

# Stroke Assessment and Triage for Large Vessel Occlusion

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IV alteplase is the only proven treatment for acute ischemic stroke to improve outcome

# Outcome After Thrombolytic Stroke Therapy

The modified Rankin Scale (mRS) Score



IV alteplase is the only proven treatment for acute ischemic stroke to improve outcome

# Outcome After Thrombolytic Stroke Therapy

The modified Rankin Scale (mRS) Score



IV alteplase is the only proven **FDA approved medication** for acute ischemic stroke to improve outcome

## Outcome After Thrombolytic Stroke Therapy

The modified Rankin Scale (mRS) Score



## NINDS TPA Stroke Trial

Excellent outcome at 3 months on all scales



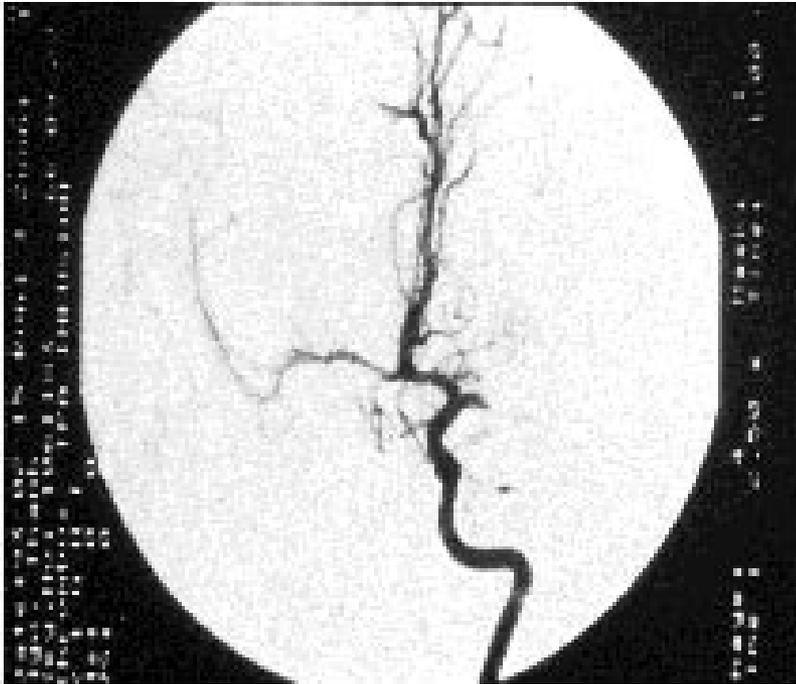
Global outcome statistic: OR=1.7, 50% v. 38% = 12% benefit

## Number Needed to Treat to Benefit from IV TPA Across Full Range of Functional Outcomes

<u>Outcome</u>	<u>NNT</u>
Normal/Near Normal	8.3
Improved	3.1

For every 100 patients treated with tPA,  
32 benefit, 3 harmed

# Treatment goals



**BEFORE TPA**  
Blocked Middle Cerebral Artery



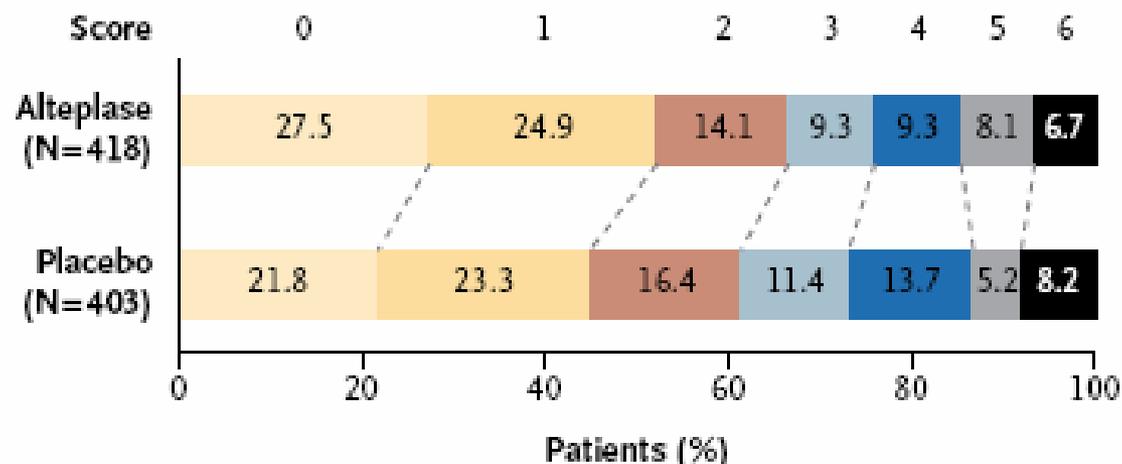
**AFTER TPA**  
Open Middle Cerebral Artery

**Table 3. Demographic and Baseline Characteristics of the Patients.**

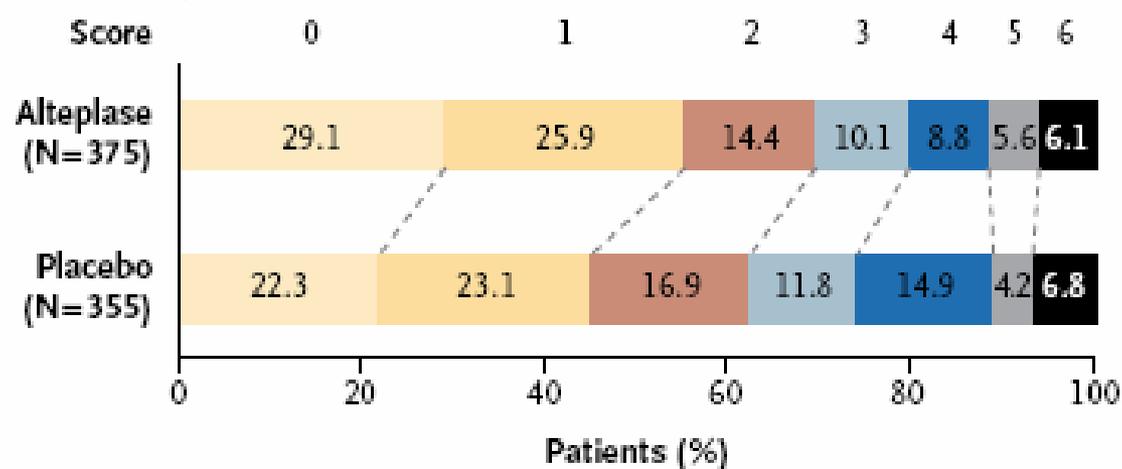
Characteristic	Study Group		P Value <sup>a</sup>
	Alteplase	Placebo	
Age (yr)			
Male sex (%)			
Weight (kg)			
NHSS score <sup>b</sup>			
Mean			
Median			
Systolic pressure (mm Hg)			
Diastolic pressure (mm Hg)			
Diabetes (%)			
Previous use of aspirin or antiplatelet drugs (%)			
Hypertension (%)			
Atrial flutter or fibrillation (%)			
History of stroke (%)			
Smoking status (%) <sup>c</sup>			
Never smoked			
Ex-smoker			
Current smoker			
Time to treatment initiation			
Median			

# ECASS 3

## A Intention-to-Treat Population

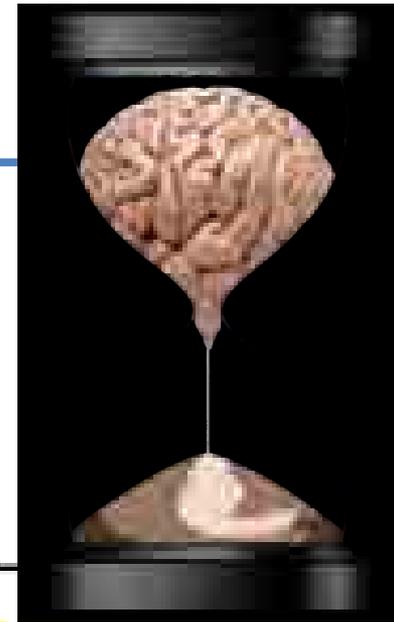


## B Per-Protocol Population



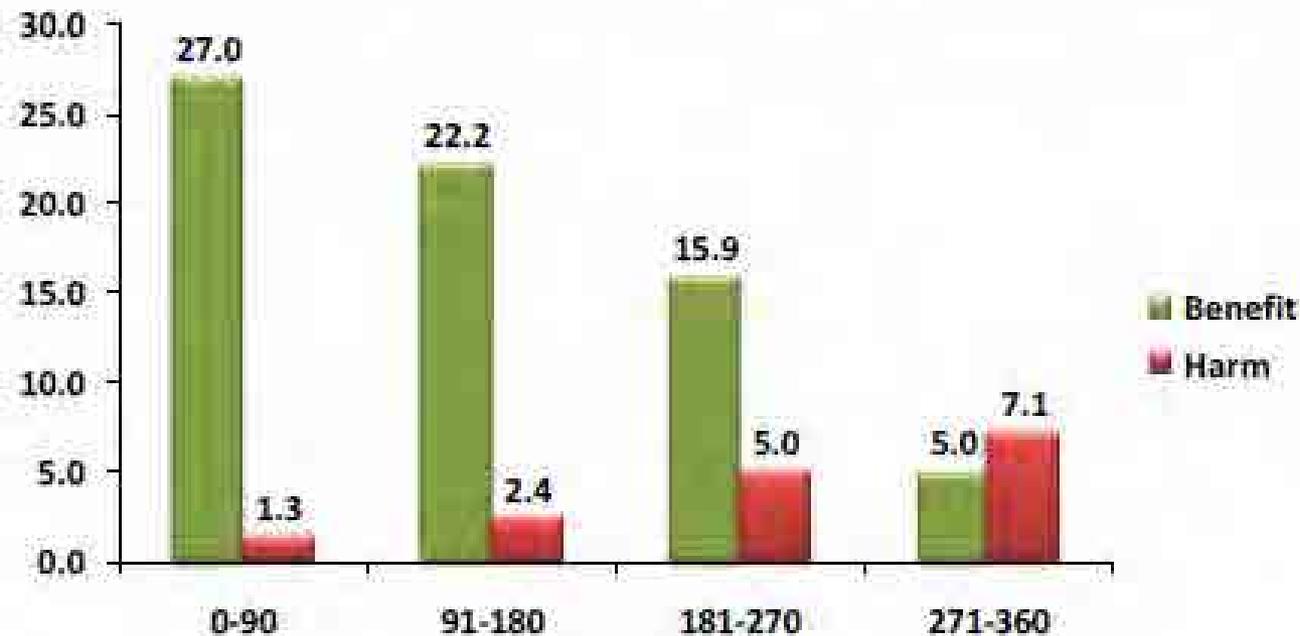
# Important points

Time frame	Neurons lost	Ages the brain by
Every second	32,000	8.7 hours
Every minute	1.9 million	3.1 weeks
Every hour	120 million	3.6 years
Every 10 hours*	1.2 billion	36 years



- ▶ 3 = NNT to result in 1 patient with better outcome than if not treated in 3 hr window
- ▶ 6 = NNT to result in 1 patient with better outcome than if not treated in 3–4.5 hr window

## Number of Patients Who Benefit and Are Harmed per 100 Patients tPA Treated in Each Time Window





The mobile stroke unit

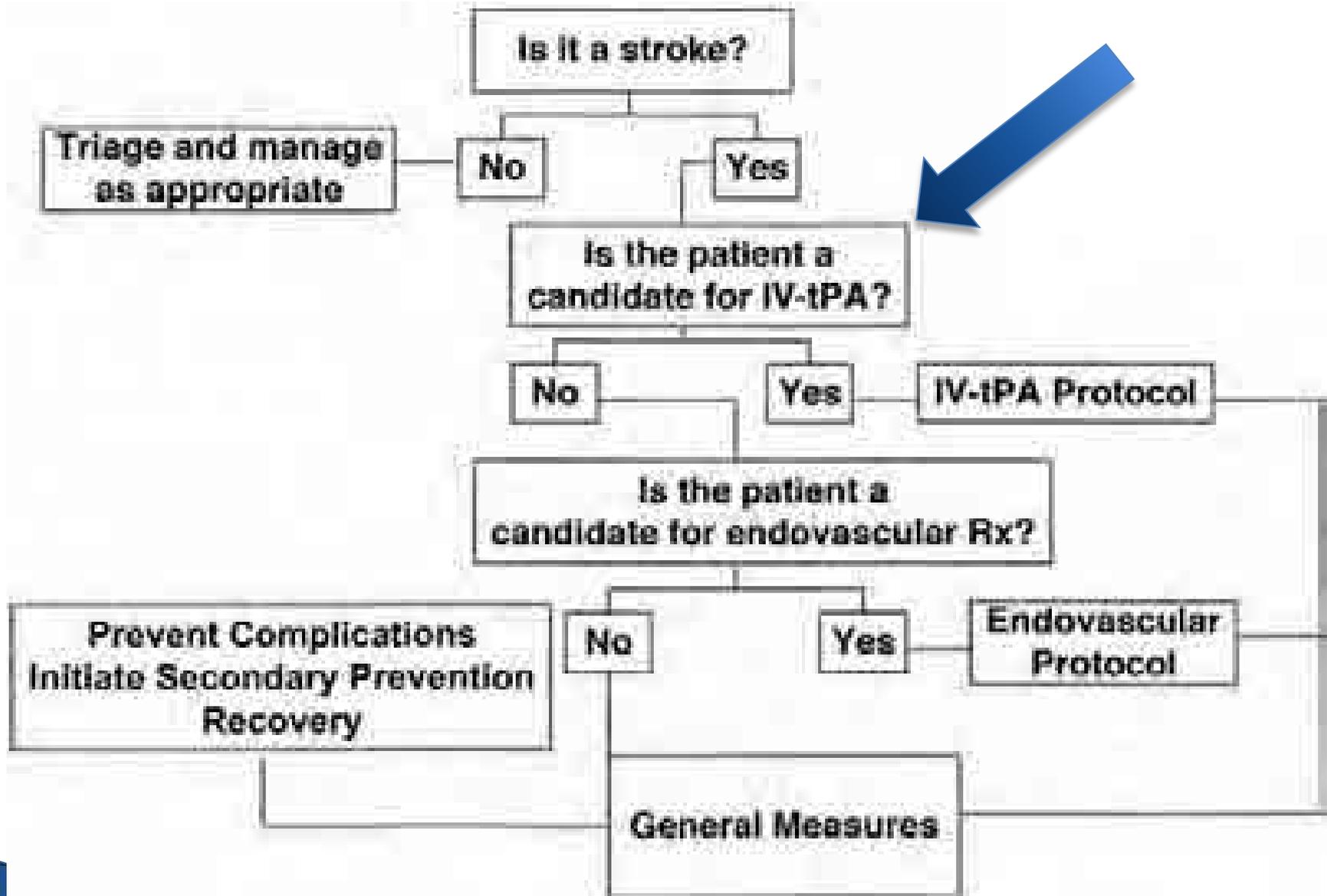
40% of patients are treated within the first hour of symptom onset

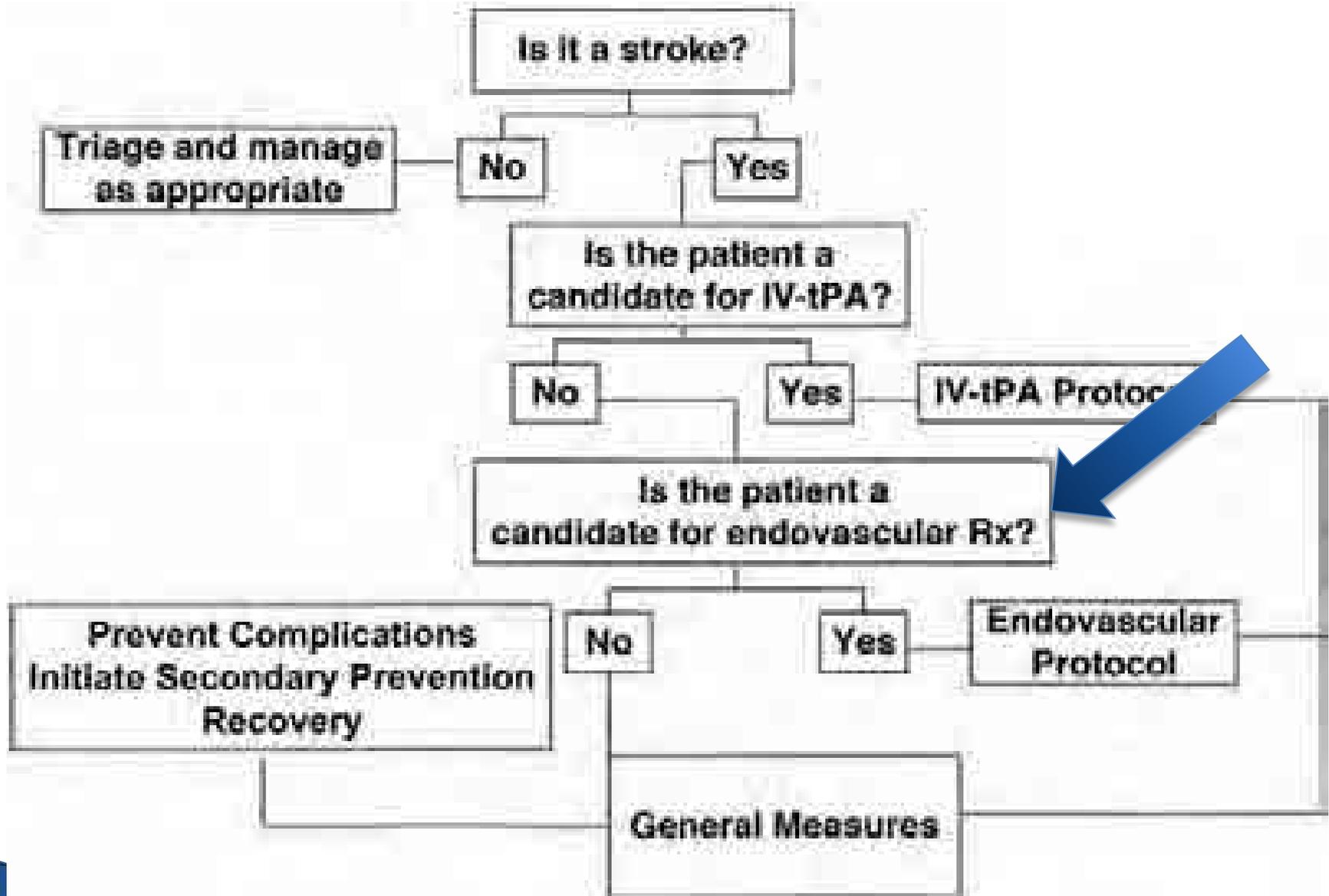
tPA given 10-18min from arrival



# Efficacy of IV tPA for LVO

- ▶ Range of recanalization rate: 13–50%
- ▶ STOPStroke study: Doubles the % of patients who have independent functional outcome (35% vs 17%,  $p < 0.031$ ) at 6 months. NNT is 7. (Stroke. 2013;44:3109–3113.)
- ▶ FIRST study:
  - any spontaneous recanalization 13%
    - 15.6% mRS 0–2 at 90 days
  - 48.4% any recanalization with IV tPA
    - 38.7% mRS 0–2 at 90 days
    - 51.6% no recanalization with IV tPA





# The New Era of Ischemic Stroke Treatment – Endovascular

# Pre-October 2014

- ▶ Clinical trials demonstrated that endovascular treatment for large vessel ischemic stroke improved rates of recanalization
- ▶ No clinical trial demonstrated that endovascular treatment for large vessel ischemic stroke improved rates of good outcome
  - Large GAP between recanalization and good outcome rates.
- ▶ Options for mechanical clot removal were developing quickly

# October 29, 2014 – World Stroke Congress in Istanbul

- ▶ On the heels of IMS-III, MR RESCUE, and SYNTHESIS Expansion trials' negative results...
- ▶ October 29<sup>th</sup>, 2014 – the day the STROKE world stood still



# MR CLEAN

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED 1812

JANUARY 1, 2015

VOLUME 368

### A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berthelsen, P.S.S. Triessen, B. Blommestein, L.A. van den Berg, H.F. Lingstra, A.J. Tim, W.J. Schoneveld, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Welzen, J. Staals, J. Holmeijer, J.A. van Gorp, G.J. Lijcklama & Nijhof, L.J. Bollen, P.A. Bruijn, B.J. Entering, S.F. de Bruijn, L.C. van Dieën, L.J. Kappelle, R.H. Li, E.J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. van den Berg, B.A.A.M. van Harselt, L.A.M. Aarden, B.J. Dallinga, M.C. Visser, J.C.J. Bat, P.C. Vroomen, C. Tsiang, T.H.C.M.J. Schreuder, R.J.J. Heijboer, K. Keizer, A.Y. Tialbeck, H.M. den Hertog, D.G. Gerrits, R.M. van den Berg-Vos, G.B. Kater, E.W. Steenberg, H.Z. Flach, H.A. Marquering, M.E.S. Sprenger, S.J.M. Janssens, L.F.M. Beenen, R. van den Berg, P.J. Koopstra, W.H. van Ziem, Y.B.W.E.M. Rom, A. van der Lugt, P.J. van Galenbrugg, C.B.L.M. Mayr, and D.W.J. Dippel, for the MR CLEAN Investigators\*

# MR CLEAN – Methods

- ▶ Phase 3, multicenter RCT
- ▶ 16 centers in the Netherlands
  - Small country with short secondary transfer time
- ▶  $\geq 18$  years of age
- ▶ NIHSS  $\geq 2$  pts
- ▶ Proximal intracranial arterial occlusion
  - anterior circulation confirmed on vessel imaging
    - tICA, M1, M2, A1 or A2 on CTA, MRA, or DSA

# MR CLEAN – Methods

- ▶ IAT must begin within 6 hrs after stroke onset
- ▶ **No study log of screened patients**
  - No idea who was not included
- ▶ Intervention – thrombolytic agent, mechanical thrombectomy, or both
- ▶ Method of IAT left to interventionalist

# MR CLEAN – Methods

- ▶ Primary outcome measure = mRS at 90 days
  - mRS 0–2 = functional independence
- ▶ Primary effect variable – adjusted common OR for a shift in the mRS to better outcome with multivariable ordinal logistic regression
- ▶ Safety variables
  - Hemorrhagic complications, progression of stroke, new ischemic stroke in different territory, death
  - sICH = increase in NIHSS  $\geq 4$  pts and hemorrhage on imaging

# MR CLEAN – Results

Most got IV tPA, and FAST!

More than half of the patients had start of procedure within 4.5 hrs

**Table 1. Baseline Characteristics of the 100 Patients.**

Characteristic	Intervention (N=50)	Control (N=50)
Age — yr		
Median	61.8	63.7
Interquartile range	54.5–70.0	54.5–70.4
Male sex — no. (%)	19 (37.8)	27 (54.0)
NIHSS score		
Median (interquartile range)	17 (14–21)	14 (14–21)
Range	4–30	4–30
Location of stroke in left hemisphere — no. (%)	28 (56.0)	23 (47.0)
History of left-brain stroke — no. (%)	7 (14.0)	8 (16.0)
Stroke recanalization — no. (%)	6 (12.0)	8 (16.0)
Previous median Rankin scale score — no. (%)		
0	10 (20.0)	21 (42.0)
1	11 (22.0)	29 (58.0)
2	12 (24.0)	18 (36.0)
3	10 (20.0)	11 (22.0)
Systemic blood pressure — mm Hg		
Median with IV alteplase — no. (%)	167 (33.4)	167 (33.4)
Time from stroke onset to start of IV alteplase — min		
Median	48	48
Interquartile range	45–140	45–110
ASPECTS — modified Alberta Stroke Program Early CT Score		
Median (interquartile range)	9 (7–10)	9 (8–10)
Interventional stroke exclusion — no. (%)		
Interventional ICA	1 (2.0)	1 (2.0)
ICA with involvement of the M1 middle cerebral artery segment	39 (78.0)	25 (50.0)
M2 middle cerebral artery segment	1 (2.0)	15 (30.0)
M3 middle cerebral artery segment	1 (2.0)	3 (6.0)
A1 or A2 anterior cerebral artery segment	0 (0.0)	2 (4.0)
Exclusion of ICA occlusion — no. (%)	15 (30.0)	25 (50.0)
Time from stroke onset to randomization — min		
Median	264	264
Interquartile range	150–314	140–304
Time from stroke onset to start of IV alteplase — min		
Median	260	264
Interquartile range	140–314	

# MR CLEAN – Results

Table 2. Primary and Secondary Outcomes and Treatment Effects\*

Outcomes	Intervention (N=232)	Control (N=267)	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)
<b>Primary outcome: modified Rankin scale score at 90 days — median (interquartile range)</b>	8 (2% to 15%)	8 (1% to 9%)	Odds ratio	1.44 (1.22 to 1.70)	1.57 (1.32 to 1.88)
<b>Secondary outcomes</b>					
<b>Clinical outcomes</b>					
Modified Rankin score of 0 or 1 at 90 days — no. (%)	27 (11.6%)	18 (6.7%)	Odds ratio	2.04 (1.48 to 2.83)	2.07 (1.47 to 2.92)
Modified Rankin score of 0-2 at 90 days — no. (%)	75 (32.3%)	81 (30.3%)	Odds ratio	1.07 (1.00 to 1.09)	1.10 (1.09 to 1.11)
Modified Rankin score of 0-3 at 90 days — no. (%)	119 (51.3%)	95 (35.6%)	Odds ratio	1.99 (1.71 to 2.31)	2.03 (1.76 to 2.33)
mRS score after 24 hr — median (interquartile range)	13 (5 to 20)	16 (12 to 22)	Ratio	1.1 (1.0 to 1.2)	1.1 (1.0 to 1.1)
mRS score at 5-7 days after discharge — median (interquartile range)	8 (2 to 17)	14 (7 to 22)	Ratio	1.2 (1.0 to 1.5)	1.3 (1.1 to 1.5)
Barthel index of 20 or 20 at 90 days — no. (%)	95 (41.0%)	71 (26.6%)	Odds ratio	2.6 (2.0 to 3.5)	2.7 (2.1 to 3.5)
DISD score at 90 days — median (interquartile range)	9.0 (6.0 to 9.8)	8.4 (6.2 to 9.1)	Ratio	0.88 (0.80 to 0.97)	0.90 (0.81 to 0.99)
<b>Imaging outcomes</b>					
No intracranial exclusion on the basis of CT angiography — no. (%)	111 (47.9%)	58 (21.7%)	Odds ratio	3.27 (1.83 to 5.74)	3.38 (1.74 to 6.54)
<b>Live patient outcomes (CT)</b>					
Patients recruited — no. (%)	138 (59.5%)	160 (59.6%)			
Mean follow-up time — no. (%)	77 (55.8%)	78 (48.5%)	Ratio	1.2 (1.0 to 1.4)	1.2 (1.0 to 1.4)

67% more likely to have a shift in mRS of at least 1 category

NNT = 18

NNT = 4

# The NEW ENGLAND JOURNAL of MEDICINE

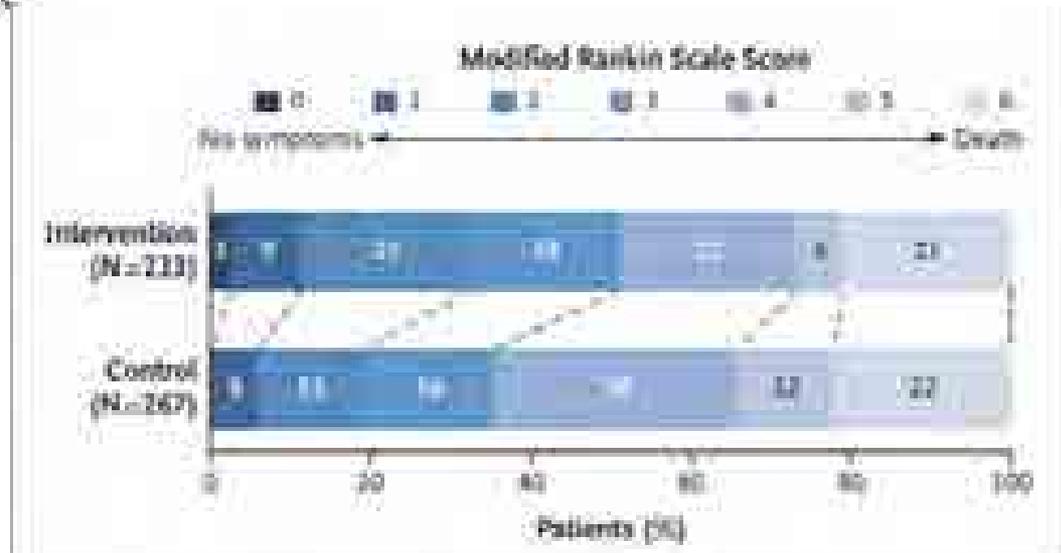
INTERNET FIRST

JANUARY 5, 2015

ISSN 0029-7875

## A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

MR CLEAN – RCT  
 IAT vs no IAT  
 ~90% IV tPA  
 <6hrs from onset



Outcomes	Intervention (N=233)	Control (N=267)	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)
Primary outcome: modified Rankin scale score at 90 days — median (interquartile range)	1 (1 to 3)	4 (1 to 6)	Common odds ratio	1.66 (1.31 to 2.24)	1.67 (1.31 to 2.10)
Secondary outcomes					
Clinical outcomes					
Modified Rankin score of 0 or 1 at 90 days — no. (%)	27 (11.6)	15 (5.6)	Odds ratio	2.08 (1.48 to 2.92)	2.07 (1.47 to 2.92)
Modified Rankin score of 0–2 at 90 days — no. (%)	76 (32.6)	51 (19.1)	Odds ratio	2.05 (1.35 to 3.06)	2.16 (1.39 to 3.34)

# EXTEND IA

ORIGINAL ARTICLE

## Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

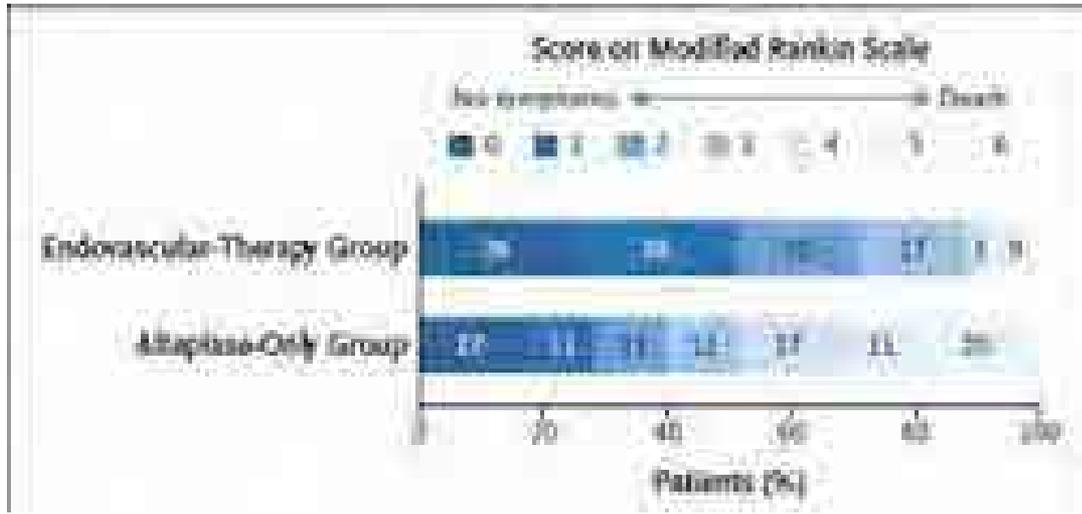
B.C.V. Campbell, P.J. Mitchell, T.J. Kleinig, H.M. Dewey, L. Churilov, N. Yassi,  
B. Yan, R.J. Dowling, M.W. Parsons, T.J. Oxley, T.Y. Wu, M. Brooks,  
M.A. Simpson, F. Miteff, C.R. Levi, M. Krause, T.J. Harrington, K.C. Faulder,  
B.S. Steinfort, M. Priglinger, T. Ang, R. Scroop, P.A. Barber, B. McGuinness,  
T. Wijeratne, T.G. Phan, W. Chong, R.V. Chandra, C.F. Bladin, M. Badve, H. Rice,  
L. de Villiers, H. Ma, P.M. Desmond, G.A. Donnan, and S.M. Davis,  
for the EXTEND-IA Investigators\*

ORIGINAL ARTICLE

# Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

## EXTEND-IA

- Advanced imaging selection
- All had IV tPA
- <70ml of ischemic core with penumbra
- <6hrs from onset



Outcome	Alteplase-Only Group (N=33)	Endovascular-Therapy Group (N=33)	Relative Risk (95% CI)	P Value	Number Needed to Treat (95% CI)	P Value
<b>Primary outcomes</b>						
Median mRS at 90 d (IQR)	3 (1-5)	2 (1-4)	0.7 (0.5-1.0)	<0.001	4.8 (2.0-11)	<0.001
Early mortality (90 d) (%)	11 (33)	3 (9)	0.3 (0.1-1.0)	0.000	8.6 (3.4-22)	<0.001
<b>Secondary outcomes</b>						
Based on the modified Rankin scale at 90 days†						
Median mRS (IQR) modified scores	3 (1-5)	2 (1-4)	0.8	0.00	2.2 (1.2-3.8)	0.00
Independently assessed — no. (%)	14 (42)	20 (61)	0.4 (0.3-0.6)	0.00	2.8 (1.9-4.0)	0.00
Quality of success — no. (%)	17 (52)	14 (42)	2.4 (0.87-6.6)	0.08	2.8 (1.3-6.1)	0.01

NNT = 3 for independence

# ESCAPE

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

## Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

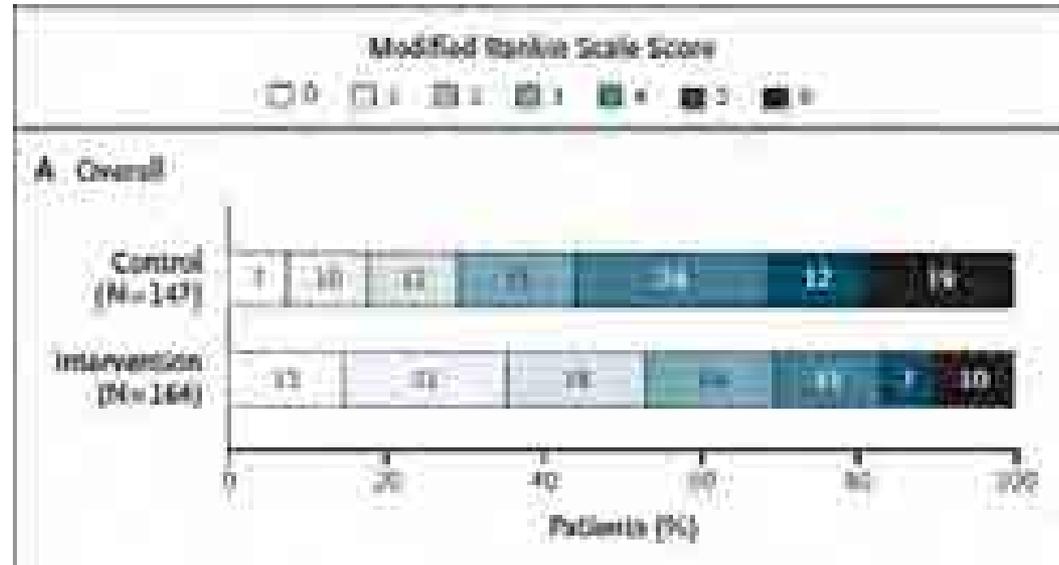
M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy, T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal, W.J. Montanera, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri, D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo, C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar, S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrison, A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison, T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators\*

ORIGINAL ARTICLE

# Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

## ESCAPE

- ♣ Within 12hrs
- ♣ 75% had IV tPA
- ♣ Excluded for large infarct or poor collaterals



Outcome	Intervention (N=144)	Control (N=147)	Difference (95% CI)*	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)
Primary outcome: modified Rankin score at 90 days				Common odds ratio	2.6 (1.3-3.8)	2.1 (1.0-4.7)
Modified Rankin score of 0-2 at 90 days — no (total no. [%])	87/144 (60.4)	49/147 (33.3)	27.8 (18.3-34.9)	Rare ratio	1.8 (1.4-2.4)	1.7 (1.4-2.1)

NNT 4.2

# SWIFT PRIME

BY NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

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

Jeffrey L. Saver, M.D., Mayank Goyal, M.D., Alain Bonafe, M.D.,  
Hans-Christoph Diener, M.D., Ph.D., Elad J. Levy, M.D., Vitor M. Pereira, M.D.,  
Gregory W. Albers, M.D., Christophe Cognard, M.D., David J. Cohen, M.D.,  
Werner Hacke, M.D., Ph.D., Olav Jansen, M.D., Ph.D., Tudor G. Jovin, M.D.,  
Hennrich P. Mattle, M.D., Raul G. Nogueira, M.D., Adrian H. Siddiqui, M.D., Ph.D.,  
Dileep R. Yavagal, M.D., Blaise W. Baxter, M.D., Thomas G. Devlin, M.D., Ph.D.,  
Demetrius K. Lopes, M.D., Vivek K. Reddy, M.D., Richard du Mesnil de Rochemont, M.D.,  
Oliver C. Singer, M.D., and Reza Jahani, M.D., for the SWIFT PRIME Investigators<sup>1</sup>

# SWIFT PRIME

## – Results

Table 2. Primary and Secondary Outcomes.<sup>a</sup>

Outcome	Intravenous I-PA Alone (N = 50)	Standard Subcutaneous plus Intravenous I-PA (N = 50)	Risk Ratio (95% CI)	P Value
<b>Primary outcome: score on modified Rankin scale at 90 days</b>				<b>&lt;0.001</b>
No. of patients with data	47	48		
Median score	1	2		
Interquartile range	1-4	1-4		
<b>Secondary outcomes</b>				
<b>Clinical efficacy outcome</b>				
Functional independence at 90 days — no./total no. (%)	23/48 (48)	33/48 (69)	1.76 (1.29–2.41)	<0.001
Change in mRS score at 90 days				
No. of patients with data	41	41		
Mean change	-1.94 (SD 1.4)	-1.84 (SD 1.4)		NS
Death at 90 days — no./total no. (%)	12/47 (26)	9/48 (19)	0.74 (0.38–1.48)	0.38
<b>Revascularization outcome<sup>b</sup></b>				
Substantial reperfusion (momentarily after thrombolysis — no./ total no. (%))	34/47 (72)	31/48 (65)		NS
Complete reperfusion at 27 hr — no./total no. (%)	11/47 (23)	9/48 (19)	1.04 (0.46–2.41)	<0.001

NNT = 3



# REVASCAT Trial

THE NEW ENGLAND JOURNAL OF MEDICINE

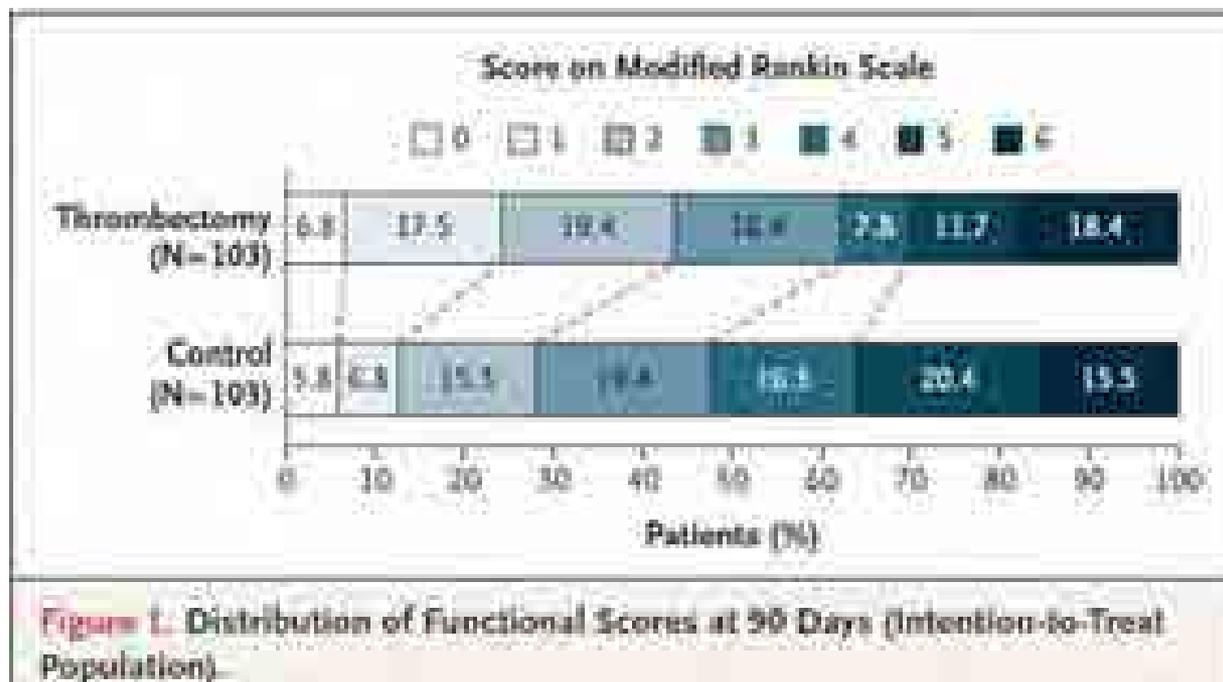
ORIGINAL ARTICLE

## Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

T.G. Jovin, A. Chamorro, E. Cobo, M.A. de Miquel, C.A. Molina, A. Rovira, L. San Roman, J. Serena, S. Abilleira, M. Ribó, M. Millán, X. Urra, P. Cardona, E. López-Cancio, A. Tomasello, C. Castaño, J. Blasco, L. Aja, L. Dorado, H. Quesada, M. Rubiera, M. Hernández-Pérez, M. Goyal, A.M. Demchuk, R. von Kummer, M. Gallofré, and A. Dávalos, for the REVASCAT Trial Investigators\*

# REVASCAT

## - Results



# What do world leaders have to say?

ISC program chair, Kyra Becker, MD

- ▶ "The data are consistent and convincing. We are now obligated to use this technology in eligible stroke patients with a large vessel occlusion."

# What do world leaders have to say?

Patrick Lyden, MD, Cedars–Sinai Medical Center, Los Angeles, California, NINDS tPA for stroke trialist

- ▶ "These data are even more impressive than the rumors have suggested. Excellent efficacy and safety has been shown across different trials and different countries. There is absolutely no question that mechanical thrombectomy should now be the standard of care."

# The New Era of Ischemic Stroke Endovascular Therapy

- ▶ Stent retriever devices
- ▶ 5 randomized clinical trials
- ▶ Median time to treatment ~4.5hrs
- ▶ NNT ~4 to get an independent outcome
- ▶ Not a replacement for IV alteplase (tPA) for eligible patients
- ▶ “standard of care” for anterior circulation large vessel occlusions

# So, what are the circumstances for which we can expect similar results?

Trial	% received IV tPA	Time to IV tPA	Time to groin puncture	Imaging requirement	NNT for 1 independent outcome
MR CLEAN	87.1	85	260	Vessel imaging only	4
EXTEND IA	100	145	210	20% penumbra; core <70ml	3
ESCAPE	72.7	110	211	ASPECTS >5; collateral >50%	4
SWIFT PRIME	100	110	224	80% penumbra; core <50ml	3
REVASCAT	68	118	269	ASPECTS >6	6.5

# AHA/ASA Guidelines

## RECOMMENDATIONS

### Endovascular Interventions

1. Patients eligible for intravenous t-PA should receive intravenous t-PA even if endovascular treatments are being considered (Class I; Level of Evidence A). (Unchanged from the 2013 guideline)
2. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A). (New recommendation)
  - (a) prestroke mRS score 0 to 1,
  - (b) acute ischemic stroke receiving intravenous t-PA within 4.5 hours of onset according to guidelines from professional medical societies,
  - (c) extensive occlusion of the internal carotid artery or proximal MCA (M1),
  - (d) age  $\geq 18$  years,
  - (e) NIHSS score of  $\geq 6$ ,
  - (f) ASPECTS of  $\geq 6$ , and
  - (g) treatment can be initiated (from puncture) within 6 hours of symptom onset

# AHA/ASA Guidelines

3. As with intravenous t-PA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TIC1 grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset (*Class I; Level of Evidence B-R*). (Revised from the 2013 guideline)
4. When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the internal carotid artery or proximal MCA (M1) (*Class IIb; Level of Evidence C*). Additional randomized trial data are needed. (New recommendation)

# AHA/ASA Guidelines

Class IIa; Level of Evidence C for:

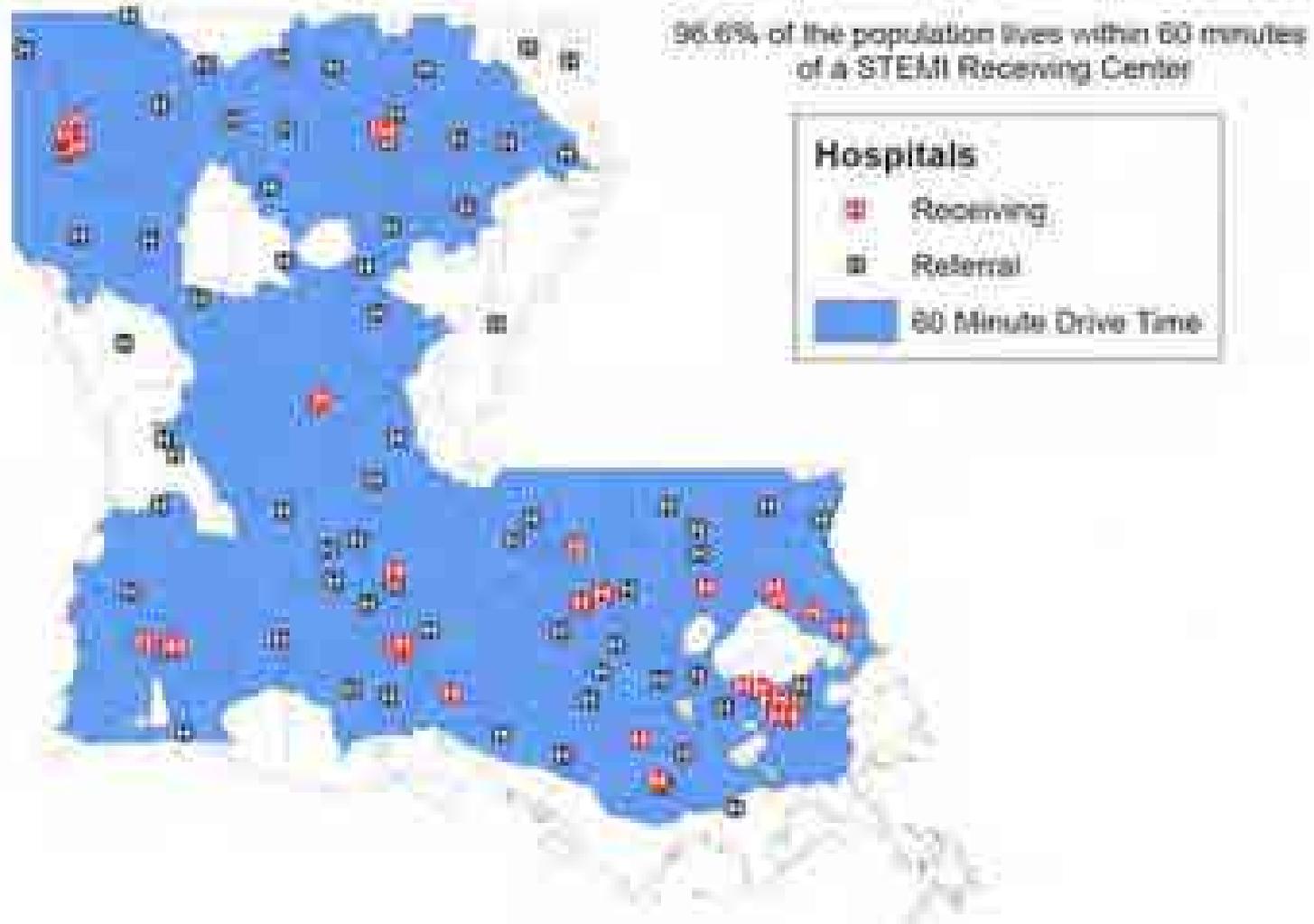
- Anterior circulation LVO with contraindication to IV tPA if < 6hrs of onset

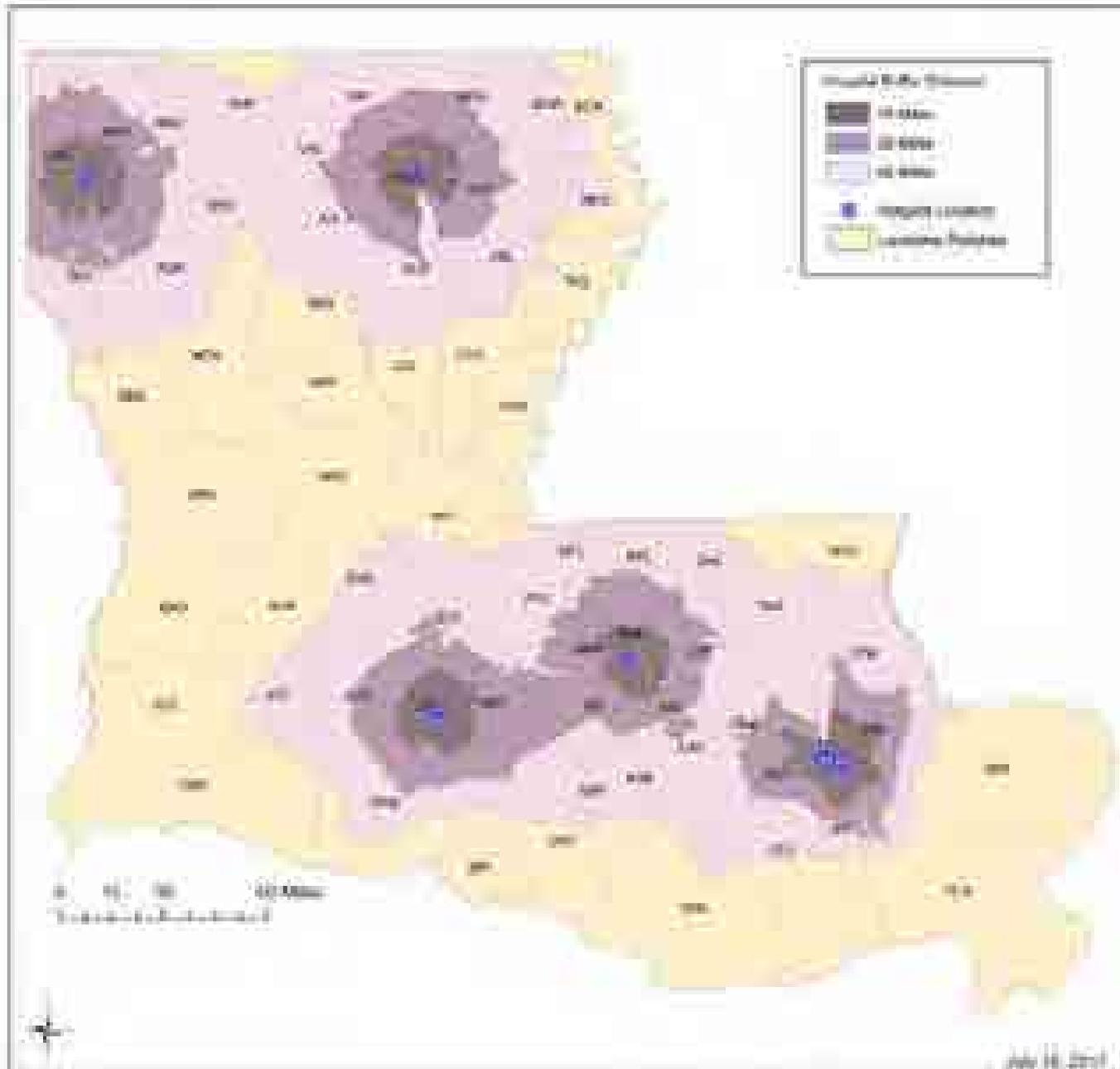
Class IIb; Level of Evidence C for:

- M2 or M3 segments of MCA, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries if < 6hrs of onset
- Pediatric population if < 6hrs of onset

# Unlike PCI centers for STEMI

## Hospital STEMI Receiving Center Attestation with Travel Time to PCI Capable Hospitals





# Priorities

- ▶ We need patients to get to the right place for what they need without compromising time to tPA, if eligible.
  - Avoid false positives = didn't have LVO, but bypassed Level II or III to go to Level I or II with ECC
  - Avoid false negative = had LVO and was missed opportunity or led to unnecessary secondary transport with inherent safety and efficiency issues
- ▶ We need safe and efficient secondary transports from spokes to hubs when endovascular therapy is considered.

Should primary destination protocols involve screening patients for large vessel occlusion?

If so...Should a patient with a positive screen bypass a tPA capable hospital to access a 24/7/365 endovascular capable hospital?

If so... How much additional travel time is acceptable? How much additional cost is involved?  
Acceptable?

# Severity-Based Stroke Triage Algorithm for EMS

EMS Dispatch center responding first call or possible stroke call. EMS crew dispatched per regional stroke protocol or in some location of acute stroke in EMS protocol

On-scene arrival- Provide any needed ABC interventions, ensure depiction of scene level of care and if necessary for stroke provide and improve patient family and other witnesses

Perform on-scene assessment of pre-hospital stroke assessment criteria (FAST, LACS, etc) and SOX through scene

Stroke criteria positive stroke suspicion

Call Stroke Alert, activate stroke protocol

Perform on-scene triage, have patient tool used to assess potential LACS, FAST, RACE, CHOC (AD) (D, etc)

Identify and document time last known well & time of symptom discovery

LACS Suspicion

LACS LESS THAN 6 HOURS

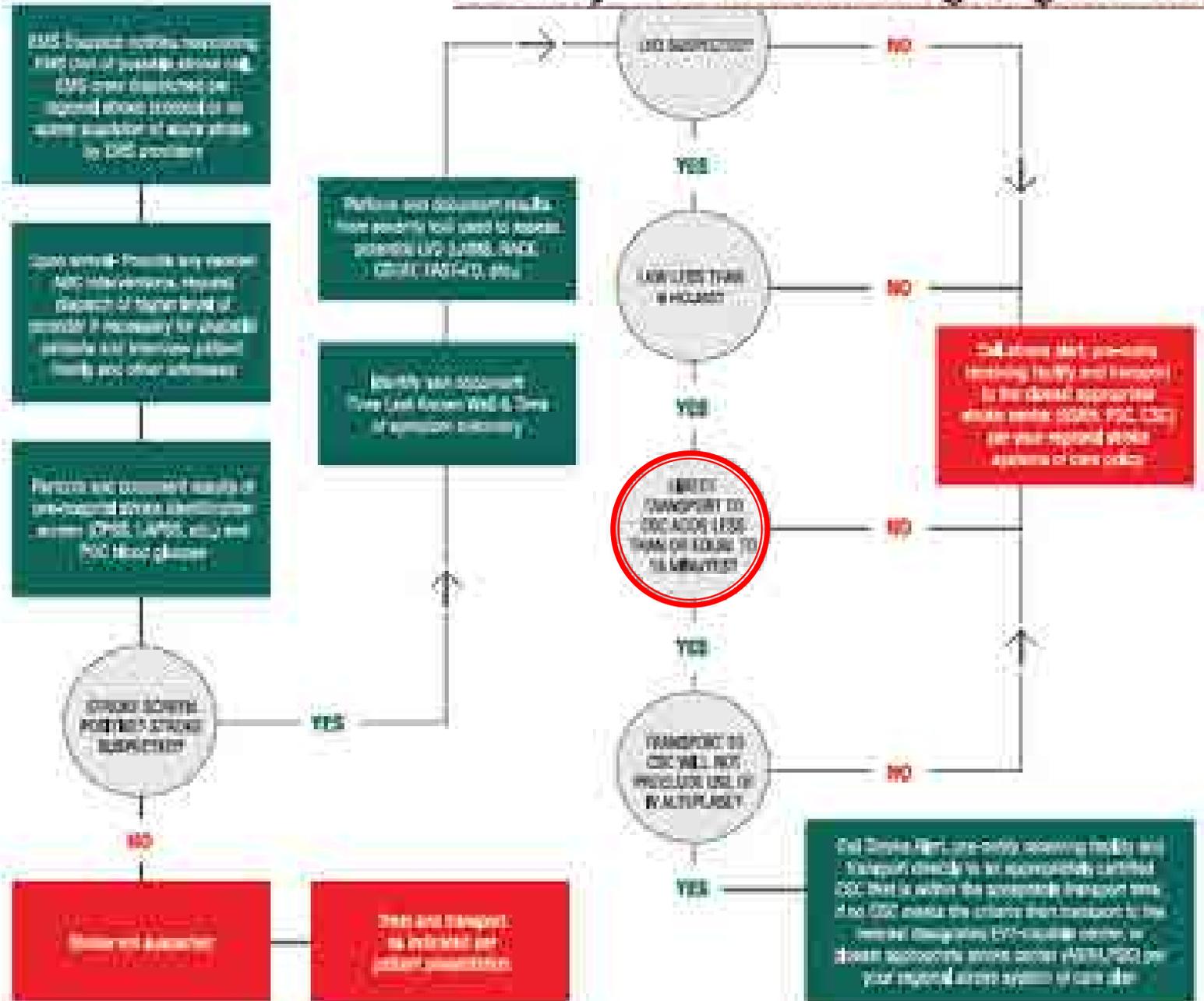
NEED TRANSPORT TO CSC ADDRESS TRANSPORT TO HOSPITAL

TRANSPORT TO CSC WILL NOT PROVIDE END OF B.Y. (PLATE)

Time and transport is critical per patient presentation

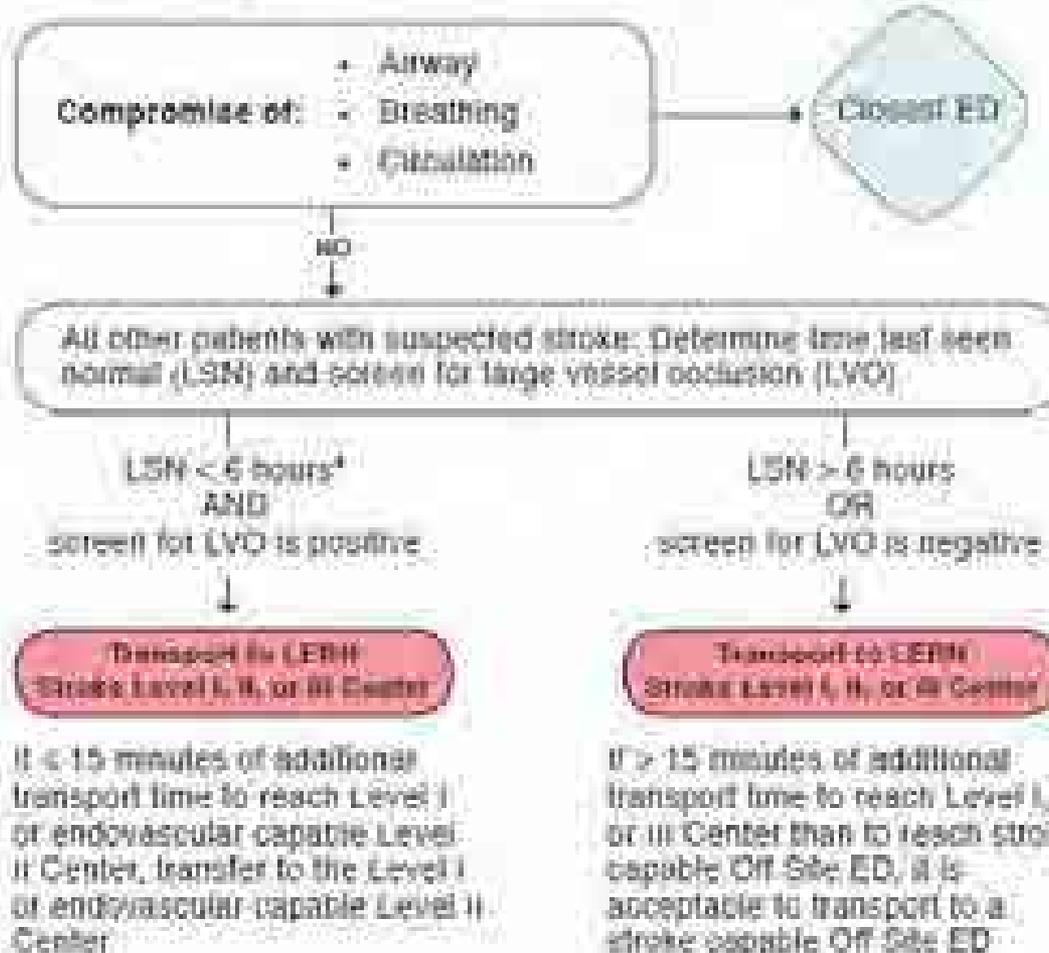
Call Stroke Alert, one-on-one assessing the patient. Transport directly to an appropriately certified CSC that is within the appropriate transport time. If no CSC meets the criteria then transport to the nearest designated EMS-eligible center or closest appropriate stroke center (ATL/POC per your regional stroke system of care plan)

Call Stroke Alert, one-on-one (training facility and transport) to the closest appropriate stroke center (ATL/POC per your regional stroke system of care plan)



## STROKE DESTINATION PROTOCOL

The following protocol applies to patients with suspected stroke:



\* The LSN < 6 hours should include patients without a definite time of LSN, but who could reasonably be assumed to be within 6 hours of onset, including patients who wake-up with stroke symptoms.

### Guiding Principles:

- Time is the critical variable in acute stroke care
- Protocols that include pre-hospital notification while en route by EMS should be used for patients with suspected acute stroke to facilitate initial destination efficiency
- Treatment with intravenous tPA is the only FDA approved medication therapy for hyperacute stroke
- EMS should identify the geographically closest hospital capable of providing tPA treatment
- Transfer patient to the nearest hospital equipped to provide tPA treatment
- Secondary transfer to facilities equipped to provide tertiary care and interventional treatments should not prevent administration of tPA to appropriate patients

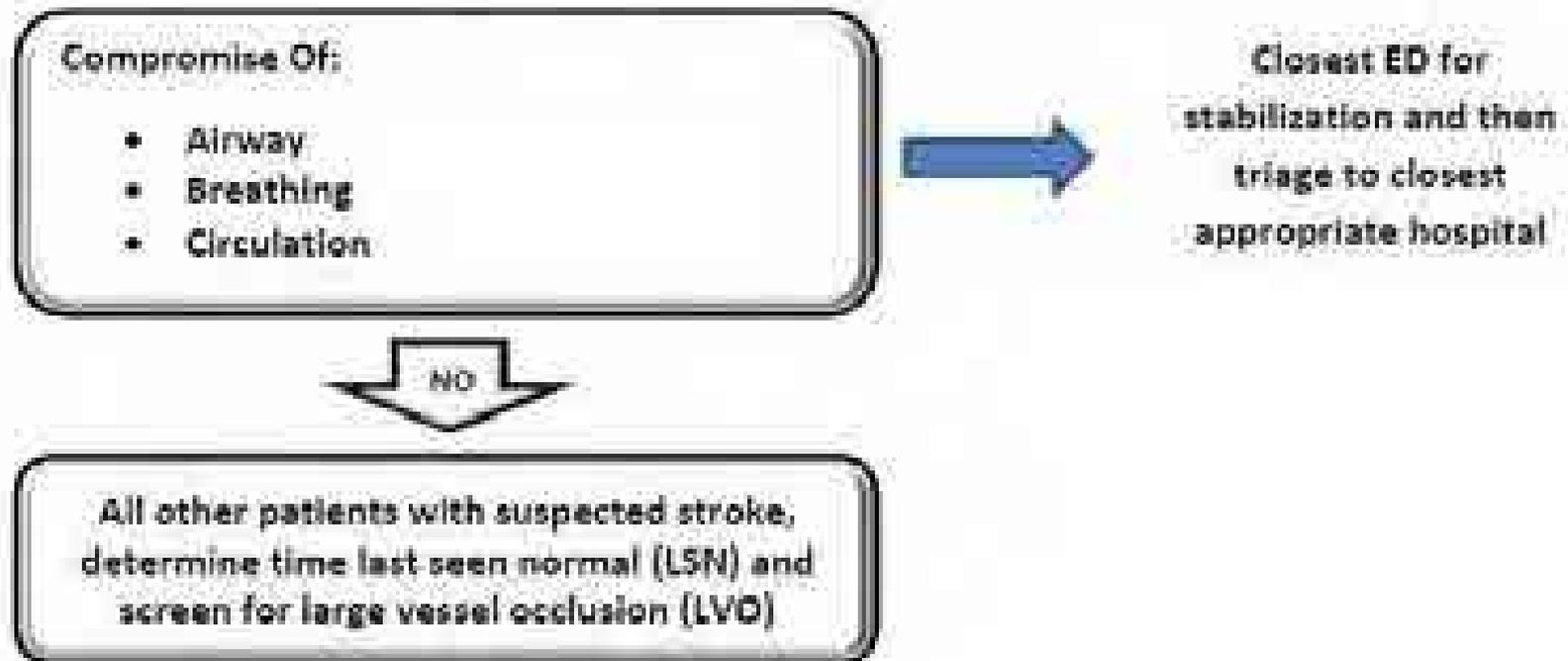
# Initial Destination Protocol

LERN Destination Protocol: Stroke



LERN Call Center: (866)320-8293

The following protocol applies to patients with suspected stroke:



Term	Definition
Last seen normal (LSN) = last known well (LKW)	<p>The time a person reports the time of symptoms onset, when able, or the time the person was last seen by a witness to be free of presenting deficits</p> <p>Important point.... If a patient is awake at the time of symptom onset AND is able to provide history, then that time serves as the LSN, even though a witness may report the last time the patient was seen normal by them was later.</p>
LSN example #1	Here is the easy one.... Woman at work during a team meeting, when at 2pm, she suddenly starts slurring her words and then develops facial paresis and arm weakness on the left side. What is the LSN? 2pm.
LSN example #2	Woman was seen normal by husband at 7am, when he left for work. He returns home at 5pm to find her on the floor and crying. She tells him that she fell at 3pm while she was walking to the kitchen, but could not get up and could not reach a phone. What is the LSN? 3pm, because she is able to provide her own history. NOT 7am when he last saw her normal.
LSN example #3	Woman was seen normal by husband at 7am, when he left for work. He returns home at 5pm to find her on the floor aphasic with a right hemiplegia. She is unable to speak. What is the LSN? 7am, because she is unable to provide her own history.
LSN example #4	Man was normal when he went to bed around 10pm. He and his wife sleep in separate bedrooms because of his loud snoring. His alarm clock woke her up at 6am. When he didn't turn it off after a couple of minutes, she went into his bedroom and found him halfway on the floor. What is the LSN?
LSN example #4a	He is able to tell his wife that he was normal when he used the bathroom an hour ago, but when his alarm went off, he couldn't stand up. What is the LSN? About 5am, because he said he was normal then.
LSN example #4b	He is unable to communicate and, therefore, not able to supplement the history. What is the LSN? 10pm

Is the patient able to provide the time of symptom onset?

YES

NO

Time of last seen normal = time symptoms noted = time of symptom onset

YES

Was the symptom onset witnessed by a bystander?

NO

Time of last seen normal comes before time symptoms noted and time of symptom onset could be anytime in between last seen normal and time symptoms noted

# Initial Destination Protocol

All other patients with suspected stroke, determine time last seen normal (LSN) and screen for large vessel occlusion (LVO)

LSN < 6 hours\* AND  
screen for LVO is positive

Transport to LERN Stroke Level I, II,  
or III Center

If < 15 minutes of additional transport time to reach Level I or endovascular capable Level II Center, transfer to the Level I or endovascular capable Level II Center

LSN > 6 hours OR  
screen for LVO is negative

Transport to LERN Stroke Level I, II,  
or III Center

If > 15 minutes of additional transport time to reach Level I, II, or III Center than to reach stroke capable Off Site ED, it is acceptable to transport to a stroke-capable Off Site ED

\*LSN < 6hrs should include patients without a definite time of LSN, but who could reasonably be assumed to be within 6hrs of onset, including patients who wake-up with stroke symptoms

# How can candidates be identified?

- ▶ Clinical features
  - $1 - \text{sensitivity} = \% \text{ missed LVO}$
  - $1 - \text{positive predictive value} = \% \text{ not LVO}$
- ▶ Radiographic features
  - Parenchymal changes – early ischemic changes
  - Vessel imaging

# Clinical features of LVO

- ▶ CPSSS – **C**incinnati **P**rehospital **S**troke **S**everity **S**core
- ▶ RACE – **R**apid **A**rterial **O**ccclusion **E**valuation
- ▶ NIHSS – arbitrary cut-off vs cortical score
- ▶ FAST-ED – **F**ield **A**ssessment **S**troke **T**riage for **E**mergency **D**estination
- ▶ VAN – **V**isual, **A**phasia, **N**eglect

# VAN = Vision, Aphasia, Neglect

## Stroke VAN

How weak is the patient?

Raise both arms up.

- Mild (minor drift)
- Moderate (severe drift—touches or nearly touches ground)
- Severe (flaccid or no antigravity)
- Patient shows no weakness. Patient is VAN negative

(exceptions are confused or comatose patients with dizziness, focal findings, or no reason for their altered mental status then basilar artery thrombus must be considered; CTA is warranted)

Visual disturbance

- Field cut (which side) (4 quadrants)
- Double vision (ask patient to look to right then left; evaluate for uneven eyes)
- Blind new onset
- None

Aphasia

- Expressive (inability to speak or paraphasic errors); do not count slurring of words (repeat and name 2 objects)
- Receptive (not understanding or following commands) (close eyes, make list)
- Mixed
- None

Neglect

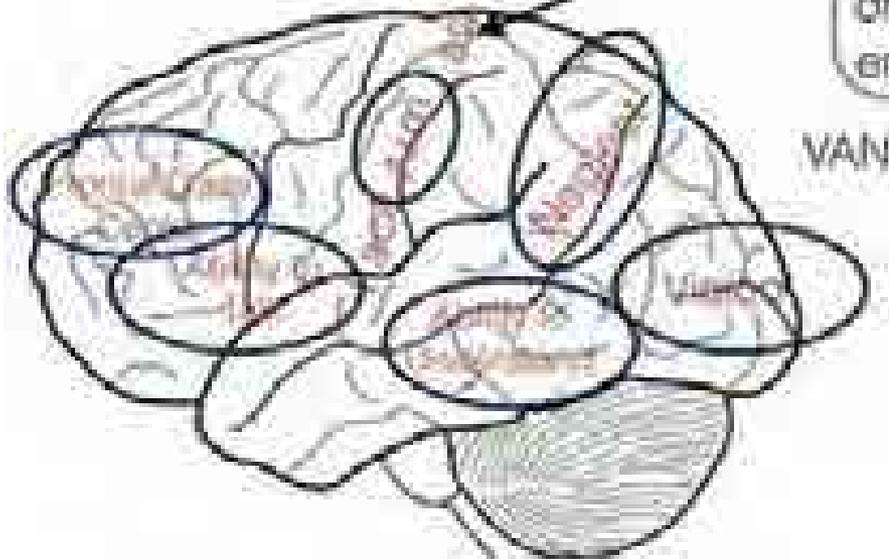
- Forced gaze or inability to track to one side
- Unable to feel both sides at the same time, or unable to identify own arm
- Ignoring one side
- None

Teleb MS, et al. *J NeuroIntervent Surg* 2016;0:1–5. doi:10.1136/neurintsurg-2015-012131

Patient must have weakness plus one or all of the V, A, or N to be VAN positive.

<https://www.youtube.com/watch?v=9g-1u3uiWb4>

Motor weakness used in all large vessel screening tools due to central location as well as its link to functional independence on modified rankin scale used for endovascular stroke trials



VAN

	Large artery clot	No large artery clot	
VAN+	14	5	19 Total VAN+
VAN-	0	43	43 Total VAN-
	14 Large artery clot	48 No large artery clot	

	Large artery clot	No large artery clot	
NIHSS $\geq 6$	14	10	24 Total
NIHSS $< 6$	0	38	38 Total
	14 Large artery clot	48 No large artery clot	

Positive predictive value of VAN =  $14/19 = 74\%$ ; sensitivity =  $14/14 = 100\%$ .

Positive predictive value of NIHSS =  $14/24 = 58\%$ ; sensitivity =  $14/14 = 100\%$ .

Negative predictive value of VAN =  $43/43 = 100\%$ ; specificity =  $43/48 = 90\%$ .

Negative predictive value of NIHSS =  $38/38 = 100\%$ ; specificity =  $38/48 = 79\%$ .

Accuracy VAN =  $57/62 = 92\%$ .

Accuracy NIHSS =  $52/62 = 84\%$ .

**Table 4** Emergent large vessel occlusion screening to comparisons

	RACE	LEGS	LAMS	Hemiparesis	VAN	3I-SS	CPSSS
Need to calculate score	Yes	Yes	Yes	No	No	Yes	Yes
No of tests	6	4	3	1	1-4	3	3-4
Length of exam 1-7 (7 is longest)	7	6	4	1	2	3	5
Positive predictive value (%)	42	60			★ 74	74	
Sensitivity (%)	85	69	81	27-48 multiple etiologies analyzed	★ 100	67	83
Negative predictive value (%)	94	86		Could not be calculated	★ 100	89	
Specificity (%)	68	81	89		90	★ 92	40
Type	Prospective	Prospective	Retro	Retro	Prospective	Prospective	Retro
Total No of patients analyzed	357	181	119	45	62	171	303

3I-SS, 3 item stroke scale; CPSSS, Cincinnati Prehospital Stroke Severity Scale; LAMS, Los Angeles Motor Scale; LEGS, legs, eyes, gaze, speech (Texas Stroke Intervention Prehospital Stroke Severity Scale); RACE, Rapid Arterial occlusion Evaluation Scale; Retro, retrospective; VAN, vision, aphasia, neglect.

- Advantages of VAN:
- ✓ Fast
  - ✓ More accurate
  - ✓ Simple + vs - (not a score)
  - ✓ Makes anatomical sense

# <https://www.strokevan.com/>

## Why VAN?

- More accurate than some.
- Easier to perform, no calculation, if any cortical symptom with arm weakness is present then VAN positive.
- It has actual tutorial on how to do exam, anatomy.
- Has potential for much better inter-observer reliability.
- Uses the simplicity of the easiest conducted tools and combines with more cortical symptoms testing of longer and more accurate tools.
- Has this website and teaches you what cortical symptoms are.
- We have video lectures going over why its important, how it changes patient outcomes, compares it to others, and how to conduct it.

Sudden neurological deficit?

No

Yes

Go to closest appropriate facility

Onset <6hrs?

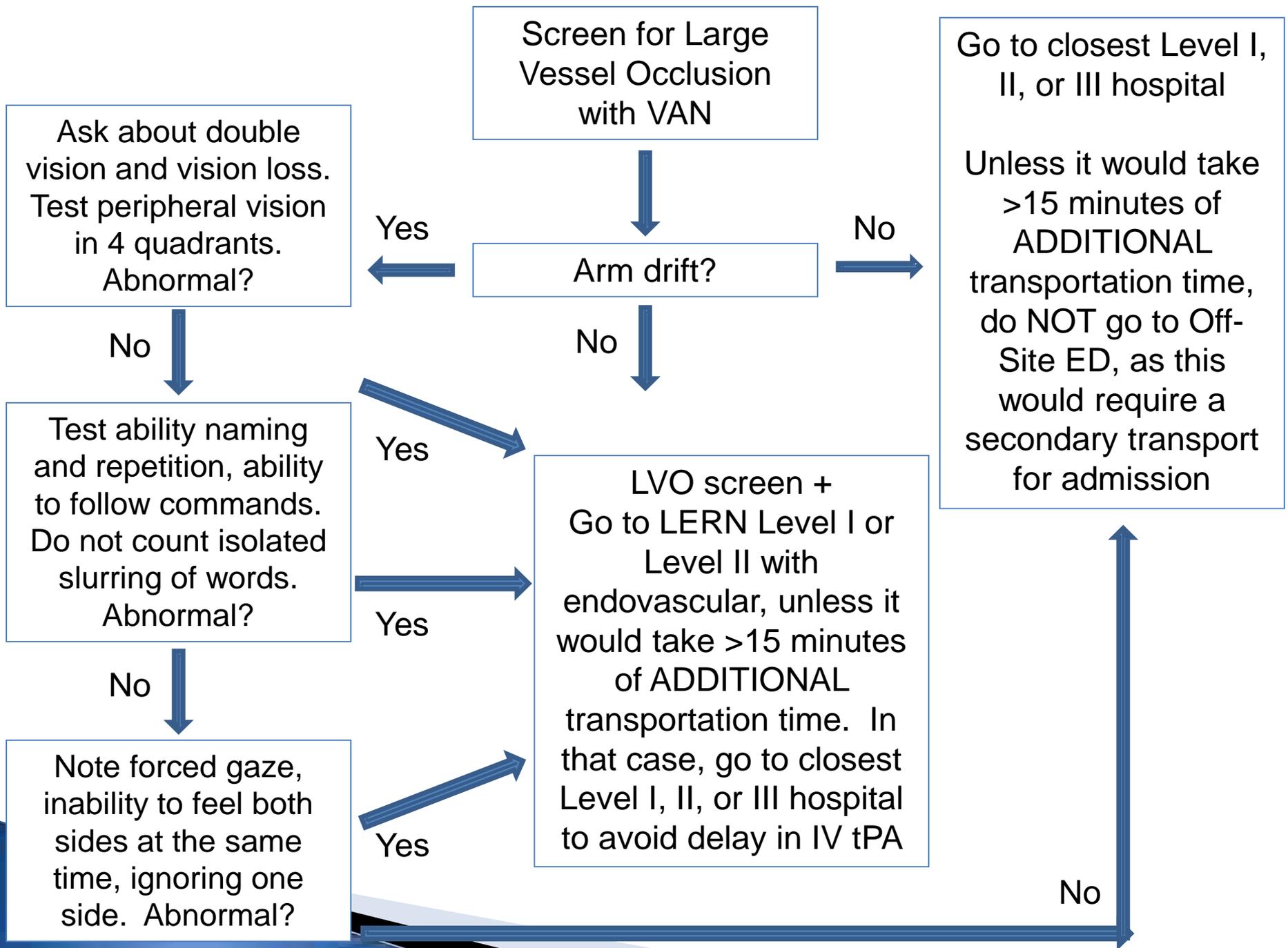
Yes

No

Screen for Large Vessel Occlusion with VAN

Go to closest Level I, II, or III hospital

Unless it would take >15 minutes of **ADDITIONAL** transportation time, do **NOT** go to Off-Site ED, as this would require a secondary transport for admission



Screen for Large Vessel Occlusion with VAN

Ask about double vision and vision loss. Test peripheral vision in 4 quadrants. Abnormal?

Arm drift?

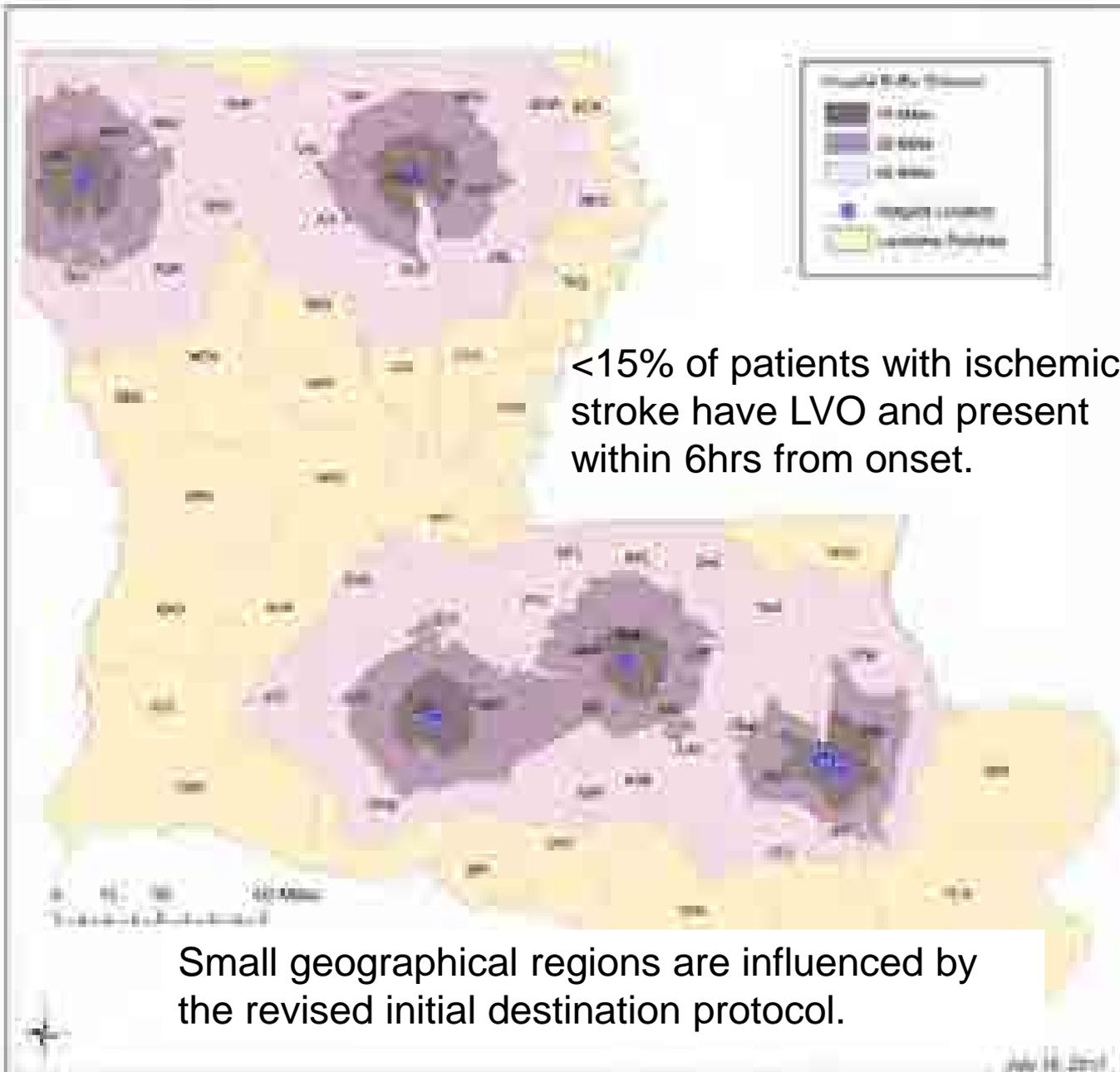
Go to closest Level I, II, or III hospital  
Unless it would take >15 minutes of ADDITIONAL transportation time, do NOT go to Off-Site ED, as this would require a secondary transport for admission

Test ability naming and repetition, ability to follow commands. Do not count isolated slurring of words. Abnormal?

LVO screen + Go to LERN Level I or Level II with endovascular, unless it would take >15 minutes of ADDITIONAL transportation time. In that case, go to closest Level I, II, or III hospital to avoid delay in IV tPA

Note forced gaze, inability to feel both sides at the same time, ignoring one side. Abnormal?

No



# The LERN Communication Center

- ▶ Implementation of LVO Screening 7/1/2017
- ▶ Q3 2017 = reference
- ▶ 337 calls for patients with suspected stroke <6hrs from LSN
  - VAN screening performed in 171 patients (50.7%)
  - 44.0% – 52.5% are screening + on VAN
  - In the trial, 30.6% screened +
- ▶ Likely sources of False Positive VAN testing
  - Misinterpreting old deficits for new deficits
  - Bilateral vs unilateral arm weakness
  - Misinterpreting dysarthria as aphasia
  - Inability to feel both sides when unable to feel one side when tested individually

# Interfacility transfer guideline

## Acute Ischemic Stroke Post-Thrombolysis EMS Inter-hospital Transfer Guideline

### Sending Hospital Must Complete

Receiving Facility Name \_\_\_\_\_  
Receiving Facility Address \_\_\_\_\_  
Accepting MD Name \_\_\_\_\_  
Accepting MD Phone # \_\_\_\_\_



Time tPA infusion started: \_\_\_\_\_ (Military Time)

Waste discarded:  Yes  No

When tPA infusion completed \_\_\_\_\_ (Military Time), start infusion of NS at same rate via tPA tubing, not to exceed 1 liter.

EMS must call the accepting physician at the receiving facility if any of the below clinical conditions occur or for any change in telemetry. Document the date/time/name of physician to whom you spoke.

Head-of-bed flat: If poor mental status or secretion management, place head-of-bed at 30°

If tPA is still running, STOP infusion for any of the following (check box):

- new severe headache - Time infusion stopped \_\_\_\_\_
- increase in mini-NDHSS by 2 or more points - Time infusion stopped \_\_\_\_\_
- inability to keep SBP  $\leq$  180 and DBP  $\leq$  105 - Time infusion stopped \_\_\_\_\_
- angioedema or new rash - Time infusion stopped \_\_\_\_\_  
Do NOT give epinephrine unless directed by accepting physician.
- nausea and vomiting - Time infusion stopped \_\_\_\_\_
- systemic bleeding not controlled by direct pressure - Time infusion stopped \_\_\_\_\_

Vital Signs every 15 minutes with continuous cardiac monitoring

BP > 180/105 must be treated per AHA/ASA guidelines

- labetalol 20 mg IV every 20 minutes per SBP > 180 or DBP > 105 - if HR > 65bpm
- hydralazine 10mg IV every 20 minutes per SBP > 180 or DBP > 105 - if HR < 65bpm
- nicardipine 0.2mg/ml IV. Initiate at 2.5 mg/hr PPN SBP > 180-200 or DBP > 105. Initiate at 5mg/hr if SBP > 200. Titrate in increments of 2.5 mg/hr as often as every 15 minutes to maintain above parameters. Max 15mg/hr.
- Nitroprusside 1/2 inch if HR < 65bpm and nicardipine is not available  
\*Confirm adequate quantity was provided for the duration of anticipated transport.
- If BP < 90/60, bolus 250cc Normal Saline. May repeat x 1 if BP remains < 90/60. Contact accepting physician for further orders if BP is refractory.

O<sub>2</sub> at 2 liters via NC, titrate to keep oxygen saturation  $\geq$  92%

Neuro checks (mini-NDHSS) every 15 minutes, notify accepting physician for signs of neurological worsening (increase in mini-NDHSS by 2 or more points).

# Monitoring of the ischemic stroke post-tPA patient en route

## Acute Ischemic Stroke Post-Thrombolysis EMS Inter-Hospital Transfer Guidelines

### Sending Hospital Must Complete:

Receiving Facility Name \_\_\_\_\_

Receiving Facility Address \_\_\_\_\_

Accepting MD Name \_\_\_\_\_

Accepting MD Phone # \_\_\_\_\_



Time tPA infusion started: \_\_\_\_\_ (Military Time)

Waste discarded:  Yes  No

When tPA infusion completed \_\_\_\_\_ (Military Time), start infusion of NS at same rate via tPA tubing, not to exceed 1 liter.

EMS must call the accepting physician at the receiving facility if any of the below clinical conditions occur or for any change in cardiac rhythm. Document the date/time name of physician to whom you spoke.

Head-of-bed flat. If poor mental status or secretion management, place head-of-bed at 30

(X) If IPA is still running, STOP infusion and contact the receiving facility physician for any of the following (check box):

- new severe headache - Time infusion stopped \_\_\_\_\_
- increase in mini-NIHSS by 2 or more points - Time infusion stopped \_\_\_\_\_
- inability to keep SBP  $\leq$  180 and DBP  $\leq$  105 - Time infusion stopped \_\_\_\_\_
- angioedema or new rash - Time infusion stopped \_\_\_\_\_  
Do NOT give epinephrine unless directed by accepting physician
- nausea and vomiting - Give Zofran 4mg IV x1 - Time infusion stopped \_\_\_\_\_
- systemic bleeding not controlled by direct pressure - Time infusion stopped \_\_\_\_\_

(X) Vital Signs every 15 minutes with continuous cardiac monitoring

BP > 180/105 must be treated per AHA/ASA guidelines

- labetalol 20 mg IV every 20 minutes prn SBP > 180 or DBP > 105 - if HR > 65bpm
- hydralazine 10mg IV every 20 minutes prn SBP > 180 or DBP > 105 - if HR < 65bpm
- nicardipine 0.2mg/ml IV. Initiate at 2.5 mg/hr PRN SBP > 180, 200 or DBP > 105. Initiate at 5mg/hr if SBP > 200

Titrate in increments of 2.5 mg/hr as often as every 15 minutes to maintain above parameters. Max 15mg/hr

- nitroglycerine 1/4 inch if HR < 65bpm and nicardipine is not available

\*Confirm adequate quantity of meds obtained for the duration of anticipated transport.

- If BP < 90/60, bolus 250cc Normal Saline. May repeat x 1 if BP remains < 90/60. Contact accepting physician for further orders if BP is refractory.

(X) O2 at 2 liters via NC. titrate to keep oxygen saturation  $\geq$  92%

(X) Neuro checks (mini-NIHSS) every 15 minutes; notify accepting physician for signs of neurological worsening (increase in mini-NIHSS by 2 or more points)



# Bottom line....

- ▶ Standard of care is IV tPA, unless contraindicated
- ▶ Faster IV tPA is better –
  - NNT for independent outcome in “golden hour” is 2
  - NNT for improved outcome in first 3 hrs is 3
  - NNT for improved outcome in 3–4.5 hrs is 6
- ▶ The stroke code isn't over until you have decided against endovascular treatment
  - Don't wait for tPA to be done to consider endovascular treatment – anticipate
  - Plan ahead –
    - notify cath lab immediately if available
    - formal agreements if endovascular is not available 24/7/365