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Impact of an emergency medicine pharmacist on door to needle alteplase time and patient outcomes in acute ischemic stroke

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ABSTRACT

Purpose: Time is a critical metric in the emergency department (ED) for acute ischemic stroke and thrombolytic therapy. National guidelines have emphasized tracking time from stroke onset to treatment and decreasing door to needle (DTN) time [1, 2]. Multidisciplinary teamwork is encouraged but, there is limited evidence demonstrating the value of the pharmacist on the stroke response team. The goal of this study is to compare DTN times in the ED with or without a pharmacist at bedside and examine the impact on subsequent patient outcomes.
Methods: This was a single-center retrospective cohort study. Investigators identified patients who presented to the ED between August 2016 – May 2020 with signs of ischemic stroke and subsequently received intravenous alteplase. Patients were excluded if they refused alteplase or received alteplase off-campus before being transferred. Pharmacist documentation of clinical interventions was used to identify participation on the stroke response team. The primary outcome was median DTN time. Secondary outcomes included severity of deficits measured by the National Institutes of Health Stroke Scale (NIHSS), hospital length of stay (LOS), 90-day Modified Rankin Scale (mRS), incidence of intracranial hemorrhage (ICH), and inpatient all-cause mortality.
Results: Of the 164 patients included, 31 had an emergency medicine pharmacist at bedside (EMP group) and 133 did not (No EMP group). The median DTN time was significantly shorter at 35 min EMP [interquartile range (IQR) 29–44] vs 42 min No EMP [IQR 34–55]; $p = 0.003$. The number of cases achieving a DTN time of 30 min or less was significantly higher when a pharmacist was involved (35.5% vs.16.5%; $p = 0.018$) as well as the number of patients receiving alteplase within 45 min (80.7% vs. 57.1%; $p = 0.015$). NIHSS scores at discharge were lower in the EMP group (2 [IQR 0–5] vs. 4 [IQR 0–8.25]; $p = 0.049$). In patients with magnetic resonance imaging (MRI) confirmed stroke, a difference was not observed in the secondary outcomes.
Conclusion: Patients with an emergency medicine pharmacist as part of their stroke response team had significantly lower DTN times. A higher proportion of these cases met benchmark DTN times less than 45 min and 30 min. An emergency medicine pharmacist on a stroke response team has the potential to improve patient care.

1. Introduction

Time is one of the most important metrics in the emergency department (ED) for acute ischemic stroke (AIS) and thrombolytic therapy. National guidelines have emphasized tracking time from stroke onset to treatment and decreasing this time [1,2]. The American Heart Association and American Stroke Association Target: Stroke initiative aims to elevate clinical performance in the care of AIS. The primary goal of Phase III of Target: Stroke for patients receiving thrombolytics is door to needle (DTN) time within 60 min in 85% or more of cases. The secondary goals are DTN within 45 min in 75% or more of cases and within 30 min in 50% or more of cases [3].

Various methods of reducing DTN time have been described that institutions can implement [3-7]. Two key strategies to improve DTN time are a multidisciplinary team-based approach and data monitoring/feedback. Most institutions are refining their stroke alert processes to meet the increasingly strict national goals and several have reported benefits of including an EMP in the care of patients with AIS [8-14]. There is limited available data quantifying the impact of pharmacist involvement. Our goal was to compare DTN times in the emergency department (ED) with or without the EMP at bedside and examine the impact on subsequent patient outcomes.

2. Methods

This was an Institutional Review Board exempt, single-center retrospective cohort study conducted at a Thrombectomy Capable Stroke

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Center in Philadelphia, Pennsylvania. Investigators utilized stroke program records that are reported annually to The Joint Commission. From these records, patients were identified that received IV alteplase from August 1, 2016 – May 31, 2020. Chart reviews were conducted to identify patients that presented to the ED and received IV alteplase for suspicion of acute ischemic stroke. Patients were excluded from the study if the ED physician documented patient refusal of alteplase or if they received alteplase off-campus before being transferred to our institution. Documentation of clinical notes by the EMP in the medical record was used to identify bedside participation.

At this institution, there is one EMP that responds with the stroke alert team during daytime hours. Standard EMP stroke alert response hours are Monday through Friday from 0800 to 1630. A neurology resident and CT technician are always on campus, and a neurology attending is available 24/7, on site during the day and over the phone at night. The EMP is a Board-Certified Pharmacotherapy Specialist with specific postgraduate training in Emergency Medicine. During a stroke alert, the pharmacist participates in screening for contraindications to alteplase, assists with blood pressure management, and facilitates administration of any necessary medications. This includes dosing and preparation of alteplase at bedside. Differences in the workflow when the EMP is not available are detailed in Table 1.

The primary outcome was median DTN time, calculated as the time from ED arrival to administration of the alteplase bolus documented by the stroke team. Secondary outcomes included severity of deficits measured by the National Institutes of Health Stroke Scale (NIHSS) at 24 h and discharge, hospital length of stay (LOS), 90-day Modified Rankin Score (mRS), radiologic evidence of intracranial hemorrhage (ICH), and inpatient all-cause mortality. Secondary endpoints were analyzed in all patients and then in a subgroup of only patients with MRI confirmed stroke. All secondary endpoints were obtained from neurology assessment notes in the patients' medical records, except mRS which was obtained with a follow up phone call from the stroke program coordinator. A sensitivity analysis was performed to determine if the shift time could be independently affecting the DTN time. To control for shift differences that might confound the impact of the EMP (present only during day shifts), DTN time was compared during day shift vs night shift in cases without an EMP at bedside. Night shift was defined as 1630–0800 Monday through Friday and weekends.

Statistics were performed using IBM SPSS Statistics software version 27.0. Continuous parametric variables were compared using a student's *t*-test. Continuous non-parametric variables were assessed using a Mann-Whitney *U* test. Fisher's exact test was utilized for nominal variables and chi-square test was used to compare proportions of each group reaching benchmark DTN times. Odds ratios and 95% confident intervals were used to assess DTN goals. Two-tailed *p*-values were used to compare groups.

Table 1
Stroke team workflow.

EMP	No EMP
Patient arrival to emergency department	
Patient transferred to stretcher; weight obtained	
Pharmacist enters current weight into chart	Unit clerk or RN enters current weight into chart
Airway, breathing, circulation assessed; vitals, blood glucose, and presenting NIHSS obtained	
Pharmacist screens for contraindications to alteplase, assists with blood pressure management, and facilitates administration of any necessary medications	Neurology resident screens for contraindications to alteplase and dictates blood pressure management
Patient transferred to ED radiology for CT +/− CTA head	
Patient placed in ED room; repeat NIHSS and vital signs obtained	
Neurology resident and attending determine if patient alteplase candidate; order placed in EMR by Neurology resident	
Pharmacist removes alteplase from automated dispensing cabinet and prepares bedside; dosing calculated/confirmed by pharmacist bedside	RN removes alteplase from automated dispensing cabinet and prepares bedside; dosing calculated/confirmed by RN and physician bedside
Neurology resident administers bolus and RN initiates infusion	
Patient monitored by RN while in the department and transferred to Neuroscience unit or Interventional Radiology if a thrombectomy candidate	

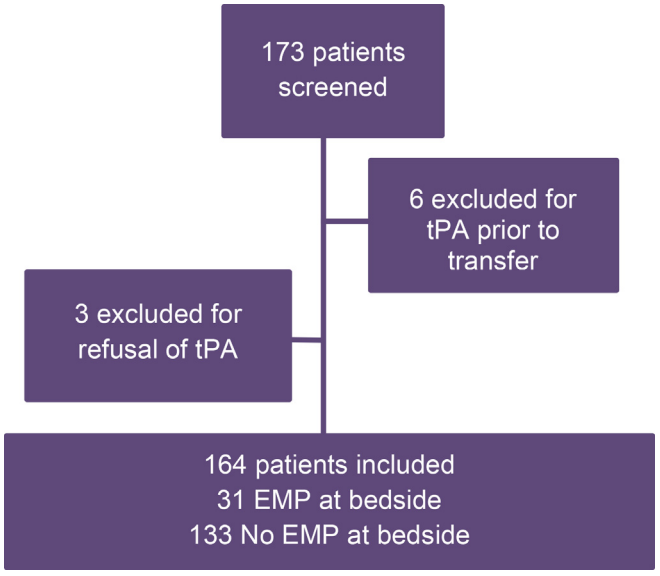

Fig. 1. Screening process.

3. Results

Investigators screened 173 patients; six patients were excluded for receiving alteplase before being transferred to our campus and three

Table 2
Baseline characteristics.

Characteristic	EMP ($n = 31$)	No EMP ($n = 133$)	p-value
Age, mean (SD)	65 (16)	63 (15)	0.691
Sex, female, n (%)	13 (42)	61 (46)	0.841
Race (%)			
Black/African American	27 (87)	111 (83)	0.787
Hispanic/Latino	2 (7)	8 (6)	1.00
Caucasian	1 (3)	7 (5)	1.00
Other/unspecified	1 (3)	3 (2)	1.00
Asian	0	4 (3)	1.00
Past medical history, n (%)			
Previous stroke or TIA	11 (35)	40 (30)	0.667
Atrial fibrillation	4 (13)	27 (20)	0.448
Hypertension	25 (81)	99 (74)	0.642
Hyperlipidemia	16 (52)	64 (48)	0.843
Smoking	13 (42)	49 (37)	0.523
Diabetes mellitus	12 (39)	53 (40)	1.00
Coronary artery disease	13 (42)	58 (44)	1.00
NIHSS at presentation, median (IQR)	8 (6–12)	10 (5–15)	0.572
mRS at presentation, median (IQR)	1 (0–2)	0 (0–1)	0.438
Systolic blood pressure, mean (SD)	168 (32)	163 (34)	0.427
Diastolic blood pressure, mean (SD)	93 (24)	91 (19)	0.561
INR at presentation, mean (SD)	1.1 (0.1)	1.1 (0.1)	0.322
Arrival by EMS (%)	25 (81)	109 (82)	0.767
Hospital pre-notification, n (%)	19 (61)	85 (64)	0.789
Time from LKW, mean, (SD)	76 (63)	74 (48)	0.823
Required HTN treatment[a] (%)	12 (39)	38 (29)	0.267
Ischemic stroke confirmed with MRI prior to discharge, n (%)	11 (35)	77 (58)	0.001

TIA, transient ischemic attack; INR, international normalized ratio; EMS, emergency medical services,
LKW, last known well; HTN, hypertension.
[a] Prior to alteplase administration.

were excluded for treatment refusal. Of the 164 patients included, 31 had an emergency medicine pharmacist at bedside participating in their care (EMP group) and 133 did not (No EMP group) (Fig. 1). The baseline characteristics were similar between the two groups (Table 2). The median DTN time was significantly shorter in the EMP group (35 min EMP [interquartile range (IQR) 29–44] vs 42 min No EMP [IQR 34–55]; $p = 0.003$) as demonstrated in Fig. 2. The number of cases achieving a DTN time within 30 min (EMP 35.5% vs. No EMP 16.5%; $p = 0.018$) as well as the number of patients receiving alteplase within 45 min (EMP 80.7% vs. No EMP 57.1%; $p = 0.015$) was significantly higher when the EMP was involved. The 60-min goal was met at a similar rate in both groups (93.6% EMP, 81.9% No EMP; $p = 0.111$) (Fig. 3).

NIHSS scores at discharge were lower in the EMP group with a median score of 2 (IQR 0–5) vs. 4 (IQR 0.25–8.75); $p = 0.049$ (Table 3). A difference was not observed between groups in 24-h NIHSS, hospital LOS, or 90-day mRS. A larger proportion of patients had a diagnosis of ischemic stroke confirmed with magnetic resonance imaging (MRI) before discharge in the No EMP group. Secondary endpoints were analyzed in a subgroup of 89 patients with MRI confirmed stroke (Table 4). In this subgroup, the secondary outcomes were similar between groups, NIHSS scores were higher, and LOS longer compared to the entire cohort. There were fewer cases of ICH and inpatient all-cause mortality in the EMP group in both analyses. In the sensitivity analysis, median DTN time was not associated with the shift time of the EMP ($p = 0.968$); day shift 42 min (IQR 30–58) vs night shift 43 min (IQR 34.5–54.5).

4. Discussion

In our study, EMP involvement in the stroke response team was associated with shorter DTN times and significant improvement in reaching the Target: Stroke DTN goals. The No EMP group had longer DTN time as well as more variation in DTN time as demonstrated by a wider range of values (Fig. 2). The authors hypothesize this could be related to variance in anticipating the need for alteplase and preventing delays in treatment when the EMP is absent. Although we could not control for all possible confounders, the DTN time was not associated with the time of day that the EMP typically responds to stroke alerts. These findings add a large patient sample to the body of evidence that supports the positive impact of emergency medicine pharmacists.

This is not the first study to demonstrate the valuable role that emergency medicine pharmacists have in improving patient care in AIS. In 2016, Gosser et al. observed a reduction in median DTN time from 89.5 min to 69.5 min with a pharmacist present ($p = 0.0027$) [8]. DTN time was reduced from 74 to 54 min and proportions of patients meeting 45-min and 60-min goals improved in a study by Montgomery et al. in 2016 [9]. In 2017, Rech et al. reported median DTN time was significantly shorter for patients with a pharmacist at bedside (48 min vs. 73 min, $p < 0.01$) [10]. In 2018, Jacoby et al. demonstrated that pharmacist involvement was independently associated with an increased proportion of DTN times less than 45 min (49% vs 25%), and lower 24-h NIHSS scores (median of 1 vs 2, $p = 0.047$) [11]. Recently, Gilbert et al. reported shorter DTN times and a higher proportion of cases meeting the DTN goal of less than 60 min with ED pharmacists present [12].

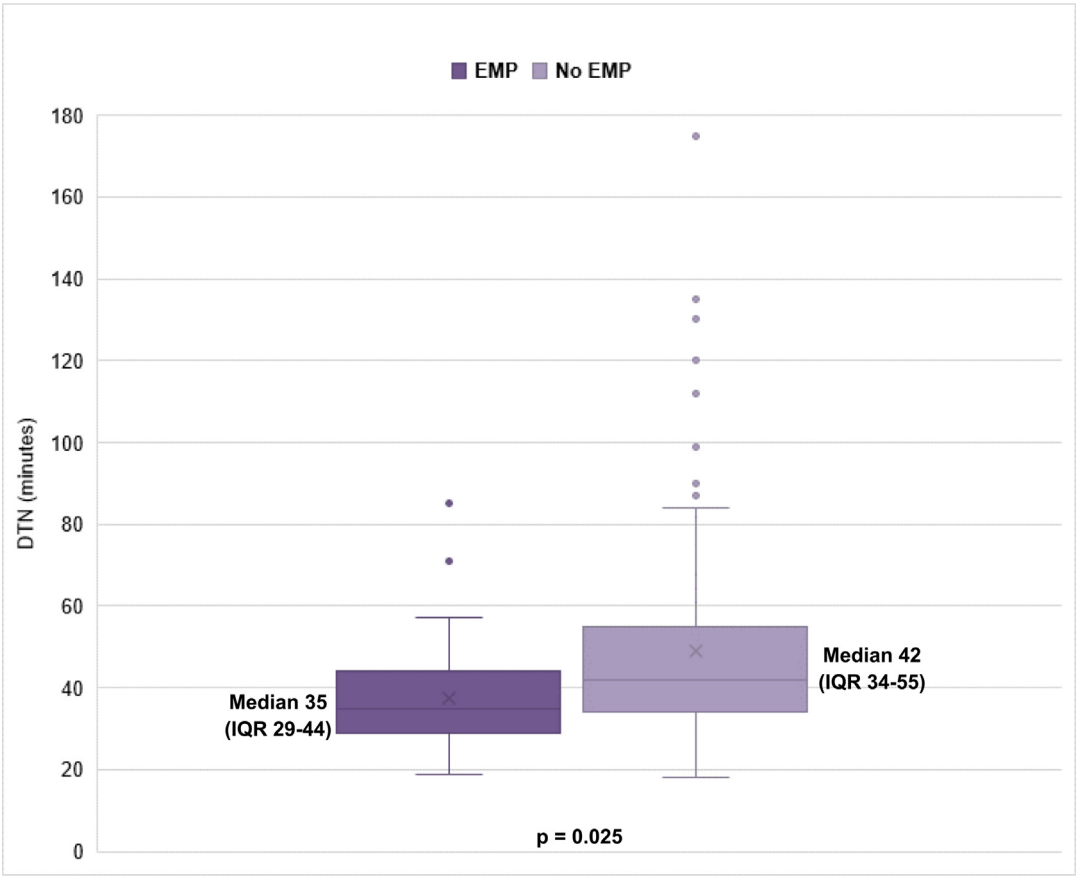

Fig. 2. Median door to needle times.
IQR, interquartile range.

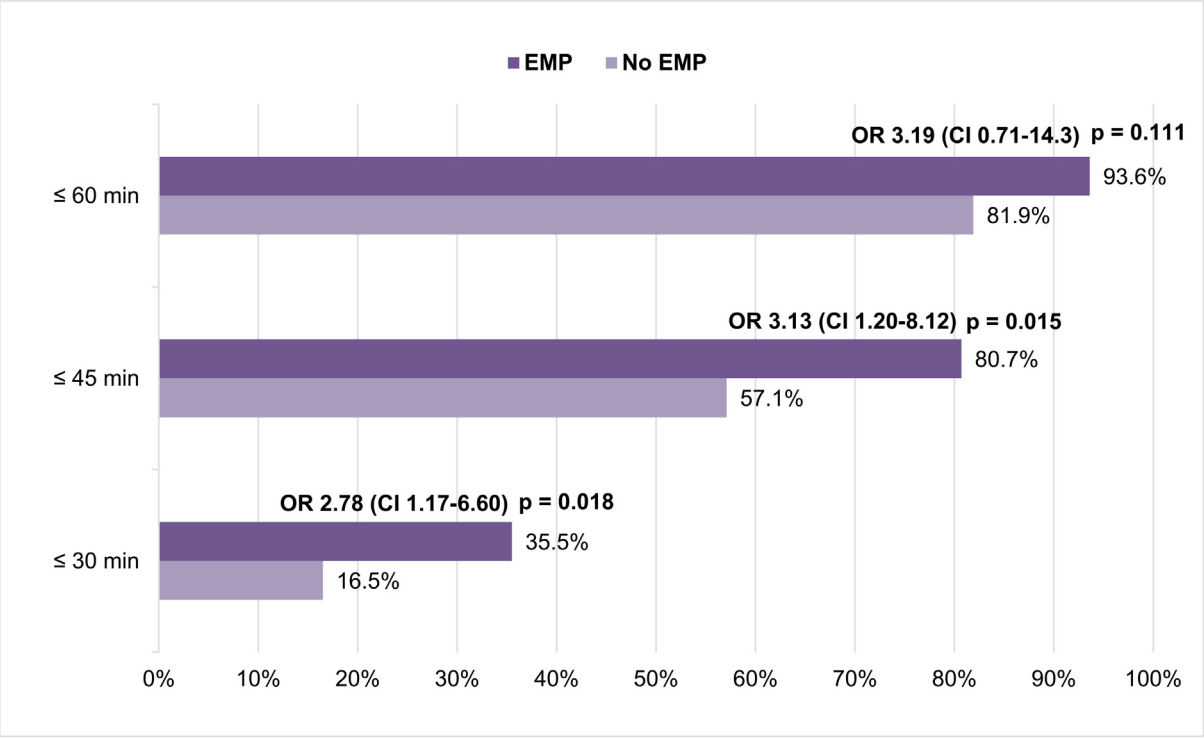

Fig. 3. Percent of cases meeting door to needle goals.
OR, odds ratio; CI, 95% confidence interval.

Table 3
Secondary endpoints in all patients.

	EMP (n = 31)	No EMP (n = 133)	p-value
24-h NIHSS, median (IQR)	3 (1–9)	6 (2−11)	0.087
Discharge NIHSS, median (IQR)	2 (0–5)	4 (0.25–8.75)	0.049
LOS, median, days (IQR)	3 (2–5)	4 (3–4)	0.063
90-day mRS[a], median, (IQR)	3 (1.25–3)	2 (1–4)	0.418
Intracranial hemorrhage, n (%)	1 (3.2)	21 (15.8)	0.081
All-cause mortality, n (%)	0	5 (3.8)	0.584

[a] $N = 47$ (EMP $n = 10$, No EMP $n = 37$).

Phase III goals of the Target: Stroke initiative were released in 2018 and became effective on January 1, 2019. Previous studies have not reported data related to the new 30-min DTN goal. In this study, the EMP group exceeded the goals of 85% of DTN within 60 min and 75% within 45 min while the No EMP group did not meet these goals. Neither group achieved the 30-min DTN goal for 50% of patients, however, the EMP group was two times more successful at reaching the 30-min goal. Secondary outcomes were similar between groups in the totality of patients as well as the subgroup of MRI confirmed stroke. NIHSS scores were lower for the EMP group before excluding patients without a documented positive MRI. NIHSS scores and LOS were worse in the MRI positive subgroup. Long term outcomes such as 90-day mRS are infrequently reported and continue to be a challenge to obtain due to loss of follow up. Rech et al. reported mRS and NIHSS scores at 90 days and did not find a difference between groups [10]. Jacoby et al. reported NIHSS scores at least 30 days from discharge and did not find a significant difference [11]. A number of patients in this study were lost to follow up, and this may have impeded our ability to evaluate 90-day mRS. High mRS scores in both groups may also be due to several challenges in this population, including access and participation in rehabilitation.

Table 4
Secondary endpoints in patients with MRI confirmed stroke.

	EMP ($n = 11$)	No EMP ($n = 78$)	p-value
24-h NIHSS, median (IQR)	10 (7–15)	8.5 (4–12)	0.64
Discharge NIHSS, median (IQR)	5 (2–7)	5 (1−10)	0.784
LOS, median, days (IQR)	4 (2.5–7)	6 (3.25–8)	0.354
90-day mRS[a], median, (IQR)	3 (2–3)	2.5 (1–4)	0.438
Intracranial hemorrhage, n (%)	0	18 (23%)	0.074
All-cause mortality, n (%)	0	2 (2.6%)	0.591

[a] $N = 34$ (EMP $n = 5$, No EMP $n = 29$).

The EMP responded to 19% of the overall patient sample. This is approximately proportional to the amount of time the EMP is available in a week (40 h). As a method of reducing DTN times, this intervention is far from its full potential impact. Our institution is continuously seeking methods to reduce our DTN times and improve outcomes for stroke patients. Even in an institution with DTN times approaching the current standards, the presence of a pharmacist had a noticeable difference. In future studies, we encourage expanding the utilization of clinical pharmacists and exploring specific barriers to meeting a DTN goal of 30 min or less.

5. Limitations

This study has several limitations that the authors recognize. As a retrospective study, the accuracy of our findings depends on the accuracy of documentation. A significant portion of mRS were not obtained at baseline and at 90 days. The number of patients lost to follow up was similar between groups. Three patients in the EMP group (9.7%) and 27 patients in the No EMP group (21%) did not receive an MRI to confirm ischemic stroke for various reasons, most commonly due to metal implants incompatible with MRI. This might have affected the secondary analyses as confirmation of stroke diagnosis was not available for these patients. Additionally, this study is limited by the fact that only one clinical emergency medicine pharmacist responds with the stroke team. This may make the results less generalizable, despite highlighting the impact that a single pharmacist can have on at a large academic medical center. There are potentially other factors not captured here related to the time of day that the EMP is on campus such

as fewer resident physicians on campus at night. However, the goal of our stroke response system is to consistently provide the necessary resources for timely care of stroke patients and the shift time was not associated with DTN time in this analysis. All other members of the multidisciplinary stroke response team respond in the same way regardless of time of day apart from the neurology attending who responds remotely at night.

6. Conclusion

Patients with an EMP as part of their stroke response team had significantly lower DTN times. The number of cases meeting goal DTN times was significantly higher in the group with pharmacist involvement. This is evidence of the benefit of including an emergency medicine pharmacist on the stroke response team. Expansion of the hours of pharmacist coverage has the potential to reach more patients and ultimately improve the care of patients with acute ischemic stroke.

Declaration of Competing Interest

None.

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