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.

The AIS* care pathway begins at symptom onset, extends through stroke recognition and rapid patient transfer to hospital, and continues to acute treatment and beyond. To achieve optimal patient outcomes, the pathway should be as efficient as possible. This can be achieved by reducing the time taken for individual steps, eliminating unnecessary stages, and carrying out some tasks in parallel. First, however, areas that can be targeted for improvement must be identified.

In this issue of the Actilyse® Publication Alert Newsletter, we highlight the procedure followed by one US CSC to identify and address in-hospital factors that delay rtPA delivery. We also look at other initiatives that can reduce in-hospital delays, together with ways in which novel technologies can be used to improve stroke care delivery.

*Abbreviations are defined at the end of the newsletter.

IDENTIFYING FACTORS THAT CAUSE TREATMENT DELAYS IS A KEY STEP IN IMPROVING STROKE CARE

Hospitals that deliver high-quality stroke care aim to assess treatment metrics regularly, so that they can identify and act upon areas where improvements can be made.

Hospital records covering a 3.7-year period at a CSC were reviewed to identify factors causing delays in DNT among patients with AIS.[1] A high proportion (80%) of patients received rtPA within 60 minutes of hospital arrival. Among the remaining 20% of patients, delays relating to CT imaging and hypertension control were common contributors to DNT >60 minutes. Multiple other delaying factors were identified and some patients had more than one reason for delayed treatment. For most of these factors, the authors suggested strategies to overcome delays and improve DNT.

The authors conclude that improvements in AIS patient care require continuous feedback, analysis, and adoption of multiple targeted strategies.

Study details

- Analysis of data from 487 patients with AIS who received rtPA at a CSC in New York State (Apr 2012–Dec 2015), to investigate causes of treatment delays among patients with DNT >60 min
  - 391 patients (80%) had a DNT ≤60 min (mean DNT 46 min; mean OTT 128 min)
  - 96 patients (20%) had a DNT >60 min (mean DNT 78 min; mean OTT 152 min)
- CT imaging acquisition was the most common source of delays, affecting 38 patients (39.5% of those with DNT >60 min)
  - 19 patients (19.8%) had delayed scan initiation, with a door-to-imaging time >25 min
  - 23 patients (24%) had prolonged imaging time (>20 min) (note that patients may have had more than one factor contributing to their delay)
- Treatment of severe hypertension was a major source of delay in 22 patients (22.9%) and the need to treat other conditions (e.g. hyperglycaemia, pulmonary oedema) before rtPA caused delays in 12 patients (12.5%)
- Strategies proposed by the authors to reduce identified delays include pre-hospital management of conditions such as glycaemia, direct transfer from ambulance to CT scanner, and administration of rtPA on the CT table (see table)

IDENTIFIED DELAYING FACTOR	N (%)	RECOMMENDED STRATEGIES TO REDUCE DELAY
Prolonged stroke imaging (>20 min)	23 (24)	• IV rtPA must be premixed and available to be given in the CT scanner • Provide IV rtPA bolus after non-contrast CT on CT table prior to CTA/CTP • Continue with CTA/CTP after rtPA
Required blood pressure management prior to rtPA	22 (23)	• Recognize severe hypertension in triage • Monitor blood pressure during CT scanning • Antihypertensive medications to be available in CT and given if needed
Unclear presentation	20 (21)	*No suggestions*

Study details (continued)

IDENTIFIED DELAYING FACTOR	N (%)	RECOMMENDED STRATEGIES TO REDUCE DELAY
Triage to imaging initiation >25 min	19 (20)	• EMS pre-notification call system in place with EMS personnel educated • Move patient from the ambulance stretcher straight to CT table • Measure blood glucose and INR with a point-of-care device, obtain venous access and draw blood samples in the CT scanner
Required treatment of other emergent conditions prior to rtPA	12 (12.5)	• Pre-hospital management if possible • Page neurology on arrival • Allow stroke team to be ready for rtPA when opportunity first arises and can prevent additional delay
Delay in paging to neurology	11 (11)	• Page neurology for all possible AIS/TIAs within time window even if symptoms have improved
MRI completed prior to thrombolysis	11 (11)	• Consider IV rtPA prior to brain MRI in case of doubt
Lengthy consenting for rtPA	9 (9)	• Initial discussion on rtPA as potential treatment early in AIS evaluation
Fluctuating neurological deficits	7 (7)	• Frequent neurological examination and treat early if needed
Logistical/other issues	6 (6)	• Measure blood glucose and INR with a point-of-care device • Laboratory confirmation of sample receipt • Two experienced personnel to attempt IV access
Difficulty identifying time of symptom onset	5 (5)	• EMS pre-notification system to provide witness/next of kin phone numbers • Call witnesses/next of kin prior to arrival

Note: Patients may have had more than one factor contributing to their delay. In 15 patients (16%) the contributor to delay was unclear

"In many cases, delay in intravenous thrombolysis was multifactorial and significant results in reducing delays are never achievable by single interventions, but rather result from continuous analysis and improvement of the whole system."[1]

RELOCATION OF IMAGING FACILITIES CAN REDUCE IN-HOSPITAL TREATMENT DELAYS

Rapid access to imaging facilities upon hospital admission can help with the timely management of patients with AIS.

At a part-time emergency hospital offering 24-hour stroke care for 3 days/week, relocating CT scanning facilities on-site led to a substantial reduction in door-to-imaging time.[2] The hospital provided round-the-clock emergency care on Tuesdays, Thursdays and Sundays only, and during the first year, CT scanning was carried out at the adjacent teaching hospital. Installation of a CT scanner within the emergency hospital more than halved door-to CT time to 35 minutes.

Stroke care procedures did not include pre-notification. This may explain why private vehicle transfer was associated with a shorter onset-to-arrival time than EMS transfer, and why referral by a neurologist or general practitioner appeared to delay hospital admission.

The authors conclude that timely rtPA administration is possible in their hospital, and that interventions targeted at EMS transfer might increase the number of patients arriving within 3 hours of AIS onset.

Study details

- Analysis of data from 435 patients with AIS admitted within 24 h of symptom onset to an emergency hospital in Egypt over a 2-year period (beginning in Jan 2012), to explore pre-hospital and in-hospital delays
  - Median onset-to-door time was 2.75 h; patients were stratified by onset-to-door time ≤3 h or >3 h
  - 246 patients (57%) were admitted within 3 h of symptom onset (14% within 1 h; 22% within 1–2 h; 21% within 2–3 h)
- Patients admitted within 3 h of stroke onset were younger, more likely to arrive by private transfer and without medical referral, and more likely to be local than those admitted >3 h from symptom onset (see table)
  - Onset-to-arrival time was not affected by gender, time of day, or stroke severity

Study details (continued)

SIGNIFICANT PRE-HOSPITAL FACTOR	ONSET–ARRIVAL ≤3 h (n=246)	ONSET–ARRIVAL >3 h (n=189)	*p* VALUE
Age, mean years (SD)	52 (13)	62 (12)	0.039
Residence, n (%)			0.000
Local	73 (30)	28 (15)	
Not local	173 (70)	161 (85)	
Mode of transport, n (%)			0.012
Private vehicle	180 (73)	115 (61)	
Ambulance	45 (18)	57 (30)	
Medical referral, n (%)			0.014
No	210 (85)	139 (74)	
Yes	36 (15)	50 (26)	

- Installation of an on-site CT scanner led to a 40-min reduction in door-to-CT scan acquisition time, from 75 min (year 1) to 35 min (year 2)
- Door-to-neurology consultation and door-to-CT scan interpretation times were also shortened in year 2

"Inhouse stroke team, CT machine and radiology team, working around the clock, significantly shortened the total inhospital time allowing rapid stroke detection and treatment in emergency department as recommended in NINDS guideslines."[2]

A STREAMLINED IN-HOSPITAL PROTOCOL CAN REDUCE DNT TO LESS THAN 30 MINUTES

Implementing a streamlined direct-to-CT protocol for patients admitted with suspected AIS has the potential to improve in-hospital efficiency and reduce treatment delays, without adversely affecting safety outcomes.[3]

By eliminating the time-consuming process of moving patients in and out of the emergency department, a dedicated multidisciplinary team at a high-volume urban US CSC developed a simplified algorithm for the evaluation and treatment of AIS:

1. Pre-hospital stroke alert by EMS
2. Patient brought to designated area (between EMS entrance and CT suite) for registration, weighing and clinical assessment
3. rtPA premixed for high-likelihood candidates
4. Transfer of patient to CT suite for scan and interpretation
5. Review and confirmation of rtPA eligibility (e.g. last known normal time, anticoagulant use, blood pressure, lab values)
6. Administration of rtPA in CT suite

Implementation of this simplified 'CT-Direct' protocol in 2014 was associated with a 10-minute reduction in median DNT to below 30 minutes and an increase in the proportion of patients with DNT ≤30 minutes, with no change in SICH rates (see table).

The results demonstrate that removing unnecessary steps from the stroke care pathway can streamline initial evaluation of patients with AIS, enabling most of those eligible to receive rtPA within 30 minutes of hospital arrival.

MEASURE	PRE-INTERVENTION JAN 2010 TO MAR 2014 (n=211)	POST-INTERVENTION APR 2014 TO MAY 2015 (n=84)	*p* VALUES
DNT, median min	38	28	<0.001
DNT treatment window, %			<0.001
≤30 min	22.7	56.0	
31–60 min	61.6	36.9	
>60 min	15.6	7.1	
SICH, n (%)	2 (0.9)	1 (1.2)	

"The implementation of a protocol that streamlined the processing of suspected patients with AIS significantly reduced door-to-needle time without negatively impacting patient safety."[3]

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INTRODUCTION OF PARALLEL WORKFLOWS CAN REDUCE AND MAINTAIN DNT BELOW 30 MINUTES

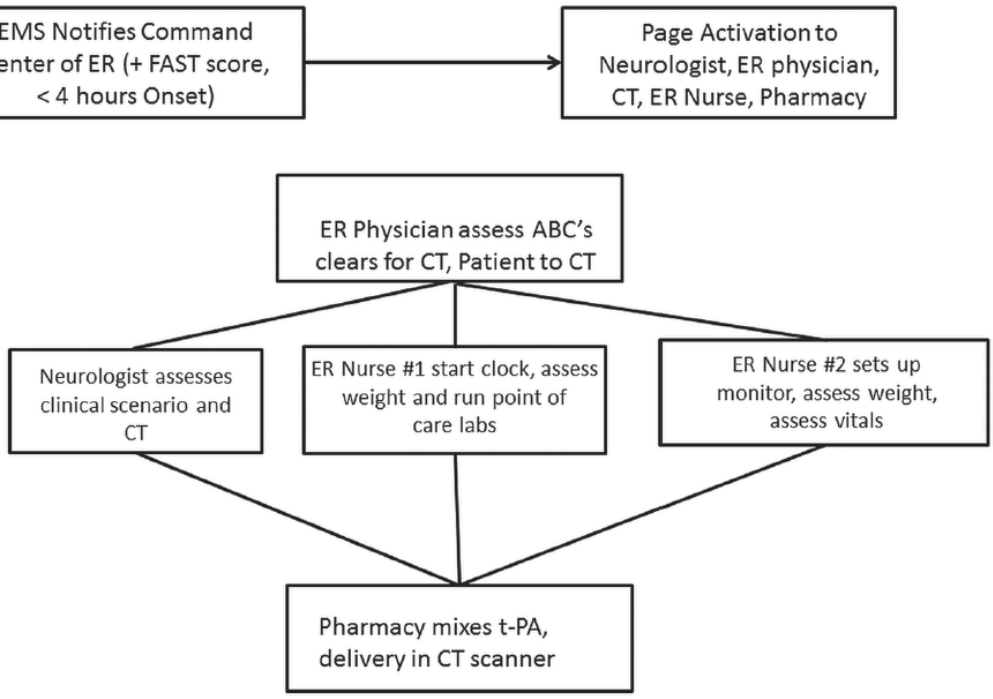
Quality improvement initiatives that introduce parallel completion of tasks by different stroke team members can successfully reduce DNT to below 30 minutes.[4]

The introduction of a CODE FAST parallel workflow protocol at a CSC halved door-to-imaging time (to 8 minutes) and significantly reduced median DNT to 25 minutes, without adversely affecting safety outcomes among rtPA-treated patients. DNT improvement was sustained throughout the 6-month post-intervention study period.

The authors observe that, with the proper implementation of a multidisciplinary protocol, DNT can be dramatically reduced and maintained at <30 minutes.

Study details

- Analysis of data from 93 patients who received rtPA at a CSC in Georgia, USA (Feb 2014–Feb 2015), before and after the implementation in September 2014 of a parallel processing protocol called CODE FAST (see Figure)
  - The new protocol included EMS pre-notification, direct patient transfer to CT, and administration of rtPA in the CT room
- The proportion of eligible patients who received rtPA was 41/141 (29%) before and 52/144 (36%) after CODE FAST
- Substantial and significant reductions in door-to-imaging time and DNT were seen post-intervention (see table)
  - Monthly DNT times showed a sudden and sustained decrease after CODE FAST implementation
  - DNT reductions outside normal working hours were similar to the overall results
  - 18/52 patients (35%) had a DNT <20 minutes
- There were no instances of SICH during the study period



CODE FAST workflow: EMS pre-notification and parallel team roles

OUTCOME	PRE-INTERVENTION (n=41)	POST-INTERVENTION (n=52)	*p* VALUE
Door-to-CT time, median (IQR) min	16 (11–25)	8 (5–11)	<0.0001
DNT, median (IQR) min	62 (49–77)	25 (18–36)	<0.0001
DNT ≤45 min, n (%)	2 (5)	45 (87)	<0.0001
Discharge to home, n (%)	20 (49)	34 (65)	0.10

"Door-to-needle time can be significantly reduced and maintained at <30 min with proper implementation of a multidisciplinary protocol."[4]

IMPROVEMENTS IN STROKE CARE CAN BE SUSTAINED OVER SEVERAL YEARS

Delivery of quality stroke care over the long term requires sustainable processes but also continuous monitoring and feedback, so that performance can be evaluated and further improvements can be incorporated.

Hillen *et al*. assessed the long-term impact of a stroke care protocol on in-hospital treatment times and found performance was sustained over several years, with DNT ≤60 minutes in most rtPA-treated patients.[5] As part of the monitoring process, several areas were identified where further improvements could be made. Having observed that immediate transfer to the CT scanner may be the most efficient way to reduce DNT, the protocol has since been modified to include direct-to-CT transfer.

The authors advocate regular performance monitoring to ensure protocols are adhered to and improvements in DNT can be achieved and maintained.

Study details

- Analysis of data from 113 patients with AIS treated with rtPA at a tertiary stroke centre in the USA, to evaluate the long-term effect on treatment times of a stroke protocol implemented in July 2010
  - The new stroke care protocol incorporated 10 evidence-based strategies (although *not* direct-to-CT transfer)
  - Performance was evaluated annually during the same 6-month period (Sep–Mar) each year for 5 years
- Door-to-CT times tended to decrease over time (see table)
  - During the last study period, median door-to-CT time was 13 min
  - The stroke care protocol has since been amended to include direct-to-CT transfer
- DNTs and proportions of patients with DNT ≤60 min were consistent over the post-intervention period
  - Overall, 56% of patients received rtPA within 60 min of arrival
  - The authors observe that shorter door-to-CT times did not translate into improved DNT due to post-imaging delays, such as: waiting for lab values; need to achieve blood pressure control; delayed rtPA request or preparation
- Rates of in-hospital fatality and symptomatic bleeding were generally consistent over time

OUTCOME	PRE-INTERVENTION	POST-INTERVENTION			
	Sep '09 – Mar '10	Sep '10 – Mar '11	Sep '11 – Mar '12	Sep '12 – Mar '13	Sep '13 – Mar '14
Treated with rtPA, n (% of AIS)	23 (17.2)	30 (18.8)	25 (16.9)	19 (14.6)	16 (12.6)
Door-to-CT time, min					
Median	20	19	16	16	13
Mean	20.6	22.3	18.2	16.4	15.9
DNT					
Median, min	61.5	58	64	49	60.5
Mean, min	66.7	68.6	69.8	51.8	65.2
≤60 min, %	48	60	44	74	56
61–90 min, %	39	20	40	26	38
≥91 min, %	13	20	16	0	6

"Continuous monitoring and education of all players involved are crucial to ensure best possible outcomes in the timely administration of intravenous tissue plasminogen activator."[5]

SMARTPHONE APPLICATIONS MAY ASSIST EMS WITH PRE-HOSPITAL TRIAGE OF AIS PATIENTS

Pre-hospital assessment and priority transport of patients with suspected AIS requires EMS to understand stroke symptoms, to know where the nearest specialist stroke hospital is, and to work out which route will be the quickest.

Nogueira *et al.* have developed a smartphone application (FAST-ED) designed to assist EMS objectively in each of these steps.[6] The application includes an automated decision-making algorithm that relies on:

- A brief series of clinical questions (e.g. age, coagulation status, 'last known well' time, symptoms) to estimate rtPA eligibility
- A database of all regional stroke centres and their capabilities
- GPS technology and real-time traffic information, enabling calculation of transfer times

Based on the information entered, the application will direct EMS to the most suitable stroke centre for any given case.

SIMPLE PRE-HOSPITAL TOOLS MAY ASSIST EMS WITH STROKE PATIENT TRIAGE

Developing a simple tool that EMS can use to identify severe strokes would potentially increase the number of patients transported to stroke care facilities offering appropriate treatment (endovascular therapy and/or rtPA).

An EMS team in Georgia, USA, used severe hemiparesis as a marker of large vessel occlusion stroke, requiring transfer to the nearest CSC.[7] This resulted in priority air transport of 45 patients between December 2014 and June 2015: 27 (60%) were diagnosed with AIS and 13 (48% of AIS patients) were treated with rtPA, either alone or in conjunction with mechanical thrombectomy.

The authors conclude that earlier identification of stroke patients may lead to faster treatment and better outcomes. They also observe that in-hospital metrics (such as DNT) may be a consideration when deciding which hospital to transport patients to.

"The ability to recognize a patient with a large stroke syndrome in the prehospital phase and bring the patient to the right destination the first time will ultimately save time, which in turn will improve outcomes"[7]

TELESTROKE USING ADVANCED CT IMAGING AIDS TREATMENT DECISION-MAKING

Incorporation of multimodal CT imaging into a telestroke network can provide patients with AIS admitted to spoke hospitals with access to advanced brain imaging, and facilitate treatment decision making by remote hub neurologists.

Over a 21-month period (starting in April 2013), 41 patients with suspected AIS were assessed by telestroke at a rural Australian spoke hospital.[8] Of these, 22 were deemed potentially eligible for rtPA based on clinical assessment but 8 were subsequently excluded from thrombolysis following multimodal CT imaging. Fourteen patients were treated with rtPA, with a median door-to-imaging time of 38 minutes and a median DNT of 91 minutes.

The authors conclude that a telestroke service with multimodal CT imaging provides rural stroke patients with rapid access to specialist review and reperfusion therapy options without impacting on service performance.

"…a telestroke service using advanced CT imaging for therapy decision assistance…can be used to guide acute stroke treatment decision-making and improve access to thrombolytic therapy."[8]

ADOPTION OF NOVEL TECHNOLOGIES CAN IMPROVE STROKE CARE

Technological advances can be adopted for use in the stroke care pathway, shortening the time from symptom onset to treatment. El-Ghanem *et al.* review the ways in which novel technologies have been used to improve stroke care:[9]

- Accessible screening tools and smartphone applications can facilitate stroke recognition by the public and EMS personnel
- Mobile stroke units enable pre-hospital evaluation and treatment initiation in AIS patients
- Telestroke networks expand stroke care expertise to wider areas
- Smartphones can be used to share real-time video and CT scan images
- Stroke registries allow analysis of medical records

These developments can streamline the rapid recognition, transport, and treatment of patients with AIS. Patients in urban areas may benefit from earlier treatment in mobile stroke units, while those in rural areas gain access to specialist care from remote neurologists. Patients with more severe stroke can be detected quickly and preferentially routed to designated CSCs.

The authors conclude:

"These modifications to traditional stroke treatment can translate to improved clinical outcomes."

AIS, acute ischaemic stroke; CSC, comprehensive stroke centre; CT, computed tomography; CTA/CTP, CT angiography/CT perfusion; DNT, door-to-needle time; EMS, emergency medical services; ER, emergency room; GPS, global positioning system; INR, international normalized ratio; IQR, interquartile range; IV, intravenous; MRI, magnetic resonance imaging; NINDS, National Institute of Neurological Disorders and Stroke; OTT, onset-to-treatment time; rtPA, recombinant tissue plasminogen activator; SD, standard deviation; SICH, symptomatic intracranial haemorrhage; TIA, transient ischaemic attack.

The Angels initiative aims to increase the number of patients treated in stroke ready hospitals and to optimise the quality of treatment in all existing stroke centres.
See more at:
https://angels-initiative.com//

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