I. REPORT CHECKLIST

The following checklist must be completed and submitted with the project report. By checking an item, *the student and advisor(s) agree that the work has been done appropriately*.

_N/A_1. If the research report will be or has been submitted for publication in a journal, provide the name of the journal here:

_____

__√__2. Project title is concise and clear; lists advisers, course no. & date submitted

__√__3. Abstract is no more than 250 words and retains headings

__√__4. Introduction provides a definition of the topic under study, the importance of the topic, and the issue addressed by the study and is no more than two (2) pages.

__√__5. There is NO literature review section

__√__6. Purpose(s) of project is clearly and concisely stated

__√__7. Methods section uses headings and represents a summary of the methods used. (Actual methods used should be described if they were modified from the proposal.)

__√__8. Data analysis described is appropriate and responds to the purpose.

__√__9. Appropriate tables are included in the results section.

__√__10. Text of results section interprets the findings reported in the tables, not repeating them.

__√__11. The discussion section includes a description of the most important findings, and relates findings to the literature.

__√__12. The final section of the discussion is the limitations section.

__√__13. The conclusions respond to the purpose statement.

__√__14. Reference list uses style from DI class (PhPr 861c) or is specific to journal.

__√__15. Data collection/recording form(s) and/or questionnaire(s)are included in the appendix.

__√__16. Information is placed in the appropriate section—introduction, methods, results, etc.

__√__17. Report does not exceed 15 pages excluding tables & figures & appendices.

Date report submitted: March 21, 2018
Student (1): Jonis Munoz
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Effect of emergent magnetic resonance imaging on alteplase utilization for acute ischemic stroke

Course title: PHPR 896B

Date: March 21, 2018

Faculty advisor: Asad E. Patanwala, PharmD, MPH, BCPS, FCCP, FASHP

Student(s): Jonis Q. Munoz and Dana M. Reyes

ABSTRACT

Objectives:

The purpose of this project was to assess appropriateness of alteplase (tPA) administration in patients undergoing magnetic resonance imaging (MRI) at Banner-University Medical Center Tucson (BUMC-T) and identify interruptions in therapy that could have been prevented.

Methods:

This descriptive quality improvement project evaluated retrospective data from the electronic health records at BUMC-T. Data was collected from patient charts using Epic. The data collection form included items based on demographics, tPA, symptoms and severity, utilization of computerized tomography, MRI, interventional radiology (IR), and complications. Wilcoxon Rank-sum test was used to compare the door-to-needle times if patients did or did not receive an MRI. Fisher's exact test was used to compare the proportion of patients with interruption of infusion with or without emergent MRI ($P<0.050$).

Main Results:

Ninety-six patients received tPA for acute ischemic stroke with 13 having an interruption in infusion. Reasons documented were placed into 4 categories: MRI related, blood pressure related, adverse reactions related to tPA, or other. Four of 13 interruptions were related to an emergent MRI. This was not statistically significant ($p>0.050$). The remainder were not preventable as tPA was discontinued because of an adverse event. Patients that received an MRI received tPA faster than those patients who did not receive an MRI (48 minutes versus 63 minutes, respectively) ($P=0.006$).

Conclusions:

Alteplase interruptions did not occur more frequently in patients who received MRI. However, all preventable interruptions were due to MRI. Alteplase administration logistics should be optimized to minimize any preventable interruptions in therapy.

INTRODUCTION

Acute ischemic stroke (AIS) is an acute occlusion of an intracranial vessel that causes reduction in blood flow to the brain region it supplies.[1] AIS claims an estimated 200,000 deaths in the United States and is the leading cause of disability among adults.[2] Intravenous thrombolytic treatment with alteplase, initiated within 3-4.5 hours after the onset of symptoms is the only medication therapy available for AIS. The American Heart Association/American Stroke Association (AHA/ASA) recommends the delivery of thrombolytic therapy within 60 minutes of arrival to the emergent department.[3] Since early stroke treatment leads to better clinical outcomes in earlier studies, time-to-treatment has been recognized as an important factor in achieving good clinical results after thrombolysis.[1,4]

To exclude hemorrhagic stroke, brain imaging is vital and the necessary first step in the process of tPA delivery. Door-to-imaging with computerized tomography (CT) screening or MRI are approved for AIS patients.[3] The time from hospital arrival to brain imaging is thought to be a main driver of door-to-needle (DTN) time. Benefits of intravenous tPA in AIS are time dependent, however the extent to which hospitals are using strategies to improve a more rapid DTN have not been well studied.[1] While there is improvement in door-to-imaging time (DIT), the DTN for intravenous administration varies widely in the United States and remain suboptimal.[1,4,5]

At BUMC-T a head CT scan is required prior to tPA administration to exclude hemorrhagic stroke. An MRI may be 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 an emergent MRI affects tPA administration in the emergency department at BUMC-T.

METHODS

Design This quality improvement project used a retrospective cohort design. This project was approved by Banner-University Medical Center Tucson.

Subjects Patients included in the study must have been 18 years or older and received alteplase for AIS at BUMC-T from January 2014 to January 2017. Patients that did not receive tPA or used tPA for indications other than AIS, like pulmonary embolism or myocardial infarction were excluded.

Measures A data collection form was created on REDCap which included the following items: 3 on demographics, 8 on tPA use and dosing, 1 on symptom onset, 1 on ED admission, 5 on utilization of computerized tomography, MRI, or interventional radiology, 2 on complications of tPA, 2 on scores of the severity of stroke, see appendices for data collection form. The dependent variables measured were the times of tPA infusion and the time the patient received the tPA from arrival to the ED.

Data collection A list of patients that used tPA during the inclusion period was provided by the advisor through a secured server through SharePoint. Data was collected from patient charts using the Epic electronic medical record system from BUMC-T. Patient names were de-identified by assigning a record number for each patient and then entered into a secured online data collection tool, REDCap.

Data analysis The Wilcoxon Rank-Sum test was used to compare median DTN times (in minutes of interquartile ranges) in patients who did or did not receive an emergent MRI. Fisher's exact test was used to analyze patients with and without interruption in infusion and with or without emergent MRI. Descriptive data such as National Institutes of Health Stroke Scale (NIHSS) scores pre-and post-TPA administration was analyzed using means and standard

deviations.

RESULTS

The summary of characteristics of the patients are shown in Table 1. A total of 96 patients were included in this project, 51 males and 45 females. The patients had an average age of 67 years ± 18 with an average weight 82 kg ± 17. The average amount of tPA dosed for each patient was 72 mg ± 13. Eight patients received a partial dose of tPA. From the 8 patients that received a partial dose, 4 of those patients had documentation on Epic of how much was wasted. The recorded amount wasted ranged from 14 to 31.7 mg.

The NIHSS score was evaluated for 95 patients prior to administration of tPA. At the 50th percentile, the patients had a score of 9. Status post tPA administration, NIHSS at the 50th percentile dramatically decreased to 2. However, this data was based off 86 patients, as not all patients had records of their score post tPA due to either death, transport to another hospital, or other complications not tPA related.

The median time from symptom onset was 59 minutes. The median time from emergency department (ED) admit to computerized tomography (CT) was 10 minutes. The median time from admit to the emergency department to tPA infusion was 61.5 minutes. The median duration of tPA infusion was 61 minutes.

Nine percent of patients received an antihypertensive agent prior to tPA infusion. These included labetalol or nicardipine. Seven percent of patients required an antihypertensive agent during infusion.

Fourteen percent of patients required an MRI scan, which was defined as having a recorded MRI time occurring before the documented tPA stop time in the electronic medical record on Epic.

Twenty-two percent of patients received emergent IR. Emergent IR was defined as having a recorded IR time within 6 hours from admit time to the ED. Of the 96 patients, 13 patients had their tPA infusions interrupted. From these patients, the reasons for interruption were documented and placed into the categories below:

1. MRI related
2. Blood pressure related
3. Adverse reactions related to tPA (eg, hematoma, headache, bleeding)
4. Other

Of the 13 patients, most of the interruptions were due to adverse effects from tPA (4%). These were reported as headache, hematoma, bleeding, and pain. The 2 patients categorized as "other" as an explanation for tPA interruption was due to a change of reported symptom onset, disqualifying the patient from receiving tPA per the institution's protocol, and the second patient was due to concern for sepsis with septic embolism and elevated risk of hemorrhage.

The duration of infusion for the patients experiencing interrupted tPA infusion was 36 minutes at 25th percentile, 61 minutes at 50th percentile, and 71 minutes at 75th percentile. The major differences in duration of infusion could be due to stopping the tPA because of ADE or discontinuing and then continuing the tPA infusion for an MRI.

Complications looked at using tPA for AIS were intracranial hemorrhage and death occurring in 15% and 9% of the patients, respectively.

Four of 13 patients who had a documented tPA interruption had an emergent MRI (31%) and 9 of 13 patients who had a documented tPA interruption did not have an emergent MRI (69%), (P >0.050) using Fisher's exact test. These proportions were not statistically significant.

Patients that received an MRI received tPA faster than those patients who did not receive an MRI. This result was statistically significant using Wilcoxon Rank-Sum (Mann-Whitney U) test.

DISCUSSION

The primary finding of this quality improvement project was emergent MRI did not affect alteplase infusion, as the results were not statistically significant. However, there were still four cases where there was an interruption due to infusion giving this project clinical significance.

Other findings of this quality improvement project were patients receiving an MRI received tPA faster than those who received a CT alone prior to infusion. Patients receiving an MRI received thrombolytic therapy 15 minutes faster at the 50th percentile. This result was similar compared to a study by Yoo et al. that showed faster DTN times with patients receiving an MRI than those with an MRI and a CT. We concluded that our patients receiving an MRI may have had more severe symptoms leading to rapid decision making by the medical team.

There were several limitations to this quality improvement project. First, this project only looked at a single site which resulted in a small sample of participants. Therefore, they are not generalizable to other institutions. The information collected was based on completeness and assumption of accuracy of the electronic health record. Thus, some of the data was not able to be extracted from the charts. Further studies looking into the involvement of a pharmacist could be

beneficial to see how the presence or absence of a pharmacist could affect time-to-treatment and preventable interruptions.

CONCLUSIONS

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 there are preventable tPA administration interruptions when MRI is utilized. Institutions should evaluate processes to minimize the potential for drug interruption when such imaging is used during drug infusion.

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Table 1. Summary Statistics

Variable	Mean	Standard deviation
Age (years)	67	18
Weight (kg)	82	17
Dose	72	13
	Mean	Percent (%)
Sex (male)	51	53
Sex (female)	45	47
	Number	Percent (%)
Patients with partial dose of alteplase (N=95)	8	8
Patients that received antihypertensive agent prior to alteplase infusion, N=96	9	9
Patients that received antihypertensive agent during alteplase infusion, N=96	7	7
Patients that received emergent interventional radiology, N=96	21	22
Number of patients with alteplase interrupted, N=96	13	14
Number of patients with reason for interruption, N=13		
MRI related	4	30
Blood pressure related	1	7.7
ADE from alteplase	6	46.2
Other	2	15.4
Number of patients with complications due to alteplase, N=96		
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	34.5-98.5
Time from door to computerized tomography (min)	10	4-16
Time from door to needle (min)	61.5	48-72.5
Duration of alteplase infusion (min)	61	60-62.5
Duration of alteplase infusion if interrupted (min)	61	36-71
	Range	
Amount of alteplase wasted (mg)	14-31.7	

Table 2. 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 3. Summary of door to needle times (min) in interquartile ranges if patient did or did not receive an MRI for Wilcoxon Ran-Sum (Mann-Whitney U) test

	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	61.5	72.5

Z=2.742

Prob > |z| =0.006

APPENDICES

Confidential

Alteplase

Record ID _____

Included/Excluded
- ◯ Included
- ◯ Excluded - Used for cardiac arrest or PE
- ◯ Excluded - Other (describe reason below)

Excluded Reason _____

Age (years) _____

Sex
- ◯ Male
- ◯ Female

Race
- ◯ White
- ◯ Hispanic
- ◯ Black
- ◯ Other

Alteplase Dose (mg) _____
(Total dose in mg (includes bolus and infusion))

Weight (kg) _____
(Weight used for dosing)

NIHSS _____
(NIH Stroke Scale Prior to TPA)

NIHSS Discharge _____
(NIH Stroke Scale (last recorded prior to hospital discharge))

Time of Symptom Onset _____
(I some cases the exact time is not recorded, so use best guess)

Time of ED Admission _____

Time of Head CT _____

Time of TPA Start _____

Time of TPA Stop _____

TPA Interrupted Documented
- ◯ Yes
- ◯ No

TPA Interrupted Reason _____

TPA Partial Dose Given
- ◯ Yes
- ◯ No

(Usually Due to Waste From Line)

TPA Amount Wasted (mg) _____
(TPA 1ml = 1mg)

BP Med Used Prior to TPA
- ◯ Yes
- ◯ No

(labetolol, nicardipine, etc for BP control in ED)