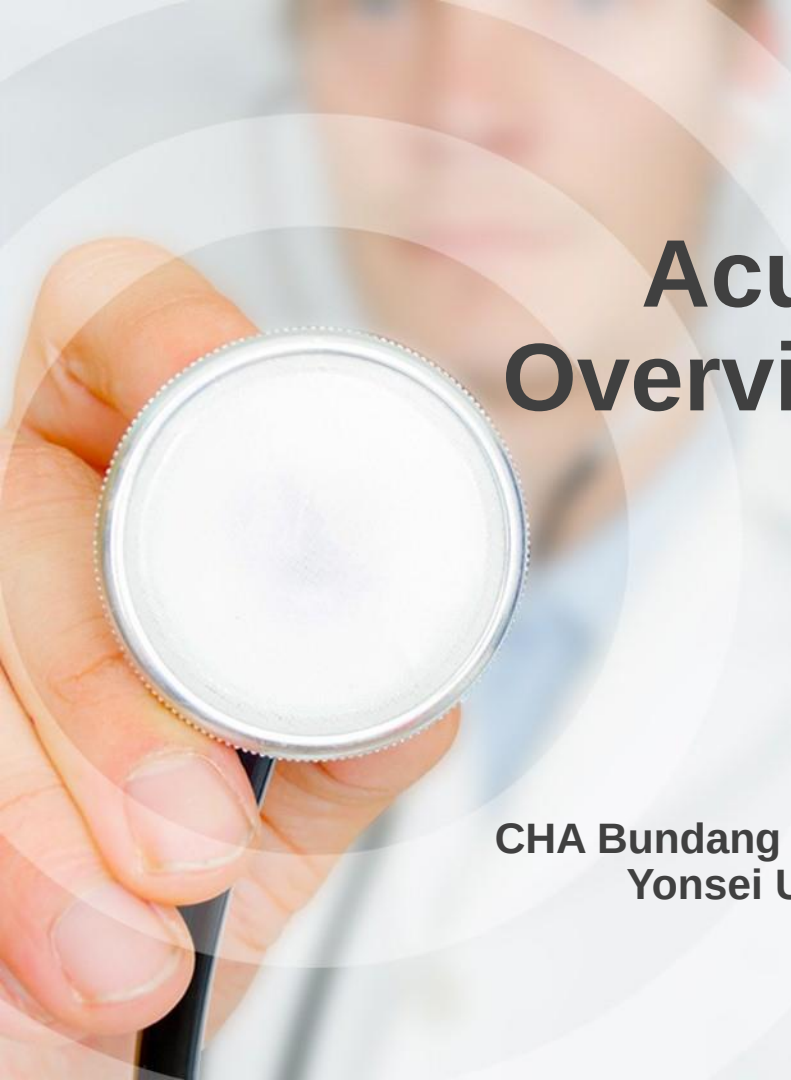

Acute Stroke Management: Overview and Recent Updates

Kee Ook Lee

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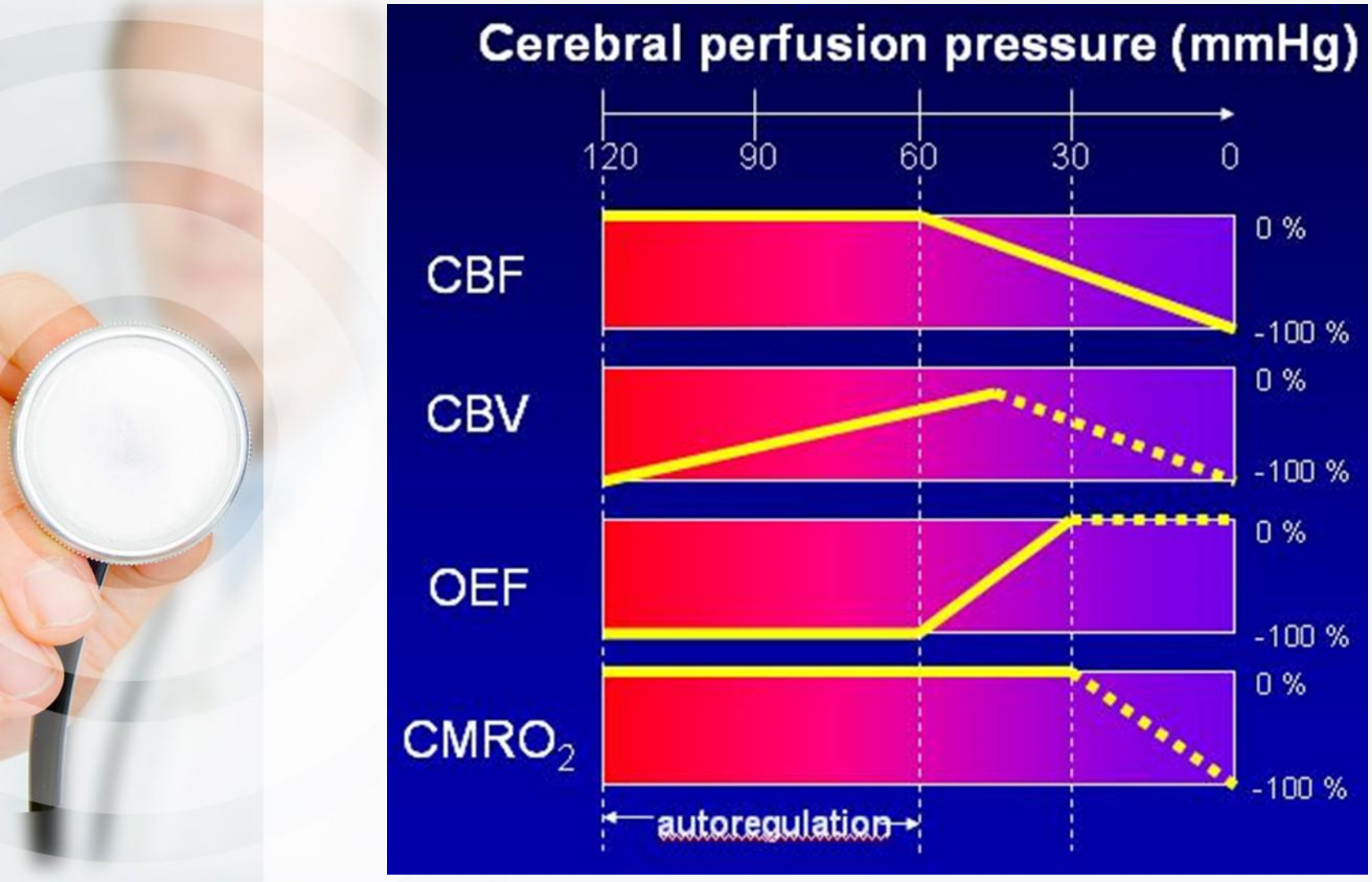
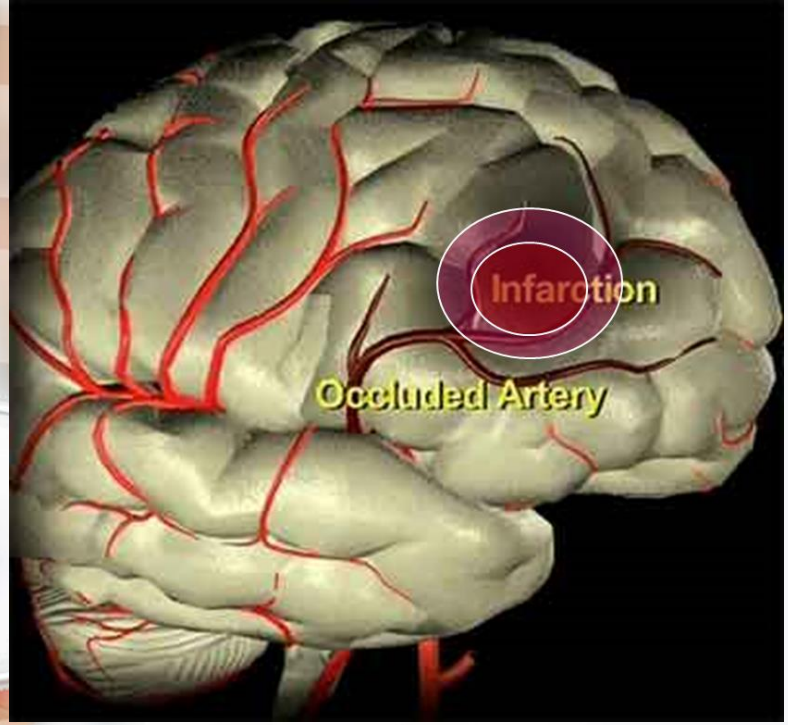
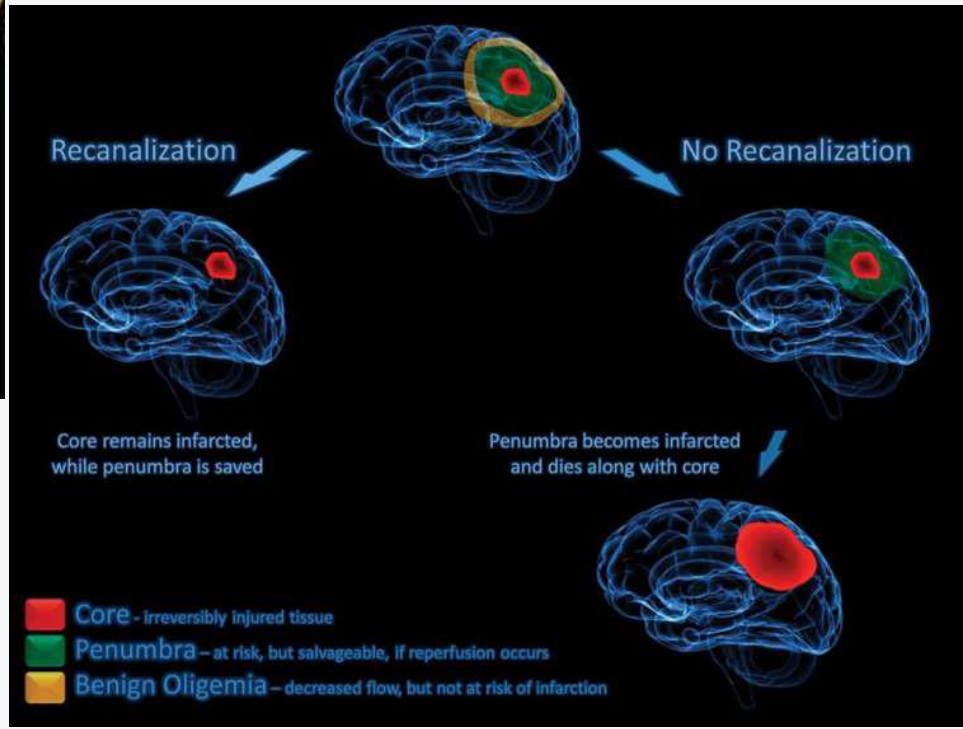
Stroke

- “apoplexy”
  - discovery by Hippocrates over 2500 years ago.
  - Greek means “struck by violence”
  - fifth leading cause of death in the United States
  - “**time is brain**”
  - timely evaluation, treatment, and care, early recognition of stroke signs is paramount

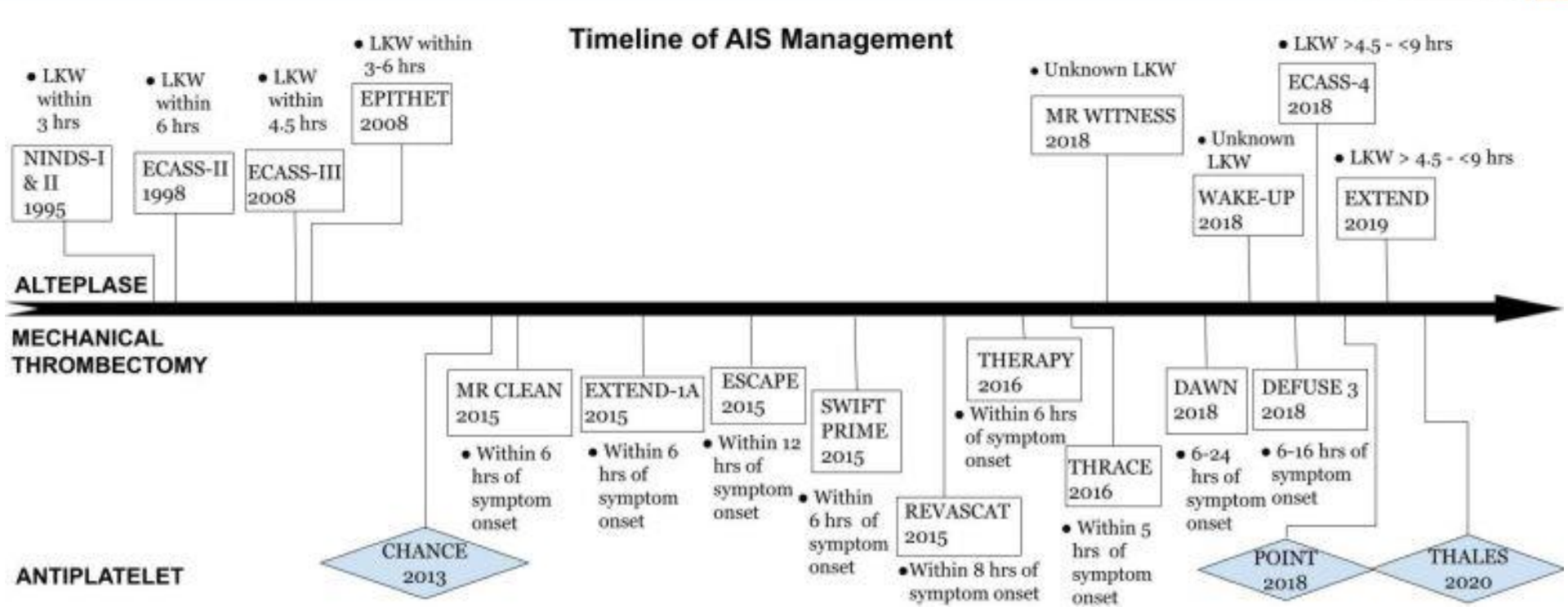

Cerebral perfusion pressure (mmHg)
120
90
60
30
0
CBF
0 %
-100 %
CBV
0 %
-100 %
OEF
0 %
-100 %
CMRO2
0 %
-100 %
autoregulation



Cell death ~ 6min central infarct area or umbra, surrounded by a penumbra of ischemic tissue that may recover



Stroke


Timeline of AIS Management
• LKW within 3 hrs
NINDS-I & II 1995
• LKW within 6 hrs
ECASS-II 1998
• LKW within 4.5 hrs
ECASS-III 2008
• LKW within 3-6 hrs
EPITHET 2008
ALTEPLASE
MECHANICAL THROMBECTOMY
ANTIPLATELET
MR CLEAN 2015
• Within 6 hrs of symptom onset
EXTEND-1A 2015
• Within 6 hrs of symptom onset
ESCAPE 2015
• Within 12 hrs of symptom onset
SWIFT PRIME 2015
• Within 6 hrs of symptom onset
REVASCAT 2015
• Within 8 hrs of symptom onset
THERAPY 2016
• Within 6 hrs of symptom onset
THRACE 2016
• Within 5 hrs of symptom onset
CHANCE 2013
• Unknown LKW
MR WITNESS 2018
• Unknown LKW
WAKE-UP 2018
DAWN 2018
• 6-24 hrs of symptom onset
• LKW >4.5 - <9 hrs
ECASS-4 2018
• LKW > 4.5 - <9 hrs
EXTEND 2019
DEFUSE 3 2018
• 6-16 hrs of symptom onset
POINT 2018
THALES 2020

Mobile Stroke Unit & Hospital Stroke Team

MSU

: potential to decreas

- **High cost & limit**

Hosp

- le
  -
  -
  -
  -
  -
  -

Hospital Stroke Teams

- Performance measures
  - anticoagulation for atrial fibrillation
  - thrombolysis when indicated
  - timely initiation and discharge on antithrombotic drugs
  - discharge on a statin
  - stroke education
  - assessment by rehabilitation.

Emergency Evaluation and Treatment

- Eligible for reperfusion therapy?
  - Hyperacute stage stroke
- **LKWT & wake up stroke**

: 24-hour clock time

  - Ways to avoid - "30 minutes ago" or "2 hours ago"
  - stroke team to operate in the same time window
  - decreases the possibility of errors
- TIA
  - completely resolved before re-setting

- **Confirmation of time is very very important**

Hospital Stroke Teams

- Laboratory evaluation
  - stroke mimics DDx.
  - blood glucose, electrolytes, CBC, PT, PTT, INR, and renal function
  - absolutely required lab is a finger-stick blood glucose test to exclude either significant hyper- or hypoglycemia (glucose <50 mg/dL or >400 mg/dL, respectively)
  - **Other laboratory tests should not delay** of IVT and or EVT

Brain and vascular imaging

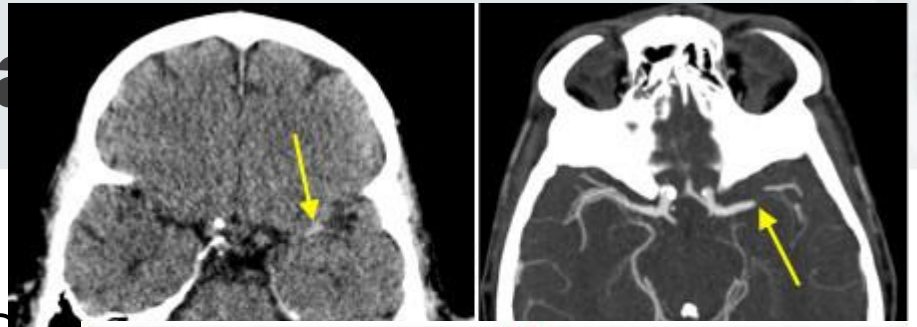
Brain and Vascular Imaging

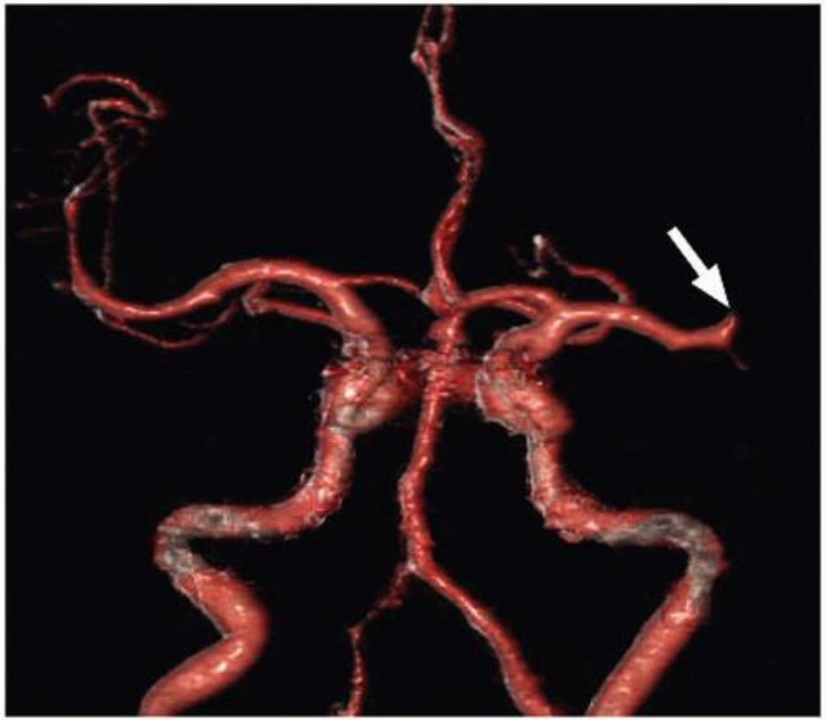
- Non-contrast CT
  - acute management decisions
- DW-MRI
  - more sensitive
  - initial routine use is neither practical nor cost effective
- **CT based or MR based**
  - CTA
  - CT or MR perfusion
  - MRA
- Performed within **15-20 minutes of arrival** in the ED
  - minimize the time to treatment initiation

Brain and Vascula

- **CTA**
  - ➢ confirm or exclude LVO
- ns
  - h
- avera
- smer
  - zed C
  - scher
  - erven

(**IMS**) III trials 권고사항





ORIGINAL RESEARCH

I.Y.L. Tan
A.M. Demchuk
J. Hopyan
L. Zhang
D. Gladstone
K. Wong
M. Martin
S.P. Symons
A.J. Fox
R.I. Aviv

CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcome

BACKGROUND AN of outcome in acu (CS) are importan stroke outcome p

MATERIALS AND M ing within 3 hours the correlation be dichotomized by regression models Receiver operating Diagnostic perfor

RESULTS: There demonstrated sm outcome (all, $P <$ outcome. A CBS confidence interva of 64.6 (95% CI, 4 activator was high 0.97 (95% CI, 0.9

CONCLUSIONS: C

Persistent anterior cerebral circulation occlus the most devastating clinical events, often ca

[Tan IY, Demchuk AM, Hopyan J angiography clot burden score a cerebral artery infarct. AJNR Am

[Kaschka IN, Kloska SP, Struffer Burden and Collaterals in Anteric CTA. Clin Neuroradiol. 2016;26:309-15.]

Clin Neuroradiol (2016) 26:309–315
DOI 10.1007/s00062-014-0359-6

ORIGINAL ARTICLE

Clot Burden and Collaterals in Anterior Circulation Stroke: Differences Between Single-Phase CTA and Multi-phase 4D-CTA

I.N. Kaschka · S.P. Kloska · T. Struffert · T. Engelhorn · P. Gölitz · N. Kurka · M. Köhrmann · S. Schwab · A. Doerfler

Received: 7 July 2014 / Accepted: 1 November 2014 / Published online: 20 November 2014

Abstract
Purpose It has been reported that the extent of intravascular thrombi and the quality of collateral filling in computed tomography (CT) angiography are predictive for the clinical outcome in patients with acute stroke. We hypothesized that multi-phase four-dimensional CTA (4D-CTA) allows better assessment of clot burden and collateral flow compared with arterial single-phase CTA (CTA).
Methods In 49 patients (33 female; age: 77 ± 12 years) with acute anterior circulation stroke, CTA and 4D-CTA reconstructed from dynamic perfusion CT data were analyzed for 5–8 (4D-CTA); $p < 0.001$), and CS (median: 2, interquartile range: 1–2 (CTA) versus median: 3, interquartile range: 2–3 (4D-CTA); $p < 0.001$). Accordingly, CTA significantly overrated clot burden and underestimated collateral flow.
Conclusions 4D-CTA more closely defines clot burden and collateral supply in anterior circulation stroke than CTA, implicating an additional diagnostic benefit.

Keywords 4D computed tomography angiography · Stroke · Perfusion imaging · Thrombus · Collateral circulation

C

Table 4: Multivariate logistic regression analysis of favorable clinical outcome (mRS score, ≤2 at 90 days), controlling for confounders

Variable	Coefficient	*P* Value	OR	Lower CI of OR	Upper CI of OR
Intercept	0.4664	.8301			
CBS	0.4448	.0089	1.560	1.118	2.177
Recanalization	1.6106	.0149	5.006	1.368	18.312
NIHSS score at presentation	−0.1734	.0025	0.841	0.751	0.941
Age	−0.0588	.0181	0.943	0.898	0.990

cerebral artery infarct. AJNR Am J Neuroradiol. 2009;30:525-31.]

Clo

ORIGINAL ARTICLE

Extensive blooming artifact predicts no recanalization after intravenous thrombolysis

S. Yan[a], Q. Chen[a], X. Zhang[a], M. Xu[a], Q. Han[a], A. Shao[b], D. S. Liebeskind[c] and M. Lou[a]

[a]*Department of Neurology, School of Medicine, Second Affiliated Hospital of Zhejiang University, Hangzhou;* [b]*Department of Neurosurgery, School of Medicine, Second Affiliated Hospital of Zhejiang University, Hangzhou, China; and* [c]*University of California – Los Angeles Stroke Center, Los Angeles, CA, USA*

Keywords:
magnetic resonance imaging, recanalization, stroke, thrombolytic therapy

Received 23 August 2015
Accepted 4 November 2015

European Journal of Neurology 2016, **23:** 737–743

doi:10.1111/ene.12930

Background and purpose: Hemosiderin exhibits a stronger T2 shortening effect than deoxyhemoglobin. The extent of the 'blooming artifact' may therefore reflect a composition of different iron forms. Our aim was to investigate the relationship between extent of susceptibility vessel sign (SVS) width beyond the lumen and middle cerebral artery (MCA) recanalization.

Methods: Clinical and imaging data from consecutive acute ischaemic stroke patients with MCA occlusion who underwent susceptibility-weighted imaging (SWI) before intravenous thrombolysis were examined. The source images of magnitude and angiography were used to obtain the width of SVS and MCA at the interface, respectively.

Results: The presence of MCA SVS was observed in 64 patients on initial SWI scans and recanalization was observed in 30 (46.9%) patients. The over-estimation ratio of thrombus width on SWI was an acceptable predictor for no recanalization [odds ratio 1.360 per 0.1; 95% confidence interval (CI) 1.093–1.691; $P = 0.006$]. The optimal cut-off point was identified at 1.943, and this yielded a sensitivity of 67.6% and a specificity of 86.7%. Extensive blooming artifact, defined as overestimation ratio ≥2, independently predicted no recanalization (odds ratio 9.687, 95% CI 1.974–47.545; $P = 0.005$) and unfavorable outcome (odds ratio 4.916, 95% CI 1.049–23.051; $P = 0.043$)

JOURNAL OF NEUROLOGY

Illustrations of
time-of-flight m
[Yan S, Chen

nages of
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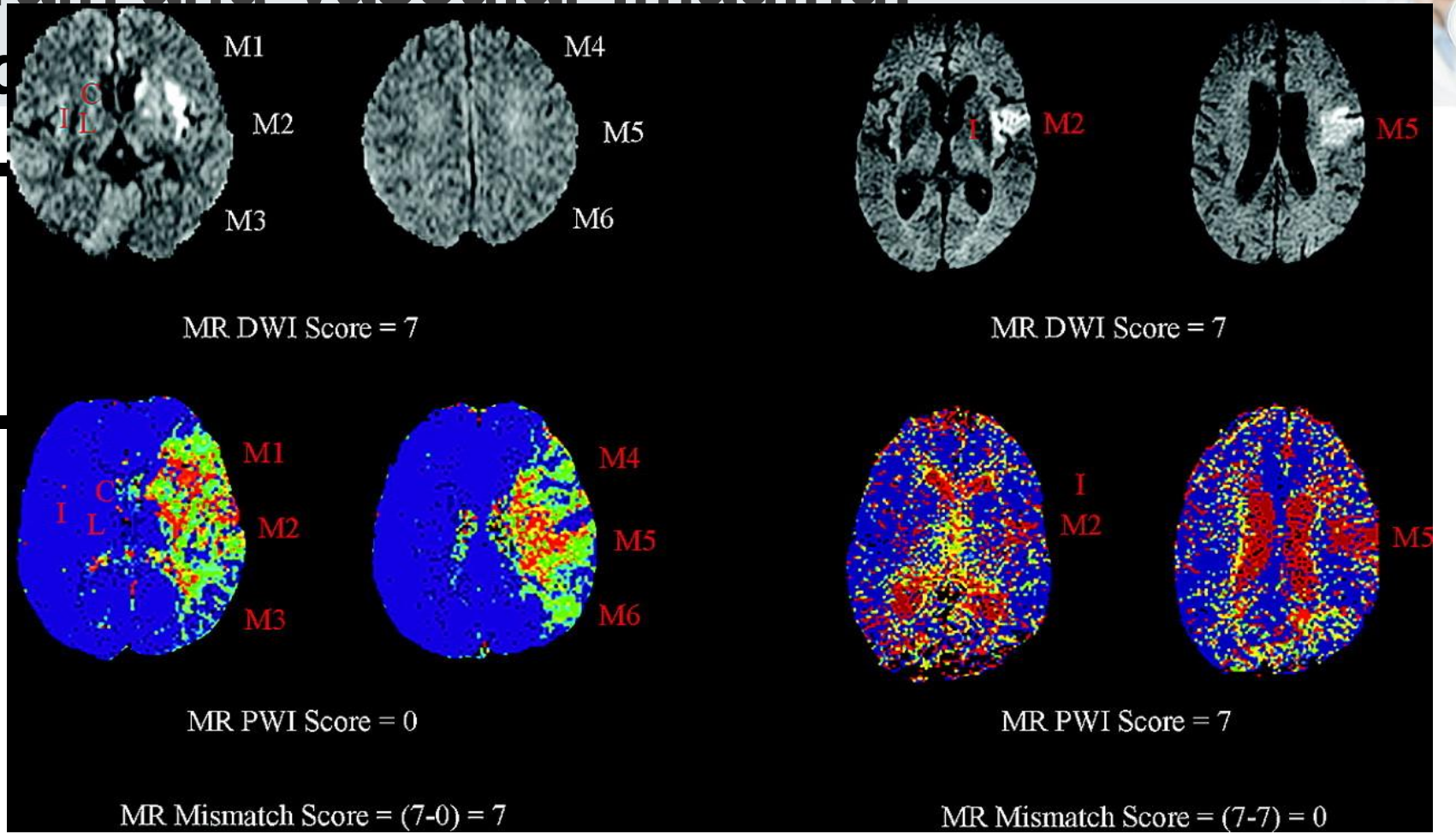
;23:737-43.]

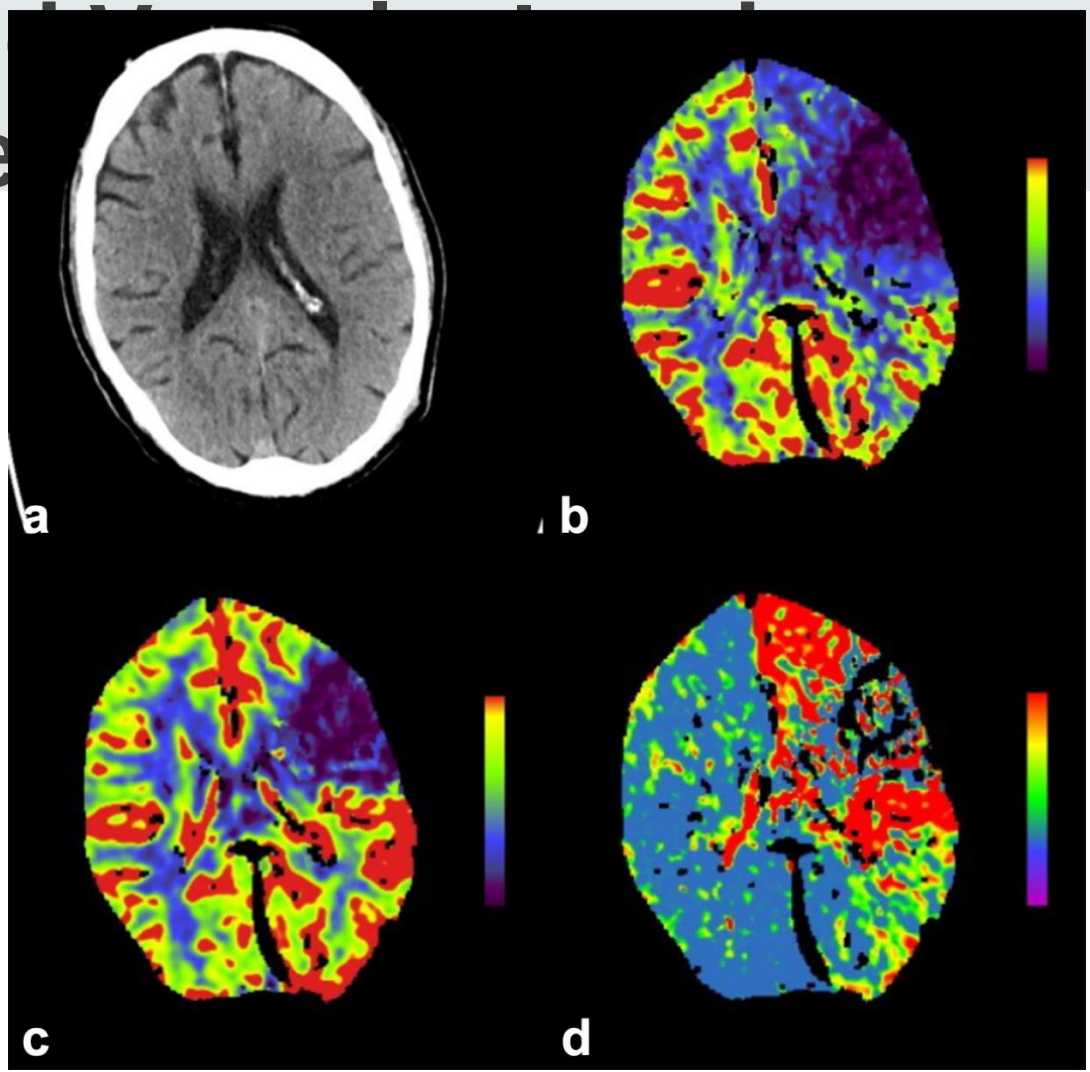
the

bus

Brain and Vascular Imaging:
Ac



Brain an
Advance



Brain and Vascular Imaging:
Advanced imaging

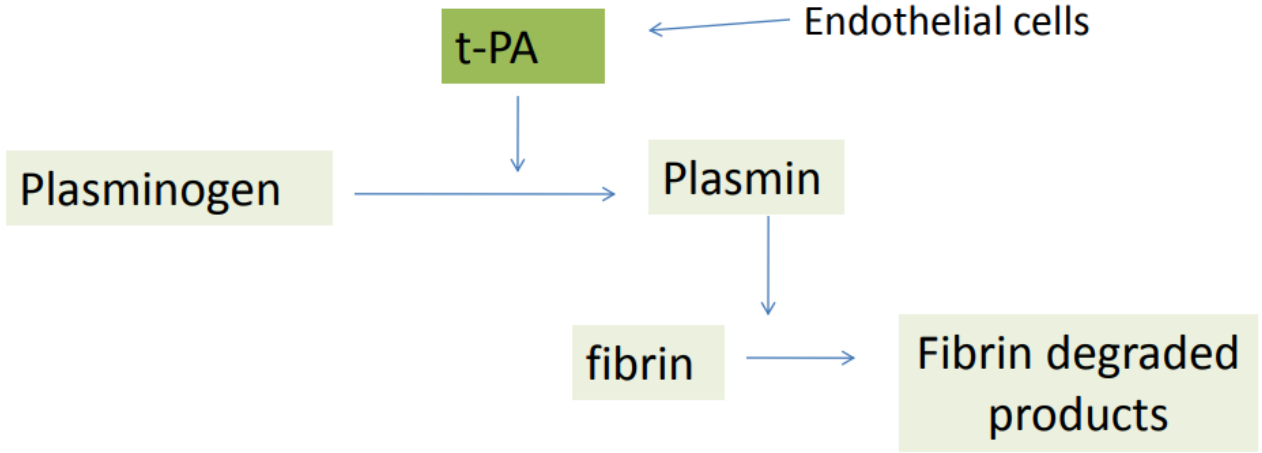
- Wake-up stroke or within 6 to 24 hours
  - useful screening tool for MT
  - Thrombectomy 6 to 12 Hours After Stroke with Mismatch Between Deficit and Infarct (**DAWN)** trial
- Between 6 and 16 hours
  - Endovascular Therapy Following Imaging Evaluation For Ischemic Stroke (**DEFUSE 3**) trial
  - perfusion-core mismatch and maximum core size with CTP or MRI perfusion
- Gold standard key
  - **Catheter angiography**

Thrombolytic agents

Thrombolysis: IVT

- Reco
  - cc
  - re
    fib
  - cc
    pl
  - pl
    ac

- The process of dissolution of clot is called fibrinolysis



Thrombolysis: IVT

- 1996, **FDA** approved the use of IV-rtPA for patients with AIS presenting within 3 h of symptom onset

- 2008, **ECASS (European Cooperative Acute Stroke Study) III** showed benefit of IV-rtPA over placebo among those treated within 3 to 4.5 h of symptom onset

- 2015, **stroke guidelines from AHA** recommended using it up to 4.5 h from onset of symptoms in eligible patients

Thrombolysis: IVT

- Tenecteplase
  - ➢ variant form
  : originates fror
  threonine, N =
  enzyme from al
  - ➢ **longer plasn**
  increased res
  - ➢ hypothesized
  - ➢ **single bolus**

Thrombolysis: IVT

- Tenecteplase (TNK)
  - ➢ NOR-TEST (Tenecteplase Similar to Altplase in Stroke)

  : compared alteplase to TNK in 1100 patients

  : **did not find any benefit in 3 month mRS**
  - ➢ **EXTEND-IA** (Extending the time for Thrombolysi in Emergency Neurological Deficits Intra-Arterial) TNK study

  : compared alteplase to TNK before thrombectomy in 200 patients

  : **increased rates of angiographic reperfusion**

  : similar rates of 90-day functional independence
  - ➢ Systematic review

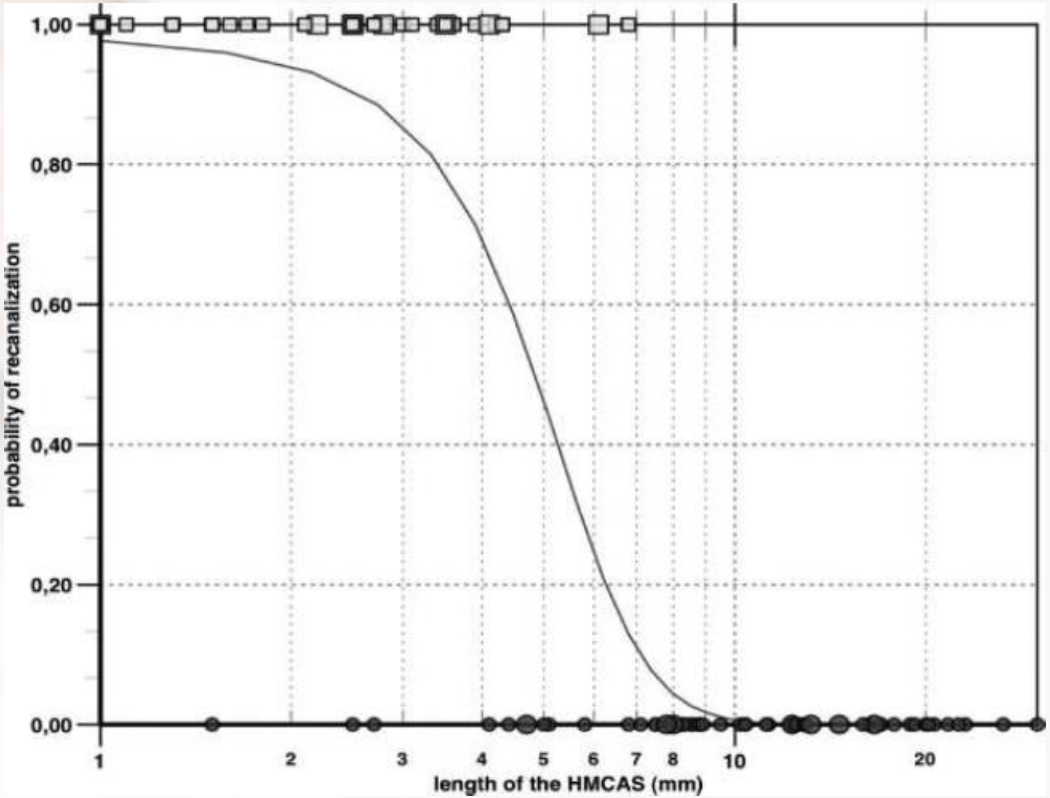
  : five prospective clinical trials more than 1500 subjects

  : non-inferiority to tPA

Thrombolysis: IVT - LIMITATIONS

- ICA and M1 occlusions have lower rate of recanalization than M2–M4 occlusions.
- 30% of MCA occlusions recanalize with IV tPA only within 2 hours
- ICA occlusions recanalize only at 1/3 of the rate of MCA occlusions
- The absolute reduction in chance of poor outcome in patients treated with IV-rtPA within 3 h is 10% (NNT-10)
- In a 3- to 4.5-h time window, the effect is reduced further, to 7% (NNT-14)

Endovascular Thrombectomy



Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by IVT depending on **thrombus length**

Christian H. Riedel et al. Stroke. 2011;42:1775-1777

Thrombolysis: EVT

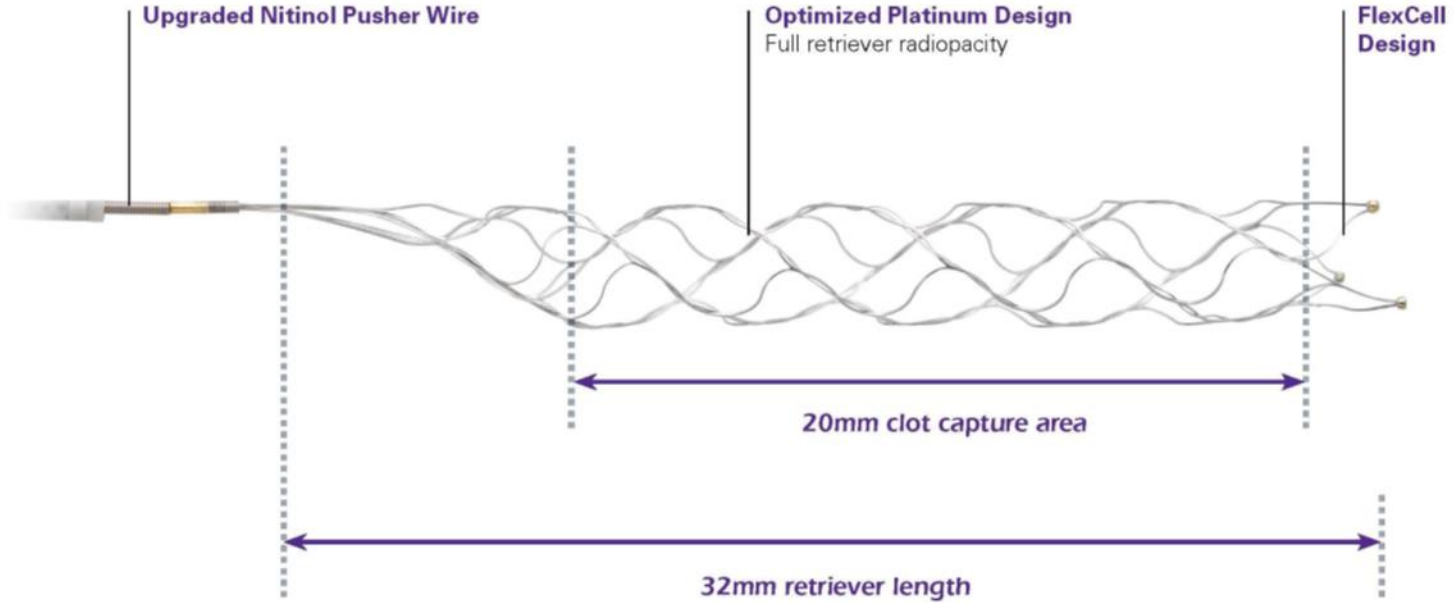
- MR CLEAN
  - First study
  - 6 hr EVT favorable data

- HERMES publication
  - Meta analysis
  - 5 positive trials conducted between 2010 to 2014
  - MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA
  - Astounding result

Thrombolysis: EVT

- Increase the rate of recanalization
  - Stent-based retrieval devices (“stentrievers”)
  - direct clot aspiration
  - combinations of the two

Th



Trevo® XP ProVue Retriever 4x20mm Specifications
Image courtesy of Stryker Neurovascular

Paradigm Shift

The NEW ENGLAND JOURNAL of MEDICINE

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

- Since 2015, the first-line tre

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.F. Lingsma, A.J. Yoo, W.J. Schonewille, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J. Staals, J. Hofmeijer, J.A. van Oostayen

TABLE 2 Comparison of Recent Trials on the Basis of Initial NIHSS, Patients Receiving IV-rtPA, ASPECTS, Functional Outcome (mRS Score at 90 Days), and Revascularization Measured by TICI Score 2b or 3

Trial (Ref. #), N (CG/IA)	NIHSS		Patients Receiving IV-rtPA (%)		ASPECTS (%)		TICI Score (2b/3)	mRS (0–2) (%)	
	CG	IA	CG	IA	CG	IA		CG	IA
MR CLEAN (27), 500 (267/237)	18	17	90	87	9	9	59	19	31.5
ESCAPE (28), 315 (150/165)	17	16	78	72	9	9	71	29.3	53
SWIFT-PRIME (29), 196 (98/98)	17	17	100	100	9	9	88	35.5	60.2
EXTEND-IA (30), 70 (35/30)	13	17	100	100	NR	NR	86	40	71
REVASCAT (32), 206 (103/103)	17	17	77	68	8	7	66	29	43

- REVASCAT

We enrolled 500 patients at 16 medical centers in the Netherlands (233 assigned to intraarterial treatment and 267 to usual care alone). The mean age was 65 years (range, 23 to 96), and 445 patients (89.0%) were treated with intravenous alteplase before randomization. Retrievable stents were used in 190 of the 233 patients (81.5%) assigned to intraarterial treatment. The adjusted common odds ratio was 1.67 (95% confidence interval [CI], 1.21 to 2.30). There was an absolute difference of 13.5 percentage points (95% CI, 5.9 to 21.2) in the rate of functional independence (modified Rankin score, 0 to 2) in favor of the intervention (32.6% vs. 19.1%). There were no significant differences in mortality or the occurrence of symptomatic intracerebral hemorrhage.

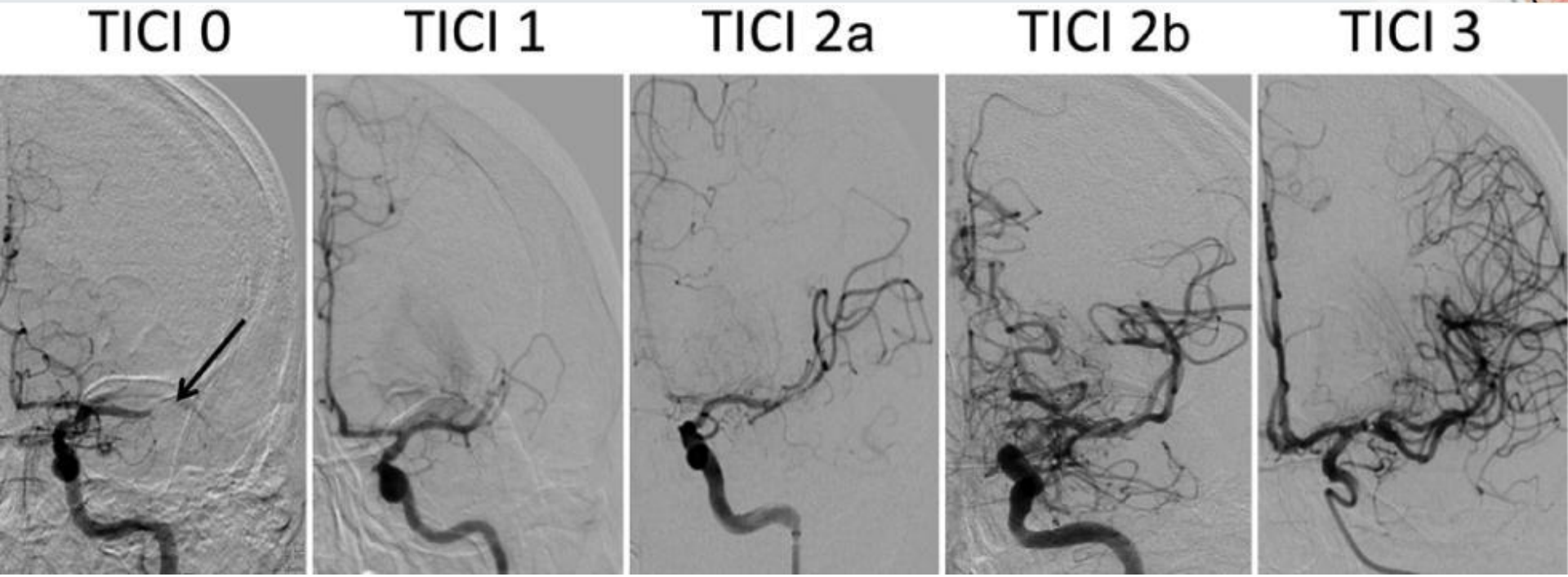
CONCLUSIONS

In patients with acute ischemic stroke caused by a proximal intracranial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe. (Funded by the Dutch Heart Foundation and others; MR CLEAN Netherlands Trial Registry number, NTR1804, and Current Controlled Trials number, ISRCTN10888758.)

This article was published on December 17, 2014, and updated on January 1, 2015, at NEJM.org.

N Engl J Med 2015;372:11-20.
DOI: 10.1056/NEJMoa1411587

TICI



Thrombolysis: EVT

- Direct Aspiration Thrombectomy
  - direct aspiration first pass technique (ADAPT)

  : **highly trackable neuro sheath** (usually 6 Fr) is placed into ICA or VA

  : proximal end of the thrombus is engaged directly

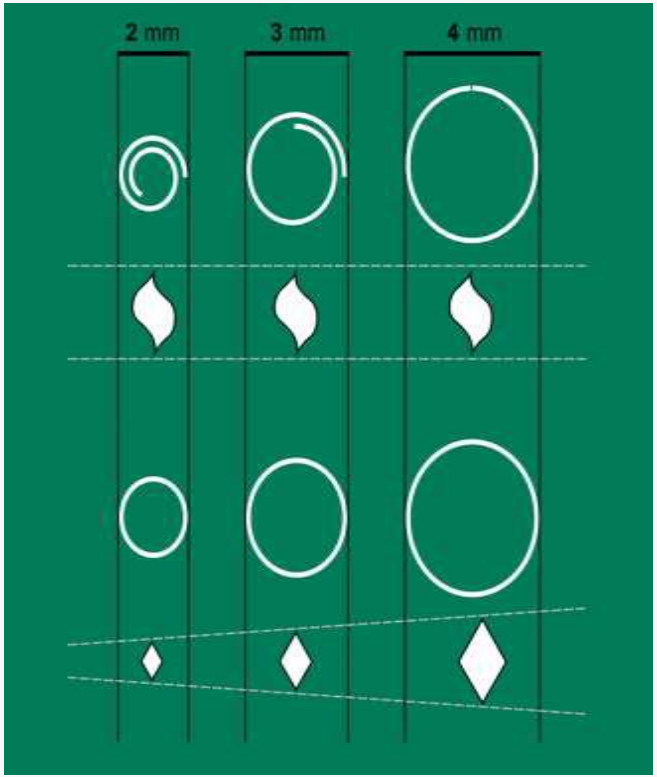
  : Aspiration performed either manually with a **large syringe or with an aspiration pump system**
- ADAPT versus stent retriever
  - decreased time to reperfusion, increased TICI 3 reperfusion, and decreased cost
  - More recent studies have suggested parity

Thrombolysis: EVT

- Combined Thrombectomy Techniques
  - “Solumbra” technique
  - placing a sheath or a BGC in ICA or VA
  - advancing an **intermediate catheter** (reperfusion catheter)
  - deploying a stent retriever across the occlusion
  - aspiration of the reperfusion catheter along with the stent retriever

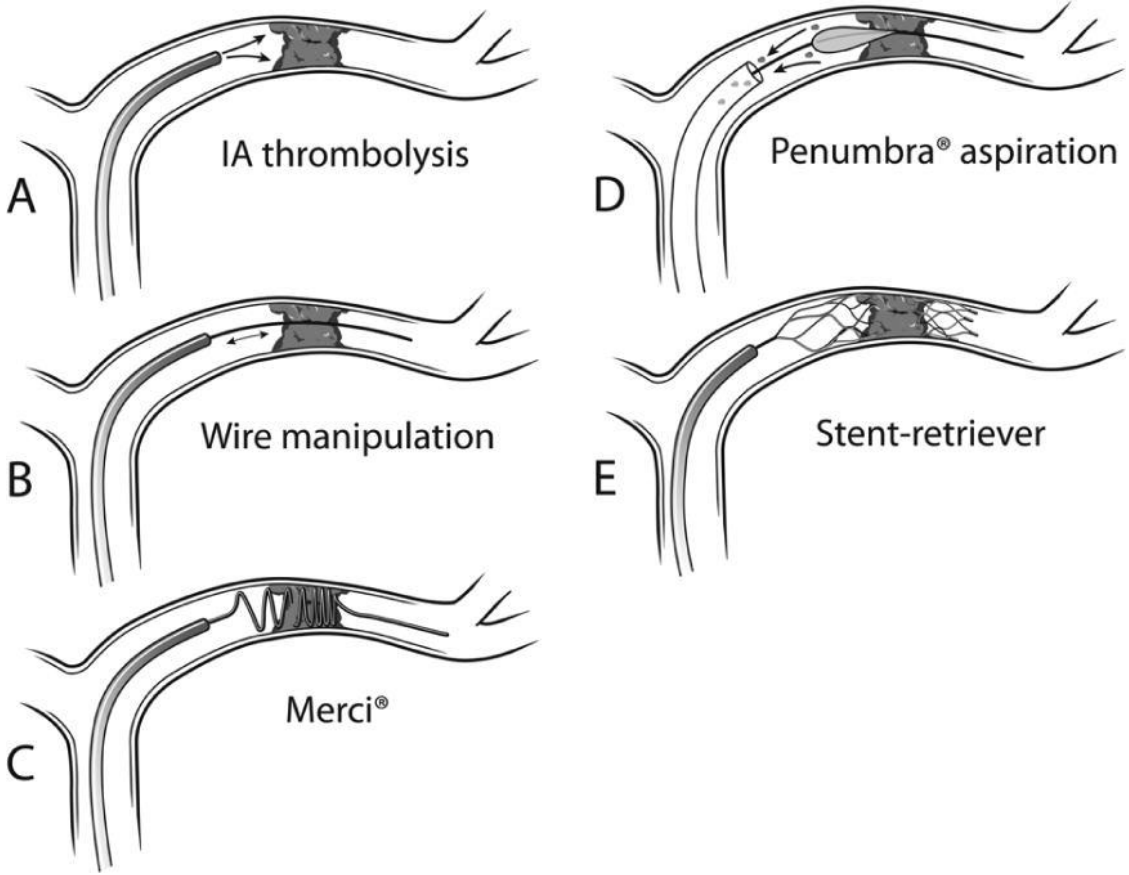
Consistent Cell Size

Variable Cell Size



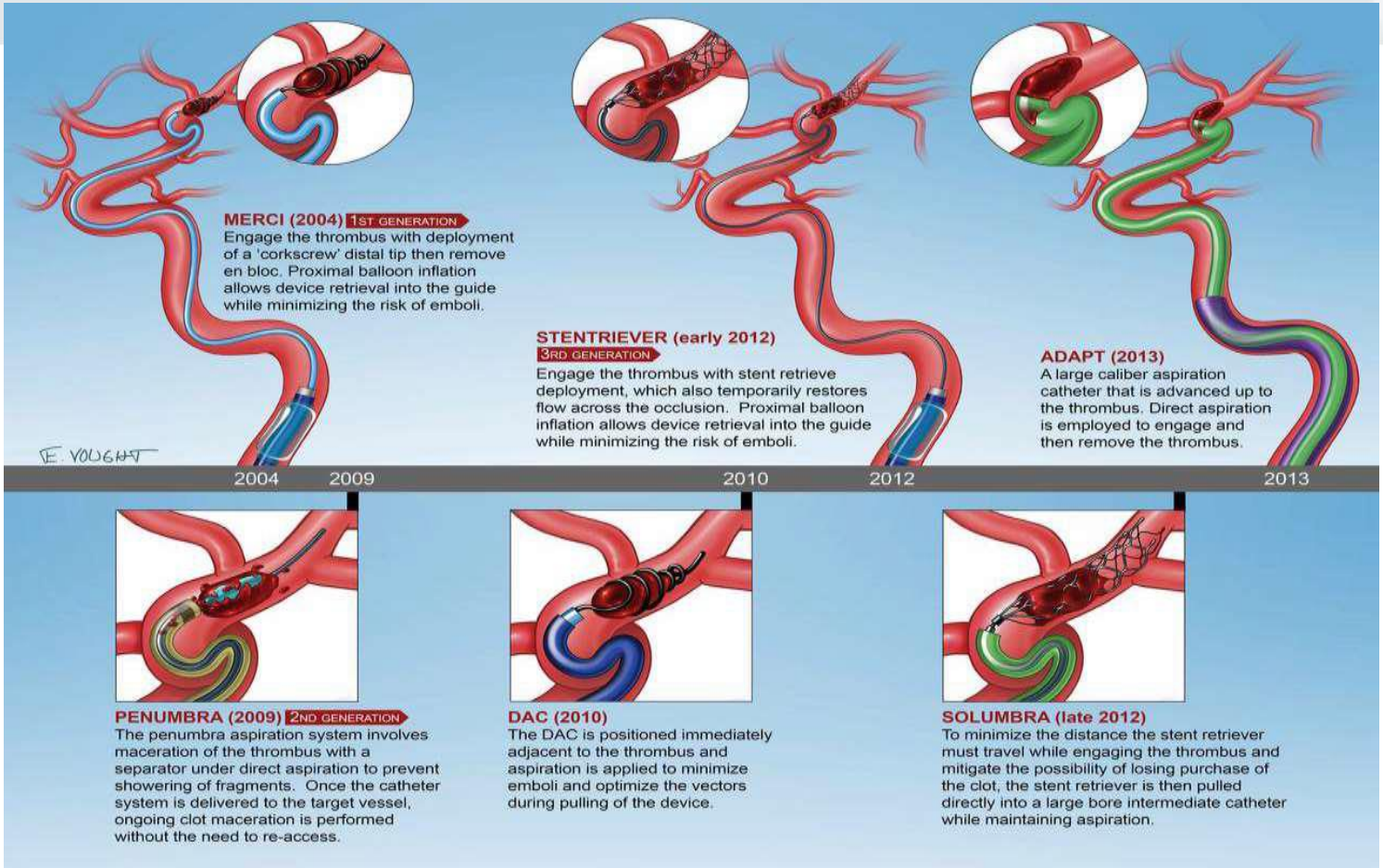
- The Solitaire™ FR device Parametric™ design that may provide multiple planes of clot contact.
- Trevo - straight cut tube ; struts of the Trevo™* device to cut into the clot

REPERFUSION STRATEGIES



Endovascular treatment of acute ischemic stroke: the end or just the beginning? Neurosurg Focus. 2014 Jan;36(1):E5. doi: 10.3171/2013.10.FOCUS13374. Maxim Mokin et al.

Major steps in evolution of thrombectomy devices



Non-treatment candidates

DAPT

- The Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack trial, (CHANCE)
  - minor stroke (NIHSS≤3) or high-risk TIA (ABCD2 score≥4)
  - first 24 hours of symptoms onset
  - 3 weeks
  - Chinese population

- Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA trial (POINT trial)
  - Multicenter, randomized
  - Similar with CHANCE
  - 3months

ADP inhibiotor

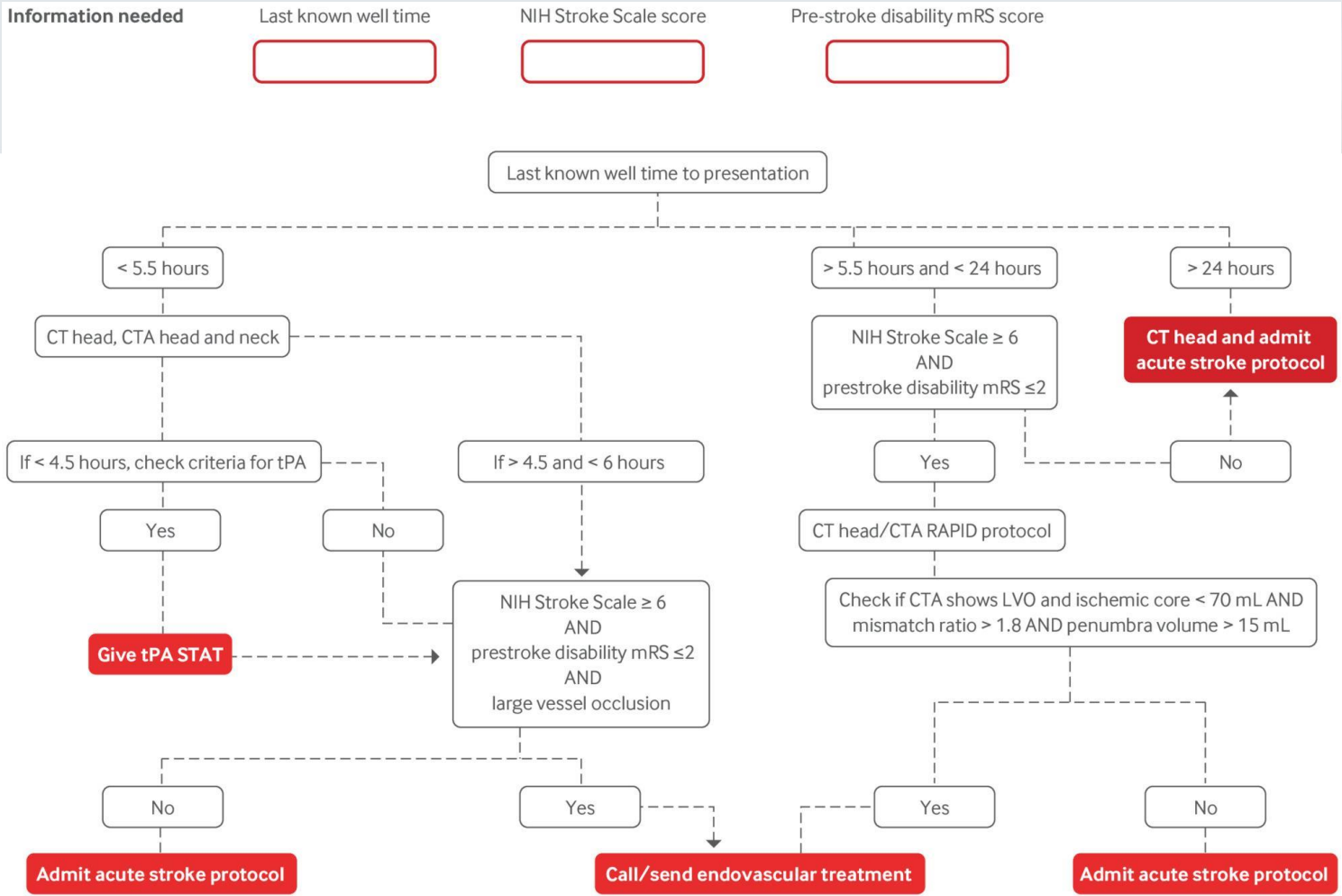
- Clopidogrel
  - polymorphism of the CYP2C19 gene

- Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA trial (THALES trial)
  - ticagrelor and aspirin vs. aspirin only
  - lower risk of stroke or death at 30 days
  - D/C due to the bleeding rates in the combination group

Clinical Trials

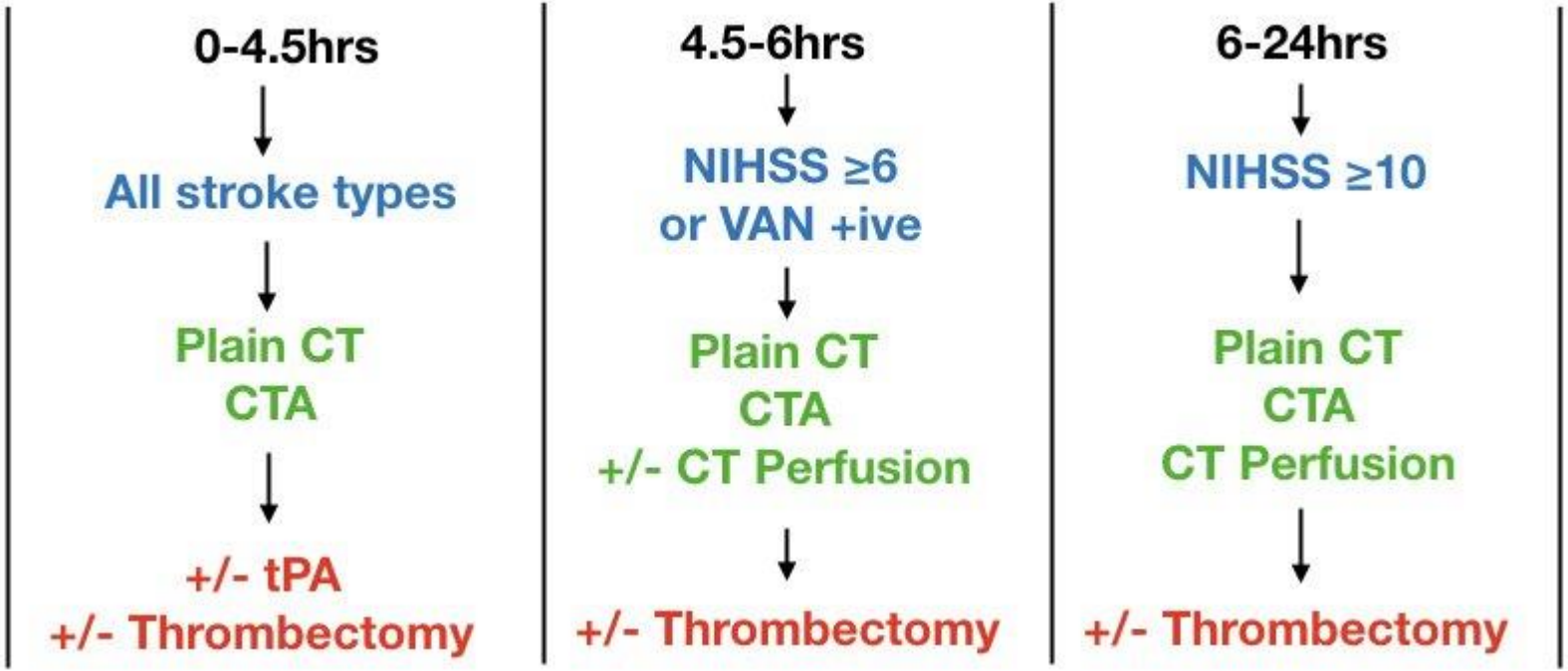
Study	Citation	Study Design	Intervention	Number of participants (n)	Rates of major/severe hemorrhage (Treatment versus Control)	Outcome
THALES	Johnston et al. NEJM 2020 [36]	Randomized, double-blind, placebo-controlled trial	Randomization within 24 hours of symptom onset	11,016	0.5% vs 0.1%, (P=0.001)	Lower risk of stroke or death within 30 days but increase risk of major hemorrhage.
POINT	Johnston et al. NEJM 2018 [25]	Randomized, double-blind multicenter trial	Randomization within 12 hours of symptom onset	4881	0.9% vs 0.4%, (P=0.02)	Lower risk of major ischemic events but a higher risk of major hemorrhage at 90 days
CHANCE	Wang et al. NEJM 2013 [24]	Randomized, double-blind, placebo-controlled trial	Randomization within 24 hours of symptom onset	5170	0.3% vs 0.3%, (P=0.73)	Lower risk of stroke but no increase risk of major hemorrhage at 90 days

Protocol



Michael S Phipps et al. 2020

Acute stroke triage



Times are symptom onset to needle times at a stroke center. CTA = CT angiogram head and neck. NIHSS = National Institute of Health Stroke Scale. VAN = Vision, Aphasia, Neglect tool

Thank you for your attention