February 2016

Publication Alert Newsletter

Please be aware that the purpose of this Newsletter is to make you familiar with the most recent scientific publications, and you must keep in mind that all aspects may not be covered by the label. Please always refer to the current prescribing information as in force in your country

Continuing efforts to improve stroke care – such as reducing treatment delays and increasing use of recombinant tissue plasminogen activator (rtPA) to treat acute ischaemic stroke (AIS) – is vital at individual hospitals and institutions. Additionally, collective benefits can be achieved by sharing best practices and transferring new approaches and improvements between healthcare settings.

This issue of the Actilyse® Publication Alert Newsletter includes a paper that describes the successful and rapid transfer of an effective stroke treatment model to a very different healthcare setting, suggesting stroke teams should look to be open-minded about how best practices can be adopted.

'Similar results should be achievable elsewhere with the same principles.'[1]

Helsinki thrombolysis model can be transferred successfully to other settings

The Helsinki stroke thrombolysis model is known to achieve short median door-to-needle times (DNT). Despite key differences between healthcare systems in Finland and Australia, the Helsinki model was implemented successfully in a Melbourne hospital, resulting in a substantial reduction in DNT.[1]

'In only 4 months, we were able to practically halve DNT to a median of 25 minutes.'

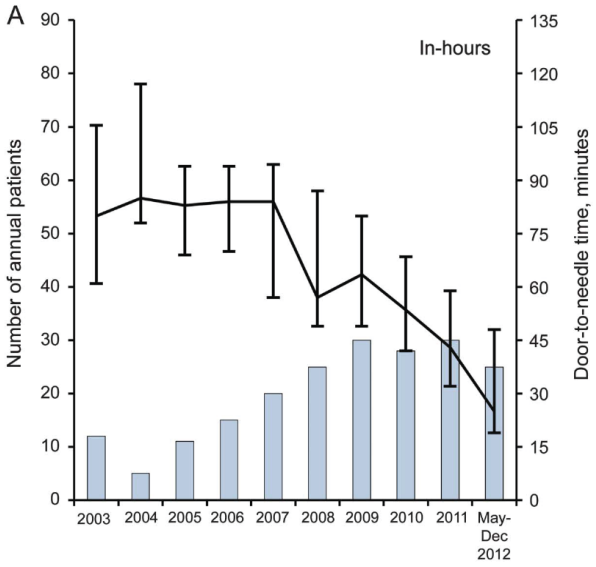
Study details

- Analysis of prospective registry data from 448 AIS patients who received rtPA at the Royal Melbourne Hospital (2003–Dec 2012), to determine the effect on DNT of a new care model implemented in May 2012
- The new protocol was applied during office hours and included key components from the Helsinki model:
  - Ambulance pre-notification of the stroke care team
  - Delivery of patients directly to the CT scanner on the ambulance stretcher
  - rtPA delivery in the CT immediately after imaging

Step	Helsinki model
Pre-notification	Ambulance calls stroke consultant, who accepts patients, takes history, and alerts the team
Medical history	Electronic province-wide picture archiving and communication system (PACS) since 2002 Electronic lab and patient records with limited access to GP text GP never called
Registration and CT request	Unique personal identification number at birth, used in all public and private systems Patient registration and CT request electronically before patient arrival
Labs	Pre-ordered blood tests for all rtPA candidates Blood samples always drawn before rtPA by lab nurse Point-of-care international normalized ratio, glucose available at rtPA decision
IV line	Ambulance always inserts large-bore antecubital cannula during transport
Straight to CT	Patients go straight to CT on ambulance stretchers
rtPA on CT table	rtPA can be initiated on CT table, but usually in adjacent room where the drug is kept

Study details (continued)

- Implementation of the new care model in 2012 reduced rtPA treatment delays compared with 2011 (figure):
  - **Overall median (IQR) DNT almost halved**, from 61 (43–75) mins to 46 (24–79) mins (p=0.04)
  - **In-hours median (IQR) DNT almost halved**, from 43 (33–59) mins to 25 (19–48) mins (p=0.009)
  - Out-of-hours DNT remained unchanged, from 67 (55–82) mins to 62 (44–95) mins (p=0.835)
- The proportion of patients receiving rtPA within 60 mins of arrival in 2012 was 80% in-hours (65% overall)
- Reduction in DNT was achieved without additional costs or reduction in diagnostic quality
  - The 'direct-to-CT' step was felt to be where the largest gains were made in reducing treatment delays



Number of patients per year (bars, left axis) and median DNT with IQR (line, right axis) in-hours (8 AM to 5 PM, Monday–Friday). Data for year 2012 are for the last 8 months, after the protocol change.

The authors attribute the successful adoption of the optimized rtPA protocol to cooperation of the ambulance, emergency and stroke teams. They conclude that the Helsinki model of stroke thrombolysis is applicable across different healthcare settings.

'We demonstrated rapid transferability of an optimized tPA protocol to a different health care setting.'[1]

Use of emergency medical services (EMS) facilitates thrombolytic therapy

Unnecessary delays in hospital arrival can exclude otherwise eligible patients from thrombolysis. Patients with AIS who present at the emergency department (ED) via EMS are more likely to arrive early enough to receive thrombolysis, and have significantly shorter onset-to-treatment (OTT) times, than patients arriving by other routes. This applies whether the stroke occurs within or outside the home, and for treatment windows of ≤3 or ≤4.5 hours.[2]

Increasing the use of EMS by AIS patients should enable more to arrive in time to receive rtPA.

Study details

- Analysis of prospective registry data from 1081 AIS patients admitted to the National Taiwan University Hospital (Jan 2010–Jul 2011) within 72 h of AIS onset, to determine impact of EMS transport on rtPA use
  - 279 patients (25.8%) arrived via EMS
  - 52.7% of patients who were transported by EMS had early ED arrival (within 3 h of stroke onset)
  - Of the 289 patients with early ED arrival, 50.9% had come via the EMS
  - Mean OTT was 26 mins shorter among EMS (101 mins) than non-EMS (127 mins) patients (p=0.01)

Arrival route, n (%)	ED arrival ≤3 h (n=289)	ED arrival >3 h (n=792)
EMS	147 (50.9)	132 (16.7)
By patient themselves	125 (43.3)	455 (57.4)
Transfer from other hospital	13 (4.5)	141 (17.8)
Transfer from outpatient department	3 (1.0)	47 (5.9)
Private ambulance	1 (0.3)	17 (2.1)

Study details (continued)

- Patients were more likely to have early ED arrival if they used EMS vs non-EMS transport (p<0.001) (table below)
- Patients who used EMS transport had a higher chance of receiving rtPA, and had a shorter treatment time
  - 76.1% of the 88 patients who received thrombolysis were transported by EMS

Variable	EMS vs non-EMS OR (95% CI)	*p* value
Onset to ED arrival ≤3 h	3.68 (2.54–5.33)	<0.001
When stroke occurred at home (n=912)	3.62 (2.49–5.27)	<0.001
When stroke occurred outside the home (n=126)	17.58 (5.10–60.59)	<0.001
Onset to ED arrival ≤4.5 h	4.07 (2.91–5.70)	<0.001
Received thrombolysis ≤3 h after stroke onset	3.89 (1.86–8.17)	<0.001

'Utilization of EMS can not only help acute ischemic stroke patients in early presentation to ED, but also effectively facilitate thrombolytic therapy and shorten the onset-to-needle time.'[2]

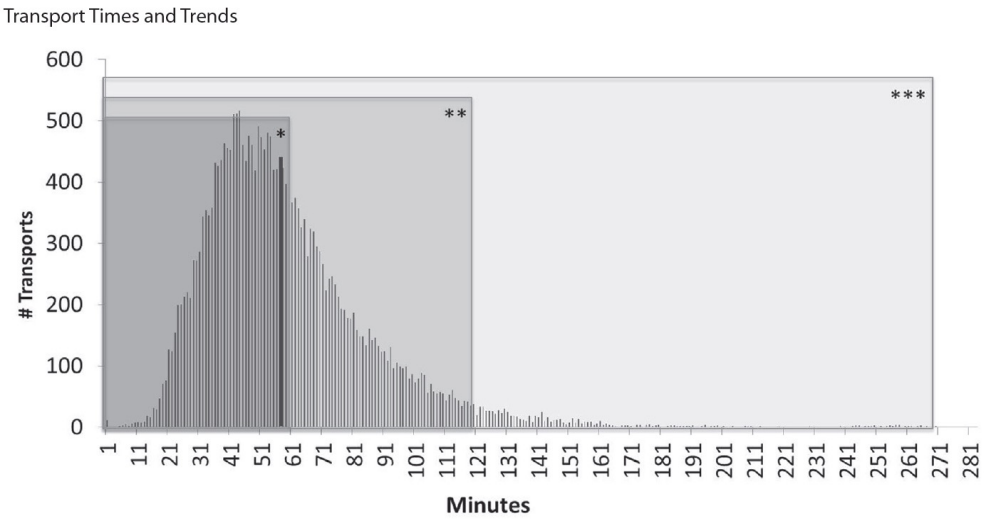
Helicopter EMS increases access to stroke care for patients in rural areas and enables rapid inter-facility transfers in urban areas

Helicopter EMS (HEMS) transport can extend timely stroke care coverage to rural and urban environments.

Analysis of data from 25 332 US helicopter transports for patients with stroke (2004–2011) revealed:[3]

- Average time of 60 min from dispatch to arrival at care facility
- 96% of patients arrived at definitive care within 2 hours (figure)
- 58% of transports were from 'rural' or 'super-rural' areas
- 72% of transports were 'inter-facility'
- 79% of transports in 2011 were to primary stroke centres (PSCs)

'…the majority of patients transported arrive in less than 2 hours from dispatch to definitive care.'[3]



*59.2% arrived at hospital within 1 h, **96.4% within 2 h and ***99.9% within 4.5 h of transport request

'HEMS is rapid, has the appropriate level of care (in the right time) to support intra-transport rtPA use, and is clearly effective at connecting stroke patients in rural and urban areas to PSCs.'[3]

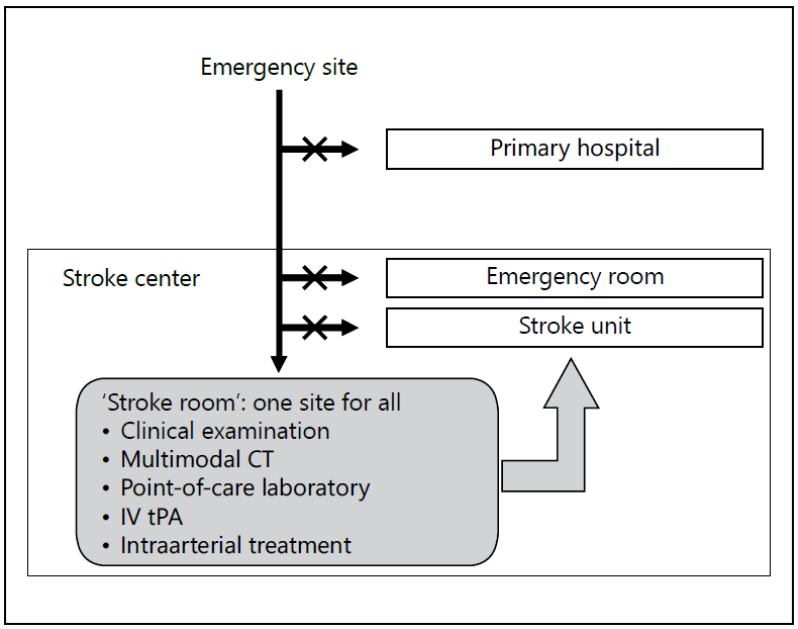
Performing all time-sensitive diagnostic and therapeutic procedures in a single 'stroke room' can reduce in-hospital delays and may increase access to rtPA

Carrying out admission, diagnosis and treatment of patients with suspected AIS at a single site ('stroke room') within a stroke centre can save crucial time.

Although the study focused on AIS patients requiring intra-arterial treatment, the stroke room protocol could also improve timely access to IV rtPA. When a tertiary university hospital implemented a stroke room protocol in 2010, significant reductions were seen in onset-to-door times and DNT compared with conventional stroke management.[4]

The stroke room intervention involved performing all time-sensitive diagnostic and therapeutic procedures at a single location (figure).

'…the stroke room protocol allowed significantly faster delivery of IV rtPA.'[4]



'Stroke room' protocol:
Patients with suspected AIS are transferred to a specialist stroke centre, bypassing hospitals without stroke expertise.

Within the stroke centre, patients are admitted directly to the 'stroke room', bypassing both the emergency room and the stroke unit.

Time-sensitive diagnostic and therapeutic procedures are all carried out in the stroke room: history taking, neurological examination, laboratory tests, imaging, medical stabilization, IV thrombolysis, and intra-arterial therapy.

'The results of this study indicate that for patients with acute stroke, performing all the time-sensitive diagnostic and therapeutic measures at a single location significantly reduces delay.'[4]

Telemedicine can be used for pre-hospital stroke evaluation

Patients with suspected AIS can be evaluated using telemedicine in mobile stroke units, resulting in shorter treatment times than conventional EMS transfer and in-hospital evaluation.[5]

A prospective study of 100 patients evaluated via telemedicine using the Cleveland mobile stroke unit (Jul–Nov 2014) demonstrated that such an approach is feasible, with a low rate of technical failure:

- On-board CT scans were completed quickly (median door-to-CT time 13 minutes)
- After telemedicine consultation, 16 patients (out of 33 with probable AIS) were administered on-board IV rtPA with a median DNT of 32 mins (26 mins quicker than the control group of 56 patients transferred to hospital by EMS)

As telemedicine alleviates the need for a neurologist to travel with a mobile stroke team, this approach could improve efficiency and reduce costs for this service while maintaining the level of stroke care.

Telestroke reduces unnecessary hospital transfers and improves rtPA use

Telestroke systems can improve stroke care decision making and shorten treatment times.

Introduction of a telestroke 'drip and ship' system in a community hospital in Madrid significantly reduced DNT (by 77 minutes) and OTT without affecting safety (table).[6] A significant improvement in clinical outcome was also seen, based on modified Rankin scale (mRS) category analysis. Only one patient in the telestroke group was transferred unnecessarily to a specialist stroke centre.

	Pre-telestroke (n=259) Mar 2008–Feb 2010	Telestroke (n=225) Mar 2010–Feb 2013	*p* value
Thrombolysis, n (%)	12 (5)	18 (8)	0.125
OTT, median (IQR) min	205 (55)	155 (121)	0.022
DNT, median (IQR) min	144 (48)	66 (54)	<0.0001
In-hospital complications (ICH, SICH, death), n (%)	3 (25)	1 (10)	–
3-month mRS 0–1, n (%)	4 (33)	10 (56)	0.145

Expanding the range of assessments during a telemedicine consultation, prior to transfer to a stroke unit, may enable more patients to receive rtPA

In addition to confirming AIS diagnosis, a telemedicine consultation can be used to interpret CT scans and assess rtPA eligibility, enabling appropriate rtPA administration before transferring patients to a stroke unit ('drip and ship'). This approach increased the number of patients who received thrombolysis five-fold compared with a model in which patients were transferred from the community hospital to a stroke unit immediately following telemedicine AIS diagnosis.[7]

The randomized controlled TRUST-tPA trial compared thrombolysis outcomes in two groups, both of which initially underwent telestroke consultation upon ED arrival:

- Telethrombolysis (n=25): videoconference used to confirm AIS diagnosis, interpret CT scan and assess rtPA eligibility (duration 73 min); 21 (84%) received rtPA *before* transfer to a stroke unit
- Usual care (n=22): videoconference used to confirm AIS diagnosis (duration 23 min) and patients then transferred to a stroke unit for CT scan and further assessment; 4 (18%) received rtPA

The delay to stroke unit admission ranged from 160 to 300 minutes in the usual care group, which precluded thrombolysis in most cases. There were no differences in thrombolysis safety or efficacy outcomes after correcting for significant baseline differences between the two groups.

The authors highlight the low number of enrolled patients (resulting in an underpowered analysis) and prolonged videoconference time in the telethrombolysis arm as possible reasons why the higher rate of thrombolysis did not translate into significantly more favourable outcomes in this study.

Introduction of telestroke enables more patients to benefit from thrombolysis

Adoption of a telestroke system by a Singapore hospital emergency department in 2010 enabled patients with AIS to receive thrombolysis when presenting outside of office hours.[8]

In a retrospective observational study, 45 patients with suspected AIS were assessed using a newly implemented telestroke protocol. Of the 18 who received rtPA, 8 presented to the ED outside of office hours. Although DNT was relatively slow (mean 92.7 min), the authors expect this to improve with experience and list six suggestions to improve treatment times.

'It is hoped that our experience can be shared with other hospitals/EDs that are planning to set up a similar system.'

AIS, acute ischaemic stroke; CT, computed tomography; DNT, door-to-needle time; ED, emergency department; EMS, emergency medical services; GP, general practitioner; HEMS, helicopter emergency medical services; ICH, intracranial haemorrhage; IQR, interquartile range; IV, intravenous; mRS, modified Rankin scale; OTT, onset-to-treatment time; PACS, picture archiving and communication system; PSC, primary stroke centre; rtPA, recombinant tissue plasminogen activator; SICH, symptomatic intracranial haemorrhage.

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