Door-to-Needle Time in Acute Stroke Treatment and the “July Effect”

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Abstract

Intravenous thrombolysis improves outcomes in acute ischemic stroke in a time-dependent fashion. As in teaching hospitals, clinical outcomes may worsen due to the arrival of new inexperienced house staff early in the academic year (July effect, JE), we evaluated the impact of the “JE” on the door-to-needle time for intravenous thrombolysis and other stroke outcomes. In this retrospective cohort study, we assessed all acute ischemic strokes treated with intravenous thrombolysis between July 2003 and June 2016. Among 101 patients, there was no detrimental July effect on the door-to-needle time, rate of thrombolysis within 60 minutes of arrival, thrombolysis of stroke mimics, post-thrombolysis intracranial hemorrhages, National Institutes of Health Stroke Scale, and modified Rankin Scale outcomes.

Keywords

stroke, thrombolytic therapy, house staff

Background and Purpose

Intravenous thrombolytic therapy (IVT) improves outcomes of patients with acute ischemic stroke in a time-dependent fashion.¹ Delays in IVT administration can occur in the pre-hospital setting or during the early hospital triage and workup. The door-to-needle time (DTNT) is the time between hospital arrival and IVT administration. Prompt diagnosis, proper logistics, and rapid response of the stroke team are key determinants of this variable.² Due to the demonstrated improvement in clinical outcomes, current guidelines recommend at least 80% of IVT treatments to be done within 60 minutes DTNT.³

The “July effect” (JE) reflects the impact of inexperienced house staff arrival on different outcomes in teaching hospitals.⁴ The lack of knowledge, fatigue, and unfamiliarity with a new system could explain the negative impact of the JE observed in some studies,⁵⁻⁸ whereas organizational factors and close supervision schemes could compensate for the lack of experience of new house staff, blunting negative outcomes.⁹⁻¹⁵

Data on the impact of the JE in stroke care are scant. In a recent study, patients with stroke admitted to tertiary stroke centers during July had similar outcomes despite slightly less frequent thrombolysis and stroke unit care.¹⁶ As the DTNT reflects a time-sensitive and complex clinical process, and residents are responsible for running stroke codes in many academic centers, this variable may be especially vulnerable to new trainees’ arrival, negatively impacting clinical

outcomes. To the best of our knowledge, there are no published data about the impact of the JE on the DTNT for acute stroke treatment. We aimed to evaluate DTNT and stroke outcome variables during the initial months of the academic year and at other periods.

Methods

Study Design

In this retrospective cohort study, we assessed all patients with acute ischemic stroke treated with IVT between June 2003 and July 2016. Patients were identified from the electronic medical record database and data extracted by retrospective chart

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review. The DTNT, rate of IVT performed within 60 minutes, thrombolysis of stroke mimics, post-IVT intracranial hemorrhage (ICH), National Institutes of Health Stroke Scale (NIHSS) on admission, and NIHSS and modified Rankin Scale (mRS) at 3 months were evaluated in all patients. Post-thrombolysis ICH was defined using European Cooperative Acute Stroke Study (ECAS III) criteria.¹⁷ Patients with uncertain DTNT and those who underwent endovascular or combined treatments were excluded.

In Argentina, new residents start their training in June. Groups were stratified for analysis as follows: June to August, (group 1), September to November (group 2), December to February (group 3), and March to May (group 4). As group 1 reflects the period with inexperienced residents and group 4 the period with most experienced house staff, we compared the above-mentioned variables between them. During the first 3 months of training, a senior resident actively supervises the new trainees while on-call. Therefore, we also compared groups 2 and 4 to determine whether the initial supervision scheme could have masked a negative impact on the DTNT. A waiver of informed consent was granted.

Hospital Structure

Our institution is a 113-bed tertiary neurological academic center located in Buenos Aires city, Argentina. The neurology department incorporates 3 residents per year. Twenty neurology staff supervises them in the inpatient setting. The stroke team, composed by 4 staff neurologists, 2 junior and 2 senior fellows, runs the stroke unit and follows all patients with stroke in the neurointensive care unit and neurology ward. They also supervise and decide treatment in all patients with acute stroke.

The institutional acute stroke protocols are mostly based on the American Heart Association (AHA) stroke guidelines. These protocols have been revised over time according to updated versions.

Statistical Analysis

Due to the nonparametric distribution of the DTNT, we performed the Kruskal-Wallis test comparing all groups. If a significant result was found, a post hoc analysis was performed using Mann-Whitney *U* test with Bonferroni correction. Additional analyses were performed by year comparing groups 1 and 4. Categorical variables were analyzed using χ^2 or Fisher exact. *P* values <.05 were considered significant. We estimated the power of our study in 0.96 for 101 patients and a 25% increase in DTNT (α = .05). Data were analyzed using Stata v12.1 (StataCorp, College Station, Texas). The study was approved by FLENI's institutional review board.

Results

During the study time frame, approximately 180 patients with acute stroke were admitted to our hospital per year (85%

ischemic and 15% hemorrhagic). Between June 2003 and June 2016, 108 patients with a diagnosis of ischemic stroke received IVT. Complete data were lacking in 7 patients; thus, 101 patients were included for the analysis (Figure 1). Demographic characteristics and vascular risk factors of these patients are depicted in Table 1.

Even though the rate of IVT varied significantly from 2003 to 2016 (Table 2), this variation was nonsignificant throughout the academic year (5.6%, 4.2%, 4.8%, and 6.5% for groups 1, 2, 3 and 4, respectively). The median DTNT down trended from 67 minutes in 2003 to 2004 to 46 minutes in 2015 to 2016 (Table 2).

The median DTNTs for groups 1 and 4 were 54 minutes (range: 20-135 minutes) and 60 minutes (range: 30-120 minutes), respectively. There were no significant differences between groups (*P* = .95; Table 3). Median DTNT for group 2 was 49 minutes (range: 20-135 minutes) and was also not significantly different compared to group 4 (*P* = .49).

In addition, no significant differences were found among groups for symptomatic TPA-related ICH, rate of thrombolysis of stroke mimics, number of thrombolysis within 60 minutes, and NIHSS and mRS at 3 months (Table 3). National Institutes of Health Stroke Scale on admission was similar in all groups.

The year-by-year comparison of DTNT was limited by the absence of events in groups 1 or 4 in most academic years with low IVT rates. The available calculations showed no significant differences except for lower DTNT in group 1 compared to group 4 during academic year 2014 to 2015 (22.5 vs 40 minutes, *P* = .004; Table 2).

Discussion

In this single academic center study, the arrival of new trainees did not adversely affect the DTNT for IVT in patients with acute ischemic stroke. The absence of a detrimental JE was also evident when studying other variables such as diagnostic errors (ie, stroke mimics receiving IVT), rate of IVT within 60 minutes of arrival, and TPA-related ICH. Outcomes at 3 months did not differ among groups and the rate of IVT remained stable throughout the academic year. A possible confounding effect of the initial supervision scheme of new trainees during the first 3 months was also ruled out.

The DTNT reflects a complex clinical process that includes triage, diagnosis, decision-making, and treatment of critically ill patients with acute ischemic stroke. It could be particularly susceptible to the arrival of new inexperienced trainees.^{18,19} For every 15-minute reduction in DTNT, there is a 5% reduction in in-hospital mortality. Also, IVT within 60 minutes of arrival is associated with lower in-hospital mortality and lower rates of symptomatic ICH.¹⁸ Therefore, current guidelines strongly recommend IVT initiation within 60 minutes after arrival.³

Resident-driven IVT protocols have shown to decrease the DTNT without increasing symptomatic hemorrhages or affecting favorable disposition.²⁰ Also, stroke mortality and

Figure 1. Patients' flowchart.

Table 1. Patients' Demographic Characteristics and Vascular Risk Factors.

Characteristics	Group 1	Group 2	Group 3	Group 4
Age, mean (SD)	68 (13)	68 (13)	68 (13)	69 (14)
Gender, female, n (%)	19 (61)	7 (41)	15 (65)	20 (67)
Hypertension, n (%)	20 (64)	12 (70)	14 (61)	18 (60)
Dyslipidemia, n (%)	4 (13)	3 (18)	8 (35)	16 (53)
Smoking, n (%)	10 (32)	5 (29)	4 (17)	8 (27)
Atrial fibrillation, n (%)	10 (32)	3 (18)	4 (17)	1 (3)
Diabetes mellitus, n (%)	4 (13)	4 (24)	5 (22)	3 (10)
Prior Stroke/TIA, n (%)	10 (13)	5 (29)	4 (17)	9 (30)
Coronary artery disease, n (%)	8 (29)	3 (18)	3 (13)	10 (33)

Abbreviations: SD, standard deviation; TIA, transient ischemic attack.

functional outcomes of patients with stroke are not negatively influenced by new house staff arrival.¹⁶ However, the impact of new residents' arrival in the DTNT has been not been fully evaluated.

Our institution's neurology department incorporates 3 residents per year. After a year of internal medicine instruction, the residents begin the 3-year neurology training. Two junior residents, a senior resident, and a stroke fellow cover the stroke unit during the day and the on-call resident after working hours. As in most teaching hospitals, the on-call resident is responsible for running the acute stroke alerts 24/7. During the first trimester of the academic year, a senior resident actively supervises new trainees while on-call. Additionally, the on-call stroke fellow and stroke attending staff

Table 2. Yearly Rate of IVT and Median DTNT.

Academic Year	IVT Rate	Median DTNT, minutes	P Value Group 1 vs 4
2003-2004	1.3	67.5	— ^a
2004-2005	4.6	90	— ^a
2005-2006	0.7	80	— ^a
2006-2007	1.3	120	— ^a
2007-2008	0.7	80	— ^a
2008-2009	3.9	72.5	— ^a
2009-2010	7.2	68	.22
2010-2011	2.6	60	1
2011-2012	4.6	47	— ^a
2012-2013	5.9	65	.8
2013-2014	8.5	55	.8
2014-2015	10.5	39	.04 ^b
2015-2016	14.5	46	.58

Abbreviations: DTNT, door-to-needle time; IVT, intravenous thrombolysis.

^aNo events in groups 1 or 4.

^bMedian DTNT: 22.5 minutes (group 1) versus 40 minutes (group 4).

actively oversee all the acute stroke alerts during the day. They can also be reached by phone overnight and remotely review patient's chart and images. To rapidly gain experience on the initial workup of patients with acute stroke symptoms, the junior residents assist to all acute stroke alerts during working hours, despite not being on-call. All IVT cases are later analyzed and discussed during daily rounds with the chief resident and vascular neurology team and at weekly stroke conferences. Additionally, during the first months of training, lectures are focused on the management of acute situations in the emergency department (ED). As part of this course, the residents are trained on the initial diagnosis, workup, and triage of acute stroke. Besides being available to assist with brain imaging interpretation 24/7, a neuroradiologist assists in the weekly stroke conference to train the residents on the interpretation of acute stroke imaging. Lastly, the nursing department is trained on a regular basis by the stroke team on the initial management of patients with acute stroke in the ED and the stroke unit.

This scheme, including a focused academic training, a close and staggered supervision scheme by senior and chief residents, stroke fellows, and stroke attending staff, allows to compensate for the inexperience, fatigue, and unfamiliarity with a new system that new residents may have early in the academic year. Additionally, their close interaction with a skilled multidisciplinary team makes less likely that their individual lack of expertise negatively impacts the studied variables, helping to assure stable care throughout the year.

This study has limitations worth mentioning. First, the small sample size and the differences in IVT during the study time frame limit the internal validity of our findings. And second, data from a single center with a relatively small neurology program limit the external validity of these results to larger academic programs in which a true JE may be observed.

Table 3. Comparison Between Groups.^a

	Group 1 (n = 27)	Group 2 (n = 20)	Group 3 (n = 23)	Group 4 (n = 31)	P Value (1 vs 4)	P Value (2 vs 4)
DTNT, minutes, median (range)	54 (20-135)	49 (20-135)	49 (20-130)	60 (30-120)	.95	.49
Thrombolysis < 60 minutes, DTNT, %	56	70	57	61	.79	.56
Stroke mimics thrombolysis, %	11	20	9	10	1	.4
Symptomatic ICH, %	0	10	4	6	.49	.62
NIHSS 3, median (range)	2 (0-9)	1 (0-14)	2 (0-11)	1 (0-10)	.95	.93
mRS 3, median (range)	1 (0-3)	1 (0-4)	2 (0-6)	1 (0-5)	.89	.65
Baseline NIHSS, mean (SD)	8 (6)	8 (6)	9 (6)	8 (6)	.96	.78

Abbreviations: DTNT, door-to-needle time; ICH, intracranial hemorrhage; mRS: modified Rankin Scale; NIHSS, National Institutes of Health stroke scale; SD, standard deviation.

^aGroup 1: June to August; group 2: September to November; group 3: December to February; group 4: March to May.

Conclusion

Our findings support the notion that the arrival of inexperienced, but highly supervised house staff may not have a negative impact on the DTNT for IVT, TPA-related ICH, and mRS–NIHSS outcomes. In accordance with previous studies, our data suggest the feasibility of participation of well-supervised in-training neurologists in the management of acute stroke in academic centers. Despite its limitations, this study raises an important hypothesis that deserves confirmation with further studies including larger samples from multiple and bigger academic programs with high and stable IVT rates over time.

Authors' Note

This study was performed at Institute for Neurological Research, FLENI, Buenos Aires, Argentina.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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