Effect of emergent magnetic resonance imaging on alteplase utilization for acute ischemic stroke

Jonis Q. Munoz Pharm.D. Candidate, Dana M. Reyes Pharm.D. Candidate; Asad E. Patanwala, Pharm.D., M.P.H., BCPS., FCCP, FASHP
Banner – University Medical Center Tucson emergency department

Introduction

Background

- Acute ischemic stroke (AIS) is an acute occlusion of an intracranial vessel reducing blood flow to region of the brain it supplies. AIS claims an estimated 200,000 deaths in the United States and is the leading cause of disability among adults.[1]
- The American Heart Association/American Stroke Association (AHA/ASA) recommends the delivery of thrombolytic therapy within 60 minutes of arrival to the emergency department.
- To exclude hemorrhagic stroke, brain imaging is necessary in the process of thrombolytic delivery. Door-to-imaging (DIT) with computerized tomography (CT) or magnetic resonance imaging (MRI) are approved for AIS patients. Guidelines recommend DIT to occur within 25 minutes of hospital arrival, highlighting the importance of a protocol for the emergency evaluation of patients with suspected stroke.
- The time from hospital arrival to brain imaging is thought to be a main driver of door-to-needle (DTN) time. While there is improvement in DITs, the DTN for intravenous administration varies widely in the United States and remain suboptimal.[3]
- Banner-University Medical Center – Tucson (BUMC-T) is an academic and comprehensive hospital located in Tucson, AZ. BUMC-T's emergency department and it's sister campus, Banner-University Medical Center – South Campus, has a combined census of 135,000 patient visits per year.[4]

Importance

- Since early stroke treatment leads to better outcomes, door-to-needle time is recognized as an important quality indicator for the management of tPA.
- A head CT scan is required prior to tPA administration to exclude hemorrhagic stroke. At BUMC-T an MRI is conducted emergently to determine the need for neurological intervention in some circumstances.
- The purpose of this quality improvement project was to determine the extent to which emergent MRI affects tPA administration in the emergency department (ED) at BUMC-T.

Prior Research

- Yoo et al. (2010) compared MRI screening and MRI plus CT screening, showing patients with MRI had longer DTN times, but improved outcomes.
- Lees et al. (2010) completed a meta analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials showing reinforcing there is increase risk of hemorrhage and the net benefit was undetectable in their sample beyond 4.5 hours.
- Fieback et al. (2002) evaluated the value of using MRI as a routine procedure compared to CT to exclude cerebral hemorrhage for tPA. Researchers concluded with the same delay after onset of AIS resulted in significant differences in diagnostic accuracy. MRI was substantially more sensitive and accurate compared to CT even with limited experience interpreters.

Objectives

Primary Objective:

- To evaluate DTN times for the administration of tPA for patients who receive an emergent MRI for AIS. We hypothesized patients receiving an emergent MRI, will have a delay in treatment with tPA.

Secondary Objective:

- To determine if patients who receive an emergent MRI for AIS will have an interruption in tPA treatment. We hypothesized patients receiving emergent MRI screenings will have an interruption during tPA infusion, prolonging tPA infusion times.

Methods

- This was a retrospective cohort quality improvement project. Adult patients who received tPA at BUMC-T for AIS from January 2014 to January 2017 were included.
- A data collection form was created and used to extract information from patient charts. This included 3 items on demographics, 8 items on tPA use and dosing, 1 item on symptom onset, 1 item of ED admission, 5 items on utilization of CT, MRI, or interventional radiology (IR), 2 items on complication of tPA, and 2 items on scores of severity of stroke.
- Data was collected from electronic medical records at BUMC-T and entered into a secured online data collection tool, REDCap.
- The Wilcoxon Rank-Sum test was used to compare DTN times (in minutes of interquartile ranges) in patients who did or did not receive an emergent MRI. Descriptive data was analyzed using means and standard deviations.

Data

Variable (n=96)	Mean	SD
Age (years)	67	18
Weight (kg)	82	17
Alteplase dose given	72	13
	Mean	**Percent (%)**
Male	51	53
Female	45	47
	Number	**Percent (%)**
Patients with partial dose of alteplase (N=95)	8	8
Patients that received antihypertensive agent prior to alteplase infusion	9	9
Patients that received antihypertensive agent during alteplase infusion	7	7
Patients that received emergent interventional radiology	21	22
Number of patients with alteplase interrupted	13	14
Number of patients with reason for interruption, (N=13)		
MRI related	4	30
Blood pressure related	1	8
ADE from alteplase	6	47
Other	2	15
Number of patients with complications due to alteplase		
Intracranial hemorrhage	14	15
Death	9	9
	Median	**IQR**
NIHSS (prior to alteplase)	9	6-16
NIHSS (s/p alteplase)	2	0-6
Time from symptom onset to door	58	35-99
Time from door to computerized tomography (min)	10	4-16
Time from door to needle (min)	62	48-73
Duration of alteplase infusion (min)	61	60-63
Duration of alteplase infusion if interrupted (min)	61	36-71
		Range
Amount of alteplase wasted (mg)	14-32	

Results

Table 1. Summary of patients with and without interruption in infusion and with and without emergent MRI

	No emergent MRI	Emergent MRI	Totals
No interruption	74	9	83
Interruption	13	4	13
Totals	83	13	96

P-value: 0.073

Table 2. Summary of DTN times (minutes) in IQR ranges if patients did or did not receive an MRI

	N	25th percentile	50th percentile	75th percentile
No MRI	83	52 min	63 min	77 min
MRI	13	36 min	48 min	56 min
Total	96	48 min	62 min	73 min

P-value: 0.0061

- A total of 96 patients were included in this project, with an average age of 67 years years and an average weight of 82 kg. Dosing on average was 72 mg.
- Eight patients received a partial dose of tPA with 4 records of amount wasted. The recorded amount wasted ranged from 14 to 32 mg.
- The National Institutes of Health Stroke Scale (NIHSS) was evaluated in all but one patient prior to tPA administration. At the 50th percentile, these patient had a NIHSS of 9, and post administration NIHSS decreased to 2. This data however, was based on 86 patients, due to incomplete records due to death, transport to another hospital or other complication not related to tPA.
- Time to symptom onset at the 50th percentile was 59 minutes and time to ED admit to CT screening was 10 minutes.
- Median DTN was 62 minutes with a median infusion time of 61 minutes.
- Nine percent of patients received an antihypertensive agent prior to infusion, these were labetalol or nicardipine. Seven percent of patients required an antihypertensive agent during infusion.
- Fourteen percent of patients required an emergent MRI screening
- Twenty-two percent of patients received emergent IR.
- Thirteen patients had interruptions during tPA infusion.

Results

- The reasoning for interruptions were documented and placed in the following categories:
  1. MRI related
  2. Blood pressure related
  3. Adverse reactions related to tPA (eg, hematoma, headache, bleeding)
  4. Other
- Most of the interruptions were due to ADE. Two patients were documented under "other" due to a change in reported symptom onset, disqualifying the patient from receiving tPA per BUMC-T's protocol and a concern for sepsis with septic embolism and elevated risk of hemorrhage.
- For the patients with an interruption in infusion, duration was 36 minutes at the 25th percentile, 61 minutes at the 50th percentile, and 71 minutes at the 75th percentile.
- Complications due to tPA were intracranial hemorrhage and death occurring in 15% and 9% of patients, respectively.
- Four of the 13 patients (31%) with a documented tPA interruption had an emergent MRI, and 9 of 13 (61%) patients who did not have an emergent MRI, using Fisher's exact test (P>0.05). This proportion was not statistically significant.
- Patients utilizing MRI screening received tPA faster than patients who did not. This result was statistically significant using Wilcoxon Rank-Sum test.

Conclusion

Overall, emergent MRI did not delay the administration of tPA. MRI patients received tPA faster, which may be related to the characteristics of the patients. However, all preventable interruptions of tPA were related to emergent MRI (4 of 13 patients).

This quality improvement project suggests that a significant proportion of patients who require an emergent MRI may have errors during tPA administration and supports the need for pharmacists to follow the patient to MRI while being infused with thrombolytic therapy.

Limitations:

- Data are from one site resulting in a small sample of participants.
- Information collected was based on completeness and assumption of accuracy of the electronic health record

References

1. Smith WS, Johnston S, Hemphill J. Cerebrovascular Disease. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. eds. Harrison's Principles of Internal Medicine, 19e New York, NY: McGraw-Hill; 2014. http://accessmedicine.mhmedical.com.ezproxy2.library.arizona.edu/content.aspx?bookid=1130&sectionid=79766261. Accessed March 28, 2017.
2. American Heart Association/American Stroke Association. (2013). Guidelines for the early management of patients with acute ischemic stroke. Retrieved from http://stroke.ahajournals.org/content/strokeaha/44/3/870.full.pdf.
3. Ying Xian, Eric E. Smith, Xin Zhao, Eric D. Peterson, DaiWai M. Olson, Adrian F. Hernandez, Deepak L. Bhatt, Jeffrey L. Saver, Lee H. Schwamm, Gregg C. Fonarow. "Strategies used by Hospitals to improve Speed of Tissue-type Plasminogen Activator Treatment in Acute Ischemic Stroke." *Stroke* 45 (2014): 1387-1395. Web.
4. About Emergency Medicine. (n.d.). Retrieved November 10, 2017, from http://emergencymed.arizona.edu/about
5. Yoo, Sung-Hee, Sun U. Kwon, Deok-Hee Lee, Sang-Joon Kim, Jong S. Kim, and Dong-Wha Kang. "Comparison between MRI Screening and CT-plus-MRI Screening for Thrombolysis within 3h of Ischemic Stroke." *Journal of the Neurological Sciences* 294.1-2 (2010): 119-23. Web.
6. Lees KR, Bluhmki E, von Kummer R, Brott TG, Toni D, Grotta JC, Albers GW, Kaste M, Marler JR, Hamilton SA, Tilley BC, Davis SM, Donnan GA, Hacke W;ECASS, ATLANTIS, NINDS and EPITHET rt-PA Study Group, Allen K, Mau J, Meier D, del Zoppo G, De Silva DA, Butcher KS, Parsons MW, Barber PA, Levi C, Bladin C, Byrnes G. "Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials." *The Lancet* 375.9727 (2010): 1695-1703. Web.
7. Fiebach, J.b., P.d. Schellinger, O. Jansen, M. Meyer, P. Wilde, J. Bender, P. Schramm, E. Juttler, J. Oehler, M. Hartmann, S. Hahnel, M. Knauth, W. Hacke, and K. Sartor. "CT and Diffusion-Weighted MR Imaging in Randomized Order: Diffusion-Weighted Imaging Results in Higher Accuracy and Lower Interrater Variability in the Diagnosis of Hyperacute Ischemic Stroke." *Stroke* 33.9 (2002): 2206-210. Web.

For more information, please contact: Jonis Q. Munoz: jmunoz@pharmacy.arizona.edu; Dana M. Reyes: reyes@pharmacy.arizona.edu; and/or Asad E. Patanwala: patanwal@pharmacy.arizona.edu