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ORIGINAL ARTICLE

Identifying and Addressing Barriers to Systemic Thrombolysis for Acute Ischemic Stroke in the Inpatient Setting: A Quality Improvement Initiative

Andrew R. Pines, MA; Devika M. Das, MS; Shubhang K. Bhatt, BS; Ham J. Shiue, PharmD, MSc; Sara Dawit, MD; Vanesa K. Vanderhye, MSN, RN; and Kara A. Sands, MD

Abstract

Objectives: To identify barriers to inpatient alteplase administration and implement an interdisciplinary program to reduce time to systemic thrombolysis.

Patients and Methods: Compared with patients presenting to the emergency department with an acute ischemic stroke (AIS), inpatients are delayed in receiving alteplase for systemic thrombolysis. Institutional AIS metrics were extracted from the electronic medical records of patients presenting as an inpatient stroke alert. All patients who received alteplase for AIS were included in the analysis. A gap analysis was used to assess institutional deficiencies. An interdisciplinary intervention was initiated to address these deficiencies. Efficacy was measured with pre- and postintervention surveys and institutional AIS metric analysis. Statistical significance was determined using the Student *t* test. We identified 5 patients (mean age, 73 years; 100% (5/5) male; 80% (4/5) white) who met inclusion criteria for the preintervention period (January 1, 2017, to December 31, 2017) and 10 patients (mean age, 71 years; 50% male; 80% white) for the postintervention period (October 31, 2018, to July 1, 2020).

Results: We found barriers to rapid delivery of thrombolytic treatment to include alteplase availability and comfort with bedside reconstitution. Interdisciplinary intervention strategies consisted of stocking alteplase on additional floors as well as structured education and hands-on alteplase reconstitution simulations for resident physicians. The mean time from stroke alert to thrombolysis was shorter postintervention than preintervention (57.4 minutes vs 77.8 minutes; P=.03).

Conclusion: A coordinated interdisciplinary approach is effective in reducing time to systemic thrombolysis in patients experiencing AIS in the inpatient setting. A similar program could be implemented at other institutions to improve AIS treatment.

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In the United States, there are approximately 795,000 strokes per year, with approximately 87% of these being classified as acute ischemic stroke (AIS).[1] Stroke is the fifth leading cause of death in the United States,[1] and an estimated 2.4% of the US population lives with disability attributed to stroke.[2]

Reports estimate that 4% to 17% of total strokes occur in patients already admitted to the hospital for other medical concerns.[3-5] Patients who develop a stroke in the inpatient setting have consistently worse outcomes than those who develop a stroke outside the hospital and present to the emergency department (ED).[3-6] Although poor outcomes can be partially attributed to an increased prevalence of vascular disease in a hospitalized population,[7,8] having a stroke on an inpatient floor has been identified as an independent risk factor for higher mortality and worse functional status on discharge.[5,9-11] These findings may appear counterintuitive, as the ease of access to health care providers in a hospital ward

From the Mayo Clinic Alix School of Medicine, Mayo Clinic, Scottsdale, AZ (A.R.P., D.M.D., S.K.B.); Department of Neurology (S.D., V.K.V., K.A.S.) and Department of Pharmacy (H.J.S.), Mayo Clinic, Phoenix, AZ.

should reduce time spent transporting, recognizing, and treating stroke patients. A plausible explanation is that the relatively low occurrence of inpatient strokes leaves providers unfamiliar with the workflow, resulting in delays in thrombolytic treatment.[6,9,10,12,13]

Timely administration of thrombolytic therapy after the onset of AIS symptoms has been found to improve patient functional outcomes[14-16] and has been identified as the most important modifiable factor to affect outcomes in the acute setting.[17] National ischemic stroke guidelines have set a benchmark of 60 minutes or less from the time patients with AIS arrive at the hospital to when eligible patients receive systemic thrombolysis.[18,19] The American Heart Association (AHA) has released an update to their guidelines that recommends eligible patients receive intravenous (IV) alteplase in the fastest achievable time.[18] Quality initiatives from the AHA recommend time from arrival at the hospital to thrombolysis as rapid as 30 minutes.[20] Similar goals would be beneficial for the inpatient setting.

To ensure the highest quality of stroke care in the inpatient setting, we conducted a quality improvement study to assess and improve our hospital response to inpatient strokes. Our primary aim was to reduce the time from when a stroke alert was activated to systemic thrombolysis to 60 minutes or less.

PATIENTS AND METHODS

Study Overview

This was a quality improvement initiative performed at a 273-bed academic hospital. This hospital is an advanced primary stroke center certified by the Joint Commission; however, the stroke center meets all the operational requirements of a comprehensive stroke center and plans on applying for this designation once volume requirements are met. The neurology department consists of 32 attending physicians, 8 advanced practice providers, 2 fellows, 12 residents, and 27 nursing staff. This study was approved by the Mayo Clinic Institutional Review Board (IRB# 17-008803). Patients were eligible for this study if they experienced AIS in the inpatient setting and were treated with IV alteplase between January 1, 2017, and July 1, 2020. Patients experiencing AIS who were brought to the ED or patients with contraindications to alteplase treatment were excluded from the study. The primary outcome was a reduction in the stroke-alert-to-needle (STN) time to the national guideline recommendation of 60 minutes or less.

Study Variables

Door-to-needle time is defined as the time it takes from patient arrival in the ED to the administration of a thrombolytic agent. The AHA recommends door-to-needle time to be 60 minutes or less.[19] On the basis of this national benchmark, we define *STN time* in the inpatient setting as the time from stroke alert activation to the administration of IV alteplase. *Decision-to-treat-to-bolus (DTB) time* is defined as the time from when the decision was made to treat with IV alteplase to subsequent administration. All these variables are documented on the stroke alert timeline in the electronic medical record (EMR) by neurology providers (physician assistant, resident, and/or attending physician). These times are extracted from the EMR by the stroke center coordinator. The primary outcome of this study was STN time, and the secondary outcome was DTB time. Satisfaction of neurology residents with our education session was assessed to measure unintended burden.

Workflow Before Intervention

The stroke team is composed of pharmacists, the stroke center coordinator, physician assistants, neurology residents, and vascular neurology physicians. When stroke symptoms are recognized in a patient, registered nurses (RNs) activate a stroke alert by calling 911 (internal), requesting stroke alert activation, and giving the callback number of the primary RN. The primary RN will notify the RN team lead that a stroke alert has been activated, and the rapid response nurse (RRN) is contacted for assistance. The RRN will perform an initial assessment and may initiate an IV if the patient does not already have a large-bore IV in place or only has 1 site of IV access. Our institution's protocol requires a large-bore (>20-G) IV to perform imaging studies in suspected large vessel occlusion strokes. Two

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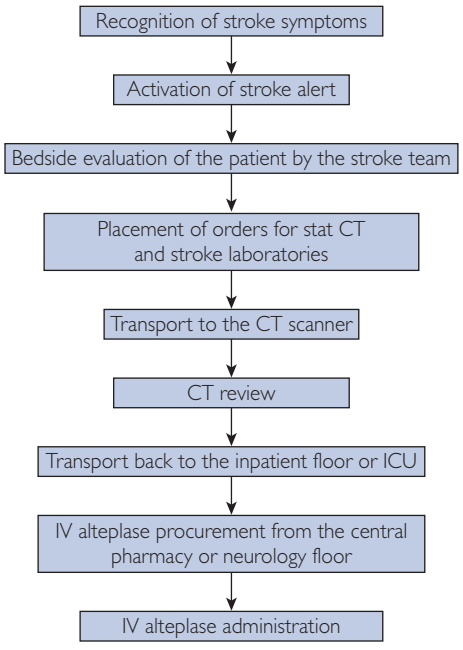

FIGURE 1. Stroke alert algorithm. CT = computerized tomography; ICU = intensive care unit; IV = intravenous.

sites of IV access are necessary to administer antihypertensive medication and/or maintenance IV fluid and to reduce the risk of bleeding from additional venous punctures after alteplase administration. The RRN assists the primary RN with preparing the patient for transport to the computerized tomography (CT) scanner. When the stroke team arrives, the patient is prepared and transported for an immediate noncontrast CT of the head. After CT imaging is reviewed and contraindications considered, the patient's candidacy for alteplase is determined. If the patient meets eligibility criteria, a pharmacist or neurologist would reconstitute alteplase and the neurologist would administer the IV bolus. At the direction of the neurologist, an RRN or an intensive care unit RN may also administer alteplase. There was not a standardized designation of the provider who reconstitutes and the provider who administers. Although it is within the scope of practice for neurology residents, a training program on reconstituting and administering alteplase did not exist before this initiative. Our institution's stroke protocol is summarized in Figure 1.

Gap Analysis

A gap analysis was performed with an interdisciplinary team consisting of an RN, neurology resident, vascular neurologist, clinical pharmacist, medical students, and the stroke center coordinator. We performed a retrospective review of all patients who experienced AIS in an inpatient setting in 2017. We reviewed the patient notes from each encounter to identify recurrent causes of treatment delay. Alteplase availability and comfort with bedside reconstitution were listed in the EMR as primary reasons for delays in the delivery of thrombolytic therapy. After consulting key stakeholders, a consensus was reached to devise and implement educational and logistical interventions to address the underlying causes of delays. The gap identified was standardization of the delivery and administration of alteplase. This gap had 2 components: (1) the physical distance between where an AIS occurred and the location of alteplase and (2) lack of provider familiarity with reconstituting and administering alteplase. We addressed these components by ensuring alteplase was strategically stocked in more automated medication dispensing cabinets (AMDCs) throughout the hospital and with an education workshop that taught neurology residents how to locate, reconstitute, and administer alteplase (Figure 2).

Intervention

An education workshop was designed to educate residents on the process of locating and reconstituting alteplase. The workshop is attended by all neurology residents. In addition, this workshop served as an update on the latest management of patients with AIS. The AIS guidelines from the AHA/American Stroke Association serve as the foundational document for the education intervention. The education workshops are led by a vascular neurologist, neurology resident, clinical pharmacist, and medical students. The didactic session was then followed up with hands-on practice with reconstituting alteplase. An alteplase simulation kit is kept in the resident workroom so that they could continually practice with the reconstitution process. Pre- and post-workshop surveys were administered to measure the efficacy of the education

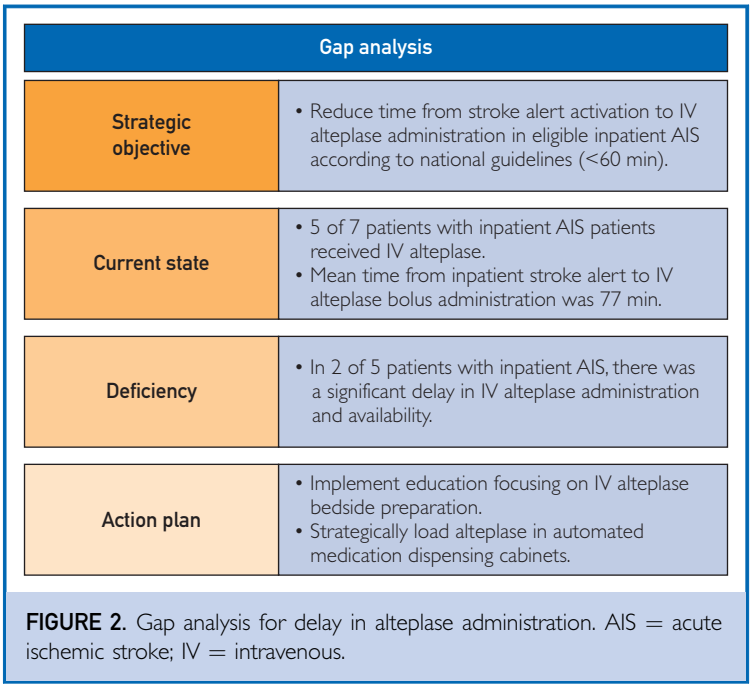

FIGURE 2. Gap analysis for delay in alteplase administration. AIS = acute ischemic stroke; IV = intravenous.

workshops. The second prong of our intervention was to stock alteplase kits in AMDCs in additional locations to improve medication access.

Define, Measure, Analyze, Improve, and Control

A quality improvement study model of define, measure, analyze, improve, and control was used for the study framework. Briefly, we defined the problem by recognizing delays in administering systemic thrombolysis in cases of inpatient AIS at our institution throughout 2017. We aimed to reduce the STN time to 60 minutes or less without causing an excessive burden on neurology providers. We measured the study variables defined above. By reviewing the EMR and learning what transpired during each stroke alert, we analyzed the data to determine a suitable intervention. We improved the process by petitioning the pharmacy administration to strategically store alteplase in more locations throughout the hospital and then educated neurology residents on reconstitution and administration of alteplase. We control the improvement with alteplase simulation kit availability in the resident workroom, an annual education session that is modified with resident feedback, and a trigger point of 3 or more cases with delayed STN times (>60 minutes) that would prompt the stroke center coordinator to engage our team to reassess the project.

Data Collection and Statistical Analyses

Continuous variables were reported as mean ± SD. Statistical significance was determined using the Student *t* test. STN and DTB times were measured from January 1, 2017, to December 31, 2017 (preintervention), and compared with times from October 31, 2018, to July 1, 2020 (postintervention). The target STN time was 60 minutes or less, whereas the target DTB time was to achieve times less than the current institutional baseline. Statistical significance was set at *P* less than .05.

RESULTS

Between January 1, 2017, and December 31, 2017 (baseline period), 5 patients met our inclusion criteria (Table 1). Between October 31, 2018, and July 1, 2020 (postintervention period), 10 patients met our study criteria (Table 2). Patients in the baseline period had a mean age of 73.6±8.3 years and were 100% male and 50% white. Their mean presenting National Institutes of Health Stroke Scale (NIHSS) score was 17.4±7.7. Patients in the postintervention period had a mean age of 71.4±15.6) years and were 50% male and 80% white. Their mean presenting NIHSS score was 8.6±7.3 (Table 3). In reviewing cases from the baseline period, we noted that the most common factors contributing to delay in IV alteplase administration were difficulty achieving IV access (n=3 [60%]), difficulty locating alteplase (n=2 [40%]), and difficulty reconstituting alteplase (n=2 [40%]). Other factors for delay included difficultly obtaining IV access (n=3 [60%]) and time of transfer from the floor to the CT scan to the intensive care unit (n=2 [40%]). We chose to target alteplase availability and reconstitution as it is the most immediately resolvable causes of delay. Difficulty in achieving IV access, which requires 1 large-bore IV and an additional IV site, and improvements in the CT workflow are challenges we hope to address in the future.

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TABLE 1. Inpatient Stroke Alert Times From January 1, 2017, to December 31, 2017

Patient no.	Symptom onset to SAA (min)	SAA to stroke team arrival (min)	Stroke team arrival to CT head review (min)	CT review to time of decision to treat (min)	DTB time (min)	STN time (min)
1	15	5	39	2	33	79
2	13	8	27	15	30	80
3	34	5	53	36	8	102
4	26	7	40	ND	ND	56
5	2	5	51	0	16	72

CT = computerized tomography; DTB = decision-to-treat-to-bolus; ND = no data available; SAA = stroke alert activation; STN = stroke alert-to-needle.

Before intervention, alteplase kits were available only in the central pharmacy and the ED, which are both located on the first floor of the hospital. When conducting the gap analysis of the 2017 inpatient AIS cases, stroke events did not occur more frequently on any particular inpatient unit. Therefore, the decision was made to add additional alteplase kits to AMDCs on a unit that met the following criteria: distant from current locations of alteplase kits (central pharmacy and ED), with a patient population with neurological diagnoses, and staffed with RNs who are NIHSS certified. All these factors led to the decision to stock alteplase kits on the neurology unit. In addition, the observation unit, in which high-risk patients with transient ischemic attack are admitted, is located on the same floor as the neurology unit.

In the preintervention analysis, patients with AIS in the inpatient setting who received IV alteplase presented to the neurology unit (n=1 [20%]), ortho/urology rehab unit (n=1 [20%]), progressive cardiac care unit (PCCU) (n=1 [20%]), hematology/oncology unit (n=1 [20%]), and oncology unit (n=1 [20%]). In the postintervention analysis, patients with AIS in the inpatient setting who received IV alteplase presented to the intensive care unit (n=1 [13%]), progressive care unit (n=3 [38%]), PCCU (n=3 [38%]), neurology unit (n=2 [25%]), and med-surg unit (n=1 [13%]).

During the baseline period, the mean STN time was 77.8±16.6) minutes. After intervention implementation, the mean STN time was reduced to 57.4±14.95 minutes (P=.03) (Figure 3). The mean DTB time

TABLE 2. Inpatient Stroke Alert Times From October 31, 2018, to July 1, 2020

Patient no.	Symptom onset to SAA (min)	SAA to stroke team arrival (min)	Stroke team arrival to CT head review (min)	CT review to time of decision to treat (min)	DTB time (min)	STN time (min)
1	10	5	34	1	13	53
2	169	10	33	13	30	86
3	9	5	12	44	3	64
4	1	6	27	2	15	50
5	18	4	28	1	4	61
6	ND	ND	ND	ND	ND	64
7	84	0	29	15	2	46
8	4	5	16	8	10	39
9	19	1	36	1	16	72
10	46	0	26	12	1	39

CT = computerized tomography; DTB = decision-to-treat-to-bolus; ND = no available dat; SAA = stroke alert activation; STN = stroke-alert-to-needle.

TABLE 3. Demographic Data by Study Period[a,b]

Characteristic	Preintervention (n=5)	Postintervention (n=10)	*P* value
Age (y)	73.6±8.3	71.4±15.6	.63
Male	5 (100)	5 (50)	.03
Female	0 (0)	5 (50)	
Race/ethnicity			.83
White	4 (80)	8 (80)	
Black	1 (20)	1 (10)	
Hispanic	0 (0)	1 (10)	
Initial NIHSS score	17.4±7.7	8.6±7.3	.17

[a]NIHSS, National Institutes of Health Stroke Scale.
[b]Data are presented as mean ± SD or as No. (percentage).

during the baseline period was 21.8±11.7 minutes and was reduced to 10.4±9.3 minutes during the postintervention period (*P*=.08) (Figure 4).

The mean score for neurology residents on knowledge assessments improved. On average, scores improved by 23% between the pretest and the posttest. Among respondents, 78% reported being "very satisfied" on the satisfaction survey and no one reported "not very satisfied" or "not at all satisfied." On a Likert scale of how confident the participants were at reconstituting alteplase ("not at all confident," "not very confident," "somewhat confident," "fairly confident," and "very confident"), confidence increased by an average of 2.2 levels after the workshop.

DISCUSSION

Summary

From our gap analysis, we identified that the predominant factors for inpatient AIS treatment delays at out institution were alteplase availability and provider comfort level with bedside alteplase reconstitution. We developed a 2-pronged interdisciplinary intervention aimed at educating neurology residents and strategically stocking alteplase in AMDCs throughout the hospital. Twenty-one months postintervention, the mean STN time was reduced (57.4 minutes vs 77.8 minutes; *P*=.03), which aligns with national guidelines. In addition, the mean DTB time for inpatient AIS improved from 21.8 to 10.4 minutes. These improved times suggest that the intervention was effective. The intervention also led to improved knowledge of AHA/American Stroke Association guidelines and alteplase administration for AIS, with the mean knowledge score increasing from preeducation to posteducation by 23%. These results indicate that education and simulation can be a valuable tool in helping providers become more comfortable with managing inpatient AIS.

Interpretation

Inpatient AIS treatment is often associated with poor outcomes and is less likely to meet quality-of-care metrics.[4,21,22] Some barriers that have been identified include increased times to neuroimaging, decreased rates of thrombolysis, lack of education in identifying stroke symptoms on inpatient units, delayed notification of necessary health care providers, and poor communication when compared with out-of-hospital strokes.[10,23,24]

Although other quality improvement projects have successfully targeted recognition of inpatient stroke symptoms, inpatient stroke workflow and protocols, communication and coordination among team members, or time to CT scan as interventions,[5,13,23,25-29] our project focused on addressing difficulty accessing alteplase and comfort with its reconstitution and administration in the inpatient setting. We attempted to resolve these barriers by increasing availability of alteplase on inpatient floors and providing education and technical training for faster delivery of systemic thrombolysis to frontline neurology residents. Previous studies have suggested targeting residents as a potential solution as residents spend

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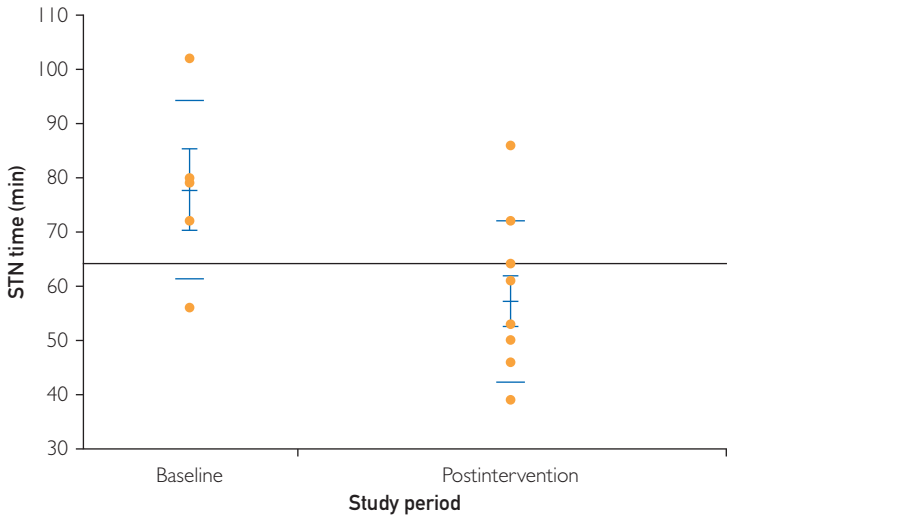


Means and SD

Level	Number	Mean	SD	SE Mean	Lower CI 95%	Upper CI 95%
Baseline	5	77.8	16.589153	7.4188948	57.201846	98.398154
Postintervention	10	57.4	14.953261	4.7286362	46.703082	68.096918

***t* test**

Postintervention-baseline
Assuming unequal variances

Difference	−20.400	*t* ratio	−2.31878
SE dif	8.798	*df*	7.369592
Upper CL dif	0.194	Prob>|*t*|	0.0517
Lower CL dif	−40.994	Prob>*t*	0.9742
Confidence	0.95	Prob<*t*	0.0258*

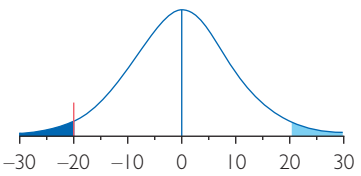


FIGURE 3. Stroke-alert-to-needle (STN) time to alteplase bolus, pre- vs postintervention periods. *Statistically significant. Dif = difference; Prob = probability.

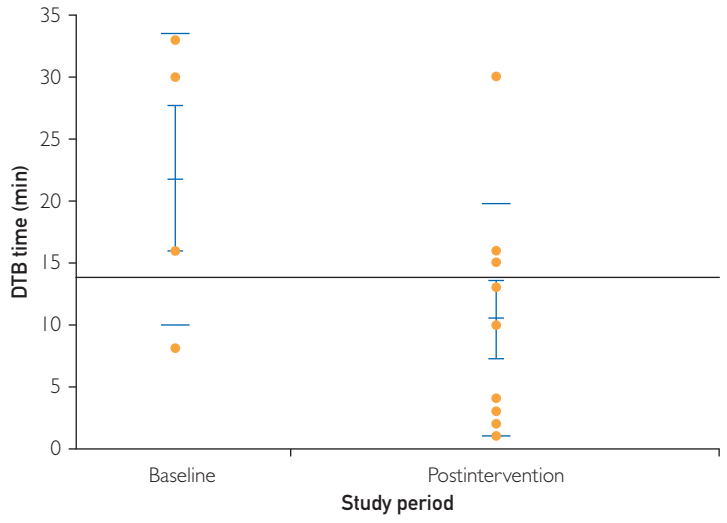
greater time on inpatient wards and play a key role in assessing patients and ensuring timely delivery of alteplase.[23] We believe this intervention to be an effective and generalizable approach to improving inpatient stroke care.

Education and increased availability of alteplase on inpatient units increased satisfaction among neurology residents, leading to more confidence in locating and reconstituting alteplase. As evidenced by the feedback we received, residents supported education workshops and appreciated the availability of simulation alteplase kits.

This intervention has no direct costs, is conducted over a 2-hour session annually, and is a low time burden on neurology residents. By training neurology residents to reconstitute alteplase at bedside, the burden is lessened on pharmacists, nurses, and other providers who may have duties elsewhere during an AIS emergency. The other prong of our intervention alleviated the burden on the ED and central pharmacy by stocking alteplase in AMDCs on additional inpatient units.

Limitations

This single-center study was limited by the small number of patients with AIS in an inpatient setting per year. In addition, preintervention data were obtained retrospectively. Nevertheless, our results are in line with previous studies that optimize inpatient stroke



Means and SD

Level	Number	Mean	SD	SE Mean	Lower CI 95%	Upper CI 95%
Baseline	4	21.75	11.786291	5.8931457	2.9953801	40.50462
Postintervention	9	10.444444	9.3422576	3.1140859	3.2633495	17.625539

***t* test**

Postintervention-baseline

Assuming unequal variances

Difference	−11.306	*t* ratio	−1.69617
SE dif	6.665	*df*	4.769845
Upper CL dif	6.080	Prob>|*t*|	0.1534
Lower CL dif	−28.691	Prob>*t*	0.9233
Confidence	0.95	Prob<*t*	0.0767

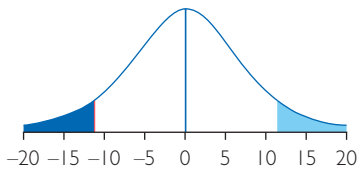


FIGURE 4. Decision-to-treat-to-alteplase bolus (DTB) time, pre- vs postintervention periods. Dif = difference; Prob = probability.

workflows. Many institutions identify similar barriers to the ones we address. Some of their strategies include emphasizing an interdisciplinary approach,[30] adapting stroke alert algorithms for the inpatient setting,[23,25] and incorporating pharmacists and dedicated nurses to the inpatient stroke team.[31-33] This study adds evidence that a similar intervention could be implemented at other hospitals to improve AIS metrics.

Our study identified a potential knowledge deficit, so we elected to use an education intervention. Education interventions have limitations that include deficiencies in content retention and lack of implementation due to habitual practice. To ensure that the neurology residents retained the education from the intervention, we scheduled an annual education workshop and encouraged practice with the alteplase simulation kits stocked in the resident workroom.

Our data also indicate delay from when the patient began experiencing symptoms to when a stroke alert was called. Further analysis revealed that the 3 longest delays in the postintervention period (Table 2) were associated with low initial NIHSS scores (3, 3, and 4; chronologically). These data suggest potential opportunities for our team to improve recognition of minor stroke symptoms.

Although baseline data did not reveal any particular pattern of inpatient unit that AIS

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events tended to present on, many patients in the postintervention period presented with AIS in the progressive care unit, located on the third floor, and the PCCU, located on the fourth floor of the hospital. However, the sample size is small and therefore limited in determining clinical significance.

Although there is suggestion that many patients with AIS in an inpatient setting are ineligible for thrombolysis, our results indicate that during the preintervention phase, 12.8% of inpatient stroke alerts who met eligibility criteria received alteplase and 10.6% of the same patient population received alteplase in the postintervention phase. The inpatient setting should not be a barrier to receiving timely thrombolysis in eligible patients. Despite our efforts, barriers still remain to achieving faster times to thrombolysis in inpatient AIS. These include IV access, travel time to the CT scanner, institutional protocols and policies, and nonneurological stroke team education. Future endeavors could target these barriers.

CONCLUSION

Patients experiencing an AIS in the inpatient setting are especially vulnerable and can have worse outcomes compared with their outpatient peers.[23] In the inpatient setting, the time from stroke alert to alteplase treatment may be reduced with targeted resident education, hands-on simulation, and increased availability of alteplase within the hospital. These interventions can subsequently reduce the overall time of brain tissue ischemia and improve patient outcomes.

Our intervention strategy was an interdisciplinary effort designed by representatives from every group that comprises the stroke team. As members of the stroke team, neurology residents are often frontline decision makers in stroke alerts. Continual resident education is therefore essential. As new residents are onboarded, annual education workshops provide an introduction to thrombolytic therapy as well as a refresher for senior residents on a continuous basis. It also makes this intervention more sustainable, as it can be updated annually. The stocking of alteplase on more inpatient units does not require additional logistical maintenance.

In the future, a similar training could be provided for other staff involved in the management of AIS. This interprofessional intervention is widely applicable and could promote better communication among team members, leading to improvements in quality care for inpatient AIS.

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Mr Pines, Ms Das, and Mr Bhatt contributed equally to this work.

Abbreviations and Acronyms: **AHA** = American Heart Association; **AIS** = acute ischemic stroke; **AMDC** = automated medication dispensing cabinet; **CT** = computerized tomography; **DTB** = decision-to-treat-to-bolus; **ED** = emergency department; **EMR** = electronic medical record; **IV** = intravenous; **NIHSS** = National Institutes of Health Stroke Scale; **PCCU** = progressive cardiac care unit; **RN** = registered nurse; **RRN** = rapid response nurse; **STN** = stroke-alert-to-needle

Potential Competing Interests: The authors report no competing interests.

Correspondence: Address to Andrew R. Pines, MA, Mayo Clinic Alix School of Medicine, Mayo Clinic, 5777 E Mayo Blvd, Phoenix, AZ 85054 (Pines.Andrew@mayo.edu; Twitter: @PinesAndrew).

ORCID

Andrew R. Pines: https://orcid.org/0000-0001-6968-2829; Shubhang K. Bhatt: https://orcid.org/0000-0002-7175-9861

REFERENCES

1. Benjamin EJ, Muntner P, Alonso A, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics—2019 Update: a report from the American Heart Association [published correction appears in *Circulation*. 2020;141(2):e33]. *Circulation*. 2019; 139(10):e56-e528.
2. Centers for Disease Control and Prevention (CDC). Prevalence and most common causes of disability among adults—United States, 2005. *MMWR Morb Mortal Wkly Rep*. 2009;58(16):421-426.
3. Aly N, McDonald K, Leathley M, Sharma A, Watkins C. Retrospective case note review of acute and inpatient stroke outcomes. *BMJ*. 2000;320(7248):1511-1512.
4. Farooq MU, Reeves MJ, Gargano J, Wehner S, Hickenbottom S, Majid A; Paul Coverdell National Acute Stroke Registry Michigan Prototype Investigators. In-hospital stroke in a statewide stroke registry. *Cerebrovasc Dis*. 2008;25(1-2):12-20.

5. Kimura K, Minematsu K, Yamaguchi T. Characteristics of in-hospital onset ischemic stroke. *Eur Neurol*. 2006;55(3):155-159.
6. Dulli D, Samaniego EA. Inpatient and community ischemic strokes in a university hospital. *Neuroepidemiology*. 2007;28(2):86-92.
7. Park HJ, Cho HJ, Kim Y-D, et al. Comparison of the characteristics for in-hospital and out-of-hospital ischaemic strokes. *Eur J Neurol*. 2009;16(5):582-588.
8. Nadav L, Gur AY, Korczyn AD, Bornstein NM. Stroke in hospitalized patients: are there special risk factors? *Cerebrovasc Dis*. 2002;13(2):127-131.
9. Masjuan J, Simal P, Fuentes B, et al. In-hospital stroke treated with intravenous tissue plasminogen activator. *Stroke*. 2008; 39(9):2614-2616.
10. Saltman AP, Silver FL, Fang J, Stamplecoski M, Kapral MK. Care and outcomes of patients with in-hospital stroke. *JAMA Neurol*. 2015;72(7):749-755.
11. Stecker MM, Michel K, Antaky K, Wolin A, Koyfman F. Characteristics of the stroke alert process in a general hospital. *Surg Neurol Int*. 2015;6:5.
12. Alberts MJ, Brass LM, Perry A, Webb D, Dawson DV. Evaluation times for patients with in-hospital strokes [published correction appears in *Stroke*. 1994;25(3):717]. *Stroke*. 1993; 24(12):1817-1822.
13. Schürmann K, Nikoubashman O, Falkenburger B, et al. Risk profile and treatment options of acute ischemic in-hospital stroke. *J Neurol*. 2016;263(3):550-557.
14. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333(24):1581-1587.
15. Hacke W, Donnan G, Fieschi C, et al; ATLANTIS Trials Investigators; ECASS Trials Investigators; NINDS rt-PA Study Group Investigators. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;363(9411):768-774.
16. Lansberg MG, Schrooten M, Bluhmki E, Thijs VN, Saver JL. Treatment time-specific number needed to treat estimates for tissue plasminogen activator therapy in acute stroke based on shifts over the entire range of the modified Rankin Scale. *Stroke*. 2009;40(6):2079-2084.
17. Khatri P, Abruzzo T, Yeatts SD, Nichols C, Broderick JP, Tomsick TA; IMS I and II Investigators. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. *Neurology*. 2009;73(13):1066-1072.
18. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association [published correction appears in *Stroke*. 2019; 50(12):e440-e441]. *Stroke*. 2019;50(12):e344-e418.
19. Jauch EC, Saver JL, Adams HP Jr, et al; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44(3):870-947.
20. Target Stroke℠ Honor Roll. Amercican Heart Association website. https://www.heart.org/en/professional/quality-improvement/target-stroke/target-stroke-honor-roll. Accessed July 15, 2020.
21. Cumbler E, Simpson J. Code stroke: multicenter experience with in-hospital stroke alerts. *J Hosp Med*. 2015;10(3):179-183.
22. Cumbler E, Murphy P, Jones WJ, Wald HL, Kutner JS, Smith DB. Quality of care for in-hospital stroke. *Stroke*. 2011;42(1):207-210.
23. Kassardjian CD, Willems JD, Skrabka K, et al. In-patient code stroke: a quality improvement strategy to overcome knowledge-to-action gaps in response time. *Stroke*. 2017; 48(8):2176-2183.
24. Del Brutto Victor, Ardelt Agnieszka, Loggini Andrea, et al. Clinical Characteristics and Emergent Therapeutic Interventions in Patients Evaluated through the In-hospital Stroke Alert Protocol. *Journal of Stroke and Cerebrovascular Diseases*. 2019;28(5): 1362-1370. https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.02.001.
25. Cumbler E, Zaemisch R, Graves A, Brega K, Jones W. Improving stroke alert response time: applying quality improvement methodology to the inpatient neurologic emergency. *J Hosp Med*. 2012;7(2):137-141.
26. Cumbler E, Anderson T, Neumann R, Jones WJ, Brega K. Stroke alert program improves recognition and evaluation time of in-hospital ischemic stroke. *J Stroke Cerebrovasc Dis*. 2010;19(6):494-496.
27. Yoo J, Song D, Baek J-H, et al. Comprehensive code stroke program to reduce reperfusion delay for in-hospital stroke patients. *Int J Stroke*. 2016;11(6):656-662.
28. Daly ML, Orto V, Wood CID. Stat: rapid response to in-hospital stroke patients. *Nurs Manage*. 2009;40(11):34-38.
29. Nolan S, Naylor G, Burns M. Code Gray—an organized approach to inpatient stroke. *Crit Care Nurs Q*. 2003;26(4): 296-302.
30. Van Schaik SM, Van der Veen B, Van den Berg-Vos RM, Weinstein HC, Bosboom WM. Achieving a door-to-needle time of 25 minutes in thrombolysis for acute ischemic stroke: a quality improvement project. *J Stroke Cerebrovasc Dis*. 2014; 23(10):2900-2906.
31. Tan BYQ, Ngiam NJH, Sunny S, et al. Improvement in door-to-needle time in patients with acute ischemic stroke via a simple stroke activation protocol. *J Stroke Cerebrovasc Dis*. 2018;27(6):1539-1545.
32. Lawrence E, Merbach D, Thorpe S, Llinas RH, Marsh EB. Streamlining the process for intravenous tissue plasminogen activator. *J Neurosci Nurs*. 2018;50(1):37-41.
33. Rech MA, Bennett S, Donahey E. Pharmacist participation in acute ischemic stroke decreases door-to-needle time to recombinant tissue plasminogen activator. *Ann Pharmacother*. 2017;51(12):1084-1089.