

Updated Development of Emergent Management in **Acute Ischemic Stroke**

林浚仁醫師

臺北榮總神經醫學中心腦血管科

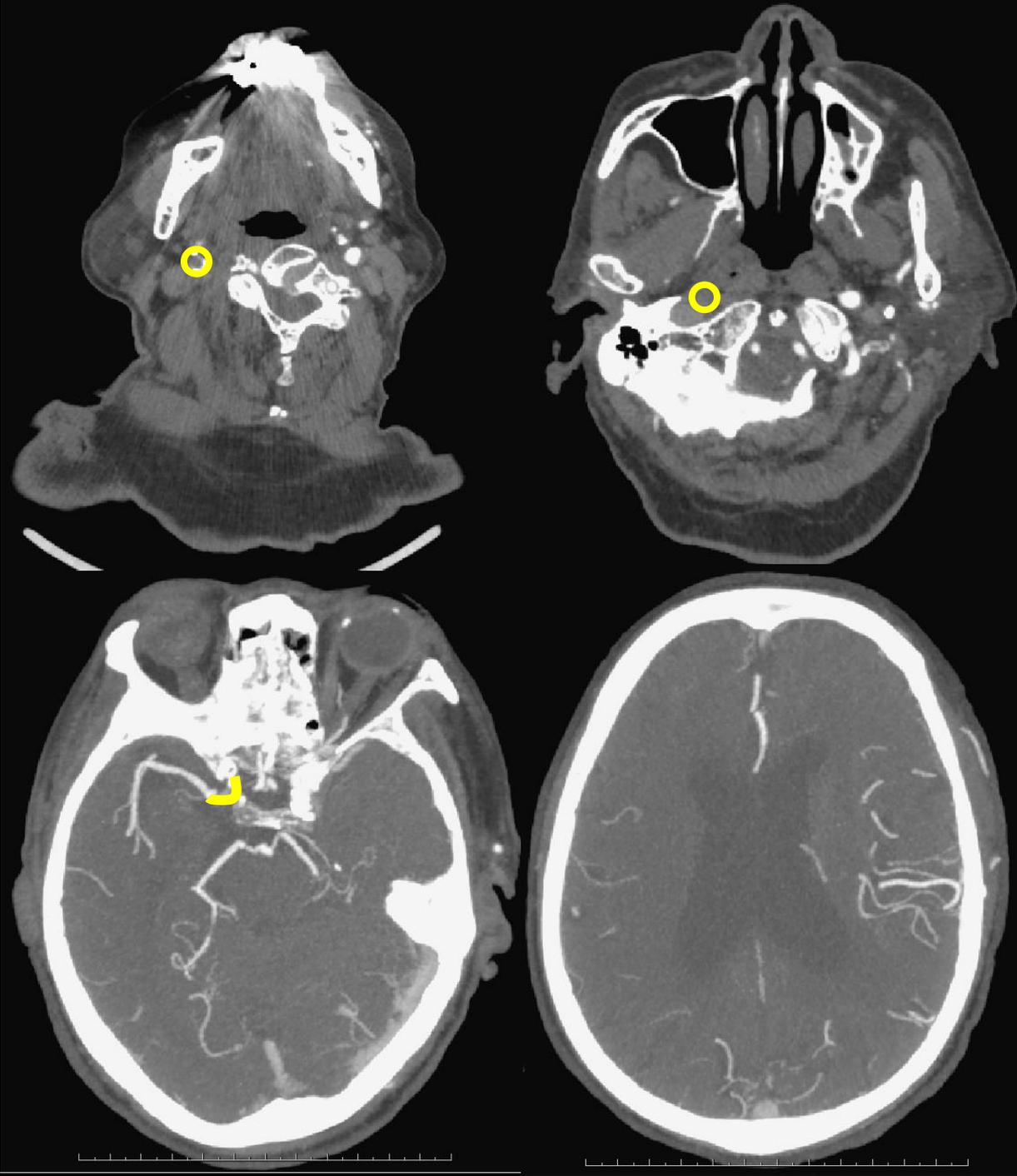


Case Sharing

#9393468

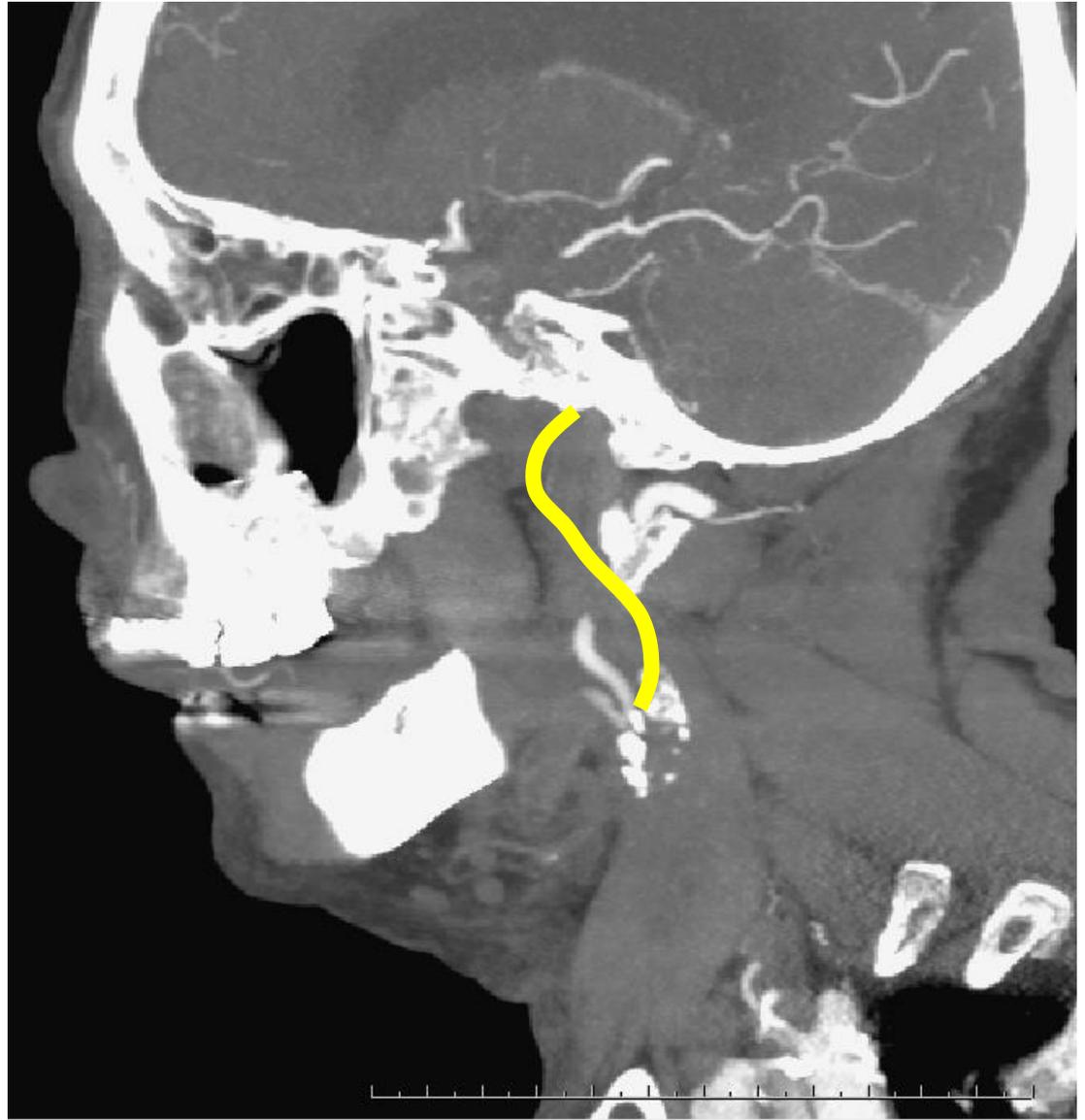
- ✓ 98y/o male
- ✓ Hx of AF under Dabigatran 110mg bid, CAD, HTN, BPH
- ✓ Suffered from acute onset of left limb weakness, facial palsy, slurred speech on 12/12 20:30
- ✓ Visited ER at 22:18
- ✓ BP: 202/91mmHg
- ✓ NIHSS at ER: 10

CTA

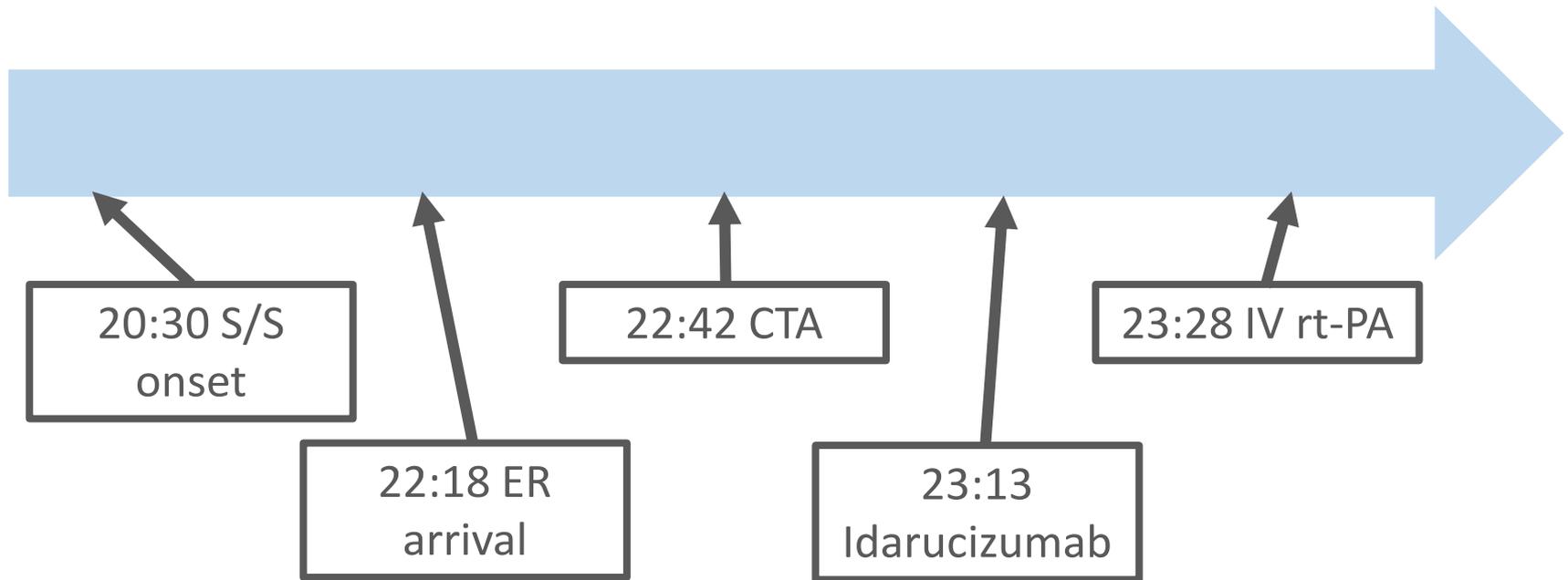


CTA

- ✓ Right ICA occlusion



- ✓ Idarucizumab 5g was given, followed by rt-PA 0.6mg/kg.
- ✓ Activate EVT simultaneously



EVT

- ✓ Aspiration with Sofia catheter x2
- ✓ Enterprise stent 4x30mm placement
- ✓ Post dilatation with balloon angioplasty

Pre



s/p stenting



Post dilatation

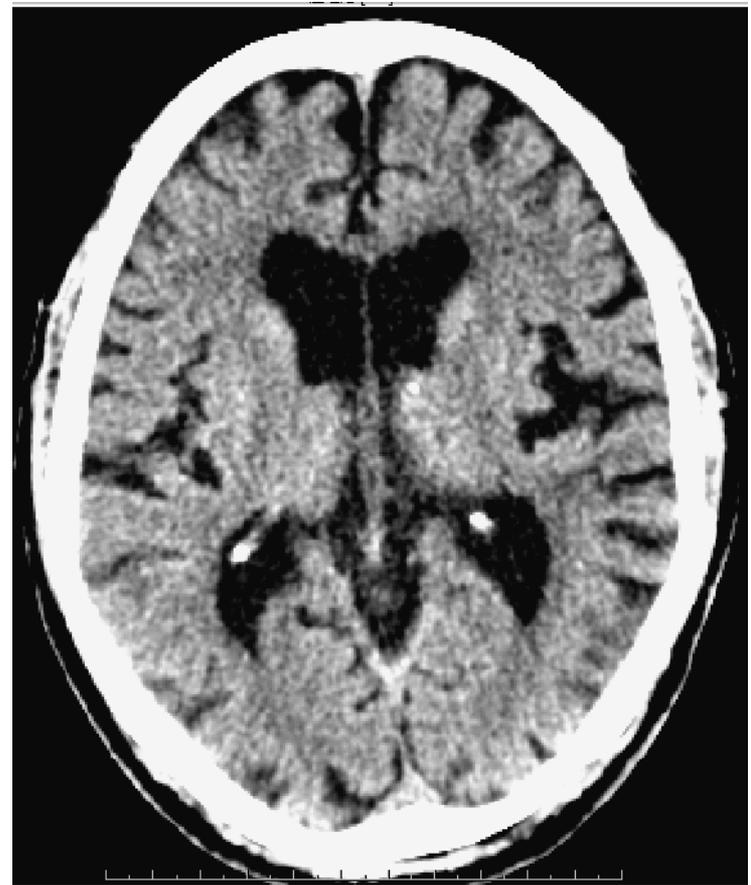
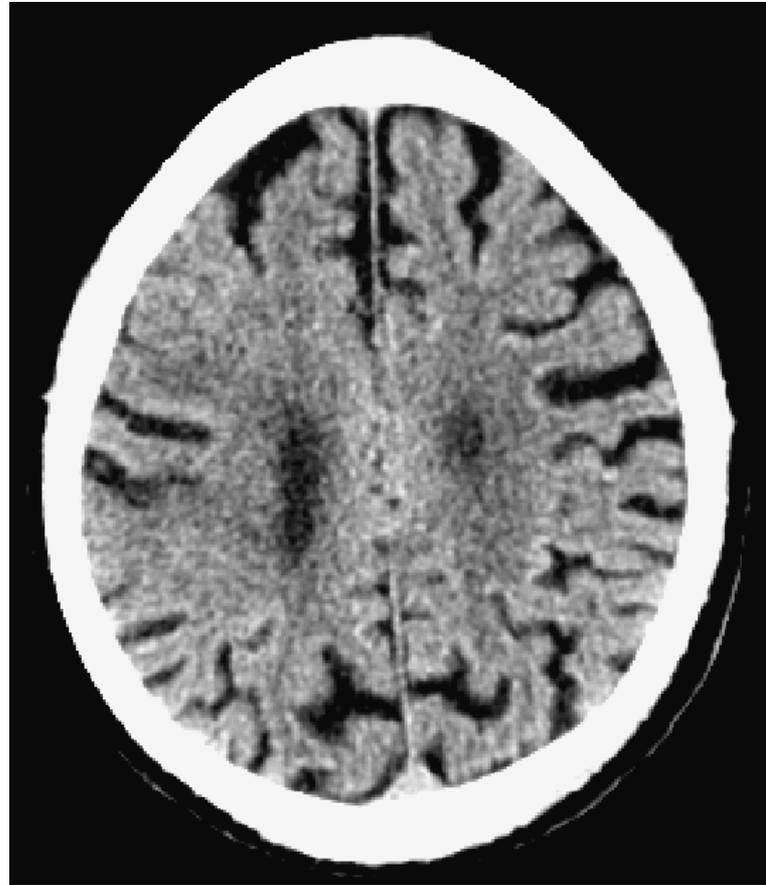


Post-operative care

- ✓ Keep sBP <120mmHg
- ✓ Tirofiban loading + low dose maintenance for 24 hours.
- ✓ Followed by DAPT with aspirin + clopidogrel
- ✓ Atorvastatin 20mg qd

- ✓ Tirofiban was stopped after 16h dripping due to UGI bleeding.
- ✓ PPI was started.
- ✓ DAPT: cilostazol instead of aspirin for 2 days

24h Brain CT



1/23 Discharge

- ✓ Clear consciousness
- ✓ NIHSS = 5
- ✓ mRS = 4
- ✓ No NG tube

2/1 & 2/25 OPD f/u

- ✓ Clear consciousness; Oriented
- ✓ NIHSS = 3; walk with small steps for <50m
- ✓ CTA f/u: Right proximal ICA 60-70% stenosis

Advance in Stroke Care

1980

1990

2000

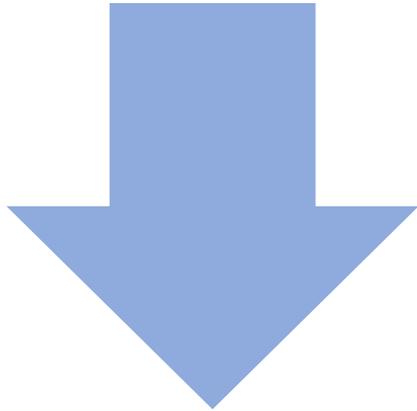
2010

- ✓ Antiplatelet
- ✓ Brain CT/MRI
- ✓ Sonogram

- ✓ Stroke Unit
- ✓ IV rt-PA

- ✓ DOACs
- ✓ Endovascular thrombectomy

IV rt-PA



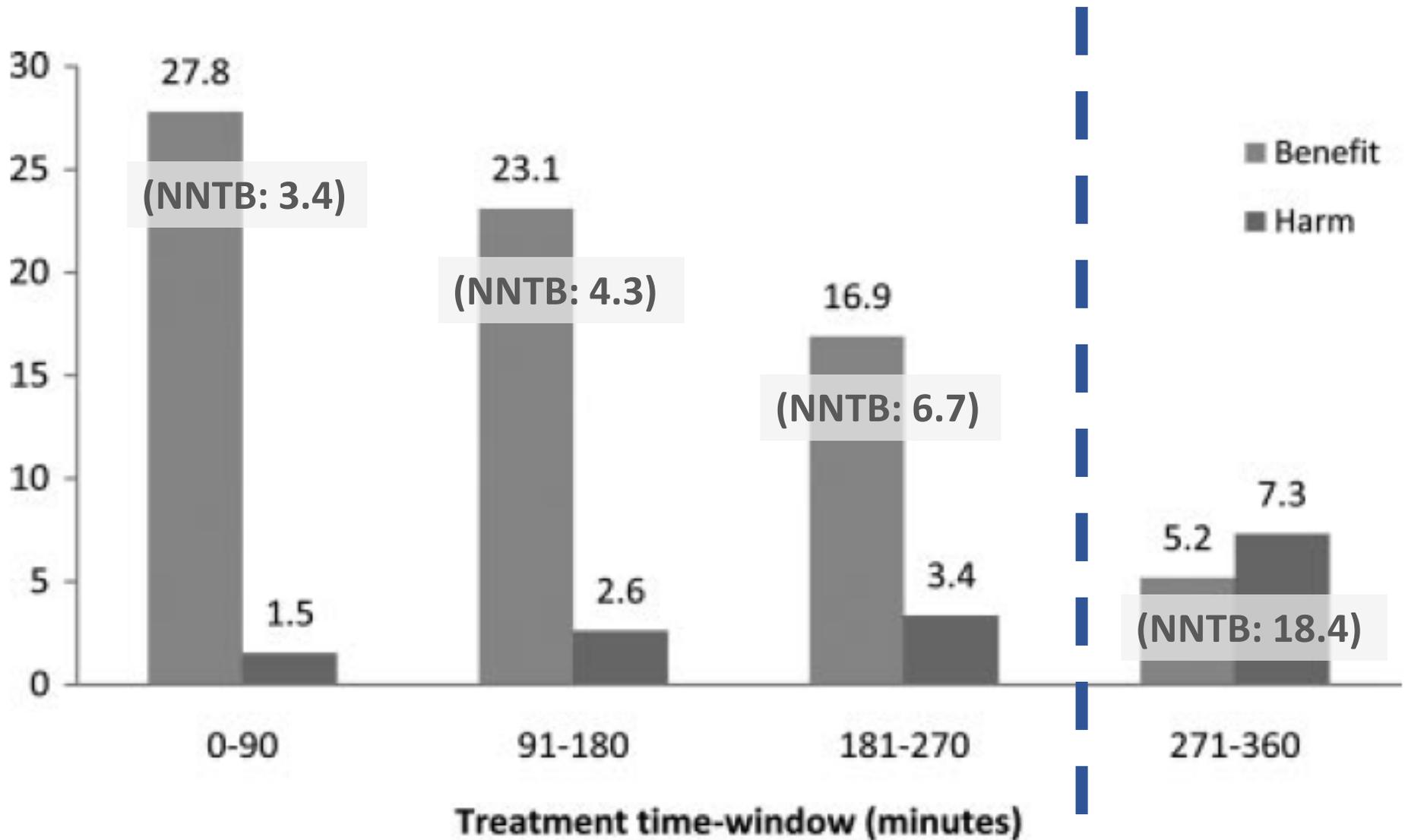
~1/3 of unfavorable outcome



~10x of symptomatic ICH (6%)

~10% in Asian American

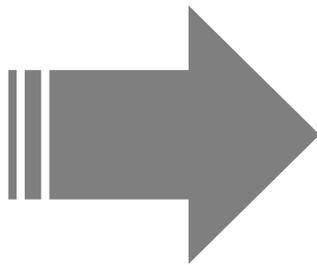
Time is Brain – IVT



IV rt-PA is associated with **low** recanalization rate in proximal a. occlusion

CTA database
N=216

Occlusion Location	Recanalization (All)	Recanalization After IV rt-PA	Recanalization After Endovascular Treatment	No Recanalization
M1-MCA	75.4% (49)	32.3% (21)	43.1% (28)	24.6% (16)
ICA terminus (T, L) occlusion	43.5% (10)	4.4% (1)	39.1% (9)	56.5% (13)
M2-MCA	92.3% (12)	30.8% (4)	61.5% (8)	7.7% (1)
BA	56.0% (14)	4.0% (1)	52.0% (13)	44.0% (11)
All	67.7% (86)	21.3% (27)	46.5% (59)	32.3% (41)



Endovascular Thrombectomy



MR CLEAN

EXTEND-IA

ESCAPE

SWIFT-PRIME

REVASCAT

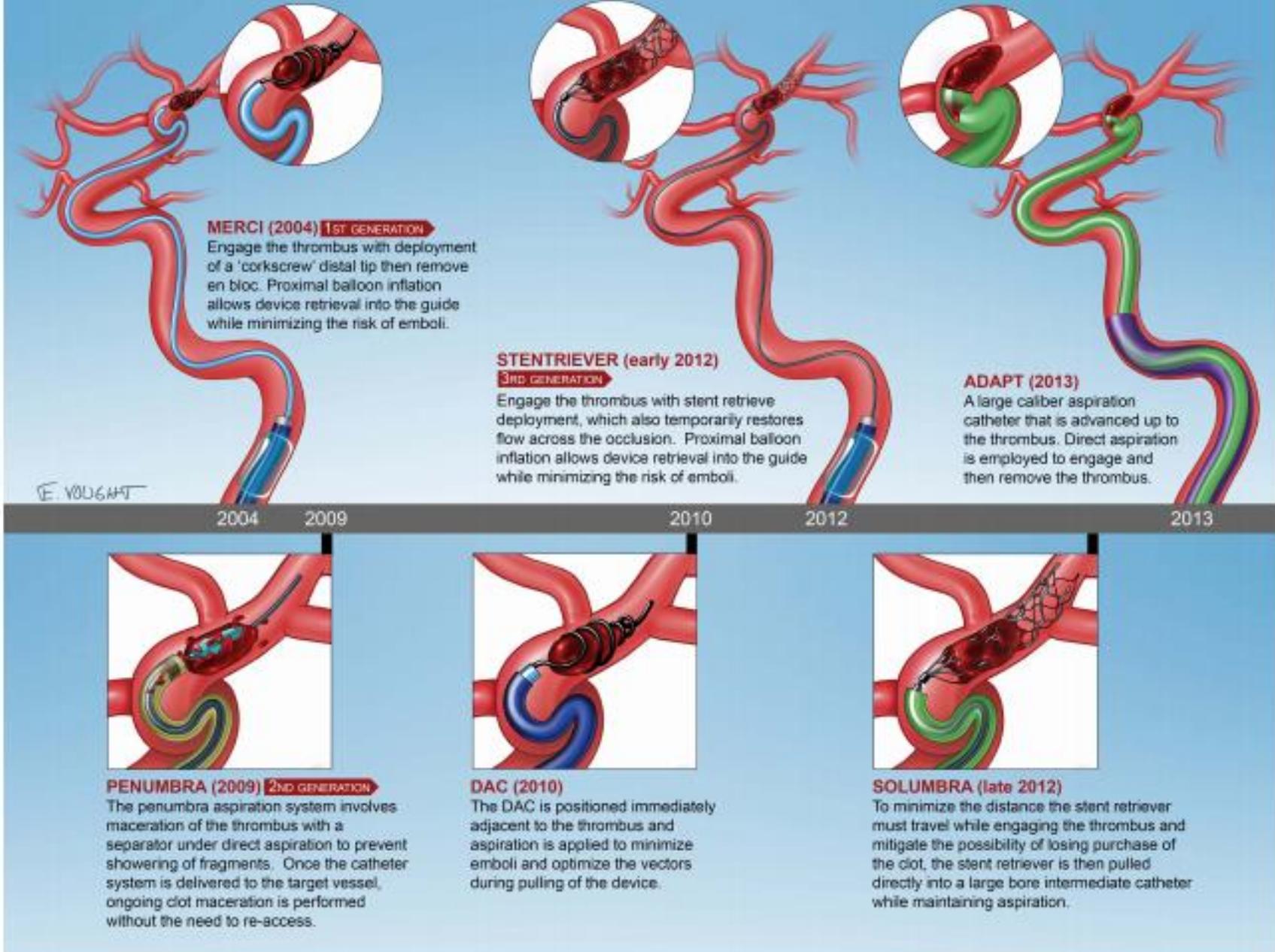


Figure 3 Illustration depicting the major steps in evolution of thrombectomy devices, beginning from the first-generation concept to state-of-the-art approaches.

A Overall

0 1 2 3 4 5 6

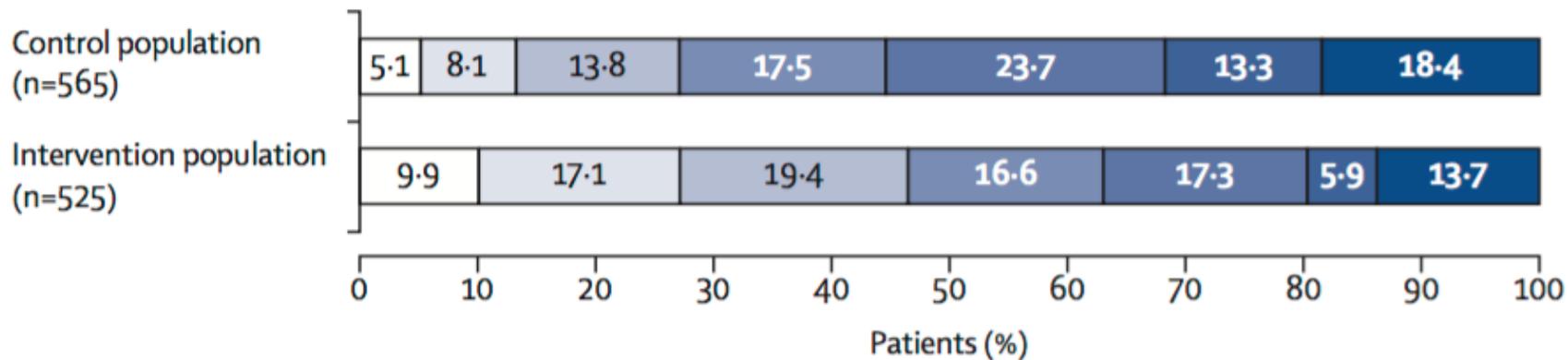


B

Ineligible for alteplase

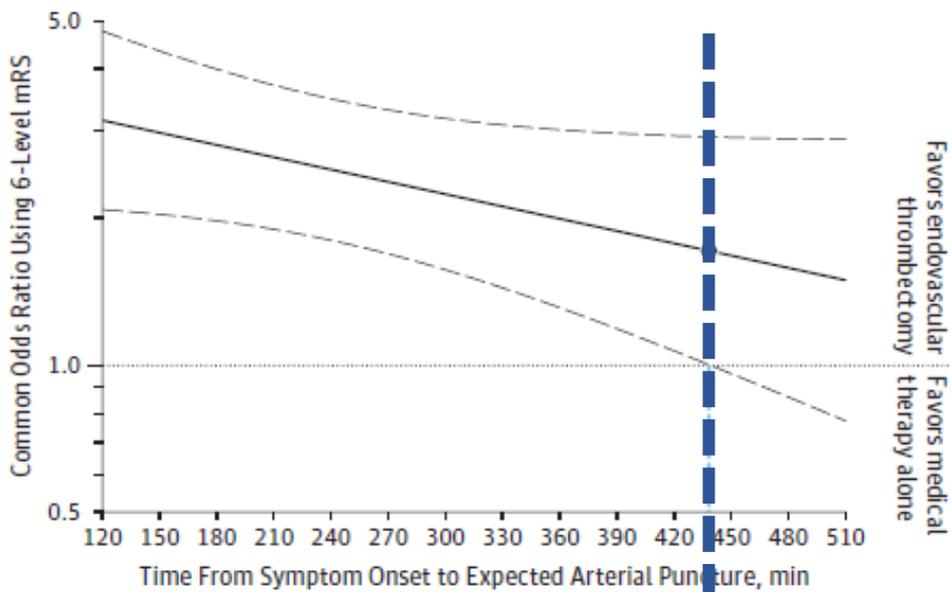


Received alteplase

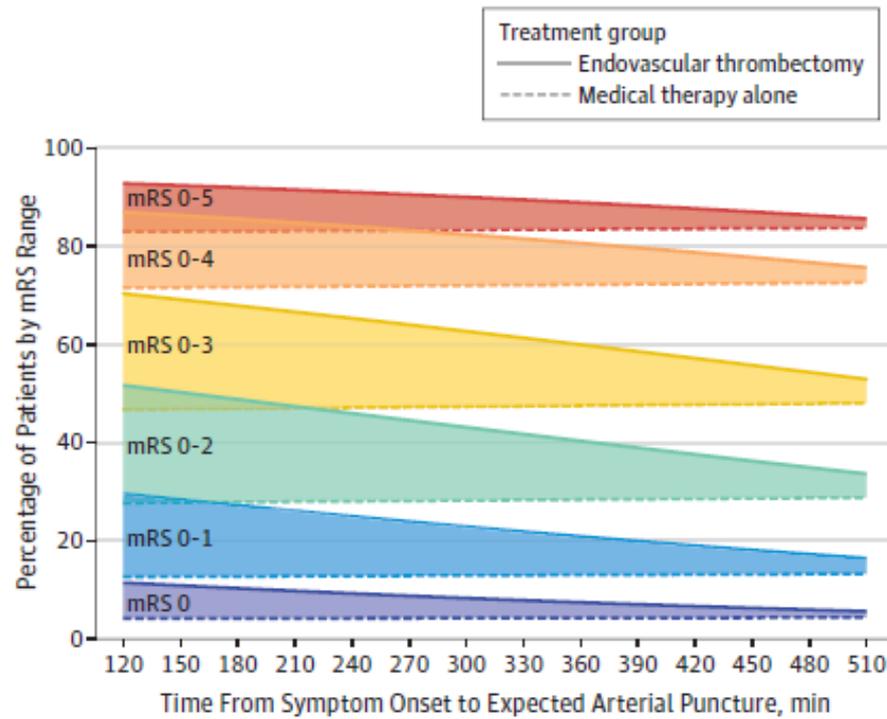


Time is Brain - EVT

A Odds ratio for less disability at 3 mo in endovascular thrombectomy vs medical therapy alone groups by time to treatment



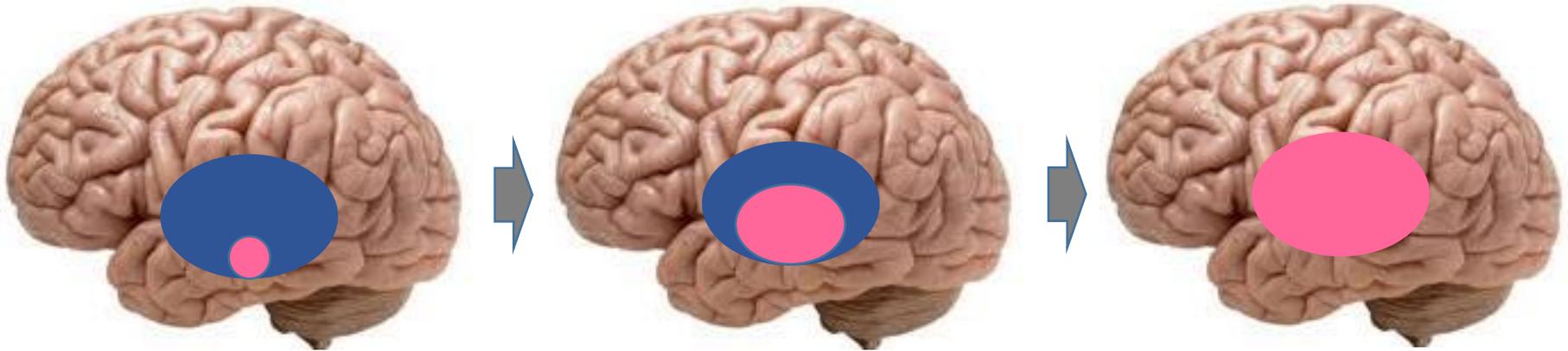
B Difference in adjusted 3-mo disability rates between endovascular thrombectomy and medical therapy alone groups by time to treatment



台灣顱內動脈內取栓健保給付條件

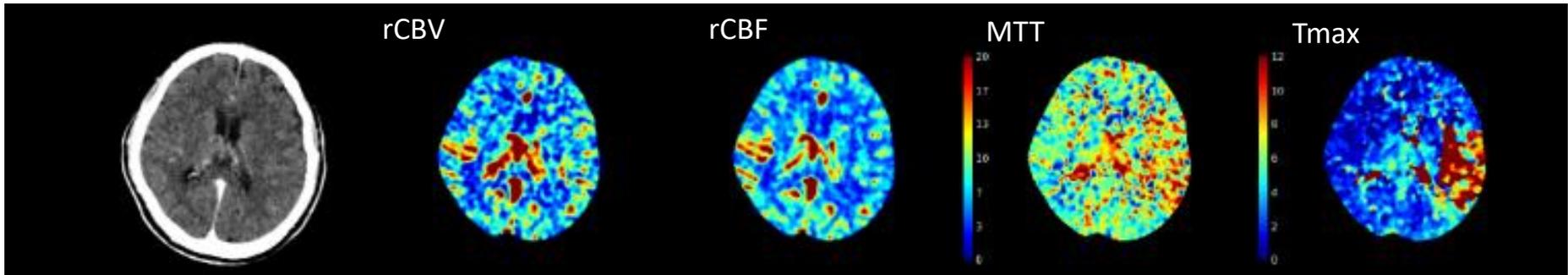
- ✓ **前循環**在發作內**8小時**內、**後循環**在發作後**24小時**內。
- ✓ 影像診斷為顱內大動脈阻塞，包括內頸動脈(**ICA**)、大腦中動脈的第1及第2段(**M1&M2**)、大腦前動脈(**ACA**)、基底動脈(**BA**)和脊椎動脈(**VA**)。
- ✓ 美國國衛院腦中風評估表(NIH Stroke Scale)評分**≥8 and ≤30**。

Tissue-Based Selection

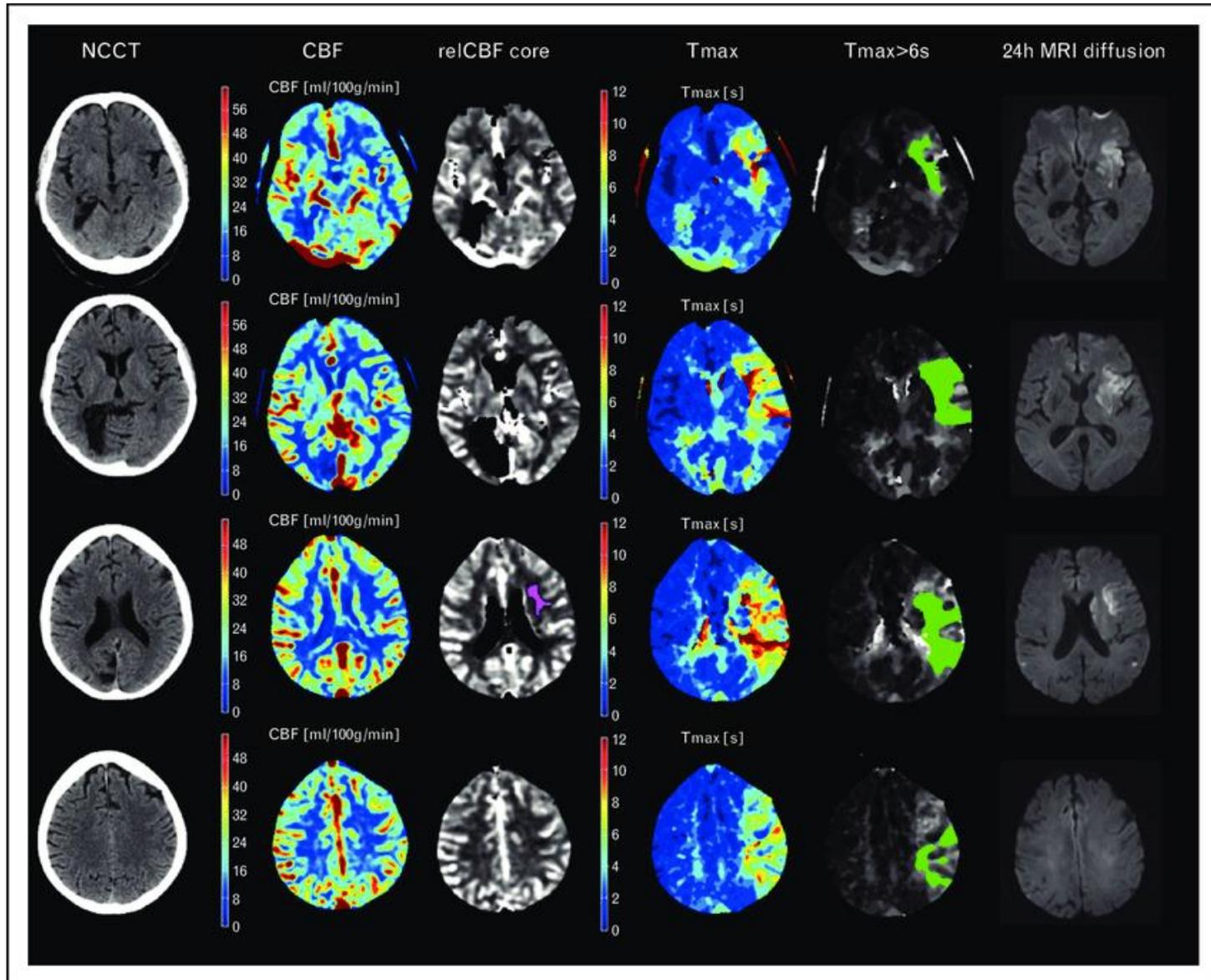


Penumbra

Infarct core



Time-based to Tissue-based patient selection



IVT with rt-PA in extended TW

	THAWS	WAKE-UP	ECASS4	EXTEND
Selection tools	DWI/FLAIR	DWI/FLAIR	DWI/PWI	DWI/PWI CBF/Tmax
Time of onset	4.5H from wake-up	4.5H from wake-up	4.5-9H WUS	4.5-9H WUS
mRS 0-1 (OR)	0.97	1.61 (p=0.02)	NA	1.44 (p=0.04)
mRS 0-2 (OR)	0.97	NA	1.34	1.36 (p=0.02)
sICH	1.4 vs 0%	2 vs 0.4% (P=0.15)	1.6 vs 0%	6.2 vs 0.9% (p=0.05)
Mortality	2.8 vs 3.3%	4.1 vs 1.2% (P=0.07)	11% vs 6.8%	11.5 vs 8.9%

EVT in extended TW

	DAWN	DIFFUSE 3
Selection tools	Clininal-Core	RAPID CBF/Tmax
Time of onset	6-24H	6-16H
mRS 0-2	RD 33%	OR 2.67
sICH	7 vs 4%	6 vs 3%
Mortality	14 vs 26%	19 vs 18%

Tissue-based patient selection is supported by current guidelines

IVT

<p>3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR.</p>	IIa	B-R	New recommendation.
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EVT

3.7.3. 6 to 24 Hours From Onset	COR	LOE	New, Revised, or Unchanged
<p>1. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.</p>	I	A	New recommendation.
<p>2. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.</p>	IIa	B-R	New recommendation.

**Is rt-PA still necessary in
such an EVT era?**

Bridging Therapy

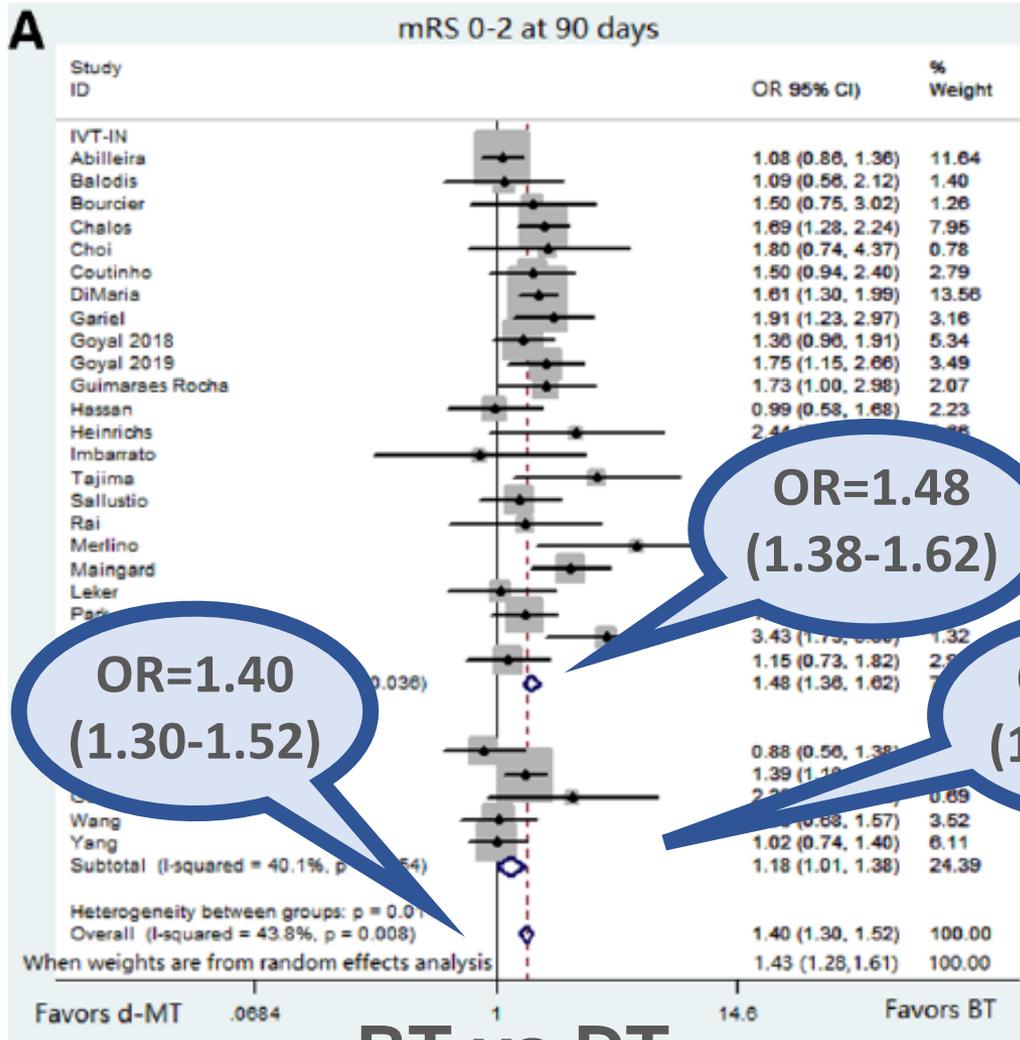
- ✓ Faster initial reperfusion therapy
- ✓ Supported by current guidelines
- ✓ Fragmentation of thrombus?
- ✓ Reduce embolus in new territory?

Direct EVT

- ✓ Faster door to puncture time
- ✓ IAT alone is cheaper
- ✓ IV rt-PA provides no additional benefits?
- ✓ IV rt-PA increases BBB disruption → increases bleeding?

What did previous studies say?

Updated meta-analysis
30 studies, N=12,082



What did current guidelines say?

3.7.1. Concomitant With IV Alteplase	COR	LOE	New, Revised, or Unchanged
1. Patients eligible for IV alteplase should receive IV alteplase even if mechanical thrombectomy is being considered.	I	A	Recommendation reworded for clarity from 2015 Endovascular. See Table XCV in online Data Supplement 1 for original wording.

2019 ASA/AHA guideline

1. 疑似或確診大血管阻塞之急性缺血性腦中風患者，可能或將進行動脈內取栓術前，若符合靜脈施打血栓溶解劑條件，可先施打靜脈血栓溶解劑治療(Class IIa; Level of Evidence A)。

2019 TSS guideline

RCTs data have been published :

DIRECT - MT vs DEVT vs SKIP
MR CLEAN - NO IV
SWIFT - DIRECT

N Engl J Med 2020; 382:1981-1993

JAMA 2021; 325: 244-253

JAMA 2021;325: 234-243

	DIRECT-MT	SKIP	DEVT	MR CLEAN-NO IV	SWIFT DIRECT
Main inclusion criteria	Age ≥18 years, mRS of 0 or 1 before onset ICA, MCA-M1, or M2 occlusion on CTA NIHSS: ≥2 ASPECTS: no limit Onset to IV rt-PA ≤4 hours 30 min	Age ≥18 and <86 years, mRS of 0, 1 or-2 before onset ICA or MCA-M1 occlusion on CTA or MRA NIHSS: ≥6 ASPECTS: DWI ≥5, CT ≥6 Onset to puncture <4 hours	Age ≥18 years, mRS of 0 or 1 before onset ICA or MCA-M1 occlusion on CTA or MRA NIHSS: no limit ASPECTS: no limit Onset to randomization ≤4 hours 15 min	Age ≥18 years, mRS of 0 or 1 before onset ICA or MCA-M1 or proximal M2 occlusion on CTA or MRA NIHSS: ≥2 ASPECTS: no limit	Age ≥18 years, mRS of 0 or 1 before onset ICA or MCA-M1 occlusion or both on CTA or MRA NIHSS of ≥5 and <30 ASPECTS: DWI/CT ≥4 Onset to randomization ≤4 hours 15 min
Treatment	MT (n=327) IVT before MT (n=329)	MT (n=101) IVT before MT (n=103)	MT (n=116) IVT before MT (n=118)	MT (n=273) IVT before MT (n=266)	MT (n=201) IVT before MT (n=207)
rt-PA	Alteplase, 0.9 mg/kg	Alteplase, 0.6 mg/kg	Alteplase, 0.9 mg/kg	Alteplase, 0.9 mg/kg	Alteplase, 0.9 mg/kg
Country	China	Japan	China	Europe	North America and Europe
Study Design	Non-inferiority,	Non-inferiority	Non-inferiority	Superiority (non-inferiority as secondary outcome)	Non-Inferiority
Non-inferiority margins	mRS shift with a non-inferiority margin OR 0.80	mRS 0-2 with a non-inferiority margin OR of 0.74	mRS 0-2 with a non-inferiority margin of 10%	mRS shift with a non-inferiority margin OR 0.80	mRS 0-2 with a non-inferiority margin of 12%
Result	non-inferiority shown	non-inferiority NOT show	non-inferiority shown	Neither superiority nor non-inferiority shown	non-inferiority NOT show

Factors Potentially Favoring Primary Thrombectomy:

Lower Chances of Reperfusion or Benefit with IVT:

- Long Clots (≥ 8 mm)¹⁵
- Low Clot Burden Scores¹⁶
- More Proximal Occlusions (ICA)¹⁷
- Tandem Occlusions¹⁸
- Absence of HDVS³¹
- Longer Times from Stroke Onset^{19, 20}
- ? Calcific Emboli

Higher Chances of Complications with IVT:

- Large Infarct Sizes/ Low ASPECTS^{21, 22}
- Antiplatelet or Anticoagulant use^{23, 24}
- Very Old Patients²³
- Severe Hyperglycemia²³
- Microbleeds/ Amyloid Angiopathy²⁴
- Severe Leukoaraiosis²⁵
- ICA/ Proximal M1 Occlusions worsened Perfusion from Clot Fragmentation²⁶
- Full Basal Ganglia Infarcts²⁷

? Requirement for Peri-Procedural Anti-Thrombotics:^{23, 24}

- Intracranial Atherosclerotic Disease
- Tandem Occlusions
- Dissections
- Calcific Emboli (due to potential need for stenting rescue)

Geographic and Center Specific Characteristics:

- High IVT Costs
- Fast Local MT Workflow²⁸
- Neuroendovascular Team immediately available

Factors Potentially Favoring Mothership Bridging:

Higher Chances of Reperfusion or Benefit with IVT:

- Very Early Time Window^{19, 20}
- Short Dense Clots (< 8 mm)^{15, 31}
- More Distal Thrombus Location¹⁷
- Higher Residual Flow/ Thrombus Permeability¹⁷
- Good Collaterals³²

Lower or Uncertain MT versus IVT Benefit:

- Low Stroke Severity (NIHSS < 10)⁵
- MCA-M2 Occlusions⁵
- Distal Occlusions (ACA, PCA, M3)
- Multi-territorial infarcts complicating MT

Expected Delays in Endovascular Reperfusion:

- Unfavorable Vascular Anatomy¹⁴
- Expected Unusual Delays related to the of Sedation or General Anesthesia

Geographic and Center Specific Characteristics:

- Low IVT Costs
- Prolonged Local MT Workflow
- Neuroendovascular team not in-house/ immediately available

- Hyperdense artery sign at CT

Thank you for your attention!

- ✓ **DOAC, IVT, EVT** are the 3 major progress in IS treatment in the recent decades.
- ✓ **Time is brain!**
- ✓ The era of **tissue-based selection** for reperfusion therapy.
- ✓ **Bridging therapy** is still the current standard.
- ✓ Direct EVT **might** be considered in certain patients (fast availability, large clot burden, easy approach...).