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Tenecteplase implementation for ischemic stroke at a large tertiary medical center

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Background

Early recognition of acute ischemic stroke (AIS) is critical as brain tissue is rapidly lost as a stroke progresses. It is also critical to determine quickly if the stroke is ischemic or hemorrhagic. A CT scan should be performed within 20 minutes of arrival to determine if thrombolytic therapy can be given. The immediate goal of stroke management is to restore the blood flow to the ischemic areas of the brain to obtain neurological recovery.

Guideline Recommendations:

- It may be reasonable to choose Tenecteplase (TNKase) single IV bolus 0.25 mg/kg (max 25 mg) over IV alteplase (tPA) in patients without contraindications for IV fibrinolysis who are also eligible for mechanical thrombectomy.
- TNKase administered at 0.4mg/kg single IV bolus has not been proven to be superior or non-inferior to IV alteplase but might be considered as an alternative in patients with minor neurological impairment and no major intracranial occlusion.

Previous Trials:

ATTEST Trial: Phase 2 prospective randomized open label trial

- TNKase 0.25mg/kg vs tPA 0.9 mg/kg
- Outcomes: penumbral salvage, early neurological recovery and incidence of intracranial hemorrhage
- Results: No difference between treatment groups

NOR-TEST Trial: Phase 3 randomized open label superiority trial

- TNKase 0.4 mg/kg versus standard dose tPA
- Outcomes: neurological improvement and intracranial hemorrhage and death within 3 months
- Results: TNKase was not superior to tPA with similar safety

EXTEND-IA TNK Trial: Prospective randomized open label trial

- TNKase 0.25 mg/kg versus standard dose tPA
- Outcomes: reperfusion, intracranial hemorrhage and functional outcomes
- Results: TNKase resulted in higher incidence of reperfusion and similar incidence of intracranial hemorrhage

Objectives

Primary outcomes

- Door to needle time with TNKase versus tPA in patients with acute ischemic stroke

Secondary outcomes

- Time from medication order to medication delivery to MD or RN
- Safety outcome is rate of symptomatic intracranial hemorrhage within 36 hours
- Cost savings with TNKase versus tPA

Methods

Study design

- Ambi-directional chart review (pre-post TNKase implementation)
 - Pre-implementation: January 1, 2021- August 17, 2021
 - Post-implementation: August 18, 2021-March 31, 2022

Inclusion criteria

- Patients with acute ischemic stroke presenting < 4.5 hours from symptom onset treated with thrombolytic therapy

Exclusion criteria

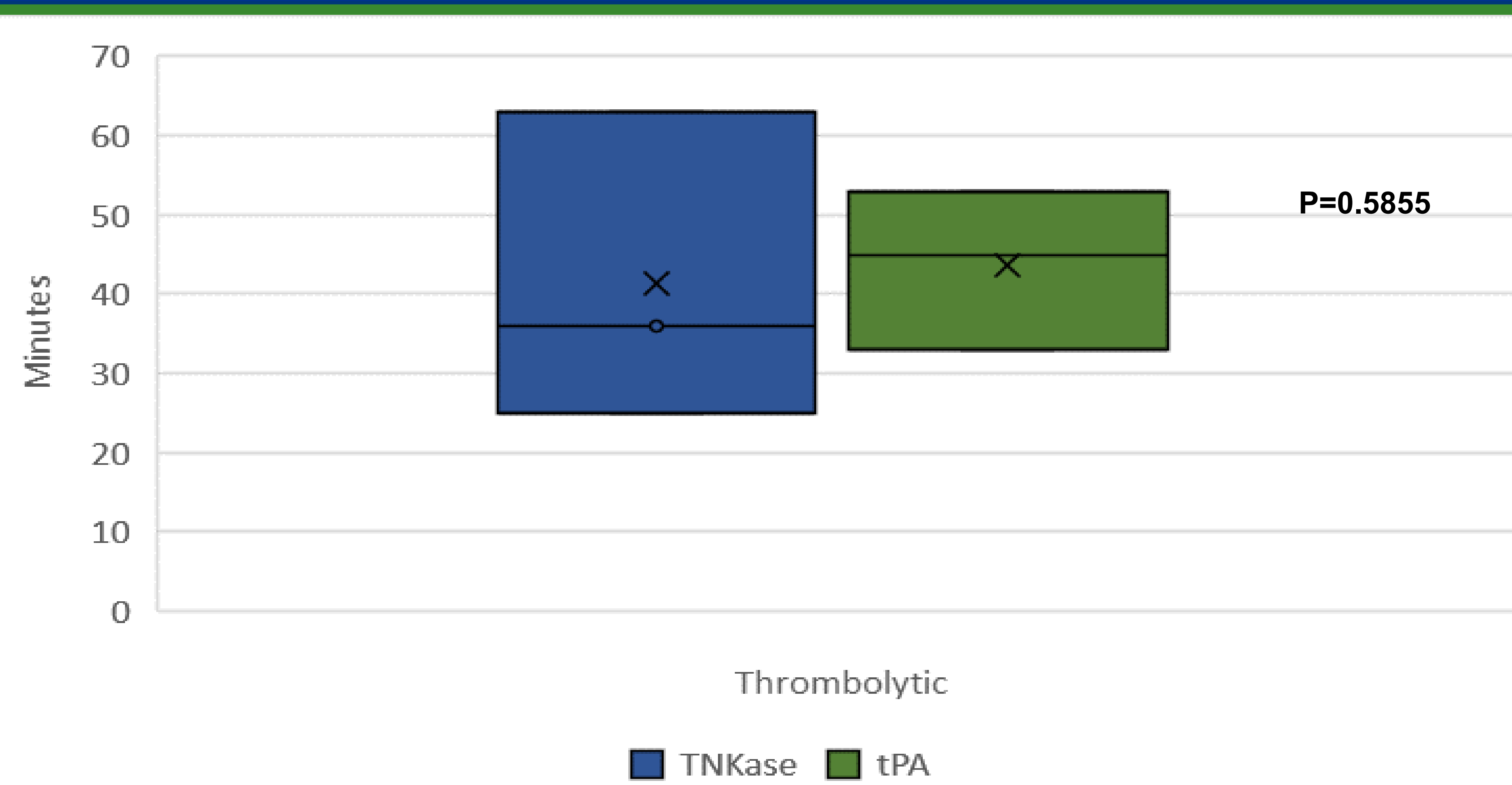
- Hemorrhagic stroke confirmed by CT scan
- Presentation > 4.5 hours from symptom onset
- Patients who undergo thrombectomy prior to thrombolytics
- Patients already admitted to the hospital at time of stroke
- Pre-stroke alert > 15 minutes after patient arrival to ED
- Door to CT time > 45 minutes if no pre-stroke given
- Documentation of a patient related reason for delay (hemodynamic instability, prolonged consent discussion, waiting for lab results, extra time needed to rule out concomitant condition)

Results

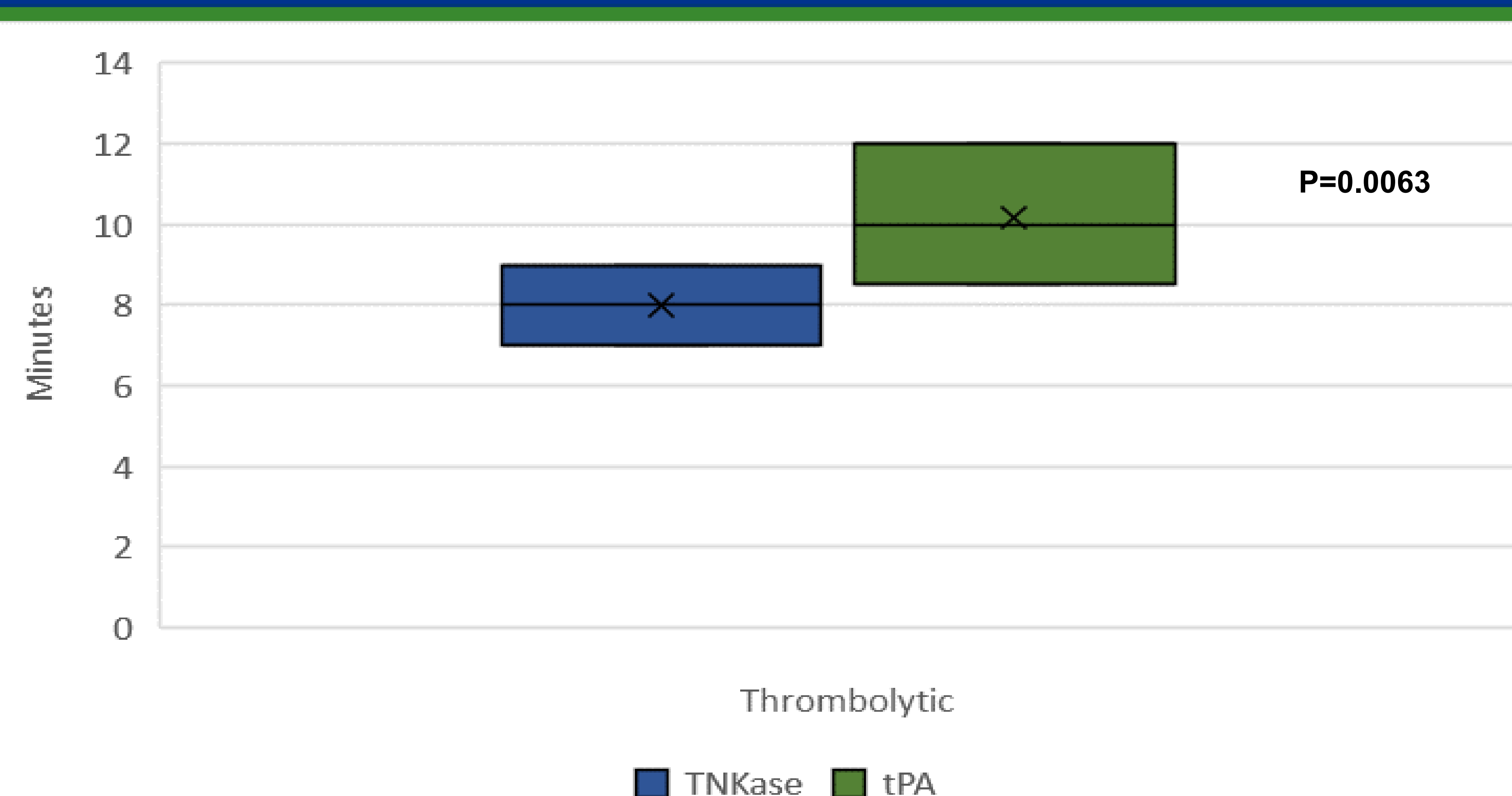
Data Summary

	Alteplase (N=20)	TNKase (N=15)	p-value
Age, mean (sd)	68 (17)	69 (15)	0.9140
Male, n (%)	10 (50%)	9 (60%)	0.5567
Patient Arrival mode, n (%)			0.4301*
EMS	17 (85%)	11 (73%)	
Walk-In	3 (15%)	4 (27%)	
Order to Delivery (min), med (q1, q3)	10 (8.5, 12)	8 (7, 9)	0.0063
Door to Needle (min), med (q1, q3)	45 (33, 53)	36 (25, 63)	0.5855
Symptomatic Intracranial Hemorrhage	0/53 (0%)	1/49 (2%)	

Door to Needle Time



Order to MD/RN Delivery Time



Cost Analysis

	tPA 100 mg Vial	tPA 50 mg Vial	TNKase 50 mg vial
N	49	4	49
WAC Cost	\$8,000	\$4,000	\$6,000
Total WAC Cost	\$392,000	\$12,000	\$294,000
Cost Savings	21% or 1,622.64 per patient and 159,018.72 based on typical annual volume		

- All costs are +/- 10%
- WAC= Wholesaler acquisition cost

Discussion

Patient Population

- A total of 103 patients were assessed for eligibility and 35 patients were included in the final analysis. (TNKase N=15, tPA N=20)
- All patients were included in the cost analysis. (N=103)
- Average age and sex were similar between groups

Study Objectives

- Median door to needle time in patients receiving tPA was 45 minutes compared to 36 minutes in patients receiving TNKase. There was no significant difference seen in door to needle time between groups. p=0.5855
- Median order to delivery time in patients receiving tPA was 10 minutes compared to 8 minutes in patients receiving TNKase. Use of TNKase significantly reduced order to delivery time by an average of 2 minutes. (p=0.0063)
- No difference was seen in occurrence of symptomatic ICH between the TNKase and tPA groups. No occurrences were documented among included patients for either group. (Of note, one patient who received TNKase did develop ICH but was excluded based on reason for therapeutic delay.)
- The average cost of a 50 mg vial of TNKase is \$6,000 compared to the average cost of a 100 mg vial of tPA which is \$8,000. (This pricing analysis is prior to any 340b price adjustments)
- The total cost spent on tPA from January 17, 2021-August 17, 2021 was \$404,000. While the total cost spent on TNKase for AIS from August 18, 2021 to March 31, 2022 was \$294,000. This reflects a cost savings amounting to \$159,018.72 annually based on typical volume for this hospital (98 patients pre-pandemic).

Limitations

- Many patients had to be excluded due to appropriate clinical delays in therapy, therefore sample size looking at door to needle and order to delivery times was small.
- Given recent switch to TNKase for AIS at this hospital, we were only able to assess ~6 months of data for each group.
- Ambi-directional chart review and not a randomized trial.

Conclusion

- Implementation of TNKase for AIS at this large tertiary medical center has resulted in shorter order to delivery times, a trend towards shorter door to needle times not reaching statistical significance, and a cost savings of 21%.
- Staff report greater satisfaction using TNKase because of simpler administration using a single 5 second bolus compared to bolus followed by a one-hour infusion when using tPA.
- More studies are needed to further assess impact of TNKase workflow on door to needle times and patient outcomes at 90 days with larger sample sizes.
- It would also be beneficial to look at this data from the entire health system versus one medical center within the system.

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