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Collaborative Interventions Reduce Time-to-Thrombolysis for Acute Ischemic Stroke in a Public Safety Net Hospital

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Background and Purpose: Shorter time-to-thrombolysis in acute ischemic stroke (AIS) is associated with improved functional outcome and reduced morbidity. We evaluate the effect of several interventions to reduce time-to-thrombolysis at an urban, public safety net hospital. *Methods:* All patients treated with tissue plasminogen activator for AIS at our institution between 2008 and 2015 were included in a retrospective analysis of door-to-needle (DTN) time and associated factors. Between 2011 and 2014, we implemented 11 distinct interventions to reduce DTN time. Here, we assess the relative impact of each intervention on DTN time. *Results:* The median DTN time pre- and postintervention decreased from 87 (interquartile range: 68-109) minutes to 49 (interquartile range: 39-63) minutes. The reduction was comprised primarily of a decrease in median time from computed tomography scan order to interpretation. The goal DTN time of 60 minutes or less was achieved in 9% (95% confidence interval: 5%-22%) of cases preintervention, compared with 70% (58%-81%) postintervention. Interventions with the greatest impact on DTN time included the implementation of a stroke group paging system, dedicated emergency department stroke pharmacists, and the development of a stroke code supply box. *Conclusions:* Multidisciplinary, collaborative interventions are associated with a significant and substantial reduction in time-to-thrombolysis. Such targeted interventions are efficient and achievable in resource-limited settings, where they are most needed. **Key Words:** Stroke—cerebrovascular disorders—thrombolytic therapy—safety net hospital.

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Introduction

Although its associated mortality is declining, stroke remains among the leading causes of long-term disability in the United States.[1,2] Additionally, stroke remains the fifth leading cause of death.[3] Thrombolysis with intravenous tissue plasminogen activator (tPA) has revolutionized the treatment of acute ischemic stroke (AIS), bestowing significant improvement in mortality and functional outcome when administered acutely.[4-6] The benefit is markedly time-dependent and wanes within hours of stroke ictus, reflecting a progression of irreparable core infarction and increasing the risk of hemorrhagic transformation.[7-10]

The American Heart Association/American Stroke Association (AHA/ASA) guidelines for early management of AIS reflect the central importance of early thrombolysis; tPA administration is recommended within 4.5 hours of symptom onset and within 1 hour of arrival at a hospital.[11] Although early thrombolysis is clearly beneficial, practical challenges persist such that the majority of stroke victims who are eligible for tPA do not receive it within the recommended times.[12,13]

Despite the clear benefits of early thrombolysis, delays in stroke recognition, hospital arrival, emergency department (ED) triage, imaging, neurology consultation, and treatment preparation and delivery impede the achievement of recommended door-to-needle (DTN) times of less than 60 minutes.[14,15] Accordingly, there exists substantial interest in targeted, effective interventions to reduce these times. Numerous studies have examined various targeted interventions to this end, including a systematic quality improvement study conducted as part of the original National Institutes of Neurologic Disorders and Stroke-sponsored trial showing benefit with tPA. In the context of this initiative, specific interventions were developed to target identified delays, and included, for example, prehospital notification by emergency medical services, use of a stroke code pager system, notification of pharmacy about potential imminent tPA use, and arrangement of expedited computed tomography (CT) scanning as part of an optimized stroke workflow.[16] Other quality improvement initiatives, including the national "Get With The Guidelines-Stroke" initiative, have demonstrated similar success.[17,18]

Interventions aimed at reducing time-to-thrombolysis are less well studied and may be more difficult to implement in public safety net hospitals. Such institutions face unique challenges related to reduced funding levels and care provision for larger proportions of socioeconomically disadvantaged patients, underinsured patients, and ethnic minorities. These patients have less access to healthcare and are less likely to receive tPA, despite having more frequent and more severe strokes.[19-24]

We present our implementation of 11 multidisciplinary, collaborative, targeted interventions to reduce DTN time in a large, urban, public safety net hospital. We analyzed DTN times before and after each intervention with the goal of understanding the combined and individual effects of our interventions on DTN time. We further subdivided DTN time into 4 components to better assess the nature and timing of treatment delays. We also sought to demonstrate the effectiveness and feasibility of implementation of such interventions in the unique setting of a public safety net hospital.

Materials and Methods

Study Design

We present an observational, retrospective study of patients diagnosed with AIS who received tPA. DTN times and their constituents are compared before and after targeted interventions using descriptive statistical methods. The study was approved by the local institutional review board. Informed consent was waived due to the retrospective, observational study design.

Study Population

The study included all patients who were judged eligible for and received intravenous tPA for AIS in the ED at our institution between 2008 and 2015, inclusively. Using a clinical electronic database, we abstracted last known well time, National Institutes of Health Stroke Scale (NIHSS) score at presentation, baseline demographic characteristics, relevant medical history, length of stay, discharge disposition, as well as times of specific ED treatment milestones: patient arrival in ED, ED physician arrival at bedside, neurologist arrival at bedside, initial laboratory test order, laboratory test result, head CT order, head CT result, and tPA administration. We also reviewed paper charts for missing data, and to confirm time intervals where there was ambiguity.

Our institution is an academic, tertiary care, urban, public safety net hospital serving 2.5 million patients annually. The center has remained continuously certified by the Joint Commission as a Primary Stroke Center since 2006. The population served is ethnically diverse, comprised nearly equal proportions of Asian, African–American, Hispanic, and Caucasian individuals, and is also largely underinsured. Additionally, our institution is growing as a referral center for patients with complex conditions requiring increasingly sophisticated care.

Interventions

Between 2011 and 2014, 11 targeted interventions were sequentially implemented in an effort to reduce DTN time (Table 1). A standardized stroke protocol CT was implemented in 2011, incorporating non-contrast head CT, CT perfusion, and CT angiography of the head and neck. Later in 2011, a dedicated stroke performance improvement coordinator was hired, who worked closely with the senior stroke coordinator to spearhead many subsequent interventions. Arrangements were made for administration of tPA in the CT scanner (typically after the non-contrast scan and prior to perfusion and angiographic imaging). A stroke code activation system was implemented in 2012, constituting pager notification of the ED attending, neurocritical care attending and fellow, neurology resident, neuroradiologist, radiology technician, pharmacist, stroke coordinator, and admission officer on duty. Concurrently, designated ED pharmacists for stroke patients were established. Monthly multidisciplinary stroke case peer review meetings were initiated, with attendance by neurocritical care attendings and fellows, neuroradiologists, neurointerventionalists, vascular neurosurgeons, and the stroke coordinator. A mobile "clot box" with tPA, labetalol,

Table 1. *Interventions implemented, chronologically*

Intervention	Date
Standardized head CT stroke protocol	January 2011
Stroke performance improvement coordinator	September 2011
tPA administered in CT scanner	February 2012
Stroke code activation system	June 2012
Dedicated ED stroke pharmacists	June 2012
Monthly stroke peer review meetings	May 2013
Mobile clot box	August 2013
Medical supply cart in CT scanner room	October 2013
Standardized tPA administration by ED RN	February 2014
Medicine dispenser in CT scanner room	March 2014
Stroke code simulation	August 2014

Abbreviations: CT, computed tomography; ED, emergency department; tPA, tissue plasminogen activator.

and other items needed to administer tPA was created; the box physically accompanies any patient for whom a stroke code is activated until a decision regarding tPA is made. Beginning in 2013, a medical supply cart with tubing, syringes, and other equipment necessary for drug administration was added to the CT suite, followed shortly thereafter by a medication dispenser. In early 2014, ED nursing staff were trained in a standardized method of tPA preparation and administration to be used in the absence of pharmacists. Finally, late 2014 saw the implementation of a stroke code simulation attended by a multidisciplinary team of ED, neurology, and radiology staff (attending physicians, fellows, residents, medical students, pharmacists, nurses, and technicians).

Study Outcomes

The primary outcome is change in DTN time for all patients who received tPA before the first intervention in January 2011 compared with all patients who received tPA after the final intervention in August 2014. The same cohorts were compared with respect to proportion receiving tPA within the goal DTN time of 60 minutes.

To compare the relative effect of different interventions, we sequentially analyzed DTN time before and after each specific intervention was implemented. Interventions implemented within 1 month of each other were considered as a single intervention to enhance sample size.

Finally, to further characterize acute stroke workflow at our institution and target potential sources of delay, we subdivided DTN time into 4 epochs based on reliably recorded milestones in ED stroke cases: patient arrival time to ED physician evaluation (door-to-MD), ED physician arrival to CT order time (MD-to-CT order), CT order time to CT preliminary interpretation time (CT turnaround time), and CT preliminary interpretation time to tPA administration (CT-to-tPA).

Statistical Analyses

Normally distributed data were described in means and standard deviations; non-normally distributed data were expressed in medians and interquartile ranges. Statistical significance of differences observed in normally distributed and non-normally distributed data was determined by Student's *t*-test and Wilcoxon rank-sum test, respectively. Relative proportions were compared with the chi-square test. All P values were 2-sided, with $P < .004$ considered statistically significant, as adjusted for multiple comparisons by Bonferroni correction. Statistical analysis was performed using Stata version 13 (College Station, TX).

Results

Between January 2008 and December 2015, 299 patients were treated with tPA in our ED and were included in the study. The baseline characteristics of the patients are described in Table 2. Sixty-seven patients were treated before any interventions commenced, and 66 patients were treated after all interventions were implemented; these groups were compared for collective effects of the implemented interventions. Patients treated with tPA before our interventions compared with those treated after all interventions had been implemented were significantly younger and had fewer comorbidities. The postintervention group had slightly more severe strokes by NIHSS, although the difference was not statistically significant.

Outcomes are described in Table 3. The median DTN time for all patients was 67 minutes (interquartile range: 48-91 minutes). DTN time was not normally distributed and was positively skewed. The median DTN time for patients in the preintervention group was 87 (68-109) minutes, compared with DTN time for patients in the postintervention group of 49 (39-63) minutes; the difference is statistically significant. The median DTN times for each intervention period are plotted in Figure 1; also shown is the contribution of each of the 4 defined epochs to overall DTN time. The prime driver of reduction in DTN times is reduction in CT turnaround time, which decreased from 41 (30-52) minutes to 13 (8-17) minutes after our targeted interventions. Other epochs comprising DTN time were also reduced but were not statistically significant. The proportion of patients receiving tPA within 60 minutes of arrival increased with our interventions from 9% (95% confidence interval: 5%-22%) to 70% (58%-81%, $P < .001$).

Discussion

With good reason, the mantra of AIS treatment has become "time is brain." Patients and healthcare providers increasingly recognize the essential importance of rapid treatment of stroke, and systematic efforts to more rapidly deliver treatment are becoming a priority. Indeed, evidence-

Table 2. *Baseline characteristics of study population*

Characteristic	All (299)	Preintervention (67)	Postintervention (66)	Significance (*P* value)
Age (year)*	67 ± 15	64 ± 15	72 ± 14	.003
Race or ethnic group (%)				
White, non-Hispanic	25	27	21	.446
Black	18	19	17	.682
Hispanic	18	13	18	.453
Asian	31	39	30	.303
Other	8	2	14	.008
Female sex (%)	50	46	58	.192
NIHSS score†	9 (5-15)	8 (5-14)	10 (5-16)	.309
Medical history (%)				
Stroke or TIA	23	15	23	.250
Diabetes mellitus	32	24	36	.080
Hypertension	78	73	86	.058
Coronary artery disease	32	33	36	.806
Dyslipidemia	67	65	70	.499
Atrial fibrillation	34	27	39	.125
Tobacco use	20	28	19	.165

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.
*Mean and standard deviation.
†Median and interquartile range.

based consensus guidelines assert that eligible stroke patients should receive tPA no longer than 60 minutes after presentation to an ED.[11] Here, we report our own efforts to this end. A longitudinal quality improvement initiative comprising 11 distinct interventions to reduce DTN time at our urban, public safety net hospital significantly reduced DTN times. More specifically, comparing DTN times before and after our interventions revealed a significant and robust decrease from 87 to 49 minutes. The proportion of patients meeting AHA/ASA goal DTN time less than 60 minutes improved from 9% to 70% over 3 years' time.

Table 3. *Outcomes in preintervention and postintervention groups*

Outcome	Preintervention (67)	Postintervention (66)	Significance (*P* value)
DTN time (min)†	87 (68-109)	49 (39-63)	**<.001**
Door-to-MD	3 (0-13)	0 (0-4)	.254
MD-to-CT order	10 (2-20)	6 (3-8)	.010
CT turnaround	41 (30-52)	13 (8-17)	**<.001**
CT-to-tPA	32 (19-50)	28 (17-40)	.513
DTN <60 min (%)*	9 (5-22)	70 (58-81)	**<.001**
Onset-to-ED arrival (min)†	59 (29-88)	59 (39-84)	.520
Onset-to-tPA (min)†	151 (120-184)	116 (90-142)	**<.001**
Discharge status			
Self-care	58 (46-70)	33 (23-46)	.004
Inpatient rehabilitation	15 (8-26)	20 (12-31)	.467
Skilled nursing facility	9 (4-19)	14 (7-25)	.393
Outside hospital	10 (5-21)	24 (15-36)	.035
Hospice	1 (0-10)	0	
In-hospital death	4 (1-13)	8 (3-17)	.452

Abbreviations: CT, computed tomography; DTN, door-to-needle; ED, emergency department; tPA, tissue plasminogen activator.
Bolded values mean $P < .004$, considered statistically significant as adjusted for multiple comparisons by Bonferroni correction.
*Mean and 95% confidence interval.
†Median and interquartile range.

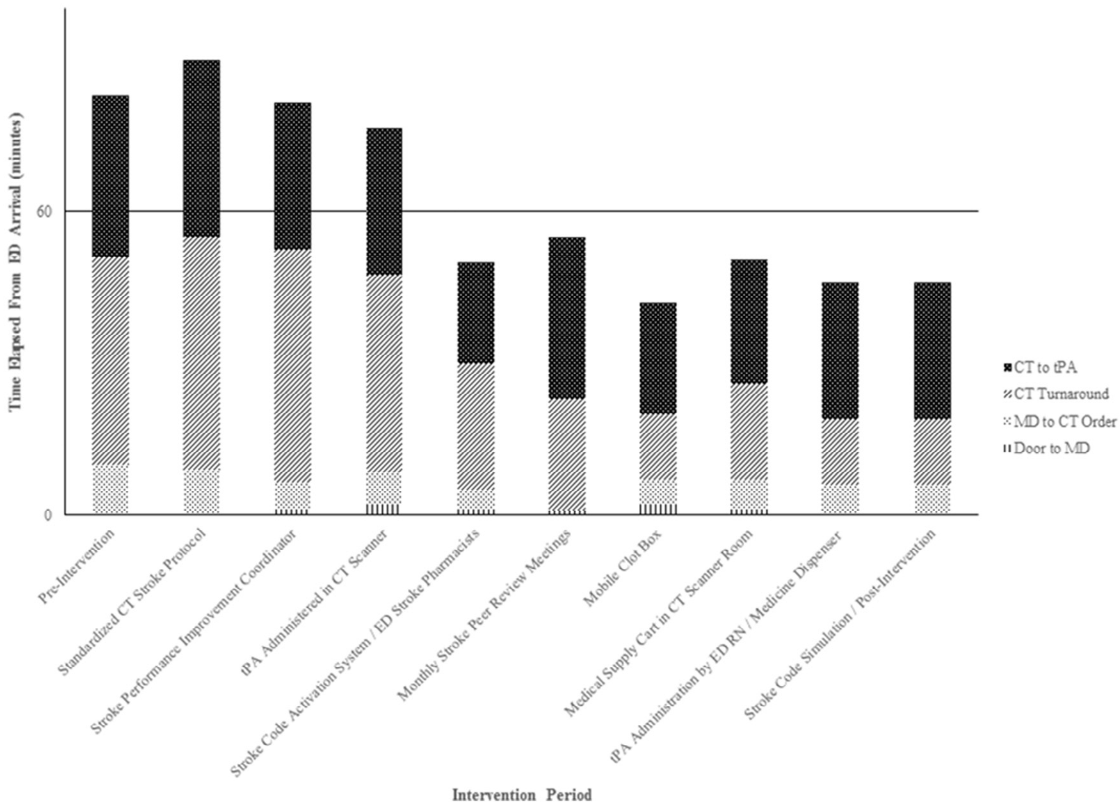

Figure 1. *Door-to-needle time and its constituents in each intervention period. Abbreviations: CT, computed tomography; ED, emergency department; tPA, tissue plasminogen activator.*

Three interventions were associated with the greatest improvements in DTN time: the institution of a stroke code activation system, the establishment of dedicated ED stroke pharmacists, and the introduction of a mobile "clot box" containing tPA, antihypertensive agents, and equipment required for tPA administration. Although these are temporally associated with improvement in DTN time, it is difficult to assess the effect of a single intervention, as the interventions are cumulative, synergistic, and may have a delayed effect. For example, hiring of a dedicated stroke performance improvement coordinator would be expected to have a delayed effect and would facilitate further interventions. Furthermore, interventions were implemented intermittently and, at times, simultaneously without randomization or other controls.

Improvement in DTN time was driven primarily by improvement in time from CT scan order to CT scan interpretation, reflecting more rapid execution of stroke evaluation workflow and emphasizing the importance of short "door-to-imaging" times. Time to stroke diagnosis and initial CT scan order remained consistently rapid, contributing little to DTN time. Instead, delays manifested primarily after stroke diagnosis was made, suggesting that delays more often resulted from systemic obstacles rather than diagnostic or cognitive error. The data suggest that we are quick to diagnose, but slow to execute. As such, hospital efforts to reduce DTN time should focus on streamlining the execution of stroke workflow. As we have shown, DTN may be effectively reduced by targeting initial stroke workflow, for example by implementing a stroke code activation system akin to systems in place for cardiac arrest and ST elevation myocardial infarction.

Although our interventions effectively reduced DTN time, we lacked the statistical power to demonstrate an effect on in-hospital mortality or functional outcome as suggested by discharge status. Fewer stroke patients in the postintervention group were discharged under self-care; however, the postintervention group was significantly older and trended toward more medical comorbidities and higher baseline NIHSS. These differences suggest that our institution is treating an aging and increasingly chronically ill population with increasing severity of illness, which confounds interpretation of longitudinal outcomes.

Although several studies have reported on means of improving the timeliness of thrombolysis in acute stroke,[14-18,25] none has specifically focused on public safety net hospitals, which generally have less funding and treat more under- or uninsured patients. As one of these hospitals, our institution treats a diverse and relatively socioeconomically disadvantaged population. Such populations, in addition to having less access to healthcare, are less likely to use emergency medical services, have longer ED wait times, and are in fact less likely to receive tPA.[21,23] Such disparities in treatment persist despite demonstrably higher incidence of stroke, worse stroke severity, poorer functional outcome, and excess associated mortality within the same populations.[19,20,22,24] As such, targeted interventions to reduce DTN times among such populations are of particular importance; these patients, more than any, demand our greatest efforts to improve stroke care.

Although the present data are more applicable to public safety net hospitals than previously published studies, our institution is privileged with luxuries not afforded to many public safety net hospitals, such as 24-hour in-house availability of neurology consultation. As a result, the generalizability of our results may be limited.

Summary and Conclusions

Multidisciplinary, collaborative, targeted interventions are associated with substantial and significant reduction in DTN time and improved compliance with AHA/ASA recommendations for treatment of AIS. Such targeted interventions are effective and achievable in resource-limited settings, where they are most needed.

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