Safer Care Victoria

2 August 2022

Clinical Conversation: Optimising hyper-acute stroke care

Stroke Clinical Network

Hosted by A/Prof Ben Clissold, Stroke Clinical Lead, Safer Care Victoria

OFFICIAL

VICTORIA State Government

Acknowledgement of Country

I acknowledge the Traditional Custodians who have lived and loved this country through the vastness of time.

I honour the Bunurong People, whose country I stand on today. I pay my respects to the old people, to the Elders and Ancestors who are the safekeepers and caretakers of the oldest living culture on the planet.

For this is the very bedrock of this place, our shared home and our special identity in the world and the source of shared pride as Australians.

For this land always was, and always will be, Aboriginal Land.

Artwork by Anmatyerr woman, Tradara Briscoe

Before we begin

This session will be recorded and made available on the SCV website and sent to Network members

Streamlining pathway to reperfusion: Pre-hospital

Skye Coote

Nurse Practitioner; Nursing Lead Melbourne Mobile Stroke Unit


elbourne
Mobile Stroke Unit
FAST
FACE
ARMS
SPEECH
TIME
Act FAST call 000
PARAMEDIC
EMERGENCY
000
NEUROSCIENCE FOUNDATION
Stroke
VICTORIA
THE FLOREY
20


The Royal Melbourne Hospital


PARAMEDIC


FACE
drooped?


ARMS
can't be raised
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slurred or confused
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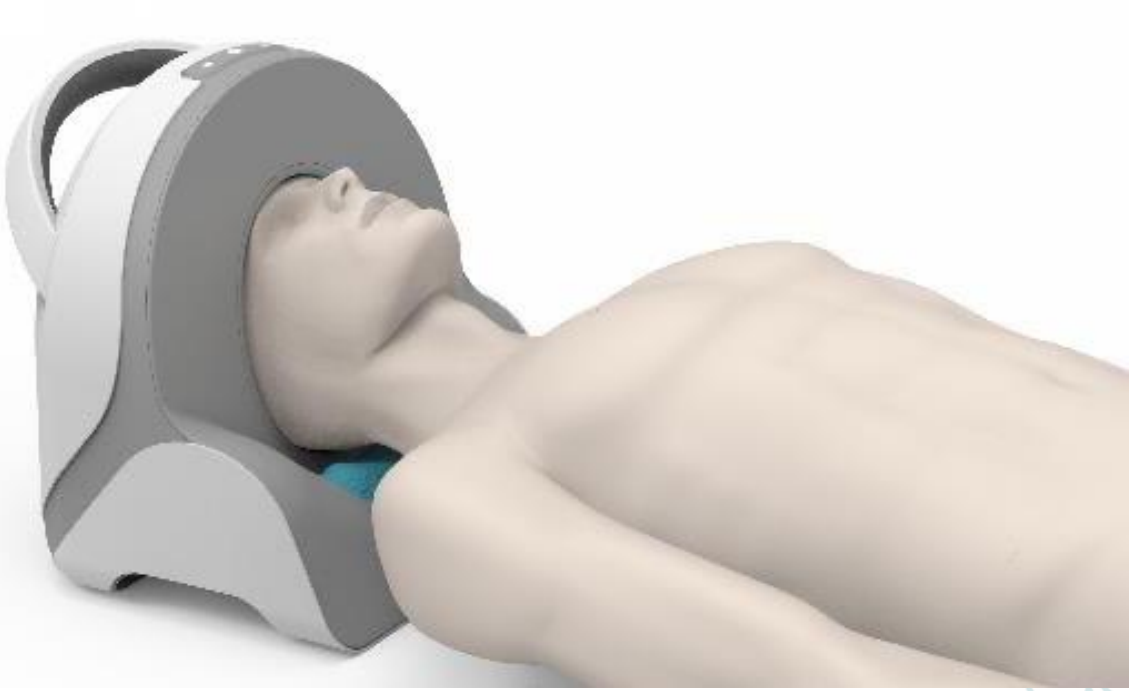

Stroke Capable Ambulances

Non-MSU ambulances


Effective code strokes start outside the hospital

Code Stroke processes reduce Door-Needle times

Helsinki measures reduced DTN times to 20 mins (median)

Implemented at the RMH

Reduced DTN times to 25 mins

Largely accepted and implemented in stroke capable hospitals

Table 1 Twelve measures to reduce treatment delays

Measure	Description	Year
EMS involvement	Education of dispatchers and EMS personnel, stroke high-priority dispatch	1998
Hospital prenotification	EMS contacts stroke physician directly via mobile phone	2001
Alarm and preorder of tests	Laboratory and CT computer-ordered and alarmed at prenotification	2001
No-delay CT interpretation	Stroke physician interprets the CT scan, not waiting for formal radiology report	2001
Premixing of tPA	With highly suspect thrombolysis candidates, tPA premixed prior to patient arrival	2002
Delivery of tPA on CT table	Bolus administered on CT table	2002
CT relocated to ER	Patient transfers of several hundred meters, including elevators, were no longer needed	2003
CT priority and CT transfer	CT emptied prior to patient arrival, and patient transferred straight onto CT table, not ER bed	2004
Rapid neurologic evaluation	Patient is examined upon arrival, on CT table	2004
Preacquisition of history	Statewide electronic patient records and eyewitness interview before/during transportation	2005
Point-of-care INR	Laboratory personnel draw blood while patient on CT table, and perform instant POC INR	2005
Reduced imaging	While all patients have a CT, advanced imaging reserved for unclear cases only	2005

Neurology. 2012 Jul 24;79(4):306-13. Neurology. 2013 Sep;81(12):1071-1076

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Neurology. 2012 Jul 24;79(4):306-13.

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Pre-hospital management

Notification

- Patient name
- Patient age
- Onset time
- Presenting symptoms
- Key medical or medication history
  - Anticoagulants
  - Residential aged care
  - Major surgery

Observations

- Only if abnormal or noteworthy
- GCS can be an immediate indicator of localisation coupled with symptoms

Pre-hospital notification is associated with improved outcomes

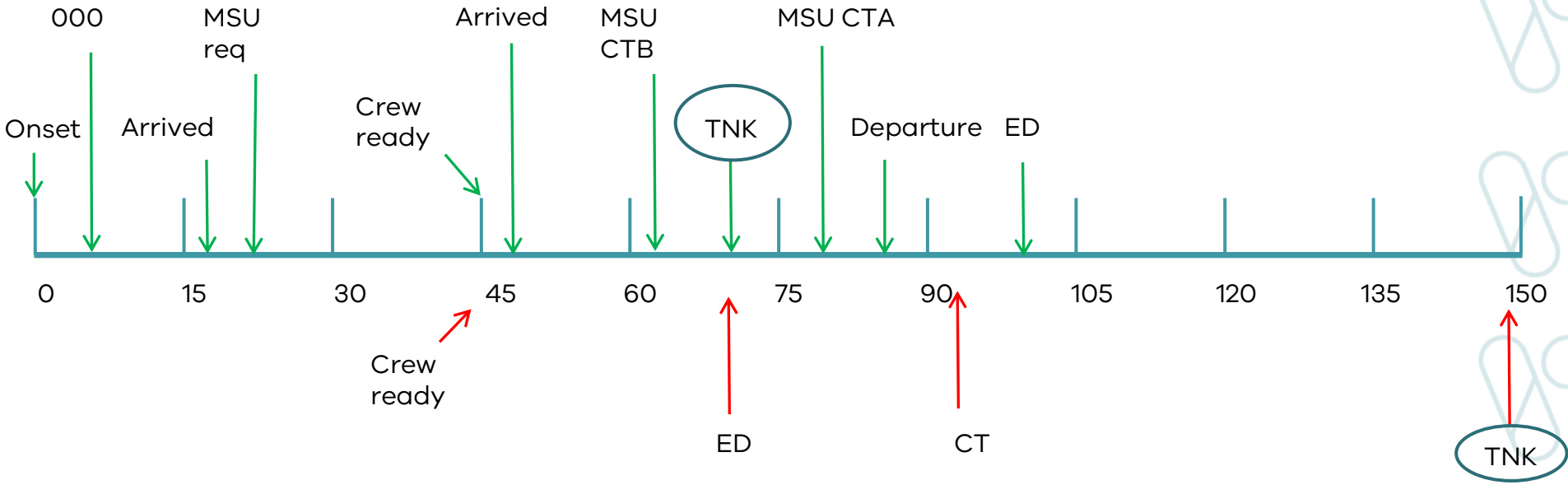
Table 1. Baseline characteristics of intravenous r-tissue plasminogen activator treated patients regarding prehospital notification status.

Characteristics	Prehospital notification		p-value
	Yes (n = 131)	*No (n = 115)*	
Age, years and median (IQR)	67 (58–75)	66 (55–77)	0.274
Male, n (%)	66 (57.4%)	72 (55.0%)	0.702
Baseline National Institutes of Health Stroke Scale, median (IQR)	15 (10–20)	11 (7.5–17)	<0.001
Onset to emergency department arrival time (min)	83 (55–121)	78 (50–120)	0.462
Door-to-CT time, min and median (IQR)	15 (10–25)	25 (18–45)	<0.001
Door-to-needle time, min, median (IQR)	42 (34–56)	70 (53–95)	<0.001

	Prenotification ($n = 727$)	No prenotification ($n = 201$)	*p*-value
Total prehospital time, median	22.5 (18.5–26.0)	22 (17.5–26.5)	0.433
Door to CT time, median	13 (10.0–18.0)	19 (13.0–34.0)	<0.001
Door to CT time ≤ 25 min	660 (90.8 %)	125 (62.2 %)	<0.001
Door to needle time, median	63 (49.0–79.0)	68 (54.0–86.0)	0.138
Door to needle time ≤ 60 min	65 (45.1 %)	7 (28.0 %)	0.110
Administering thrombolytic therapy	144 (19.8 %)	25 (12.4 %)	0.017

	Total (n=252)	Hotline group (n=218)	Non-hotline group (n=34)	P value
Primary outcome				
Good neurological outcome at 90 days, n (%)	102 (40.5)	94 (43.1)	8 (23.5)	0.030
Secondary outcomes				
Hospital arrival to t-PA time[a], median (IQR), min	31 (24 to 41)	30 (24 to 38)	48 (37 to 65)	<0.001
Hospital arrival to groin puncture time, median (IQR), min	42 (33 to 57)	40 (32 to 54)	76 (50 to 97)	<0.001
Hospital arrival to recanalization time, median (IQR), min	90 (69 to 136)	88 (67 to 127)	121 (83 to 176)	0.003
t-PA use, n (%)	141 (56.0)	127 (58.3)	14 (41.2)	0.062
Successful recanalization (modified TICI2b-3), n (%)	225 (89.3)	193 (88.5)	32 (94.1)	0.33

Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine (2016) 24:57 **Scientific Reports** | (2022) 12:1010 ***Future Neurol.*** (2018) 13(1), 5–11



78 mins faster

Streamlining pathway to reperfusion: Emergency department

Dr Philip Choi & Tanya Frost

Head of stroke services, Eastern Health

Acute stroke nurse, Eastern Health


London Evening Standard

Thursday 20 October 2016 | FREE | standard.co.uk

ES Magazine

Russell Brand on looking forward to fatherhood

PLUS London's newest all-night party pits

Available today and tomorrow

WEST END FINAL

STROKE PATIENTS 'BROUGHT TO LIFE'

REVOLUTIONARY NEW TREATMENT AT LONDON HOSPITAL

GIRL RECOVERS ON OPERATING TABLE AND CAN SPEAK AGAIN

EXCLUSIVE

Ross Lydall Health Editor

CRITICALLY ill patients left paralysed by strokes are being "brought back to life" on the operating table by a ground-breaking rapid-response treatment at a London hospital.

Doctors revealed to the Standard that people left unconscious or unable to speak or move by major strokes are making dramatic – sometimes almost instant – recoveries due to the first 24/7 UK centre offering a revolutionary procedure.

Experts say that getting the time-critical treatment within hours after a stroke can be the difference between a full recovery and serious disability or even death.

A girl of 17 was the first to receive the new "gold standard" out-of-hours care at St George's Hospital, Tooting, after being rushed late at night from Surrey when conventional clot-busting drugs failed to work.

She was unable to speak or move one side of her body – but suddenly recovered on the operating table when doctors fed a 3ft-long catheter wire through her groin to "fish out" life-threatening blood clots in her brain.

Consultant neurologist Dr Bhavini Patel said: "The whole of her right side had no power. She was mute. As soon as the

Continued on Page 4

Challengers: Donald Trump has refused to commit to accepting the US Presidential election result if he loses. His Democratic rival Hillary Clinton, seen with him after their final TV debate today, described his stance as "horrifying" REPORT, Pages 10 & 11

TRUMP: I COULD REJECT RESULT

Inside

City plea for visa deal for skilled staff PAGE 2

Hero wife: Tube thug was rude PAGE 5

Sport

England fight back after top order fails PAGE 76

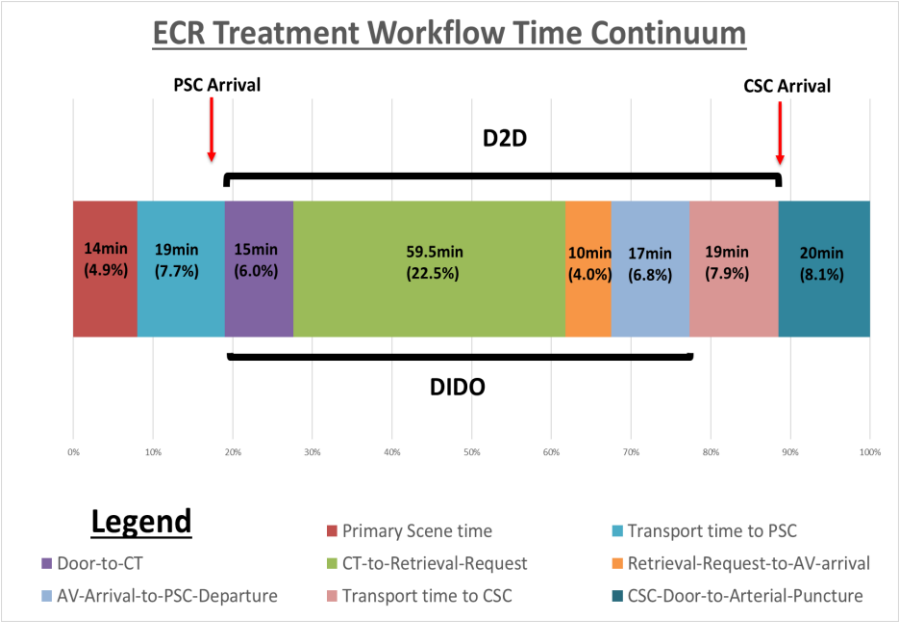
2016

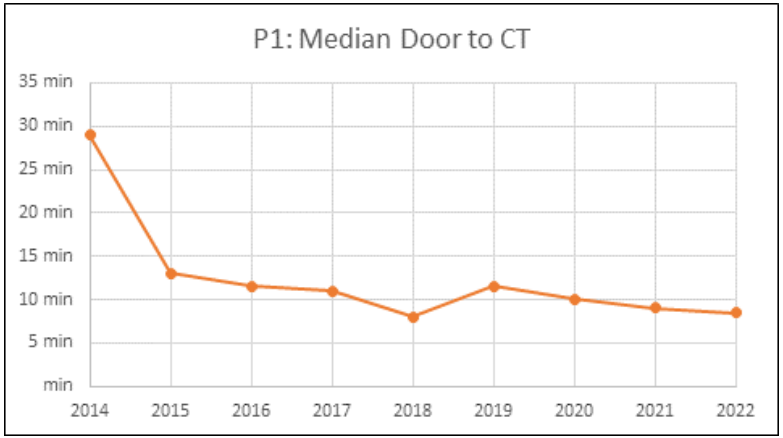
2017

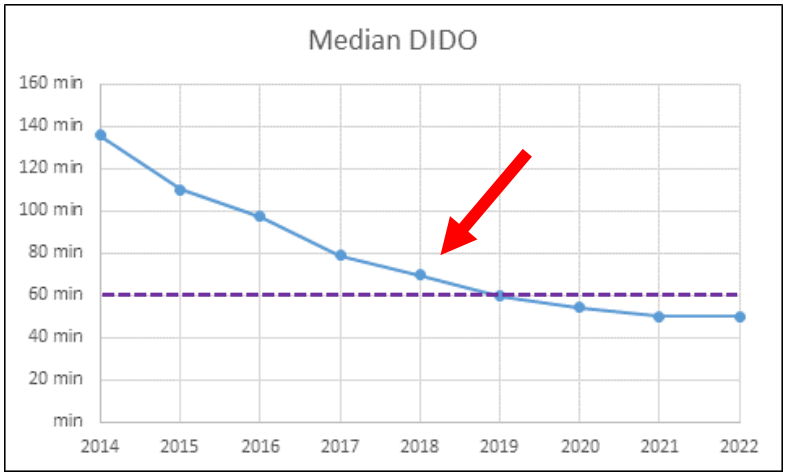
Door-in-Door-out time:

U.S: 104.5 mins

Running time of Finding Nemo is...

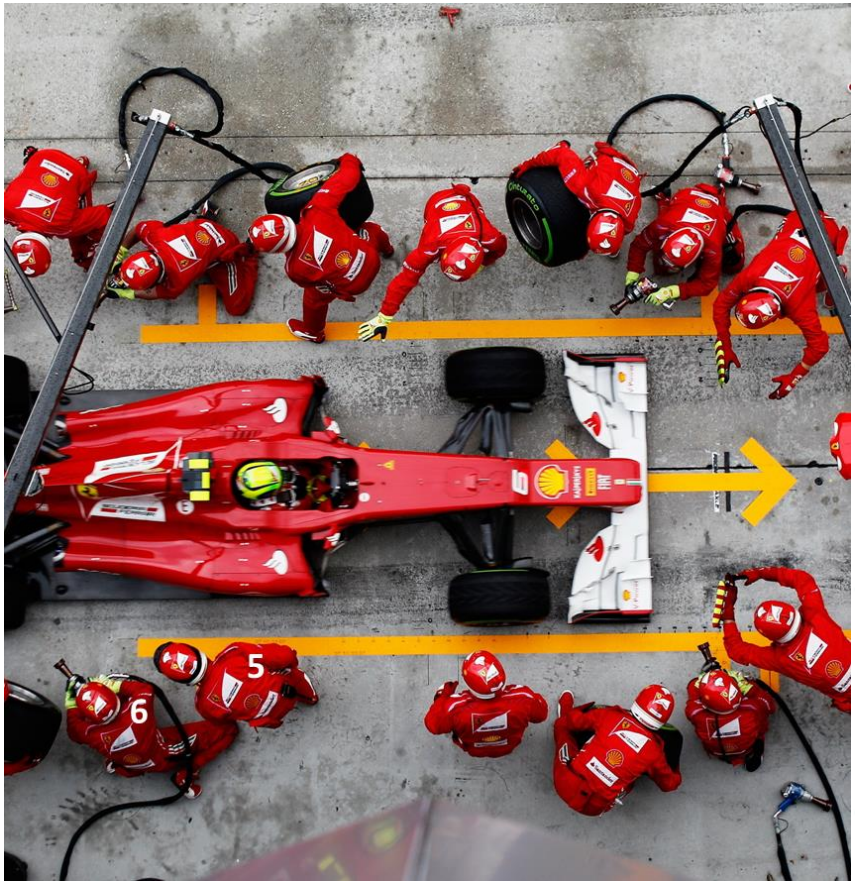






Ross Cody, unpublished

Eastern Health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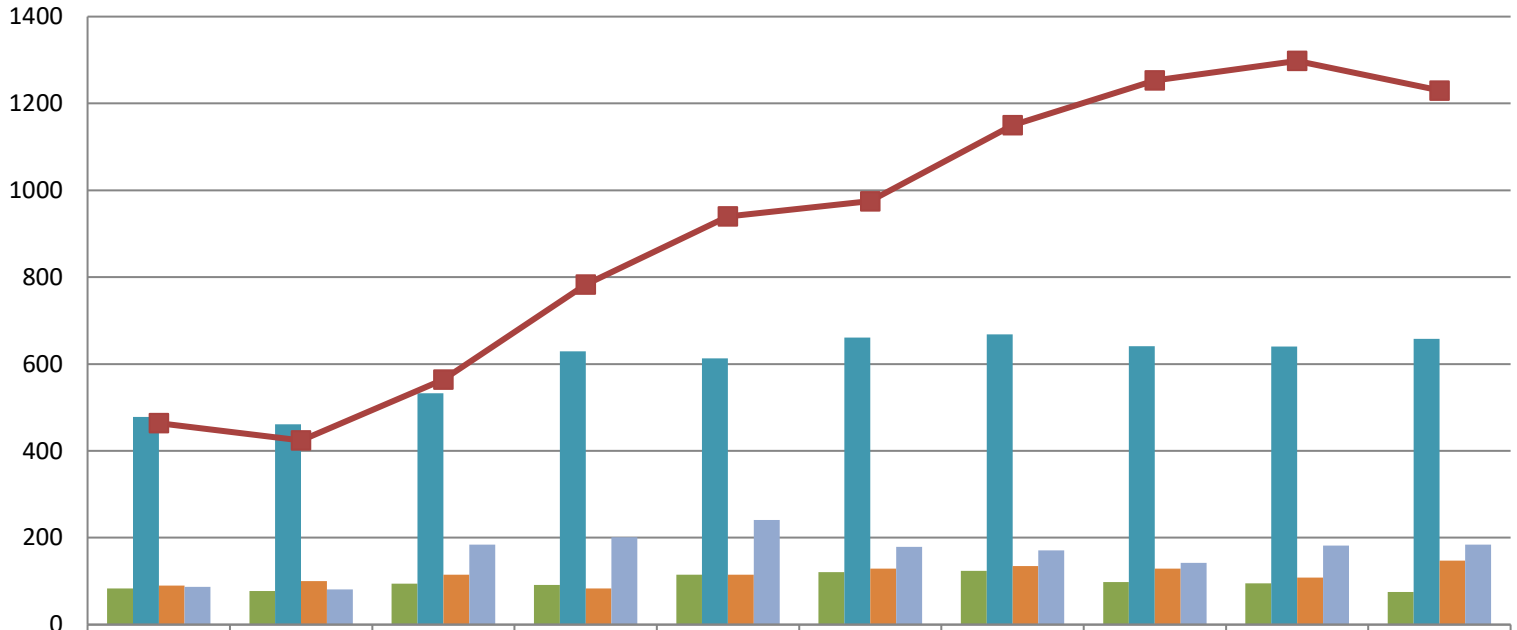
QI Activities

- CT – Images, transfer, length of time
- Workflow- codes - roles/CT/ASU/Ambulance
- Triage Processes- flow chart
- Code Stroke Forms
- Feedback of KPI's- ED, ward, management
- Monitor for themes
- Know your data
- Team Consistency
- Communication- right people right room
- Review of practice: Know your IQR
- Expectations of excellence
- Continuous quality improvement – how long does it really take?

Stroke Service 2011-2020



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
t-PA	83	77	94	91	115	121	124	98	95	75
Ischaemic Stroke	478	461	533	629	613	661	668	641	640	658
Haemorrhagic Stroke	90	100	115	83	115	129	135	129	108	147
TIA	87	81	184	201	241	179	171	142	182	184
Code Stroke	464	424	564	783	940	975	1150	1253	1298	1230

Thrombolysis beyond 4.5 hours and Thrombectomy beyond 6 hours of stroke onset

Professor Henry Ma

Director of Neurology, Head, Stroke Unit, Monash Health

Professor, Department of Medicine, Monash University

Acute Reperfusion Therapy

- Acute ischemic stroke is due to occlusion of the vessel(s) supplying the brain

- The concept of Ischemic Penumbra – salvage the brain

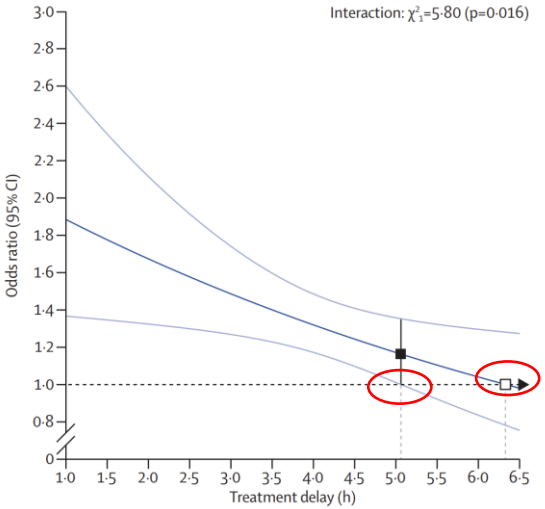
- Time is Brain – need to open up the vessel as soon as possible

Thrombolysis < 4.5 hours from Stroke Onset

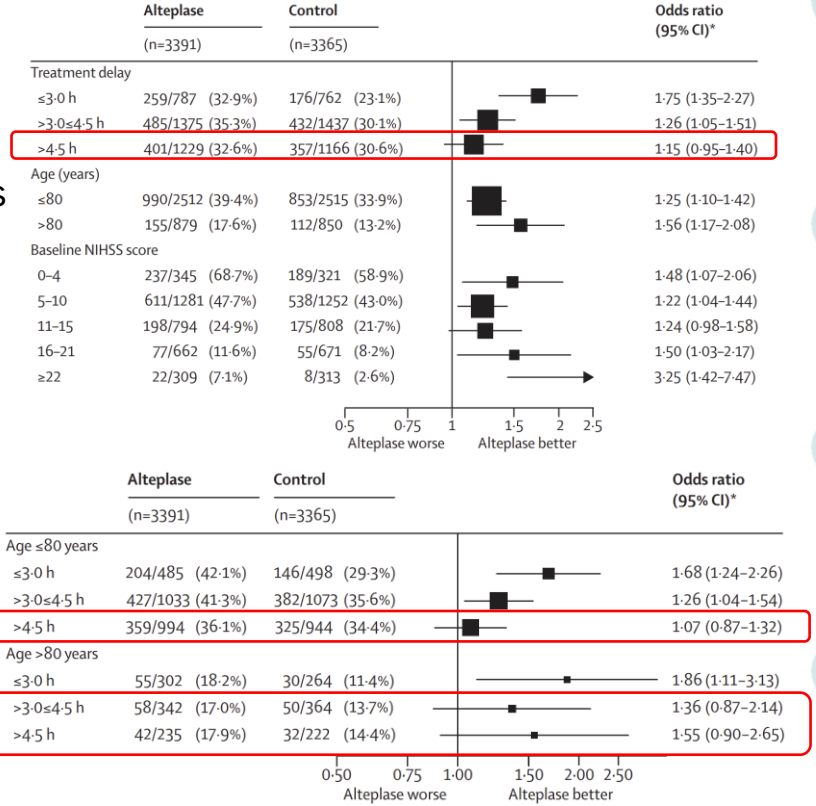
NINDS =< 3 hours of stroke onset

ECASS 3 3 – 4.5 hours of stroke onset

Emberson et al 9 tPA clinical trials analysis



Used **non-contrast** CT Brain to assess patients



Excellent Clinical outcome mRS 0-1

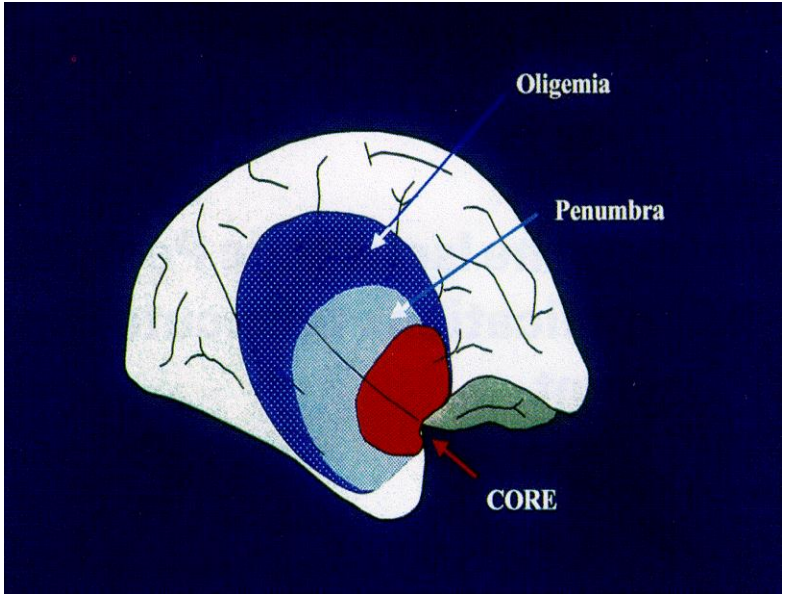
Lancet 2014; 384: 1929–35

Excellent Clinical outcome mRS 0-1

Extending the re-perfusion time window
Enriched Cohort
The principle – the ischemic penumbra

- Identify patient with the ischemic penumbra and salvage it

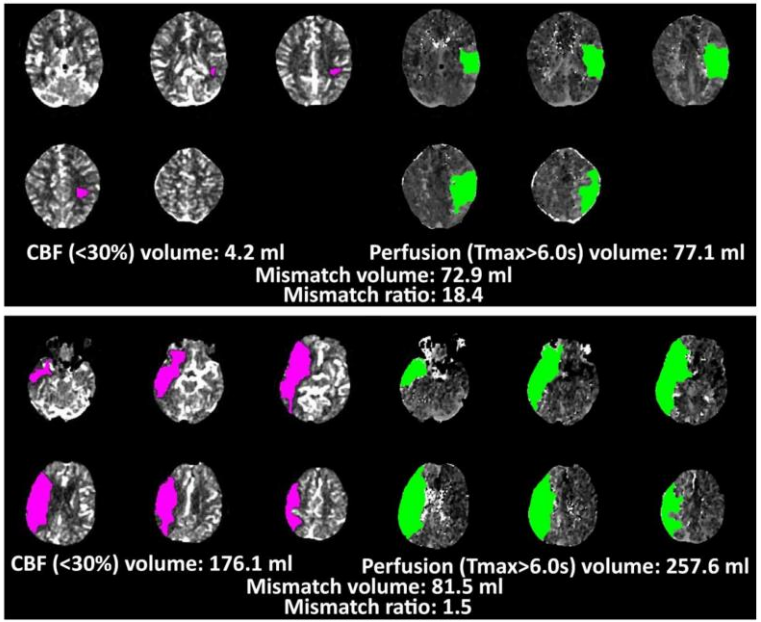
- Patients without the ischemic penumbra are less likely to benefit from reperfusion therapy



Baron JC. Cerebrovas Dis 1999;9:193-201 Fig1

Thrombolysis 4.5 – 9 Hours from stroke onset and Wake Up Stroke – Perfusion imaging

CT Perfusion



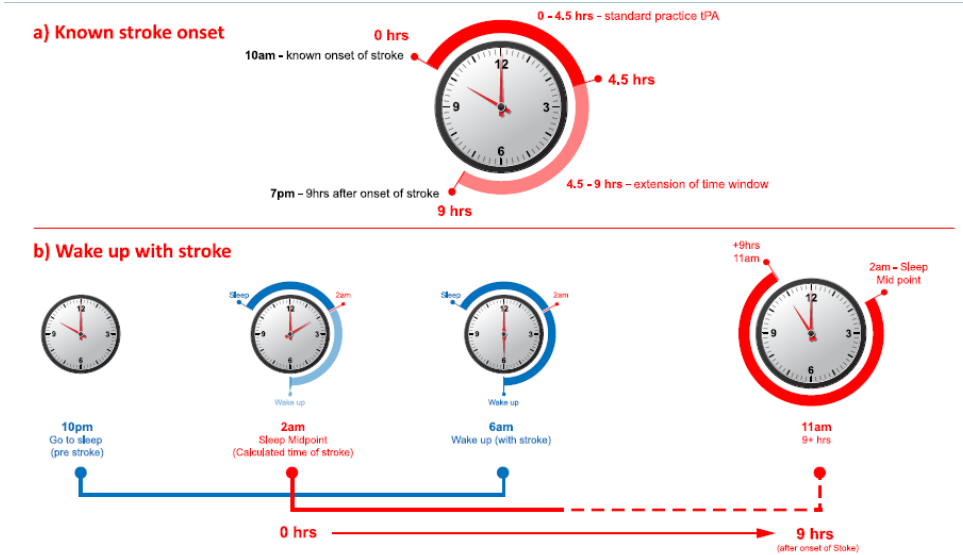
Aim to identify penumbral tissues (Benefit) and core (risk)

ANN NEUROL 2017;81:849–856

Thrombolysis 4.5 – 9 Hours from stroke onset and Wake Up Stroke – Perfusion imaging

EXTEND

EXtending the time for Thrombolysis in Emergency Neurological Deficits



RAPID* automated CT perfusion or MR perfusion

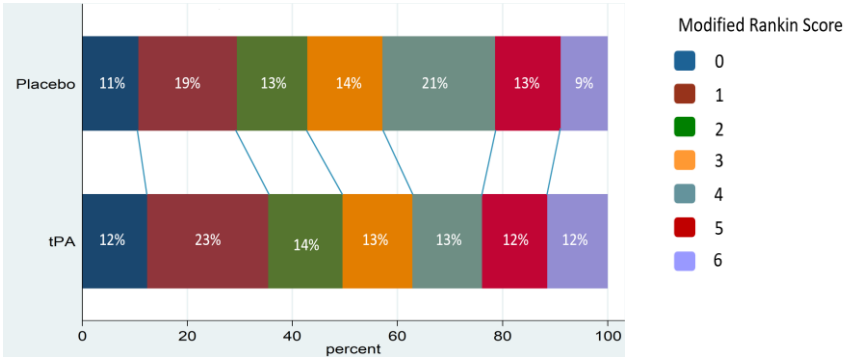
- **Penumbral mismatch criteria**

1. Hypoperfusion to core volume ratio > 1.2
2. Perfusion lesion - core absolute difference >10 ml
3. Ischaemic core lesion volume ≤70 ml

Need to have a clinically relevant penumbra

Thrombolysis 4.5 – 9 Hours from stroke onset and Wake Up Stroke – Perfusion imaging

EXTEND



mRS -0-1

Adjusted Relative Risk **1.44** (95%C.I. 1.01, 2.06) **P=0.04**

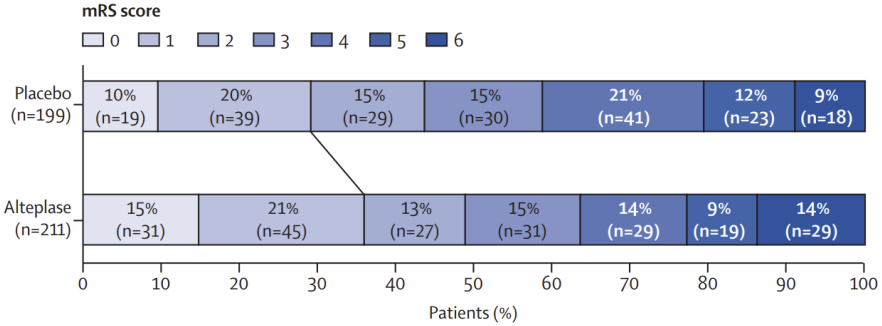
Death at 90 days

- **Adjusted Relative Risk: 1.17 (CI 0.57, 2.4) p=0.67**

Symptomatic Intracranial Haemorrhage at 36 hours

- **Adjusted Relative Risk 7.22 (CI 0.97, 53.54) p =0.053**

Pooled Analysis: EXTEND EPITHET ECASS 4



mRS 0-1

36% vs 29% adjusted OR 1.86 (95% CI 1.15 – 2.99) P=0.011

Death at 90 days

- **Odd Ratio 1.55 (CI 0.81, 2.97) p=0.19**

Symptomatic Intracranial Haemorrhage at 36 hours

- **Odd Ratio 9.70 (CI 1.23, 76.55) p =0.03**

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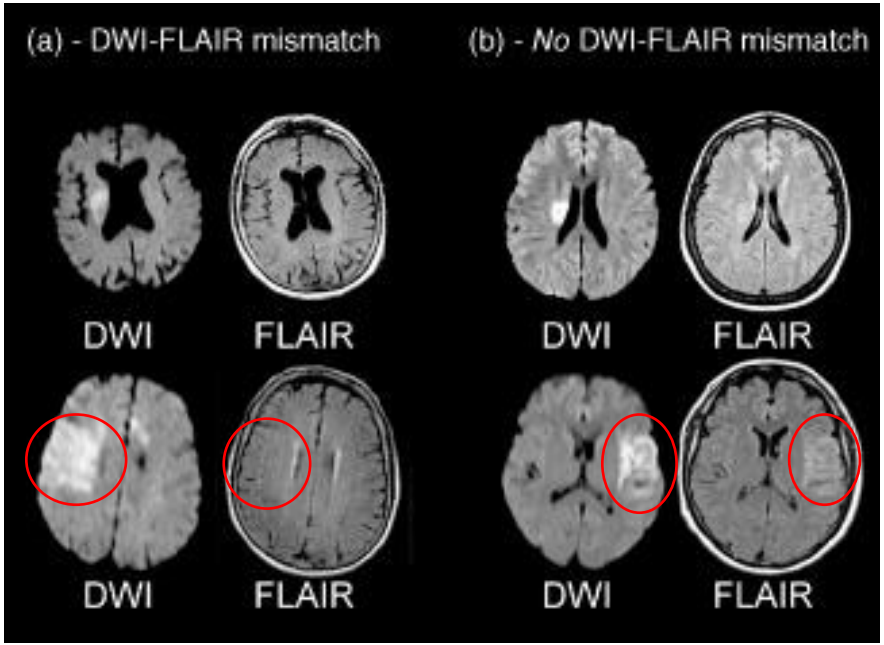
Stroke with unknown time of onset
DWI:FLAIR Mismatch

YES



NO

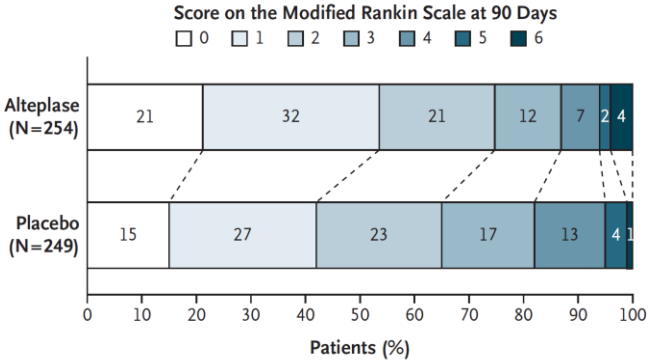
DWI-FLAIR Mismatch

Thomalla et al. Mar 2013 · International Journal of Stroke

Stroke with unknown time of onset

Within 4.5hour of wake up with symptoms or found to have symptoms but the exact time of onset unclear

WAKE UP



Favourable outcome 0-1 mRS

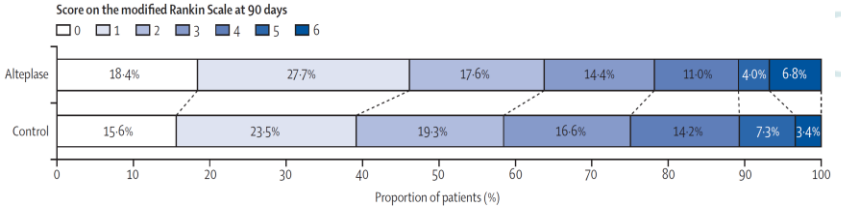
53.3% vs 41.8% aOR 1.61 p=0.02

Symptomatic ICH

Adjusted Odd Ratio 4.95 (0.57-42.87) p=0.15

NEJM 16 May 2018

EOS pooled analysis of WAKEUP, EXTEND, THAWS, ECASS4 and MR Witness



Favourable outcome 0-1 mRS

Adjusted Odd Ratio 1.49 (1.1-2.03) p=0.011

Symptomatic ICH

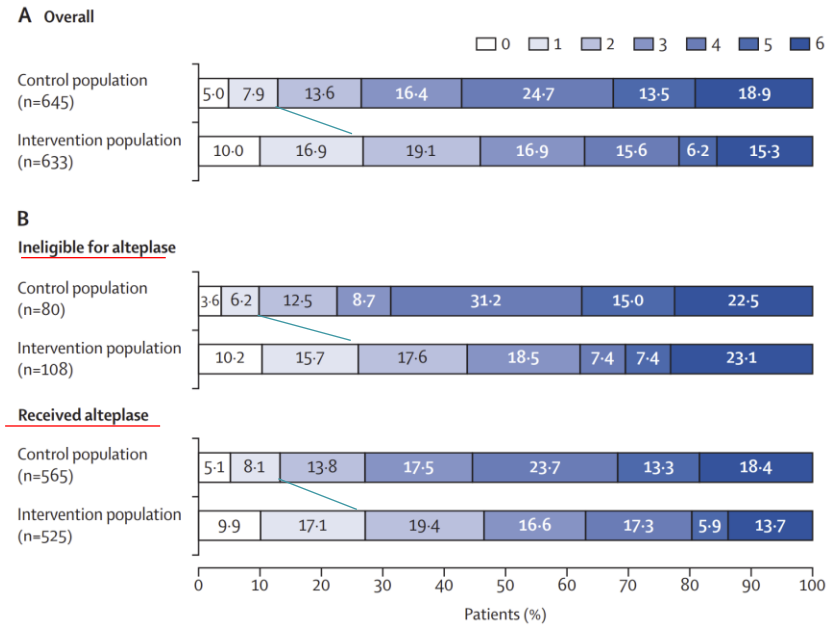
Adjusted Odd Ratio 5.58 (1.22-25.05) p=0.024

LANCET Nov 8 2020 published online

Thrombectomy < 6 Hours

HERMES: 5 trials EXTEND IA, ESCAPE, MR CLEAN, SWIFT PRIME, REVASCAT

Stroke onset within 12 hours (imaging selection used in < 6 hours)



mRS 0-1 (Excellent Functional Outcome)

Control 12.9% Intervention 26.9%

Adjusted odds ration 2.72 (1.99-3.71) P <0.0001

Symptomatic ICH

Control 4.3% Intervention 4.4%

Adjusted odds ratio 1.07 (0.62-1.84) p = 0.81

Mortality

Control 15.3% Intervention 18.9%

Adjusted odds ratio 0.732 (0.47-1.13) p=0.16

Lancet 2016; 387: 1723–31

Thrombectomy 6 - 24 hours

DAWN

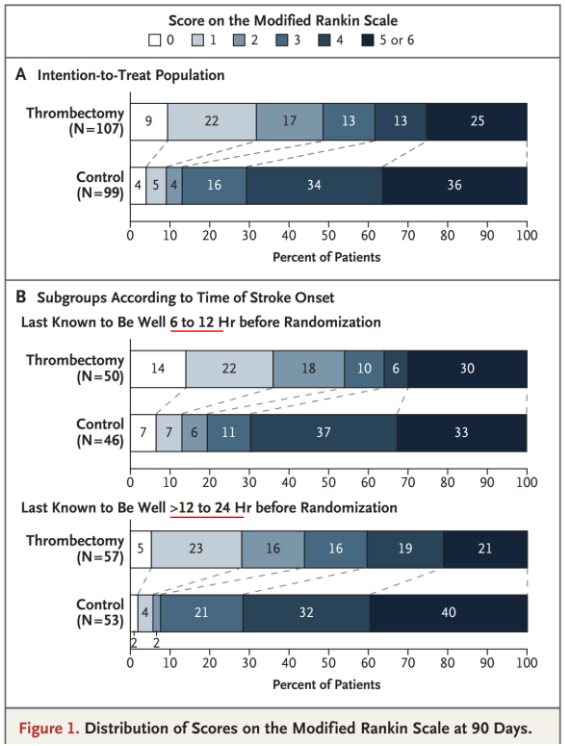


Figure 1. Distribution of Scores on the Modified Rankin Scale at 90 Days.

DAWN

Based on clinical severity and infarct volume mismatch based on aged group (80 yo younger or older)

DEFUSE 3

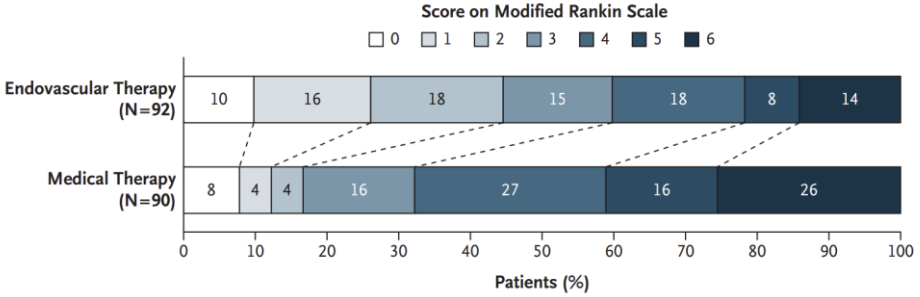
6-16 hours

Based on Perfusion mismatch (RAPID)

Infarct < 70ml

Mismatch ratio 1.8

DEFUSE 3



DEFUSE 3

mRS 0-2

45% vs 17% p<0.001

Mortality 90 days

14% vs 26% p=0.05

Symptomatic ICH

7% vs 4% p=0.75

DAWN

Mean score of utility weighted mRS 90 days

5.5 vs 3.4

Symptomatic ICH

6% vs 3% p=0.5

Mortality 90 days

19% vs 18% p=1

N Engl J Med 2018;378:11-21.

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N Engl J Med 2018;378:708-18.

Summary: NSF Guideline for extended time window

Thrombolysis

Strong recommendation

For patients with potentially disabling ischaemic stroke who meet perfusion mismatch criteria in addition to standard clinical criteria, intravenous alteplase (dose of 0.9 mg/kg, maximum of 90 mg) should be administered up to 9 hours after the time the patient was last known to be well, or from the midpoint of sleep for patients who wake with stroke symptoms, unless immediate endovascular thrombectomy is planned. (Ma et al 2019 [64], Campbell et al 2019 [58])

Weak recommendation

For patients with potentially disabling ischaemic stroke of unknown onset time who meet MRI FLAIR-diffusion mismatch criteria in addition to standard clinical criteria, intravenous alteplase (dose of 0.9 mg/kg, maximum of 90 mg) may be administered (Thomalla et al 2019 [61]).

Thrombectomy

Strong recommendation

For patients with ischaemic stroke caused by a large vessel occlusion in the internal carotid artery, proximal middle cerebral artery (M1 segment), or with tandem occlusion of both the cervical carotid and intracranial large arteries, endovascular thrombectomy should be undertaken when the procedure can be commenced between 6-24 hours after they were last known to be well if clinical and CT perfusion or MRI features indicate the presence of salvageable brain tissue. (Nogueira et al. 2017 [71], Albers et al. 2018 [72])

https://app.magicapp.org/#/guideline/QnoKGn/section/EaWDdL

Questions need to be answered....

Strong recommendation

NSF Guideline

In selected stroke patients with occlusion of the basilar artery, endovascular thrombectomy should be undertaken. (Kumar et al. 2015 [86])

Posterior Circulation stroke

- Recent presentation at ESOC
- ATTENTION:
  - Chinese study within 12 hours of basilar artery occlusion
  - Thrombectomy vs best medical therapy (46% vs 23%)
  - Thrombectomy better functional outcome and lower mortality
  - Awaiting full publication

Thrombolysis beyond 9 hours

ETERNAL – up to 24 hours from stroke onset using TNK and perfusion selection in patients with large vessel occlusion

ETERNAL POSTERIOR

Thrombectomy in more distal vessels (Distal M2 and beyond)

A number of clinical trials underway

Large Infarct Core for thrombectomy

Ongoing trials

Thrombolytic eligibility and complications

Prof Bruce Campbell

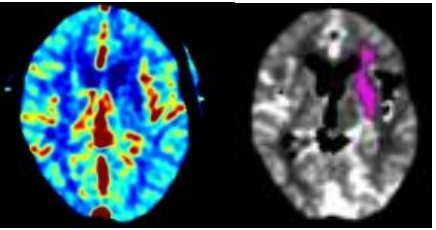
Director of Neurology & Stroke

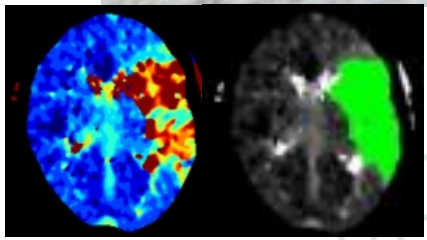
Royal Melbourne Hospital

Victorian Stroke Telemedicine Neurologist, Ambulance Victoria

Professor of Neurology, University of Melbourne

Chair of Clinical Council, Stroke Foundation, Australia





MELBOURNE BRAIN CENTRE at The Royal Melbourne Hospital

Stroke FOUNDATION

Ambulance Victoria OFFICIAL

RMH Comprehensive Stroke Centre

Outline

- Standardising & simplifying thrombolytic eligibility
- Role of lytics before thrombectomy
- Complications
    - symptomatic haemorrhagic transformation
    - malignant cerebral oedema
    - orolingual angioedema
- Primary ICH
- Concluding remarks

Thrombolytic Indications and Contraindications

Indications:

last known well <4.5h *or CTP-selected for 4.5-9hr/WUS*

potentially disabling deficit and potential quality of life benefit

Contraindications:

hemorrhage on CT brain

extensive hypodensity on CT brain (subacute infarct) – re-check onset time

recent/active bleeding, surgery or trauma – risk vs benefit, may be suitable for thrombectomy

irreversible anticoagulants

BP >185/105 or BSL <2.7mmol/L – fix then treat

Eliquis® apixaban

Xarelto® rivaroxaban

Thrombolytic Contraindications - detail

- **Previous hemorrhage?**
  -subdural many years ago – generally OK if scan normal now

- **Aneurysm/AVM?**
  -unruptured, incidental – limited experience but thought not to be a contraindication
  -clipped or coiled in past – regarded as secured

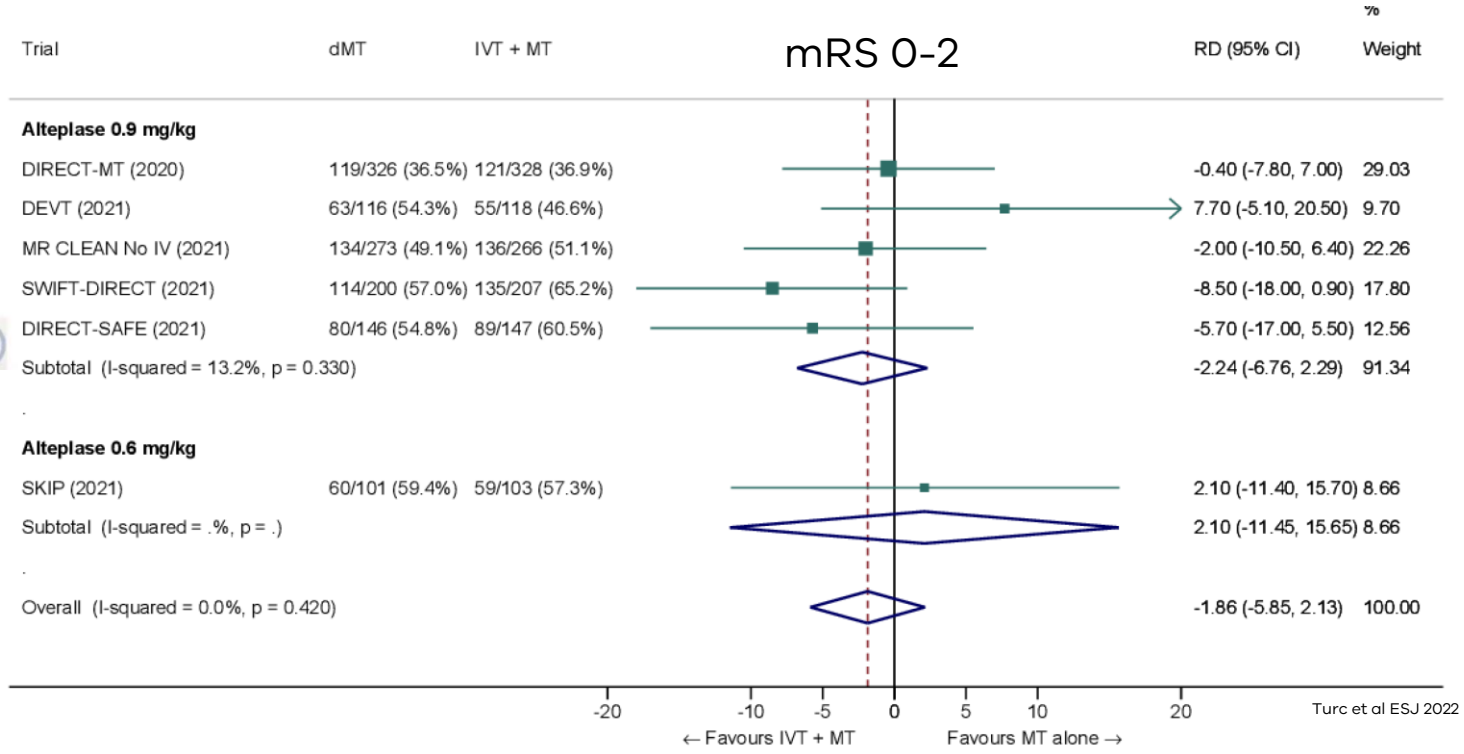
- **Brain tumour?**
  -meningioma not a problem
  -glioma/metastases can bleed - contraindication

- **Recent/active bleeding, surgery or trauma – risk vs benefit, IVT vs EVT**
  compressible sites are OK (e.g. skin lesions)
  cataract surgery – avascular – OK
  joint surgery – d/w ortho, often comfortable to lyse (may need to wash out)
  abdo/chest – riskier
  LP/epidural or non-compressible arterial puncture – 1 week?

Thrombolytic Contraindications - detail

- DVT prevention dose of enoxaparin – OK, therapeutic is not;
- INR <=1.7 OK, platelets <100 unknown, DOACS<48h - evolving
- aortic dissection – contraindication
- cervical artery dissection – OK
- known infective endocarditis - contraindication
- non-STEMI OK
- STEMI – probably OK – d/w cardiology, highest risk rupture after anterior STEMI
- Pregnancy – OK (risk is placental bleed), post-partum uncertain –consult O&G
- Menstruation – OK
- Lactation – no issue (but other factors may warrant pause)

Do we still need lytic before thrombectomy?



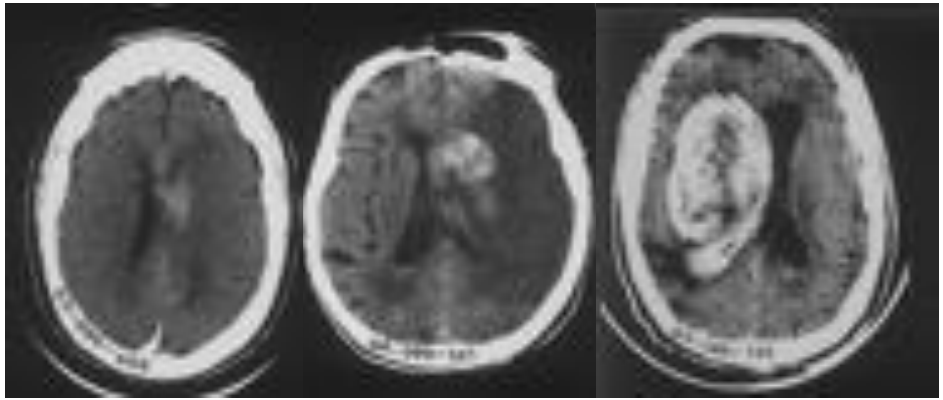
Why IV thrombolytics are still important before thrombectomy?

- "Direct" trials only enrolled patients at EVT centres (not applicable to transfers)
  – EVT is still restricted to major metro centres
- "Direct" trials used alteplase and delayed treatment compared to standard care but even so did not demonstrate non-inferiority and final reperfusion consistently better with thrombolytics
  – Tenecteplase may be more effective, improved outcomes
- Early (pre-hospital) thrombolysis in MSU appears more effective
- "Cardiac paradigm" argument?
  - Workflow is still slow compared to STEMI and revascularization outcomes imperfect
  - Stroke is mostly embolic – if the clot dissolves the underlying artery is often normal, no further Tx required

Complications after lytics

Neurological deterioration

- Bleeding
- Reocclusion/recurrent embolism



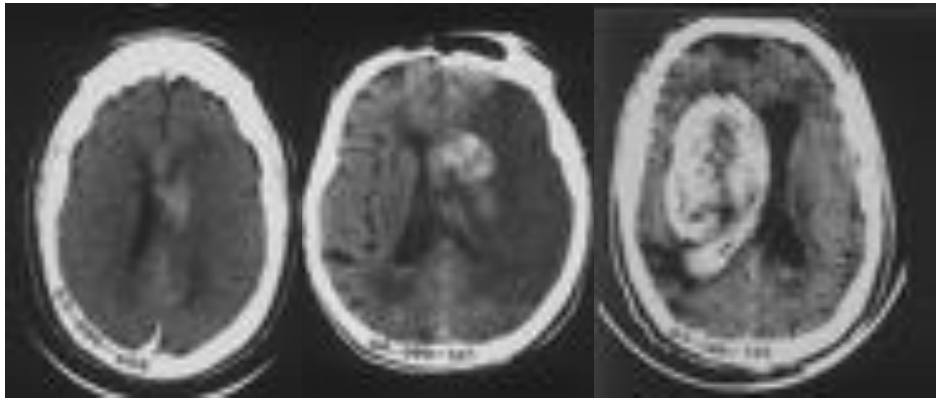
Angioedema

Blood Pressure targets

- Ask why BP is elevated?
- Raised ICP, pain, retention…

Complications after thrombectomy

- Neurological deterioration
  - Bleeding
  - Reocclusion/recurrent embolism



- Puncture site
  - Bleeding – external, retroperitoneal
  - Ischemic limb
- Hyperperfusion post-sent
- Hypotension post-sent
- Blood pressure targets
  - Ask why BP is elevated?
  - Raised ICP, pain, retention…

Recognising deterioration

- Increased limb weakness

  -aim to have “NIHSS” style assessment (10sec UL drift, 5sec LL drift)

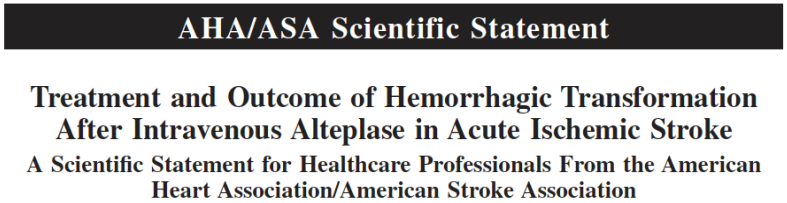
  -changes from flexion to extension less meaningful

- Aphasia – questions and commands, naming
- Reduced conscious state
- Headache and vomiting
- BP changes

Symptomatic ICH

- Tends to occur a few hours after lysis (median 5-10h) but within 24h unless anticoagulated too early
- Most deterioration during the infusion is not ICH but stop and re-scan, if no blood think why?
  -?recurrent embolism
  -?collateral failure
  -?hypoperfusion

- Check fibrinogen/coags
- Consider cryoprecipitate and tranexamic acid
- Fibrinogen usually back to normal after a few hours
- Mostly supportive care


AHA/ASA Scientific Statement

Treatment and Outcome of Hemorrhagic Transformation After Intravenous Alteplase in Acute Ischemic Stroke

A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Yaghi et al Stroke 2017

Orolingual Angioedema

- Tends to occur during or immediately after the infusion
  - ~2% patients
  - (~5% if ACEI vs 1.5% not taking ACEI)
  - 15-105min post-bolus,
  - mean 70min post-bolus
- More common if ACEI (bradykinin mediated)
- Usually unilateral tongue/lip on side *opposite* affected hemisphere
- Hydrocortisone
- Consider icatibant (bradykinin inhibitor)
- Rarely requires intubation

Malignant cerebral oedema

- Tends to peak day 3-5 after ischemic stroke but can occur within 24h, particularly after reperfusion
- Large middle cerebral artery territory infarcts
- Large PICA cerebellar infarcts

- Watch for reduced conscious state but that can go off rapidly
- Increasing BP concerning
- Serial imaging in those at risk
- Consider hemicraniectomy or posterior fossa decompression
- Early discussion with Neurosurgery

Post-carotid endarterectomy care

- Cranial nerve injury – tongue, vocal cord
- Neck hematoma – airway risk
- Hyperperfusion – risk ICH – control BP
- Post-op stroke

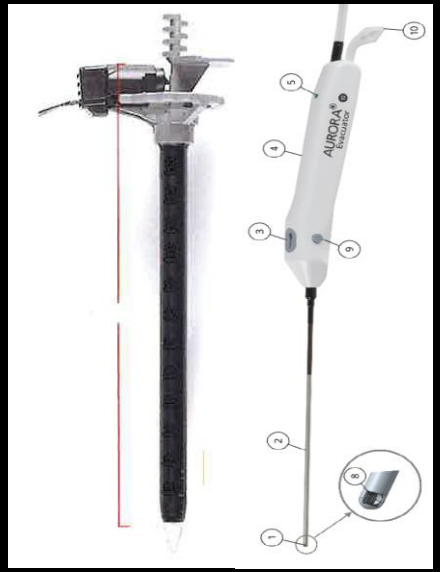
Can we effectively treat intracerebral haemorrhage?

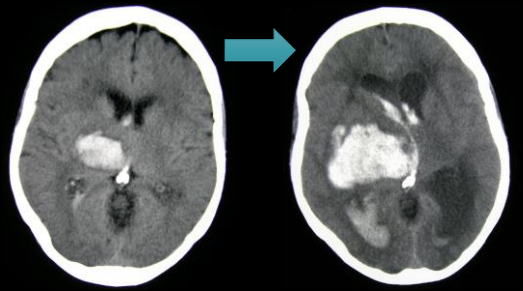
Hematoma growth occurs early & larger ICH = worse outcome

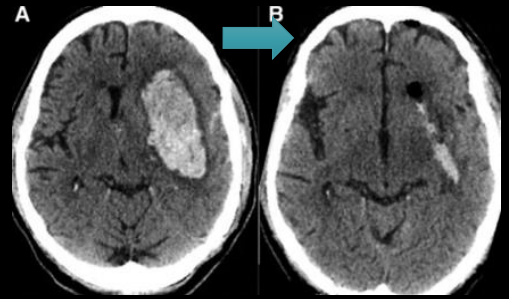
Hemostatic agents ?tranexamic acid (STOP-MSU) ?rVIIa
Minimally invasive surgery
Aim of early surgery = prevent haematoma expansion and toxicity related to thrombin and iron

Pitfalls of previous surgical trials:
too late, too disruptive to normal brain, insufficiently effective haematoma removal

EVACUATE







Conclusions

- Rapid reperfusion remains the proven treatment paradigm in ischemic stroke
    - Thrombectomy is highly effective in a broad range of patients 0-6h and more selected patients >6h (boundaries of efficacy still expanding)
    - Thrombolytics remain the foundation of reperfusion in stroke (including before thrombectomy) and are particularly effective when given pre-hospital in an MSU

      0-4.5h broad criteria, 4.5-9h/wake-up stroke – perfusion mismatch selection

- Intracerebral hemorrhage remains challenging but there are promising treatments in trials

- Simply delivering thrombolytics (ideally pre-hospital) & thrombectomy faster and increasing access to appropriate patients is essential to maximise effectiveness
  – focus on systems of care, including pre-hospital
  – simplified and consistent protocols, understanding potential complications

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