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Brief Reports

PHARMACIST IMPACT ON ISCHEMIC STROKE CARE IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: The Froedtert Acute Stroke Team (FAST) is composed of various health professionals who respond to stroke calls, but it does not formally include a pharmacist at this time. However, emergency department (ED) pharmacists have been actively involved in patient evaluation and facilitation of i.v. recombinant tissue plasminogen activator (rtPA) preparation and administration in the ED. ED pharmacists are qualified to dose and prepare rtPA, as well as screen for contraindications to therapy. Objective: The primary objective was to compare the accuracy of rtPA dosing, mean door-to-rtPA time, and identification of contraindications to rtPA therapy when a pharmacist was present vs. absent in the ED. Methods: This is a retrospective study of 105 patients who received rtPA for acute ischemic stroke in the ED at a comprehensive stroke center from January 1, 2008 to October 1, 2012. Results: A total of 105 patients were included in this study. Dosing accuracy was similar when a pharmacist was present vs. absent (96.6% vs. 95.6%; $p = 0.8953$). The median door-to-rtPA time when a pharmacist was present was statistically significantly shorter than when a pharmacist was absent (69.5 vs. 89.5 min; $p = 0.0027$). When a pharmacist was present, a door-to-rtPA time of < 60 min was achieved 29.9% of the time, as compared with 15.8% in the pharmacist-absent group ($p = 0.1087$). Conclusions: Pharmacist involvement on stroke teams may have a beneficial effect on door-to-rtPA time and patient care in the ED.** © **2016 Elsevier Inc.**

☐ **Keywords—pharmacist; ischemic stroke; alteplase; recombinant tissue plasminogen activator; rtPA**

INTRODUCTION

Quick action is critical to restoring cerebral blood flow and preserving brain tissue in patients with acute ischemic stroke. Intravenous alteplase or recombinant tissue plasminogen activator (rtPA) has been shown to provide neurologic improvement and better outcomes if administered early to ischemic stroke patients (1,2). A shorter time to treatment is associated with greater benefit, especially if rtPA is initiated within 90 min of symptom onset. In a pooled analysis of six large rtPA studies, the odds ratio for favorable outcome at 3 months was 2.81 (95% confidence interval [CI] 1.75–4.50), 1.55 (95% CI 1.12–2.15), 1.40 (95% CI 1.05–1.85), and 1.15 (95% CI 0.9–1.47) in patients initiated on rtPA within 90 min, 1.5 to 3 h, 3 to 4.5 h, and 4.5 to 6 h, respectively (3). The 2013 American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend rtPA for treatment-eligible patients diagnosed with acute ischemic stroke who present within 3 h of symptom onset (1). The

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treatment window may be extended to 4.5 h in patients who do not meet the following additional exclusion criteria: age older than 80 years, National Institute of Health Stroke Scale >25, current oral anticoagulant therapy regardless of international normalized ratio (INR), evidence of >1/3 of middle cerebral artery territory ischemic injury, or a history of both diabetes and ischemic stroke (1). However, rtPA is not completely benign, as it carries a high risk of spontaneous intracranial hemorrhage if administered erroneously or to patients who possess known contraindications to therapy.

Target: Stroke[SM], a national quality initiative of the AHA/ASA, has identified Ten Best Practice Strategies (Table 1) to achieve door-to-rtPA times of <60 min in eligible ischemic stroke patients (4). Pharmacists are in a unique position to enhance Best Practice Strategies 7, 8, and 9, which include mixing rtPA ahead of time, rapid access to i.v. rtPA, and utilizing a team-based approach (4). Froedtert & The Medical College of Wisconsin, a Level I trauma center and comprehensive stroke center in Milwaukee, WI, utilizes a stroke team composed of neurologists, emergency department (ED) physicians, and nurse specialists to respond to stroke calls. Although the Froedtert Acute Stroke Team (FAST) did not formally include a pharmacist member at the time of this study, ED pharmacists had been actively involved in patient evaluation and facilitation of rtPA preparation and administration within the ED. Pharmacists are qualified to dose and prepare rtPA for immediate administration, screen for contraindications to therapy, and ensure that patients receive the correct dose every time. Formal integration of the pharmacist in the response to acute ischemic stroke may contribute to greater attainment of goal door-to-rtPA times and the potential for improved patient outcomes. The purpose of this study is to retrospectively examine the pharmacist's impact on door-to-rtPA time and dosing accuracy within the ED at Froedtert.

Table 1. Target Stroke[SM] Ten Best Practice Strategies (4).

Strategy	Best Practice
1	Advance hospital notification by EMS
2	Rapid triage protocol and stroke team notification
3	Single call activation system
4	Stroke tools
5	Rapid acquisition and interpretation of brain imaging
6	Rapid laboratory testing (including point of care testing if indicated)
7	Mix tPA medication ahead of time
8	Rapid access to i.v. tPA
9	Team-based approach
10	Prompt data feedback

EMS = Emergency Medical Services; tPA = tissue plasminogen activator.

METHODS

Study Design and Setting

This study is a retrospective analysis comparing door-to-rtPA time, identification of contraindications, and dosing accuracy of rtPA for patients treated for acute ischemic stroke with and without a pharmacist present in the ED of a comprehensive stroke center. During the study period, ED pharmacists staffed daily and were available for consult from 10:00 AM to 6:30 PM.

Selection of Participants

Patients were included in the study if they received i.v. rtPA for acute ischemic stroke in the ED from January 1, 2008 to October 1, 2012. Patients were excluded if they were younger than 18 years old, received a partial dose of rtPA, initiated on rtPA at an outside institution, hypertensive and antihypertensive agents were unable to lower blood pressure to <185/110 mm Hg for rtPA initiation, had missing or incomplete documentation in the electronic medical record, or if rtPA was given for another U.S. Food and Drug Administration labeled indication, such as ST-elevation myocardial infarction, pulmonary embolism, or central venous catheter occlusion. The electronic medical records of patients who met inclusion criteria were then reviewed to determine whether or not a pharmacist was involved during rtPA administration. Pharmacist involvement was defined as encounters with documentation in the notes, order entry, or automating dispensing cabinet override. Patients who received rtPA with pharmacist involvement were categorized to the pharmacist present group. The remaining patients were assigned to the pharmacist absent group.

Data Collection

Data collected from the medical record included demographic information, time of patient presentation to the ED, rtPA bolus and infusion doses and times administered, weight used to calculate rtPA dose, staff who dispensed rtPA, medication history status on ED arrival, blood pressure, antihypertensive agents administered if applicable, INR, platelets, and glucose values. The weight used to dose rtPA was extrapolated by dividing the dose administered by 0.9, with the assumption that the intended dose was 0.9 mg/kg. To assess whether or not the rtPA was dosed accurately, the extrapolated weight was then compared with actual patient weight obtained and documented in the electronic health record. Door-to-rtPA time was defined as the time of presentation to the ED to the time of administration of the rtPA bolus. Expedited review was granted and approved by the Froedtert Institutional Review Board.

Statistical Analysis

A power analysis completed before initiation of the study indicated that a sample size of 72 patients (36 patients per group) would be needed to detect a medium to large effect size of $d = 0.60$, with power set at 80% and a 5% level of significance.

Descriptive statistics were used to summarize the collected data. Frequency distributions were calculated for categorical variables. The independent *t*-test was used to compare dosing accuracy. The Wilcoxon Mann-Whitney nonparametric test was used to compare door-to-rtPA times for the two groups. A χ^2 test was utilized to determine the proportion of instances when the door-to-rtPA time was <60 min for each group. Statistical analyses were performed using SAS software, version 9.2 (SAS Institute, Inc, Cary, NC).

RESULTS

Characteristics of Study Patients

Of the 120 patients identified and screened for inclusion, 105 patients met the inclusion criteria. Fifteen patients were excluded from analysis due to one or more of the following: incomplete medical record documentation; partial doses of rtPA administered; high blood pressure resistant to lowering with antihypertensive agents, disallowing administration of rtPA; and an adverse reaction resulting in the discontinuation of rtPA. One patient experienced epistaxis that was difficult to control, and the other patient experienced a rapid decline in condition during the infusion. In total, 67 patients were included in the pharmacist-present group and 38 patients were included in the pharmacist-absent group (Figure 1).

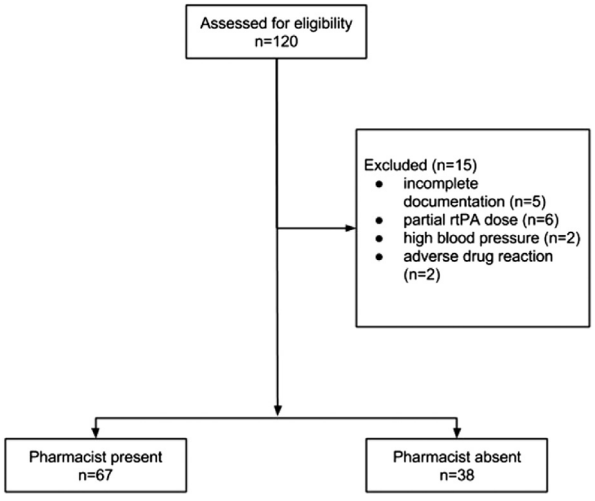


Figure 1. Patient group stratification and disposition. rtPA = recombinant tissue plasminogen activator.

Main Results

A door-to-rtPA time of <60 min was achieved 24.8% of the time for all patients during the study period (Figure 2). Median door-to-rtPA time for the study period for all patients was 75.0 min. Dosing accuracy was similar in both groups (pharmacist-present 96.6% vs. pharmacist-absent 95.6%; $p = 0.8953$). Median door-to-rtPA time was 69.5 min when a pharmacist was present and 89.5 min when a pharmacist was absent ($p = 0.0027$) (Figure 3). When a pharmacist was present, a door-to-rtPA time of <60 min was achieved 20 out of 67 times (29.9%), as compared with 6 out of 38 times (15.8%) in the pharmacist-absent group ($p = 0.1087$) (Table 2).

High blood pressure, defined as >185/110 mm Hg, was the only contraindication present upon admission for patients in both study groups. rtPA was administered only if blood pressure could be lowered to <185/110 mm Hg. Of all patients, 37.9% required intervention with antihypertensive agents to control blood pressure in order to receive rtPA. There were no instances where rtPA was given to patients whose blood pressure remained >185/110 mm Hg at the time of administration. Thirty-eight patients (36.2%) had a medication history note recorded by the ED pharmacist. All patients had a medication history completed and documented after admission to the inpatient unit.

DISCUSSION

The Target: Stroke™ initiative recommends incorporation of several strategies to approach acute ischemic stroke care (1). A recent study examining use of these strategies by hospitals found that stroke team notification, use of a single-call activation system, and rtPA storage in the ED were all strategies independently associated

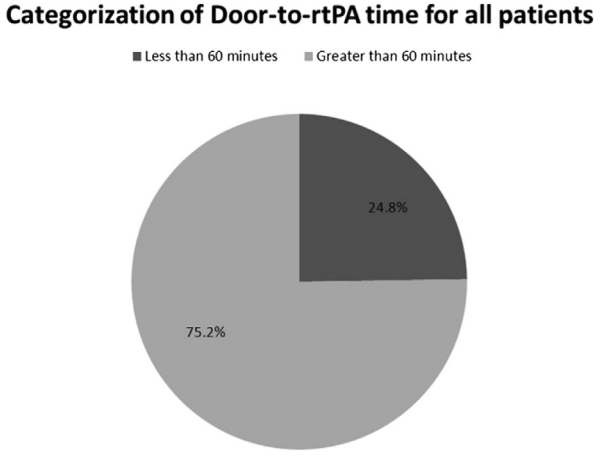
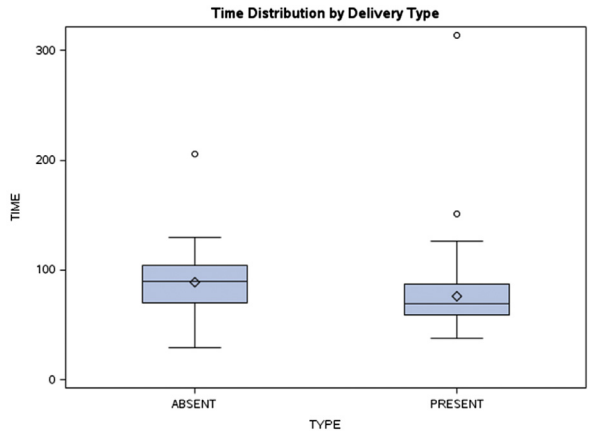


Figure 2. Categorized dosing time by goal of <60 min. rtPA = recombinant tissue plasminogen activator.



TYPE	N	Median Time (mins)	25th Pctl	75th Pctl
Pharmacist Absent	38	89.50	70.00	104.00
Pharmacist Present	67	69.50	59.00	87.50

p=0.0027

Figure 3. Boxplot of door-to-recombinant tissue plasminogen activator time (min) for pharmacist-absent and pharmacist-present groups.

with shorter door-to-rtPA time (5). Incorporation of pharmacists in acute ischemic stroke care, however, was not explored in this study. The percentage of patients with door-to-rtPA time <60 min (24.8%) in this study is comparable with the < 30% found in the AHA/ASA Get With The Guidelines quality-improvement program and other analyses (6–8). Several factors might contribute to a delay in rtPA administration, including but not limited to delay in attainment of head computed tomography (CT) scan, delay in provider assessment, delay in the decision to give rtPA, need for blood pressure reduction, inability to determine weight, and delay in obtaining patient consent. Although no longer needed currently, patient consent had been required at our institution during the study period. In this study, 37.9% of patients had blood pressures of >185/110 mm Hg, requiring intervention before rtPA administration.

Table 2. Proportion of Times Door-to-Recombinant Tissue Plasminogen Activator Time Achieved by Patient Group

Patient Group	Dosing Time ≤60 min	Dosing Time >60 min	Total
Pharmacist absent, n (%)	6 (15.8)	32 (84.2)	38
Pharmacist present, n (%)	20 (29.9)	47 (70.1)	67
Total, n (%)	26 (24.8)	79 (75.3)	105

$\chi^2 = 2.57$, $p = 0.1087$ for proportion of times the dosing time was ≤60 min for pharmacist-present and pharmacist-absent groups.

There were a few instances in which less than ideal antihypertensive agents (e.g., metoprolol) were chosen to lower blood pressure, prolonging the door-to-rtPA time. This was found most often outside of pharmacist staffing hours of 10:00 AM to 6:30 PM in the pharmacist-absent group (Table 3). The AHA/ASA Early Management of Acute Ischemic Stroke guidelines recommend use of antihypertensive agents, such as i.v. labetalol, nicardipine, and hydralazine (1). The pharmacist-present group had more instances of nicardipine drip utilization after labetalol dose escalation failed to adequately lower blood pressure in a timely manner (Table 3). Pharmacist involvement on the stroke team can allow for more efficient lowering of blood pressure with the appropriate agents, dose, and frequency.

When patients present to the ED with symptoms of acute ischemic stroke, weight is usually obtained via use of a bed scale. If the situation is very acute and the patient is unable to be weighed, the patient or family might be asked to report the current weight, or an estimation can be made by the medical team. This weight is then used to dose rtPA. In examining dosing accuracy, the weight was back calculated from the rtPA dose administered and compared to the actual bed weight as documented in the electronic health record, which might have occurred after admission. There was no statistical difference between dosing accuracy between the study groups. This is most likely attributed to similar methods being used to obtain the patient weight within both study groups.

The proportion of patients in the pharmacist-present group who had a door-to-rtPA time <60 min was nearly two times that of the pharmacist-absent group, however, this was not statistically significant. Several reasons might be attributed to this difference between the groups. The pharmacist might be more familiar with the

Table 3. Patient Demographics

Patient Demographics	Pharmacist Present (n = 67)	Pharmacist Absent (n = 38)
Age (y), median (range)	72 (40–96)	73 (41–97)
No. of patients with hypertension* on presentation to ED, n (%)	28 (42)	10 (26)
Baseline BP in patients with hypertension* on presentation		
Systolic BP	211	214
Diastolic BP	106	106
Total number of antihypertensive doses given		
Labetalol, 10–20 mg i.v.	32	7
Hydralazine, 10–20 mg i.v.	2	0
Metoprolol, 5 mg i.v.	0	2
Nicardipine infusion†	15	2

BP = blood pressure; ED = emergency department.
* Hypertension defined as BP > 185/110 mm Hg.
† Nicardipine infusion numbers represent patients initiated on nicardipine in the ED.

preparation of the agent than a nurse who might not prepare rtPA as often. For the majority of the study period, rtPA was not stocked in the ED automated dispensing cabinets. This could have impacted door-to-rtPA times for both groups, as additional time was required to retrieve rtPA from the central pharmacy. Pharmacists might have been more adept at obtaining the medication from the central pharmacy when needed, allowing for more rapid acquisition of the rtPA. When rtPA was stocked in the ED automated dispensing cabinets, pharmacists were more actively involved in the preparation of rtPA onsite in the ED, which might have also led to decreased door-to-rtPA time. Pharmacist ownership of acquisition and preparation of rtPA allows physicians and nurses to focus on the assessment and care of the patient.

Medication histories are the pharmacist's opportunity to screen for medication contraindications that can potentially exclude a patient from receiving rtPA, as it can increase risk of bleed or harm. The documentation rate of medication histories by the ED pharmacist was low in this study. Although this formal documentation was low, it is not fully indicative of medication history screening that may have been done by the pharmacist. The American Society of Health-System Pharmacists (ASHP) Guidelines on Emergency Medicine Pharmacist Services recommends that pharmacists provide medication history services to patients most in need (9). All patients had complete medication histories documented within 24 h of admission to the hospital.

Limitations

Incomplete documentation was prevalent in patient charts from 2008 to 2010, due to the use of paper charts instead of an electronic health record. Some patients during this time period were excluded from the study because the time or dose of rtPA administration was unclear or not documented in the paper chart. Patients were excluded from this study if they received partial doses of i.v. rtPA to allow for subsequent intra-arterial rtPA, as dosing varies from i.v. administration.

Pharmacists staffed the ED from 10:00 AM to 6:30 PM during the study period. This timeframe provides a well-staffed ED, with potentially better access to resources. It is possible that this provided some benefit to the door-to-rtPA in some cases, however, there were cases during this timeframe that were assigned to the pharmacist-absent group, as the ED pharmacist was not notified of the stroke call.

During the retrospective study period, pharmacists were not formally notified of patients with suspected stroke because they were not a part of the FAST. If pharmacists were notified of a potential stroke before the patient actually needed rtPA, it could have assisted in the workup facilitation and decreased door-to-rtPA time more frequently than what was found in this retrospective analysis. ED pharmacists at Froedtert now receive stroke pages via their personal pagers. Adoption of resolution 44 and recognition of ED pharmacist services by the Council of The American College of Emergency Physicians paves the way for further development of clinical pharmacy services within the ED (10,11).

CONCLUSIONS

In summary, there were no statistically significant differences in dosing accuracy, however the median door-to-rtPA time was significantly less in the pharmacist-present group. Patient outcome comparisons as a result of this decreased door-to-rtPA time between the two groups were not evaluated. There is a need for further investigation to correlate pharmacist involvement and decreased door-to-rtPA time to patient outcomes. Increased pharmacist involvement within FAST may be beneficial to stroke response teams and patient care.

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ARTICLE SUMMARY

1. Why is this topic important?

Intravenous alteplase or recombinant tissue plasminogen activator (rtPA) has been shown to provide neurologic improvement and better outcomes if administered early to ischemic stroke patients.

2. What does this study attempt to show?

This retrospective study attempts to show that pharmacists can have a beneficial impact on the door-to-rtPA time and patient care in the emergency department.

3. What are the key findings?

This study found a median door-to-rtPA time of 69.5 min when a pharmacist was present and 89.5 min when a pharmacist was absent ($p = 0.0027$). Dosing accuracy and number of times door-to-rtPA time was <60 min was not statistically significant between the two groups. Patient outcomes between the two groups were not evaluated.

4. How is patient care impacted?

Pharmacist ownership of acquisition and preparation of rtPA allows physicians and nurses to focus on the assessment and care of the patient.