COMPARISON OF FUNCTIONAL OUTCOMES IN EARLY VERSUS DELAYED ADMINISTRATION OF ALTEPLASE FOR ACUTE ISCHEMIC STROKE IN THE EMERGENCY DEPARTMENT

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PURPOSE

To determine whether alteplase door-to-needle time (<45 minutes vs ≥45 minutes) influences a patient's functional status at hospital discharge

BACKGROUND

- Stroke is the fifth most common cause of death and a leading cause of disability in the United States
- Alteplase is an effective treatment for Acute Ischemic Stroke (AIS), however its utility is diminished when there is a delay in administration[1,2]
- Alteplase is a high-risk medication associated with intracranial hemorrhage
- Administration of alteplase within 4.5 hours has shown to correlate with improvement in in-hospital mortality and functional outcomes at hospital discharge[2-7]
- With this known benefit, there continues to be a need to identify the ideal administration window for optimization of patient outcomes[8,9]
- A previous study found a significant association between longer door-to-needle times (specifically > 45 minutes) and increased in-hospital mortality and readmission rates[8,10]
- Currently, the rapid administration of alteplase is the focus of many stroke centers, with a goal of < 45 minutes from hospital arrival
- Even though administration of alteplase within 45 minutes has shown mortality benefit in previous studies, it is unknown whether this earlier administration of alteplase is associated with an improvement in quality of life

METHODS

IRB-approved, single center, retrospective, cohort study

Inclusion Criteria

- ≥18 years old
- Received alteplase within 4.5 hours of symptom onset for AIS in the emergency department (ED)

Exclusion Criteria

- Pregnancy
- Prisoners
- mRS>2 at baseline
- Patients without documented mRS at discharge

A total of **200** patients who presented to Advocate Christ Medical Center ED between December 2018 – March 2022 were identified. This sample size is based on feasibility.

METHODS (CONT.)

Primary Endpoint:

- Patient functional status at the time of hospital discharge, measured by MRS

Secondary Endpoints:

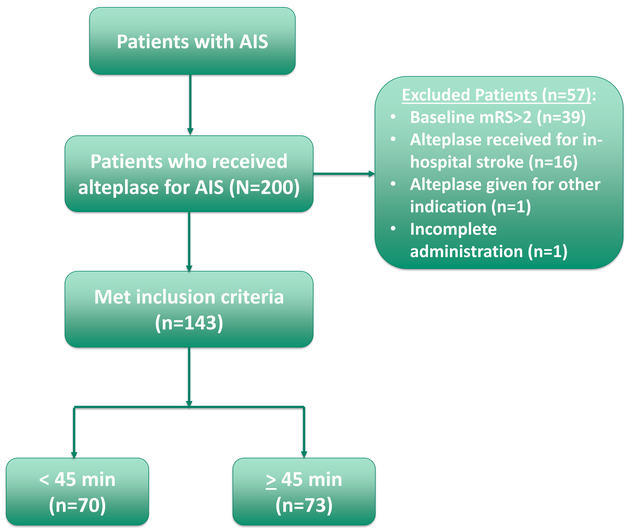
- **Barriers to early administration of alteplase:**
  - Unable to obtain medication history
  - Delay in neuroimaging
  - Unclear last known normal (LKN)
  - Delay in obtaining consent
  - Delay in receiving drug from pharmacy
  - Blood pressure (BP) control
- **Hospital Course:** ICU/hospital length of stay
- **Readmission:** stroke/cardiac-related event

Safety Endpoints:

- Any intracranial hemorrhage (ICH)
- Symptomatic ICH
- In-hospital mortality rate
- Alteplase administered for stroke mimic

RESULTS

Patient Enrollment

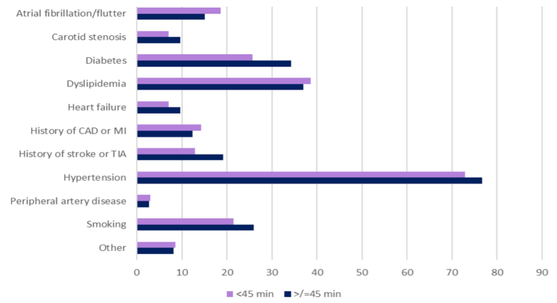


RESULTS (CONT.)

Baseline Characteristics

Demographics	<45 min	≥45 min	*p*-value
Males, *n(%)*	38 (54.3)	33 (45.2)	0.2776
Age (years), *median [IQR]*	66 [59-79]	63 [57-73]	0.2178
NIHSS, *median [IQR]*	7 [4-15]	7 [4-13.5]	0.5587
VAN positive, *n(%)*	37 (52.9)	43 (58.9)	0.7660
Baseline mRS:			**0.0449**
0, *n(%)*	54 (77.1)	64 (87.7)	
1, *n(%)*	11 (15.7)	9 (12.3)	
2, *n(%)*	5 (7.1)	0	
Onset-to-arrival (min), *median [IQR]*	42 [27-71]	49 [33-95]	0.0864
Door-to-needle (min), *median [IQR]*	35.5 [31-41]	63 [53-80]	**<0.0001**
Onset-to-needle (min), *median [IQR]*	79 [63-106]	119 [94-177]	**<0.0001**
Large vessel occlusion, *n(%)*	41 (58.6)	51 (69.9)	0.1588
Thrombectomy, *n(%)*	22 (31.4)	13 (17.8)	0.0583
EMS hospital arrival mode, *n(%)*	58 (82.9)	54 (74.0)	0.2486

Vascular Risk Factors



Primary Outcome

Outcome	<45 min	≥45 min	*p*-value
mRS at discharge:			0.9920
<2, *n(%)*	22 (31.4)	23 (31.5)	
≥2, *n(%)*	48 (68.6)	50 (68.5)	

Secondary Outcomes

Outcome	<45 min	≥45 min	*p*-value
ICU LOS (days), *median [IQR]*	2 [1-3]	2 [1-3]	0.7594
Hospital LOS (days), *median [IQR]*	4 [3-7]	4 [3-7]	0.3576
Death in hospital, *n(%)*	5 (7.1)	4 (5.5)	0.7416
Readmission for stroke/cardiac-related events within 90 days, *n(%)*	6 (8.6)	5 (6.9)	0.3720

RESULTS (CONT.)

Reasons for Alteplase Delay

Reason	<45 min	≥45 min	*p*-value
Obtaining medication history, *n(%)*	3 (4.3)	10 (13.7)	0.0503
Neuroimaging, *n(%)*	0	13 (17.8)	0.0001
Unclear LKN, *n(%)*	5 (7.1)	6 (8.2)	0.8092
Obtaining consent, *n(%)*	7 (10)	30 (41.1)	<0.0001
Receiving alteplase from pharmacy, *n(%)*	0	1 (1.4)	1.0000
Blood pressure control, *n(%)*	14 (20)	21 (28.8)	0.2229

Safety Outcomes

Outcome	<45 min	≥45 min	*p*-value
Any ICH within 36h, *n(%)*	15 (21.4)	7 (9.6)	**0.0498**
Symptomatic ICH, *n(%)*	6 (8.6)	2 (2.7)	0.1601
Need for alteplase reversal, *n(%)*	3 (4.3)	1 (1.4)	0.3593
Stroke mimic, *n(%)*	8 (11.4)	9 (12.3)	0.8679

CONCLUSIONS

- No difference in functional outcome comparing early versus delayed administration of alteplase
- Trend towards increased incidence of symptomatic ICH in early administration group, with statistically significant increase of any ICH
- Obtaining consent and neuroimaging were the biggest contributors for delayed alteplase administration

Limitations

- Retrospective chart review
- Single center study
- Feasibility study

Future Direction

- Continue data collection

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