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SVIN Society of Vascular and Interventional Neurology

International Perspectives on Stroke Triage, Diagnosis and Treatment

Episode 3: Treatment with IV Lytics

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Overview

- Jointly presented by ASA and SVIN
- No CEs available for webinar
- Certificate of Completion is available

Disclosures

- **Dr. Pooja Khatri**: Payment to UC Dept of Neurology from: Cerenovus (IIS grant for ENDOLOW MPI), Lumosa (consultant), Nervive (NIH SBIR grant coinvestigator), Diamedica (Stroke Advisory Board); Bayer (effort as PACIFIC-Stroke National PI); Royalties from UpToDate, Inc
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- **Dr. Alexandra Czap**: none
- **Dr. Ashu Jadhav**: none
- **Dr. Liping Liu**: none

To Ask a Question

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Panelists

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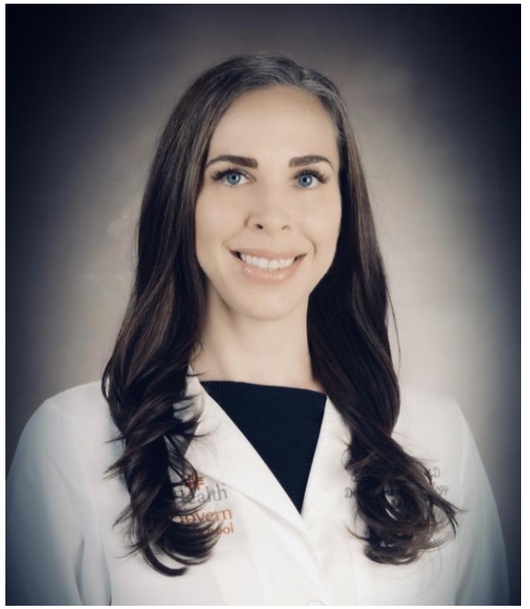

Panelists

Liping Liu, MD, PhD

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IV Alteplase: Eligibility Considerations

Pooja Khatri, MD, MSc

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The opinions expressed during this webinar are those of the speakers and do not necessarily reflect the opinions, recommendations or guidance of American Stroke Association or Society of Vascular and Interventional Neurology.

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Who should we....

Definitely treat?
Definitely not treat?
Probably treat?
Debate about treating?

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Endorsed by the Society for Academic Emergency Medicine and The Neurocritical Care Society

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons.

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CLASS (STRENGTH) OF RECOMMENDATION	
CLASS I (STRONG)	Benefit >>> Risk
CLASS IIa (MODERATE)	Benefit >> Risk
CLASS IIb (WEAK)	Benefit ≥ Risk
CLASS III: No Benefit (MODERATE) *(Generally, LOE A or B use only)*	Benefit = Risk
CLASS III: Harm (STRONG)	Risk > Benefit

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
▪ High-quality evidence‡ from more than 1 RCT ▪ Meta-analyses of high-quality RCTs ▪ One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
▪ Moderate-quality evidence‡ from 1 or more RCTs ▪ Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
▪ Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies ▪ Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
▪ Randomized or nonrandomized observational or registry studies with limitations of design or execution ▪ Meta-analyses of such studies ▪ Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
Consensus of expert opinion based on clinical experience	

Alteplase Eligibility <4.5 Hours

CLASS I (STRONG)

Benefit >>> Risk

Indications

- Ischemic stroke (no ICH on CT)
- Disabling deficits (regardless of NIHSS)

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*)
Prior antiplatelet therapy	IV alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke on the basis of evidence that the benefit of alteplase outweighs a possible small increased risk of sICH.† (*COR I; LOE A*)
	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.

Powers et al, Stroke, 2020

Microbleeds?

2.2.2. IV Alteplase Eligibility	COR	LOE
1. Administration of IV alteplase in eligible patients without first obtaining MRI to exclude cerebral microbleeds (CMBs) is recommended.	**I**	**B-NR**

CMBs are common in patients receiving IV alteplase, occurring in 15% to 27%.[89–94] Such patients were undoubtedly included in the pivotal NINDS and ECASS III trials that established the benefits of IV alteplase treatment.[48,49] Two meta-analyses of the association of baseline CMBs and the risk of sICH after IV alteplase reported that sICH is more common in patients with baseline CMBs, whereas 2 other meta-analyses and 1 multicenter study did not.[89–93] In 2 studies using ECASS II sICH criteria, the rates in patients with CMBs were 5.8% and 6.5% compared with 5.3% in ECASS III.[49,90,91] One study analyzing the risk of sICH in patients with CMBs detected after IV alteplase treatment reported sICH of 5% using the NINDS criteria compared with 6.4% in the NINDS tPA trials.[48,94] The risk of sICH in patients with >10 CMBs (30%–47%) is consistently reported as significantly greater than in those with no CMBs (1%–4.4%). However, these data are based on <50 patients, constituting <2% of these series.[90,91,93,94] No RCTs of IV alteplase in AIS with baseline MRI to identify CMBs have been conducted, so no determination of the effect of baseline CMB on the treatment effect of alteplase with CMB is available. In the absence of direct evidence that IV alteplase provides no benefit or produces harm in eligible patients with CMBs, withholding treatment on the basis of the presence of CMBs could lead to the exclusion of patients who would benefit from treatment.

Benefit of Intravenous Thrombolysis in Acute Ischemic Stroke Patients With High Cerebral Microbleed Burden

Ludwig Schlemm, MD, MSc; Matthias Endres, MD; David J. Werring, MD; Christian H. Nolte, MD

Conclusions—High CMB burden modifies the treatment effect of IVT. In patients with >10 CMBs, IVT is associated with higher mortality and, in older patients with severe strokes and longer treatment delays, a net utility loss. Patients with higher-than-average pretest probability of >10 CMB might profit from magnetic resonance imaging screening if it does not increase the treatment time. **(*Stroke*. 2020;51:232-239. DOI: 10.1161/STROKEAHA.119.027633.)**

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*)‡

Powers et al, Stroke, 2020
Schlemm, Stroke, 2020

Alteplase Contraindications

- Mild, nondisabling stroke (NIHSS 0-5)
- Extensive, clear ischemic hypodensity (ex:>1/3 MCA territory) on CT
- >185/110 mm Hg that cannot be safely and stably lowered
- Severe head trauma, ischemic stroke, or intracranial/intraspinal surgery <3 months
- Previous intracranial hemorrhage
- Suspected subarachnoid hemorrhage, infective endocarditis, aortic arch dissection
- Intracranial intra-axial neoplasm
- Gastrointestinal malignancy/bleeding <21 days
- Bleeding diathesis or coagulopathy
  - INR>1.7, heparin use <48h with abnormal PTT, LMWH <24h, platelets <100,000 mm3
  - *only wait for them if suspected abnormality*
- Current use (<48h) of direct oral anticoagulant with any abnormal coagulation tests
  - anti-Xa-activity for FXa inhibitors, thrombin time for dabigatran, or DOAC blood level

Powers et al, Stroke, 2020

Generally Treat…

CLASS IIa (MODERATE) **Benefit >> Risk**

- Early improvement
- Seizure at onset
- Glucose <40 or >400
- Menstruation
- Extracranial cervical dissections
- Unruptured intracranial aneurysm
- Extra-axial intracranial neoplasm
- Acute MRI
- Recent MI
- Procedural stroke
- Sickle cell disease

Early improvement	IV alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner.† (*COR IIa; LOE A*)
Seizure at onset	IV alteplase is reasonable in patients with a seizure at the time of onset of acute stroke if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon.† (*COR IIa; LOE C-LD*)§
Blood glucose	Treatment with IV alteplase in patients with AIS who present with initial glucose levels <50 or >400 mg/dL that are subsequently normalized and who are otherwise eligible may be reasonable. (Recommendation modified from 2015 IV Alteplase to conform to text of 2015 IV Alteplase. [*COR IIb; LOE C-LD*])§
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*)§
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*)§
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*)§
Extra-axial intracranial neoplasms	IV alteplase treatment is probably recommended for patients with AIS who harbor an extra-axial intracranial neoplasm.† (*COR IIa; LOE C-EO*)§
Acute MI	For patients presenting with concurrent AIS and acute MI, treatment with IV alteplase at the dose appropriate for cerebral ischemia, followed by percutaneous coronary angioplasty and stenting if indicated, is reasonable.† (*COR IIa; LOE C-EO*)§
Recent MI	For patients presenting with AIS and a history of recent MI in the past 3 mo, treating the ischemic stroke with IV alteplase is reasonable if the recent MI was non-STEMI.† (*COR IIa; LOE C-LD*)§
	For patients presenting with AIS and a history of recent MI in the past 3 mo, treating the ischemic stroke with IV alteplase is reasonable if the recent MI was a STEMI involving the right or inferior myocardium.† (*COR IIa; 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*)§
Sickle cell disease	IV alteplase for adults presenting with an AIS with known sickle cell disease can be beneficial. (*COR IIa; LOE B-NR*)‡

Powers et al, Stroke, 2020

Grey Areas…

CLASS IIb (WEAK)

Benefit ≥ Risk

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*)§
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*)§
	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*)§

Grey Areas Continued…

CLASS IIb (WEAK) — Benefit ≥ Risk

Acute pericarditis	For patients with major AIS likely to produce severe disability and acute pericarditis, treatment with IV alteplase may be reasonable† (*COR IIb; LOE C-EO*)§; urgent consultation with a cardiologist is recommended in this situation.
	For patients presenting with moderate AIS likely to produce mild disability and acute pericarditis, treatment with IV alteplase is of uncertain net benefit.† (*COR IIb; LOE C-EO*)§
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*)§
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*)§
Preexisting dementia	Patients with preexisting dementia may benefit from IV alteplase. Individual considerations such as life expectancy and premorbid level of function are important to determine whether alteplase may offer a clinically meaningful benefit.† (*COR IIb; LOE B-NR*)§

Time Considerations

Powers et al, Stroke, 2020

Additional Considerations for 3-4.5 Hours

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*)§

Powers et al, Stroke, 2020

Wake Up/Unknown Time of Onset Strokes?

CLASS IIa (MODERATE)

Benefit >> Risk

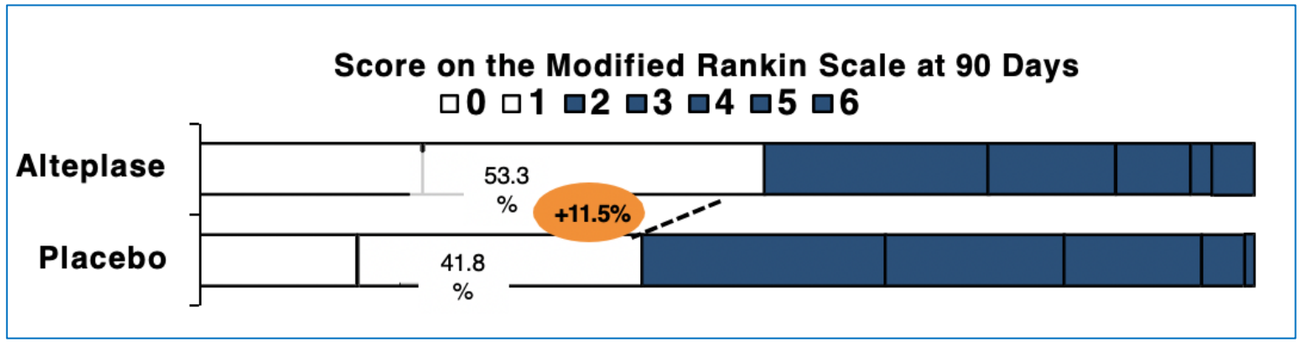
3. In patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last known well or at baseline state, MRI to identify diffusion-positive FLAIR-negative lesions can be useful for selecting those who can benefit from IV alteplase administration within 4.5 hours of stroke symptom recognition.	**IIa**	**B-R**
The WAKE-UP trial (Efficacy and Safety of MRI-based Thrombolysis in Wake-Up Stroke) randomized 503 patients with AIS who awoke with stroke or had unclear time of onset >4.5 hours from last known well 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 middle cerebral artery (MCA), NIHSS score >25, contraindication to treatment with alteplase, or planned thrombectomy were all exclusions. The trial was terminated early for lack of funding before the designated 800 patients were randomized. Ninety-four percent were wake-up strokes. Median NIHSS score was 6. Median time from last known well was slightly over 10 hours. At baseline, one-third of the patients had vessel occlusion on time-of-flight MRA, and three-quarters of the FLAIR lesions were <9 mL. The end point of an mRS score of 0 to 1 at 90 days was achieved in 53.3% of the IV alteplase group and in 41.8% of the placebo group (P=0.02).[88]		

Powers et al, Stroke, 2020

>4.5 Hours?

WAKE-UP (unwitnessed)

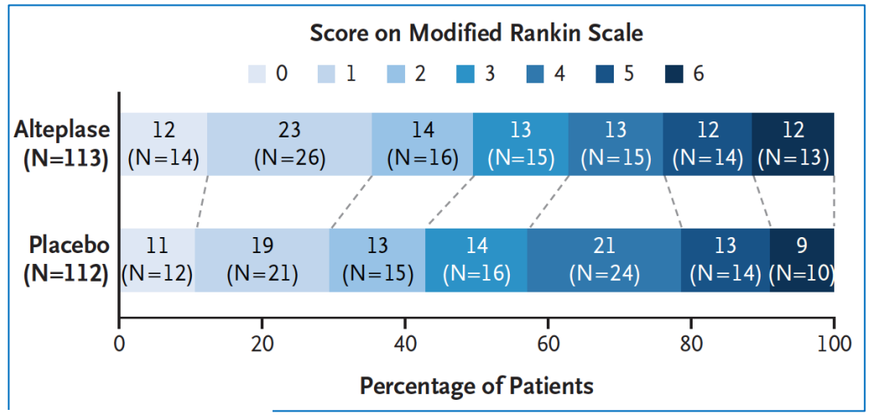
- Clinical benefit: NNT 9



- Imaging
  - WAKEUP: FLAIR-DWI mismatch

EXTEND (4.5-9h)

- Clinical benefit: NNT 17



- Imaging
  - EXTEND:
    - Tmax >6 sec
    - Mismatch >1.2
    - Core <70 cc

Thomalla, NEJM, 2018; Ma, NEJM, 2019

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International Considerations for Alteplase Administration…

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Thank You.

Bypass IV Alteplase for LVO

Alexandra Czap, MD

Assistant Professor of Neurology and Neurosurgery
University of Texas Health Science Center at Houston

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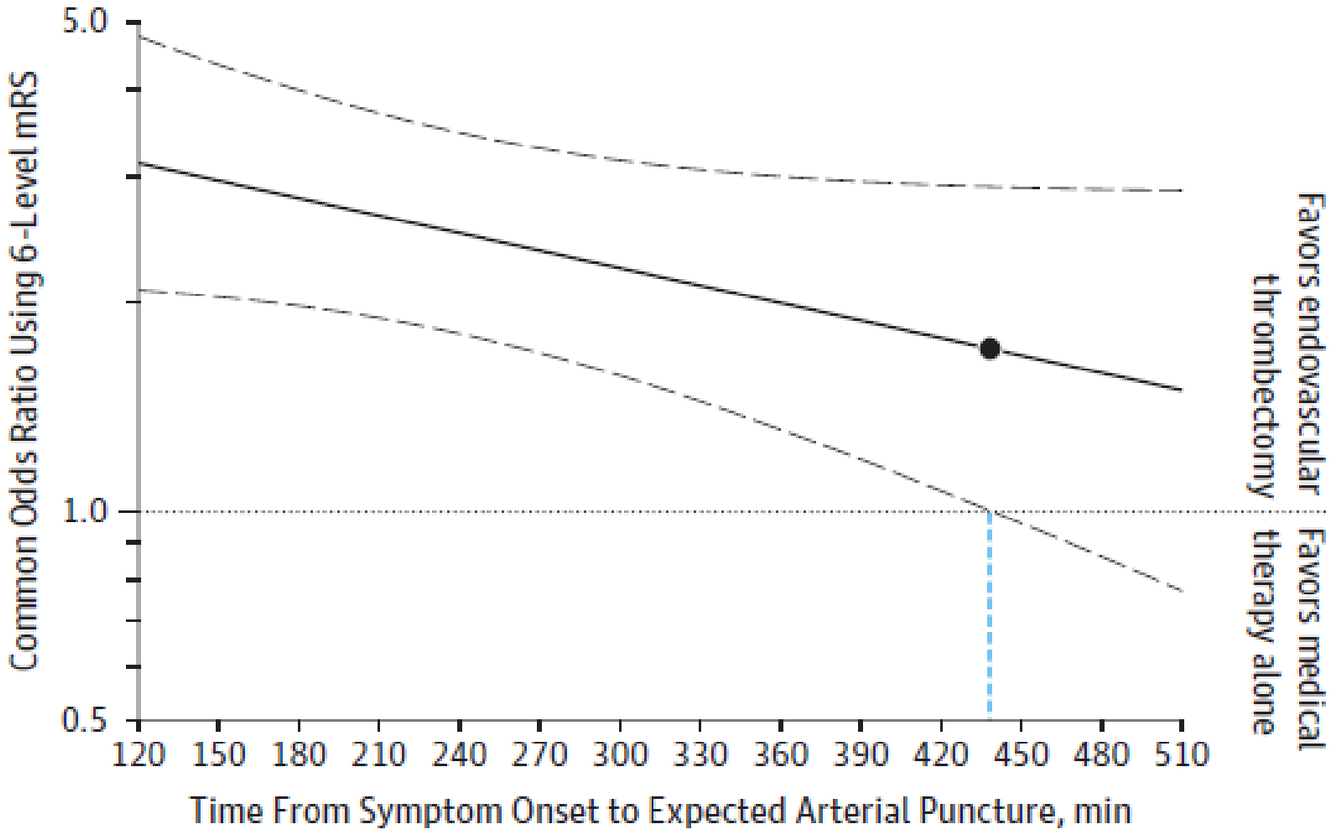
Goals of Acute Stroke Therapy

Open vessels in a cost-effective manner as quickly as possible with maximal clinical benefit

Impact of Time on Outcomes



Among every 1000 patients achieving substantial endovascular reperfusion, for every 15-minute faster emergency department door–to-reperfusion time, an estimated 39 patients would have a less-disabled outcome at 3 months, including 25 more who would achieve functional independence (mRS 0-2)

Saver et al (JAMA 2016)

Does alteplase open LVOs?

Table 2. Differences in Preinterventional Reperfusion in IV-tPA Versus no IV-tPA Patients Stratified According to Occlusion Sites

COS with TICI ≥2a	No IV-tPA	IV-tPA	*P* Value
All	1.3% (5/377)	13.6% (34/250)	<0.001
Posterior circulation	0% (0/38)	25% (5/20)	0.003
iICA/carotid-T	0% (0/96)	2.5% (1/40)	0.294
M1 proximal	2.9% (2/68)	4.5% (3/66)	0.678
M1 distal	1% (1/100)	16.9% (13/77)	<0.001
M2	3.1% (2/65)	27.9% (12/43)	<0.001
Other	0% (0/10)	0% (0/4)	…

In 13.6% of patients yes, however…..

Kaesmacher et al (Stroke 2018)

Does alteplase open LVOs?

Table 2. Differences in Preinterventional Reperfusion in IV-tPA Versus no IV-tPA Patients Stratified According to Occlusion Sites

COS with TICI ≥2a	No IV-tPA	IV-tPA	COS with TICI ≥2b			
All	1.3% (5/377)	13.6% (34/250)	All	0.8% (3/377)	6.0% (15/250)	<0.001
Posterior circulation	0% (0/38)	25% (5/20)	Posterior circulation	0% (0/38)	20.0% (4/20)	0.011
ilCA/carotid-T	0% (0/96)	2.5% (1/40)	ilCA/carotid-T	0% (0/96)	0% (0/40)	…
M1 proximal	2.9% (2/68)	4.5% (3/66)	M1 proximal	1.5% (1/68)	3.0% (2/66)	0.617
M1 distal	1% (1/100)	16.9% (13/77)	M1 distal	0% (0/100)	5.2% (4/77)	0.034
M2	3.1% (2/65)	27.9% (12/43)	M2	3.1% (2/65)	11.6% (5/43)	0.112
Other	0% (0/10)	0% (0/4)	Other	0% (0/10)	0% (0/4)	…

In 13.6% of patients yes, however….. often incomplete

Kaesmacher et al (Stroke 2018)

Alteplase Recanalization dependent on

Table 2 Recanalization rate in digital subtraction angiography/control imaging dependent on occlusion location

	Relevant recanalization before EVT			Partial recanalization before EVT		
	Total	Mother-ship paradigm	Drip-and-ship paradigm	Total	Mother-ship paradigm	Drip-and-ship paradigm
Total	28 (8.8%)	12/194 (6.2%)	17/125 (13.6%)	54/319 (16.9%)	15/194 (7.7%)	10/125 (8%)
ICA	5/93 (5.4%)	2/52 (3.8%)	3/41 (7.3%)	3/93 (3.2%)	2/52 (3.8)	1/41 (2.4%)
M1	12/148 (8.1%)	6/101 (5.9%)	6/47 (12.8%)	15/148 (10.1%)	11/101 (10.9%)	4/47 (8.5%)
M2	6/34 (17.6%)	2/21 (9.5%)	4/13 (30.8%)	3/34 (8.8%)	1/21 (4.8%)	2/13 (15.4%)
BA	5/44 (11.4%)	1/20 (5%)	4/24 (16.7%)	4/44 (9.1%)	1/20 (5%)	3/24 (12.5%)

BA, basilar artery; EVT, endovascular therapy; ICA, internal carotid artery; M1, middle cerebral artery segment M1; M2, middle cerebral artery segment M2.

Mueller et al (Eur J Neuro 2017)

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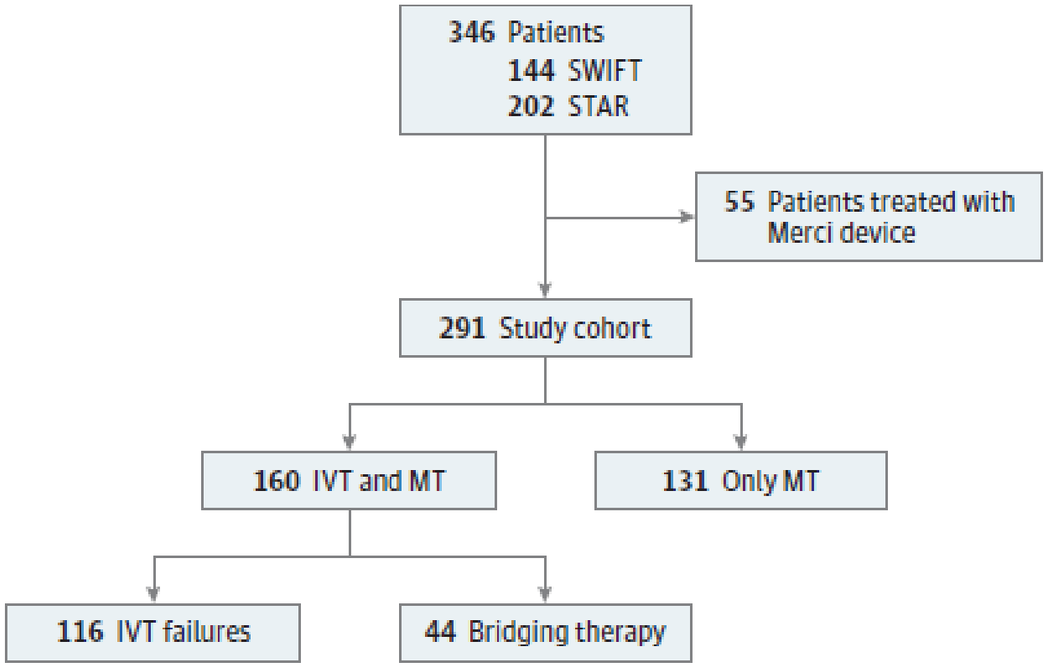
BA, basilar artery; EVT, endovascular therapy; ICA, internal carotid artery; M1, middle cerebral artery segment M1; M2, middle cerebral artery segment M2.

Mueller et al (Eur J Neuro 2017)

Limitations of IV Alteplase

- Incomplete recanalization (especially for large clot burden)

Figure. Flowchart of Patient Selection



A total of 346 patients were enrolled in the Solitaire With the Intention for Thrombectomy (SWIFT) (n = 144) and Solitaire Flow Restoration Thrombectomy for Acute Revascularization (STAR) (n = 202) clinical trial studies, of whom 55 patients were excluded from the analysis because they were not treated with the Solitaire FR (flow restoration) stent retriever. The remaining 291 patients comprised the analysis population.

Coutinho et al (JAMA Neurology 2017)

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Table 4. Multivariate Analyses

Variable	No. (%) of Patients		OR (95% CI)	
	MT and IVT (n = 160)	MT Alone (n = 131)	Unadjusted	Adjusted
Times[a]				
Hospital arrival to groin puncture ≤90 min	97/156 (62.2)	72/121 (59.5)	1.12 (0.69-1.82)	1.63 (0.83-3.21)
Groin puncture to reperfusion ≤45 min	82/152 (53.9)	59/118 (50.0)	1.17 (0.72-1.90)	1.31 (0.75-2.29)
Technical details of the MT procedure[b]				
mTICI 2b or 3	127/151 (84.1)	105/124 (84.7)	0.96 (0.50-1.84)	0.68 (0.28-1.66)
mTICI 3	86/151 (57.0)	66/124 (53.2)	1.16 (0.72-1.87)	1.38 (0.76-2.51)
>3 Passes with stent retriever	30/132 (22.7)	30/120 (25.0)	0.88 (0.49-1.58)	0.90 (0.44-1.85)
Procedural complications[b]				
sICH	2/160 (1.3)	5/131 (3.8)	0.32 (0.06-1.67)	0.03 (0.00-1.28)
Emboli to uninvolved territory	7/156 (4.5)	3/126 (2.4)	1.93 (0.49-7.61)	4.12 (0.75-22.54)
Vasospasm	40/160 (25.0)	17/131 (13.0)	2.24 (1.20-4.17)	1.41 (0.58-3.42)
Outcome at 90 d[c]				
mRS scores of 0-2[d]	90/156 (57.7)	61/128 (47.7)	1.50 (0.94-2.40)	1.48 (0.80-2.74)
Mortality	13/160 (8.1)	16/131 (12.2)	0.64 (0.29-1.37)	0.90 (0.35-2.30)

Coutinho et al (JAMA Neurology 2017)

Limitations of IV Alteplase

- Incomplete recanalization (especially for large clot burden)
- **Unclear clinical benefit**

Not all LVO strokes are the same

Theoretically, immediately after a large vessel occlusion of the ICA/MCA M1
- Ischemic Core Volume is 0 ml, Penumbra is the entire MCA territory

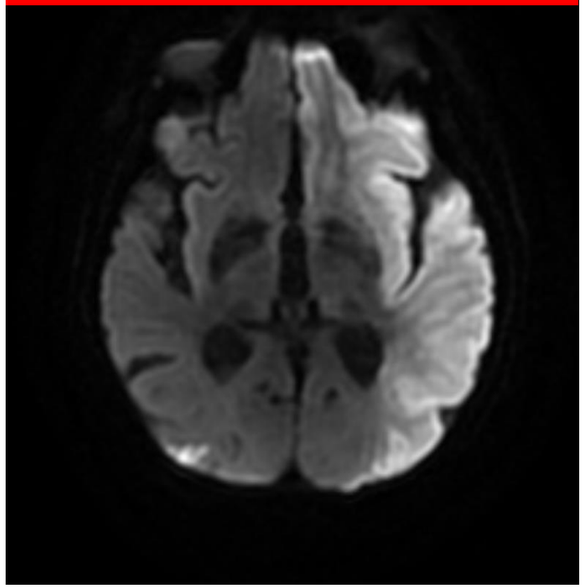
Large phenotypic differences exist among LVO strokes

Patient 1:

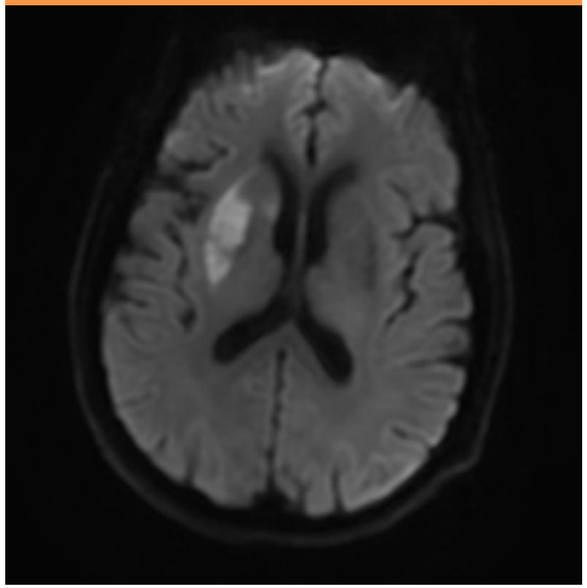
Stroke onset: 2hours

Occlusion: Left M1

Ischemic Core= 163 ml



Ischemic Core= 7 ml

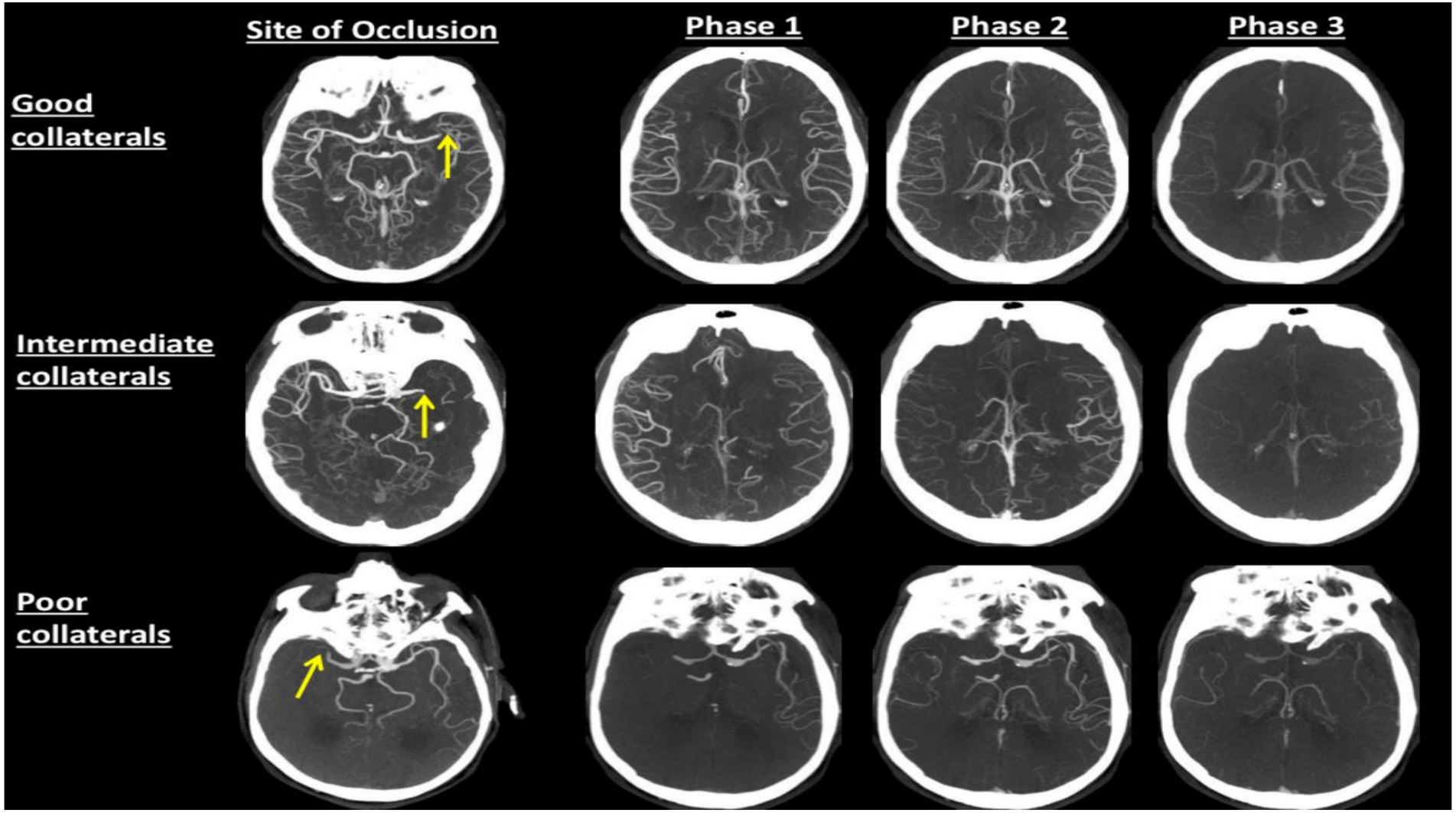


Patient 2:

Stroke onset: 2hours

Occlusion: Right M1

‘Fast’ versus ‘Slow’ Progressors



Time is brain (quantified)

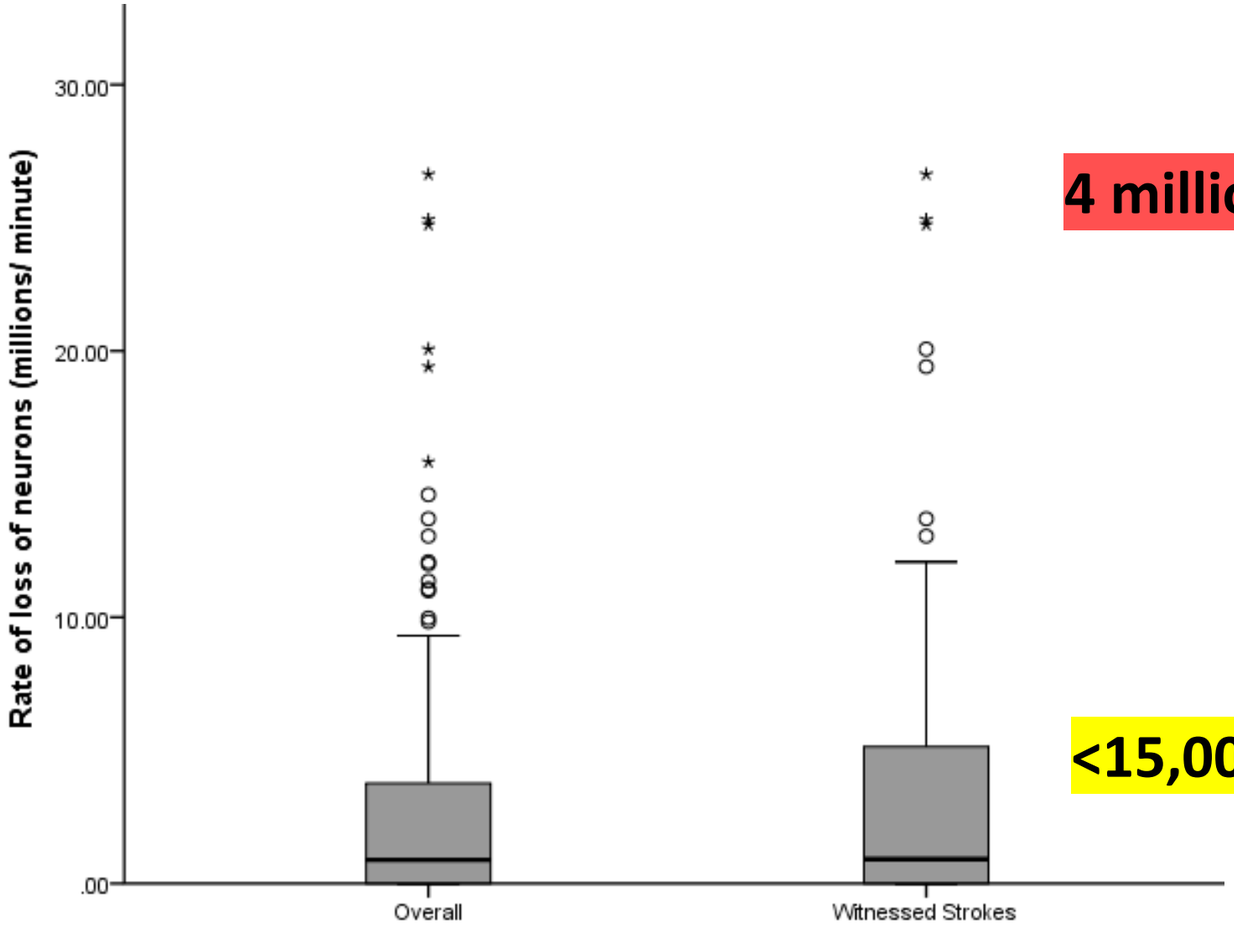
Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

1.9 million neurons lost per minute

Saver (Stroke 2006)

High Variability in Neuronal Loss

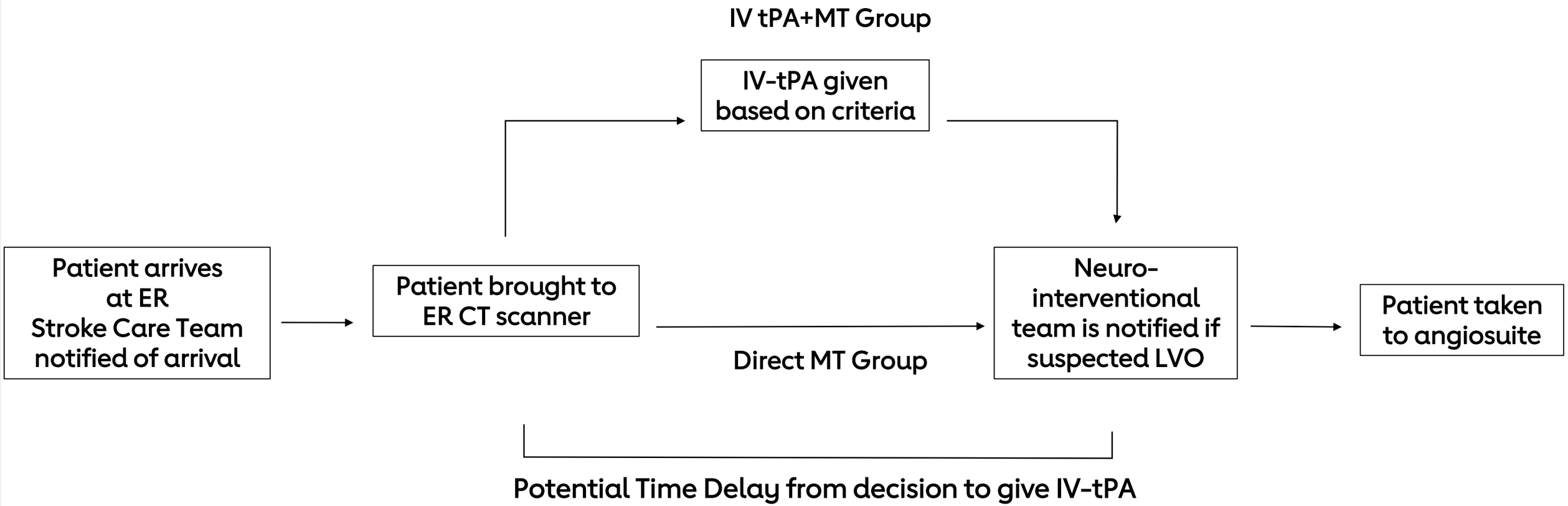


4 million neurons/min to >24 million neurons/min

<15,000 neurons/min to 1.7 million neurons/min

Desai et al (Stroke 2019)

Impact of Alteplase on Workflow



*tPA given immediately after NCCT is completed en route to angiosuite to prevent delay

Atchaneeyasakul et al (SVIN 2019)

Impact of Alteplase on Workflow

Feature	IV-tPA	Direct MT	P value
LKW-to-door, mins	85 (61.5-85)	176 (125-222)	<0.001
Door-to-needle, mins	40 (31-56)	N/A	N/A
Door-to-needle ≤ 60m (%)	75.3%	N/A	N/A
Door-to-needle ≤ 45m (%)	59.3%	N/A	N/A
Door-to-puncture, mins	74 (59.5-90.5)	52 (18-80.75)	<0.001
Door-to-puncture ≤ 90m (%)	69.1%	75%	0.34

Atchaneeyasakul et al (SVIN 2019)

Limitations of IV Alteplase

- Incomplete recanalization (especially for large clot burden)

- Unclear clinical benefit

- **Delays mechanical thrombectomy (penalty: fast progressors)**

Hospital Costs with Alteplase

Table 3 Comparison of length of stay and hospital costs between the two treatment groups

	EV-Only vs IV+EV Entire cohort (n=90)			EV-Only vs IV+EV Onset to presentation ≤4.5 hours (n=64)		
	EV-Only (n=52)	IV+EV (n=38)	p Value	EV-Only (n=26)	IV+EV (n=38)	p Value
Total cost, $	33 810 (13 505)	40 743 (17 177)	0.024*	31 621 (12 874)	40 743 (17 177)	0.027*
Direct cost, $	23 034 (8786)	28 711 (11 406)	0.007*	22 087 (9228)	28 711 (11 406)	0.017*
Indirect cost, $	10 777 (5104)	12 032 (6311)	0.39	9534 (3928)	12 032 (6311)	0.09
Length of stay, days	8 (6)	8 (6)	0.86	6 (4)	8 (6)	0.34
Length of ICU stay, days†	2.1 (2.1)	2.2 (1.5)	0.48	2 (2.2)	2.2 (1.5)	0.23

Rai et al (JNIS 2018

Limitations of IV Alteplase

- Incomplete recanalization (especially for large clot burden)
- Unclear clinical benefit
- Delays mechanical thrombectomy (penalty: fast progressors)
- **Increase costs**

Limitations of IV Alteplase

- Incomplete recanalization (especially for large clot burden)
- Unclear clinical benefit
- Delays mechanical thrombectomy (penalty: fast progressors)
- **Increase costs**

… why not SKIP and go Direct MT?

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Protocol

International Journal of Stroke
WSO

The randomized study of endovascular therapy with versus without intravenous tissue plasminogen activator in acute stroke with ICA and M1 occlusion (SKIP study)

International Journal of Stroke
2019, Vol. 14(7) 752–755
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DOI: 10.1177/1747493019840932
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SAGE

Suzuki et al (Int J Stroke 2019)

SKIP Trial Design

Multicenter prospective RCT with open label treatment and blinded outcome assessment

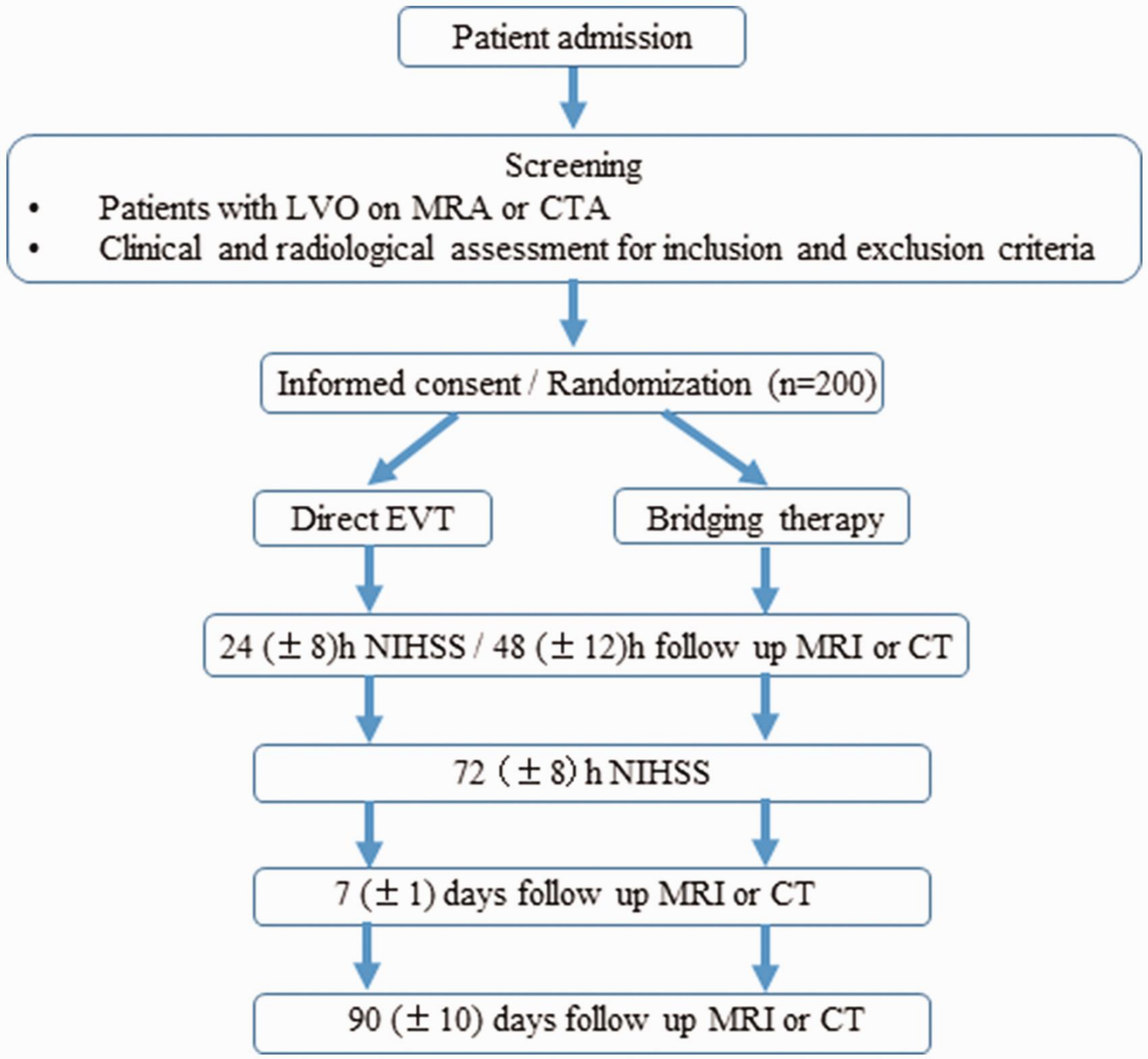
Arms: direct endovascular thrombectomy (EVT) vs bridging therapy (IVT + EVT)

Randomized 1:1

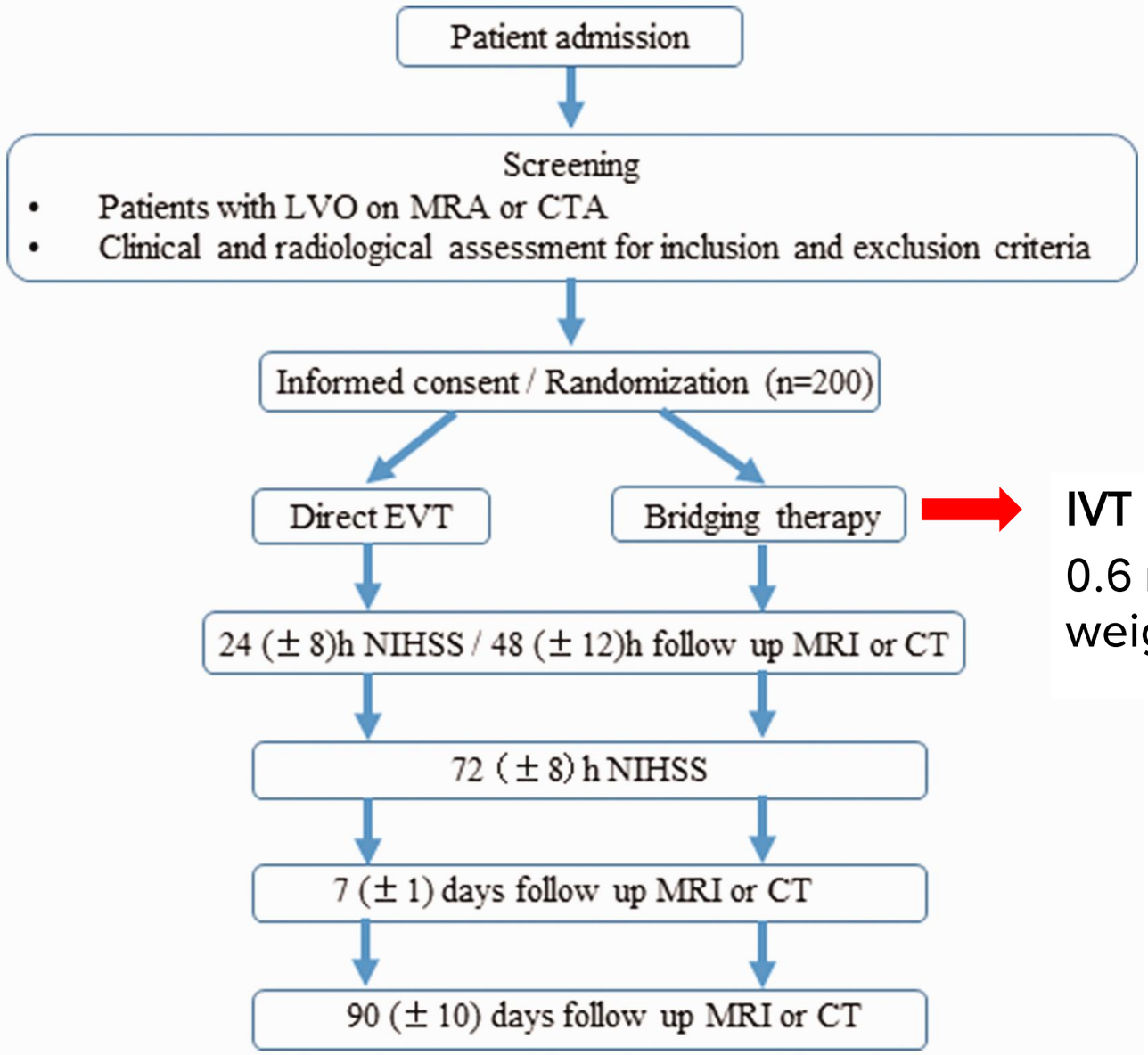
Inclusion: ICA/M1 occlusions, 4 hours, NIHSS > 6, NIHSS 18-85, ASPECTS > 6

Endpoint: mRS 0-2 at 90 days

Suzuki et al (Int J Stroke 2019)



Suzuki et al (Int J Stroke 2019)



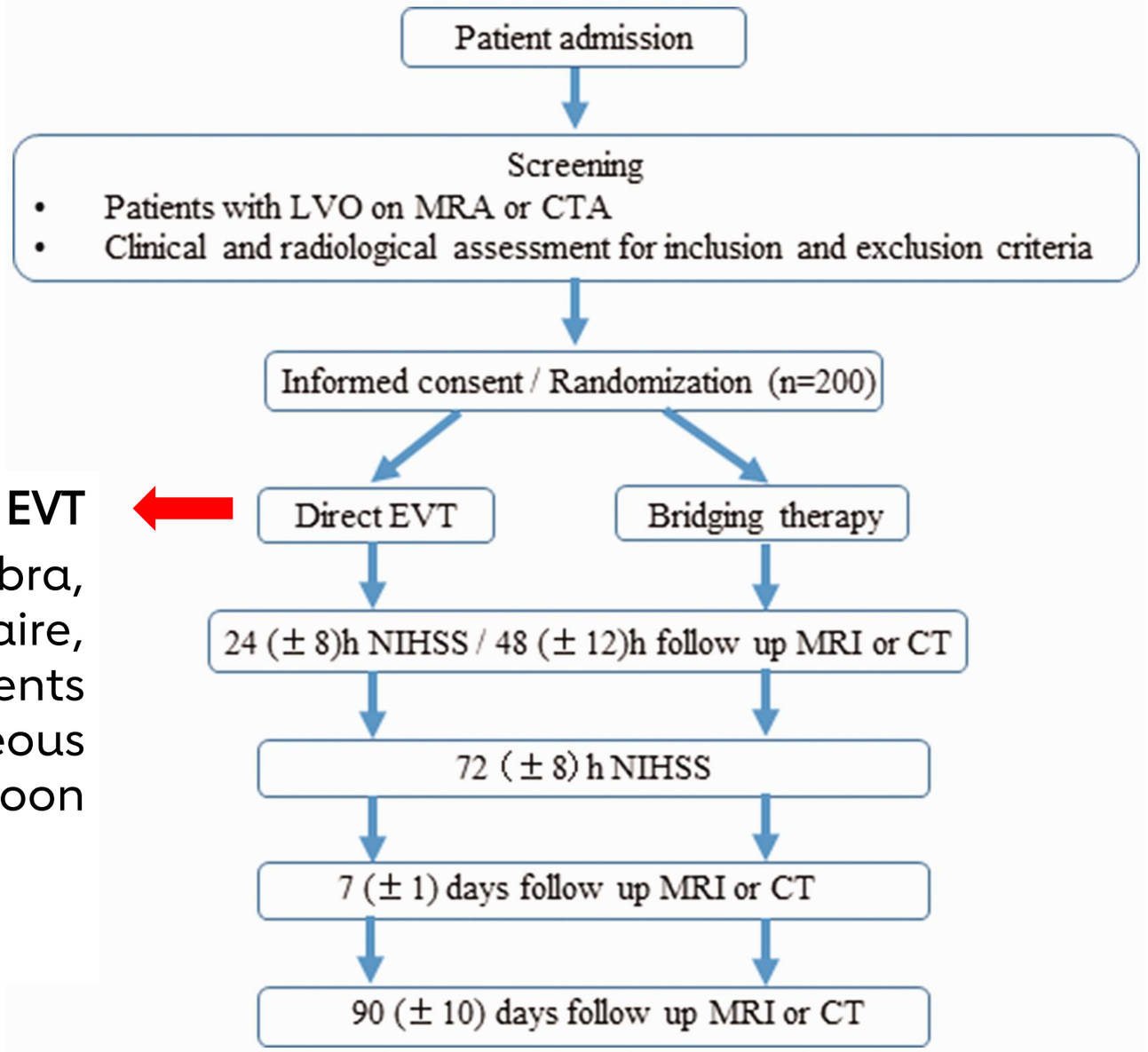
IVT

0.6 mg/kg body weight dose given

Suzuki et al (Int J Stroke 2019)

Direct EVT

Merci, Penumbra, Trevo, Solitaire, Revive, any stents and percutaneous angioplasty balloon



Suzuki et al (Int J Stroke 2019)

SKIP Results

	Direct EVT	IV tPA + EVT	P value
90 day mRS ≤ 2 (%)	59.4	57.3	0.78
mTICI ≥ 2b (%)	90	92	0.78
Symptomatic ICH (%)	6	8	0.78
Any ICH (%)	34	50	0.02
90 day mortality	7.9	8.7	1.00

Unable to demonstrate the noninferiority of primary EVT over combined therapy

Suzuki et al (ISC 2020)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke

P. Yang, Yongwei Zhang, L. Zhang, Yongxin Zhang, K.M. Treurniet, W. Chen, Y. Peng, H. Han, J. Wang, S. Wang, C. Yin, S. Liu, P. Wang, Q. Fang, Hongchao Shi, J. Yang, C. Wen, C. Li, C. Jiang, J. Sun, X. Yue, M. Lou, M. Zhang, H. Shu, D. Sun, H. Liang, Tong Li, F. Guo, K. Ke, H. Yuan, G. Wang, W. Yang, Huaizhang Shi, Tianxiao Li, Z. Li, P. Xing, P. Zhang, Y. Zhou, H. Wang, Y. Xu, Q. Huang, T. Wu, R. Zhao, Q. Li, Y. Fang, Laixing Wang, J. Lu, Y. Li, J. Fu, X. Zhong, Y. Wang, Longde Wang, M. Goyal, D.W.J. Dippel, B. Hong, B. Deng, Y.B.W.E.M. Roos, C.B.L.M. Majoie, and J. Liu, for the DIRECT-MT Investigators*

DIRECT MT Trial Design

Multicenter Phase III prospective RCT with open label treatment and blinded outcome assessment

Arms: direct mechanical thrombectomy (MT) vs MT with IV tPA (IVT)

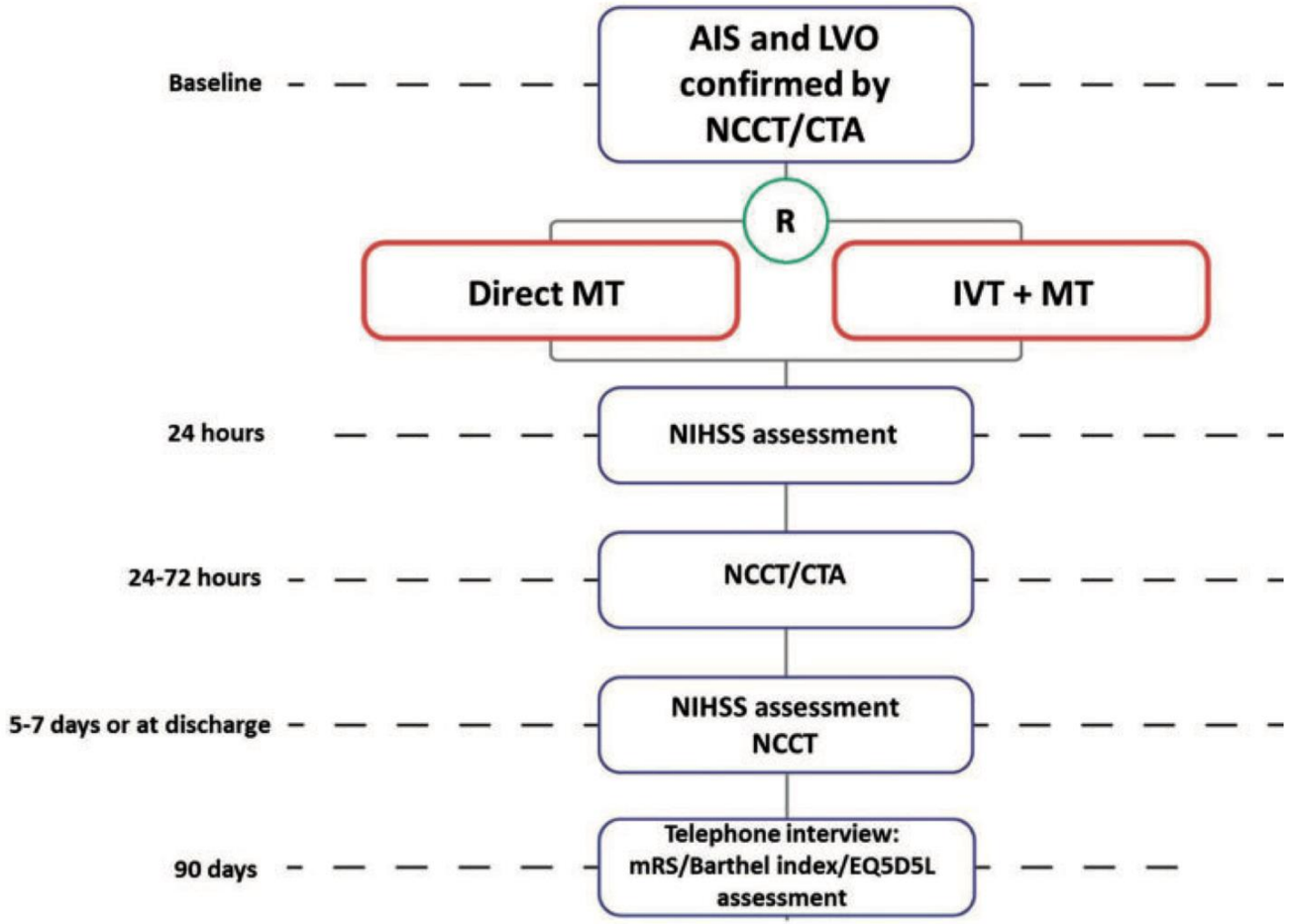
Randomized 1:1

Inclusion: ICA/M1/M2 occlusion, 4.5 hours, NIHSS ≥ 2, Age ≥ 18

Endpoint: mRS at 90 days

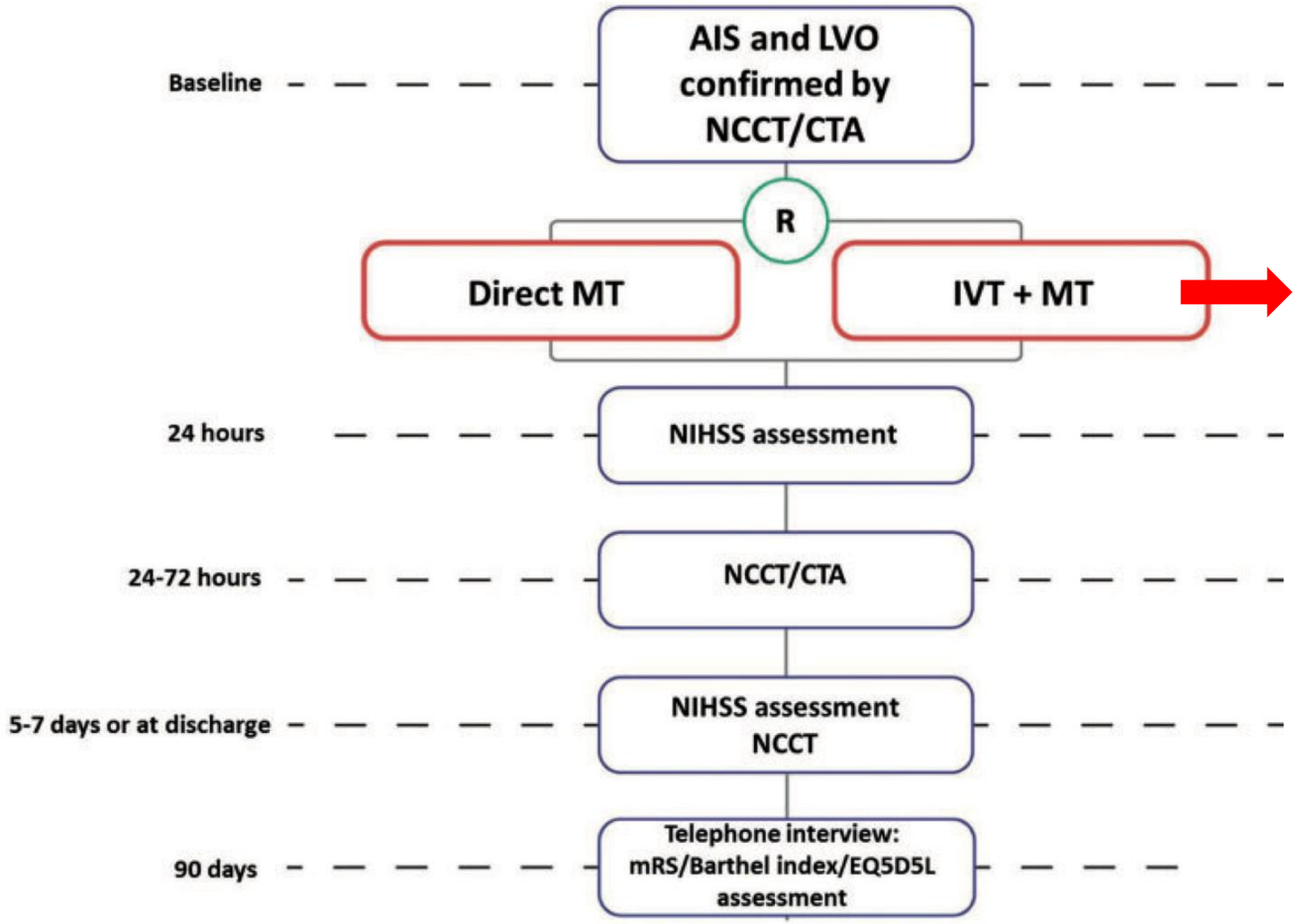
Yang et al (N Engl J Med 2020)

Figure 1. Patient flow in direct MT.



Yang et al (N Engl J Med 2020)

Figure 1. Patient flow in direct MT.



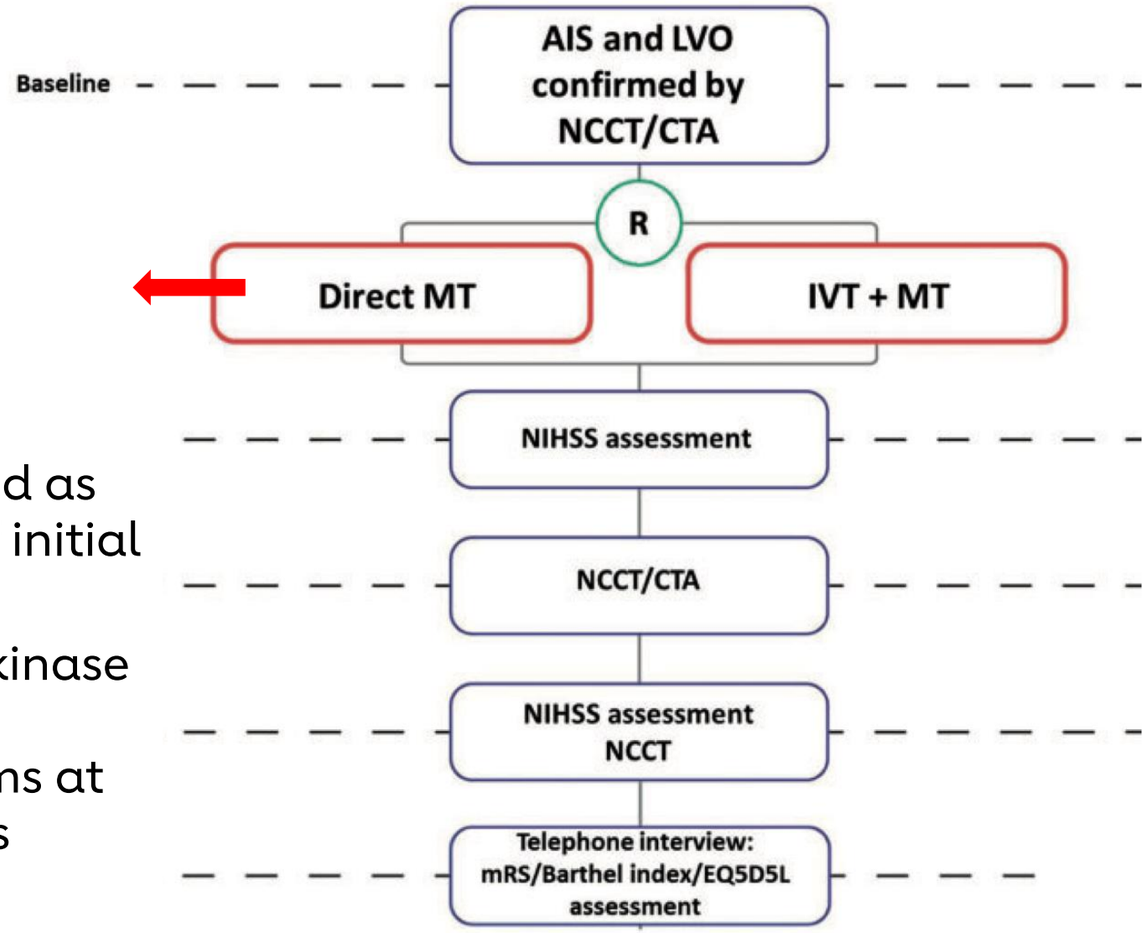
IVT

Standard 0.9 mg/kg body weight dose given

Infusion continued through MT procedure even if recanalization accomplished prior to completion

Yang et al (N Engl J Med 2020)

Figure 1. Patient flow in direct MT.



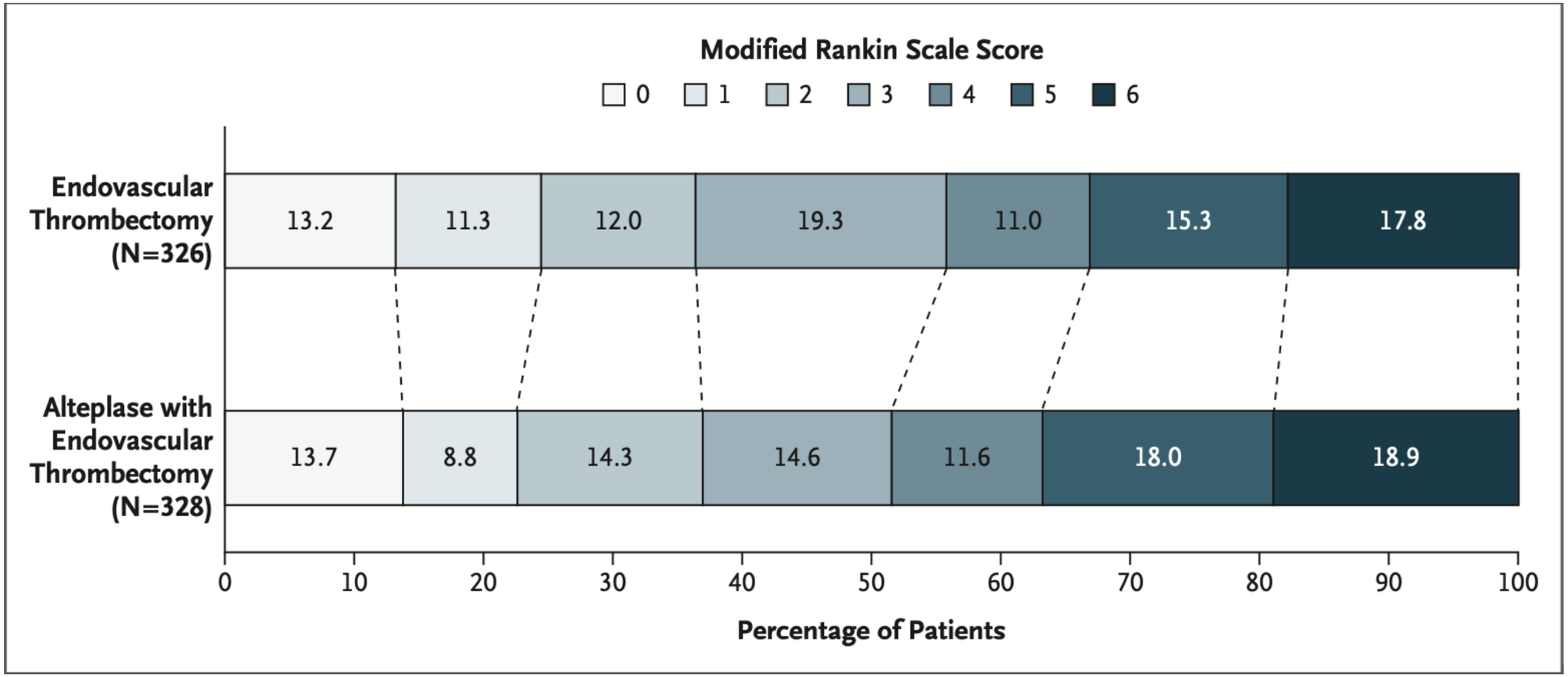
MT

Stent retriever was primary device

Aspiration permitted as secondary device if initial reperfusion failed

IA Alteplase or Urokinase accepted as rescue therapy in both arms at treating physician's discretion

Yang et al (N Engl J Med 2020)



Thrombectomy alone is non-inferior to combination therapy for 90 day mRS
aOR (95% CI) 1.07 (0.81-1.40)

Yang et al (N Engl J Med 2020)

Direct to Thrombectomy Trials

- SKIP
- DIRECT-MT
- **SWIFT DIRECT** (NCT03192332; 168/40)
- **MR CLEAN NO IV** (ISRCTN80619088; 435/540)
- **DIRECT-SAFE** (NCT03494920; 135/780)
- **DEVT** (ChiCTR-IOR-17013568; 240/970)

Nogueira and Tsivgoulis (Stroke 2020)

Summary for bypassing Alteplase

- Lower rates of reperfusion or clinical benefit with alteplase
- Higher rates of complications with alteplase
- Impact on geographic or center specific characteristics
- Potential limitations of peri-procedural therapies
- Ongoing RCTs to provide further evidence

…. however next question may be, bridging with TNK?

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Society of Vascular and Interventional Neurology

Thank You.

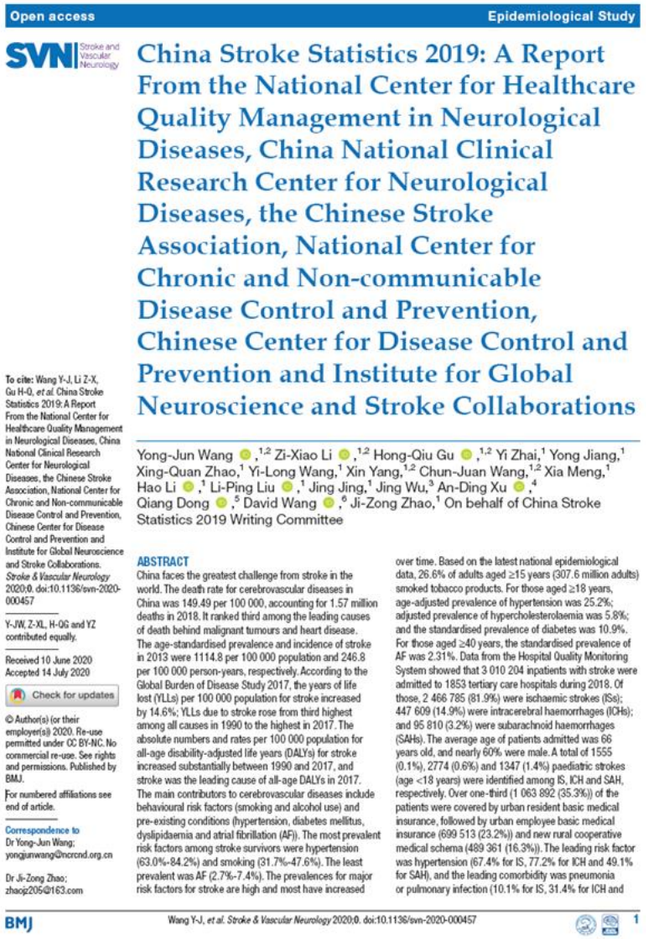
International Perspectives on Stroke Triage, Diagnosis, and Treatment

Liping Liu, MD

Dept. of Neurology
Beijing Tiantan Hospital
Capital Medical University

The opinions expressed during this webinar are those of the speakers and do not necessarily reflect the opinions, recommendations or guidance of American Stroke Association or Society of Vascular and Interventional Neurology.

China Stroke Statistics 2019



Open access Epidemiological Study

SVN Stroke and Vascular Neurology

China Stroke Statistics 2019: A Report From the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations

Yong-Jun Wang ,[1,2] Zi-Xiao Li ,[1,2] Hong-Qiu Gu ,[1,2] Yi Zhai,[1] Yong Jiang,[1] Xing-Quan Zhao,[1] Yi-Long Wang,[1] Xin Yang,[1,2] Chun-Juan Wang,[1,2] Xia Meng,[1] Hao Li ,[1] Li-Ping Liu ,[1] Jing Jing,[1] Jing Wu,[3] An-Ding Xu ,[4] Qiang Dong ,[5] David Wang ,[6] Ji-Zong Zhao,[1] On behalf of China Stroke Statistics 2019 Writing Committee

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Y-JW, Z-XL, H-QG and YZ contributed equally.

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ABSTRACT

China faces the greatest challenge from stroke in the world. The death rate for cerebrovascular diseases in China was 149.49 per 100 000, accounting for 1.57 million deaths in 2018. It ranked third among the leading causes of death behind malignant tumours and heart disease. The age-standardised prevalence and incidence of stroke in 2013 were 1114.8 per 100 000 population and 246.8 per 100 000 person-years, respectively. According to the Global Burden of Disease Study 2017, the years of life lost (YLLs) per 100 000 population for stroke increased by 14.6%; YLLs due to stroke rose from third highest among all causes in 1990 to the highest in 2017. The absolute numbers and rates per 100 000 population for all-age disability-adjusted life years (DALYs) for stroke increased substantially between 1990 and 2017, and stroke was the leading cause of all-age DALYs in 2017. The main contributors to cerebrovascular diseases include behavioural risk factors (smoking and alcohol use) and pre-existing conditions (hypertension, diabetes mellitus, dyslipidaemia and atrial fibrillation (AF)). The most prevalent risk factors among stroke survivors were hypertension (63.0%-84.2%) and smoking (31.7%-47.6%). The least prevalent was AF (2.7%-7.4%). The prevalences for major risk factors for stroke are high and most have increased over time. Based on the latest national epidemiological data, 26.6% of adults aged ≥15 years (307.6 million adults) smoked tobacco products. For those aged ≥18 years, age-adjusted prevalence of hypertension was 25.2%; adjusted prevalence of hypercholesterolaemia was 5.8%; and the standardised prevalence of diabetes was 10.9%. For those aged ≥40 years, the standardised prevalence of AF was 2.31%. Data from the Hospital Quality Monitoring System showed that 3 010 204 inpatients with stroke were admitted to 1853 tertiary care hospitals during 2018. Of those, 2 466 785 (81.9%) were ischaemic strokes (ISs); 447 609 (14.9%) were intracerebral haemorrhages (ICHs); and 95 810 (3.2%) were subarachnoid haemorrhages (SAHs). The average age of patients admitted was 66 years old, and nearly 60% were male. A total of 1555 (0.1%), 2774 (0.6%) and 1347 (1.4%) paediatric strokes (age <18 years) were identified among IS, ICH and SAH, respectively. Over one-third (1 063 892 (35.3%)) of the patients were covered by urban resident basic medical insurance, followed by urban employee basic medical insurance (699 513 (23.2%)) and new rural cooperative medical schema (489 361 (16.3%)). The leading risk factor was hypertension (67.4% for IS, 77.2% for ICH and 49.1% for SAH), and the leading comorbidity was pneumonia or pulmonary infection (10.1% for IS, 31.4% for ICH and

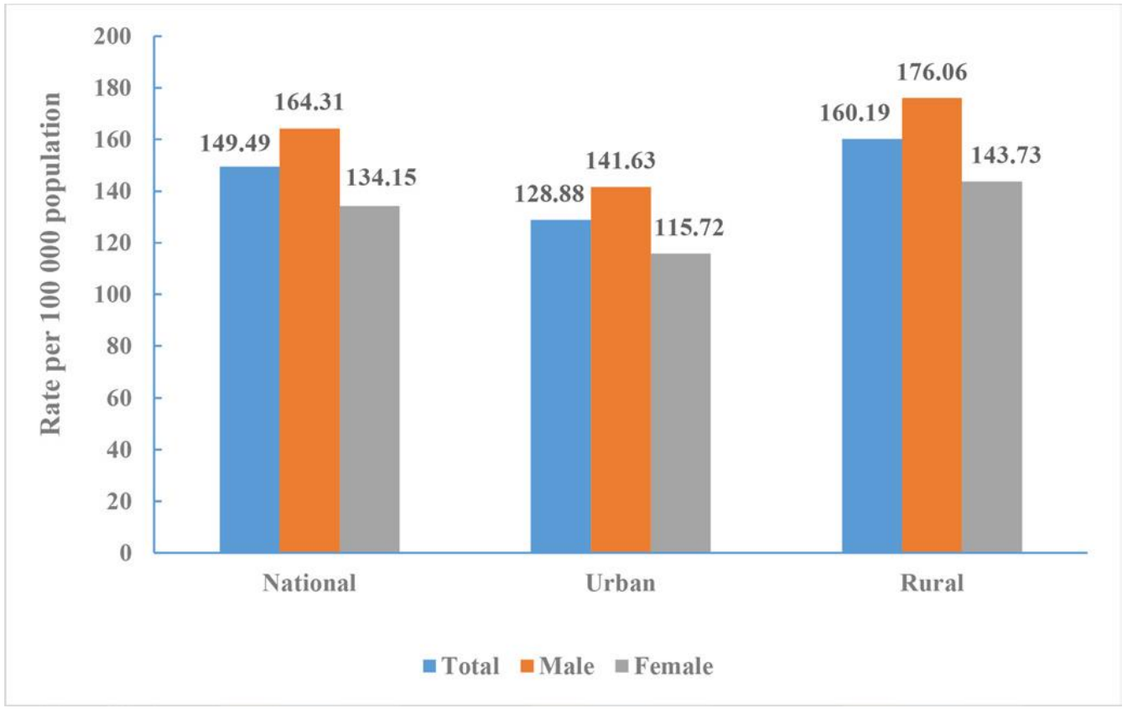

Figure 1 Crude mortality rate of cerebrovascular disease in Chinese residents by sex and region, National Mortality Surveillance System 2018.

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A division of the American Heart Association.

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Using Recombinant Tissue Plasminogen Activator to Treat Acute Ischemic Stroke in China

Analysis of the Results From the Chinese National Stroke Registry (CNSR)

Yilong Wang, MD; Xiaoling Liao, MD; Xingquan Zhao, MD; David Z. Wang, DO; Chunxue Wang, MD; Mai N. Nguyen-Huynh, MD, MAS; Yong Zhou, MD; Liping Liu, MD; Xianwei Wang, MD; Gaifen Liu, PhD; Hao Li, PhD; Yongjun Wang, MD; on behalf of the China National Stroke Registry (CNSR) Investigators

Table 1. Reasons Documented for Not Giving IV rtPA to 1045 Patients Within 3 Hours of Symptom Onset

Reasons (n=1045)*	No. (%)
Age >80 y	139 (13.30%)
Stroke too severe (NIHSS >25)	56 (5.36%)
Stroke symptoms had significantly improved before rtPA therapy	437 (41.82%)
Major early infarct signs involving greater than one third of the middle cerebral artery territory on the CT scan	54 (5.17%)
Seizure at onset	23 (2.20%)
Prior stroke or head trauma within the last 3 mo	13 (1.24%)
Uncontrolled hypertension	17 (1.63%)
Known history of ICH, brain aneurysm, or hemorrhagic diathesis within the last 6 mo	18 (1.72%)
Blood glucose <50 or >400 mg/dL	2 (0.19%)
Platelet count <100 000/mm^3	3 (0.29%)
PT (INR) >1.4, PT >15, or APTT >40 s	6 (0.57%)
Time window became >3 h because of delay in hospital	712 (68.13%)
Consent was not available	171 (16.36%)
Others	37 (3.54%)

Stroke. 2011;42:1658-1664.)

Trend of the Alteplase treatment recent 5 years

Supplemental Table II. Trend analysis of quality measurement

Variables	2015 (N=26173 [2.6%])	2016 (N=220403 [21.9%])	2017 (N=253971 [25.2%])	2018 (N=319014 [31.7%])	2019 (N=187237 [18.6%])	Relative Increasement from 2015 to 2019 (%)	P for trend
Acute performance measures							
IV rt-PA ≤ 4.5h	658 (17.9)	5949 (16.5)	9290 (21.0)	16270 (24.2)	11582 (28.7)	60.3	<0.0001
Early antithrombotics	18657 (84.6)	165093 (86.2)	190324 (85.0)	241213 (84.4)	145122 (85.7)	1.3	0.0481
DVT prophylaxis	4184 (43.9)	30965 (42.4)	34403 (41.1)	43098 (42.7)	22542 (42.5)	-3.2	0.2374
Dysphagia screen	17455 (66.7)	155507 (70.6)	177773 (70.0)	236666 (74.2)	143317 (76.5)	14.7	<0.0001

Data from comparation of CNSR I/II/III

Primary outcomes

The proportion of patients who received IV-rtPA treatment was stable across CNSR I and II; a marked increase was observed in CNSR III for both patient groups:

- 3h IV-rtPA-treated among 2h-IVT eligible patients (Group C)
- 4.5h IV-rtPA-treated among 3.5h-IVT eligible patients (Group C')

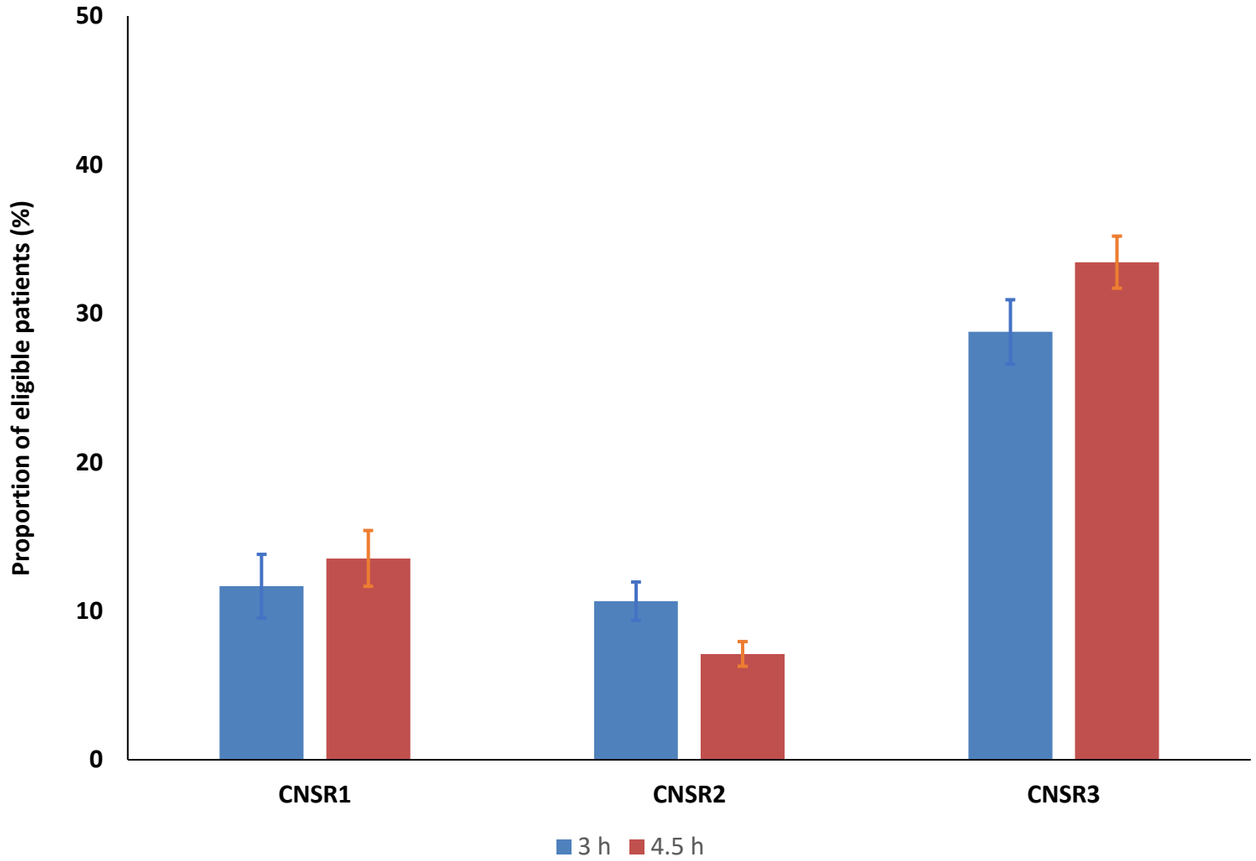
Patients	CNSR I	CNSR II	CNSR III
3h IV-rtPA / 2h-IVT eligible, % (n/N) [95%CI]	11.7 (101/866) [9.5-13.8]	10.7 (236/2214) [9.4-11.9]	28.8 (483/1679) [26.6-30.9]
4.5h IV-rtPA / 3.5h-IVT eligible, % (n/N) [95%CI]	13.5 (172/1271) [11.7-15.4]	7.1 (262/3684) [6.3-7.9]	33.4 (932/2787) [31.7-35.2]

CNSR: Chinese National Stroke Registry

n, number of 3h or 4.5h-IV-rtPA-treated patients; N, number of 2h or 3.5h-IVT eligible patients.

Primary outcomes

Proportion of 3h IV-rtPA-treated among 2h-IVT eligible patients (Group C) and 4.5h IV-rtPA-treated among 3.5h-IVT eligible patients (Group C')



n, number of 3h or 4.5h-IV-rtPA-treated patients; N, number of 2h or 3.5h-IVT eligible patients.

Secondary outcomes

The proportion of 3h IV-rtPA-treated (Group C) and 4.5h IV-rtPA-treated (Group C') among all AIS patients increased over time

Patients	CNSR I	CNSR II	CNSR III
3h IV-rtPA / All AIS patients,% (n/N) [95%CI]	0.9 (101/10968) [0.7-1.1]	1.3 (236/17823) [1.2-1.5]	3.6 (483/13397) [3.3-3.9]
4.5h IV-rtPA / All AIS patients, % (n/N)[95%CI]	1.6 (172/10968) [1.3-1.8]	1.5 (262/17823) [1.3-1.7]	7.0 (932/13397) [6.5-7.4]

n, number of 3h or 4.5h IV-rtPA-treated patients; N, number of all the AIS patients who met the criteria.

Secondary outcomes (group C)

DTN time, onset-to-needle time and proportion of 3h IV-rtPA-treated patients (group C) with DTN ≤ 60 minutes were stable across CNSR I and II; marked improvements were observed in CNSR III

	CNSR I (N = 101)	CNSR II (N = 236)	CNSR III (N = 483)
Median DTN time, minutes (IQR), Mean [SD]	90.0 (60.0–120.0) 89.4 [36.6]	100.0 (74.0–113.0) 94.2 [28.1]	58.0 (38.0–77.0) 58.8 [30.3]
DTN time ≤ 60min, % [95%CI]	28.7 [20.0-37.5]	12.3 [8.1-16.5]	59.2 [54.8-63.6]
Median onset-to-door time[a] , minutes (IQR), Mean [SD]	60.0 (32.0–90.0) 60.3 [32.3]	59.0 (43.0–75.0) 59.2 [24.1]	69.0 (50.0–93.0) 70.5 [30.1]
Median onset-to-needle time[b], minutes (IQR), Mean [SD]	150.0 (138.0–170.0) 149.6 [25.8]	156.0 (141.0–165.0) 153.4 [15.4]	134.0 (108.0–155.0) 129.3 [33.2]

NTD, Door-to-Needle; a, time between symptom onset and arrival at hospital; b, time between symptom onset and the administration of IV-rtPA treatment

Opportunities to increase access to stroke treatment

- Further detailed data analysis regarding the challenge and opportunity
- Take the recommendation from other international or national guidelines
- Promoting the education to physicians and patients/ families of the awareness and therapeutic strategy for acute stroke

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Thrombolysis in AIS, a Panorama from developing country , Egypt

Ossama Mansour MD, PhD, FSVIN, FINR, FESO

Professor of Clinical & Interventional Neurology
Director of Stroke & Neurointerventional Section
Founder of Egyptian Stroke Network- Alexandria prototype
On behalf of ESN group

The opinions expressed during this webinar are those of the speakers and do not necessarily reflect the opinions, recommendations or guidance of American Stroke Association or Society of Vascular and Interventional Neurology.

Points

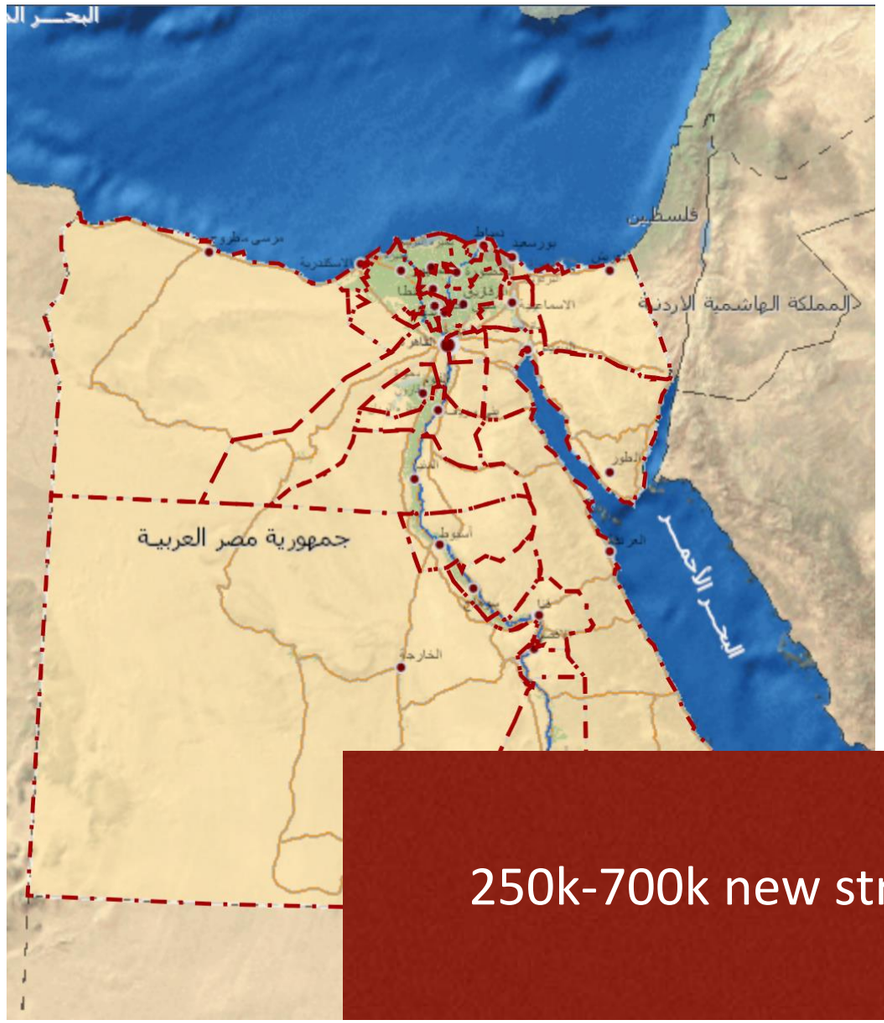
1-State the IV alteplase eligibility requirements

2-Differentiate between the use of alteplase via IV or IA for acute stroke

3- List the barriers to treatment delivery: cost, systems issues, and gaps

4-Summarize opportunities to increase access to stroke treatment

5-Compare various considerations in providing alteplase in various countries and regions of the world



The official national statistics revealed that cardiovascular disorders, including stroke, are the primary cause of death in Egypt.[2]

In Egypt the most populous country in Middle East region (92 millions population), the crude prevalence rate of stroke, according to recent estimates, is of 270-963/100 000 inhabitants.[1]

That means, more than new 250 000 - 700 000 acute strokes occurs every year

250k-700k new stroke every year

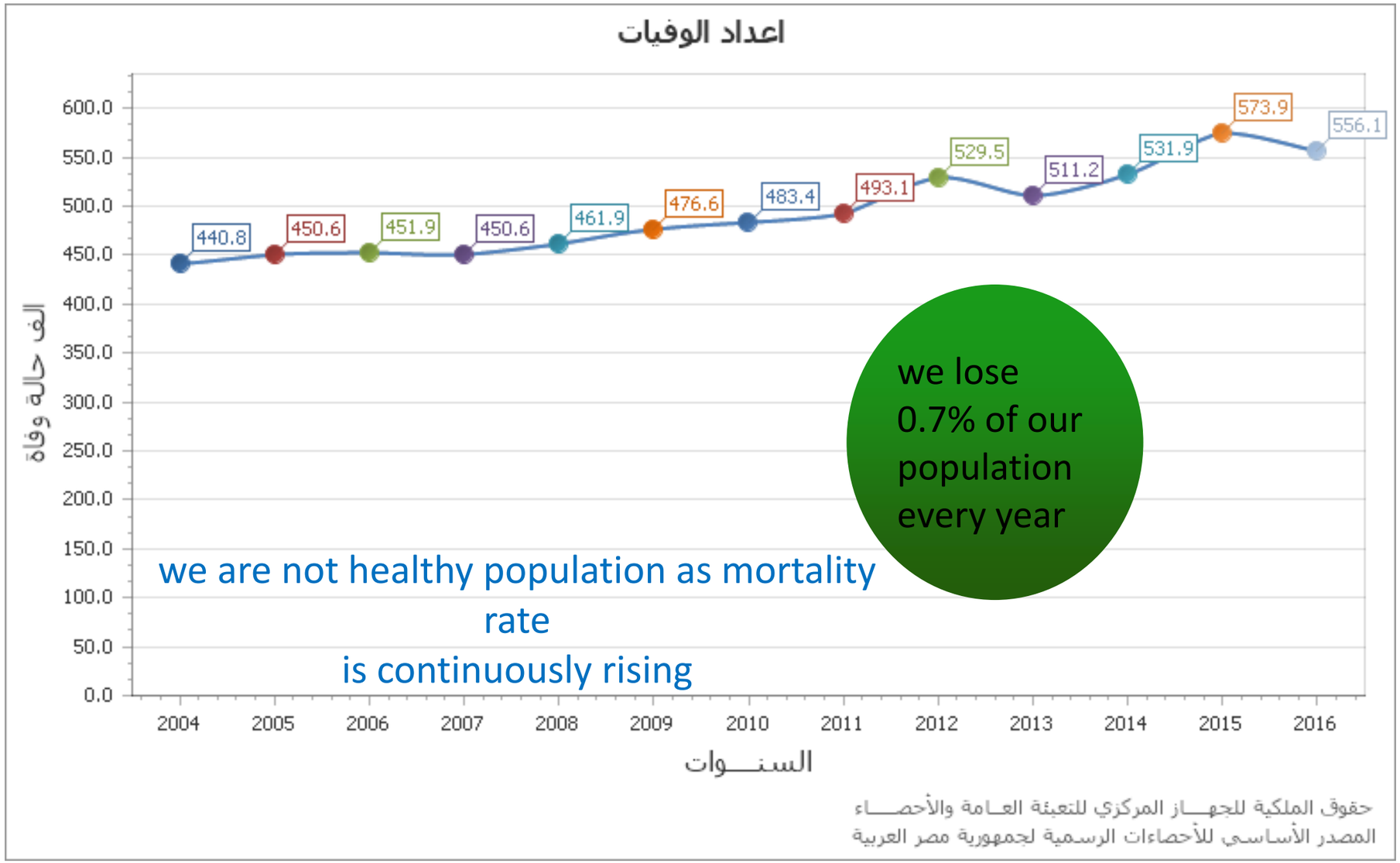
Why is there a high stroke burden and mortality in Egypt ?

Inadequate level primary prevention programmes

- socioeconomic status
- education
- cultural beliefs

Weak healthcare system setups

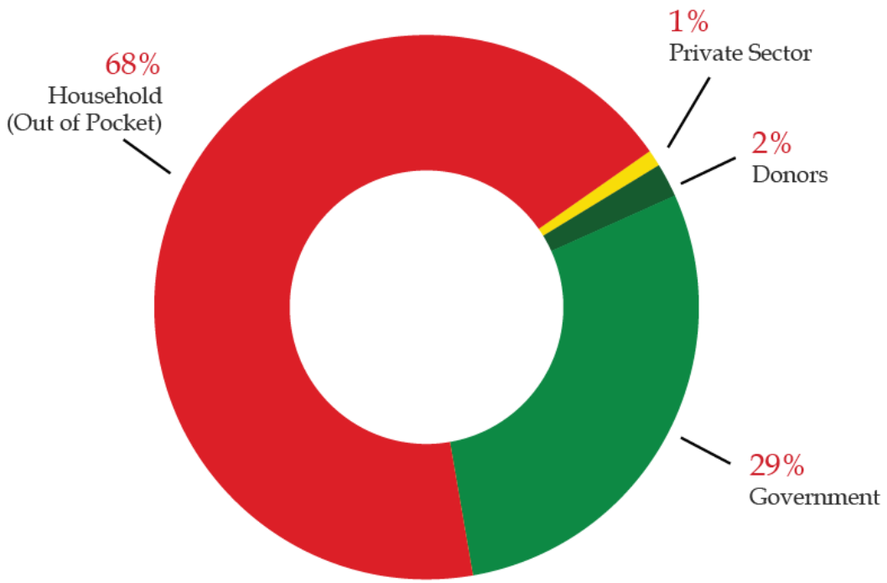
- uneven distribution of stroke services (if accepted definition)
- very weak referral systems
- very limited capacity to provide emergency stroke care
- data collection not readily available to inform policy decisions



Mortality Rate

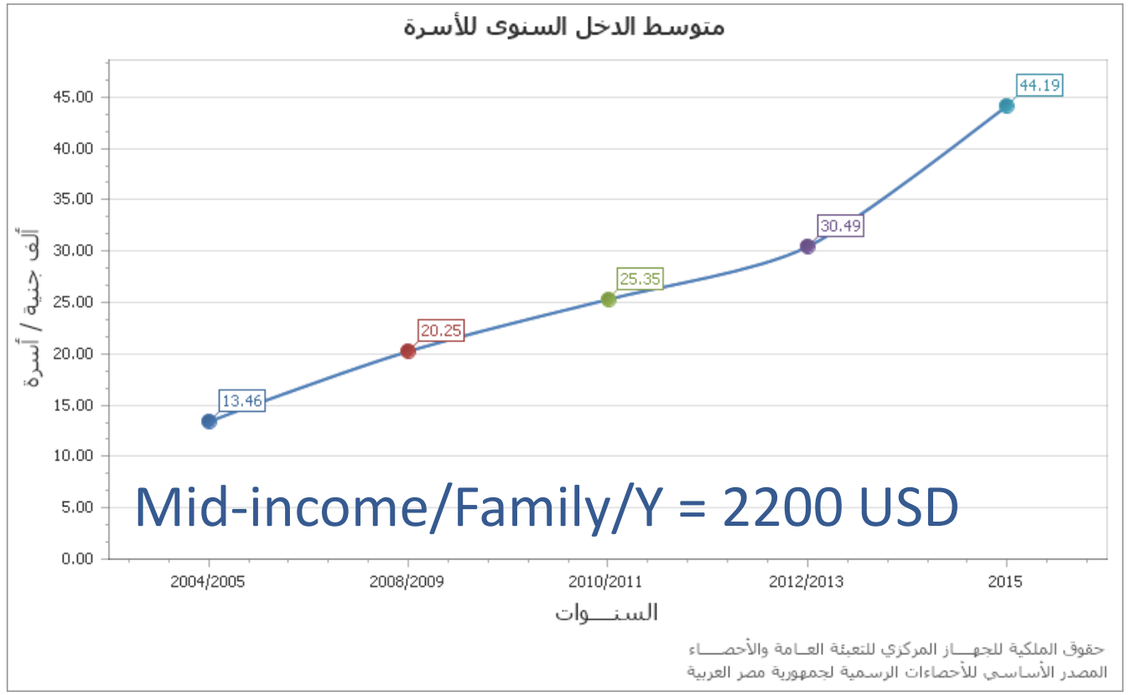
https://www.capmas.gov.eg/Pages/IndicatorsPage.aspx?Ind_id=1092

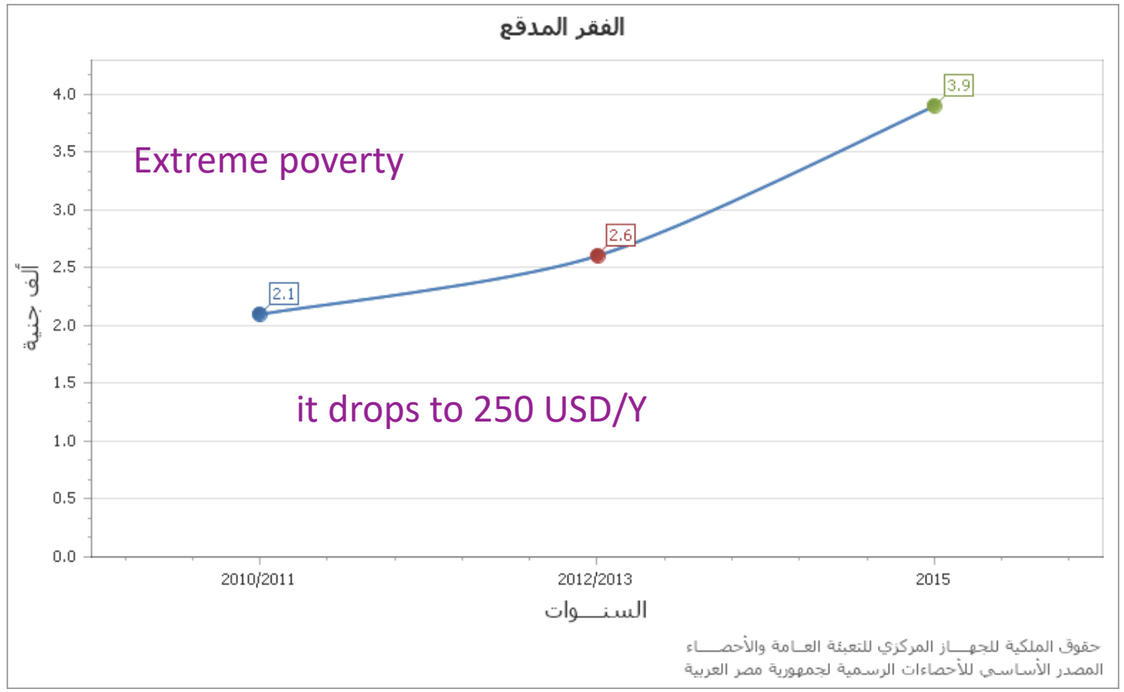
The majority of NCDI services are financed by household (out of pocket) payments



Fianacing for NCDI services in Egypt

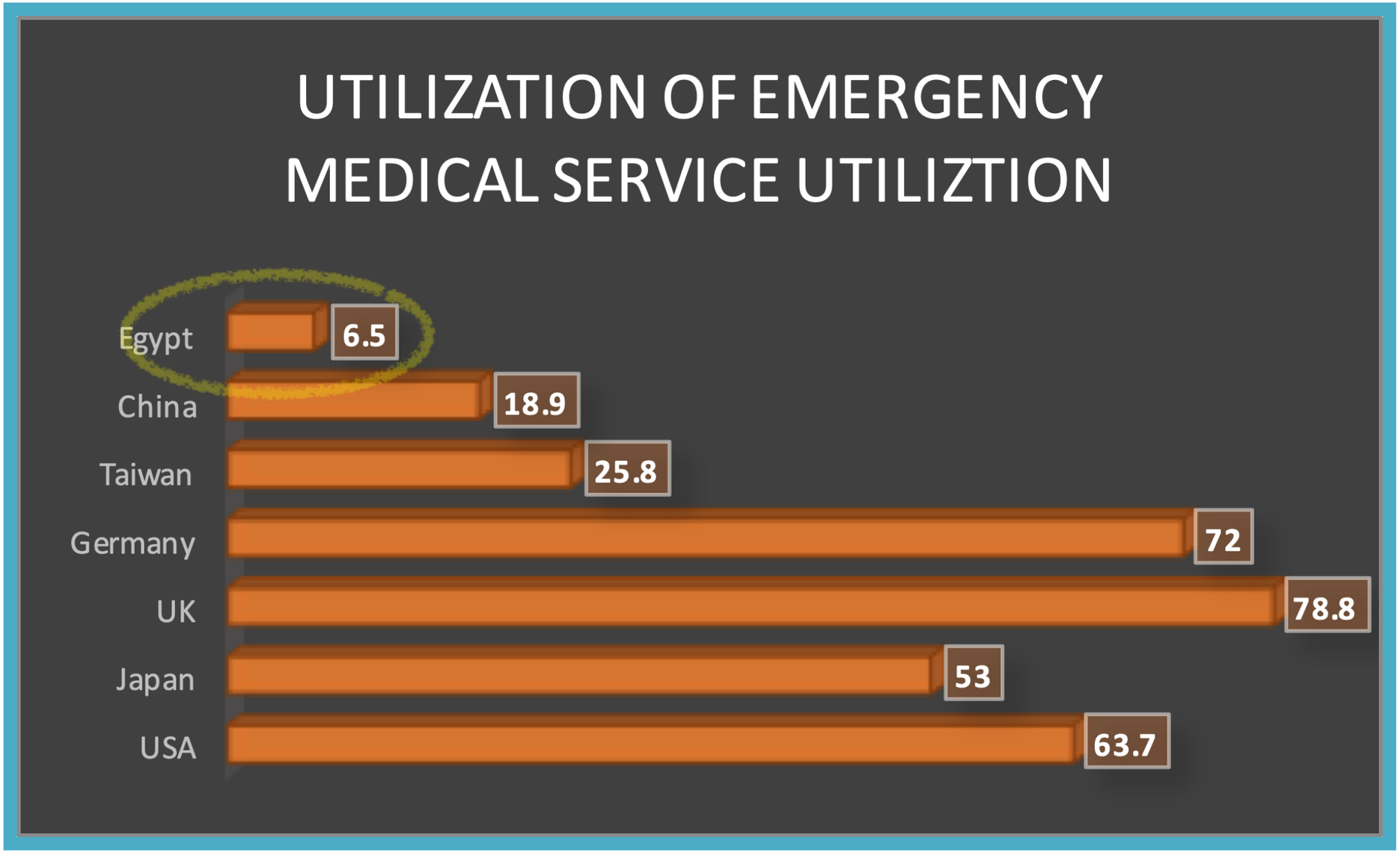
Wide geographical disparities and increased burden of NCDs and their risk factors are identified as key challenges facing the healthcare system in Egypt. Priority setting in the light of these findings is crucial to support nation- al efforts to attain health equity and UHC.





Poverty

https://www.capmas.gov.eg/Pages/IndicatorsPage.aspx?Ind_id=1092



Traffic Inj Prev. 2012;13 Suppl 1:44-56. doi: 10.1080/15389588.2011.639417.

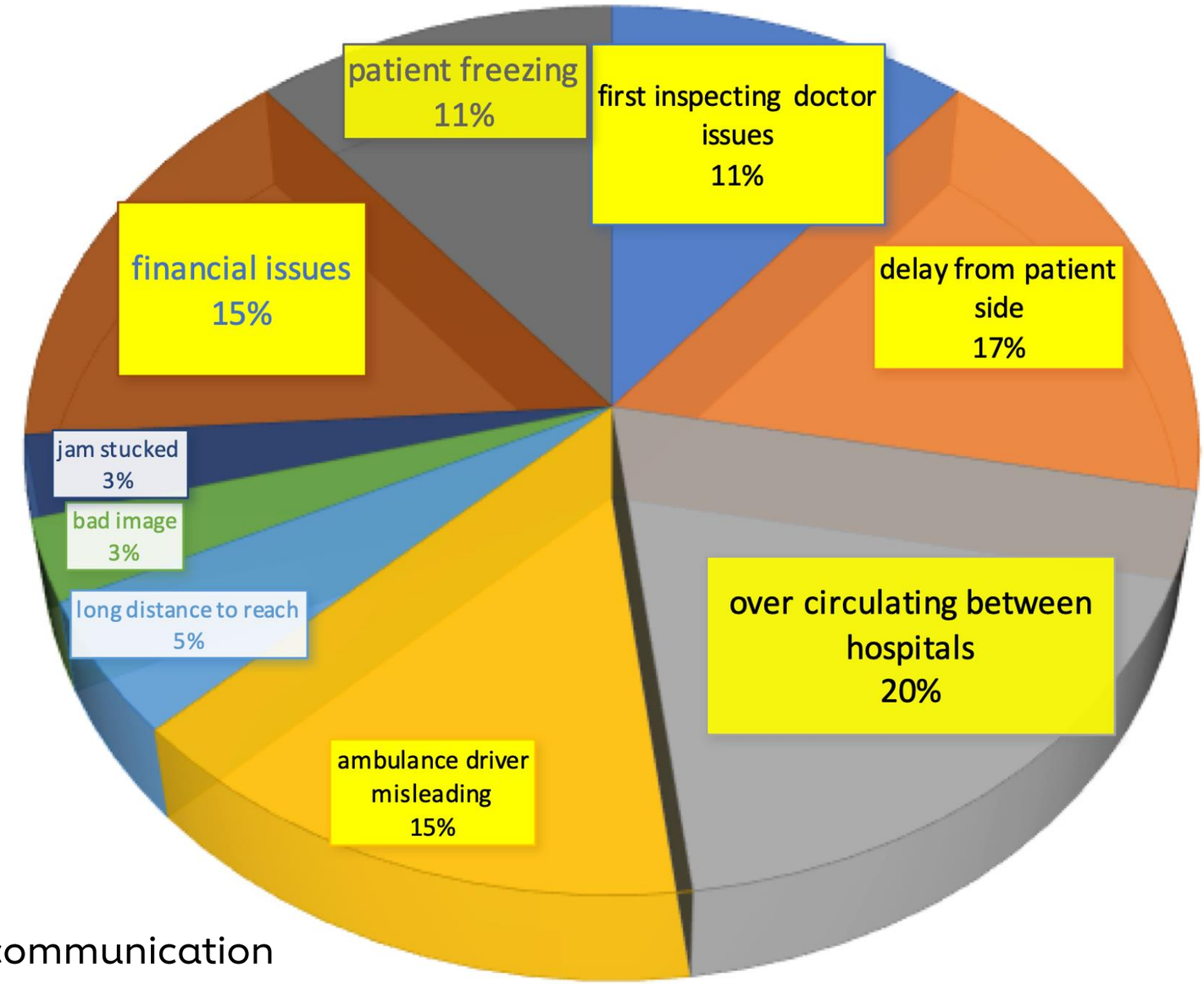
Triage Problems

Extrahospital pathway (swirl)

- patient delivery
- communication between stroke centers

Intra-hospital pathway

Reasons for Futile Transfer (510 Patients)



- awareness
- education
- triage system
- inter & intra hospital communication

Challenges facing Egypt in acute stroke Care

- Infrastructure organization
  - (models & Paradigms0
- Effective coverage
- (city vs rural)
- Transportation
- Telestroke

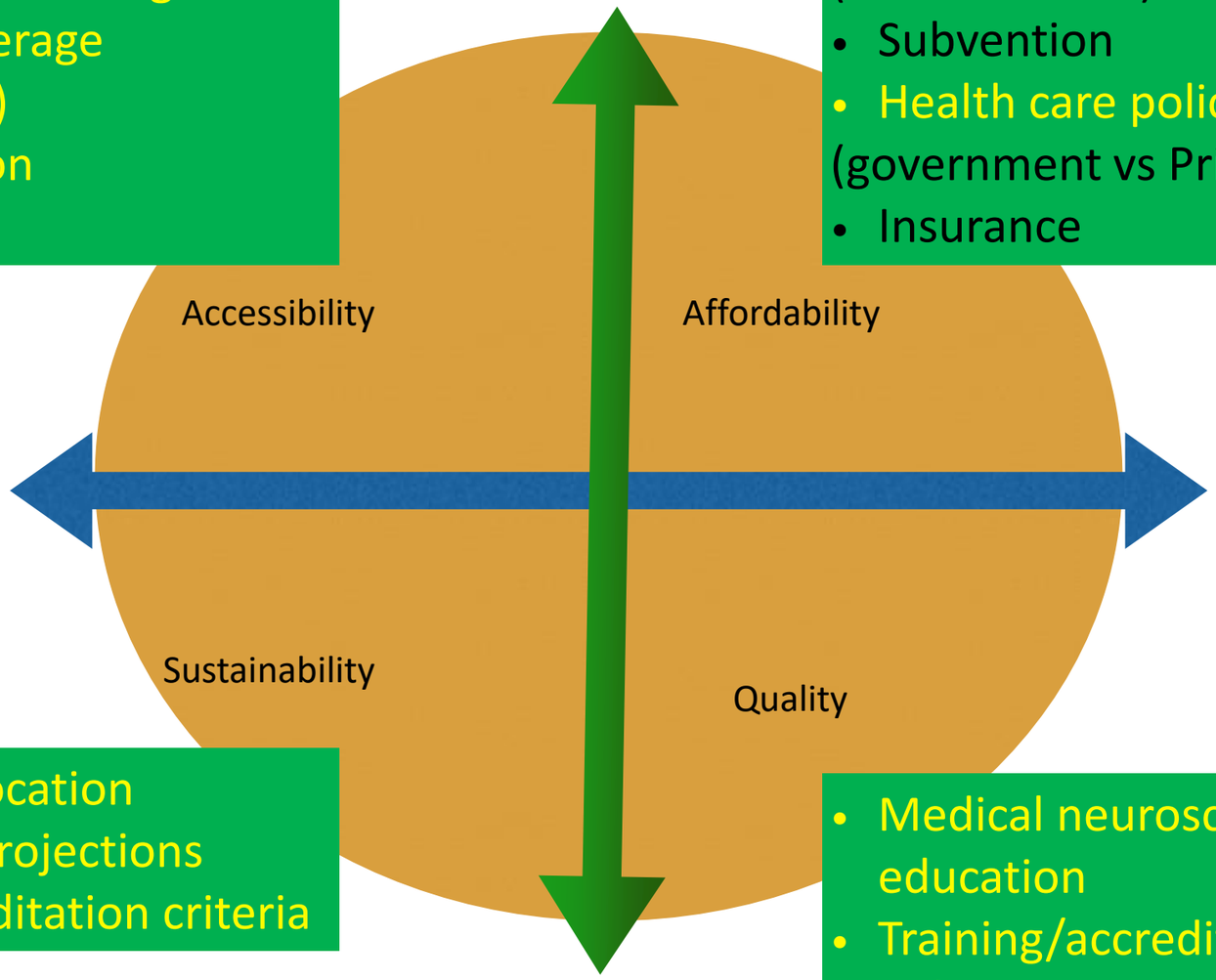
- Socio-economic status

(Fiscal Policies)

- Subvention
- Health care policies

(government vs Private)

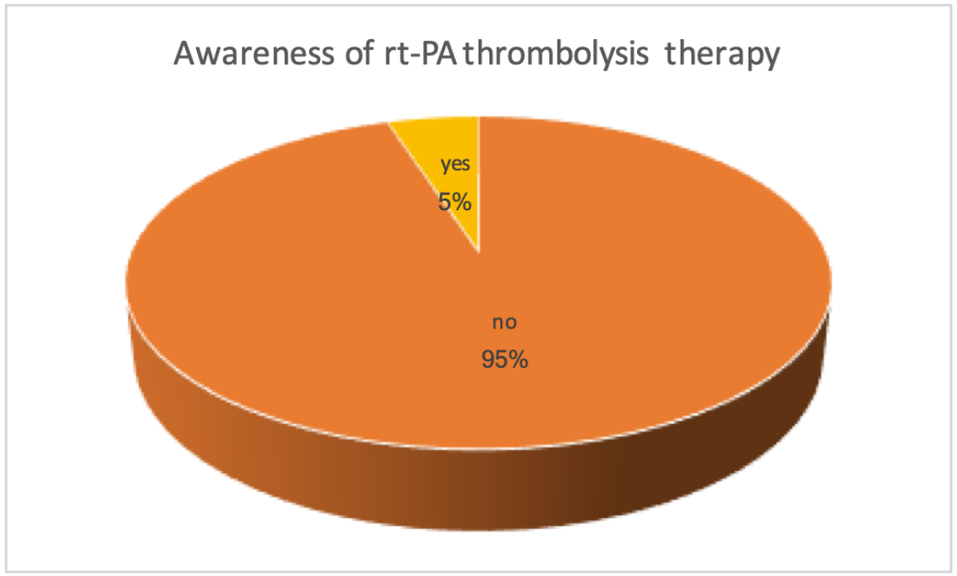
- Insurance

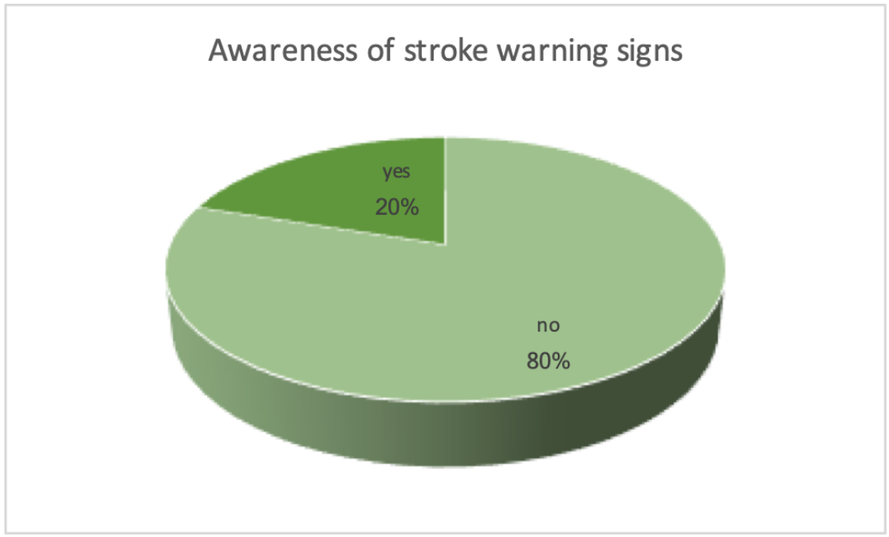


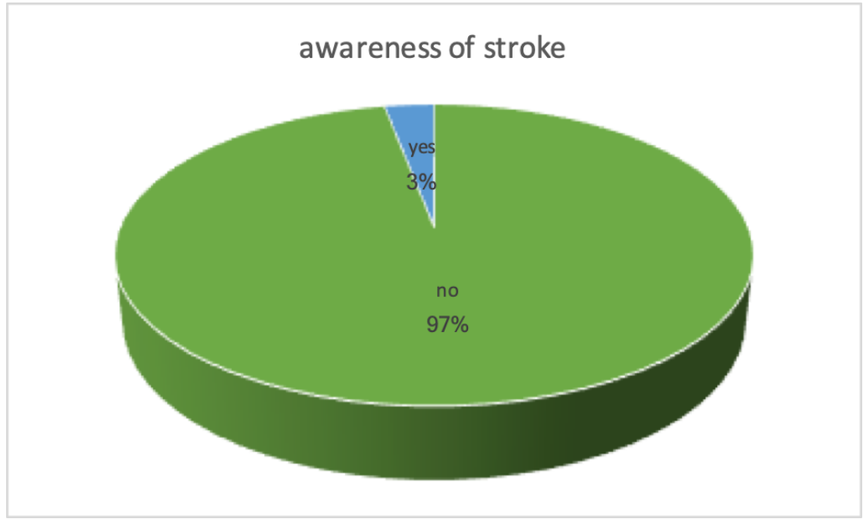
- Resource allocation
- Manpower projections
- EVT re-accreditation criteria

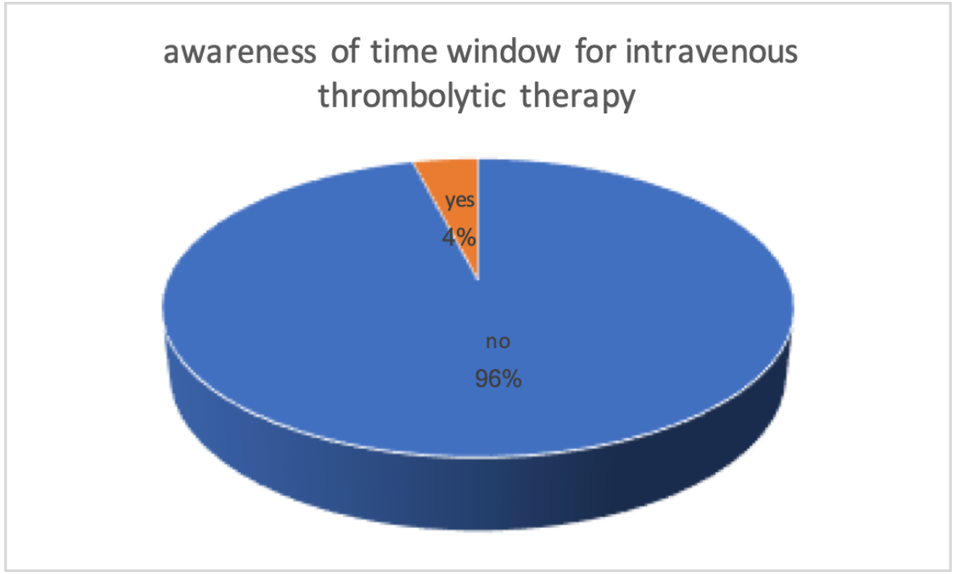
- Medical neuroscience education
- Training/accreditation
- industries

Insufficient Public Awareness of Stroke







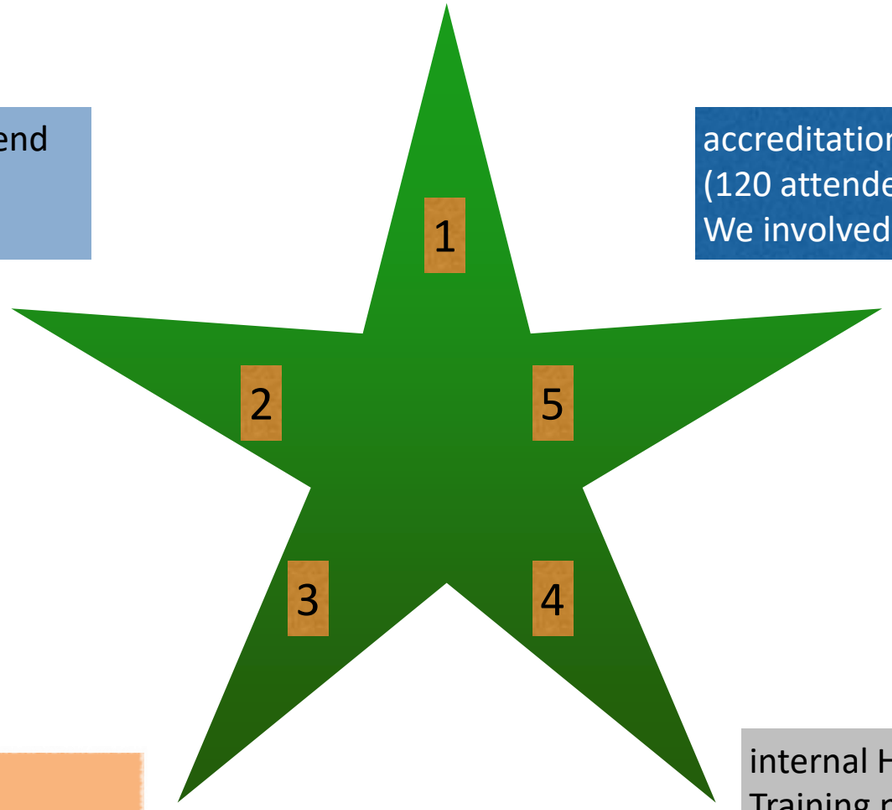


Stroke prevention & treatment Training programs

more than 4 training
hubs were established by 2017
(All are Tertiary academic hospitals)

regional and community hospital send
care providers to the training hub
(15 courses held)

accreditation & certification
(120 attendees)
We involved syndicate to be more formal



EgyStrokeSchool

Network training &
online classes
240 candidates

internal Hospital
Training programs
supervision
(1000 attendees)

www.egyptianstrokenetwork.com

Till aproval of IV tPA in 2016

الصحة تطلق المشروع القومي لعلاج السكتات الدماغية

الصحة تطلق المشروع القومي لعلاج السكتات الدماغية

5 Compare various considerations in providing tPA in various countries and regions of the world

Level of barrier	Type of barrier	Reference number
Pre-hospital	Lack of stroke helpline Insufficient infrastructure Unavailable/inadequate transportation facilities (Ambulance)	[12–14, 16, 18, 19, 25, 37]
Hospital triage	Under-resourced emergency departments Under-resourced imaging and radiologist	[38, 39, 41] [16, 32, 33, 35]
Stroke unit	Lack of neurologist/stroke experts in rural areas Lack of trained personnel High cost of drugs	[45, 48] [94] [45, 88, 92]
Post stroke care	Limited rehabilitation facilities Deficient numbers of physiotherapists speech therapist and occupational therapists	[94] [32]
Community support	Lack of social workers	[94]

Neuroepidemiology 2017;49:45–61 DOI: 10.1159/00047951

Some Strategies from Around the World

Thrombolysis					
51	Abstract MP25: Intravenous thrombolysis in India: the Indo–US stroke project	– Eleven percent (227/2066) patients thrombolysed	India	Establishing SUs in teaching referral hospitals can dramatically improve thrombolysis rate	
52	Telestroke in resource-poor developing country model	– Telestroke between 2 tertiary care hospitals (with neurologist) and 17 district hospitals (without neurologist) between June 2014 and May 2015, thrombolysed 26 patients	Shimla, India	tPA is offered free of charge by the state government Telestroke is feasible	Needs government support

Reference number	Title	Observations and potential area of improved care	Country(ies)	Strategy	Limitation
53	Problems and limitations in thrombolysis of acute stroke patients at a tertiary care centre	– In this retrospective audit, lack of triaging stroke patients at every level was identified as a potential area for saving time. – Educating EM staff about triaging stroke patients – Suggested that incase the first on call neurologist is busy, a second neurologist can be on call only for patients with acute stroke. – Suggested to establish a "stroke-code". This code is a pre-notification call to all the concerned departments about any stroke patient within the hospital	Pune, India	Pre-notification within the hospital can reduce door to needle time Second on call neurologist/ stroke expert only for patients with acute stroke in ED may be helpful	

Neuroepidemiology 2017;49:45–61 DOI: 10.1159/00047951

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Alexandria Strategy

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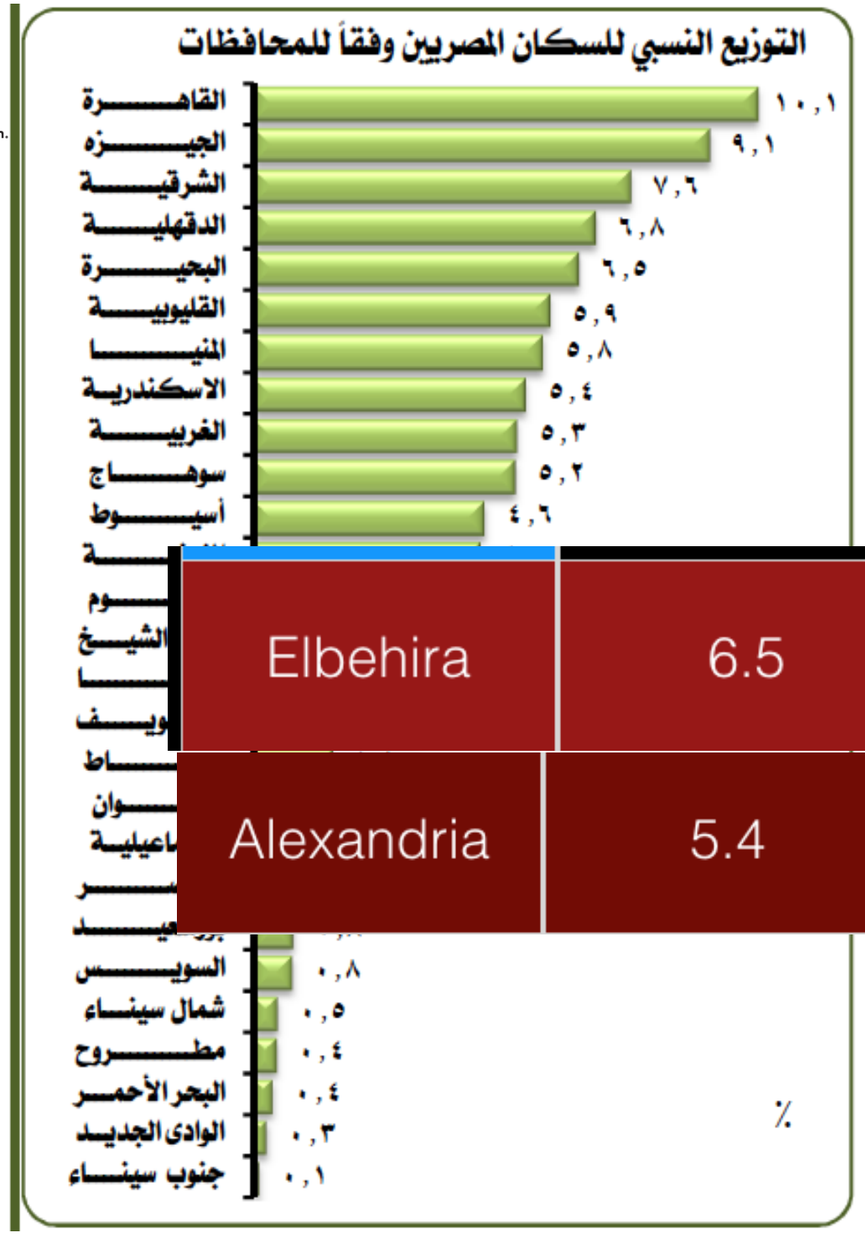
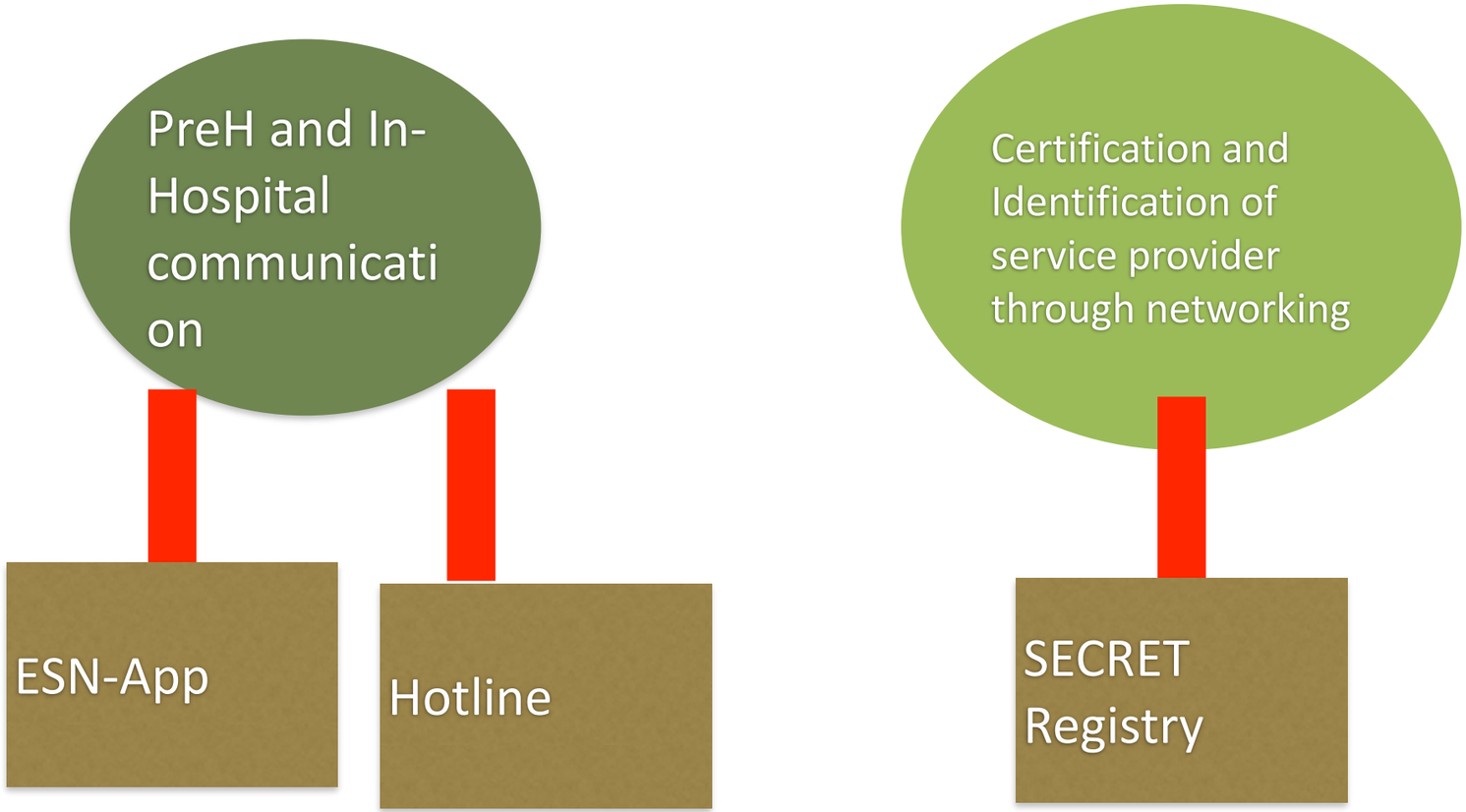
what seems impossible at large scale could be possible in smaller one



Egypt:
projected numbers of EVT each govern ate per year

governate	population 2017 (milion)	estimated no of Mts (3-6 pe100000 P/Y)	estimated no of Eligible EVT (21 pe100000 P/Y)
Cairo	10,1	300-600	2100
Giza	9.1	273-546	1911
			96
			28
Elbehira	6.5	195-390	1365
Alexandria	5.4	162-324	1134
			65
ElQaliobia	5.9	177-354	1239
ElMENIA	5.8	174-348	1218
Alexandria	5.4	162-324	1134

Our Solution Bundle depends on




1-Certification and Identification of service provider through networking
Registry

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Stroke Egyptian Clinical REgisTry

www.strokeregistry.eg

www.mena-secret.org

www.strokecenters.com

Our Registry Types

Hospital Based improvement Program for stroke care

A 6 levels grading system was designed according to the the capability of each service spot (hospital , center , etc) to present a range of the 5 stroke service bundles of care.each Service Spot (SS) will have

© Can Stock Photo

Cost-effectivness registry Based SOPs

SECRET is the first of its type registry to study the parameters for cost/effectiveness for specific steps in the chain of treatment and care for stroke patient. The only convincing tool which could

Aneurysm Registry

This registry is dedicated for the cerebral aneurysm disorders and their type of clinical presentation. The options of treatment and each option effectiveness and cost outcome.

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Green Program Stroke care

Bundles presented

- EVT variables Bundle+
- tPA capabilities bundle+
- Telemedicine Core Bundle+
- DISMAST Bundle +
- Process of care Bundle

Learn More

Yellow Program Stroke Care

Bundles Presented

- tPA capabilities bundle +
- Telemedicine Core Bundle+
- DISMAST Bundle+
- Process of care Bundle

Learn More

Red Program of Stroke Care

Bundles Presented

- EVT variables Bundle +
- Telemedicine Core Bundle+
- tPA capabilities bundle+
- Process of care Bundle

Learn More

Purple Program Stroke

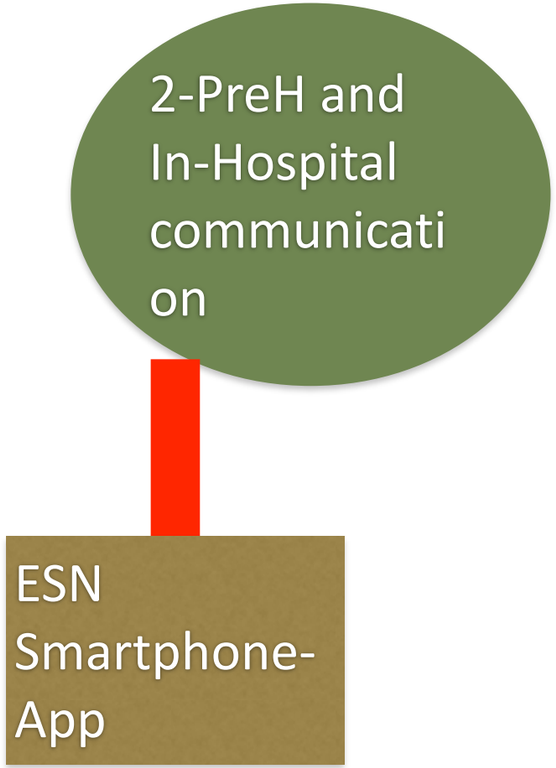
Blue Program Stroke

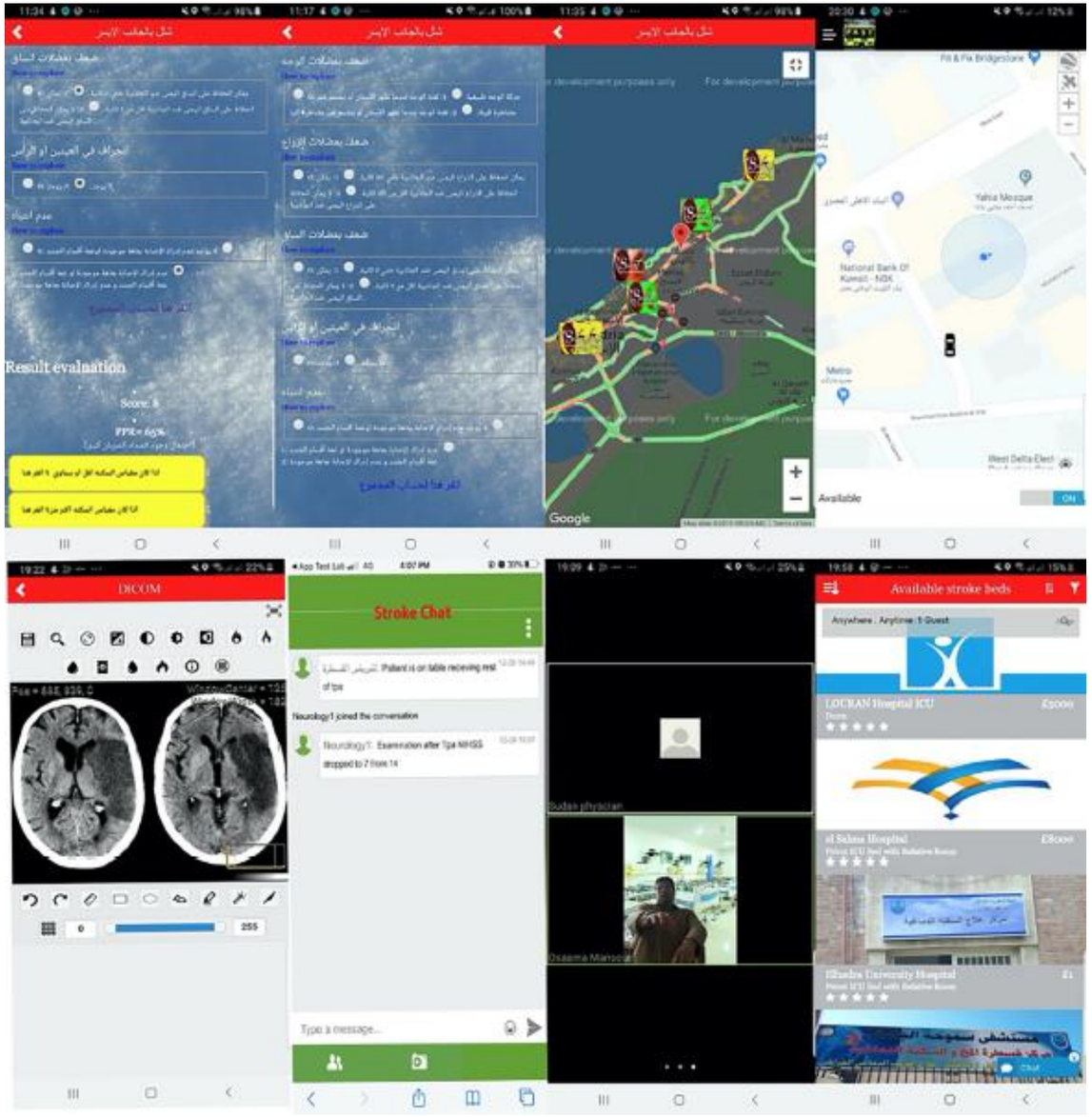
Black Program Stroke

Our Solution Bundle depends on

Mark	ID	Icon	Title	Category	Address	Description	Image	Link	Action
☐	10		kaser el shefa hospital (مستشفى قصر الشفا)		31.137970, 29.826700			>>	
☐	9		Elnozha Hospital (ستشفى النزهة التخصصى						
☐	8		Elsalama Hospital (ستشفى أندلسية السلامة						
☐	7		Nareman Hospital (ستشفى الحضرة الجامعى						
☐	6		Mostafa Kamel Hospit For Armed Forces (مستشفى مصطفى كامل للقوات المسلحة)						
☐	5		Gamal Abdelnaser Hospital (ستشفى جمال عبد الناصر)						
☐	4		Semoha University Hospital (ستشفي سموحة الجامعي)						
☐	3		Loran Hospital (ستشفى لوران)						
☐	2		Mabaret Alasafra Hospital (مبرة العصافرة)						

Our Solution Bundle depends on





1) EgyptianStrokeNetwork APP
   A customized mobile smartphone application, “ الشبكة المصرية لعلاج السكتات الدماغية” (MENA-SINO, Inc, Alexandria, Egypt) was developed in an effort to streamline our Alex-Stroke-60/75 min workflow model described above.
2) Important features of this application include:

- Prehospital detection of the stroke type using Arabic version RACE interactive algorithm which direct the user to the nearest hospital suitable for stroke services using GPS functionality and according the calculated score at this point of time. Additionally , Real-time tracking of the patient's exact position during transport using global positioning system (GPS).
- Notification to the stroke team of basic patient information and demographics
- Recording events in the workflow in Automated time-stamping fashion.
- The ability for communication among stroke team members in Real-time, secure Fashion
- Ability to open secure 2 way A/V Telecommunication channel to help ER physcian in remote facility to triage the patient properly.
- Ability for transmission of patient demographics and clinical information.
- Generation of a summary document in portable document format (PDF) format that can be uploaded into the electronic medical record

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Stroke Egyptian Clinical Registry

www.strokeregistry.eg

www.mena-secret.org

www.strokecenters.com

Will be available online within 2 weeks

Pilot Study

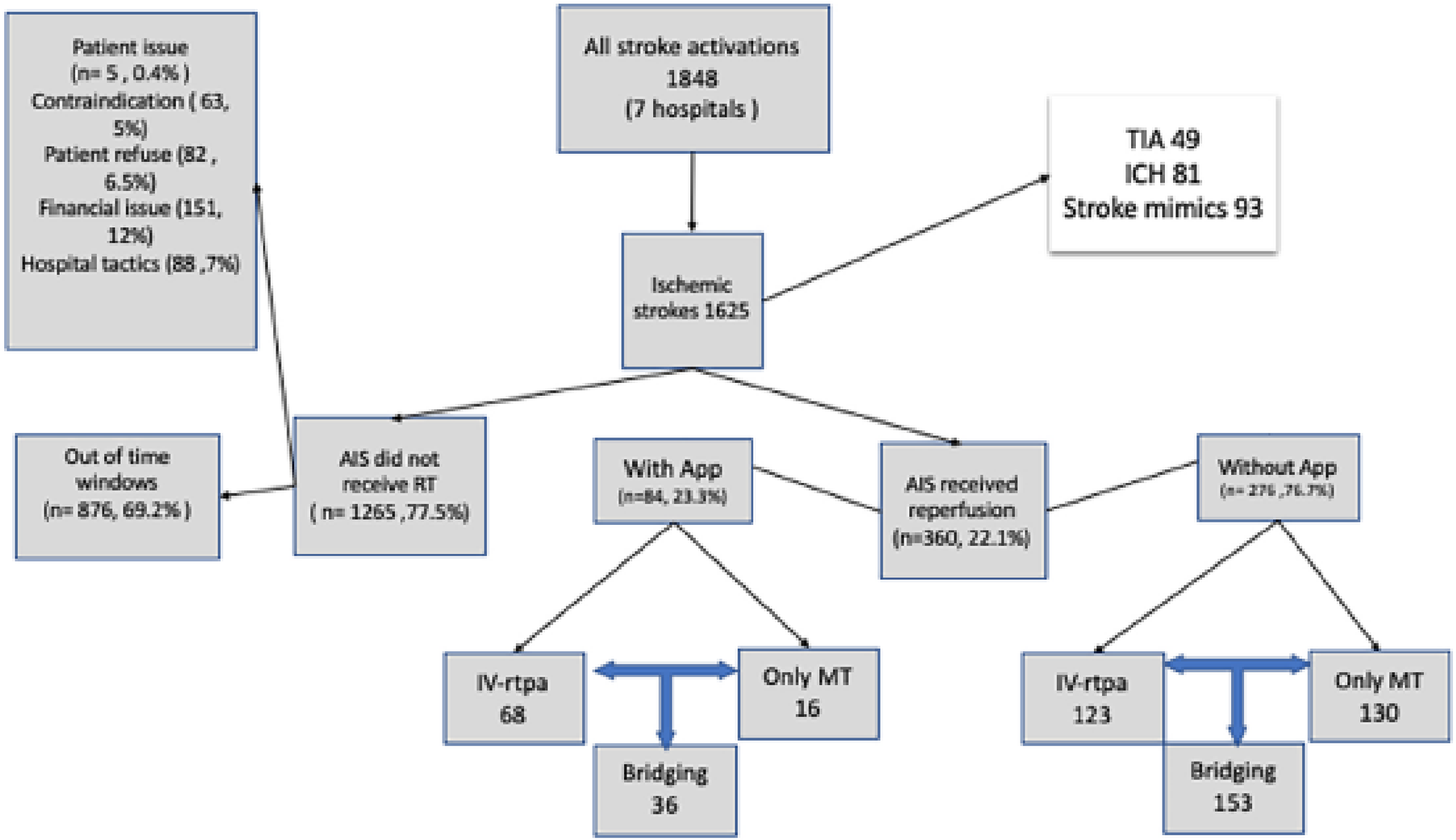
All stroke activations
1848
(7 hospitals)
Patient issue
(n= 5 , 0.4%)
Contraindication (63, 5%)
Patient refuse (82 , 6.5%)
Financial issue (151, 12%)
Hospital tactics (88 ,7%)
TIA 49
ICH 81
Stroke mimics 93
Ischemic strokes 1625
Out of time windows
(n= 876, 69.2%)
AIS did not receive RT
(n= 1265 ,77.5%)
With App
(n=84, 23.3%)
AIS received reperfusion
(n=360, 22.1%)
Without App
(n= 276 ,76.7%)
IV-rtpa
68
Only MT
16
Bridging
36
IV-rtpa
123
Only MT
130
Bridging
153

Table 1: Patient data uploaded by participating hospitals

Pilot hospital	IV-tpa patients		MT patients		Transferred patients	
	App (n= 68 alone)	Non (n=123 alone)	App (n= 36) (all received both)	Non (n=153) (n= 42 received both)	App (n= 31)	Non (n=47)
1 (loran) (176MT+51 IV)	41	4	31	145	25	23
2 (Smouha) (6MT+101 IV)	41	60	2	4	6	24
3 (Narmean) (55 IV)	21	34	0	0	0	
4 (Damanhur) (9 IV)	9	0	0	0	0	0
5 (Shark el-madina) (8IV)	8	0	0	0	0	0
6 (Mbret el Asafra) (19IV)	10	9	0	0	0	0
7 (Andalusia) (7MT+26IV)	10	16	3	4	0	0

Characteristics of patients entered into the registry

All pilot hospitals	App Patients (n=84)	NON app Patients (n=276)	
Males	44 (52.3%)	149 (54%)	
LVO	36	153	
Non LVO	48	123	
Mean age	60±5 y	63±2 y	
Mean NIHSS	14.5±2.5	10.4±3.6	
Recurrent stroke/TIA	21 (25%)	60 (21.7%)	
Stroke subtype (TOAST)			
Cardioembolic, n (%)	28 (33.3%)	87 (31.5%)	0.78
Large vessel Athrosclerosis , n (%)	26 (30.9%)	102 (37%)	0.36
Lacunar, n (%)	14 (16.6%)	43 (15.6%)	0.86
Functional independence (mRS <3) at 3 mo , n (%)	57 (67.9%)	130 (47.1%)	0.0011
sICH	4 (4.8%)	14 (5.1%)	> 0.05

Type of reperfusion therapy and time metrics in treatment workflow

Process of hospital care	App triaged patients		Non-App triaged patients		
	n	%	n	%	
In ischaemic stroke, patients received intravenous thrombolysis (tPA)	68	81%	123/276	44.6%	
LVO Patient transferred from another hospital within 6 hours window	31/36	86.1%	47/153	30.7%	
In ischemic stroke, patients received MT	36/84	43%	153/276	55.4%	
Confirmed LVO (transferred) within 6h	30 /36	(96.7%)	23 /47	(48.9%)	0.0001
Received MT	28/30	(93.3%)	16/23	(69.6%)	0.03
Door to needle time	55±12 min		78±16 min		0.001
Door in- Door out time	56±34 min		96±45 min		<0.0001
Door to groin time	50±7 min		120±25 min		<0.001
Ambulance to ER time	45±5 min		98±20min		0.0001
Time to image	14±4 min		23±9 min		0.000

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Thank you

Conclusion:

Our area needs more efforts

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Panel Discussion

Audience Q & A

To Ask a Question

Upcoming Opportunities

- On-demand viewing

- Remainder of *International Perspectives on Stroke Triage, Diagnosis and Treatment* series
  - Episode 4: Treatment with Thrombectomy (October 28)

- World Stroke Day (October 29)
  - One CycleNation with ASA
  - Discounted educational opportunities with SVIN

- AHA Scientific Sessions (November 13 – 17)

- SVIN Annual Conference (November 18 – 21)

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Thank You.

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