



Brief Report

Pharmacoeconomic impact of an alternative workflow process for stroke

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ABSTRACT

Objective: The objective of this study was to evaluate a new multidisciplinary process in which intravenous alteplase (tPA) waste, used for acute ischemic stroke (AIS), was salvaged in an attempt to maximize cost effectiveness without impacting door-to-needle (DTN) administration times.

Design: This was a retrospective cohort between May 2017 and February 2018. The primary endpoint evaluated for this study was the total tPA salvaged and total cost savings in U.S. dollars. Secondary endpoints evaluated included overall DTN time in minutes.

Setting: Emergency department of a primary stroke center.

Patients: A convenience sample of sequential adult (>18 years) patients who received tPA in the ED for AIS were included for analysis.

Interventions: New stroke process which involved bedside mixing of tPA and salvaging of excess waste in the main central pharmacy.

Measurements and main results: A total of 50 patients were included in the final analysis. There were 25 patients included in the new process and old process groups respectively. A total of 605 mg of alteplase was salvaged from 25 patients in the new process group which was associated with an estimated cost savings of over \$120,000 annually. Patients in the new process group had statistically faster average (52 min vs. 60 min; $p = 0.01$) and median (50 min vs. 58 min; $p = 0.03$) DTN administration times.

Conclusion: Preliminary data, in this pilot study, utilizing a multidisciplinary model for tPA administration led to significant cost savings of tPA and decreases in overall DTN administration times.

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1. Background

Delays in the administration of alteplase (tPA) and its overall cost burden remain a central focus of institutions across the country [1]. While recent interest has centered around comprehensive stroke centers, primary stroke centers still comprise a large fraction of stroke care delivered in the U.S which may not have the budget or resources of a comprehensive center [2]. The current benchmark for door to needle (DTN) administration time of tPA is ≤ 60 min for $\geq 50\%$ of acute ischemic stroke (AIS) patients [3]. Prolonged administration times are associated with worsen neurological outcomes, therefore focuses of stroke centers have evaluated ways in which to reduce DTN times [1,3]. Previous studies have shown the ability to reduce DTN administration times utilizing various different strategies [4–7]. In an effort to reduce DTN times, many facilities have implemented processes that utilize 100 mg vials prepared at the bedside, however this practice often results in a significant amount of drug waste.

The drug cost of tPA has more than doubled over the past decade according to Centers for Medicare and Medicaid Services (CMS) data [8]. A CMS payment amount for 1 mg of tPA in 2005 was \$30.50 compared to > \$64 per 1 mg in 2015. In 2006, tPA amounted to roughly 27% of the diagnosis-related group (DRG) associated payment to hospitals for AIS compared to 53% in 2013 [8]. The DRG associated reimbursement for AIS to institutions has not increased enough to account for inflation of tPA cost to institutions, therefore it becomes valuable to maximize efficiency of its use. The American Heart Association/American Stroke Association 2018 guidelines recommend the utilization of a multidisciplinary stroke team in the management of patients with AIS (LOE 1-B) [3]. The purpose of this pilot study was to measure a multidisciplinary teams approach to improve tPA utilization without negatively effecting DTN time.

2. Methods

This was a retrospective cohort study at a primary stroke center emergency department (ED) between May 2017 and February 2018. The previous ED AIS algorithm (old process) had the main centralized pharmacy prepare the entire tPA dose and hand delivered to the nurse

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for administration. Fig. 1 describes the multidisciplinary approach (new process), implemented in October 2017, which utilizes bedside mixing of tPA and also salvaging waste in the main centralized pharmacy.

The first syringe mixed bedside, which included the initial bolus and the first portion of the infusion, was prepared by ED nursing staff using the entirety of a 50 mg vial (dose permitting) and was used to begin timely administration to the patient. The amount needed to complete the patient's remaining infusion dose, was prepared from a second 50 mg vial into a second syringe by the main pharmacy and the excess tPA salvaged into 1 mg/mL aliquots and frozen. Per USP 797 guidelines,

these aliquots are useable for up to 45 days [9]. The majority of the salvaged tPA was utilized for catheter clearance. Using a 60 mL syringe 50 mL of sterile water was drawn up then used to reconstitute 50 mg of tPA. Once the dilution was prepared within the 60 mL syringe, the dose was then verified by two nurses independently and placed onto a syringe pump. The bolus dose (i.e. – 10% of the total target dose) was administered over 1 min and the subsequent infusion dose was initiated using the remaining volume within the first syringe. The second syringe, also verified by two nurses independently, would begin to infuse immediately after the first syringe completed. The infusion dose

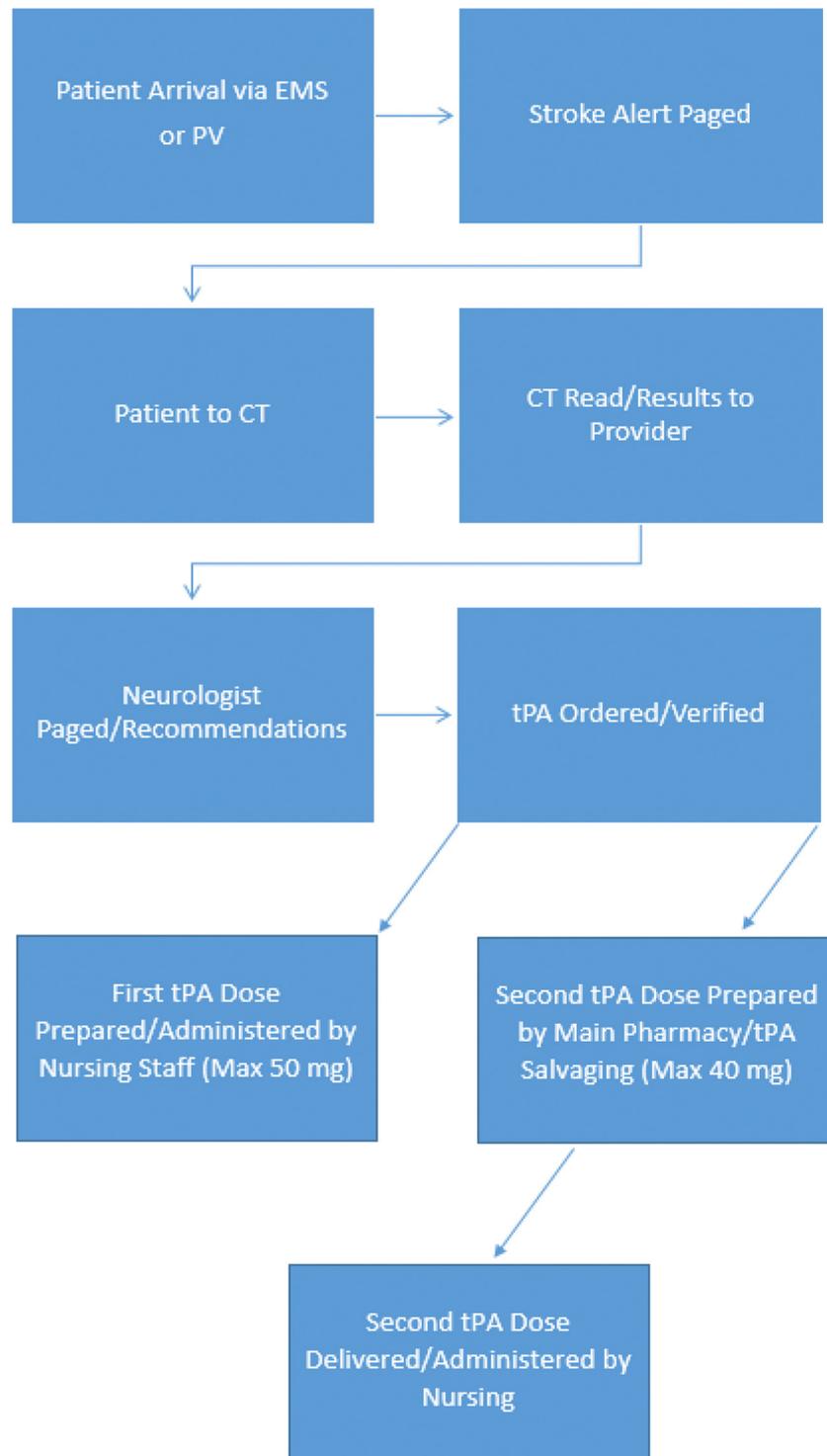


Fig. 1. Multidisciplinary process.

for each syringe was set to a rate based on the volume to be completed in 1 h.

The primary endpoint evaluated for this study was the total tPA salvaged and total cost savings in U.S. dollars. Secondary endpoints evaluated included overall DTN time in minutes. With respect to cost savings, CMS reported data as of April 1, 2018; tPA had a reimbursement rate of \$84.58 per 1 mg [10].

Patients were included if they were >18 years old and received tPA for AIS in the ED. Patients were excluded if they received tPA outside of the ED, or those who received tPA for a diagnosis other than AIS. Patients evaluated from October 2017 to February 2018 were included in the new process group with patients prior to October 2017 being included in the old process group. Factors believed to influence DTN administration times were evaluated in an attempt to limit confounders. The electronic medical records (EMR) of patients who received tPA in the ED were reviewed for age, sex, arrival time, tPA administration times, tPA dose, initial National Institute of Health Stroke Scale (NIH) score, whether the patient was on anti-platelet or anticoagulation medication prior to arrival, and whether the patient had an arrival via EMS.

Categorical variables were summarized using counts and analyzed using either Chi-square or Fisher exact *t*-tests. Continuous variables were summarized using means or medians + standard deviations and analyzed with either a Student *t*-test or Wilcoxon rank sum test. This study was approved by the institutional review board.

3. Results

The electronic medical record (EMR) of 140 patients was evaluated with 50 being included in the final analysis. Table 1 describes the baseline characteristics, which appeared similar. There were 25 patients included in the new process and old process groups respectively. A total of 605 mg of alteplase was salvaged from 25 patients in the new process group which was associated with \$51,170.90 in cost savings during the 5 month new process study period (estimated over \$120,000 annually). Of the 25 patients that were included in the new process, 24.2% of tPA was salvaged based off a 2500 mg total if 100 mg vials of tPA had been utilized.

Patients in the new process group had statistically faster average (52 min vs. 60 min; $p = 0.01$) and median (50 min vs. 58 min; $p = 0.03$) DTN administration times. There was no difference found between the median times of door to CT time or CT to tPA order time. However, there was a statistically significant difference between the

timeframe of tPA order to administration which we contribute to the bedside availability of tPA. There was no difference in the percentage of patients who had a goal DTN ≤ 60 min between either group (80% vs. 64%; $p = 0.21$). The old process group's percentage of patients receiving tPA within the goal time was consistent with previous years institutional data. Of the 25 patients in the new process group there were no delays between administration of the first and second doses noted within the EMR.

4. Discussion

Large focuses of stroke centers have been on the reduction of overall DTN times using processes that are not cost effective. Different strategies have included the creation of a code stroke team, reductions in door to CT times, and bed side mixing of tPA among the few [4–10]. However, to our knowledge this is the first study that has evaluated not only DTN times but also cost effective utilization of tPA for AIS. This pilot study showed that the new process implemented at a primary stroke center was associated with large cost savings and associated decreases in DTN administration times. The average and median DTN times of 59 and 50 min in the new process group are consistent with previously reported DTN times [4,8]. Other studies have reported median DTN as low as 25 min, however there has been no reported data to suggest that patients who receive tPA within 30 min is superior to those who receive it within 60 min [5–7,9,10]. Approaches utilized by previous studies that decrease DTN do not allow for salvaging of tPA and would be associated with significantly increased cost burden at most institutions.

While bedside mixing of tPA to reduce DTN time is not a new concept, this is the first, to the authors knowledge, of utilizing the 50 mg vials instead of 100 mg and salvaging the waste. It is important to note this process was not implemented as a way to reduce DTN times, but rather as a way to utilize tPA in a more cost effective process which would not affect DTN times in a negative way. Currently, at our institution, the cost of tPA is based on the \$84.58/mg value, therefore two 50 mg vials of tPA is equal to one 100 mg vial (i.e. no increased associated cost with utilizing two 50 mg vials vs. one 100 mg vial).

Some strengths of this study include the inclusive patient population, which we believe is representative of those evaluated for AIS in EDs across the country. The DTN administration times are consistent with previously reported data. The results of this study are suggestive that a multidisciplinary team and aspects of this new protocol could be implemented in many institutions who would like to either reduce DTN times, reduce cost burden, or both.

This study has some inherent limitations beyond its retrospective design. While the sample size is not robust, it does deliver a large enough sample size to warrant further investigation in a larger trial. This pilot study only enrolled patients within the ED and does not address those who may receive tPA within other hospital units. Estimated cost savings may differ by each institution as it pertains to tPA dosing weights and utilization of salvaged tPA. Also, the study only evaluates the impact of the pharmacoeconomic impact of drug utilization and does not take into account the cost associated with having to process, prepare, and handling of the second tPA syringe/salvaged tPA. Lastly, due to the variability of emergency departments throughout the country this data may not be generalizable to all institutions, however the multidisciplinary approach, which is guideline recommended, could be tailored to each institution.

5. Conclusion

Preliminary data, in this pilot study, utilizing a multidisciplinary model for tPA administration led to significant cost savings of tPA and decreases in overall DTN administration times. The utilization of bedside mixing with the ability to salvaging tPA could potentially lead to significant decreases in cost burden and DTN times in stroke centers.

Table 1
Baseline characteristics.*

Variable	Old Process; n = 25	New Process; n = 25	p Value
Average Age; years (range)	64 (38–87)	67 (35–91)	0.62
Males; n (%)	7 (46.6)	14 (56)	0.97
Average tPA Dose in mg (range)	74.4 (55–90)	73.8 (55–90)	0.35
Average Initial NIHSS (range)	6 (2–11)	5 (0–28)	0.29
EMS Arrival; n (%)	16 (64)	20 (80)	0.21
Administration of tPA in CT; n (%)	0	1 (4)	0.99
History of Stroke; n (%)	6 (24)	7 (28)	0.75
History of Diabetes; n (%)	8 (32)	6 (24)	0.53
History of TIA; n (%)	3 (12)	4 (16)	0.68
History of Hypertension; n (%)	21 (84)	16 (64)	0.11
History of HLD; n (%)	17 (68)	12 (48)	0.15
History of Atrial Fibrillation; n (%)	7 (28)	5 (20)	0.51
Outpatient Anti-coagulation/Anti-platelet Use; n (%)	12 (48)	13 (52)	0.78
Patients Receiving tPA within 3 h of Symptoms Onset; n (%)	22 (86.7)	23 (92)	0.64
Median Door to CT; mins	8	6	0.53
Median CT to tPA Order; mins	25	25	0.98
Median tPA Order to Administration; mins	22	12	0.04

* NIHSS; national institute of health stroke scale, CT; computed tomography, TIA; transient ischemic attack, MI; myocardial infarction, HLD; hyperlipidemia.

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None.

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