How Should Acute Stroke Severity (NIHSS) Influence Timing To Therapeutic Intervention: For tPA Use; For CEA And CAS; For Intracranial Arterial Clot Removal: It Matters To Neurologic Outcomes

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No Relevant Financial Disclosures

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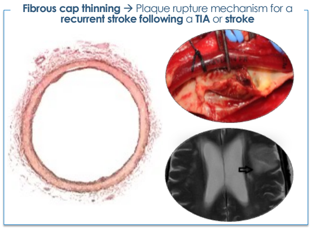
Vulnerable (Unstable) Plaque is Mechanism in Acute Carotid-Related Stroke and Recurrence Risk

Risk Recurrence within **7 - 14 days significant**

Fibrous cap thinning → Plaque rupture mechanism for a **recurrent stroke following** a **TIA** or **stroke**



*Risk of ipsilateral ischemic stroke recurrence after **initial carotid-related TIA** or **stroke***

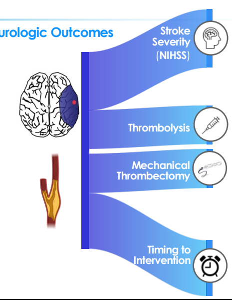
% Risk	Days
2 - 8	2
4 - 17	3
4 - 22	7
7.5 - 25	**14**

Bazan HA et al. *A Pro-Inflammatory and Fibrous Cap Thinning Transcriptome Profile Accompanies Carotid Plaque Rupture Leading to Stroke*. **Scientific Reports** 2022
De Rango, P et al. *Summary of evidence on early carotid intervention for recently symptomatic stenosis based on meta-analysis of current risks*. **Stroke**. 2015
AbuRahma A et al. *SVS clinical practice guidelines for management of extracranial cerebrovascular disease*. **J Vasc Surg** 2022
Naylor AR et al. *ESVS 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease*. **Eur J Vasc Endovasc Surg** 2023

3

Stroke Severity (NIHSS), MER, Thrombolysis & Timing to CEA / CAS

Influence Clinical & Neurologic Outcomes



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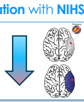
NIHSS → Objective Criteria to Assess Stroke Severity
mRS → Outcome Measure for Post-Stroke Functional Dependence

Ischemic brain lesion on imaging has **strong correlation** with **NIHSS**

Stroke severity – NIHSS

NIHSS	Severity
< 4	minor
5 – 15	moderate
16 – 20	moderate-severe
21 – 24	severe

Impacted Brain Density



Neurologic Outcomes – modified Rankin Scale – mRS

mRS	Description	
0	asymptomatic	Functional Independence
1	no significant disability (facial droop)	Functional Independence
2	slight disability (grip problems)	Functional Independence
3	moderate disability (walks w/out assistance)	Functional Dependence (on caregiver)
4	moderate severe disability (needs assistance to walk)	Functional Dependence (on caregiver)
5	Severe disability (bedridden)	Functional Dependence (on caregiver)
6	Death	

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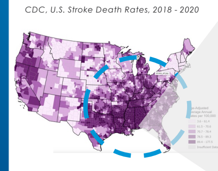
U.S. 'Stroke Belt'

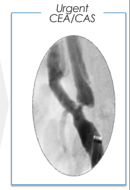
Regionalization Stroke Care with *Increasing* **Comprehensive Stroke Centers**

CDC, U.S. Stroke Death Rates, 2018 - 2020



Ochsner Tele-Stroke Network

Urgent CEA/CAS

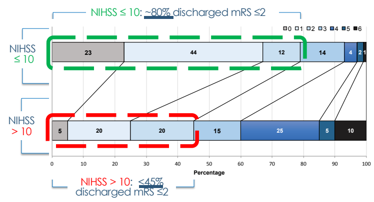


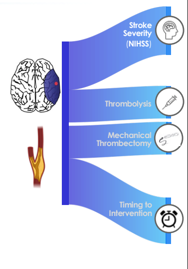
St Hilaire C … Bazan HA. Frailty scores impact the outcomes of urgent carotid interventions in acute stroke patients: A comprehensive analysis of risk and prognosis. ***J Vasc Surg*** 2024 (in press)
Loftus IM, Paraskevas KI, Naylor AR. Urgent Carotid Endarterectomy Does Not Increase Risk and Will Prevent More Strokes. ***Angiology***. 2017

6

Presenting Stroke Severity (NIHSS) Important Predicting Outcomes

CEA > 48h is also associated with mRS ≤ 2





n=120

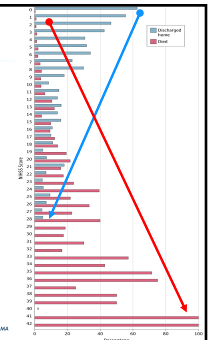
Mihindu E...Bazan HA. *Patients with moderate to severe strokes (NIHSS > 10) undergoing urgent carotid interventions within 48h have worse functional outcomes.* ***J Vasc Surg*** 2019

As stroke severity (NIHSS) Increases, Outcomes worsen

For all Ischemic Strokes

As stroke severity ↑:

- ✓ the worse the **outcome**
- ✓ More likely **not** to be **discharged home**
- ✓ More likely to **die** in **hospital**



ReSaber, H., Saver, J.L.. *Distributional Validity and Prognostic Power of the National Institutes of Health Stroke Scale in US Administrative Claims Data.* ***JAMA Neurology*** 2020

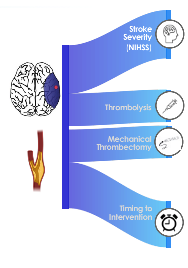
Presenting Stroke Severity & Outcomes in Acute Stroke Interventions

Stroke score strongly influences neurologic function

Presenting NIHSS Score Influences Odds of Functional Independence (mRS ≤ 2)

- ✓ The **odds** of **functional independence** (**mRS** ≤ **2**) following uCEA/uCAS are **3x-higher** if the presenting **NIHSS ≤ 10** vs. NIHSS > 10
- ✓ Those presenting with an **NIHSS ≤ 10** do significantly better with urgent carotid interventions (**3x better**) compared to NIHSS > 10

Functional independence (mRS of ≤2)[c]	
NIHSS 0-10 vs >10	**3.11 (1.33-7.33)**



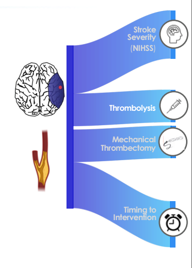
n=10,975 (all ischemic strokes)

Rivera A...Bazan HA. *Neurologic outcomes of carotid and other emergent interventions for ischemic stroke over 6 years with dataset enhanced by machine learning.* ***J Vasc Surg*** 2022

Thrombolysis Use

Thrombolysis safe?

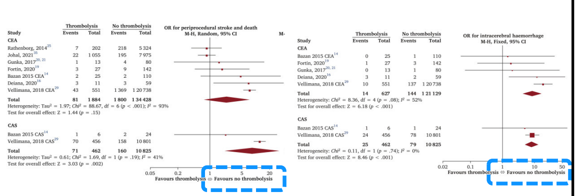
- ✓ Concern over increased **risk** of **bleeding**
  - Infarct → ICH conversion
  - Neck (CEA or TCAR); Groin (TF-CAS) hematoma
- ✓ Patients receiving thrombolysis are presenting with **more severe stroke** (**higher NIHSS scores**), requiring more aggressive intervention



Bazan HA et al. Urgent carotid intervention is safe after thrombolysis for minor to moderate acute ischemic stroke. ***J Vasc Surg*** 2015
Kakkos SK, Vega de Ceniga M, Naylor R. A Systematic Review and Meta-analysis of Peri-Procedural Outcomes in Patients Undergoing Carotid Interventions Following Thrombolysis. ***Eur J Vasc Endovasc Surg*** 2022
Rivera A...Bazan HA. *Neurologic outcomes of carotid and other emergent interventions for ischemic stroke over 6 years with dataset enhanced by machine learning.* ***J Vasc Surg*** 2022

Thrombolysis may Pose Increased Risk

Stroke & Death; ICH / bleeding



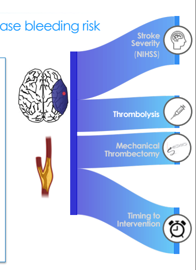
Kakkos SK, Vega de Ceniga M, Naylor R. A Systematic Review and Meta-analysis of Peri-Procedural Outcomes in Patients Undergoing Carotid Interventions Following Thrombolysis. ***Eur J Vasc Endovasc Surg*** 2022

Thrombolysis may Pose Increased Risk but …

Thrombolysis safe in minor to moderate strokes, but may increase bleeding risk

Don't deny a patient CEA or CAS simply because they received thrombolysis

- ✓ **Patients receiving thrombolysis are presenting with more severe stroke** (**higher NIHSS scores**), requiring more aggressive intervention.
- ✓ **Patient selection is crucial: CEA or CAS be done safely in select neurologically stable patients** with minor-moderate strokes (NIHSS < 10).
- ✓ **Caveat: May incur increased peri-procedural risks** (e.g., **ICH**, **hematoma**) with CEA/CAS after thrombolysis, suggesting careful patient selection and possibly deferring intervention for 6–7 days.
- ✓ **Limitations exist** due to lack of RCTs and potential biases (i.e., thrombolysis presenting with worse strokes).



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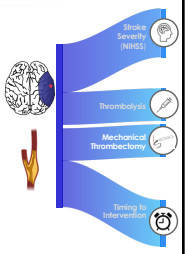
Rivera A...Bazan HA. *Neurologic outcomes of carotid and other emergent interventions for ischemic stroke over 6 years with dataset enhanced by machine learning.* ***J Vasc Surg*** 2022

Mechanical Thrombectomy – Intracranial Clot Removal (MER, Mechanical Endovascular Reperfusion)

Influence Clinical & Neurologic Outcomes

- ✓ **Occurring with higher frequency with proliferation of stroke centers, neuro-interventionalists and neuro-rescue technologies**



Rivera A., Baron HA. Neurologic outcomes of carotid and other emergent interventions for ischemic stroke over 6 years with dataset enhanced by machine learning. *J Vasc Surg* 2022

Intracranial Clot Retrieval (MER)-Outcomes in Acute Stroke Interventions

Neurologic outcomes (mRS) are influenced by **presenting NIHSS**

MER cohort

↑↑ Stroke severity presentation

Worse Neurologic outcomes vs. CEA/CAS alone

	uCEA/uCAS (n = 189)	tPA only (n = 1055)	MER only (n = 418)	tPA + MER (n = 199)	No intervention (n = 3311)	*P* value
Presenting stroke severity						
NIHSS	4.9 ± 5.3	8.6 ± 6.8	15.9 ± 7.5	16.0 ± 6.8	6.9 ± 7.9	<.001*
NIHSS						<.001*
No symptoms (0)	41 (21.7)	44 (4.2)	5 (1.2)	0 (0)	652 (19.7)	
Minor (1-4)	72 (38.1)	310 (29.4)	25 (6.0)	6 (3.0)	1166 (35.2)	
Moderate (5-15)	64 (33.9)	528 (50.1)	164 (39.2)	89 (44.7)	971 (29.3)	
Moderate to severe (16-20)	9 (4.8)	78 (7.4)	106 (25.4)	53 (26.6)	228 (6.9)	
Severe (21-42)	3 (1.6)	95 (9.0)	118 (28.2)	51 (25.6)	294 (8.9)	
Discharge neurologic outcome						
mRS	1.7 ± 1.4	1.8 ± 1.3	2.6 ± 1.5	2.3 ± 1.5	1.8 ± 1.5	<.001*
No symptoms (0)	11 ± 1.3	1.0 ± 0.9	2.0 ± 1.5	—	0.6 ± 1.0	<.001*
Minor (1-4)	1.6 ± 1.2	1.4 ± 1.2	1.5 ± 1.3	2.5 ± 2.1	1.4 ± 1.2	.111*
Moderate (5-15)	2.1 ± 1.3	1.9 ± 1.3	2.4 ± 1.5	2.1 ± 1.5	2.4 ± 1.4	<.001*
Moderate to severe (16-20)	2.7 ± 1.9	2.5 ± 1.4	2.8 ± 1.4	2.4 ± 1.5	3.0 ± 1.4	.064*
Severe (21-42)	2.7 ± 1.5	2.5 ± 1.4	2.9 ± 1.5	2.5 ± 1.4	3.0 ± 1.5	.055*
Functional independence (mRS of =2)†						
NIHSS 0-4 vs >4	**2.81 (1.49-5.39)**	**2.99 (2.20-4.15)**	**2.96 (1.36-7.07)**	—	**6.91 (5.07-8.16)**	
NIHSS 0-10 vs >10	**3.11 (1.33-7.33)**	**3.09 (2.35-4.06)**	**2.35 (1.49-3.71)**	1.89 (0.98-3.70)	**5.90 (4.98-7.01)**	
NIHSS 0-15 vs >15	2.60 (0.82-8.28)	**3.13 (2.24-4.37)**	**2.25 (1.52-3.33)**	1.27 (0.75-2.22)	**4.07 (4.00-5.94)**	

n=10,975 (all ischemic strokes)

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Thrombolysis, Intracranial Clot Retrieval (MER)-Outcomes in Acute Stroke Interventions

Neurologic outcomes (mRS) are influenced by **presenting NIHSS**

MER + Thrombolysis cohort

↑↑ Stroke severity presentation

Some improvement in Neurologic outcomes vs. CEA/CAS alone

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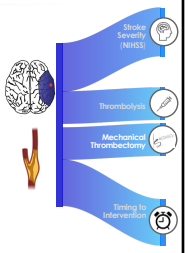
Mechanical Thrombectomy – Intracranial Clot Removal (MER, Mechanical Endovascular Reperfusion)

Influence Clinical & Neurologic Outcomes

CEA / CAS may need to be considered in patients undergoing MER ***and*** MER + Thrombolysis

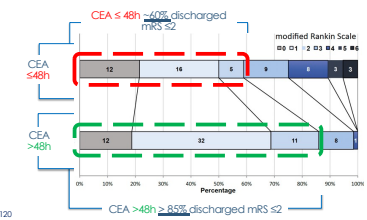
- ✓ **Patients receiving MER present with largest stroke severity**
- ✓ **This in itself is risk for worse complications**
- ✓ **Patient selection is crucial**, consider CEA or CAS in **select neurologically stable patients with vulnerable plaque at-risk of repeat atheroembolization**



Rivera A., Baron HA. Neurologic outcomes of carotid and other emergent interventions for ischemic stroke over 6 years with dataset enhanced by machine learning. *J Vasc Surg* 2022

CEA > 48h is Associated with Best Neurological Outcomes (mRS ≤ 2)

Wait >48 hrs in neurologically stable patient with non-fluctuating symptoms (i.e., no cTIAs or SIE)



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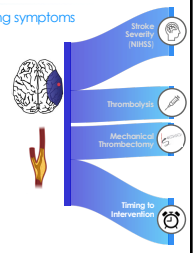


Mikhno E., Baron HA. Patients with moderate to severe strokes (NIHSS > 15) undergoing urgent carotid interventions within 48h have worse functional outcomes. *J Vasc Surg* 2019

Revascularize in non-disabling stoke (mRS ≤ 2)

(Or … in **'minor-to-moderate' stroke, NIHSS < 10**)

		Strength of Recommendation	Evidence Quality
GUIDELINES ESVS 2023	✓ Patients with a **disabling stroke** (**mRS≥3**), or where the area of infarction exceeds 1/3 MCA territory, altered consciousness should not undergo CEA/CAS until neurological improvement has occurred b/c higher risks of hemorrhagic transformation of an infarct or ICH.	I: Strong	Low
SVS 2022	✓ In patients with **recent stable stroke** (**mRS 0-2**), carotid revascularization…as soon as the patient is ***neurologically stable after 48 hours***	I: Strong	Moderate
	✓ Recommend **against** revascularization…in patients who suffered a ***disabling stroke***, ***mRS > 3***…to minimize the risk of postoperative parenchymal hemorrhage	I: Strong	Low
	✓ Revascularize later if neurologic recovery		

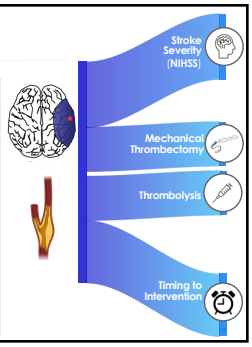
Naylor AR et al, European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg* 2023
Aziz Rivera, Ali et al. SVS Clinical Practice Guidelines for Management of Extracranial Cerebrovascular Disease. *J Vasc Surg* 2022

Conclusions

For Optimal Clinical Outcomes & Neurologic Functional Independence (mRS ≤ 2)

Patient selection is most crucial

- ✓ **NIHSS**: Incoming stroke severity (NIHSS) is predictive of functional neurologic outcomes (mRS) … NIHSS ≤ 10 are more likely to leave the hospital with functional independence
- ✓ **Mechanical Thrombectomy**: Largest risk, due to fact these patients presenting with the most severe strokes
  - Control SBP < 120 or 140 post-procedure
- ✓ **Thrombolysis**: Don't deny a patient CEA or CAS simply because they received thrombolysis
  - Lysis patients present with more severe strokes
- ✓ **Timing**: Wait >48 hrs in neurologically stable patient with non-fluctuating symptoms (i.e., no cTIAs or SIE)



Acute Stroke Severity (NIHSS) DOES Matter To Neurologic Outcomes
Timing (>48 hrs), Thrombolysis Use & Intracranial Arterial Clot Removal (MER) also Matter

Thank you

OchsnerHealth