Talk About Thrombolysis. Regular Case-Based Discussions of Stroke Thrombolysis Improve Door-to-Needle Time by 20%

Caroline Klingner, MD,* Albrecht Günther, MD,* Stefan Brodoehl, MD,*,† Otto W. Witte, MD,* and Carsten M. Klingner, MD*,†

Background: The outcome of stroke patients can be improved by a rapid initiation of thrombolytic therapy. Here, we sought to determine whether an additional simple but thorough case-based discussion of recent thrombolysed cases with the entire neurologic staff can improve the door-to-needle time without changes to the implemented stroke protocol. *Methods:* For every performed thrombolysis, a route card, consisting of a timeline with 3 time points and target times, had to be completed by the attending neurologist. Times and reasons for delays were noted. All thrombolysed cases were then reviewed in a 14-day-rhythm with the entire neurologic staff. The responsible stroke consultant gave details and reasons for delays. Possibilities to avoid delays were then discussed with the whole team. All thrombolyses were prospectively recorded and compared with thrombolyses of the 2 preinterventional years. The primary outcome parameter was the door-to-needle time. *Results:* The door-to-needle time decreased from 37 minutes in the preintervention period (N = 154) to 28 minutes during the intervention (N = 97; $P < .001$). Performance was improved for residents (<6 years of neurologic training) as well as for the specialists (>6 years of neurologic training). Improvements in the performance of specialists were significantly greater than those of residents. *Conclusions:* The present study demonstrates improved treatment of stroke patients by a simple, non−time-consuming intervention that combines education with a potential increase in staff motivation. This intervention is effective in a tertiary academic stroke center with a previously implemented sophisticated stroke protocol but should also improve treatment delays in primary stroke centers.

Key Words: Stroke management—thrombolysis—education—door-to-needle—t-PA

Introduction

The recanalization of occluded vessels is the best therapeutic option for patients in the acute phase of stroke.[1,2,3,4] Multiple studies have demonstrated substantial benefits of tissue plasminogen activator (t-PA) within the first hours.[2,5] As the efficacy of t-PA declines over time, a rapid initiation of thrombolytic therapy is of utmost importance.[5,6-8]

It is known that the door-to-needle time can be improved by implementing a stroke protocol.[9,10] This also requires staff training for an optimal protocol adherence. Most studies have investigated training effects bundled together with other interventions to improve the acute management of stroke patients.[9,11,12] However, there is no consensus on how this training should be implemented as well as what a reasonable compromise between time-consumption and

From the *Hans Berger Department of Neurology, Jena University Hospital, Jena, Germany; and †Biomagnetic Center, University Hospital, Germany.

Received August 29, 2018; revision received November 12, 2018; accepted December 5, 2018.

Funding Disclosure: The authors were supported by BMBF (IRESTRA 16SV7209 and Schwerpunktprogramm BU 1327/4-1).

Conflict of Interest: The authors declare that there are no conflicts of interest.

Address correspondence to Carsten M. Klingner MD, Hans Berger Department of Neurology, University Hospital Jena, Erlanger Allee 101, Jena D 07747, Germany. E-mail: carsten.klingner@med.uni-jena.de.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.12.002

effect is. Additionally, it remains unknown whether staff training alone has an effect on an already streamlined acute stroke management.

In the current study, we sought to determine whether an additional, simple but steady training program for neurology staff members can improve the door-to-needle time in an academic stroke center with an already implemented sophisticated stroke protocol with an average door-to-needle time of 37 minutes. The investigated staff training model was inspired by the suggestions of the American Heart Association.[13] The intervention consisted mainly of the introduction of a case-based review and discussion of all performed thrombolyses by the entire neurologic staff. All details of the thrombolyses included a timeline of 3 timesteps and written comments about delays that were presented without anonymity. Possibilities to avoid delays and optimize acute management were discussed by the whole team, including senior neurologists.

We hypothesized that the repetitive discussion and identification of individual barriers will improve acute stroke management. All thrombolyses were prospectively recorded since the start of this intervention in January 2017 until January 2018. The effectiveness of this intervention was evaluated by comparing door-to-needle times, as the primary outcome parameter, with the 2 preceding years.

Methods

Intervention Design and Implementation

A training program for the neurologic staff was developed and implemented in January 2017. All neurology staff members who participated in the acute management of stroke patients in the emergency department were required to attend. Sessions were scheduled every second week. In these sessions, all thrombolyses of the 2 previous weeks were discussed. For each thrombolysis, the physician who treated the patient was required to complete a route card (the route card is shown in the supplementary material). This route card was presented to and discussed by the whole team. Special attention was given to time delays in different steps, while possible solutions for encountered problems were given. In each session, an average of 4-5 thrombolyses were discussed. Sessions did not exceed 10 minutes. The investigated staff training model was inspired by the suggestions of the American Heart Association.[13]

Primary outcome measure was the door-to-needle time. Secondary outcome measures were door-to-imaging time, the number of thrombolysed stroke mimics, and differences in performance improvements between residents and specialists.

Data Management and Statistical Analysis

All required information that was entered into the statistical analysis was taken from the hospital electronic documentation system. Particularly, the time from arrival of the patient to the start of imaging as well as the door-to-needle time were taken from the electronic documentation system and not from the route card to avoid any bias and maximize comparability between pre- and post-intervention periods. However, from the route card, we extracted the following information: time from start of imaging to image review by neurologist and radiologist; and time from image review to start of thrombolysis. This information was not accessible from the preceding years and was therefore not entered into the statistical analysis but instead was accessed for informative value. We further determined whether thrombolysis was performed by a neurology specialist or neurology resident.

We included all patients who received thrombolytic therapy from 2015 to 2017. The single exclusion criterion was a documented decision against thrombolytic therapy that was reversed due to a worsening of symptoms within the hospital. The rationale for this exclusion criterion is that the door-to-needle time for these patients did not depend on the acute stroke management and stroke protocols. All data were prospectively collected during the year 2017 and compared with retrospectively collected data from the years 2015 and 2016.

Quantitative data were described using mean and standard deviation. Qualitative data were described using absolute and relative frequencies. Comparison of age was performed using Student's t test. Since all other quantitative data were presumably non-normally distributed, group differences were accessed by using Wilcoxon rank-sum tests. Comparisons of qualitative data were performed by using Fisher's exact test.

Results

During the survey (2015-2017), 2108 patients with ischemic stroke were admitted primarily to the University Hospital of Jena. 259 (12.3%) of these stroke patients were treated with t-PA. Eight patients were excluded because of a thrombolysis due to secondary worsening of symptoms after a documented initial decision against thrombolytic therapy. The resulting study group consisted of 251 patients. Seventy-three were thrombolysed in the year 2015, 81 in 2016, and 97 in 2017. Patient characteristics are shown in Table 1. None of the patient characteristics showed a significant difference between the preintervention period and intervention period.

The mean door-to-needle time decreased significantly by 8.8 minutes, from 37.1 ± 23.0 minutes in the preintervention period to 28.3 ± 14.3 minutes in the intervention period ($P = .001$). A significant decrease was also found for the door-to-imaging time from 15.0 ± 9.5 minutes in the preintervention period to 10.2 ± 7.7 minutes in the intervention period ($P < .001$). The decreased imaging-to-needle time of 3.6 minutes was not nonsignificant ($P = .73$).

Table 1. *Baseline demographic and resident characteristics for thrombolysed patients*

	Preintervention period		Intervention period	*P* value
	2015	2016	2017	pre vs post
Characteristic				
N	73	81	97	
Female (N)	44% (32)	49% (40)	51% (49)	.56
Age ± SD	73.4±12.7	70.6 ± 12.8	73.2 ± 12.8	.75
NIHSS ± SD	10.0±6.6	10.2 ± 5.7	11.6 ± 7.3	.19
CHA_2DS_2VASc ± SD	2.7±1.6	2.8 ± 1.5	3.0 ± 1.5	.09
Dementia (N)	12 % (9)	9% (7)	8% (8)	.57
Malignant tumor (N)	5% (4)	2% (2)	4% (4)	.92
Peripheral arterial disease (N)	8 % (6)	5% (4)	5% (5)	.66
Renal insufficiency (N)	8 % (6)	9% (7)	15% (15)	.09
Congestive heart failure (N)	14% (10)	16% (13)	22% (21)	.17
Hypertension (N)	74% (54)	75% (61)	79% (77)	.40
Diabetes (N)	30% (22)	21% (17)	29% (28)	.54
Coronary artery disease (N)	16% (12)	4% (3)	12% (12)	.51
Deep venous thrombosis (N)	3% (2)	1% (1)	5% (5)	.16
Pulmonary embolism (N)	3% (2)	2% (2)	6% (6)	.16
Adipositas (N)	4% (3)	5% (4)	8% (8)	.23
Prior stroke (N)	12% (9)	15% (12)	10% (10)	.44
Treated by resident (N)	57% (42)	60% (49)	54% (52)	.43
Treated by specialist (N)	43% (31)	40% (32)	46% (45)	.43

± SD, standard deviation; N, number of patients.

The proportion of patients with a door-to-needle time of less than 30 minutes (53% versus 68%) and less than 20 (19% versus 35%) minutes significantly increased (see Table 2 and Fig 1 for details).

The proportion of thrombolyses performed by a specialist versus a resident did not change during the survey. Both groups showed a significantly decreased door-to-needle time. The door-to-needle time decreased by 10.8 minutes for patients treated by specialists, while a decrease of 6.3 minutes was found for treatments performed by residents.

In the preintervention period, there was no difference in the door-to-needle time between specialists and residents (36.4 ± 28.0 versus 37.6 ± 18.9; $P = .82$), while in the intervention period, we found a significant difference with lower door-to-needle times for specialists compared to

Table 2. *Outcome parameters*

	Preintervention period		Intervention period	*P* value
	2015	2016	2017	pre vs post
Characteristic				
N	73	81	97	
Symptom-to-door time ± SD	73.4 ± 12.7	70.6 ± 12.8	73.2 ± 12.8	.81
Door-to-imaging time ± SD	15.5 ± 7.8	14.2 ± 10.5	10.2 ± 7.7	<.001
Imaging start-to-viewing ± SD			6.8 ± 5.8	
Image viewing-to-needle time ± SD			11.3 ± 7.9	
Door-to-needle time ± SD	37.5 ± 23.5	36.7 ± 22.7	28.3 ± 14.3	<.001
Symptom-to-door time ± SD	73.4 ± 12.7	70.6 ± 12.8	73.2 ± 12.8	.75
DTN time <15 min (N)	11% (8)	12% (10)	17% (16)	.344
DTN time <20 min (N)	16% (12)	21% (17)	35% (34)	.007
DTN time <30 min (N)	52% (38)	53% (43)	68% (66)	.025
DTN time <60 min (N)	88% (64)	91% (74)	97% (94)	.074
Door-to-needle time for patients treated by residents ± SD	38.5±19.6	37.2±18.5	30.8 ± 14.5	.019
Door-to-needle time for patients treated by specialists ± SD	36.7±28.4	36.0±28.1	25.4 ± 13.7	.026
Stroke mimic (N)	1% (1)	7% (6)	4% (4)	.74
Favorable outcome (mRS ≤2) (N)	59% (43)	57% (46)	65% (63)	.26

All times are in minutes; ± SD, standard deviation; N, number of patients.

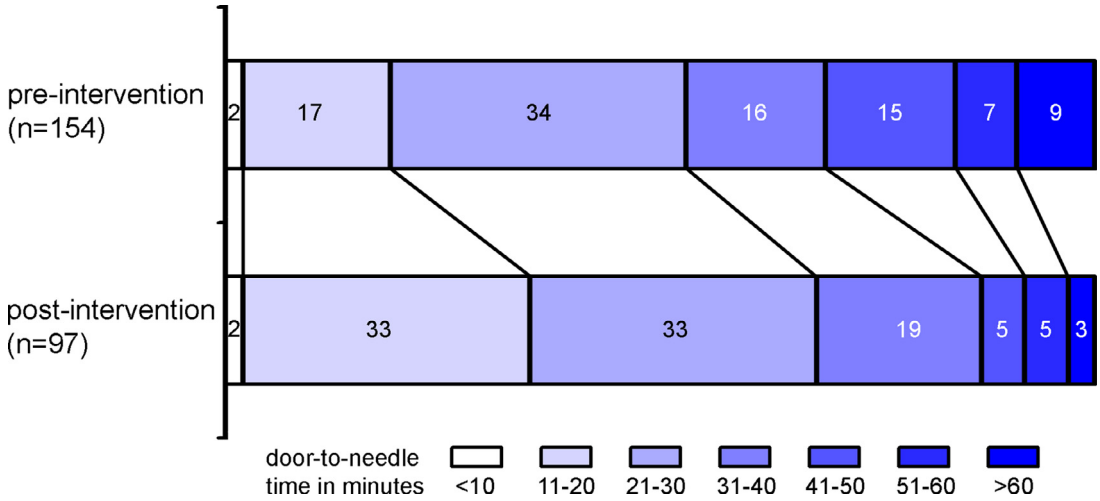

Figure 1. *Distribution of door-to-needle time intervals according to the preintervention period (upper part) and intervention period (lower part). (Color version of figure is available online.)*

residents (25.4 ± 13.7 versus 30.8 ± 14.5; $P = .008$; Fig 2). No significant difference was found for the symptom-to-door time ($P = .84$). We found no significant difference for a favorable outcome at the time of discharge. In the preintervention period, 58% of patients showed a favorable outcome (mRS ≤2 at the time of discharge), while 65% showed a favorable outcome during the intervention period ($P = .26$). Additionally, no significant difference was found for the treatment of stroke mimics, with 5% in both the preintervention and intervention period ($P = .083$).

From our experiences of the case-based discussions during the intervention as well as from the delay-reasons noted in the thrombolysis protocols, there are some repetitive problems encountered that prevented a timely start of the imaging (see Table 3 for key discussion points).

Discussion

In the current study, we investigated the effects of neurological staff training on the hyperacute management of stroke patients. The main finding was a significantly

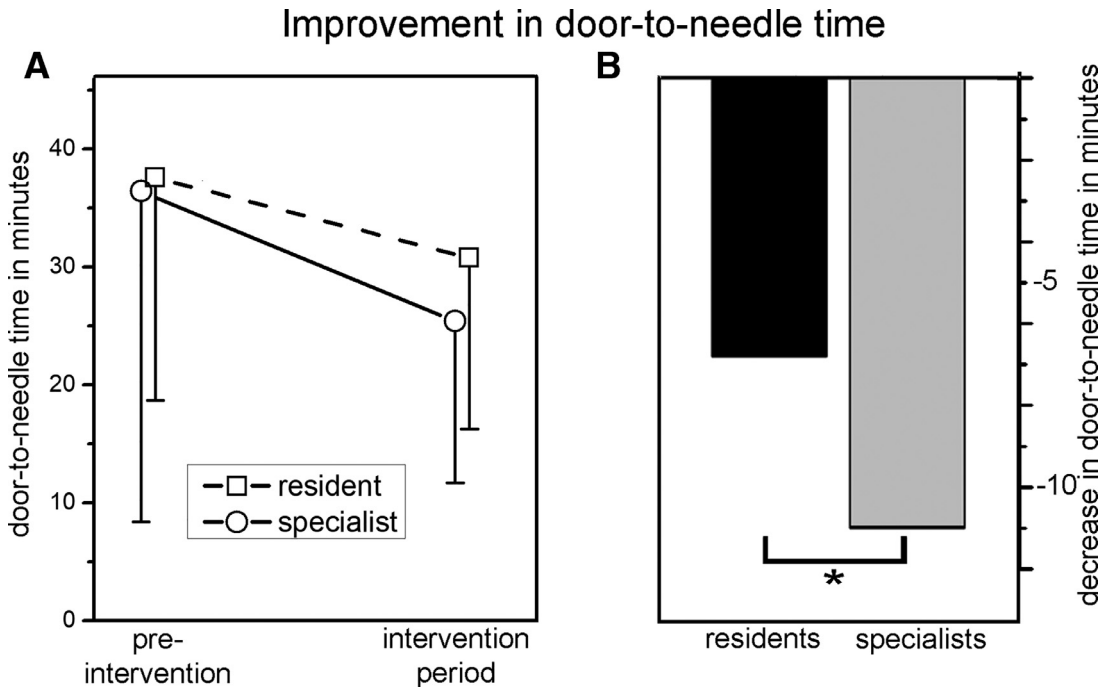

Figure 2. *Impact of the current intervention on door-to-needle times (DNT) depending on treatment by a neurologic resident (year 1-6 of neurologic training) or neurologic specialist (>6 years of neurologic training). (A), Median DNT in minutes and standard deviation for the preinterventional- and interventional period. (B), Intervention-associated changes in DNT depending on treatment by a neurologic resident (black column) or neurologic specialist (gray column).*

Table 3. *Key discussion points*

1	door-to-imaging and imaging-to-thrombolysis procedures
2	balancing "swift or sure" in clinical examination
3	challenges in taking the medical history (eg, aphasia or neglect)
4	indication and contraindication of t-PA
5	evidence-based balancing of individual risks and benefits in the presence of relative contraindications
6	effective communication in the emergency department
7	handling of difficult agitated patients

t-PA, tissue plasminogen activator.

improved door-to-needle time. In most available studies, staff training is one part of a more complex intervention and mostly combined with structural changes.[12,14] There are only a few studies available that primarily focused on staff training. For example, Haesebaert et al performed a training program targeting emergency physicians and nurses with videos and interactive simulation workshops. They demonstrated a significant increase in performed thrombolyses but no decrease in door-to-needle time[11]. Another study found a decreased door-to-needle time (from 79 minutes to 58 minutes) by implementing a structured, educational 1-time training for neurology residents.[15] These interventions differ considerably from the current intervention, as these studies have used education and training to induce protocol changes in the management process of stroke patients. In the current study, however, the staff training was an isolated intervention and not combined with any changes on the management process of stroke patients. It was also a permanent and not a 1-time intervention. Moreover, most previous studies that included staff training in their interventions started with a door-to-needle time beyond 60 minutes.[12,15] The current study, however, was performed at a tertiary academic stroke center with a previously implemented sophisticated stroke protocol. Except for the premixing of t-PA (prior to the patients arrival), all measures suggested by the Helsinki protocol were implemented in our hospital.[9,10] Therefore, the current intervention aimed to improve the management of acute stroke patients while it did not induce protocol changes. We found a significantly improved door-to-needle time that was mainly caused by a reduced door-to-imaging time. From our experiences, during the time of intervention and particularly from the case-based discussions, we suggest that the reasons for this result included an increased protocol adherence and improved performance in difficult cases (eg, the handling of an agitated patient). In contrast to the door-to-imaging time, the reduction in the imaging-to-needle time did not reach statistical significance. The image-to-needle time consists of the image acquisition, image viewing (together with the radiologist), the decision making, and mixing of t-PA. Most of the noted delays in the imaging-to-needle time are difficult to avoid, such as an unknown symptom onset or an unknown medication.

One of the most interesting results of the current study was the finding that specialists improved their performance significantly more than did residents. This finding seems counterintuitive, as one might assume higher learning effects for staff members with little knowledge and experience. Particularly, additional knowledge on practical stroke management and hospital-specific circumstances should have a minor effect on neurologic specialists, as all our specialists are former residents of our hospital and therefore well aware of hospital-specific processes.

If we further assume that residents indeed acquire more knowledge than specialists from the current intervention, then the stronger improvement found in specialists must not have been caused by the knowledge domain. We hypothesize that the nonanonymous presentation of cases acts as an additional, extrinsic motivational factor that improves the motivation of staff members to perform thrombolyses as fast as possible. This is a somewhat provocative hypothesis, as one might assume that the well-being of patients is the primary objective of all medical staff members. However, although this may be a convincing way to think, psychologic science has clearly shown that motivation is not a binary attribute but is instead a continuous state that is generated not solely by intrinsic factors.[16] According to current psychological theories, motivation for a specific activity is determined by weighing the expected benefits and expected costs of this activity.[16] One could assume that intrinsic benefits are the dominant motivational factor for medical staff members; however, as with nearly all other mechanisms of neuronal systems, intrinsic benefits underlie habituation.[17,18] Therefore, it is quite conceivable that the additional extrinsic motivation induced by the nonanonymous presentation of performance has a stronger effect on specialists than on residents. Moreover, even if extrinsic motivation in residents and specialists is improved equally, the performance of specialists should improve more greatly than that of residents, as their performance prior to the current intervention was similar; therefore, one may assume a greater potential for improvements in specialists.

In conclusion, the present study demonstrates improved treatment of stroke patients by a simple, non−time-consuming intervention that combines education with a potential increase in staff motivation. This

intervention was demonstrated as effective in a tertiary academic stroke center with a previously implemented sophisticated stroke protocol and should also improve treatment delays in primary stroke centers.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2018.12.002.

References

1. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-1731.
2. Emberson J, Lees KR, Lyden P, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet 2014;384:1929-1935.
3. Fonarow GC, Reeves MJ, Smith EE, et al. Characteristics, performance measures, and in-hospital outcomes of the first one million stroke and transient ischemic attack admissions in get with the guidelines-stroke. Circ Cardiovasc Qual Outcomes 2010;3:291-302.
4. Fonarow GC, Smith EE, Saver JL, et al. Timeliness of tissue-type plasminogen activator therapy in acute ischemic stroke: patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes. Circulation 2011;123:750-758.
5. Lees KR, Emberson J, Blackwell L, et al. Effects of alteplase for acute stroke on the distribution of functional outcomes: a pooled analysis of 9 trials. Stroke 2016;47:2373-2379.
6. Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 2004;363:768-774.
7. Lees KR, Bluhmki E, von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. Lancet 2010;375:1695-1703.
8. Marler JR, Tilley BC, Lu M, et al. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. Neurology 2000;55:1649-1655.
9. Meretoja A, Strbian D, Mustanoja S, et al. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. Neurology 2012;79:306-313.
10. Meretoja A, Kaste M. Pre- and in-hospital intersection of stroke care. Ann N Y Acad Sci 2012;1268:145-151.
11. Haesebaert J, Nighoghossian N, Mercier C, et al. Improving access to thrombolysis and inhospital management times in ischemic stroke: a stepped-wedge randomized trial. Stroke 2018;49:405-411.
12. Prabhakaran S, Lee J, O'Neill K. Regional learning collaboratives produce rapid and sustainable improvements in stroke thrombolysis times. Circ Cardiovasc Qual Outcomes 2016;9:585-592.
13. Fonarow GC, Smith EE, Saver JL, et al. Improving door-to-needle times in acute ischemic stroke: the design and rationale for the American Heart Association/American Stroke Association's target: stroke initiative. Stroke 2011;42:2983-2989.
14. Van Schaik SM, Van der Veen B, Van den Berg-Vos RM, et al. Achieving a door-to-needle time of 25 minutes in thrombolysis for acute ischemic stroke: a quality improvement project. J Stroke Cerebrovasc Dis 2014;23:2900-2906.
15. Ruff IM, Liberman AL, Caprio FZ, et al. A resident boot camp for reducing door-to-needle times at academic medical centers. Neurol Clin Pract 2017;7:237-245.
16. Studer B, Knecht S. Motivation: what have we learned and what is still missing? Prog Brain Res 2016;229:441-450.
17. Thompson RF. Habituation: a history. Neurobiol Learn Mem 2009;92:127-134.
18. Klingner CM, Hasler C, Brodoehl S, et al. Excitatory and inhibitory mechanisms underlying somatosensory habituation. Hum Brain Mapp 2014;35:152-160.