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CLINICAL PHARMACY RESEARCH REPORT

Impact of clinical pharmacist participation in stroke team activations on tissue plasminogen activator door-to-needle time

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Abstract

INTRODUCTION: Current stroke guidelines recommend that treatment with tissue plasminogen activator (tPA) should be initiated as quickly as possible in eligible patients to provide maximum therapeutic benefit. Pharmacists possess multiple skills including knowledge of dosing, reconstitution, and improved access to medication that may positively impact door-to-needle (DTN) times for patients with acute ischemic stroke.

OBJECTIVE: The objective was to evaluate the impact of a clinical pharmacist on time to tPA administration in patients with acute ischemic stroke.

METHODS: This was a retrospective, single-center cohort study at a community teaching hospital and certified primary stroke center from January 1, 2014 to December 31, 2018. The primary outcome of this study was to compare the average DTN time with a pharmacist present at a stroke team activation vs no pharmacist present. Secondary outcomes included the proportion of patients in each group meeting a DTN time of less than 60 minutes and the proportion of patients in each group meeting a DTN time of less than 45 minutes. Statistical analysis utilized included Wilson's *t*-test to compare average DTN time and the odds ratio to determine a DTN time <60 or 45 minutes between the pharmacist and non-pharmacist groups.

RESULTS: Pharmacist involvement was associated with a reduction in the average DTN time: 66 minutes vs 78 minutes ($P = .038$). The DTN time of less than 60 minutes was met in 60% of cases with a pharmacist present compared with 35% without a pharmacist ($P = .005$). The DTN time of less than 45 minutes was met in 18% of cases with a pharmacist present vs 20% without a pharmacist ($P = .71$).

CONCLUSION: Pharmacist participation in stroke teams in the emergency department may reduce DTN times and increase the likelihood of a patient receiving tPA in less than 60 minutes.

KEYWORDS
clinical pharmacist, emergency department, ischemic stroke, tissue plasminogen activator (tPA)

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1 | INTRODUCTION

Current stroke guidelines recommend that treatment with intravenous (IV) tissue plasminogen activator (tPA) be initiated as quickly as possible in eligible patients to provide maximum therapeutic benefit.[1] In the United States, IV alteplase is the only thrombolytic agent at the time of this publication that is Food and Drug Administration (FDA)-approved for the treatment of acute ischemic stroke (AIS). High-quality studies have demonstrated a treatment benefit with IV alteplase administration up to 4.5 hours after symptom onset, with the greatest benefit occurring with earlier administration.[1] The door-to-needle (DTN) time, which is the time interval from hospital arrival to the start of alteplase administration, is a metric reported to the Joint Commission for stroke center certification. Guidelines recommend that hospitals employ an organized, protocolized, multidisciplinary approach to assessing patients with potential stroke.[1] For every 10-minute delay in the start of thrombolytic therapy within the treatment window, one less patient has an improved disability outcome.[2] Consequently, patients who present to the hospital within the first 60 minutes of onset have the greatest opportunity to benefit. However, problems or challenges that hospitals may face when trying to improve their DTN time include eligibility challenges (refusal and social or religious concern), management of concomitant conditions (hypoglycemia and seizure), and in-hospital delay (diagnosis or equipment issues). Strategies for improving DTN times in patients with AIS have been recommended by the "Target: Stroke" initiative.[2] The American Heart Association has established 12 key best practices and pharmacists may assist with best practices #4 A stroke toolkit containing clinical decision support, stroke-specific order sets, guidelines, hospital-specific algorithms, critical pathways, National Institutes of Health (NIH) Stroke Scale, and other stroke tools should be available and used for each patient, #7 (mix tPA medication ahead of time), #8 (rapid access to intravenous tPA), and #9 (team-based approach).[2]

Clinical pharmacists (CPs), especially emergency medicine pharmacists (EMPs), may play an active role in the assessment and treatment of stroke patients in the emergency department (ED) and can positively impact DTN times for patients with AIS. Pharmacists can participate with the team in the assessment of candidacy for tPA by assessing home medications, assisting with blood pressure management, and assessing recent laboratory values, thereby expediting tPA dose calculations, medication procurement, admixing, and administration. The objective of this study was to evaluate the impact of a clinical pharmacist on time to tPA administration in patients with AIS.

2 | METHODS

2.1 | Study design and setting

This study was designed as a retrospective, single-center cohort study at a community teaching hospital (Holy Cross Hospital) located in Silver Spring, Maryland. Institutional Review Board approval was granted on November 13, 2017 and a waiver of informed consent was obtained. Retrospective data were reviewed from January 1, 2014 to December 31, 2018.

This institution is a 449-bed not-for-profit community teaching hospital. The ED is a Joint Commission and Maryland Institute for Emergency Medical Services Systems (MIEMSS)-certified primary stroke center, MIEMSS-certified cardiac interventional center, and home to the nation's first Seniors Emergency Center for people aged 65 and older. The ED treats nearly 90 000 patients per year.

In 2012, Holy Cross Hospital developed a stroke team improvement project to reduce IV alteplase DTN times and improve processes that were identified to create delays in IV alteplase administration. Efforts in 2012 included the "define" phase, where current processes and procedures were assessed for delays and performance improvement areas were defined (Figure 1). In 2015-2016, the "improve" phase was implemented. This improvement phase resets timelines for processes to occur in the ED stroke team workflow (Figure 2). The addition of an ED pharmacist during peak hours (15:00-01:30) also occurred during this phase to provide additional support to ED nursing and medical staff. Within less than 1 week of each stroke team activation/tPA, the case is analyzed by the stroke nurse practitioner and feedback provided to individuals and groups, as appropriate. Feedback (verbal and written) includes areas where guidelines/protocols were followed appropriately and areas for improvement to help meet DTN goals. Case studies are reviewed and presented by the stroke medical directory at monthly tPA meetings.

At our institution, ED pharmacists respond to stroke team activations and assist with review of medication histories, screening for contraindications to thrombolytic therapy, managing blood pressure therapy, and dosing/reconstituting alteplase. Pharmacists assist with obtaining accurate weight documentation, expediting access to alteplase, including prospective order verification, and pre-mixing, if indicated. Pharmacists are also involved in providing education and training to ED nurses and participate in stroke committee and tPA meetings.

2.2 | Participant selection

Patients were included in the study if they received IV alteplase in the ED from January 1, 2014 to December 31, 2018. Patients were excluded from this study if they were less than 18 years of age or received IV alteplase for any indication other than AIS. Electronic health records were then retrospectively reviewed to determine pharmacist participation based on ad hoc clinical intervention documentation or record of a pharmacist pulling tPA from the ED-automated dispensing cabinet. Pharmacist documentation was required; however, given that the ED is a high acuity setting, there may have been instances where documentation was missed. Documentation included a brief summary of patient presentation, alteplase dosing and timing, and any blood pressure management recommendation. If pharmacist documentation or any evidence the pharmacist participated in the stroke team was not present, the patients were included in the non-pharmacist group.

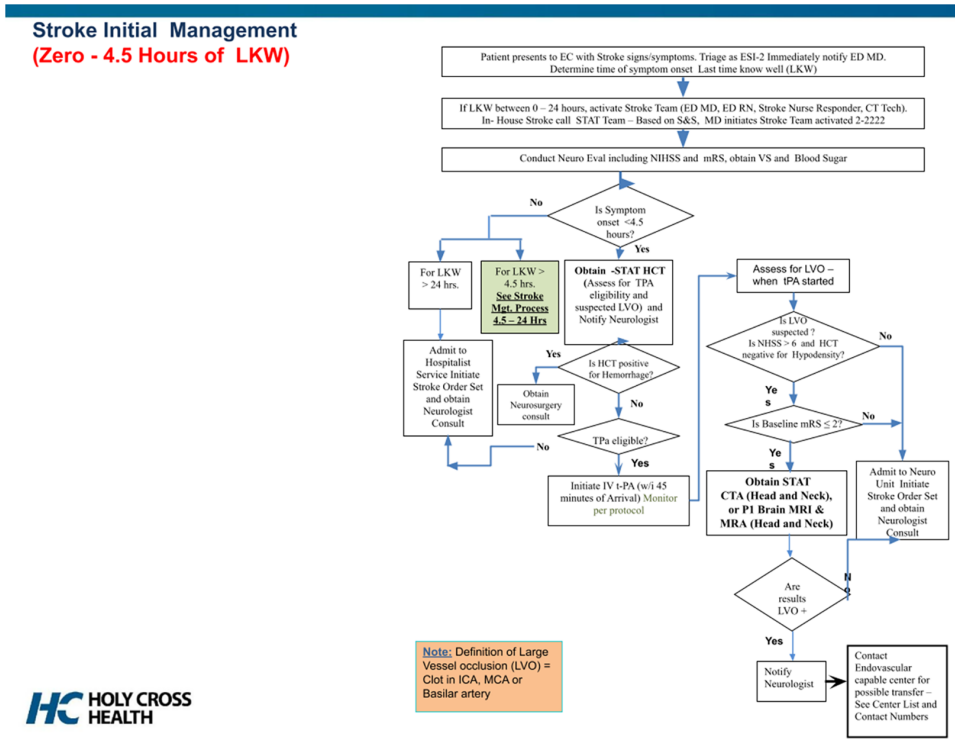

FIGURE 1 Stroke initial management process. Stroke management algorithm based on last time known well (LKW), imaging results, and which patients should receive thrombolytic therapy. CTA, computed tomography angiogram; EC, emergency center; ED, emergency department; ESI, emergency service index; HCT, head computed tomography; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; mRS, modified rankin score; NIHSS, national institutes of health stroke scale; S&S, signs & symptoms; tPA, alteplase; VS, vital signs

<35 Minutes	<45 minutes
• ED MD consults with neurologist • RN/PharmD pulls tPA from Pyxis and obtains IV supplies for high probability cases	• RN/PharmD calculates tPA dosing, if ordered • RN/PharmD double checks tPA dose • RN/PharmD mixes tPA • Second RN/PharmD checks dosing

FIGURE 2 Improve phase (2015-2016) timelines for stroke management. ED, emergency department; IV, intravenous; MD, medical doctor; PharmD, doctor of pharmacy/clinical pharmacist; RN, registered nurse: tPA, tissue plasminogen activator

2.3 | Outcomes

The primary outcome of this study was to compare the average DTN time (in minutes) with a pharmacist present at a stroke team activation vs no pharmacist present. Secondary outcomes included the proportion of patients in each group meeting a DTN time of less than 60 minutes and the proportion of patients in each group meeting a DTN time of less than 45 minutes.

2.4 | Data collection

All data collected were obtained through the electronic health record system, Cerner. Demographic data collected included age, gender, and baseline National Institutes of Health Stroke Scale (NIHSS) score. The NIHSS score was obtained from the stroke neurologist consultation note. The DTN time was collected from the medication administration record. The DTN time was defined as the time from hospital arrival to charting of tPA administration by a nurse.

2.5 | Statistical analysis

To detect a 10-minute difference in DTN time between the pharmacist and non-pharmacist groups, approximately 126 patients would be required to achieve 80% power at a two-sided significance level of 5%. Categorical data were summarized using frequency distributions and Fisher's exact test. Continuous data were analyzed using the *t*-test unless otherwise stated. Welch's *t*-test was used to compare the average DTN time between the pharmacist and non-pharmacist

groups. Welch's *t*-test was utilized due to the unequal sample sizes between the pharmacist and non-pharmacist groups. The odds ratio was used to compare DTN time less than 60 or less than 45 minutes, respectively between the pharmacist and non-pharmacist groups.

3 | RESULTS

A total of 159 patients were included in the study. Baseline characteristics were similar in both the pharmacist and non-pharmacist groups, with the exception of the percentage of severe admission NIHSS scores between the two groups (Table 1). The non-pharmacist group had 37% NIHSS severe patients on admission vs 14% in the pharmacist group. Despite the difference, the average admission NIHSS score between the groups was not statistically significant; both average admission NIHSS scores were classified as moderate severity. Pharmacists were involved in the care of 40 patients (25%), while 119 (75%) had no pharmacist present. Pharmacist involvement was associated with a reduction in the average DTN time: 66 minutes vs 78 minutes ($P = .038$). The DTN time of less than 60 minutes was met in 60% of cases with a pharmacist present compared with 34% without a pharmacist ($P = .005$). The DTN of less than 45 minutes was met in 18% of cases with a pharmacist present vs 20% without a pharmacist ($P = .71$).

4 | DISCUSSION

In this retrospective, single-center cohort study involving patients admitted for AIS requiring IV alteplase administration, pharmacist involvement in the stroke team reduced the DTN time by an average of 12 minutes. The DTN time of less than 60 minutes was improved with a pharmacist vs without a pharmacist and was statistically significant; however, the DTN time of less than 45 minutes was not improved (Table 2). With a larger sample size in the pharmacist group, statistical significance may have potentially been reached. Figure 3 displays the average DTN time trend between pharmacist and non-pharmacist groups throughout the study period. During the "improve" phase 2015-2016, average DTN decreased in both groups and then increased during 2017-2018. During 2018, there was a larger increase in the non-pharmacist versus pharmacist groups potentially due to the removal of IV alteplase from the override list secondary to a Joint Commission recommendation. Without having IV alteplase on override, the non-pharmacist group would have an additional barrier of waiting on pharmacist verification. It is unclear why DTN times increased in both groups during 2017-2018 and perhaps, if the study continued for a longer period of time, a better trend would be visualized. Some studies have utilized "image to needle" times to identify pharmacist benefit on DTN time; however, this was not reviewed in

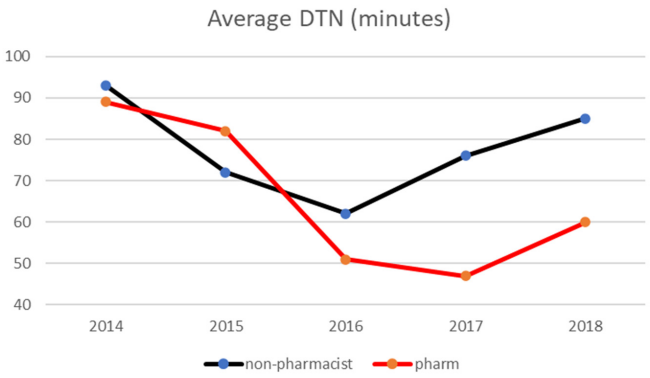

FIGURE 3 DTN time throughout the study period (2014-2018). DTN, door-to-needle

TABLE 1 Baseline demographics and characteristics

	Pharmacist n = 40	Non-pharmacist n = 119	*P* value
Age (y), mean (range)	64 ± 20 (28-95)	67 ± 16 (23-96)	.46
Male sex, n (%)	18 (45)	58 (49)	.72
Female sex, n (%)	22 (55)	61 (51)	.72
Arrival NIHSS score, median (range)	8 (1-27)	12 (1-25)	.12
Mild (1-4)	7/29 (24)	10/104 (10)	0.06
Moderate (5-15)	18/29 (62)	55/104 (53)	0.41
Severe (>20)	4/29 (14)	39/104 (37)	0.02

Abbreviations: NIHSS, National Institute of Health Stroke Scale; y, years.

TABLE 2 Time to thrombolytic therapy

	Pharmacist n = 40	Non-pharmacist n = 119	Odds ratio	95% CI	*P* value
Mean DTN time, min, SD	66 ± 27	78 ± 38	–	0.68-23.87	.038
DTN < 60 min, n (%)	24 (60)	41 (34)	2.85	1.37-5.96	.005
DTN < 45 min, n (%)	7 (18)	24 (20)	0.83	0.33-2.13	.71

Abbreviations: CI, confidence interval; DTN, door-to-needle; SD, SD.

TABLE 3 Literature review

	Gosser et al.[3]	Montgomery et al.[4]	Rech et al.[5]	Jacoby et al.[6]	Gilbert et al.[7]
Sample size	105	97	125	100	65
Average DTN time (minutes)	69.5 vs 89.5	54 vs 74	48 vs 73	46 vs 58	49 vs 63
PharmD vs no PharmD	20-minute difference	20-minute difference	25-minute difference	12-minute difference	14-minute difference
DTN < 60 minutes	29.9% vs 15.8%	71% vs 39%	71% vs 29%	Not measured	OR 3.3 (95% CI: 1.1-9.6) $P = .04$
DTN < 45 minutes	Not measured	42% vs 19%	Not measured	49% vs 25%	Not measured

Abbreviations: CI, confidence interval; DTN, door-to-needle; OR, odds ratio; PharmD, doctor of pharmacy/clinical pharmacist.

this study. Previously published studies have also demonstrated positive outcomes with pharmacist participation in interdisciplinary stroke teams (Table 3).[3-7] In our study, reduction in DTN time (12 minutes) with pharmacist involvement in stroke teams was consistent with similar studies, with a reduction in DTN time ranging from 14 to 25 minutes (Table 3).[3-7] In the Gosser and colleagues (29.9% vs 15.8%), Montgomery and colleagues (71% vs 39%), and Rech and colleagues studies (71% vs 29%), DTN was achieved in less than 60 minutes twice as often in the pharmacist vs non-pharmacist groups.[3-5] Similar to our study, in the Gilbert and colleagues study, the odds ratio of achieved DTN less than 60 minutes with a pharmacist present in the stroke team was three times more likely.[7] Contrasting to our study, in the Montgomery and colleagues (42% vs 19%) and Jacoby and colleagues studies (49% vs 25%), DTM was achieved in less than 45 minutes twice as often in the pharmacist vs non-pharmacist groups.[3,6] Unlike previous studies, there was no concurrent improvement phase; however, it is important to note that all stroke centers are constantly reviewing DTN and identifying areas for improvement.

4.1 | Limitations

Confounding factors that were not controlled for that could have contributed to delays in IV alteplase administration were delays in obtaining actual body weight, imaging, blood pressure management, provider assessment (emergency medicine/neurologist assessment [overnight neurologist available via telephone only]), and family decision-making. An additional confounder that was introduced during the study period was the removal of IV alteplase from the override list that could have potentially increased DTN in the non-pharmacist group. The non-pharmacist group was three times larger than the pharmacist group. This unequal distribution may have led to better results in the pharmacist group. The Welch's *t*-test was specifically chosen to analyze the average DTN between groups because it takes into account unequal sample sizes. The smaller sample size may have been due to limited hours of emergency room support. In 2014, the emergency medicine pharmacist was a new position and although attending stroke teams was an expectation, there may have been lower attendance due to balancing responsibilities or concurrent emergencies. Another limitation of this study that may have led to an underestimation of reduction in DTN time in the pharmacist group was that the identification of pharmacist participation in a stroke team was based on documentation in the electronic health record. Due to the various responsibilities and workload of the pharmacist, they may have forgotten to document an intervention, which led to pharmacist group patients being placed in the non-pharmacist group.

5 | CONCLUSION

The involvement of a clinical pharmacist in the care of patients with AIS at our institution was associated with a 12-minute reduction in the average DTN time and a statistically significant proportion of patients receiving alteplase with a DTN time less than 60 minutes. These findings support the inclusion of pharmacists on a multidisciplinary stroke team. Given the strong evidence demonstrating pharmacist involvement and improvement in DTN times, there is a need for investigation into pharmacist impact on patient-centered outcomes, such as improvement in the NIHSS score and morbidity/mortality.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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