

## 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 involves many sequential steps, with the resulting potential for bottlenecks and treatment delays. To achieve optimal patient outcomes, the entire pathway should be as efficient as possible: this can be achieved by implementing parallel workflow processes and by adopting strategies that promote cooperation among all stroke care team members.

In this issue of the Actilyse® Publication Alert Newsletter, we highlight the positive impact that multidisciplinary interventions can have on in-hospital delays and rtPA treatment. We also look at how different workflow initiatives can streamline in-hospital processes, and how stroke centre certification can address geographical disparities and improve quality in stroke care.

\*Abbreviations are defined at the end of the newsletter.

### A MULTIDISCIPLINARY APPROACH TO STROKE CARE DECREASES DELAYS AND IMPROVES OUTCOMES

Identifying factors that cause in-hospital delays and addressing these by introducing strategic changes throughout the stroke care pathway has the potential to improve rtPA treatment rates and outcomes for patients admitted with suspected AIS.

Jeon *et al.* implemented a multidisciplinary intervention at their hospital to identify and address in-hospital delays in stroke care.<sup>1</sup> Designed to be active 24 hours a day, new measures included ambulance pre-notification, a streamlined rtPA protocol and regular team feedback. Following implementation, rtPA use increased from 7% to 11% and median DNT more than halved from 46 min to 20.5 min; post-thrombolysis ICH rate was reduced to 4%. Looking only at those patients for whom ambulance pre-notification was used, median DNT was shortened even further to 15 minutes. The intervention was equally effective in office hours and after hours.

The authors conclude that a multidisciplinary approach can reduce in-hospital delays for rtPA treatment both during office hours and after hours, increase thrombolysis rate, and positively affect safety outcomes.

#### Study details

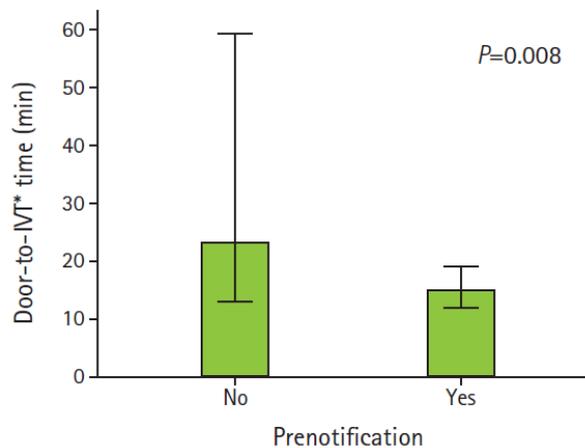
- Analysis of data from 245 patients with AIS who received thrombolysis at a hospital in Korea (Jan 2014–Aug 2016), to investigate the impact on in-hospital treatment times of a multidisciplinary intervention implemented on 2 May 2016
- The SAT (stroke alert team) intervention identified factors causing in-hospital delays, removed unnecessary steps and introduced key measures to reorganize round-the-clock in-hospital care and reduce treatment times. Measures included:
  - Ambulance pre-notification; updated thrombolysis protocol; rtPA administration on the CT table; specified time limits for each step; point-of-care tests; advance notification of neuroradiology team; real-time and regular team feedback
- SAT implementation increased rtPA rates, and reduced door-to-imaging time, DNT and onset-to-needle time (see table)
  - Onset-to-door time remained unchanged by the intervention
  - Post-thrombolysis ICH rate decreased from 13% to 4%
- Following SAT intervention, no differences were found between office hours and after-hours treatment times (onset-to-door, door-to-imaging, door-to-needle, or onset-to-needle)
- Ambulance pre-notification was used in 13/47 cases and, when used, shortened door-to-CT time (7 vs 17 minutes;  $p < 0.001$ ) and DNT (15 vs 26 min,  $p < 0.001$ ) (see also figure); onset-to-door time was not affected

OUTCOME	PRE-INTERVENTION (n=198) 1 JAN 2014 TO 1 MAY 2016	POST-INTERVENTION (n=47) 2 MAY 2016 TO 31 AUG 2016	p VALUE
Onset-to-door time, median (IQR) min	107 (45.5–218.5)	91 (36–199)	0.144
Door-to-imaging time, median (IQR) min			
Door-to-CT	18 (15–23)	13 (8–19)	<0.001
Door-to-MRI	56 (44.5–70)	37.5 (30.3–52)	<0.001
Received rtPA, n/n eligible (%)	141/2012 (7.0)	34/297 (11.4)	0.007
DNT, median (IQR) min	46 (36–57)	20.5 (15.8–32.5)	<0.001
Onset-to-needle time, median (IQR) min	129 (84.3–183.3)	102.5 (49–153.5)	0.024
ICH, n (%)	26 (13.1)	2 (4.3)	0.035

August 2017

**THE FULL PRESCRIBING INFORMATION FOR ACTILYSE IS PROVIDED AT THE END OF THIS NEWSLETTER. IT IS IMPORTANT THAT YOU CHECK THE PRESCRIBING INFORMATION AS APPLICABLE FOR YOUR OWN COUNTRY BEFORE USE.**

### Study details (continued)



Median DNT in 22 EMS-transported patients according to whether pre-notification was used (No, n=9; Yes, n=13) (an additional 25 patients who were not transported by EMS, and therefore did not have pre-notification, are not included in the figure)

**“Using a multidisciplinary approach, we showed that SAT significantly reduced in-hospital delay for thrombolysis treatment.”<sup>1</sup>**

### EFFICIENT STROKE TEAM WORKFLOW COORDINATION BY NURSES REDUCES IN-HOSPITAL DELAYS

Effective cooperation and coordination among stroke team members and between hospital departments is essential to minimize in-hospital delays and achieve a streamlined workflow.<sup>2</sup>

To reduce in-hospital delays, a teaching hospital in China expanded their stroke care team to include a designated ED nurse, who coordinated workflow, and a stroke unit nurse who assisted with rtPA administration. The new standardized nursing cooperation workflow resulted in improved rtPA rates, shorter treatment times and favourable outcomes: almost one-third of eligible patients received rtPA, with a mean DNT of 56 min, and almost all treated patients had a good functional outcome.

The results demonstrate that a standardized nursing cooperation workflow, involving skilled and experienced nurses with appropriate training, promotes effective interdepartmental communication and reduces delays in acute stroke care.

#### Study details

- Analysis of data from 319 patients who received rtPA within 4.5 h of AIS onset at a university hospital in Shanghai, China (Mar 2015–Mar 2016), to examine the impact of a new protocol designed to improve team coordination and reduce delays
- The new protocol, a standardized nursing cooperation workflow, included 24-h support from:
  - An ED ‘coordinator’ nurse, who arranged the CT scan and provided timely information to the ‘cooperating’ nurse
  - A stroke unit ‘cooperating’ nurse, who carried the thrombolysis kit and assisted with rtPA delivery and monitoring
- A thrombolysis kit (containing rtPA and other useful items) was established as part of the new protocol
- The proportion of eligible patients who received rtPA more than doubled under the new workflow protocol, and there were significant reductions in door-to-imaging time and DNT (see table)

OUTCOME	PRE-INTERVENTION (n=689) MAR 2015 TO SEP 2015	POST-INTERVENTION (n=712) OCT 2015 TO MAR 2016	p VALUES
Received rtPA, n (%)	88 (12.8)	231 (32.4)	0.009
Treatment times, mean (SD) [range] min			
Door-to-CT initiation	38.7 (5.2) [16–62]	14.4 (4.4) [3–36]	<0.001
CT completion-to-needle	55.1 (4.8) [38–102]	30.3 (3.7) [6–62]	<0.001
DNT	100.4 (6.1) [56–175]	55.7 (3.6) [18–108]	<0.001
3-month mRS score 0–1, n (%)	85 (96.5)	223 (96.8)	0.863

**“The new standardized nursing cooperation workflow significantly reduced the stroke thrombolysis delays in our emergency department.”<sup>2</sup>**

August 2017

THE FULL PRESCRIBING INFORMATION FOR ACTILYSE IS PROVIDED AT THE END OF THIS NEWSLETTER. IT IS IMPORTANT THAT YOU CHECK THE PRESCRIBING INFORMATION AS APPLICABLE FOR YOUR OWN COUNTRY BEFORE USE.

## MULTIPLE SIMPLE INTERVENTIONS CAN REDUCE AND MAINTAIN DNT ≤60 MINUTES

Assessment of existing practices followed by implementation of new protocols can successfully reduce DNT to below 60 minutes. Practice changes need not be large, but they must be sustainable to ensure improvements can be maintained.<sup>3</sup>

Multiple strategies, including EMS pre-notification and rtPA administration in the CT room, were introduced simultaneously in a Canadian hospital with the aim of reducing in-hospital delays. Median DNT was significantly reduced from 75 minutes to 46 minutes and the proportion of patients treated within 60 minutes increased from 29% to 76%, without adversely affecting safety outcomes. Modifications were implemented in less than a month; reductions in treatment times were achieved within 6 months and were sustained through to the end of the study almost 2 years later.

The authors observe that it is possible to implement multiple simple interventions in a very short timeframe, resulting in improvements in treatment times that are achieved rapidly and yet can be maintained. They advocate a parallel workflow and recommend that all strategies are continuously re-evaluated and optimized to ensure durability and continued safety.

### Study details

- Analysis of data from 106 consecutive patients who received rtPA at a tertiary academic centre in Montreal, Canada (Jan 2012–Mar 2015), before and after implementation (June 2013) of a new stroke care model designed to achieve DNT ≤60 min (see below)

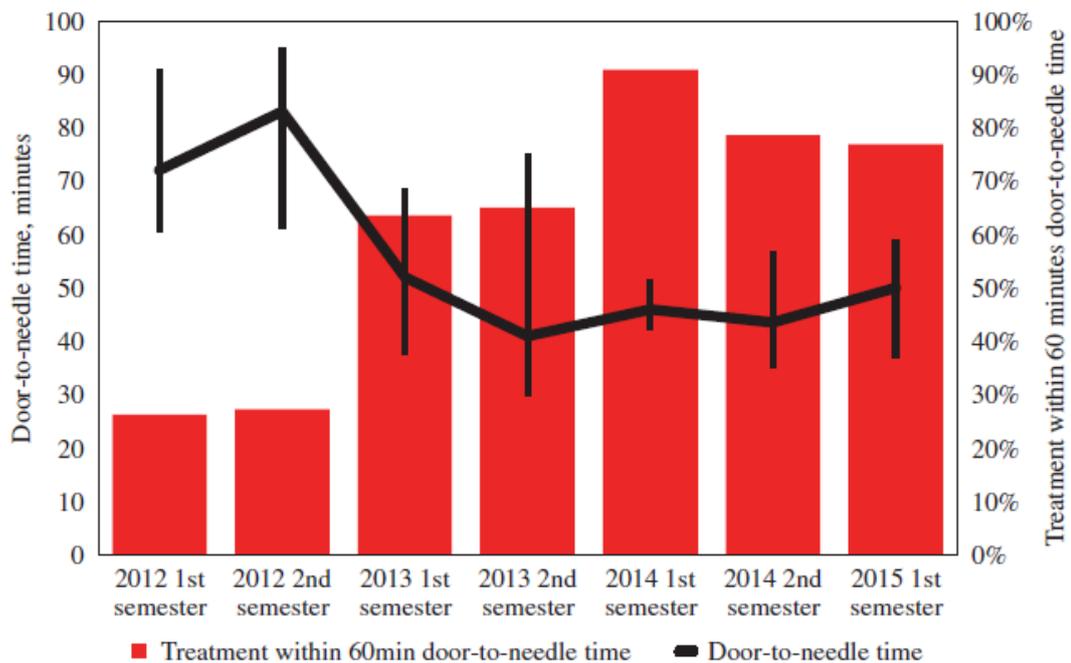
STEP IN CARE PATHWAY	MODIFICATIONS TO REDUCE DNT
Stroke team notification	<ul style="list-style-type: none"> <li>• Pre-notification of stroke team by EMS via single-call activation system</li> </ul>
Laboratory tests	<ul style="list-style-type: none"> <li>• Priority access to point-of-care glycaemia measurement</li> <li>• INR only used if anticoagulation suspected</li> </ul>
Transfer to CT	<ul style="list-style-type: none"> <li>• Direct transfer from EMS to CT upon hospital arrival</li> <li>• Reserved access to elevator</li> </ul>
CT scan	<ul style="list-style-type: none"> <li>• CT technician available 24/7 and directly accessible by stroke team</li> <li>• CT scan interpreted by stroke neurologist without waiting for radiology report</li> </ul>
rtPA delivery	<ul style="list-style-type: none"> <li>• rtPA administration on CT table</li> </ul>
Feedback	<ul style="list-style-type: none"> <li>• Regular feedback to nursing and radiology personnel</li> <li>• Posting of DNT times for personnel to see</li> </ul>

- Rapid, substantial and sustained reductions in median DNT were seen post-intervention (see table below and figure)
  - Median DNT showed a rapid and sustained decrease
  - More than 75% of patients had a DNT ≤60 min
- Door-to-CT and onset-to-needle times were also reduced post-intervention
- The proportion of SICH remained low during the study period

OUTCOME	PRE-INTERVENTION (n=48) JAN 2012 TO MAY 2013	POST-INTERVENTION (n=58) JUL 2013 TO MAR 2015	p VALUES
Door-to-CT time, median (IQR) min	25 (16–42)	19 (14–25)	0.020
DNT, median (IQR) min	75 (60–94)	46 (33–59)	<0.0001
DNT ≤60 min, %	29.2	75.9	<0.001
Onset-to-needle time, median (IQR) min	151 (127–173)	130 (96–176)	0.090
Onset-to-needle time ≤90 min, %	2.1	19.0	0.006
SICH, %	4.2	1.7	0.361

**“We were able to decrease our door-to-needle time for acute stroke thrombolysis by implementing relatively simple modifications and these improvements persisted over time.”<sup>3</sup>**

### Study details (continued)



Median DNT (line, error bars show interquartile range) and proportion of patients with DNT within 60 minutes (bars) before and after implementation of DNT reduction strategies in June 2013

## EMERGENCY DEPARTMENT CROWDING CAN DELAY INITIAL ASSESSMENT AND IMAGING OF STROKE PATIENTS

Streamlined workflow between the ED and the stroke team helps to minimize in-hospital delays. For example, locating the CT scanner next to the ED reduces door-to-CT times. Identifying additional reasons for delays within the ED might highlight areas where coordination of resources could further improve stroke treatment times.<sup>4</sup>

Tsai *et al.* assessed the impact of ED crowding on stroke management efficiency and found door-to-assessment and door-to-CT times – but not DNT – were delayed when there were more patients in the ED and fewer attending physicians available. Patients who did not arrive by ambulance or who were first assessed by less qualified physicians also experienced delays in assessment and imaging. It is possible that DNT was not affected by these factors because patients identified for rtPA treatment received priority physician care. In contrast, having fewer ED nurses available did adversely affect DNT, perhaps due to delays in preparing patients for rtPA treatment (e.g. establishing IV access, taking blood samples).

The authors emphasize the key role of attending physicians in coordinating timely stroke care, and advocate collaboration between ED nurses and the stroke team to improve the efficiency of stroke management.

### Study details

- Analysis of data from 1142 patients presenting to the ED within 3 hours of stroke onset at a large tertiary academic hospital in Taiwan (May 2008–Dec 2013), to evaluate impact of ED crowding and medical staff numbers on stroke care efficiency
  - 72% of stroke patients were assessed within 10 min; median door-to-assessment time was 7 min
  - 78% of stroke patients completed a CT scan within 25 min; median door-to-CT time was 15 min
  - 90/785 AIS patients (11.5%) received rtPA with a mean DNT of 67 min
  - 42/90 rtPA-treated patients (47%) had a DNT ≤60 min
- Delayed door-to-assessment (>10 min) and door-to-CT (>25 min) times **were** associated with greater ED crowding, fewer attending physicians, initial assessment by a resident rather than by an attending physician, and not arriving by ambulance. They **were not** associated with number of nurses.
  - For each additional attending physician available, door-to-assessment time decreased by 2 min and door-to-CT time decreased by 7 min
- Delayed DNT (>60 min) **was** associated with fewer nurses, but **was not** associated with ED crowding, not arriving by ambulance, number of attending physicians, or initial assessment by a resident
  - For each additional nurse available, DNT decreased by 15 min

August 2017

THE FULL PRESCRIBING INFORMATION FOR ACTILYSE IS PROVIDED AT THE END OF THIS NEWSLETTER. IT IS IMPORTANT THAT YOU CHECK THE PRESCRIBING INFORMATION AS APPLICABLE FOR YOUR OWN COUNTRY BEFORE USE.

**“Attending physicians play the key role in the early management of stroke patients including early activation of the treatment protocol and timely collaboration of resources both inside...and outside the ED.”<sup>4</sup>**

### IMPROVING STROKE CARE REQUIRES A MULTIDISCIPLINARY STRATEGIC APPROACH

Stroke directors are tasked with leading the stroke care team and achieving the highest possible standards of stroke care. This requires bringing together many elements:<sup>5</sup>

- Understanding existing stroke care processes and identifying areas where improvements could be made
- Building a multidisciplinary stroke care team (with core team members from: EMS, nurses, physicians, radiologists, pharmacists, laboratory technicians, neurologists, and rehabilitation specialists), and developing a streamlined workflow
- Implementing incremental changes that have a good chance of translating into better care (e.g. EMS pre-notification)
- Engaging and collaborating with ED staff
- Setting goals and reviewing performance regularly

These strategies are relevant to different types of stroke care centre, from community hospitals to CSCs.

### CT IMAGING PROVIDES REAL-TIME EVIDENCE OF THROMBOLYSIS FOLLOWING rtPA ADMINISTRATION

Administration of rtPA to patients while they are still on the CT table shortens DNT and provides an opportunity to image IV thrombolysis in real time. This may help to identify patients with successful recanalization following rtPA administration, and those for whom additional intra-arterial therapy may be beneficial.<sup>6</sup>

Among 10 patients with acute anterior circulation stroke who received rtPA while still on the CT scanner (mean DNT 53 min), imaging evidence of recanalization was seen in 5 patients (50%; 2 with early recanalization, 3 with late recanalization). In the control group of 22 patients, who received rtPA after completing the full imaging protocol (mean DNT 87 min), 8 (36%) showed evidence of recanalization on follow-up imaging (all of which was late recanalization).

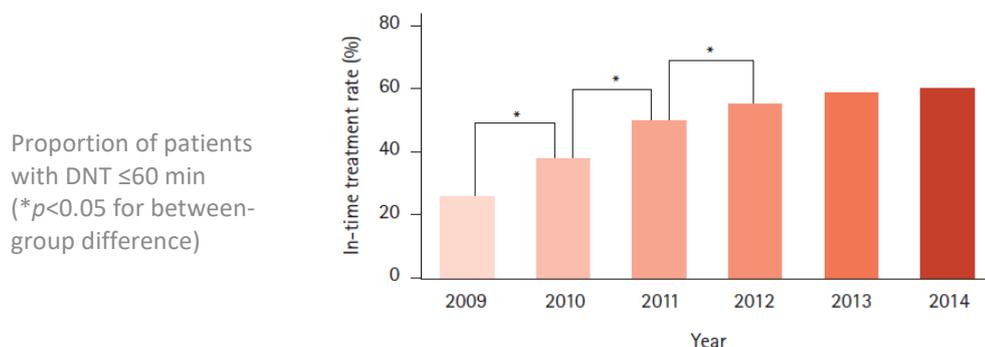
Administering rtPA to patients while still in the CT scanner reduces DNT, while continued imaging of the patient provides evidence of early recanalization following rtPA treatment.

### HOSPITAL CERTIFICATION INITIATIVES CAN LEAD TO IMPROVEMENTS IN THROMBOLYSIS TREATMENT

Nationwide improvements in stroke care quality may be achieved through government initiatives, which encourage individual hospitals to seek stroke centre certification by meeting requirements for acute stroke management.<sup>7</sup>

One such project in Taiwan (‘HECAL-Stroke’) was launched in 2009. By 2014, there were 112 certified hospitals; rtPA treatment rates had increased (from 3% to 4.5%) and the proportion of patients with DNT ≤60 minutes had reached 60% (see figure), without adversely affecting safety outcomes. Improvements were seen across different types of institution, from community hospitals to academic medical centres.

The authors conclude that the government-initiated project led to significant improvements in rtPA treatment in Taiwan.



**“...a thoughtfully designed and well reported project initiated by the government to improve stroke treatment quality can be effective in both academic medical centers and community hospital settings.”<sup>7</sup>**

August 2017

THE FULL PRESCRIBING INFORMATION FOR ACTILYSE IS PROVIDED AT THE END OF THIS NEWSLETTER. IT IS IMPORTANT THAT YOU CHECK THE PRESCRIBING INFORMATION AS APPLICABLE FOR YOUR OWN COUNTRY BEFORE USE.

## HOSPITAL CERTIFICATION STATUS AND GEOGRAPHIC LOCATION AFFECT STROKE CARE QUALITY

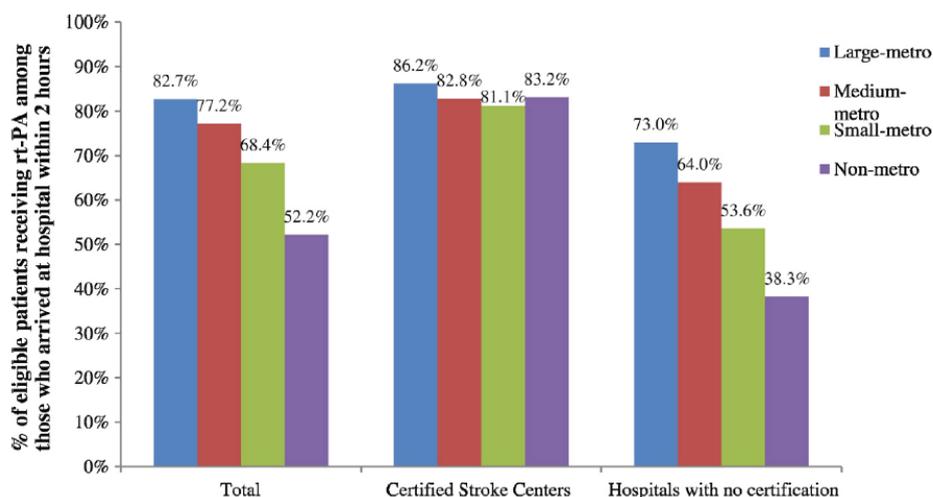
Quality of stroke care within regional networks may vary according to hospital certification status and geographical location. A stroke care network in Kentucky and West Virginia, USA, was set up in 2008 to provide better, more coordinated stroke care. As the initial step in a continuous quality improvement process, a gap analysis was performed in 2014 on affiliated hospitals.<sup>8</sup> Elkins *et al.* analysed data from 17 out of 23 network hospitals and found that certified PSCs or CSCs were most likely to meet stroke care criteria, hospitals with more than 200 beds were moderately successful and rural hospitals were least successful, with none meeting the required stroke care criteria. Only 3 of the 23 hospitals had a stroke programme coordinator. The authors believe that hospital certification drives stroke care quality success, and they encourage affiliated hospitals to seek this. Stroke care quality can be improved throughout the network, and particularly in rural areas, through increased collaboration with top-performing hospitals.

## HOSPITAL CERTIFICATION MAY REDUCE REGIONAL VARIATIONS IN STROKE CARE

Geographical disparities in stroke care quality may be partly addressed by hospital certification as a PSC or CSC.<sup>9</sup> Performance information provided by the US Hospital Compare database illustrates the wide variation and gaps that exist in stroke care delivery, particularly in rtPA use, between urban and rural areas. Non-metropolitan hospitals generally perform worse than metropolitan hospitals, on multiple measures of stroke care quality. However, this gap appears to be abolished in non-metropolitan hospitals that are certified stroke centres. The authors of the study conclude that the care quality gap between metropolitan and non-metropolitan areas is significant, but adequate access to neurological services may improve rtPA treatment rates. In particular, adopting the care protocols that are required for stroke centre certification may help to eliminate quality gaps based on geographical location.

### Study details

- Analysis of stroke care performance data from 2758 US institutions (reported between Apr 2013 and Mar 2014), to document quality gaps in stroke care based on geographical area, size and hospital Joint Commission certification status
- Metropolitan hospitals performed better than non-metropolitan hospitals on all assessed stroke care measures
- Certified stroke centres provided higher quality of care than non-certified hospitals across all geographical areas
  - Non-certified hospitals showed wider variation in stroke care quality than certified hospitals
- Overall, 77.9% of eligible patients received rtPA across all hospitals (see figure)
  - Metropolitan hospitals had 16–31% higher rtPA administration rates than non-metropolitan hospitals
  - Certified hospitals had higher rtPA administration rates than non-certified hospitals; this gap was widest in non-metropolitan areas (83% vs 38%)
  - Hospital certification of a non-metropolitan hospital could improve rtPA treatment rate by as much as 45%
- Greater access to neurological services was associated with higher rtPA treatment rates
  - Telemedicine adoption by a non-metropolitan hospital could improve rtPA treatment rate by 22%



Hospital quality performance in rtPA use by geographical area and certification level

August 2017

“...telemedicine...could improve outcomes for rt-PA-eligible patients with stroke in under-resourced hospitals by facilitating access to neurological services.”<sup>9</sup>

## CLINICAL AND RADIOLOGICAL ASSESSMENT ARE THE KEY COMPONENTS OF TELESTROKE

Laghari and Hammer summarize the benefits of real-time telestroke in providing access to specialist care from remote or rural locations and enabling timely administration of rtPA to a greater number of eligible AIS patients.<sup>10</sup>

They note that telestroke combines remote clinical and radiological components:

- Clinical assessment includes history (e.g. **time of symptom onset**, risk factors) and physical examination
- Radiological assessment includes **head CT scan** and vessel studies (e.g. CT angiography)

The authors observe that, provided telestroke images are of sufficient quality, the time of symptom onset and non-contrast head CT scan are enough information for a decision regarding rtPA administration.

## “Telestroke solves the problems of distance and of shortage of neurologists”

AIS, acute ischaemic stroke; CSC, comprehensive stroke centre; CT, computed tomography; DNT, door-to-needle time; ED, emergency department; EMS, emergency medical services; ICH, intracranial haemorrhage; INR, international normalized ratio; IQR, interquartile range; IV, intravenous; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; PSC, primary stroke centre; rtPA, recombinant tissue plasminogen activator; SAT, stroke alert team; SD, standard deviation; SICH, symptomatic intracranial haemorrhage.

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//>

## References

1. Jeon SB, Ryoo SM, Lee DH *et al*. Multidisciplinary approach to decrease in-hospital delay for stroke thrombolysis. *J Stroke* 2017;19:196-204.
2. Zhou Y, Xu Z, Liao J *et al*. New standardized nursing cooperation workflow to reduce stroke thrombolysis delays in patients with acute ischemic stroke. *Neuropsychiatr Dis Treat* 2017;13:1215-20.
3. Chen BY, Moussaddy A, Keezer MR *et al*. Short- and long-term reduction of door-to-needle time in thrombolysis for acute stroke. *Can J Neurol Sci* 2017;44:255-60.
4. Tsai MT, Yen YL, Su CM *et al*. The influence of emergency department crowding on the efficiency of care for acute stroke patients. *Int J Qual Health Care* 2016;28:774-8.
5. Miller EC, Blum C, Rostanski SK. Developing a stroke center. *Stroke* 2017;48:e155-e156.
6. Tan J, Aysenne A, Singh V. Thrombolysis in real time: demonstration of revascularization with intravenous thrombolysis therapy in the CT scanner. *J Neuroimaging* 2017;27:50-8.
7. Cheng TJ, Peng GS, Jhao WS *et al*. Nationwide "Hospital emergent capability accreditation by level-stroke" improves stroke treatment in Taiwan. *J Stroke* 2017;19:205-12.
8. Elkins K, Bellamy L, Guo J *et al*. Small Rural hospitals have a harder time achieving success in continuous quality improvement: an example from a stroke care network. *Qual Manag Health Care* 2017;26:165-70.
9. Seabury S, Bogner K, Xu Y *et al*. Regional disparities in the quality of stroke care. *Am J Emerg Med* 2017.
10. Laghari FJ, Hammer MD. Telestroke imaging: a review. *J Neuroimaging* 2017;27:16-22.

[ACTILYSE® PRESCRIBING INFORMATION](#)

August 2017

THE FULL PRESCRIBING INFORMATION FOR ACTILYSE IS PROVIDED AT THE END OF THIS NEWSLETTER. IT IS IMPORTANT THAT YOU CHECK THE PRESCRIBING INFORMATION AS APPLICABLE FOR YOUR OWN COUNTRY BEFORE USE.