone G, Ladurner G, Waldstein N, Rendl KH, Prenner K. Eur Neurol 1990; 30; 214-7

- 64 patients equally randomized to op vs non-op
  - Acute stroke
  - Angiographic confirmed ipsilater
- Outcomes
  - Normal
  - Mild/moderate def
  - Severe deficit
  - Mortality

BETTER?

	NON-OP	OP
	16%	16%
	53%	31%
	28%	25%
	3%	25%

MORTALITY
Blaisdell—42%
Wylie—55%

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ICA Occlusion—90's

- 4 pts w/ acute occlusion of ICA & severe hemiparesis—w/in 2hrs
  - 3 patients were alert
  - 1 patient was lethargic at the time of hospital admission (1990-1999)
- Head
- ICA o
  - 3 pts→MCA occlusion was noted
  - Collateral circulation in all pts.
  - IA fibrinolysis→Partial recanalization of occl'd ICA in all pts w/in 4 h
  - 2 pts with severe residual ICA stenosis→emergency CEA
  - 2 pts→ CEA in the subacute or chronic stage

? ROLE FOR CEA IF EARLY TIME COURSE

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ICA OCCLUSION—2000-PRESENT

- EC-IC BYPASS REVISITED----COSS TRIAL
- GUIDELINES
  - SVS (2021)
  - ESVS (2023)
- RANDOMIZED TRIALS→LARGE ISCHEMIC STROKE
  - Japan→Rescue-Japan-Limit
  - US, Canada, EU, Aus, NZ→Select 2
  - China→Angel-Aspect

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MODIFIED RANKIN SCALE--mRS

Modified Rankin Scale (MRS)

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

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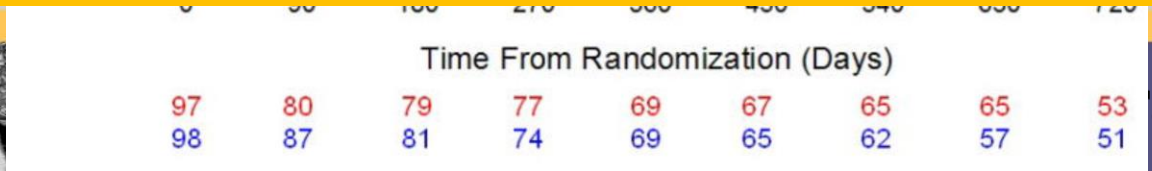
Extracranial-Intracranial Bypass Surgery for Stroke Prevention in Hemodynamic Cerebral Ischemia

The Carotid Occlusion Surgery Study Randomized Trial

- 1° Endpt – published 2011
  - SURGICAL ARM
    - 30d STROKE & DEATH
    - IPSI ISCHEMIC STROKE w/in 2 yrs
  - MEDICAL ARM
    - 30d STROKE & DEATH POST RANDOMIZATION
    - IPSI ISCHEMIC STROKE w/in 2 yrs

CAROTID OCCLUSION SURGERY STUDY (COSS)

- The trial was terminated early for futility. Two-year rates for the primary end point were 21.0% (95% CI, 12.8% to 29.2%; 20 events) for the surgical group and 22.7% (95% CI, 13.9% to 31.6%; 20 events) for the nonsurgical group (P=.78, Z test), a difference of 1.7% (95% CI, −10.4% to 13.8%). Thirty-day rates for ipsilateral ischemic stroke were 14.4% (14/97) in the surgical group and 2.0% (2/98) in the nonsurgical group, a difference of 12.4% (95% CI, 4.9% to 19.9%)



ESVS GUIDELINES—CNO W/ SXS

- Sx CAROTID NEAR OCCLUSION (CNO)
  - 262 ECST AND NASCET pts
    - 16 total collapse distal ICA
    - 246 partia
  - No decreased stroke--CEA vs BMT
    - Meta-analysis
    - Carotid Endart Trial Collaborists
      - @ 5 & 8 yrs

CNO=NO INTERVENTION

Recommendation 56			Unchanged
For symptomatic patients with carotid near occlusion and distal vessel collapse, carotid endarterectomy and carotid stenting are not recommended, unless as part of a randomised controlled trial.			
Class	**Level**	**References**	**ToE**
		Rothwell *et al.* (2003)[357]	

Recommendation 57			New
For patients with carotid near occlusion and distal vessel collapse with recurrent carotid territory symptoms (despite best medical therapy), carotid endarterectomy or carotid artery stenting may be considered only after multidisciplinary team review.			
Class	**Level**	**References**	**ToE**
IIb	C	Meershoek *et al.* (2019)[78], Xue *et al.* (2020)[110], García-Pastor *et al.* (2017)[126], Meershoek *et al.* (2018)[423]	

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ESVS GUIDELINES—FREE FLOATING THROMBUS

- FREE FLOATING THROMBUS (FFT)
- POOR QUALITY DATA
  - ↑'d s
- DECISIO
  - probable etiology (e.g., thrombophilia requiring AC)
  - whether patients had recurrent events on APRx or AC
  - interval since TIA/stroke onset
  - size of infarct
  - whether FFT is located at the carotid bifurcation (accessible) or extends towards the skull base (less accessible).
  - Serial DUS/CTA/MRA to assess resolution/progression

FFT=AC +/- CEA/CAS

Recommendation 58 — **New**

For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus within the carotid artery, therapeutic anticoagulation is recommended.

Class	Level	References	ToE
I	C	Bhatti *et al.* (2007)[49], Fridman *et al.* (2019)[54]	

New

with recent carotid territory symptoms and free floating thrombus who develop recurrent symptoms whilst receiving anticoagulation therapy, surgical or endovascular removal of the thrombus may be considered.

Class	Level	References
IIb	C	Consensus

Recommendation 60 — **New**

For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus, intravenous thrombolysis is not recommended.

Class	Level	References	ToE
III	C	Fridman *et al.* (2019)[54]	

CLINICAL PRACTICE GUIDELINES | VOLUME 75, ISSUE 1, SUPPLEMENT , 4S-22S, JANUARY 2022

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PDF [100

Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease

Ali F. AbuRahma, MD • Efthymios D. Avgerinos, MD, PhD • Robert W. Chang, MD • ... Richard J. Powell, MD • Caron B. Rockman, MD • Wei Zhou, MD • Show all authors

Open Archive • Published: June 18, 2021 • DOI: https://doi.org/10.1016/j.jvs.2021.04.073 •

JVS Journal of Vascular Surgery

SVS | Society for Vascular Surgery

SVS Recommendations--2021

3.3. We recommend against revascularization, regardless of the extent of stenosis for patients who experienced a disabling stroke, have a modified Rankin scale score of ≥3, whose area of infarction is >30% of the ipsilateral middle cerebral artery territory, or who have altered consciousness to minimize the risk of postoperative parenchymal hemorrhage. **These patients can be reevaluated for revascularization later if their neurologic recovery is satisfactory. Level of recommendation: grade 1 (strong); quality of evidence: C (low).**

ESVS GUIDELINES—NEUROLOGICALLY UNSTABLE

- DEFINITION
  - mRS ≥ 3
  - > 1/3 MCA territory involved
  - ↓'d LOC
- Large infarct→HIGHER RISKS of
  - ICH
  - Hemorrhagic transformation
  - Hyperperfusion

Recommendation 46			Unchanged
For patients with 50–99% stenoses who experience a disabling stroke (modified Rankin score ≥3), or whose area of infarction exceeds one third of the ipsilateral middle cerebral artery territory, or who have altered consciousness/ drowsiness, it is recommended to defer carotid interventions to minimise the risks of post-operative parenchymal haemorrhage.			
Class	**Level**	**References**	**ToE**
I	C	Rantner *et al.* (2006)[388], Wolfle *et al.* (2004)[389]	

NO RECOMMENDATION FOR CAROTID OCCLUSION

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RESCUE-JAPAN-LIMIT

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Endovascular Therapy for Acute Stroke with a Large Ischemic Region

Yoshimura S et al. DOI: 10.1056/NEJMoa2118191

CLINICAL PROBLEM

Although endovascular therapy is standard treatment for ischemic stroke caused by large-vessel occlusion, it is not typically used in patients with a large ischemic region because of a lack of data from randomized trials and concern about the risk of hemorrhage with reperfusion.

CLINICAL TRIAL

Design: An open-label, multicenter, randomized clinical trial in Japan compared endovascular therapy with medical therapy alone in patients with large-vessel stroke and a large ischemic area.

Intervention: 203 patients underwent randomization; 100 patients assigned to endovascular therapy and 102 assigned to medical care alone completed follow-up. The primary outcome was a modified Rankin scale score of 0 (no disability) to 3 (moderate disability but ambulatory) at 90 days after stroke onset.

RESULTS

Efficacy: The percentage of patients with a modified Rankin scale score of 0 to 3 at 90 days was significantly higher with endovascular therapy than with medical care alone.

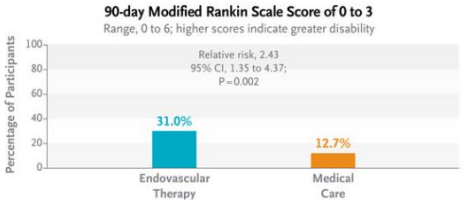
Safety: The percentage of patients who had any intracranial hemorrhage within 48 hours after randomization was significantly higher with endovascular therapy than with medical care alone. However, the percentage of patients who had symptomatic intracranial hemorrhage within 48 hours, decompressive craniectomy within 7 days, or ischemic stroke recurrence within 90 days or who died within 90 days did not differ significantly between the groups.

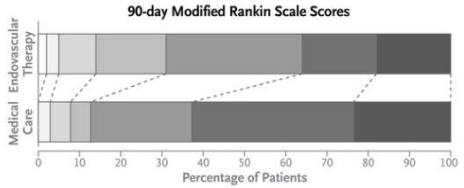
LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

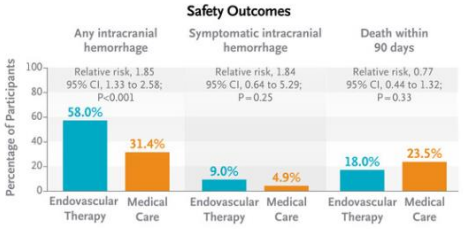
- The difference in how ischemic area is determined by computed tomography, as is common practice in the United States, and by diffusion-weighted magnetic resonance imaging, which was used more often in this trial, should be considered.
- Generalizability of the findings is limited outside Japan; approximately 27% of the patients in each group received intravenous thrombolysis at a dose of 0.6 mg per kilogram according to Japanese guidelines — a lower dose than that used in some other countries.
- Whether causes of death were related to the assigned trial treatment could not be determined.

Links: Full Article | NEJM Quick Take



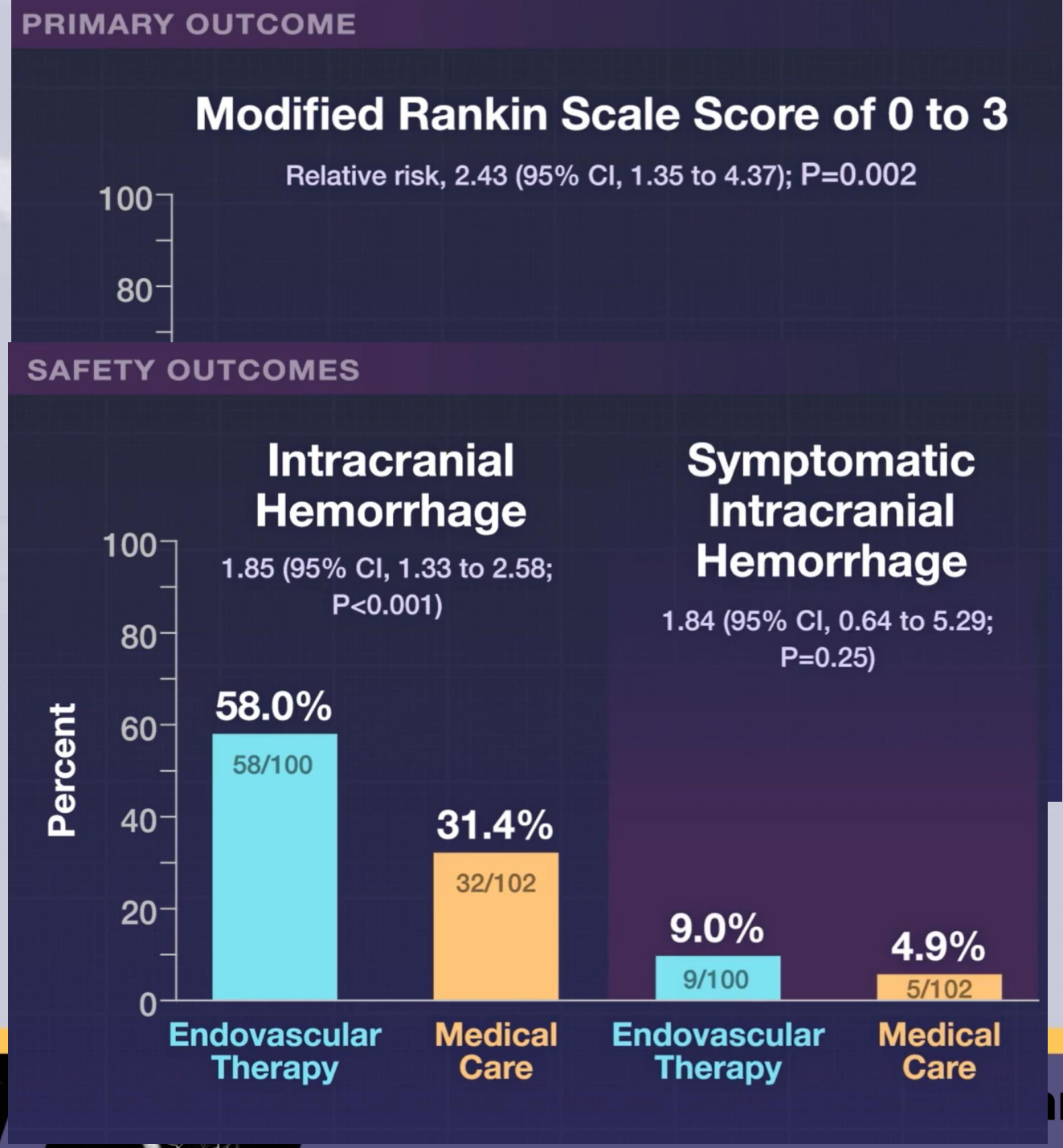


Modified Rankin Scale Scores	0	1	2	3	4	5	6
Endovascular Therapy — no. (%)	2 (2.0)	3 (3.0)	9 (9.0)	17 (17.0)	33 (33.0)	18 (18.0)	18 (18.0)
Medical Care — no. (%)	0	3 (2.9)	5 (4.9)	5 (4.9)	25 (24.5)	40 (39.2)	24 (23.5)



CONCLUSIONS

Patients with large cerebral infarctions had better functional outcomes but more overall intracranial hemorrhages with endovascular therapy added to medical therapy than with medical therapy alone.



SELECT-2

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Trial of Endovascular Thrombectomy for Large Ischemic Strokes

Sarraj A et al. DOI: 10.1056/NEJMoa2214403

CLINICAL PROBLEM

Endovascular thrombectomy has been shown to be more beneficial than medical therapy alone in selected patients with ischemic stroke due to occlusion of a large cerebral vessel. However, patients with large strokes, who have a poor prognosis, have been underrepresented in thrombectomy trials.

CLINICAL TRIAL

Design: A phase 3, international, randomized, open-label trial evaluated endovascular thrombectomy plus medical care, as compared with standard medical care alone, in patients with acute ischemic stroke due to occlusion of the internal carotid artery or the first segment of the middle cerebral artery (or both), with a large ischemic-core volume on noncontrast computed tomography (CT), CT perfusion imaging, or diffusion-weighted magnetic resonance imaging.

Intervention: 352 patients were assigned to undergo endovascular thrombectomy within 24 hours after stroke onset in addition to standard medical care or to receive standard medical care alone. The primary outcome was the ordinal score on the modified Rankin scale at 90 days (range, 0 to 6, with higher scores indicating greater disability). Functional independence was a secondary outcome. Safety outcomes included symptomatic intracranial hemorrhage and death from any cause.

RESULTS

Efficacy: Endovascular thrombectomy outperformed medical care with respect to the modified Rankin scale score at 90 days.

Safety: Procedural complications occurred in 18.5% of the patients in the thrombectomy group. Mortality and the incidence of intracranial hemorrhage were similar in the two groups.

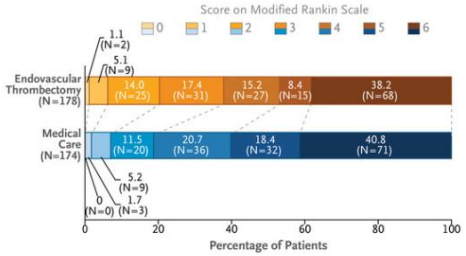
LIMITATIONS

- The trial was terminated early for efficacy, potentially leading to overestimation of the effects of thrombectomy.
- Only about 20% of the patients received intravenous thrombolytic agents before randomization.

Links: Full Article | NEJM Quick Take | Editorial

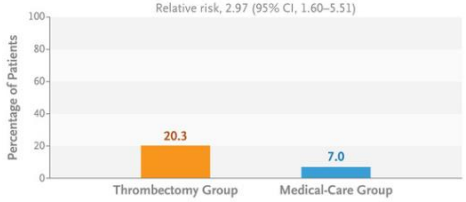
Efficacy at 90 Days

Generalized OR, 1.51 (95% CI, 1.20–1.89); P<0.001



Functional Independence at 90 Days

Relative risk, 2.97 (95% CI, 1.60–5.51)

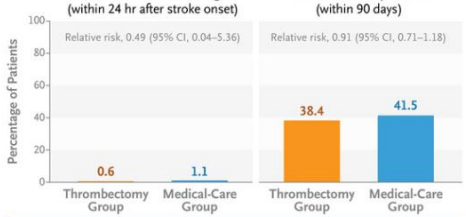


Symptomatic Intracranial Hemorrhage (within 24 hr after stroke onset)

Relative risk, 0.49 (95% CI, 0.04–5.36)

Death from Any Cause (within 90 days)

Relative risk, 0.91 (95% CI, 0.71–1.18)

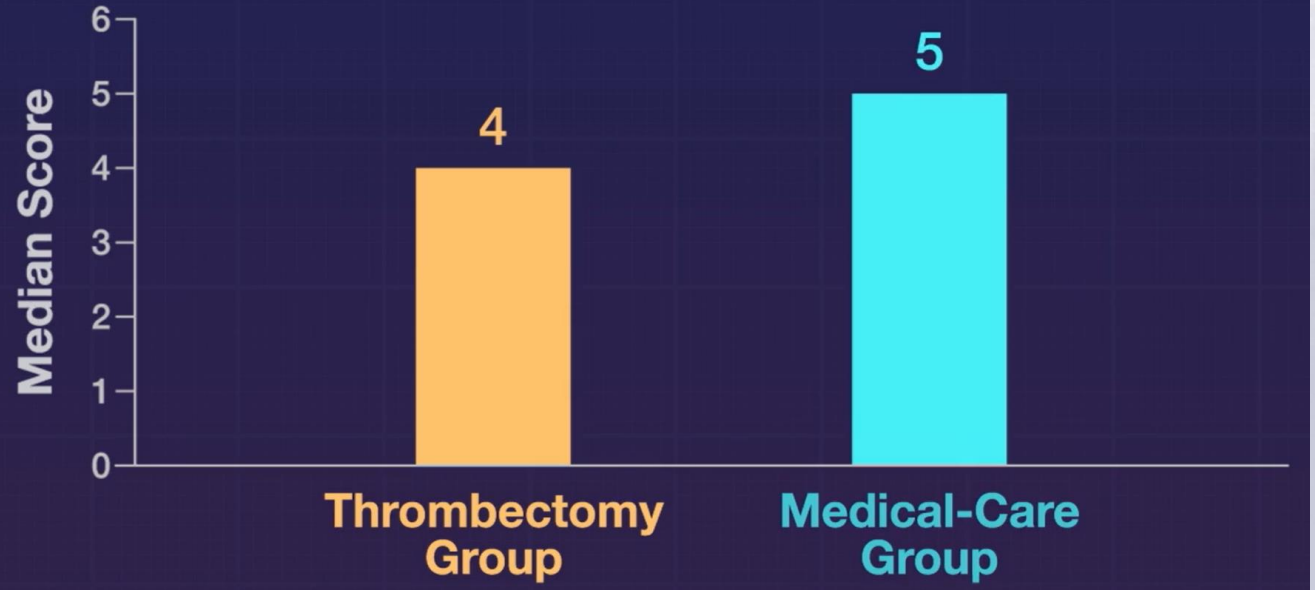


CONCLUSIONS

In patients with acute ischemic stroke due to a proximal large-vessel occlusion and with a large ischemic-core volume, endovascular thrombectomy in addition to standard medical care resulted in better functional outcomes at 90 days than medical care alone but was associated with procedural vascular complications.

PRIMARY OUTCOME

Median Score on Modified Rankin Scale at 90 Days



Total (0–6):

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ANGEL-ASPECT

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct

Huo X et al. DOI: 10.1056/NEJMoa2213379

CLINICAL PROBLEM

Endovascular therapy is a standard approach in patients with acute ischemic stroke due to cerebral large-vessel occlusion. However, whether endovascular therapy benefits patients with a large infarct core remains uncertain.

CLINICAL TRIAL

Design: A multicenter, open-label, randomized trial with blinded end-point assessment investigated the efficacy and safety of endovascular therapy, as compared with medical management alone, in patients with a large infarct core caused by acute large-vessel occlusion in the anterior circulation.

Intervention: 456 adults in China presenting within 24 hours after stroke onset who had an Alberta Stroke Program Early Computed Tomography Score of 3 to 5 (range, 0 to 10, with lower scores indicating larger infarct) or an infarct-core volume of 70 to 100 ml were assigned to undergo endovascular thrombectomy — and, if needed, balloon angioplasty, stent implantation, or intraarterial thrombolysis — and receive medical management or to receive medical management alone. The primary outcome was the score on the modified Rankin scale at 90 days (range, 0 to 6, with higher scores indicating greater disability).

RESULTS

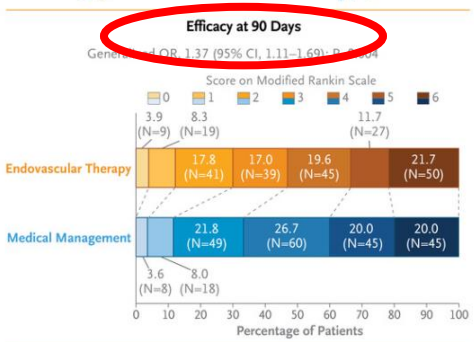
Efficacy: At 90 days, a shift in the distribution of the scores on the modified Rankin scale indicated better outcomes with endovascular therapy than with medical management alone.

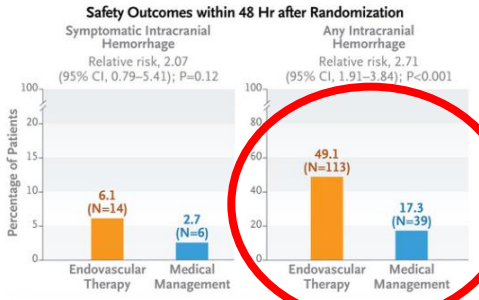
Safety: Symptomatic intracranial hemorrhage and any intracranial hemorrhage were more common with endovascular therapy than with medical management alone.

LIMITATIONS

- Less than one third of patients received intravenous thrombolysis, which may have disadvantaged the medical-management group.
- Urokinase was used instead of alteplase in some patients; alteplase is probably more effective.
- Patients >80 years of age were excluded.

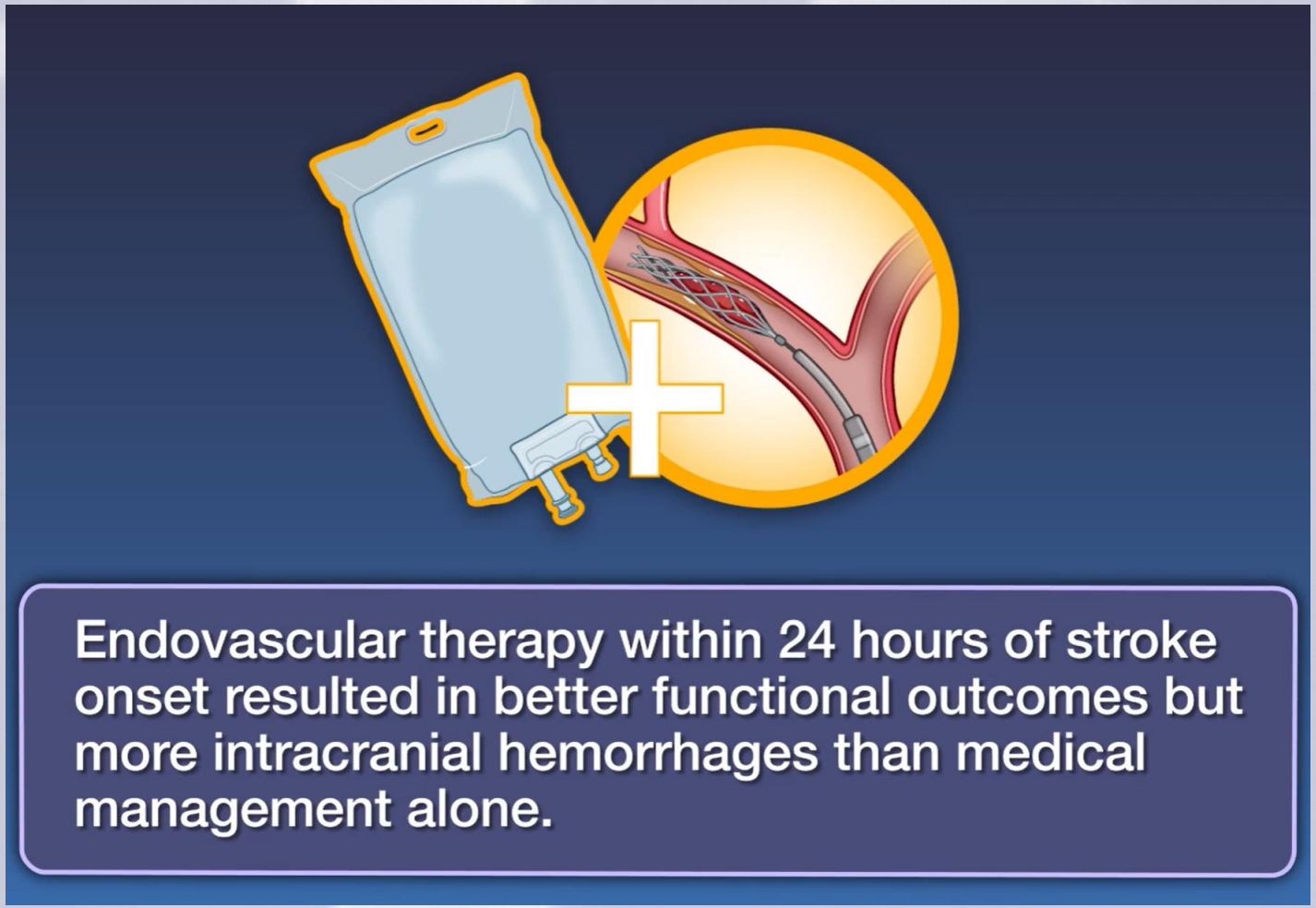
Links: Full Article | NEJM Quick Take | Editorial





CONCLUSIONS

In patients in China with a large infarct-core volume caused by acute large-vessel occlusion in the anterior circulation, endovascular therapy within 24 hours after stroke onset resulted in better functional outcomes at 90 days but more intracranial hemorrhages than medical management alone.



Endovascular therapy within 24 hours of stroke onset resulted in better functional outcomes but more intracranial hemorrhages than medical management alone.

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ALL THREE LARGE INFARCT RANDOMIZED TRIALS

- IMPROVED NEUROLOGIC STATUS @ 90D

EXTRACRANIAL/INTRANCRANIAL INTERVENTION AFTER LARGE STROKE
? BENEFIT

- IN EXCHANGE FOR
  - INCREASED ICH
  - INCREASED VASCULAR COMPLICATIONS

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ESVS GUIDELINES—CEA/CAS after THROMBOLYSIS

- 10-20% of Thombolysis pts have underlying ICA stenosis of 50-99%

- Intervention too soon after TT may lead to ICH or neck hematoma

Table 30. Peri-operative outcomes in pooled series undergoing carotid endarterectomy (CEA) or carotid artery stenting (CAS) after intravenous thrombolysis therapy for patients with acute ischaemic stroke*

Outcome	CEA (n = 2 076)	CAS (n = 481)
Stroke or death (95% CI) — %	5.2 (3.3–7.5)	14.9 (11.9–18.2)
ICH (95% CI) — %	3.4 (1.7–5.6)	5.5 (3.7–7.7)
Haemorrhage (95% CI) — %	Neck: 3.8 (2.9–4.9)	Local: 4.9 (0.09–16.2)

CI = confidence interval; ICH = intracranial haemorrhage.
* Data derived from Kakkos.[66]

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ESVS GUIDELINES—Timing of CEA/CAS after THROMBOLYSIS

- ½ life of rtPA—5 min and tenectaplase—24 min
- Fibrinogen and plasminogen levels only revert back to ≥ 80% baseline @ ≥ 24h
- rtPA increases circulating fibrin degration products to > 200ng/dl which increases BBB permeability leading to increased risk of ICH
- Thus Heparin & antiplt should be held x 24h after TT
- Restarted only after f/u CT shows no hemorrhagic transformation

ESVS GUIDELINES—CEA/CAS after THROMBOLYSIS

- Early CEA
  - rapid neurological recovery (mRS 0-2)
  - infarction area less than one third the MCA territory
  - recanalization of a previously occluded MCA mainstem on repeat CTA
  - ipsilateral 50-99% stenosis
  - no evidence of parenchymal haemorrhage or significant brain edema

ESVS GUIDELINES—CEA/CAS after THROMBOLYSIS

- Contraindications for CEA
  - severe persistent neurological deficit (mRS 3)
  - anticipated high surgical risk
  - parenchymal hemorrhage on CT
  - previous radical neck dissection or radiotherapy

Table 31. Peri-operative outcomes for case control studies in carotid endarterectomy (CEA) and carotid artery stenting (CAS) patients who did or did not have intravenous thrombolysis therapy for acute ischaemic stroke

Outcome	CEA			CAS		
	TT − %	No TT − %	OR (95% CI)	TT − %	No TT − %	OR (95% CI)
Stroke	4.1	1.2	2.74 (0.62–12.07)			
Death	2.1	0.7	2.84 (0.85–17.3)			
Stroke / death	4.3	1.5	2.34 (0.74–7.47)	5.2	1.5	8.49 (2.12–33.95)
Intracranial haemorrhage	2.2	0.1	7.82 (4.07–15.2)	5.4	0.7	7.48 (4.69–11.92)
Neck haematoma	3.6	2.3	1.65 (1.17–2.33)			

Data derived from Kakkos et al.[66] OR = odds ratio; CI = confidence interval.

ESVS GUIDELINES—Timing of CEA/CAS after THROMBOLYSIS

- A US National Inpatient Sample
  - ↑'d post-op CVA and ICH if performed early
  - ↓'d to levels in non-TT grp by 7 d
- UK National Vascular Registry reported
  - No assoc b/t CEA timing after TT and procedural risks.
- 136 Meta-regression analyses of published data
  - Inverse relationship b/t the time interval between TT and CEA and the risk of peri-operative stroke/death→performing CEA early after TT was associated with higher risks of peri-procedural stroke/ death.

ESVS GUIDELINES—TIMING OF CEA/CAS after TT

- Meta-regression analysis (Figure 7), peri-operative stroke/death was 13% when CEA was performed three days after TT completion and 10.6% after four days. The risk was predicted to reduce to within the currently accepted 6% threshold after six days had elapsed, suggesting that CEA should probably be deferred until six days after TT.

In a Finnish study (n=128), the risk of recurrent stroke between TT and under going CEA was 5.5% when performed a median of four days after TT (range 0 -8) This is lower than the predicted 10.6% risk associated with performing CEA four days after TT in the meta-regression analysis.

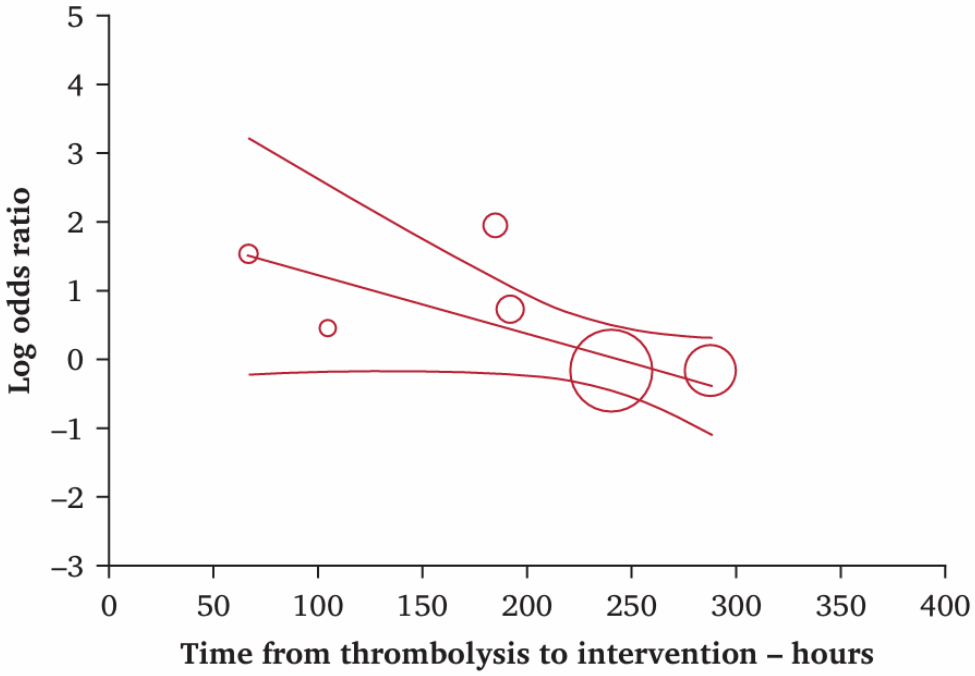

Figure 7. Regression of log odds ratio on time (hours) for peri-operative death/stroke in patients with stroke undergoing carotid endarterectomy after thrombolysis or without thrombolysis. Reproduced with permission from: Kakkos S, Vega de Ceniga, Naylor AR. A systematic review and meta-analysis of periprocedural outcomes in patients undergoing carotid interventions following thrombolysis. *Eur J Vasc Endovasc Surg* 2021;**62**:340—9.

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ESVS GUIDELINES—TIMING OF CEA/CAS after TT

Recommendation 48			Unchanged
For symptomatic patients undergoing thrombolysis, it is recommended that intravenous heparin and antiplatelet therapy be withheld for 24 hours after completion of thrombolysis, but antiplatelet therapy should then be commenced before any carotid intervention is undertaken.			
Class	**Level**	**References**	**ToE**
I	C	Berge *et al.* (2021)[399]	

Recommendation 49			New
For patients with acute ischaemic stroke due to a symptomatic 50–99% carotid stenosis who have received intravenous thrombolysis, delaying carotid endarterectomy or carotid stenting by six days following completion of thrombolysis should be considered.			
Class	**Level**	**References**	**ToE**
IIa	B	Kakkos *et al.* (2021)[66], Vellimana *et al.* (2018)[157]	

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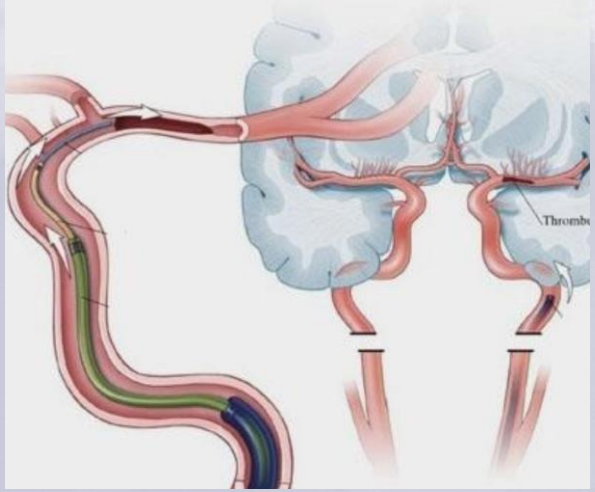
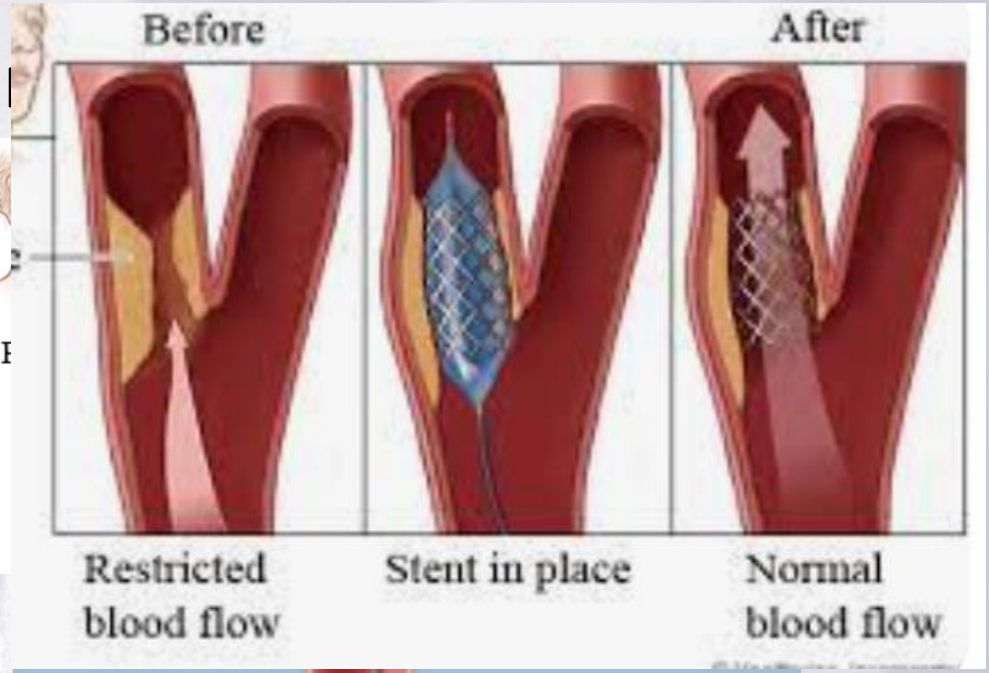
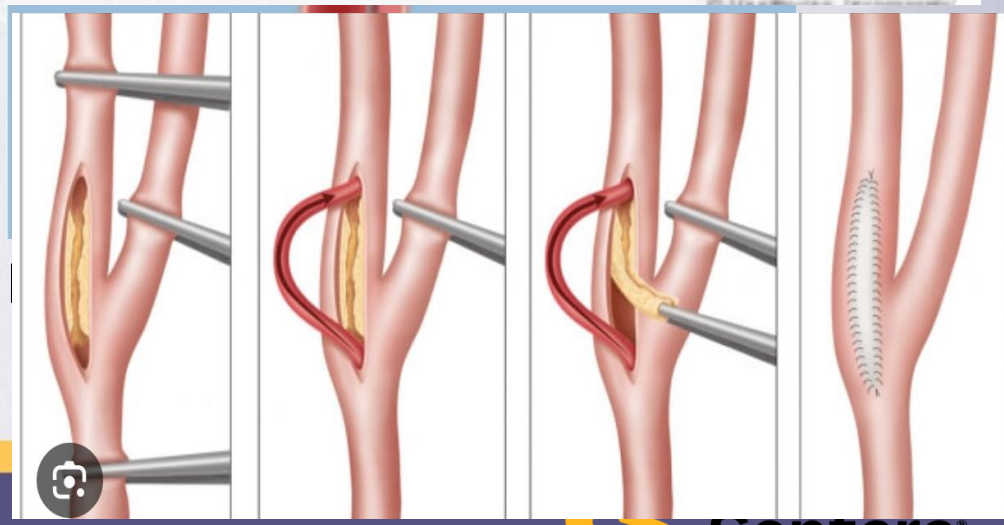
ESVS GUIDELINES—TIMING OF CEA/CAS after MT

- Meta-analysis of 5 RCT's→ 2 fold improve
- 10-20% of MT pts
  - Embolic MCA
  - Tandem ICA stenosis
- Rx options
  - Synchronous MT + CAS + AP rx
  - Synchronous MT + CAS w/o AP rx
  - Synchronous MT + PTA w/o stent or AP
  - Synchronous MT +/- deferred CEA/CAS







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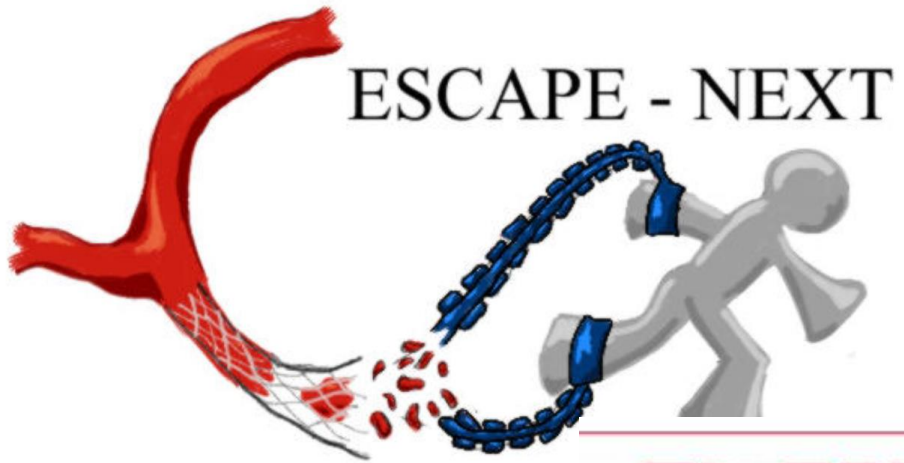
PMID: 30915023



usion Strokes Treated

nelet,[1] Liang Liao,[1]

nad Anadani,[4]

REVASCAT

EXTEND - IA

EM OCCLUSIO

[SWIFT PRIME]

my

trials

- MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA
  - aka HERMES Collaboration

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HERMES REGISTRY

- 1287 patients 634 assigned to endovascular thrombectomy, 653 assigned to control
- Endovascular thrombectomy led to significantly reduced disability at 90 days compared with control
- NNT w/ MT to reduce disability by one level on mRS was 2.6
- Treatment effect of mechanical thrombectomy (MT) in patients with **TANDEM OCCLUSIONS** was comparable to **Isolated** intracranial occlusion
- HOWEVER, MR CLEAN tandom lesions 70-80%

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HERMES REGISTRY

- Effect sizes favouring endovascular thrombectomy over control were present in several strata of special interest
  - >80 yrs
  - [redacted]
  - [redacted]
- NO DIFFERENCE
  - Mortality at 90 days
  - Risk of parenchymal hematoma
  - Symptomatic intracranial hemorrhage (sICH)

REDUCED DISABILITY @ 90d w/ ENDOVASCULAR THROMBECTOMY

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Front Neurol. 2019; 10: 206.
Published online 2019 Mar 11. doi: 10.3389/fneur.2019.00206
PMCID: PMC6421313
PMID: 30915023

Impact of Emergent Cervical Carotid Stenting in Tandem Occlusion Strokes Treated by Thrombectomy: A Review of the TITAN Collaboration

François Zhu,[1] Serge Bracard,[1,2] René Anxionnat,[1,2] Anne-Laure Derelle,[1] Romain Tonnelet,[1] Liang Liao,[1] Gioia Mione,[3] Lisa Humbertjean,[3] Jean-Christophe Lacour,[3] Gabriela Hossu,[2] Mohammad Anadani,[4] Sébastien Richard,[3,5] and Benjamin Gory[1,2,*]

- Pooled NON-randomized MT databases from 18 stroke ctrs
- Jan 2012-Sept 2016
- Tandem lesion
  - Proximal intracranial
    - intracranial ICA
    - proximal M1 or M2
  - Extracranial
    - Cervical ICA Occlusion or $\geq$ 90% stenosis

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TITAN REGISTRY ENDPOINTS

- 1° Outcome →90 day modified Rankin Scale (mRS) 0–2.
- 2° Outcomes
  - Successful reperfusion--modified Thrombolysis In Cerebral Infarction (mTICI) score 2b-3
  - All-cause mortality at 90 d
  - Any procedural related complications
  - Any intracranial hemorrhage (ICH) and symptomatic ICH.
  - Symptomatic ICH (sICH) was defined as any PH, SAH, or IVH assoc'd w/ worsening NIHSS score by 4 points or more

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TITAN REGISTRY—OUTCOMES

- 295 PTS—MT/CAS/AP vs MT
  - CERVICAL LESION TYPE→NO DIFFERENCE IN OUTCOME →
    - 230—ATHEROSCLEROTIC
    - 65--DISSECTION
- BETTER mTICI w/ statistical signif
- HOWEVER, once confounders accounted for, statistical signif of 90 d improved mRS NO LONGER SIGNIFICANT

Table 1

Efficacy and safety outcomes between patients treated by intracranial thrombectomy alone vs. those treated by intracranial thrombectomy and cervical carotid artery stenting with antiplatelets [from Papanagiotou et al. (8)].

Outcomes	Intracranial thrombectomy and cervical ICA stenting with antiplatelets (*n* = 256)	Intracranial thrombectomy alone (*n* = 108)	Unadjusted analysis		Adjusted analysis[a]	
			OR (95%CI)	*P*	OR (95%CI)	*P*
mTICI 2b-3	212/255 (83.1)	65/108 (60.2)	3.26 (1.96–5.41)	<0.001	2.66 (1.38–5.10)	0.003
mTICI 3	105/255 (41.2)	25/108 (23.2)	2.32 (1.39–3.88)	0.001	1.91 (1.08–3.40)	0.026
90-day mRS 0-2	147/254 (57.9)	43/105 (41.0)	1.98 (1.24–3.15)	0.004	1.44 (0.77–2.67)	0.25

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TITAN REGISTRY—OUTCOMES

- 295 PTS—MT/CAS/AP vs MT
- SIGNIFICANT SURVIVAL BENEFIT
- PREDICTORS OF MORTALITY
  - AGE
  - CURRENT SMOKER
  - NIHSS score
  - ASPECTS score
  - PRIOR THROMBOLYSIS

Outcomes	Intracranial thrombectomy and cervical ICA stenting with antiplatelets (*n* = 256)	Intracranial thrombectomy alone (*n* = 108)	Unadjusted analysis		Adjusted analysis[a]	
			OR (95%CI)	*P*	OR (95%CI)	*P*
90-day mortality	24/254 (9.5)	18/105 (17.1)	0.50 (0.26–0.98)	0.042	0.44 (0.21–0.94)	0.033
Symptomatic intracerebral hemorrhage	13/255 (5.1)	5/108 (4.6)	1.11 (0.38–3.18)	0.85	1.24 (0.36–4.23)	0.73

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TITAN REGISTRY—OUTCOMES--HEMORRHAGE

A

	CAS+MT+tPA+AP	CAS+MT without tPA+AP	CAS+MT+tPA without AP	CAS+MT without tPA, without AP	Total
No sICH	130 (52.85%)	85 (34.55%)	10 (4.06%)	7 (2.84%)	232 (94.31%)
sICH	6 (2.44%)	7 (2.85%)	1 (0.41%)	0 (0%)	14 (5.69%)
Total	136 (55.29%)	92 (37.40%)	11 (4.47%)	7 (2.84%)	246

B

Predictors	OR (95% CI)*	P*
ICA occlusion	2.24 (1.08 to 4.60)	0.005
Diabetes	2.80 (1.28 to 6.16)	0.010
MRI-based treatment	0.44 (0.22 to 0.86)	0.015
Prior use of thrombolysis	0.50 (0.28 to 0.89)	0.018
ASPECTS score <7	2.24 (1.08 to 4.61)	0.029
Extracranial ICA occlusion	0.55 (0.31 to 0.96)	0.034
Admission NIHSS (per 5 point increase)	1.24 (0.95 to 1.60)	0.10

OF NOTE HEPARIN, TT & AP rx NOT PREDICTORS

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TITAN REGISTRY—OUTCOMES—IV THOMBOLYSIS

- IMPROVED REPERFUSION w/ IV THROMBOLYSIS FOR ALL API
- ONLY W
PERFORMED WAS SAFETY PROFILE NOT ADVERSELY AFFECTED

TITAN→SURVIVAL BENEFIT w/ COMBINED INTRA AND EXTRACRANIAL THERAPY

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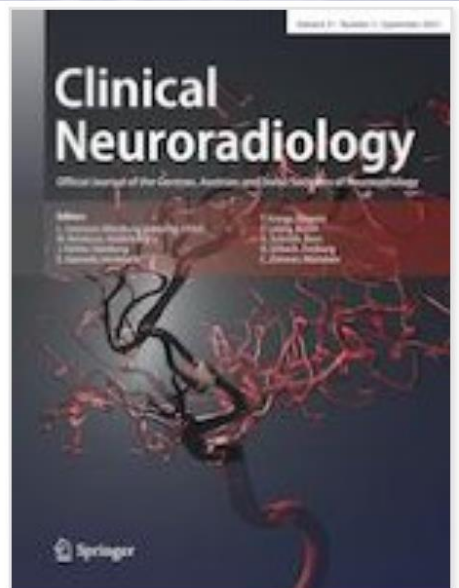
OPEN ACCESS 17.09.2020 | Original Article

Emergency Carotid Endarterectomy Instead of Carotid Artery Stenting Reduces Delayed Hemorrhage in Thrombectomy Stroke Patients

verfasst von: Raveena Singh, Sven Dekeyzer, Arno Reich, Drosos Kotelis, Alexander Gombert, Martin Wiesmann, Omid Nikoubashman

Erschienen in: Clinical Neuroradiology | Ausgabe 3/2021

- CAS and DAPT assoc'd w/ ↑'d intraparenchymal hemorrhage
- Simultaneous MT and CEA or CAS
- 1° outcome→PH
- Prospectively maintained stroke registry



OPEN ACCESS 17.09.2020 | Original Article

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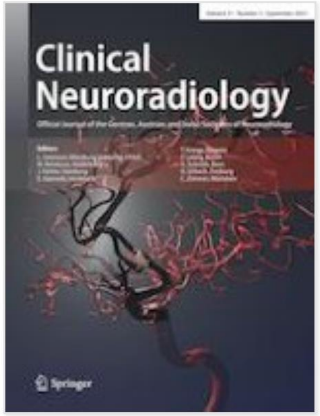
Erschienen in: Clinical Neuroradiology | Ausgabe 3/2021



- Our rationale is to avoid acute treatment of ICA stenosis altogether whenever possible
- Perform CEA before or after thrombectomy whenever necessary **(SAME SETTING)**
- Notify our vascular surgery team if
  - Surgical access to the occlusion site is needed because access to the occlusion site via femoral or radial/brachial access is expected to be difficult and to take longer than 45 min
  - CAS and DAPT after the procedure are to be avoided (↑'d hemorrhagic risk)
    - Already on AC
    - Large volume infarct

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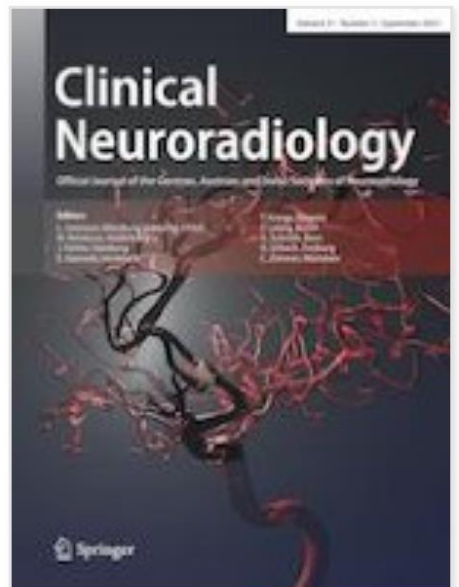
Emergency Carotid Endarterectomy Instead of Carotid Artery Stenting Reduces Delayed Hemorrhage in Thrombectomy Stroke Patients

verfasst von: Raveena Singh, Sven Dekeyzer, Arno Reich, Drosos Kotelis, Alexander Gombert, Martin Wiesmann, Omid Nikoubashman

Erschienen in: Clinical Neuroradiology | Ausgabe 3/2021

- CONTINUE thrombolysis during surgery
- GpIIb/IIIa for CAS and DAPT afterwards
- June 2013-Sept 2018
- 114 pts (21 excluded for dissection)
  - 27 CEA—62 CAS



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Emerg Stenti Patier ery Stroke

verfasst von: ubashman

Erschienen

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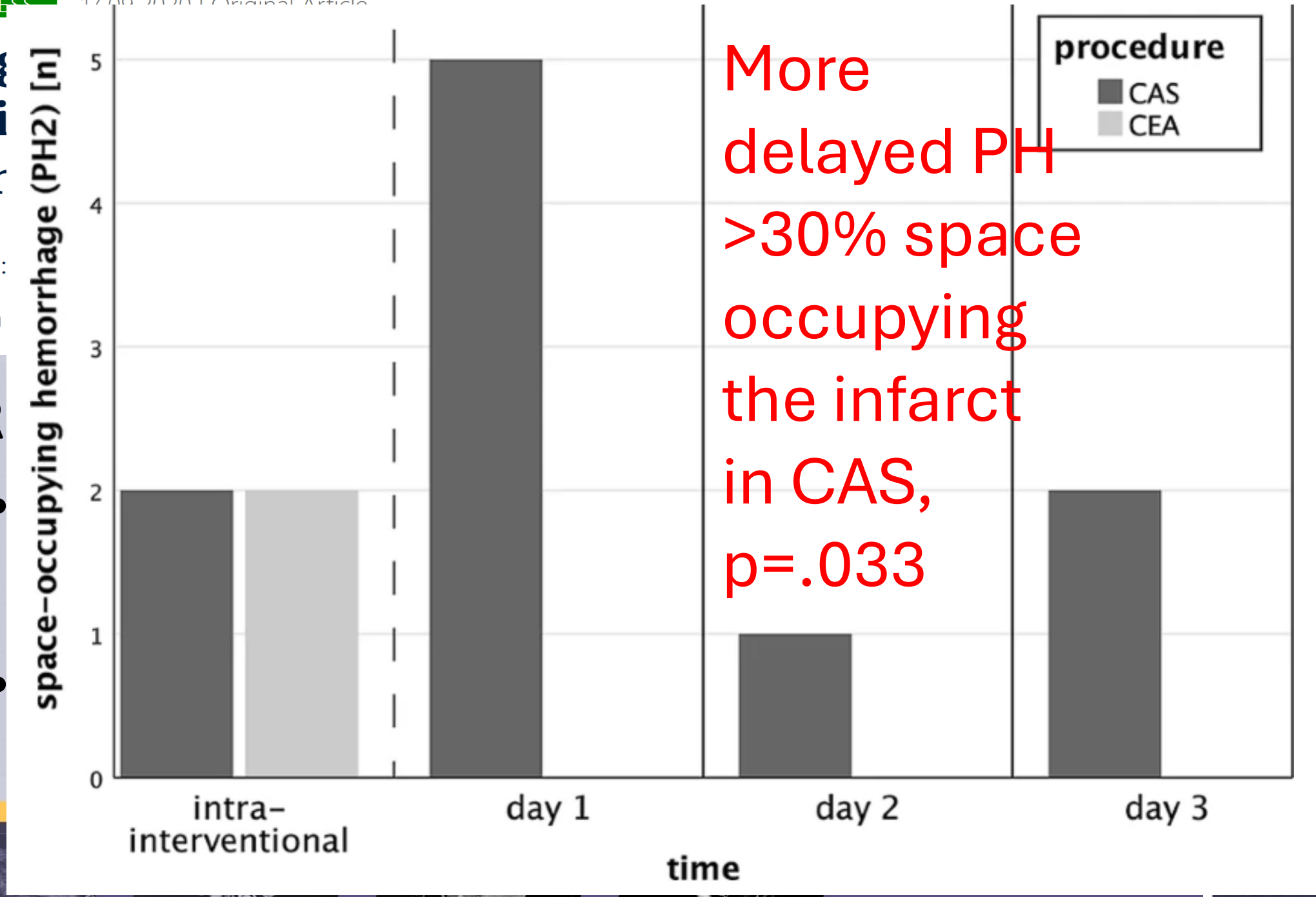

Urgent endarterectomy for symptomatic carotid occlusion is associated with a high mortality

CAROTID ARTERY INTERVENTIONS | VOLUME 76, ISSUE 3, E41, SEPTEMBER 2022

Jamie A. Schlacter, BS,[a] Molly Ratner, MD,[b] Jeffrey J. Siracuse, MD,[c] Virendra Patel, MD,[d] William Johnson, MD,[b] Jose Torres, MD,[e] Heepeel Chang, MD,[f] Glenn Jacobowitz, MD,[b] Caron Rockman, MD,[b] *and* Karan Garg, MD,[b] *New York and Valhalla, NY; and Boston, MA*

OUTCOMES

	CAROTID OCCLUSION	≥80%
MORTALITY	2.8%	0.9%

1991—25%→2020—2.8%

COMPOSITE	8.7%	5.4%

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SUMMARY—WHAT DO WE DO FOR CAROTID OCCLUSION

- It all
  - Ac
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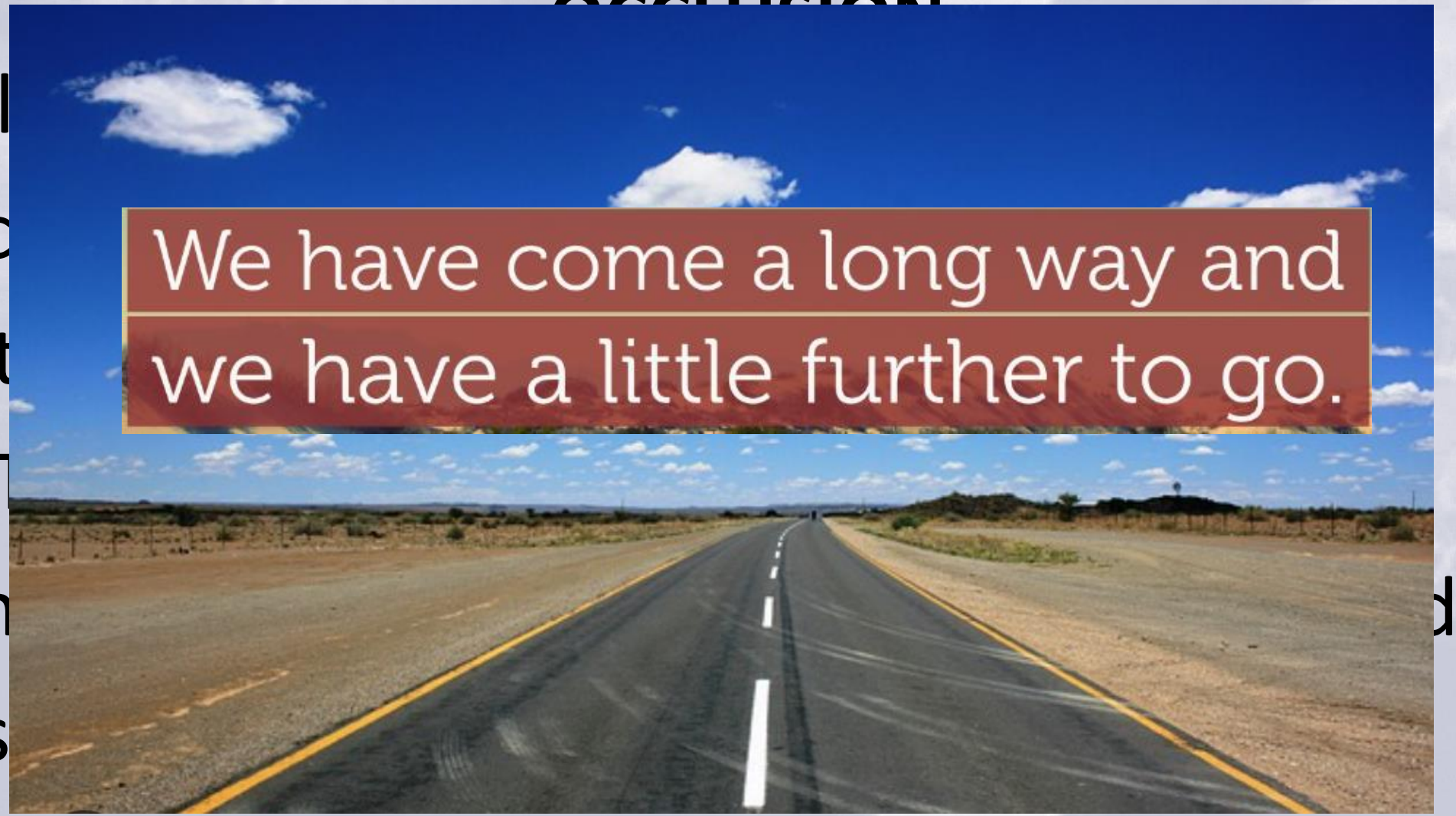
    - T
  - Ch dart
  - As




THANK
YOU

COMMON CAROTID OCCLUSIONS

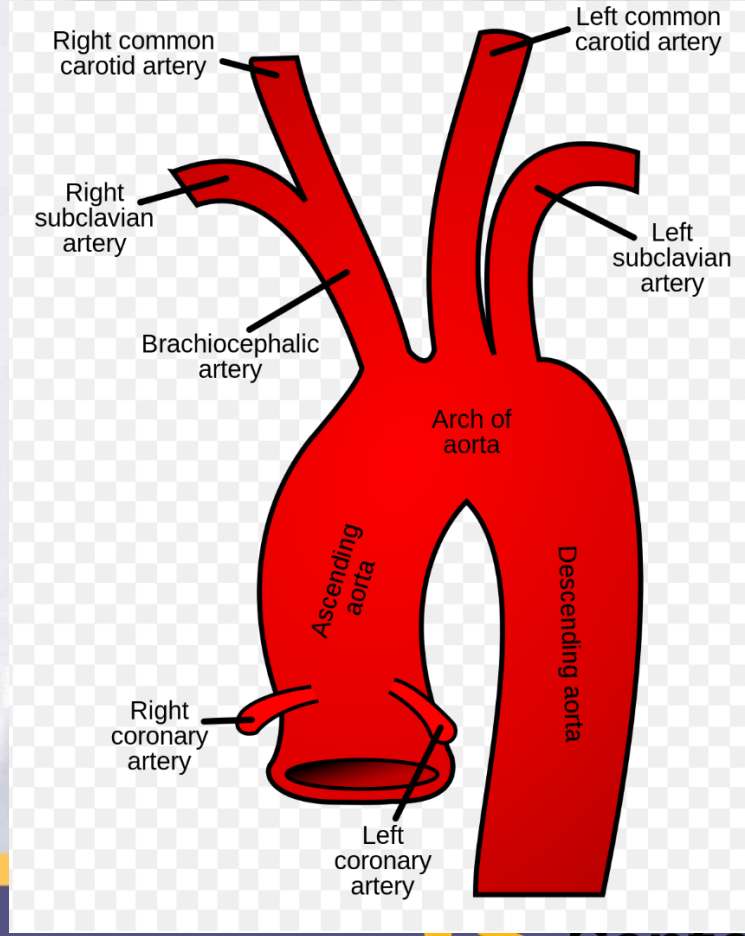
- Stenosis/occlusion at the aortic arch branch vessel origins is 0.5-6.4%
- Higher frequency in the IA & LSA vs L CCA

Technical and Clinical Success and Long-Term Durability of Endovascular Treatment for Atherosclerotic Aortic Arch Branch Origin Obstruction: Evaluation of 144 Procedures

M.A.J. van de Weijer [a], E.J.P.A. Vonken [b], J.-P.P.M. de Vries [c], F.L. Moll [a], J.A. Vos [d], G.J. de Borst [a]

European Journal of Vascular and Endovascular Surgery

Volume 50, Issue 1, July 2015, Pages 13-20



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COMMON CAROTID OCCLUSIONS

Technical and Clinical Success and Long-Term Durability of Endovascular Treatment for Atherosclerotic Aortic Arch Branch Origin Obstruction: Evaluation of 144 Procedures

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European Journal of Vascular and Endovascular Surgery

Volume 50, Issue 1, July 2015, Pages 13-20

- 1969 pts
- 3 different approaches
  - Hybrid (CEA w/ retrograde IA or CCA stenting)—700 pts
  - Isolated Open to prox IA or CCA—686 pts
  - Isolated Endovascular to prox IA or CCA—583 pts

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COMMON CAROTID OCCLUSIONS OUTCOMES

Technical and Clinical Success and Long-Term Durability of Endovascular Treatment for Atherosclerotic Aortic Arch Branch Origin Obstruction: Evaluation of 144 Procedures

M.A.J. van de Weijer [a], E.J.P.A. Vonken [b], J.-P.P.M. de Vries [c], F.L. Moll [a], J.A. Vos [d], G.J. de Borst [a]

European Journal of Vascular and Endovascular Surgery
Volume 50, Issue 1, July 2015, Pages 13-20

	30d S/D	Restenosis	Late ipsi stroke
Hybrid	3.3%	10.5%-p/4.1%-d	3.3% @ 6y
Open	7%	2.6%	1% @12y
Endo	1.5%	9%	1% @ 4y

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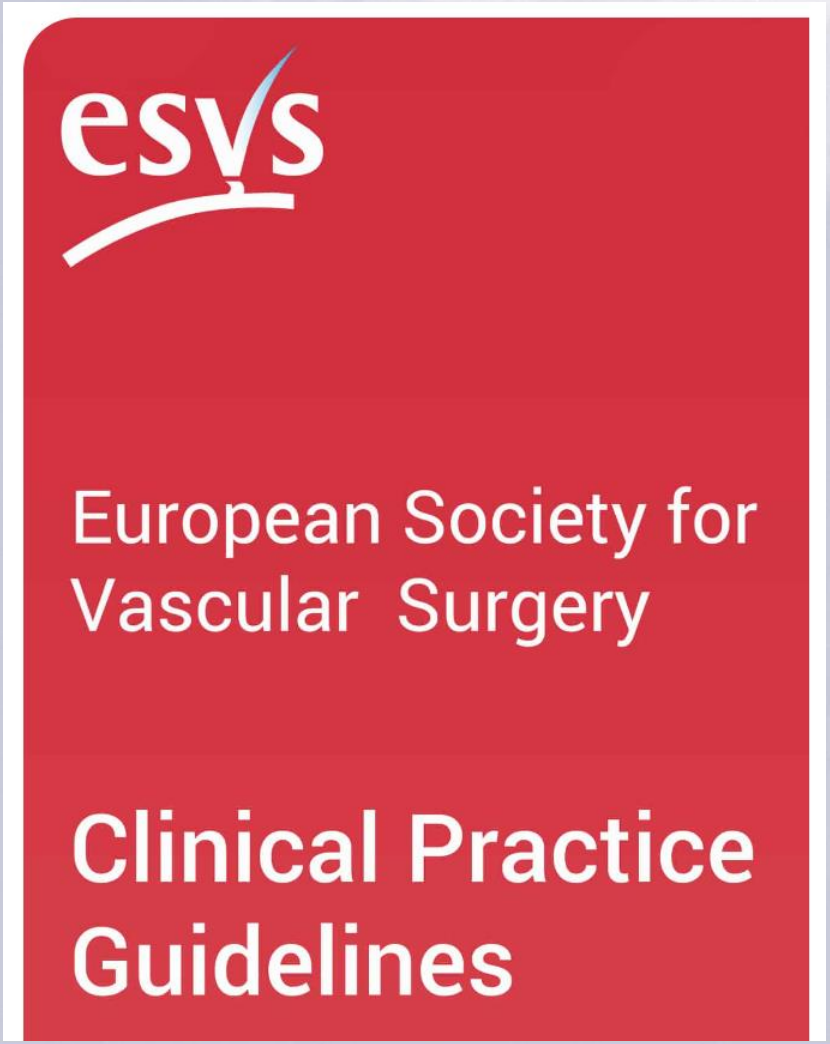
COMMON CAROTID STENOSIS/OCCLUSION



Recommendation 123		Unchanged
For asymptomatic patients with proximal common carotid artery or innominate artery stenoses/occlusions, open or endovascular interventions are not recommended.		
Class	**Level**	**References**
III	C	Consensus

Recommendation 124		Unchanged
For symptomatic patients with proximal common carotid artery or innominate stenoses, open retrograde angioplasty and stenting should be considered.		
Class	**Level**	**References** ToE
IIa	C	Robertson *et al.* (2020)[90], Van de Weijer *et al.* (2015)[596]

CLINICAL PRACTICE GUIDELINE DOCUMENT

European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease☆

Ross Naylor [a,*], Barbara Rantner [a], Stefano Ancetti [a], Gert J. de Borst [a], Marco De Carlo [a], Alison Halliday [a], Stavros K. Kakkos [a], Hugh S. Markus [a], Dominick J.H. McCabe [a], Henrik Sillesen [a], Jos C. van den Berg [a], Melina Vega de Ceniga [a], Maarit A. Venermo [a], Frank E.G. Vermassen [a]

ESVS Guidelines Committee [b], George A. Antoniou, Frederico Bastos Goncalves, Martin Bjorck, Nabil Chakfe, Raphael Coscas, Nuno V. Dias, Florian Dick, Robert J. Hinchliffe, Philippe Kolh, Igor B. Koncar, Jes S. Lindholt, Barend M.E. Mees, Timothy A. Resch, Santi Trimarchi, Riikka Tulamo, Christopher P. Twine, Anders Wanhainen

Document Reviewers [c], Sergi Bellmunt-Montoya, Richard Bulbulia, R Clement Darling, III, Hans-Henning Eckstein, Athanasios Giannoukas, Mark J.W. Koelemay, David Lindström, Marc Schermerhorn, David H. Stone

ESVS Guidelines

New Class IIb recommendations

51. For a patient with acute ischaemic stroke undergoing intracranial mechanical thrombectomy with a tandem 50–99% carotid stenosis and a small area of ipsilateral infarction, synchronous carotid stenting may be considered in the presence of poor antegrade internal carotid artery flow or poor collateralisation via the circle of Willis after mechanical thrombectomy.

57. For patients with carotid near occlusion and distal vessel collapse with recurrent carotid territory symptoms (despite best medical therapy), carotid endarterectomy or carotid artery stenting may be considered only after multidisciplinary team review.

59. For patients presenting with recent carotid territory symptoms and free floating thrombus who develop recurrent symptoms whilst receiving anticoagulation therapy, surgical or endovascular removal of the thrombus may be considered.

New Class III recommendations

60. For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus, intravenous thrombolysis is not recommended.

Urgent endarterectomy for symptomatic carotid occlusion is associated with a high mortality

CAROTID ARTERY INTERVENTIONS | VOLUME 76, ISSUE 3, E41, SEPTEMBER 2022

Jamie A. Schlacter, BS,[a] Molly Ratner, MD,[b] Jeffrey J. Siracuse, MD,[c] Virendra Patel, MD,[d] William Johnson, MD,[b] Jose Torres, MD,[e] Heepeel Chang, MD,[f] Glenn Jacobowitz, MD,[b] Caron Rockman, MD,[b] *and* Karan Garg, MD,[b] *New York and Valhalla, NY; and Boston, MA*

- SVS VQI 2003-2020
- 390 symptomatic patients with CAROTID OCCLUSION
  - 60% male
  - Mean age 67
- CEA w/in 24 hrs of presentation
- Control group—urgent CEA for ≥80% stenosis

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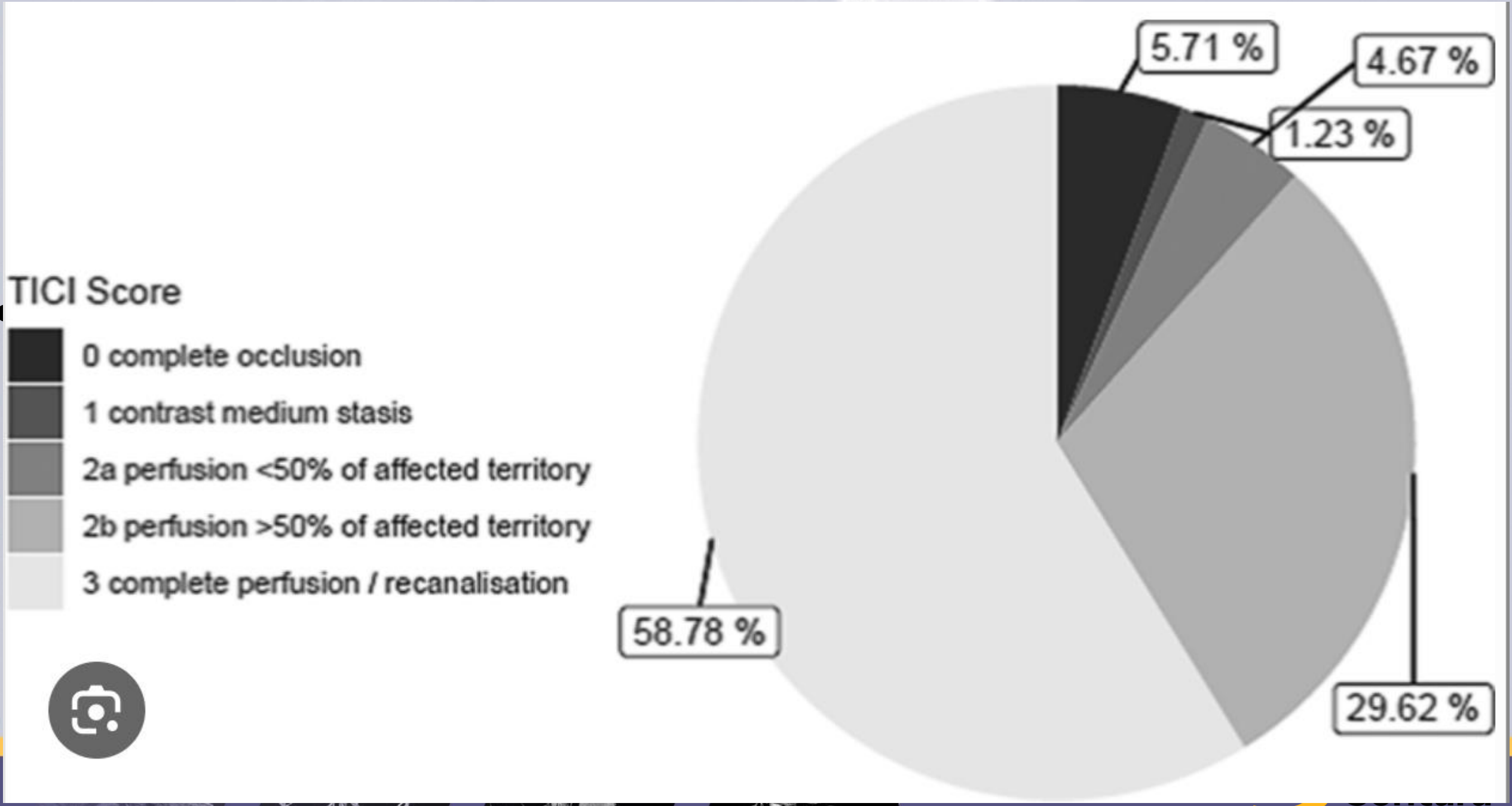

TICI Score
0 complete occlusion
1 contrast medium stasis
2a perfusion <50% of affected territory
2b perfusion >50% of affected territory
3 complete perfusion / recanalisation
5.71 %
4.67 %
1.23 %
58.78 %
29.62 %

TITAN REGISTRY—OUTCOMES—HEAD vs NECK

- HEAD 1st
  - Earlier reperfusion
  - Increased risk of distal emboli
- NECK 1st
  - Provides accessibility to d
- NO BENEFIT TO EITHER APP
- BENEFIT TO HEAD 1st

Review › J Neurointerv Surg. 2018 Aug;10(8):721-728. doi: 10.1136/neurintsurg-2017-013707. Epub 2018 Mar 9.

Management of tandem occlusions in acute ischemic stroke - intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis

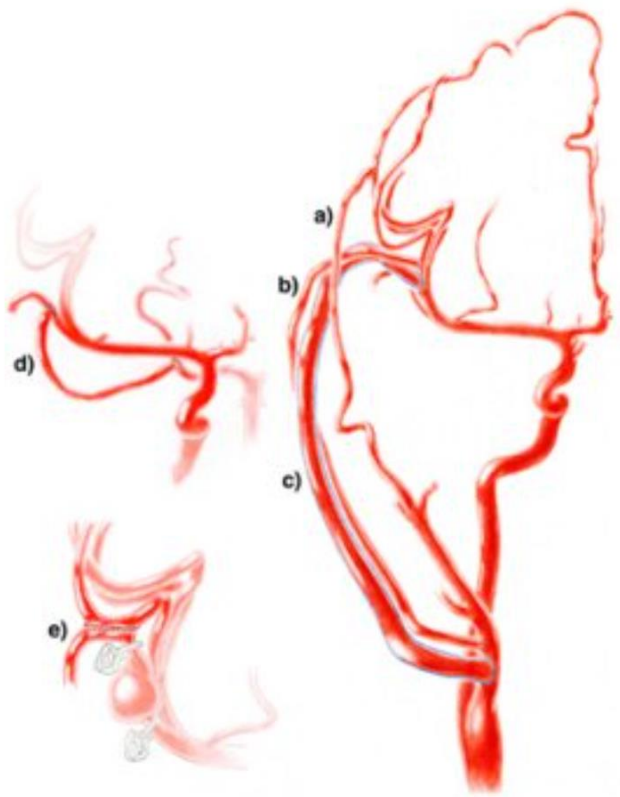
Mitchell P Wilson [1], Mohammad H Murad [2], Timo Krings [3], Vitor M Pereira [3], Cian O'Kelly [4],

› J Neurointerv Surg. 2019 Mar;11(3):237-240. doi: 10.1136/neurintsurg-2018-014114. Epub 2018 Jul 27.

Stent retriever placement in embolectomy: the choice of the post-bifurcational trunk influences the first-pass reperfusion result in M1 occlusions

Volker Maus [1], Alex Brehm [1], Ioannis Tsogkas [1], Silja Henkel [1], Marios-Nikos Psychogios [1]

EC-IC Bypass



Bypass type	Common techniques	Typical indications
a) Standard flow (20-70 ml/min)	STA-MCA[7] STA-PCA[8] STA-ACA[11]	Chronic cerebral ischemia in Moyamoya vasculopathy and arteriosclerotic cerebrovascular disease with hemodynamic compromise Vessel sacrifice with needed blood flow of 20-70 ml/min, Tumors and aneurysms with chronic ischemia
b) Intermediate flow (60-100 ml/min)	ECA-MCA[3,14] ECA-ACA[13,14] ECA-PCA[13,14] Direct end-to-side, multiple reimplantation[16] or Y-bypass[17]	Chronic cerebral ischemia, failed STA-MCA or no STA Vessel sacrifice with needed blood flow of 60-100ml/min
c) High flow (100-200 ml/min)	ECA-MCA[12] ECA-PCA[12] ECA-ACA[12]	Vessel sacrifice with needed blood flow of 100-200 ml/min
d) IC-IC	M2-P2 Radial artery graft	Revascularisation of posterior circulation
e) In-situ	PICA-PICA[18] MCA reanastomosis [12]	Aneurysms, most often used in PICA aneurysms Complex M3 aneurysms

Figure

Caption

In (a)–(c), all three types of EC-IC bypass are shown with the provided blood flow and the common indications as well as with the typical technical variations. In (d), an IC-IC bypass from the MCA to a P2 segment is shown. In (e), in situ bypass between the two M2 segments after aneurysm trapping is shown

Bypass in neurosurgery—indications and techniques

June 2019 · Neurosurgical Review 42(2)

DOI: 10.1007/s10143-018-0966-9

Lars Wessels · N. Hecht · P. Vajkoczy

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ICA OCCLUSION and THROMBOLYSIS—80's

- First reported animal model in rabbits

Tissue Plasminogen Activator Reduces Neurological Damage After Cerebral Embolism

JUSTIN A. ZIVIN, MARC FISHER, UMBERTO DEGIROLAMI, CARL C. HEMENWAY, AND JOAN A. STASHAK Authors Info & Affiliations

SCIENCE • 13 Dec 1985 • Vol 230, Issue 4731 • pp. 1289-1292 • DOI: 10.1126/science.3934754

- Streptokinase had caused significant ICH and NINDS investigators began protocols w/ tPA

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ESVS GUIDELINES—Timing of CEA/CAS after THROMBOLYSIS

- Meta-regression analysis (Figure 7), peri-operative stroke/death was 13% when CEA was performed three days after TT completion and 10.6% after four days. The risk was predicted to reduce to within the currently accepted 6% threshold after six days had elapsed, suggesting that CEA should probably be deferred until six days after TT.

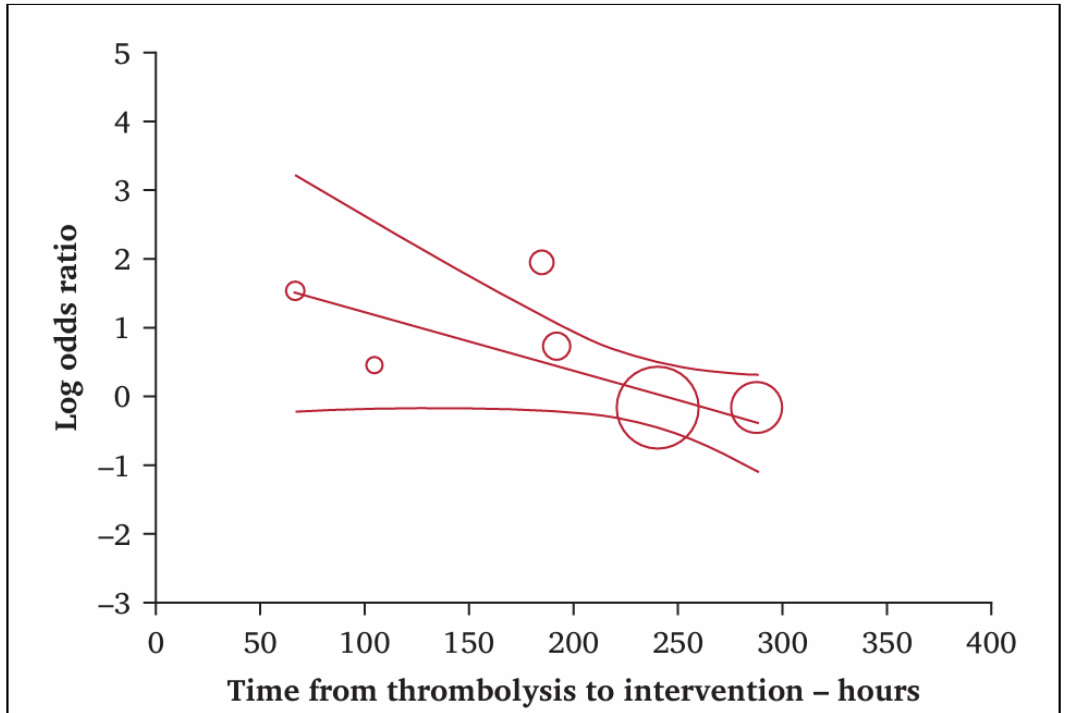

Figure 7. Regression of log odds ratio on time (hours) for peri-operative death/stroke in patients with stroke undergoing carotid endarterectomy after thrombolysis or without thrombolysis. Reproduced with permission from: Kakkos S, Vega de Ceniga, Naylor AR. A systematic review and meta-analysis of periprocedural outcomes in patients undergoing carotid interventions following thrombolysis. *Eur J Vasc Endovasc Surg* 2021;**62**:340—9.

CLINICAL RESEARCH STUDY | CAROTID ARTERY DISEASE | VOLUME 68,
ISSUE 4, P1047-1053, OCTOBER 2018

Emergent carotid endarterectomy versus stenting i acute stroke patients with tandem occlusion

Diana E. Slawski, BS • Mouhammad A. Jumaa, MD • Hisham Salahuddin, MD • ...
Aixa Espinosa-Morales, MD • Andrea Korsnack, RN • Syed F. Zaidi, MD • Show all authors

Open Archive • Published: May 19, 2018 • DOI: https://doi.org/10.1016/j.jvs.2017.12.077 •

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      - Fourth level
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Two-stage carotid saphenous vein interposition graft and superficial temporal artery bypass for acute carotid occlusion

Lukas Andereggen, MD • Robert H. Andres, MD • Marcel Arnold, MD • Andreas Raabe, MD • Jürg Schmidli, MD • Michael Reinert, MD

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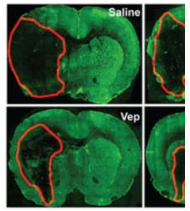
Stroke



Adjunct Therapy of Vepoloxamer W

Volume 50, Number 12, December 2019

3.5.2. Time Windows	COR	LOE	New, Revised, or Unchanged
1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who can be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	I	A	Recommendation reworded for clarity from 2013 AIS Guidelines. COR and LOE unchanged. See Table XCV in online Data Supplement 1 for original wording.
The safety and efficacy of this treatment when administered within the first 3 hours after stroke onset are solidly supported by combined data from multiple RCTs[155–157] and confirmed by extensive community experience in many countries.[158] The eligibility criteria for IV alteplase have evolved over time as its usefulness and true risks have become clearer. A recent AHA statement provides a detailed discussion of this topic.[14] Eligibility recommendations for IV alteplase in patients with AIS are summarized in Table 8. The benefit of IV alteplase is well established for adult patients with disabling stroke symptoms regardless of age and stroke severity.[78,159] Because of this proven benefit and the need to expedite treatment, when a patient cannot provide consent (eg, aphasia, confusion) and a legally authorized representative is not immediately available to provide proxy consent, it is justified to proceed with IV alteplase in an otherwise eligible adult patient with a disabling AIS. In a recent trial, a lower dose of IV alteplase (0.6 mg/kg) was not shown to be noninferior to standard-dose IV alteplase for the reduction of death and disability at 90 days.[160]			See Table XX in online Data Supplement 1.
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	I	B-R	Recommendation reworded for clarity from 2013 AIS Guidelines. COR unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System.
3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR.	IIa	B-R	New recommendation.
The WAKE-UP RCT randomized 503 patients with AIS who awoke with stroke or had unclear time of onset and could be treated with IV alteplase within 4.5 hours of stroke symptom recognition. Eligibility required MRI mismatch between abnormal signal on DW-MRI and no visible signal change on FLAIR. DW-MRI lesions larger than one-third of the territory of the MCA, NIHSS score >25, contraindication to treatment with alteplase, or planned thrombectomy were all exclusions. Ninety-four percent were wake-up strokes. Median NIHSS score was 6. Median time from last known well to symptom recognition was ≈7 hours and to alteplase administration slightly over 10 hours. The primary end point of an mRS score 0 to 1 at 90 days was achieved in 53.3% of the alteplase group and in 41.8% of the placebo group (P=0.02). Only 20% had LVO of the intracranial internal carotid or proximal middle cerebral arteries.[88]			See Table XIX in online Data Supplement 1.

Stroke

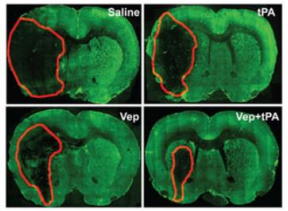


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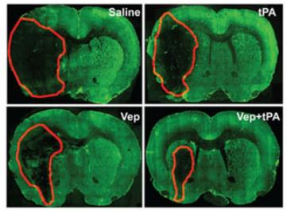
Table 8. Eligibility Recommendations for IV Alteplase in Patients With AIS (Table view)

Indications (COR I)	
Within 3 h*	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) is recommended for selected patients who may be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in this table to determine patient eligibility.† (*COR I; LOE A*)
Within 3 h–Age	For otherwise medically eligible patients ≥18 y of age, IV alteplase administration within 3 h is equally recommended for patients ≤80 and >80 y of age.† (*COR I; LOE A*)
Within 3 h–Severe stroke	For severe stroke, IV alteplase is indicated within 3 h from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms.† (*COR I; LOE A*)
Within 3 h–Mild disabling stroke	For otherwise eligible patients with mild but disabling stroke symptoms, IV alteplase is recommended for patients who can be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state (*COR I; LOE B-R*)‡
3–4.5 h*	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) is also recommended for selected patients who can be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined in this table to determine patient eligibility.† (*COR I; LOE B-R*)§
3–4.5 h–Age	IV alteplase treatment in the 3- to 4.5-h time window is recommended for those patients ≤80 y of age, without a history of both diabetes mellitus and prior stroke, NIHSS score ≤25, not taking any OACs, and without imaging evidence of ischemic injury involving more than one-third of the MCA territory.† *(COR I; LOE B-R)*§
Urgency	Treatment should be initiated as quickly as possible within the above-listed time frames because time to treatment is strongly associated with outcomes.† (*COR I; LOE A*)
BP	IV alteplase is recommended in patients with BP <185/110 mm Hg and in those patients whose BP can be lowered safely to this level with antihypertensive agents, with the physician assessing the stability of the BP before starting IV alteplase.† (*COR I; LOE B-NR*)§
Blood glucose	IV alteplase is recommended in otherwise eligible patients with initial glucose levels >50 mg/dL.† (*COR I; LOE A*)
CT	IV alteplase administration is recommended in the setting of early ischemic changes on NCCT of mild to moderate extent (other than frank hypodensity).† (*COR I; LOE A*)
Prior antiplatelet therapy	IV alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke on the basis of evidence that
	IV alteplase is recommended for patients taking antiplatelet drug combination therapy (eg, aspirin and clopidogrel) before stroke on the basis of evidence that the benefit of alteplase outweighs a probable increased risk of sICH.† (*COR I; LOE B-NR*)§
End-stage renal disease	In patients with end-stage renal disease on hemodialysis and normal aPTT, IV alteplase is recommended.† (*COR I; LOE C-LD*)§ However, those with elevated aPTT may have elevated risk for hemorrhagic complications.

Stroke



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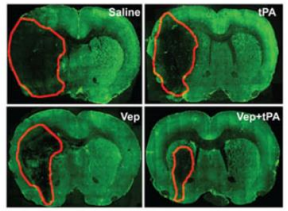
Additional recommendations for treatment with IV alteplase for patients with AIS (COR IIa)	And (COR IIb)
3 to 4.5 h–Age	For patients >80 y of age presenting in the 3- to 4.5-h window, IV alteplase is safe and can be as effective as in younger patients.† (*COR IIa; LOE B-NR*)§
3 to 4.5 h–Diabetes mellitus and prior stroke	In AIS patients with prior stroke and diabetes mellitus presenting in the 3- to 4.5- h window, IV alteplase may be as effective as treatment in the 0- to 3-h window and may be a reasonable option.† (*COR IIb; LOE B-NR*)§
3 to 4.5 h–Severe stroke	The benefit of IV alteplase between 3 and 4.5 h from symptom onset for patients with very severe stroke symptoms (NIHSS score >25) is uncertain.† (*COR IIb; LOE C-LD*)§
3 to 4.5 h–Mild disabling stroke	For otherwise eligible patients with mild disabling stroke, IV alteplase may be reasonable for patients who can be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well or at baseline state. (*COR IIb; LOE B-NR*)‡
Wake-up and unknown time of onset	IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 min) administered within 4.5 h of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 h from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR. (*COR IIa; LOE B-R*)‡
Preexisting disability	Preexisting disability does not seem to independently increase the risk of sICH after IV alteplase, but it may be associated
Coagulopathy	IV alteplase may be reasonable in patients who have a history of warfarin use and an INR ≤1.7 or a PT <15 s.† (*COR IIb; LOE B-NR*)§
	The safety and efficacy of IV alteplase for acute stroke patients with a clinical history of potential bleeding diathesis or coagulopathy are unknown. IV alteplase may be considered on a case-by-case basis.† (*COR IIb; LOE C-EO*)§
Dural puncture	IV alteplase may be considered for patients who present with AIS, even in instances when they may have undergone a lumbar dural puncture in the preceding 7 d.† (*COR IIb; LOE C-EO*)§
Arterial puncture	The safety and efficacy of administering IV alteplase to acute stroke patients who have had an arterial puncture of a noncompressible blood vessel in the 7 d preceding stroke symptoms are uncertain.† (*COR IIb; LOE C-LD*)§
Recent major trauma	In AIS patients with recent major trauma (within 14 d) not involving the head, IV alteplase may be carefully considered, with the risks of bleeding from injuries related to the trauma weighed against the severity and potential disability from the ischemic stroke. (Recommendation modified from 2015 IV Alteplase to specify that it does not apply to head trauma. [*COR IIb; LOE C-LD*])§
Recent major surgery	Use of IV alteplase in carefully selected patients presenting with AIS who have undergone a major surgery in the preceding 14 d may be considered, but the potential increased risk of surgical-site hemorrhage should be weighed against the anticipated benefits of reduced stroke related neurological deficits.† (*COR IIb; LOE C-LD*)§
GI and genitourinary bleeding	Reported literature details a low bleeding risk with IV alteplase administration in the setting of past GI/genitourinary bleeding. Administration of IV alteplase in this patient population may be reasonable.† (*COR IIb; LOE C-LD*)§ (Note: Alteplase administration within 21 d of a GI bleeding event is not recommended; see Contraindications.)
Menstruation	IV alteplase is probably indicated in women who are menstruating who present with AIS and do not have a history of menorrhagia. However, women should be warned that alteplase treatment could increase the degree of menstrual flow.† (*COR IIa; LOE C-EO*)§
	When there is a history of recent or active vaginal bleeding causing clinically significant anemia, then emergency consultation with a gynecologist is probably indicated before a decision about IV alteplase is made.† (*COR IIa; LOE C-EO*)§
	Because the potential benefits of IV alteplase probably outweigh the risks of serious bleeding in patients with recent or active history of menorrhagia without clinically significant anemia or hypotension, IV alteplase administration may be considered.† (*COR IIb; LOE C-LD*)§
Extracranial cervical dissections	IV alteplase in AIS known or suspected to be associated with extracranial cervical arterial dissection is reasonably safe within 4.5 h and probably recommended.† (*COR IIa; LOE C-LD*)§
Intracranial arterial dissection	IV alteplase usefulness and hemorrhagic risk in AIS known or suspected to be associated with intracranial arterial dissection remain unknown, uncertain and not well established.† (*COR IIb; LOE C-LD*)§

Stroke



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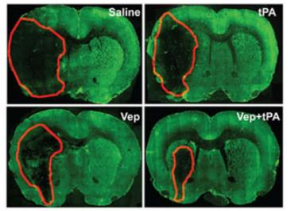
Unruptured intracranial aneurysm	For patients presenting with AIS who are known to harbor a small or moderate-sized (<10 mm) unruptured and unsecured intracranial aneurysm, administration of IV alteplase is reasonable and probably recommended.† (*COR IIa; LOE C-LD*)§
	Usefulness and risk of IV alteplase in patients with AIS who harbor a giant unruptured and unsecured intracranial aneurysm are not well established.† (*COR IIb; LOE C-LD*)§
Intracranial vascular malformations	For patients presenting with AIS who are known to harbor an unruptured and untreated intracranial vascular malformation the usefulness and risks of administration of IV alteplase are not well established.† (*COR IIb; LOE C-LD*)§
	Because of the increased risk of ICH in this population of patients, IV alteplase may be considered in patients with stroke with severe neurological deficits and a high likelihood of morbidity and mortality to outweigh the anticipated risk of ICH.† (*COR IIb; LOE C-LD*)§
CMBs	In otherwise eligible patients who have previously had a small number (1–10) of CMBs demonstrated on MRI, administration of IV alteplase is reasonable. (*COR IIa; Level B-NR*)‡
	In otherwise eligible patients who have previously had a high burden of CMBs (>10) demonstrated on MRI, treatment with IV alteplase may be associated with an increased risk of sICH, and the benefits of treatment are uncertain. Treatment may be reasonable if there is the potential for substantial benefit. (*COR IIb; Level B-NR*)‡
Concomitant tirofiban, epifibatide	The efficacy of the IV glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide coadministered with IV alteplase is not well established. (*COR IIb; Level B-NR*)‡
Extra-axial intracranial	IV alteplase treatment is probably recommended for patients with AIS who harbor an extra-axial intracranial neoplasm.†
Left atrial or ventricular thrombus	For patients with major AIS likely to produce severe disability and known left atrial or ventricular thrombus, treatment with IV alteplase may be reasonable.† (*COR IIb; LOE C-LD*)§
	For patients presenting with moderate AIS likely to produce mild disability and known left atrial or ventricular thrombus, treatment with IV alteplase is of uncertain net benefit.† (*COR IIb; LOE C-LD*)§
Other cardiac diseases	For patients with major AIS likely to produce severe disability and cardiac myxoma, treatment with IV alteplase may be reasonable.† (*COR IIb; LOE C-LD*)§
	For patients presenting with major AIS likely to produce severe disability and papillary fibroelastoma, treatment with IV alteplase may be reasonable.† (*COR IIb; LOE C-LD*)§
Procedural stroke	IV alteplase is reasonable for the treatment of AIS complications of cardiac or cerebral angiographic procedures, depending on the usual eligibility criteria.† (*COR IIa; LOE A*)§
Systemic malignancy	The safety and efficacy of IV alteplase in patients with current malignancy are not well established.† (*COR IIb; LOE C-LD*)§ Patients with systemic malignancy and reasonable (>6 mo) life expectancy may benefit from IV alteplase if other contraindications such as coagulation abnormalities, recent surgery, or systemic bleeding do not coexist.
Pregnancy	IV alteplase administration may be considered in pregnancy when the anticipated benefits of treating moderate or severe stroke outweigh the anticipated increased risks of uterine bleeding.† (*COR IIb; LOE C-LD*)§
	The safety and efficacy of IV alteplase in the early postpartum period (<14 d after delivery) have not been well established.† (*COR IIb; LOE C-LD*)§
Ophthalmological conditions	Use of IV alteplase in patients presenting with AIS who have a history of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions is reasonable to recommend, but the potential increased risk of visual loss should be weighed against the anticipated benefits of reduced stroke-related neurological deficits.† (*COR IIa; LOE B-NR*)§
Sickle cell disease	IV alteplase for adults presenting with an AIS with known sickle cell disease can be beneficial. (*COR IIa; LOE B-NR*)‡
Hyperdense MCA sign	In patients with a hyperdense MCA sign, IV alteplase can be beneficial. (*COR IIa; LOE B-NR*)‡
Illicit drug use	Treating clinicians should be aware that illicit drug use may be a contributing factor to incident stroke. IV alteplase is reasonable in instances of illicit drug use–associated AIS in patients with no other exclusions.† (*COR IIa; LOE C-LD*)§
Stroke mimics	The risk of symptomatic intracranial hemorrhage in the stroke mimic population is quite low; thus, starting IV alteplase is probably recommended in preference over delaying treatment to pursue additional diagnostic studies.† (*COR IIa; LOE B-NR*)§

Stroke



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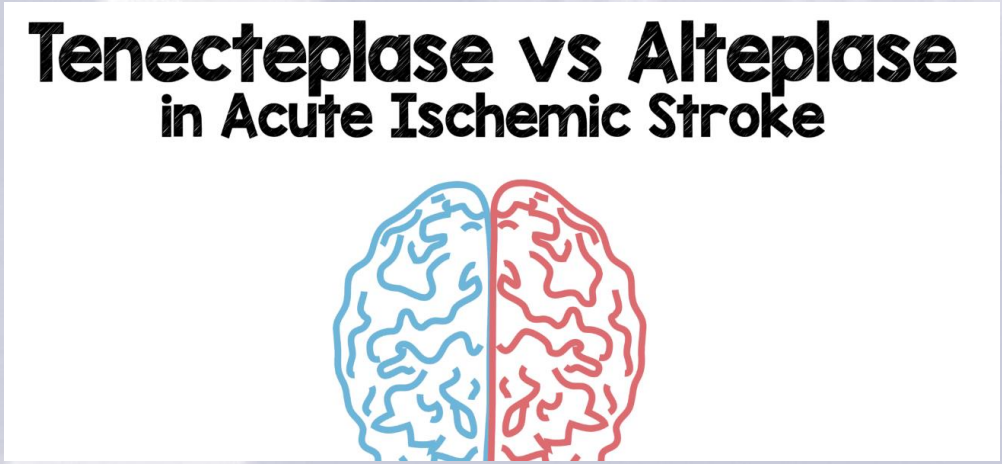
Contraindications (COR III: No Benefit)	And (COR III: Harm)
0- to 3-h window–Mild nondisabling stroke	For otherwise eligible patients with mild nondisabling stroke (NIHSS score 0–5), IV alteplase is not recommended for patients who could be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state. (*COR III: No Benefit, LOE B-R*)‡
3- to 4.5-h window–Mild nondisabling stroke	For otherwise eligible patients with mild nondisabling stroke (NIHSS score 0–5), IV alteplase is not recommended for patients who could be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well or at baseline state. (*COR III: No Benefit, LOE C-LD*)‡
CT	There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to alteplase. However, administering IV alteplase to patients whose CT brain imaging exhibits extensive regions of clear hypoattenuation is not recommended. These patients have a poor prognosis despite IV alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury.† (*COR III: No Benefit; LOE A*)‖
ICH	IV alteplase should not be administered to a patient whose CT reveals an acute intracranial hemorrhage.† (*COR III: Harm; LOE C-EO*)§‖
Ischemic stroke within 3 mo	Use of IV alteplase in patients presenting with AIS who have had a prior ischemic stroke within 3 mo may be harmful.† (*COR*
Coagulopathy	The safety and efficacy of IV alteplase for acute stroke patients with platelets <100 000/mm^3, INR >1.7, aPTT >40 s, or PT >15 s are unknown, and IV alteplase should not be administered.† (*COR III: Harm; LOE C-EO*)§‖ (In patients without history of thrombocytopenia, treatment with IV alteplase can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm^3. In patients without recent use of OACs or heparin, treatment with IV alteplase can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.) (Recommendation wording modified to match COR III stratifications.)
LMWH	IV alteplase should not be administered to patients who have received a full treatment dose of LMWH within the previous 24 h.† (*COR III: Harm; LOE B-NR*)§‡ (Recommendation wording modified to match COR III stratifications.)
Thrombin inhibitors or factor Xa inhibitors	The use of IV alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful.† (*COR III: Harm; LOE C-EO*)§‖ IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 h (assuming normal renal metabolizing function). (Alteplase could be considered when appropriate laboratory tests such as aPTT, INR, ecarin clotting time, thrombin time, or direct factor Xa activity assays are normal or when the patient has not taken a dose of these ACs for >48 h and renal function is normal.) (Recommendation wording modified to match COR III stratifications.)
Concomitant Abciximab	Abciximab should not be administered concurrently with IV alteplase. (*COR III: Harm; LOE B-R*)‡
Concomitant IV aspirin	IV aspirin should not be administered within 90 min after the start of IV alteplase. (*COR III: Harm; LOE B-R*)‡
Infective endocarditis	For patients with AIS and symptoms consistent with infective endocarditis, treatment with IV alteplase should not be administered because of the increased risk of intracranial hemorrhage.† (*COR III: Harm; LOE C-LD*)§‖ (Recommendation wording modified to match COR III stratifications.)
Aortic arch dissection	IV alteplase in AIS known or suspected to be associated with aortic arch dissection is potentially harmful and should not be administered.† (*COR III: Harm; LOE C-EO*)§‖ (Recommendation wording modified to match COR III stratifications.)
Intra-axial intracranial neoplasm	IV alteplase treatment for patients with AIS who harbor an intra-axial intracranial neoplasm is potentially harmful.† (*COR III: Harm; LOE C-EO*)§‖

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

Authors: Bruce C.V. Campbell, Ph.D., Peter J. Mitchell, M.Med., Leonid Churilov, Ph.D., Nawaf Yassi, Ph.D., Timothy J. Kleinig, Ph.D., Richard J. Dowling, M.B., B.S., Bernard Yan, M.B., B.S., +47, for the EXTEND-IA TNK Investigators* Author Info & Affiliations

Published April 25, 2018 | N Engl J Med 2018;378:1573-1582 | DOI: 10.1056/NEJMoa1716405 | VOL. 378 NO. 17

- Tenectaplase
  - Greater fibrin specificity
  - Longer half life
  - Can be given as bolus as opposed to infusion



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- Randomized ICA, Basilar, MCA occl in pts w/ ischemic stroke
- TNK vs Alteplase
- Excluded mRS 3-6
- 1° endpt
  - 50% reperfusion of ischemic area
  - Absence of thrombus at angio
- 2° endpt—mRS @ 90 d
- Safety endpt
  - ICH
  - Death

Outcome	Tenecteplase Group (N=101)	Alteplase Group (N=101)
Primary efficacy outcome		
Substantial reperfusion at initial angiographic assessment — no. (%)*	22 (22)	10 (10)
Difference — percentage points		
Adjusted incidence ratio		
Adjusted odds ratio		

Mostly MCA

Outcome	Tenecteplase Group (N=101)	Alteplase Group (N=101)	Effect Size (95% CI)
Adjusted incidence ratio			1.2 (0.9–1.6)
Adjusted odds ratio			1.4 (0.8–2.6)
Early neurologic improvement — no. (%)§¶	72 (71)	69 (68)	
Adjusted incidence ratio			1.0 (0.9–1.2)
Adjusted odds ratio			1.1 (0.6–2.1)
Safety outcomes			
Death — no. (%)§	10 (10)	18 (18)	
Adjusted risk ratio			0.5 (0.3–1.0)
Adjusted odds ratio			0.4 (0.2–1.1)
Symptomatic intracerebral hemorrhage — no. (%)§‖	1 (1)	1 (1)	
Risk ratio			1.0 (0.1–15.9)
Odds ratio			1.0 (0.1–16.2)
Parenchymal hematoma — no. (%)§**	6 (6)	5 (5)	
Risk ratio			1.2 (0.4–3.8)
Odds ratio			1.2 (0.4–4.1)

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

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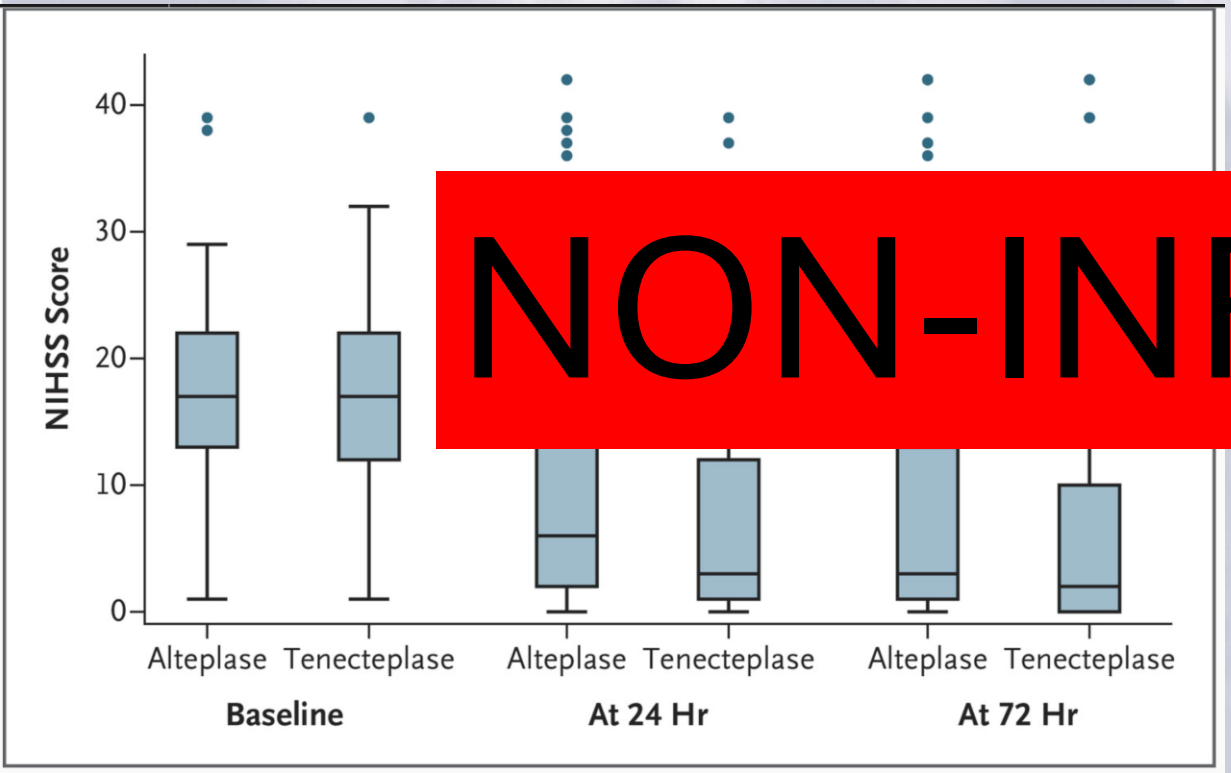
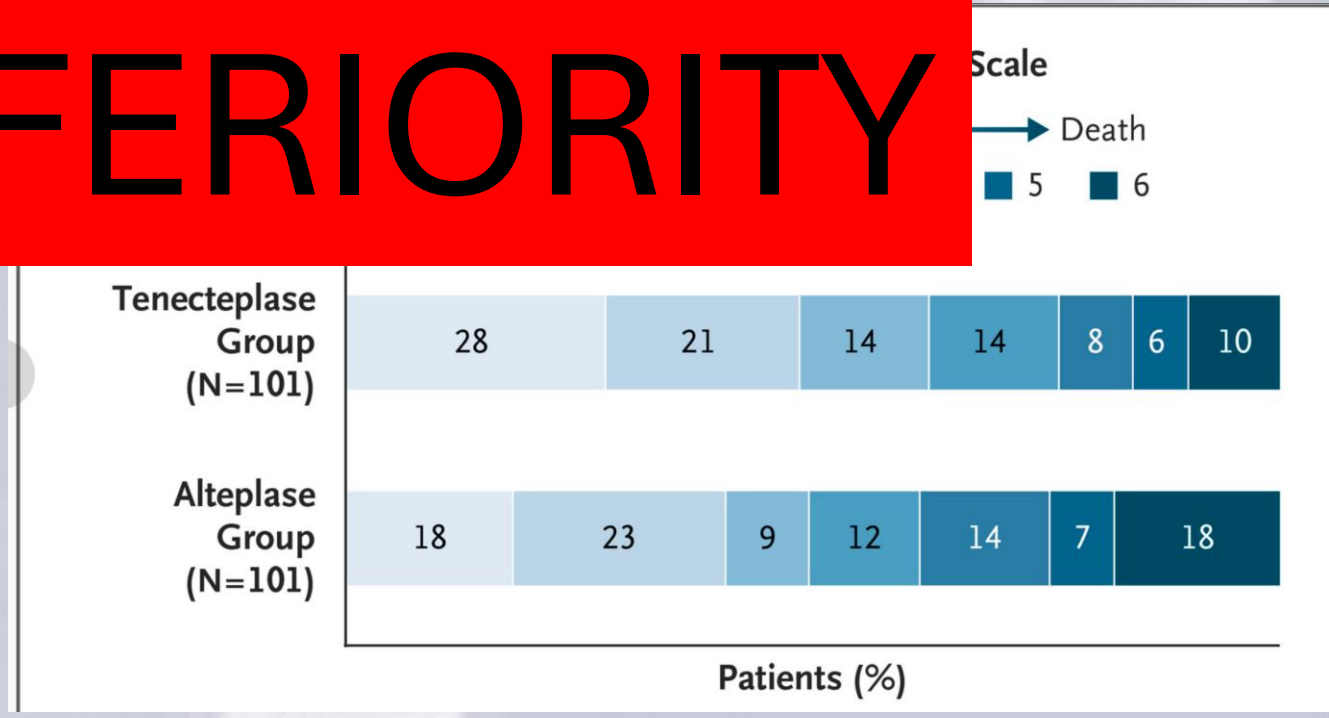


NON-INFERIORITY



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THROMBECTOMY W/ or W/O THROMBOLYSIS

- THROMBOLYTICS
  - may increase early reperfusion of the ischemic area and dissolve residual distal thrombi after endovascular thrombectomy.[7-10]
  - For large, proximally located thrombi, however, the lytic effect of intravenous alteplase is limited, and partial lysis could fragment the target thrombus or cause it to migrate distally, potentially complicating endovascular thrombectomy.[11,12]
  - Intravenous alteplase may also increase the risk of cerebral hemorrhage.[13]

Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke

Authors: Pengfei Yang, M.D., Yongwei Zhang, M.D., Lei Zhang, M.D., Yongxin Zhang, M.D., Kilian M. Treurniet, M.D., Wenhuo Chen, M.D., Ya Peng, M.D., +52, for the DIRECT-MT Investigators* Author Info & Affiliations

Published May 6, 2020 | N Engl J Med 2020;382:1981-1993 | DOI: 10.1056/NEJMoa2001123 | VOL. 382 NO. 21

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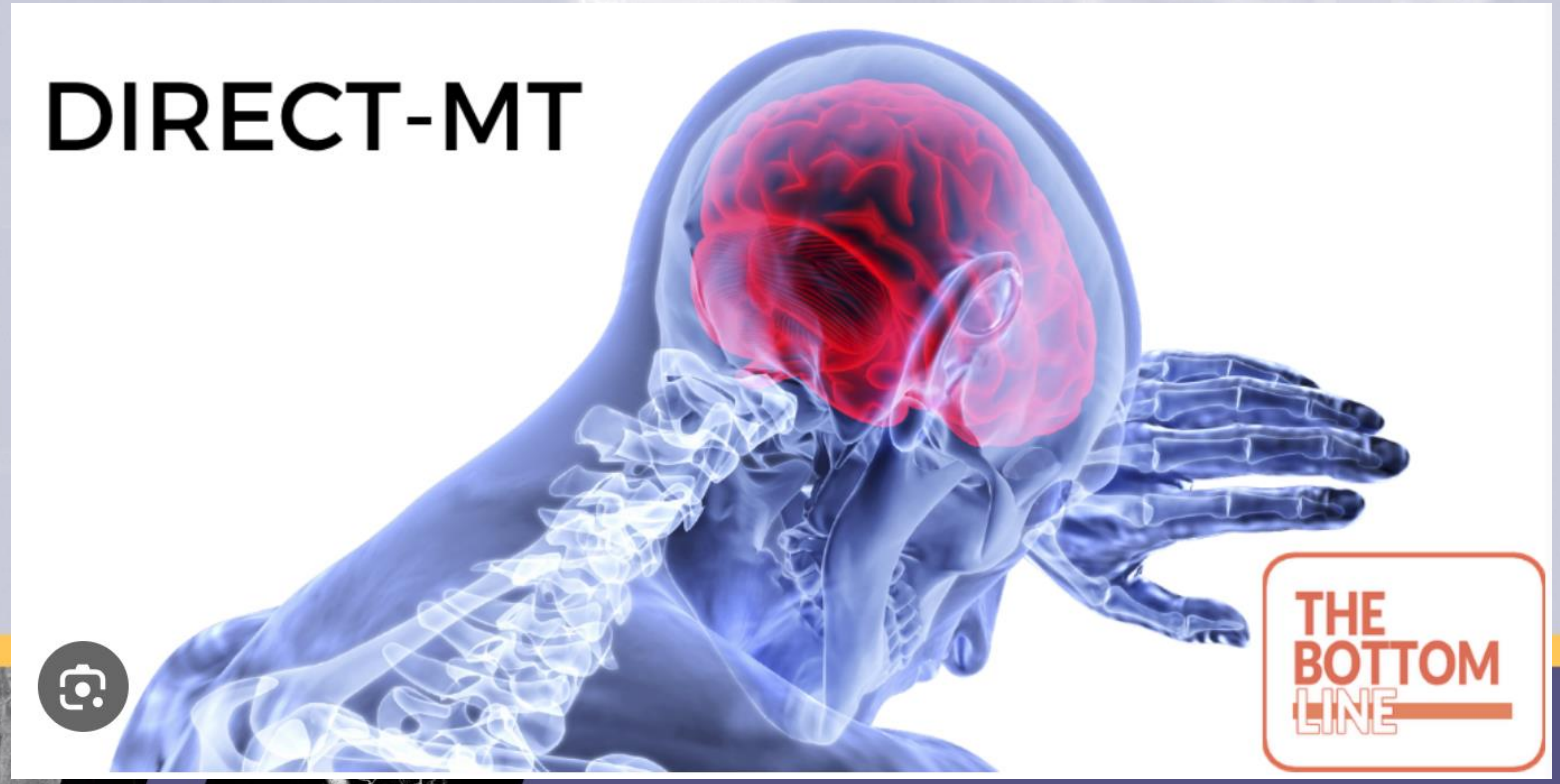
THROMBECTOMY vs THROMBECTOMY/THOMBOLYSIS DIRECT MT(2020)

- Chinese study w/ 656 pts
  - Thrombectomy
  - Thrombectomy + Thrombolysis
- 1° Endpts
  - mRS @ 90 d
  - Reperfusion
- Safety
  - ICH
  - Death



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Thrombectomy with or without Alteplase for Stroke

MULTICENTER, RANDOMIZED, NONINFERIORITY TRIAL IN CHINA

656 Patients with acute ischemic stroke

	Endovascular thrombectomy alone (N=327)	Alteplase (0.9 mg/kg) + Endovascular thrombectomy (N=329)
Median modified Rankin score at 90 days	3	3

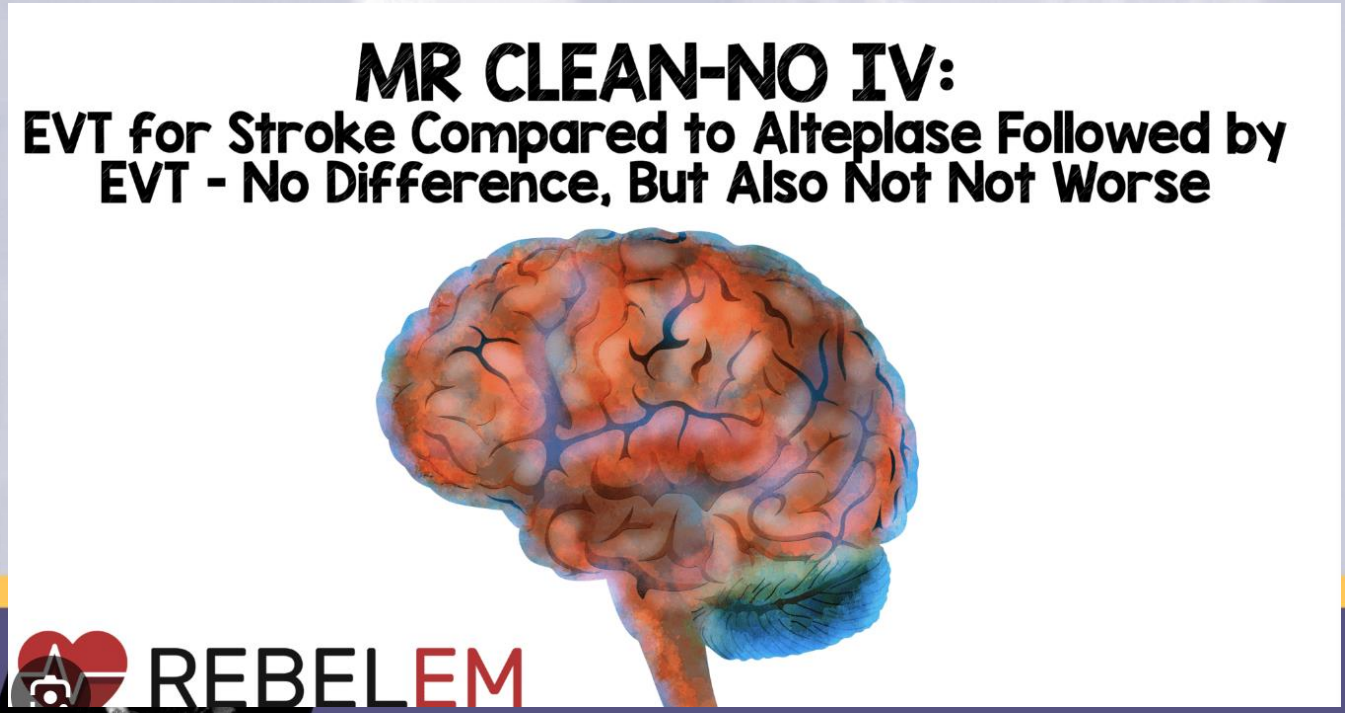
Adjusted common OR, 1.07; 95% CI, 0.81 to 1.40; P=0.04

Death		17.7%	≈	18.8%
Intracranial hemorrhage	Symptomatic:	4.3%	≈	6.1%
	Asymptomatic:	33.3%	≈	36.2%

Endovascular thrombectomy alone was not inferior to intravenous alteplase plus endovascular thrombectomy

THROMBECTOMY vs THROMBECTOMY/THOMBOLYSIS
MR CLEAN—NO IV (2021)

- European study w/ 539 pts
  - Thrombectomy
  - Thrombectomy + Thrombolysis
- 1° Endpt—mRS @ 90 d
- Safety
  - ICH
  - Death



RESEARCH SUMMARY

A Randomized Trial of Intravenous Alteplase before Endovascular Treatment for Stroke

LeCouffe NE et al. DOI: 10.1056/NEJMoa2107727

CLINICAL PROBLEM

Guidelines recommend use of intravenous thrombolysis before endovascular treatment (EVT) for anterior-circulation ischemic stroke, but trials involving Asian patients have suggested that outcomes with EVT alone are noninferior to those with EVT preceded by thrombolysis.

CLINICAL TRIAL

Design: A multicenter, randomized, open-label trial in Europe compared the use of EVT with or without intravenous alteplase pretreatment for ischemic stroke.

Intervention: 539 patients with stroke caused by occlusion of a proximal anterior-circulation artery were randomly assigned to receive EVT alone or EVT after standard-dose intravenous alteplase (usual care). The primary end point was functional outcome at 90 days according to the modified Rankin scale.

RESULTS

Efficacy: The median score on the modified Rankin scale at 90 days was 3 in the group treated with EVT alone and 2 in the group treated with EVT plus alteplase, with overlapping interquartile ranges. The odds ratio for a shift in modified Rankin scale score indicated neither noninferiority nor superiority of EVT alone.

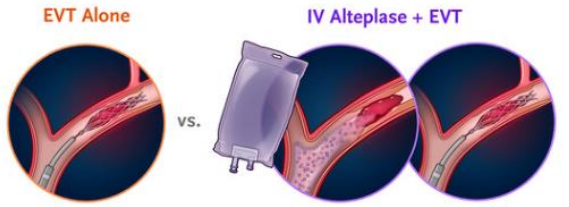
Safety: The incidences of death from any cause and symptomatic intracerebral hemorrhage at 90 days did not differ significantly between the two treatment groups.

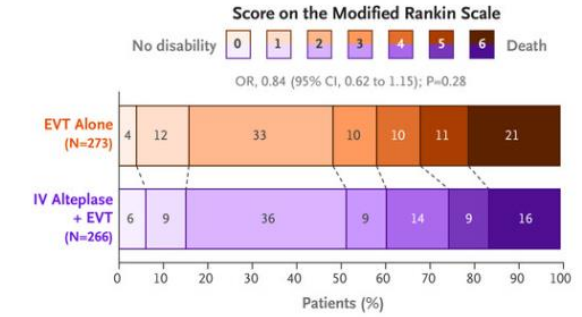
LIMITATIONS AND REMAINING QUESTIONS

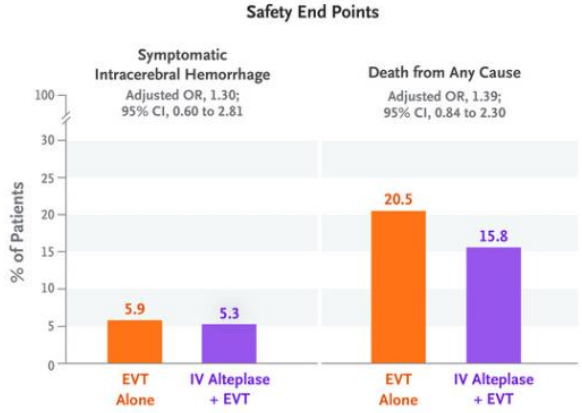
Further study is required to understand whether the findings would apply to other groups of patients:

- patients not presenting directly to a center with EVT capability.
- patients with longer times to hospital arrival.

Links: Full Article | NEJM Quick Take







CONCLUSIONS

In this randomized trial focusing on 90-day functional outcomes in European patients, EVT alone was neither superior nor noninferior to intravenous alteplase plus EVT for ischemic stroke.

90 Days after EVT

Median Score on Modified Rankin Scale

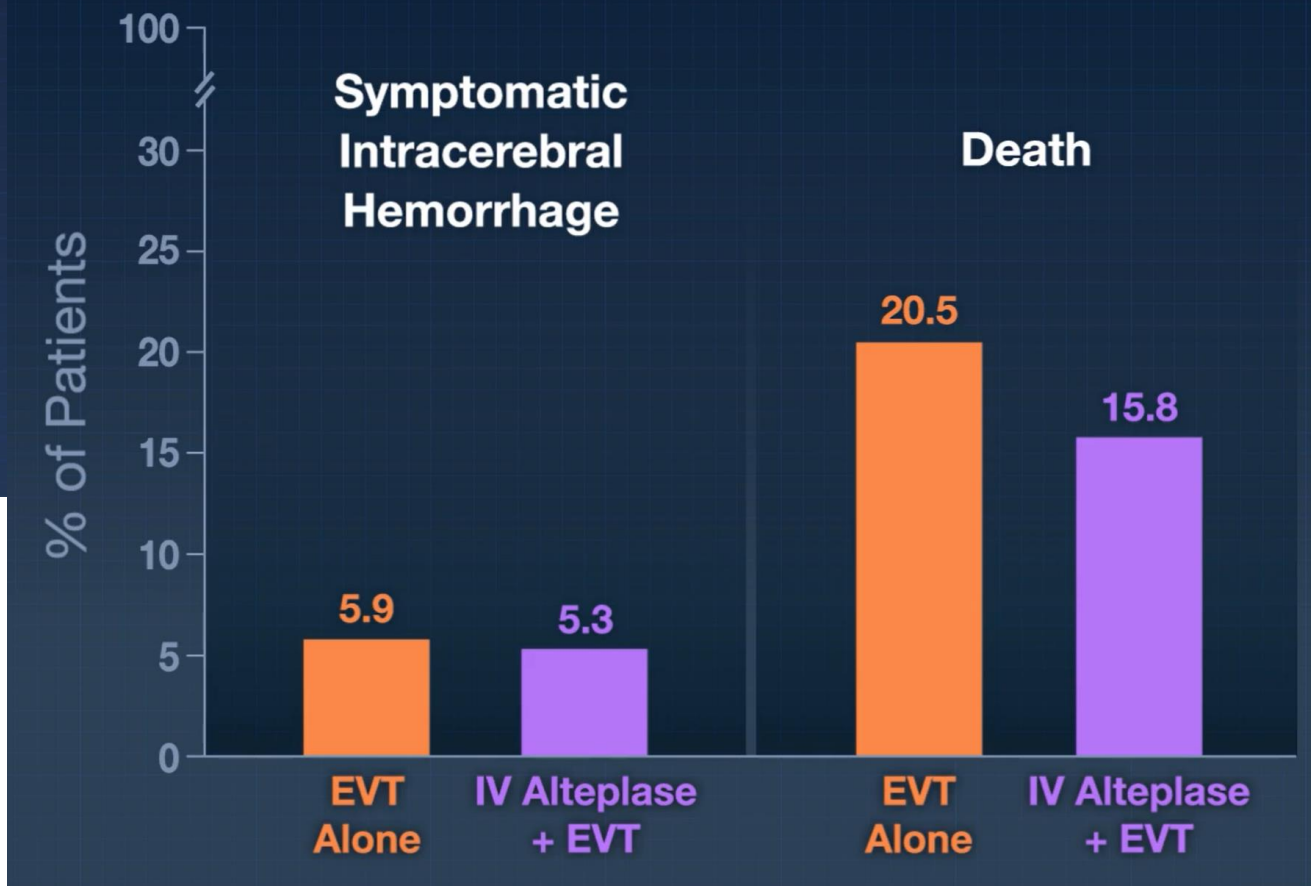
Neither superior nor noninferior

Common Odds Ratio, 0.84

95% CI, 0.62 to 1.15; P=0.28

2

Safety End Points



ENDOVASCULAR THROMBECTOMY vs MEDICAL THERAPY RESCUE-JAPAN LIMIT TRIAL--2022

- THERAPY w/in 24 hrs onset (27% rec'd thrombolytics)
  - Thrombectomy
  - Med mgmt
    - BP, Critical care, In-hospital and Outpt Rehab
- Large volume—ASPECTS value 3-5
  - NCCT
  - DW MRI

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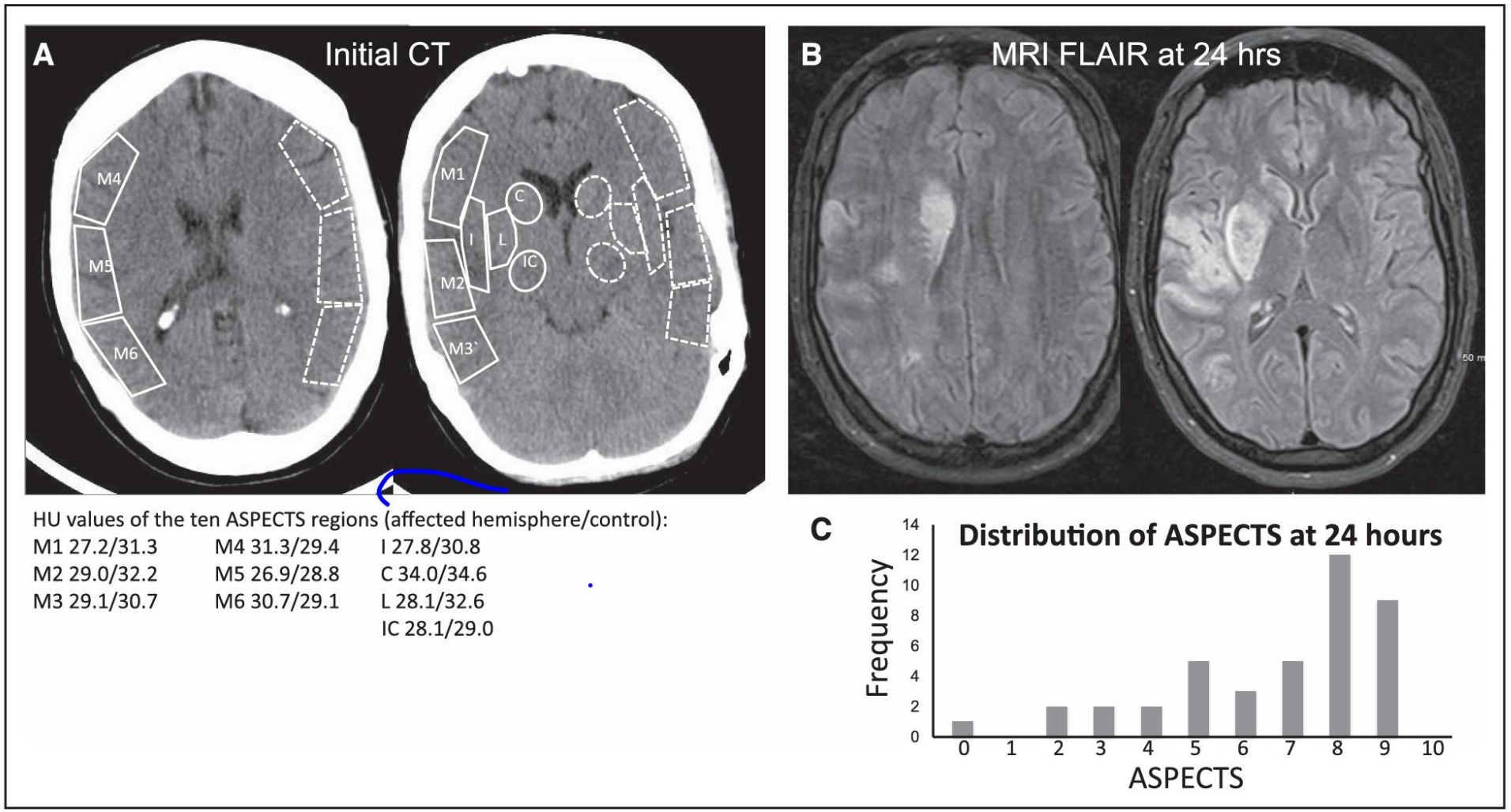

Figure 2. An example of initial computerized tomography head with Hounsfield unit (HU) values calculated between the 2 hemispheres. **A**, Ten ASPECTS (Alberta Stroke Program Early CT Score) regions are outlined manually. HU values representing each individual region are shown at the bottom. Solid lines label the affected hemisphere and dotted lines label contralateral (control) hemisphere. **B**, Follow-up magnetic resonance imaging fluid-attenuated inversion recovery repeated at 24 hours shows the extent of final stroke, ASPECTS=5. **C**, Distribution of ASPECTS at 24 hours. C indicates caudate; I, insular ribbon; IC, internal capsule; L, lentiform; and M1–6, middle cerebral artery cortical regions 1 to 6.

Higher ASPECTS Score=> Less Extensive CVA

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RESEARCH SUMMARY

Endovascular Therapy for Acute Stroke with a Large Ischemic Region

Yoshimura S et al. DOI: 10.1056/NEJMoa2118191

CLINICAL PROBLEM

Although endovascular therapy is standard treatment for ischemic stroke caused by large-vessel occlusion, it is not typically used in patients with a large ischemic region because of a lack of data from randomized trials and concern about the risk of hemorrhage with reperfusion.

CLINICAL TRIAL

Design: An open-label, multicenter, randomized clinical trial in Japan compared endovascular therapy with medical therapy alone in patients with large-vessel stroke and a large ischemic area.

Intervention: 203 patients underwent randomization; 100 patients assigned to endovascular therapy and 102 assigned to medical care alone completed follow-up. The primary outcome was a modified Rankin scale score of 0 (no disability) to 3 (moderate disability but ambulatory) at 90 days after stroke onset.

RESULTS

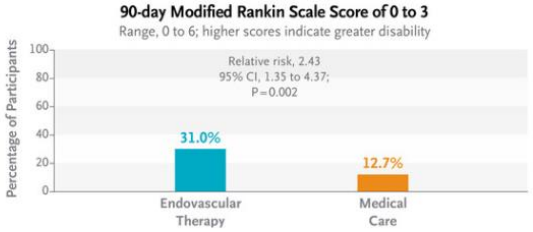
Efficacy: The percentage of patients with a modified Rankin scale score of 0 to 3 at 90 days was significantly higher with endovascular therapy than with medical care alone.

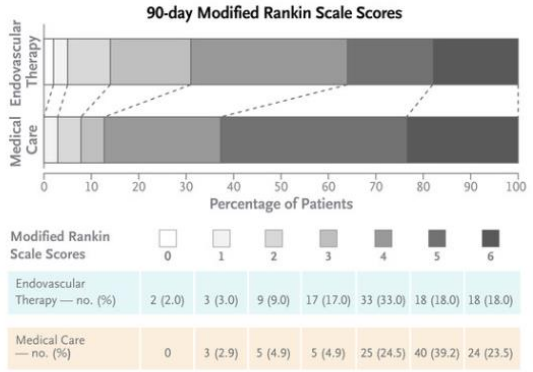
Safety: The percentage of patients who had any intracranial hemorrhage within 48 hours after randomization was significantly higher with endovascular therapy than with medical care alone. However, the percentage of patients who had symptomatic intracranial hemorrhage within 48 hours, decompressive craniectomy within 7 days, or ischemic stroke recurrence within 90 days or who died within 90 days did not differ significantly between the groups.

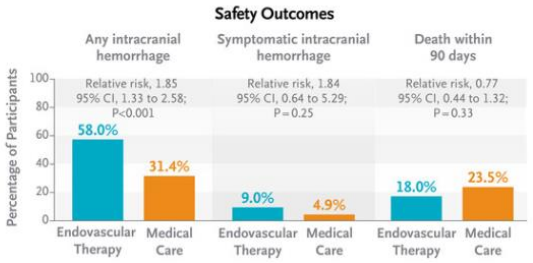
LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- The difference in how ischemic area is determined by computed tomography, as is common practice in the United States, and by diffusion-weighted magnetic resonance imaging, which was used more often in this trial, should be considered.
- Generalizability of the findings is limited outside Japan; approximately 27% of the patients in each group received intravenous thrombolysis at a dose of 0.6 mg per kilogram according to Japanese guidelines — a lower dose than that used in some other countries.
- Whether causes of death were related to the assigned trial treatment could not be determined.

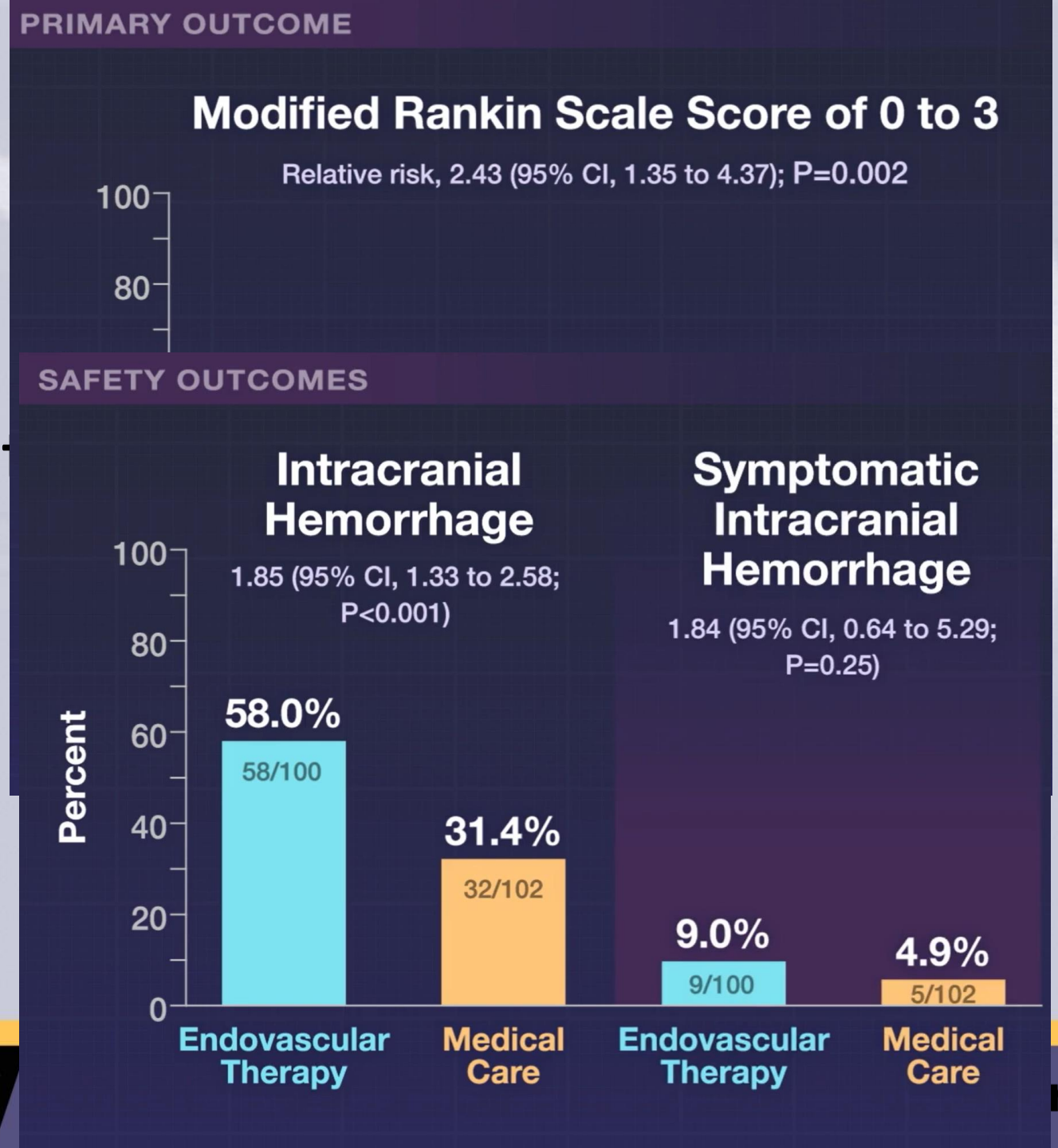






CONCLUSIONS

Patients with large cerebral infarctions had better functional outcomes but more overall intracranial hemorrhages with endovascular therapy added to medical therapy than with medical therapy alone.



ENDOVASCULAR THROMBECTOMY vs MEDICAL THERAPY SELECT 2—(2023)

- THERAPY w/in 24 hrs onset (20% rec'd thrombolytics)
  - Thrombectomy
  - Med mgmt.
    - BP, Critical care, In-hospital and Outpt Rehab
- Large volume
  - ASPECTS 3-5
  - CORE INFARCT VOLUME—50ML

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RESEARCH SUMMARY

Trial of Endovascular Thrombectomy for Large Ischemic Strokes

Sarraj A et al. DOI: 10.1056/NEJMoa2214403

CLINICAL PROBLEM

Endovascular thrombectomy has been shown to be more beneficial than medical therapy alone in selected patients with ischemic stroke due to occlusion of a large cerebral vessel. However, patients with large strokes, who have a poor prognosis, have been underrepresented in thrombectomy trials.

CLINICAL TRIAL

Design: A phase 3, international, randomized, open-label trial evaluated endovascular thrombectomy plus medical care, as compared with standard medical care alone, in patients with acute ischemic stroke due to occlusion of the internal carotid artery or the first segment of the middle cerebral artery (or both), with a large ischemic-core volume on noncontrast computed tomography (CT), CT perfusion imaging, or diffusion-weighted magnetic resonance imaging.

Intervention: 352 patients were assigned to undergo endovascular thrombectomy within 24 hours after stroke onset in addition to standard medical care or to receive standard medical care alone. The primary outcome was the ordinal score on the modified Rankin scale at 90 days (range, 0 to 6, with higher scores indicating greater disability). Functional independence was a secondary outcome. Safety outcomes included symptomatic intracranial hemorrhage and death from any cause.

RESULTS

Efficacy: Endovascular thrombectomy outperformed medical care with respect to the modified Rankin scale score at 90 days.

Safety: Procedural complications occurred in 18.5% of the patients in the thrombectomy group. Mortality and the incidence of intracranial hemorrhage were similar in the two groups.

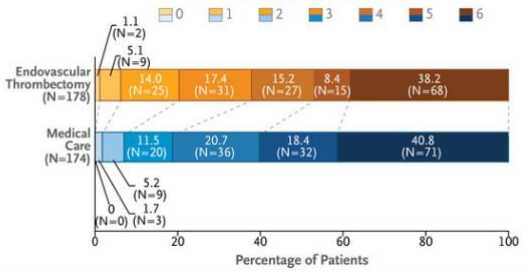
LIMITATIONS

- The trial was terminated early for efficacy, potentially leading to overestimation of the effects of thrombectomy.
- Only about 20% of the patients received intravenous thrombolytic agents before randomization.

Links: Full Article | NEJM Quick Take | Editorial

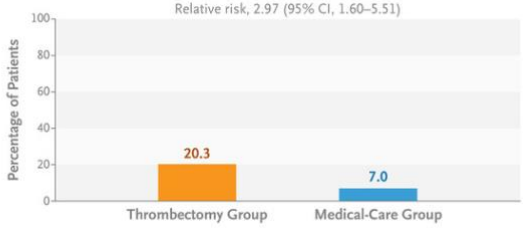
Efficacy at 90 Days

Generalized OR, 1.51 (95% CI, 1.20–1.89); P<0.001



Functional Independence at 90 Days

Relative risk, 2.97 (95% CI, 1.60–5.51)

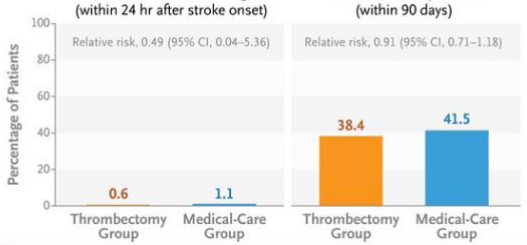


Symptomatic Intracranial Hemorrhage (within 24 hr after stroke onset)

Relative risk, 0.49 (95% CI, 0.04–5.36)

Death from Any Cause (within 90 days)

Relative risk, 0.91 (95% CI, 0.71–1.18)



CONCLUSIONS

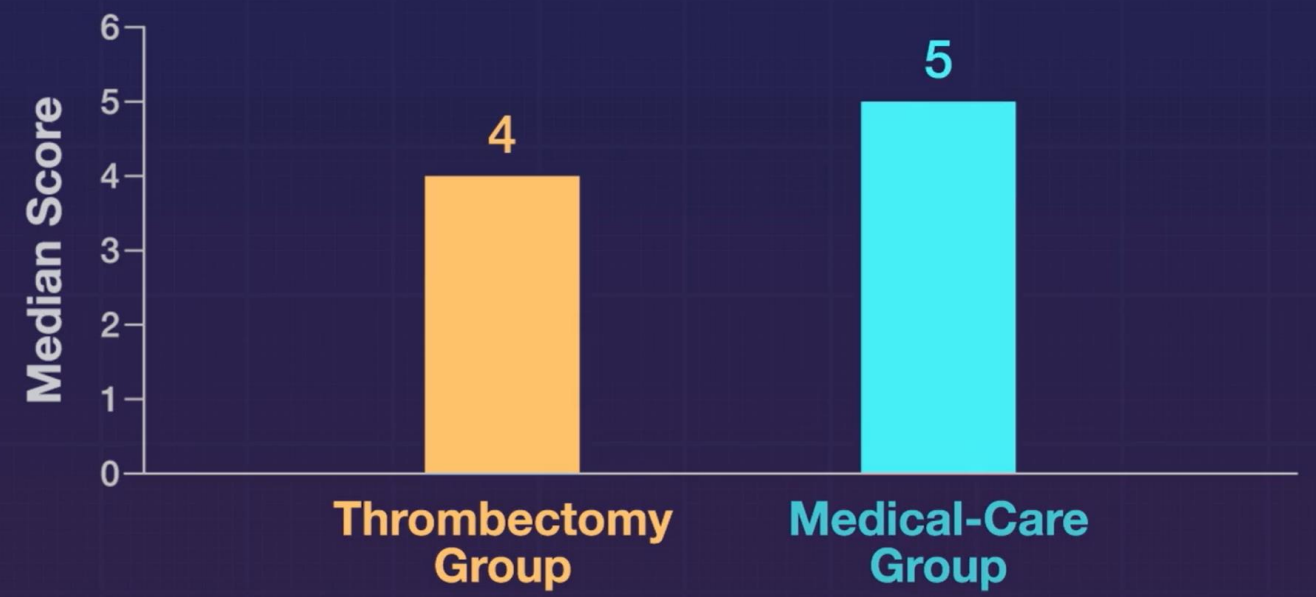
In patients with acute ischemic stroke due to a proximal large-vessel occlusion and with a large ischemic-core volume, endovascular thrombectomy in addition to standard medical care resulted in better functional outcomes at 90 days than medical care alone but was associated with procedural vascular complications.

Supplementary Table 1: Modified Rankin Scale

Score	Description

PRIMARY OUTCOME

Median Score on Modified Rankin Scale at 90 Days



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Design: A phase 3, international, randomized, open-label trial evaluated endovascular thrombectomy plus medical care, as compared with standard medical care alone, in patients with acute ischemic stroke due to occlusion of the internal carotid artery or the first segment of the middle cerebral artery (or both), with a large ischemic-core volume on noncontrast computed tomography (CT), CT perfusion imaging, or diffusion-weighted magnetic resonance imaging.

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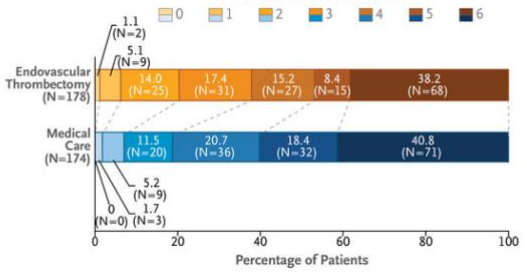

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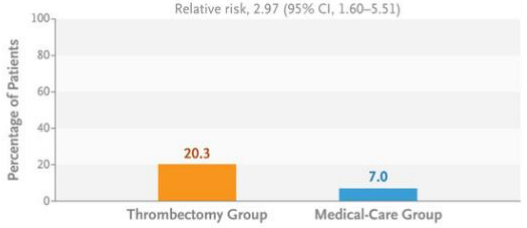

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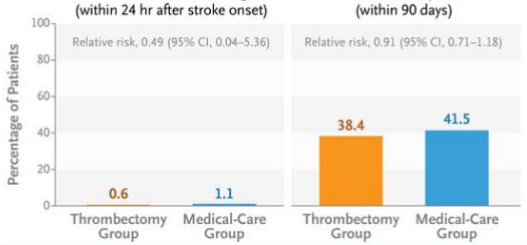
Death from Any Cause (within 90 days)

Relative risk, 0.91 (95% CI, 0.71–1.18)



CONCLUSIONS

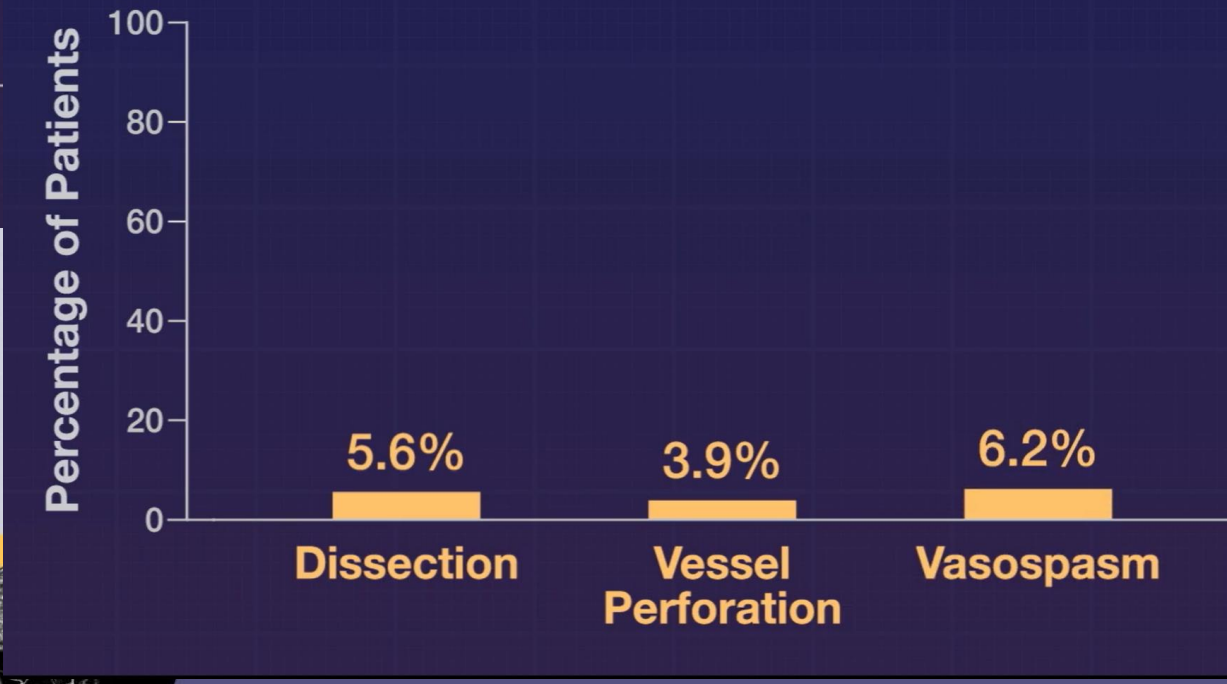
In patients with acute ischemic stroke due to a proximal large-vessel occlusion and with a large ischemic-core volume, endovascular thrombectomy in addition to standard medical care resulted in better functional outcomes at 90 days than medical care alone but was associated with procedural vascular complications.

ADVERSE EVENTS

Procedural Complications

ADVERSE EVENTS

Procedural Complications



ENDOVASCULAR THROMBECTOMY vs MEDICAL THERAPY ANGEL-ASPECT (2023)

- THERAPY w/in 24 hrs onset (28% rec'd thrombolytics)
  - Thrombectomy
  - Med mgmt.
    - BP, Critical care, In-hospital and Outpt Rehab
- Large volume
  - ASPECTS 3-5
  - CORE INFARCT—70-100ML

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RESEARCH SUMMARY

Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct

Huo X et al. DOI: 10.1056/NEJMoa2213379

CLINICAL PROBLEM

Endovascular therapy is a standard approach in patients with acute ischemic stroke due to cerebral large-vessel occlusion. However, whether endovascular therapy benefits patients with a large infarct core remains uncertain.

CLINICAL TRIAL

Design: A multicenter, open-label, randomized trial with blinded end-point assessment investigated the efficacy and safety of endovascular therapy, as compared with medical management alone, in patients with a large infarct core caused by acute large-vessel occlusion in the anterior circulation.

Intervention: 456 adults in China presenting within 24 hours after stroke onset who had an Alberta Stroke Program Early Computed Tomography Score of 3 to 5 (range, 0 to 10, with lower scores indicating larger infarct) or an infarct-core volume of 70 to 100 ml were assigned to undergo endovascular thrombectomy — and, if needed, balloon angioplasty, stent implantation, or intraarterial thrombolysis — and receive medical management or to receive medical management alone. The primary outcome was the score on the modified Rankin scale at 90 days (range, 0 to 6, with higher scores indicating greater disability).

RESULTS

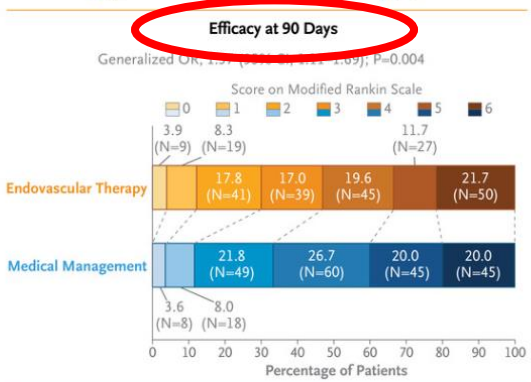
Efficacy: At 90 days, a shift in the distribution of the scores on the modified Rankin scale indicated better outcomes with endovascular therapy than with medical management alone.

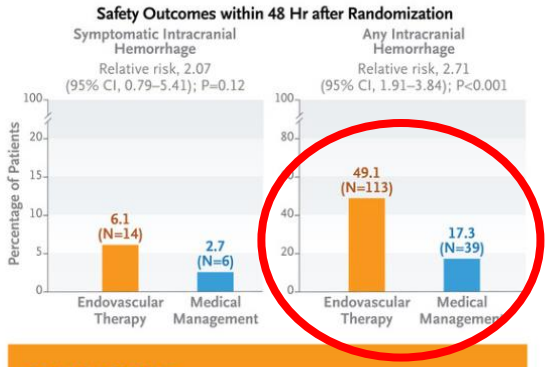
Safety: Symptomatic intracranial hemorrhage and any intracranial hemorrhage were more common with endovascular therapy than with medical management alone.

LIMITATIONS

- Less than one third of patients received intravenous thrombolysis, which may have disadvantaged the medical-management group.
- Urokinase was used instead of alteplase in some patients; alteplase is probably more effective.
- Patients >80 years of age were excluded.

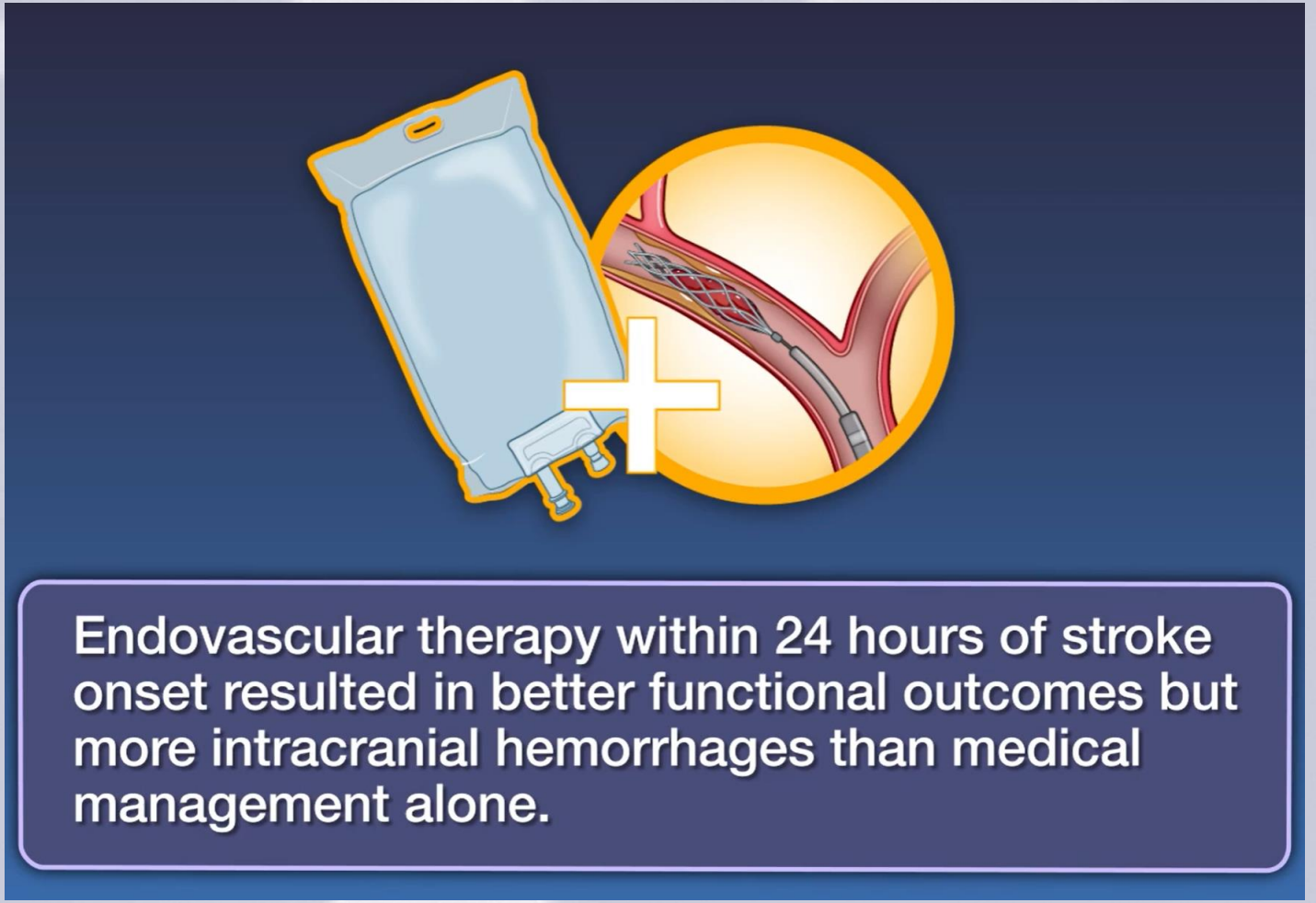
Links: Full Article | NEJM Quick Take | Editorial





CONCLUSIONS

In patients in China with a large infarct-core volume caused by acute large-vessel occlusion in the anterior circulation, endovascular therapy within 24 hours after stroke onset resulted in better functional outcomes at 90 days but more intracranial hemorrhages than medical management alone.



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Tenecteplase for Stroke at 4.5 to 24 Hours with Perfusion-Imaging Selection

Albers GW et al. DOI: 10.1056/NEJMoa2310392

CLINICAL PROBLEM

Tenecteplase, an alternative thrombolytic agent to alteplase for treatment of acute ischemic stroke, has been shown to be noninferior to alteplase when administered within 4.5 hours, but its use beyond the 4.5-hour time window has not been well studied.

CLINICAL TRIAL

Design: A multicenter, double-blind, randomized, placebo-controlled trial evaluated the safety and efficacy of tenecteplase administered 4.5 to 24 hours after stroke onset in patients with evidence of occlusion of the internal carotid or middle cerebral artery and evidence of salvageable brain tissue on perfusion imaging.

Intervention: 458 adults with ischemic stroke were randomly assigned to receive tenecteplase (0.25 mg per kilogram of body weight; maximum dose, 25 mg) or placebo, both administered as an intravenous bolus over a 5-second period. Eligible patients were anticipated to receive endovascular thrombectomy thereafter. The primary outcome was the ordinal score on the modified Rankin scale — a measure of disability with scores ranging from 0 (no symptoms) to 6 (death) — at day 90.

RESULTS

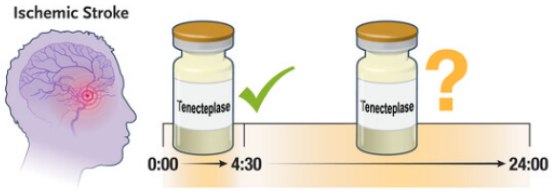
Efficacy: Among patients who could be evaluated, the median modified Rankin scale score at 90 days among patients who received tenecteplase was similar to that among patients who received placebo.

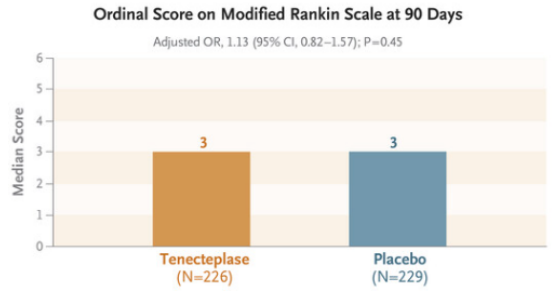
Safety: Mortality at 90 days did not differ appreciably between the two groups, and the incidence of symptomatic intracranial hemorrhage within 36 hours was similar in the two groups.

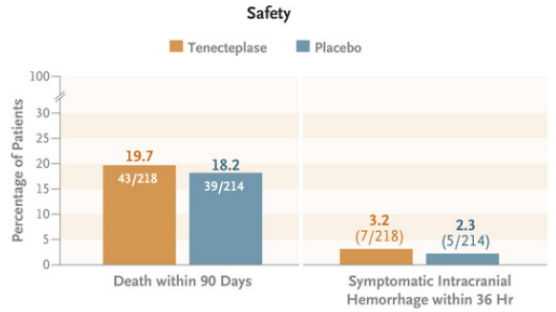
LIMITATIONS AND REMAINING QUESTIONS

- The number of patients who did not undergo endovascular thrombectomy was too small to support firm conclusions about the effect of tenecteplase in that patient population.

Links: Full Article | NEJM Quick Take | Editorial







CONCLUSIONS

In patients with ischemic stroke and a favorable perfusion-imaging profile, most of whom underwent endovascular thrombectomy, treatment with intravenous tenecteplase at 4.5 to 24 hours after the time they were last known to be well did not result in outcomes better than those with placebo, and the incidence of brain hemorrhage was similar in the two groups.