

PUBLICATION ALERT NEWSLETTER – JUNE 2016

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.

Achieving high-quality care of patients with acute ischaemic stroke (AIS), including timely treatment with recombinant tissue plasminogen activator (rtPA), can be challenging. The American Stroke Association emphasizes three main principles for developing systems of stroke care:

“effective communication among agencies, services, and providers; an organized and standardized approach to acute stroke care at each facility; and performance feedback for continual improvement.”¹

As stroke care evolves, initiatives are continually being developed to monitor and improve performance within stroke teams and across stroke care networks.

This issue of the Actilyse® Publication Alert Newsletter focuses on papers that highlight the positive impact on AIS treatment times and outcomes that can be achieved by implementing and adapting standardized processes and protocols, and using performance metrics to drive further improvements.

SHORTER TREATMENT TIMES LEAD TO REDUCED LENGTH OF HOSPITAL STAY AND BETTER PATIENT OUTCOMES

The benefits to patients and their families of timely rtPA administration include a shorter length of hospital stay (LOS) and a greater chance of being discharged home.

Among patients with AIS receiving rtPA in the US state of Georgia, shorter door-to-needle times (DNTs) were associated with reduced LOS, greater likelihood of favourable discharge disposition, and better ambulatory status at discharge.²

Based on these findings, if hospitals administered rtPA to each eligible patient within 60 minutes of arrival, the average LOS would be reduced to ~4 days and more patients would be discharged home.

Study details

- Data from 3154 patients with AIS who received rtPA within 4.5 h of symptom onset at 36 hospitals participating in the Georgia Coverdell Acute Stroke Registry (Jan 2007–Dec 2013), to assess the impact of shorter DNT on patient LOS, bleeding complications, and discharge status and disposition
 - Median DNT decreased during the study period from 81 to 60 min; overall median DNT was 69 min
 - 1201 patients (38%) were treated within 60 min of arrival
 - Median LOS was 5 days
- Shorter DNT was associated with decreased LOS ($p < 0.05$ in multivariable analysis)
 - DNT ≤ 30 min: **19% shorter LOS** vs patients with DNT ≥ 2 h ($p = 0.04$)
 - DNT 30–60 min: **15% shorter LOS** vs patients with DNT ≥ 2 h
- Patients treated ≤ 60 min after arrival were more likely to have a favourable discharge disposition and to be walking than patients treated > 60 min after arrival, with a similar rate of bleeding complications (table)

OUTCOME MEASURE	ADJUSTED OR (95% CI) FOR THOSE WITH DNT ≤ 60 min VS DNT > 60 min	p VALUE
Favourable discharge disposition	1.28 (1.06–1.56)	0.01
Ambulating at discharge	1.26 (1.02–1.56)	0.03
Bleeding complication	0.71 (0.44–1.45)	0.16

Discharge disposition categories: home; facilities other than hospice; hospice/died

Ambulatory status categories: independent (with or without a device); with help from another person; unable to ambulate

“Hospitals should be encouraged to measure, monitor, and reduce door-to-treatment time progressively for a better patient outcome.”²

SHORTER DNT CAN BE ACHIEVED BY USING AN APP TO COORDINATE ACUTE STROKE CARE

Using technology to provide real-time patient updates may heighten the sense of urgency and improve communication efficiency within the stroke team, resulting in shorter treatment times.

Using a medical app to alert and inform the stroke care team and monitor the timeliness of therapy led to a 40-minute decrease in mean DNT, and a four-fold increase in the proportion of patients treated within 60 minutes of arrival at the emergency department (ED) of a primary stroke centre (PSC).³

The app was developed by physicians to facilitate the rapid assessment and care of patients with AIS, enhance coordination and communication within the stroke care team, provide immediate feedback on time elapsed for each case, and track metrics on all patients receiving rtPA.

Study details

- ‘Stop Stroke[®]’ acute care coordination app:
 - Activated by medical personnel (EMS, ED, or rapid response team) when stroke is suspected
 - Siren tone and details of the new patient are transmitted to all members of the stroke care team
 - Stroke care team members indicate their readiness status via the app, to facilitate coordination of care
 - Patient information is updated in real time
 - Universal clock compares the current case against national benchmarks and provides immediate feedback on elapsed time
- Data from 85 patients with AIS treated with rtPA at a single centre (Feb 2014–Aug 2015), analysed retrospectively to evaluate the impact on DNT of stroke team activation using the stroke app
 - 63 stroke activations used the app and 22 did not
- When the stroke app was used, mean DNT was reduced from 87 to 47 min (46% reduction; $p < 0.001$)
- Proportion of patients treated within 60 min of stroke onset increased from 18% to 85% (3.7x improvement)

SHORTER TREATMENT TIMES FOR IN-HOSPITAL STROKE CAN BE ACHIEVED WITH STANDARDIZED PROTOCOLS

Patients with in-hospital stroke may benefit from implementation of hospital-wide code stroke programmes, similar to those already in place for patients with AIS onset outside of hospital.⁴

Following implementation of a comprehensive code stroke programme developed specifically for patients with in-hospital stroke, AIS evaluation and treatment times were significantly shortened. The programme combined new protocols for identifying in-hospital stroke and notifying the neurology team with pre-existing protocols for stroke evaluation and treatment.

The authors concluded that, “...the findings of the present study suggest that the in-hospital code stroke programme should be implemented in the entire hospital.”

Study details

- Data from 70 consecutive patients who developed in-hospital stroke in non-neurology departments and received reperfusion therapy at a single PSC in Seoul (Jul 2002–Feb 2015), to determine the effect on treatment times of a standardized programme for treating in-hospital stroke
 - Programme included a computerized alert system (for activation of code stroke, notification, and communication), specific in-hospital stroke protocols, and regular staff education
 - Programme implemented initially in the cardiology and cardiovascular surgery wards in Nov 2008
- Delays to notification of the neurology department and imaging were reduced after programme implementation
- Delays to IV rtPA were also reduced, with median onset-to-needle time almost halved to 65 min (table)

MEDIAN (IQR), min	BEFORE IMPLEMENTATION (n=15)	AFTER IMPLEMENTATION (N=27)	p VALUE
Onset to neurology notification	50 (24.5–122)	28 (11.5–55)	0.033
Recognition to neurology notification	22 (17–45)	9 (5–15)	0.011
Onset to imaging	91 (72–119.5)	41 (27–66)	<0.001
Notification to IV rtPA	77 (46–93) [n=9]	45 (33–54) [n=17]	0.052
Onset to IV rtPA	120 (120–149) [n=9]	65 (50–87) [n=17]	0.001

“The comprehensive program for in-hospital stroke...was effective in reducing time intervals to evaluation and reperfusion therapy.”⁴

SYSTEM-WIDE BENCHMARKING MAY HELP IMPROVE STROKE CARE PROCESSES

Although integrated stroke care systems share some common practices, there may be variations in performance between hospitals.

Despite overall improvements in use of rtPA and DNT over time in a US integrated health system, there was wide variation in the level and rate of improvement in rtPA delivery at individual hospitals.⁵

Understanding why stroke care varies within a health system may help to ensure that quality improvements happen at all hospitals and successful processes are adopted at lower-performing centres.

Study details

- Data from 11 630 patients with AIS admitted to 14 hospitals in Southern California (2009–2013)
- AIS care generally improved during the study period, with increased probability of receiving rtPA coupled with reduced DNT over time (table)
- Delivery of rtPA varied widely between hospitals, both at baseline and in rates of change
 - Some hospitals showed marked improvement, whereas others remained more static

METRIC	2009	2010	2011	2012	2013	ALL YEARS
Total number of patients	2475	2343	2334	2163	2315	11 630
rtPA-treated patients, n (%)	64 (2.6)	53 (2.3)	87 (3.7)	100 (4.6)	149 (6.4)	453 (3.9)
Door to imaging time, median (IQR), min						
All patients	58 (35–87)	55 (34–84)	48 (25–79)	47 (23–76)	46 (23–78)	51 (29–81)
rtPA-treated patients	23 (14.5–28)	16 (8–29)	13 (9–20)	13 (8–22)	15 (9–22)	15 (9–23)
DNT, median (IQR), min	94 (67–128)	79 (62–112)	74 (58–96)	73.5 (54.5–103.5)	67 (50–89)	73 (55–103)
DNT <60 min, %	20.3	22.6	27.6	32	40.3	31.1

“...it is important to better understand factors that drive differences in stroke care delivery between hospitals.”⁵

INTERNATIONAL BENCHMARKING CAN HELP IMPROVE STROKE CARE PROCESSES

International benchmarking can highlight opportunities to improve rtPA treatment rates and workflow speed, and may be used as a tool to improve stroke care systems.

In a benchmarking study to compare hospitals in Australia and Japan, Kawano et al found that the Australian hospital had higher rtPA treatment rates while the Japanese hospital had faster DNT and imaging-to-needle times.⁶

Such studies can highlight potential areas for improvement, such as more efficient imaging protocols in the Australian centre and the need for a critical assessment of patient selection in the Japanese centre.

Study details

- International benchmarking of prospectively collected data from a tertiary referral hospital in Australia and a teaching hospital in Japan, for all patients receiving rtPA within 4.5 h of AIS onset (Oct 2012–May 2014)
- rtPA treatment rates were higher in the Australian (41%) than in the Japanese (25%) hospital ($p=0.0016$)
- In-hospital delays were significantly longer in the Australian than in the Japanese hospital (table)

MEDIAN (IQR), min	AUSTRALIAN HOSPITAL (n=62)	JAPANESE HOSPITAL (n=60)	p VALUE
Onset-to-door time	95 (64–137)	81 (50–130)	0.09
Onset-to-needle time	171 (130–198)	142 (105–189)	0.0028
Door-to-CT scan time	27 (14–39)	13 (11–15)	<0.0001
CT scan-to-needle time	34 (25–44)	41 (36–46)	0.0007
DNT	63 (48–74)	54 (47–62)	0.0355
DNT ≤60 min, n (%)	28 (45)	44 (73)	0.0016

“International benchmarking...for thrombolytic therapy provides opportunities to improve the system of care for acute stroke patients.”⁶

MANY HOSPITALS LACK A PROTOCOL FOR DOCUMENTING 'LAST KNOWN WELL' TIME

“73% of those surveyed reported that their hospital did not have a protocol to establish ‘last known well’ times.”⁷

Establishing the time of stroke onset (‘last known well’ time) is necessary to determine eligibility for rtPA treatment.

If this time is not captured, the patient is – possibly incorrectly – deemed ineligible for thrombolysis.

A survey of 57 hospitals in the Northeast region of the US found that most lacked an established protocol for ‘last known well’ documentation.⁷

The authors suggest that ‘last known well’ times are being assessed informally, in order to determine eligibility for rtPA treatment, but are not being documented. They encourage nursing staff to question the patient and their family to establish a ‘last known well’ time, even if it is a best estimate.

Standardized documentation of stroke onset time could increase rtPA rates, and more accurate tracking of this metric may reduce prehospital delays and inform future public education efforts.

SCHOOL-BASED STROKE EDUCATION HAS THE POTENTIAL TO REDUCE PREHOSPITAL DELAYS

Raising public awareness of stroke symptoms and the need to seek urgent medical attention is a critical step in reducing prehospital delays for patients with AIS.

There is good evidence that school-based education programmes improve knowledge of stroke symptoms among children, and that this knowledge is then passed on to parents.⁸ School-based initiatives may thus improve stroke recognition among families, who will then know to contact EMS immediately.

REDUCING PREHOSPITAL DELAY CAN INCREASE THE PROBABILITY OF SURVIVAL IN PATIENTS WITH AIS, EVEN WHEN THROMBOLYSIS IS NOT AVAILABLE

The benefits of early hospital admission, which have already been established for patients who are eligible for thrombolysis, apply to all stroke patients regardless of subsequent treatment.

Even when time-dependent interventions – such as thrombolysis – are not available, early hospital admission can increase the probability of survival in patients with AIS.⁹

Study details

- Data from 1847 patients with AIS admitted to an Italian hospital (Jan 2003–Dec 2011), for whom time of symptom onset was prospectively recorded, to examine impact of onset-to-door time on stroke outcome
 - No patients received rtPA (the hospital was only recently given approval to offer thrombolysis)
 - Median onset-to-door time was 4 h 52 min; 512 patients (28%) arrived within 2 h of symptom onset
- Early arrival at the ED was associated with reduced risk of 1-month mortality (table)
 - Each 60-minute increase in delay was associated with a significant increase in mortality
 - Survival advantage associated with early ED arrival was limited to those with the most severe symptoms
 - Higher chance of survival did not translate into a better overall outcome

	1-MONTH MORTALITY ADJUSTED HR (95% CI)	p VALUE
Onset-to-arrival time <2 h (vs ≥2h)	0.65 (0.48–0.89)	0.02
Onset-to-arrival time <3 h	0.66 (0.47–0.91)	0.01
Onset-to-arrival time <4 h	0.67 (0.49–0.93)	0.02
Delay in minutes (for each 1 h increase)	1.03 (1.01–1.06)	0.005
Onset-to-arrival time <2 h (vs ≥2 h); more severe stroke	0.54 (0.34–0.85)	0.008
Onset-to-arrival time <2 h (vs ≥2 h); less severe stroke	1.40 (0.72–2.73)	0.32

“patients who need high-complexity interventions, including but not limited to thrombolysis, benefit the most from early hospital admission.”⁹

STROKE CARE INFRASTRUCTURE MAY NEED TO BE REORGANIZED TO ENABLE ELIGIBLE PATIENTS TO BENEFIT FROM MECHANICAL THROMBECTOMY AFTER THROMBOLYSIS

Up to 15% of patients eligible for rtPA thrombolysis may benefit from additional mechanical thrombectomy. To ensure these patients have timely access to thrombolysis *and* endovascular therapy, stroke care infrastructure may need to be reorganized in every country.¹⁰

Initiatives can include increasing the number of comprehensive stroke centres, linking stroke centres via telemedicine, training emergency physicians and endovascular radiologists, and public education.

REORGANIZING THE STROKE CODE PROTOCOL ENABLES FAST REFERRAL OF CANDIDATES TO HOSPITALS PROVIDING MECHANICAL THROMBECTOMY

Existing protocols and infrastructure can be adapted to enable potential candidates for mechanical thrombectomy to be treated as quickly as possible.

In one region of Spain, the code stroke protocol was modified to permit immediate referral of patients with severe stroke (National Institutes of Health Stroke Scale score ≥ 10 and age ≤ 80 years) to hospitals offering endovascular therapy.¹¹

The authors conclude that this change enabled them to “apply reperfusion therapies with good results” and “offer the best and safest treatment for each patient as soon as possible.”

NATIONWIDE INITIATIVES TO IMPROVE STROKE CARE SERVICES CAN BE HIGHLY SUCCESSFUL

A recent news article highlights the positive impact that inclusive, multidisciplinary initiatives can have on national stroke care provision.¹²

“...pharma-funded initiatives can be catalysts for positive changes in health care.”¹²

In 2014 only four hospitals in South Africa were able to provide acute stroke care in accordance with guideline recommendations. Following introduction of the MyStroke initiative, championed by Lynn Katsoulis and supported by Boehringer Ingelheim, 17 new stroke units were registered by the end of 2015 and many more are expected in 2016.

The MyStroke initiative set out to improve the provision of acute stroke care in South Africa by: petitioning for funding; finding specialist champions to help establish stroke units; assisting with the formation of stroke teams; sharing and setting up stroke care protocols; organizing multidisciplinary stroke management congresses; offering training; and raising public awareness of stroke.

PHARMACISTS PERFORM IMPORTANT ROLES WITHIN MULTIDISCIPLINARY ‘CODE STROKE’ RESPONSE TEAMS

Including pharmacists in ED stroke teams may provide rapid access to rtPA and improve patient care.

In 2011, to improve stroke care provision and prepare for PSC certification, a US community hospital established a multidisciplinary ‘code stroke’ response team that included an ED pharmacist.¹³

A pharmacist was available round-the-clock to participate in code stroke activations. They assisted with patient evaluation and – using standardized ‘stroke kits’ placed within the ED – helped to provide timely access to rtPA.

By 2015, median DNT at this hospital was 44 minutes with 81% of cases treated within 60 minutes.

The authors conclude that, “the pharmacy department played an important role in enabling the medical center to provide consistent, excellent care for all patients with stroke.”

AIS, acute ischaemic stroke; CI, confidence interval; CT, computed tomography; DNT, door-to-needle time; ED, emergency department; EMS, emergency medical services; IQR, interquartile range; IV, intravenous; ; PSC, Primary Stroke Centre; OR, odds ratio; rtPA, recombinant tissue plasminogen activator.

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