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.

Specialist stroke teams working within stroke units offer expert treatment and care to patients with AIS.* However, patients must first access this expertise, with the support of pre-hospital and emergency department personnel. Timely transfer of AIS patients to stroke team care requires multidisciplinary teamwork and co-ordinated protocols. Continual efforts to improve stroke care delivery are therefore needed and include initiatives to enhance cooperation among first responders and hospital departments, and adjustments to streamline the patient care pathway.

In this issue of the Actilyse® Publication Alert Newsletter, we look at collaborative and targeted changes to improve timely access to thrombolysis for as many patients as possible, particularly where stroke care resources may be limited.

*Abbreviations are defined at the end of the newsletter.

CONTINUAL EFFORTS TO IMPROVE MULTIDISCIPLINARY STROKE CARE PROTOCOLS REDUCE TREATMENT DELAYS

To improve the timeliness and effectiveness of treatment and increase the proportion of patients able to receive rtPA, stroke care protocols need to be continually re-evaluated and revised.

Evaluation and subsequent modification of an existing acute stroke care protocol at a tertiary centre in Singapore resulted in stepwise improvements in rtPA delivery.[1] Firstly, introducing EMS pre-notification and direct-to-CT transfer reduced mean door-to-CT time by 17 minutes (to 14 minutes) and mean DNT by 15 minutes (to 69 minutes). Secondly, adding dedicated stroke nurses to the 24-hour stroke response team supported streamlined workflow and led to further reductions in treatment delays: mean DNT was reduced to below 60 minutes and two-thirds of patients received rtPA within an hour of hospital arrival.

The authors conclude that, "the application of a simple systems-based, multidisciplinary stroke activation protocol may help in significant reduction in DNT." Adding round-the-clock dedicated stroke nurses to the care team, to accompany the patient and facilitate care, was described as the most important action taken to expedite steps in the treatment pathway.

Study details

- Analysis of data from 410 consecutive patients with AIS who received rtPA at a tertiary stroke care centre in Singapore during a 3-year period (Jan 2014–Dec 2016), to evaluate the impact on DNT and functional outcome of two protocol amendments
  - Original protocol (up to Feb 2015): sequential stroke team workflow without EMS pre-notification
  - Amendment 1 (Mar 2015 – Feb 2016): EMS pre-notification; direct transfer to CT scanner; rapid patient assessment
  - Amendment 2 (Mar 2016 – Dec 2016): streamlined workflow; specialist stroke nurse to expedite treatment
- Both protocol amendments resulted in stepwise improvements in door-to-CT time and DNT (see table)
  - Improvements remained consistent over several months
  - Onset-to-needle times were unchanged, suggesting gains in DNT were offset by longer onset-to-arrival times
- Involvement of a dedicated stroke nurse to facilitate patient care had a significant impact on door-to-CT time and DNT
  - After amendment 2, more than 68% of patients received rtPA within 60 min of symptom onset
- Functional outcomes (SICH, mRS score 0–2 at 3 months, mortality) were similar after amendments 1 and 2

OUTCOME	ORIGINAL PROTOCOL (n=129)	AMENDMENT 1 (n=137)	AMENDMENT 2 (n=144)
ONT, mean min	167	153	160
Door-to-CT time, mean min	31	**14***	**10***
CT-to-needle time, mean min	53	54	49
DNT, mean min	84	**69***	**59*†**
DNT ≤60 min, %	19.4	**48.2***	**68.1*†**

*p<0.005 vs original protocol; †p<0.05 vs amendment 1

"Our study showed that better organization of various concurrent multidisciplinary activities involved in acute stroke care effectively reduced the DNT."[1]

TIMELY THROMBOLYSIS CAN BE ACHIEVED BY MULTIDISCIPLINARY, TARGETED, COLLABORATIVE INTERVENTIONS

Targeted interventions are the most efficient way to improve stroke care delivery, particularly in settings with limited resources.

Safety net hospitals in the USA offer care to all people, regardless of whether they can pay for it or not. As such, safety net hospitals face unique funding and resource challenges in providing stroke care. By introducing a series of specific, targeted interventions within a 4-year period, a safety net hospital in San Francisco, California, was able to significantly reduce DNT and increase the proportion of patients who received rtPA within an hour of hospital arrival.[2]

The decrease in DNT was driven by reductions in imaging delays. Interventions that had the greatest individual impact on DNT were implementation of a stroke code activation system, which included dedicated ED stroke pharmacists, and the introduction of a mobile supply box containing all items needed to administer rtPA.

The authors conclude that multidisciplinary, collaborative, targeted interventions are effective and achievable in resource-limited settings, where they are most needed. Hospital efforts to reduce DNT should focus on streamlining stroke workflow.

Study details

- Analysis of data from 299 consecutive patients with AIS who received rtPA at a tertiary care urban PSC during an 8-year period (Jan 2008–Dec 2015), to evaluate the combined and individual impact on DNT of 11 distinct protocol amendments implemented sequentially between Jan 2011 and Aug 2014
  - Initiatives included: a standardized CT stroke protocol; rtPA administration in the CT scanner; a stroke code activation system; designated ED stroke pharmacists; regular performance review; a box containing items needed to administer rtPA (to accompany the patient); rtPA administration by trained ED nurses
- Patients treated after all interventions were implemented (post-Aug 2014) had a significantly shorter median DNT than patients treated before any interventions were introduced (pre-Jan 2011) (see table)
  - The reduction in DNT was driven mainly by a reduction in CT turnaround time
- The reduction seen in median ONT was due to the reduction in DNT, as onset-to-arrival time was unchanged
- The proportion of patients who received rtPA within an hour of arrival increased from 9% to 70%
- Median DNT was reduced to below 60 minutes after concurrent introduction of the stroke code activation system and dedicated ED stroke pharmacists; a further reduction in DNT occurred after establishing the mobile rtPA supply box

PERFORMANCE INDICATOR	PRE-INTERVENTION (n=67)	POST-INTERVENTION (n=66)	*p* VALUE
Onset-to-arrival time, median (IQR) min	59 (29–88)	59 (39–84)	0.520
ONT, median (IQR) min	151 (120–184)	116 (90–142)	**<0.001**
Door-to-physician time, median (IQR) min	3 (0–13)	0 (0–4)	0.254
Physician-to-CT order time, median (IQR) min	10 (2–20)	6 (3–8)	**0.010**
CT turnaround time, median (IQR) min	41 (30–52)	13 (8–17)	**<0.001**
CT-to-rtPA time, median (IQR) min	32 (19–50)	28 (17–40)	0.513
DNT, median (IQR) min	87 (68–109)	49 (39–63)	**<0.001**
DNT <60 min, mean %	9	70	**<0.001**

"Multidisciplinary, collaborative, targeted interventions are associated with substantial and significant reduction in door-to-needle time."[2]

ED–STROKE UNIT COLLABORATION CAN IMPROVE TIMELY THROMBOLYSIS OF PATIENTS WITH AIS

Involving ED staff and stroke unit personnel in multidisciplinary, collaborative training initiatives may reduce in-hospital delays by improving the efficiency of the stroke care pathway from ED admission through to imaging and rtPA administration.

To improve stroke recognition by triage staff and to refine in-hospital stroke care pathways, one-day training sessions involving ED physicians and nurses, and stroke unit radiologists and neurologists, were carried out at 18 centres in France.[3] The training programme was associated with significant improvements in thrombolysis rates and imaging-to-stroke unit time – although not door-to-imaging time or DNT – without affecting safety outcomes.

Multivariate analysis revealed that admission via EMS had the largest impact on rtPA use and in-hospital delays:

- significantly higher proportions of patients received thrombolysis (overall and within 4.5 h of onset)
- door-to-imaging time was reduced by 76 minutes
- all other metrics were also significantly improved (see table).

However, only 54% of patients were admitted via EMS.

The authors conclude that increasing the awareness and skills of ED professionals significantly increased thrombolysis rates, and that the "optimal strategy to reduce delays and improve access to stroke treatment should associate several complementary measures to act at each step of the chain". Increasing the number of patients admitted via EMS, with pre-notification and direct transfer to the stroke unit, may also reduce in-hospital delays and increase access to rtPA.

PERFORMANCE INDICATOR	PRE-INTERVENTION (n=328)	POST-INTERVENTION (n=363)	*p* VALUE
Received rtPA, n (%)	114 (34.8)	140 (38.6)	**0.04**
Received rtPA within 4.5 h of symptom onset, n (%)	84 (25.6)	124 (34.2)	**<0.001**
Door-to-imaging time, median min	71	80	0.77
Imaging-to-stroke unit time, median min	53	39	**0.03**
Door-to-stroke unit time, median min	113	106	0.14
DNT, median min	95	96	0.40
Death, n (%)	22 (6.7)	14 (3.9)	0.289
Complications, n (%)	40 (12.2)	44 (12.1)	0.976

EMS NOTIFICATION OF THE ON-CALL NEUROLOGIST REDUCES IN-HOSPITAL DELAYS FOR PATIENTS WITH AIS

In a tertiary university hospital in Iran, direct EMS notification of the on-call neurologist (rather than the ED physician) significantly reduced door-to-CT time and DNT, and improved rtPA treatment rates for patients with AIS.[4]

The authors suggest that earlier involvement of the attending neurologist provides the stroke team with more time to prepare for the patient's arrival. They conclude that simple, brief, and continuing training sessions for EMS, and direct 24/7 telephone contact between dispatch and a neurologist can reduce door-to-CT time and DNT effectively for acute stroke patients.

Study details

- Analysis of data from 379 patients with AIS for whom stroke code was activated at a tertiary care centre in Iran during a 4-year period (Jan 2013–Dec 2016) to evaluate the impact on door-to-CT and DNT of a pre-hospital notification (PHN) protocol implemented in Dec 2012
  - Under the PHN protocol, trained EMS staff notified the on-call neurologist *directly,* via a 24/7 hotline, of any patient with suspected AIS with symptom onset within 3 h; the on-call neurologist then activated the hospital stroke code
  - Patients admitted with PHN were compared with patients admitted without PHN during the same period
- Just under half of all patients (180/379) with stroke code activation were admitted with PHN
  - Code activation via EMS was correct in 161/180 cases (89%); 12 cases did not meet the symptom onset time criterion
  - Patients without PHN were typically transferred to hospital by family members and were more likely to arrive outside of the rtPA treatment window
- Use of PHN increased the rtPA treatment rate and significantly shortened in-hospital delays (see table)
  - 87% of patients with PHN received rtPA ≤3 h after symptom onset, compared with 70% of those without PHN

PERFORMANCE INDICATOR	NO PRE-NOTIFICATION (n=115)	PRE-NOTIFICATION (n=131)	*p* VALUE
Received rtPA, n/N (%)	115/199 (58)	131/180 (73)	
Onset-to-arrival time, median (IQR) min	78 (50–120)	83 (55–121)	0.462
Door-to-CT time, median (IQR) min	25 (18–45)	15 (10–25)	**<0.001**
DNT, median (IQR) min	70 (53–95)	42 (34–56)	**<0.001**

PROVIDING ROUND-THE-CLOCK STROKE CARE, INCLUDING AN EMERGENCY TELEPHONE NUMBER, REDUCES IN-HOSPITAL DELAYS FOR PATIENTS RECEIVING rtPA

Developing and implementing a multidisciplinary stroke care protocol that covers the AIS pathway from symptom onset to treatment can reduce in-hospital treatment delays and increase access to thrombolysis.

A tertiary care hospital in China adopted a stroke care protocol that included a dedicated 24-hour emergency stroke number and round-the-clock thrombolysis provision. Following protocol adoption, in-hospital treatment delays were significantly shorter and the proportion of eligible patients who received rtPA more than doubled.[5]

The authors conclude that the successful implementation of a 24-hour stroke thrombolysis protocol can increase the rate of rtPA use and reduce in-hospital treatment delays.

Study details

- Analysis of data from 188 patients with AIS treated with rtPA within 4.5 h of stroke onset at a tertiary care centre during a 3-year period (Jan 2012–Dec 2014), to evaluate the impact of a 24-h stroke thrombolysis protocol implemented in Jan 2013
  - 24-h protocol included: a universal emergency number for patients with stroke symptoms to call; priority EMS dispatch and assessment within 10 min; dedicated ED stroke nurses; neurologist notification; rapid evaluation; CT scan within 25 min of arrival; transfer of eligible patients to the stroke unit for rtPA administration within 60 min of arrival
  - 2467 of 2702 patients admitted with AIS were ineligible to receive rtPA due to ED arrival >4.5 h after symptom onset
- Number and proportion of patients who received rtPA increased significantly after the intervention (see table)
- Door-to-CT time, CT-to-needle time, and DNT all decreased significantly after the intervention, to within target times (see table)
  - Onset-to-treatment time decreased after the intervention, although not significantly
- Safety outcomes were unaffected while functional outcomes improved, albeit not significantly (see table)

PERFORMANCE INDICATOR	2012 (PRE-INTERVENTION) (n=36)	2013 (n=62)	2014 (n=90)	*p* VALUE
Received rtPA, n/N (%)	36/878 (4.1)	62/968 (6.4)	90/856 (10.5)	**0.001**
Onset-to-treatment time, median (IQR) min	176 (157–209)	147 (121–173)	124 (97–142)	0.26
Door-to-CT time, median (IQR) min	21 (15–29)	18 (13–27)	16.5 (11–25)	**<0.01**
CT-to-needle time, median (IQR) min	24 (17–32)	22 (16–30)	21 (15–27)	**0.04**
DNT, median (IQR) min	81 (73–94)	52 (43–65)	42 (30–51)	**<0.01**
SICH, n (%)	1 (2.8)	2 (3.2)	2 (2.2)	0.93
90-day mRS score 0–2, n (%)	17 (47.2)	32 (51.6)	51 (56.7)	0.60
3-month mortality, n (%)	7 (19.4)	10 (16.1)	11 (12.2)	0.56

USING A REGIONAL TELESTROKE NETWORK TO TREAT AIS IS EFFECTIVE, WITH GOOD SAFETY

A potential shortage of stroke units and neurologists in France led to introduction of a new regional telestroke network in Burgundy in 2012, which was associated with good results in terms of safety and efficacy for AIS management.[6] Following teleconsultation, more than a third of patients with suspected AIS received rtPA, and more than half of these had a good functional outcome at 3 months. Time to treatment, safety and effectiveness outcomes were generally similar to those of patients treated in person.

The authors conclude that the proportion of patients who receive thrombolysis will increase due to the telestroke network.

Study details

- Retrospective review of data from 132 consecutive patients with AIS treated with rtPA in a 10-hospital telestroke network (1 stroke unit connected to 9 local hospitals), to evaluate safety and effectiveness of telestroke thrombolysis
  - 361 patients with suspected AIS received teleconsultation (April 2012–Dec 2014); 132 (36.6%) received rtPA
  - Control group of 222 patients received rtPA after in-person consultation at the hub hospital (Jan 2011–Dec 2012)
  - Decision to administer rtPA was made by the same neurologists for both groups of patients
- Outcomes were similar in the telestroke and in-person groups (see table), with two exceptions:
  - A higher proportion of telestroke patients died in hospital, possibly due to greater stroke severity in this group
  - A lower proportion of telestroke patients had an mRS score of 0 or 1 at 3 months; however, no significant association between telestroke and worse outcome was found after adjustment for confounding factors

PERFORMANCE INDICATOR	IN-PERSON CONSULTATION (n=222)	TELECONSULTATION (n=132)	*p* VALUE
Time to rtPA treatment, mean ±SD min	195 ±58	192 ±48	0.94
In-hospital mortality, n (%)	14 (6.3)	18 (13.6)	0.02
SICH, %	14 (6.3)	8 (6.1)	0.93
3-month mRS score, mean ±SD*	2.3 ±2.2	2.7 ±2.2	0.12
mRS score 0–1, n (%)	103 (48.6)	47 (35.6)	0.02
mRS score 0–2, n (%)	124 (55.9)	68 (51.5)	0.43
3-month mortality, n (%)	35 (16.5)	25 (18.9)	0.56

*4.5% of patients from the in-person consultation group had missing data for mRS score

AIS, acute ischaemic stroke; CT, computed tomography; DNT, door-to-needle time; ED, emergency department; EMS, emergency medical services; IQR, interquartile range; mRS, modified Rankin Scale; ONT, onset-to-needle time; PHN, pre-hospital notification; PSC, primary stroke centre; rtPA, recombinant tissue plasminogen activator; SD, standard deviation; SICH, symptomatic intracranial haemorrhage.

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

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