Three Easily-Implementable Changes Reduce Median Door-To-Needle Time for Intravenous Thrombolysis by 23 Minutes

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Abstract

Background:The benefit of intravenous thrombolysis (IVT) for acute ischemic stroke (AIS) is time dependent. Despite great effort, the median door-to-needle time (DNT) was 60 minutes at the U.S. stroke centers. We investigated the effect of a simple quality improvement initiative on DNT for IVT. Methods: This is a single-center study of patients treated with IVT between 2013 and 2017. A simple quality improvement initiative was implemented in January 2015 to allow the Stroke team to manage hypertension in the emergency room, to make decision for IVT before getting blood test results unless patients were taking oral anticoagulants, and to give IV tPA in the CT suite. Baseline characteristics, DNT and outcomes at hospital discharge were compared between pre- and post-intervention groups. Results: Ninety and 136 patients were treated with IVT in pre- and post-intervention groups, respectively. The rate of IVT was significantly higher in the post-intervention group (20% vs. 14.4%, p=0.007).The median DNT with interquartile range (IQR) was reduced significantly by 23 minutes (63[53-81] versus 40[29-53],p<0.001) with more patients in the post-intervention group receiving IVT within 60 minutes (81.6% versus 46.7%) and 45 minutes (64.0% versus 17.8%). There was no significant difference in symptomatic intracerebral hemorrhage rate (1.5% vs 1.1%), functional independence at discharge (mRS 0-1, 29.4% vs 23.3), and hospital mortality (7.4% vs 6.7%) between the 2 groups. Conclusions:Three easily-implementable quality improvement initiative increases IVT rate and reduces DNT significantly. It is safe and can be easily adopted at other stroke centers.

Introduction

Intravenous thrombolysis (IVT) with tissue-type plasminogen activator (tPA) is the proven medical therapy for acute ischemic stroke (AIS), with faster administration resulting in better outcomes.[1,2] However, the diagnosis and treatment of AIS are often delayed for various reasons, including lack of pre-notification, unclear last-known-well (LKW) time, waiting for blood test results, lag in getting CT scan and reports of imaging findings, holdup in mixing tPA or transportation between emergency room (ER) and CT scan suite, management of uncontrolled hypertension, performing CT angiography and CT perfusion, and determination of eligibility.[3-10]

Researchers at Helsinki University Central Hospital in Finland were able to implement measures to reduce delays and cut the median door-to-needle time (DNT) to 20 minutes with interquartile range (IQR) 14-32 minutes.[4] The Helsinki protocol was successfully replicated at the Royal Melbourne Hospital to reduce DNT to 25 (IQR, 19-48) minutes during business hours (8AM to 5PM Monday-Friday) in 2012.[5] A few hospitals in Canada and Netherlands were also able to reduce median DNT to 25-37 minutes.[6-8]

In contrast, the quality improvement endeavors have not worked out very well in the United States. Despite the launch of American Heart Association (AHA)/American Stroke Association (ASA) Target: Stroke initiatives in 2010 and comprehensive stroke center (CSC) certification by the Joint Commission in 2012,[9-10] the IVT rate and median DNT at the U.S. stroke centers remains suboptimal. A study of AIS patients registered in *Get With The Guidelines*-Stroke from October 2012 to April 2015 showed that the median DNT was 60 minutes with only 50% patients treated within 60 minutes.[11] The Target: Stroke phase II was launched in April 2014. The median DNT from 888 surveyed hospitals between June 2014 and April 2015 was still 56 (IQR, 42-75) minutes.[12] In a recent study comparing stroke care and outcomes between comprehensive stroke centers (CSCs) and primary stroke

centers (PSCs) in the U.S. from 2013 to 2015, the median DNT was 52 (IQR, 39-70) minutes at CSCs and 60 (IQR, 47-83) minutes at PSCs.[13] The IVT rates were only 10.4% and 9.2%, respectively.

It appears that centralized hospital system in developed countries were able to implement quality improvement initiatives efficiently.[4-8] The healthcare system is decentralized with numerous community hospitals in the U.S., with average annual IV tPA volumes at 40 and 22 at CSCs and PSCs, respectively.[13] Due to low annual volumes and labor-intensive code stroke protocols, the stroke centers in the U.S., including academic medical centers and community hospitals, appear to have significant logistic restraints in implementing comprehensive quality improvement initiatives 24/7.[10,12,13]

We decided to focus on 3 easily-implementable changes in January 2015 to improve stroke care at our CSC. This study aimed to explore the effect and safety of this simple initiative.

Methods

Patients and design

This is a single-center study approved by the University of California Irvine Institutional Review Board, and written informed consent was waived. Consecutive patients with AIS receiving IV tPA at the University of California Irvine Comprehensive Stroke Center between January 2013 and December 2017 were included. A simple quality improvement protocol was developed in January 2015 to allow the stroke team to 1) manage hypertension in the ER, 2) make decision for IVT before getting blood test results (complete blood count, comprehensive metabolic panel, cardiac enzymes and coagulation) unless patients were taking anticoagulants, and 3) give IV tPA in the CT suite. The patients were divided into pre-intervention (January 2013 to December 2014) and post-intervention (January 2016 to December 2017) groups, with one-year washout period (January 2015 to December 2015) allowing for the full implementation of the initiative.

The following information was collected and compared between the pre- and post- intervention groups: age, gender, past medical history (hypertension, diabetes, hyperlipidemia), National Institutes of Health Stroke Scale (NIHSS) score at admission, DNT, symptomatic intracranial hemorrhage (sICH), in-hospital mortality, and modified Rankin Scale (mRS) at hospital discharge. sICH was defined as intraparenchymal hematoma, subarachnoid hemorrhage, or intraventricular hemorrhage associated with a worsening of the NIHSS score by $\geq$ 4 points within 24 h.[2] A mRS score 0-1 at discharge was defined as functional independence.

Statistical analysis

Continuous variables were described by mean ± standard deviation (SD) or median with interquartile range (IQR) based on the results of normality testing. Categorical variables were expressed by counts with percentages. Baseline characteristics and outcomes at discharge were compared between pre- and post-intervention groups by t test or Wilcoxon rank-sum test for continuous variables and $\chi 2$ test for categorical variables. The proportions of sICH, functional independence (mRS 0-1), poor outcome (mRS 5-6), and in-hospital mortality were further compared between the 2 groups using multivariate logistic regression analysis after adjusting for age, hypertension, diabetes, hyperlipidemia and baseline NIHSS score. Analyses were performed using SPSS software (version 23.0). A 2-tailed value of $P<0.05$ was considered statistically significant.

Results

A total of 1305 patients with AIS were admitted to our medical center during the study period and 294 of them received IV tPA. After excluding 68 patients treated during the transitional year of the quality improvement initiative, there were 90 patients in pre-intervention group (from January 2013 to December 2014) and 136 in post-intervention group (from January 2016 to December 2017). The demographics and treatment benchmarks of the 2 groups are shown in Table 1. Compared with pre-intervention group, significantly more patients were treated with IVT in the post-intervention group (20.2% versus 14.4%, p=0.07). There was no difference in patient age, gender, history of hypertension or diabetes between the 2 groups. The post-interventional group had significantly higher rate of hyperlipidemia and lower NIHSS scores at admission than pre-intervention group. The patients with minor stroke (NISSS £ 4) appeared to be more likely to receive IVT in the post-intervention group (27.2% versus 10%, p<0.001).

The median DNT time was reduced by 23 minutes from 63 (IQR, 53-81) minutes in the pre-intervention group to 40 (IQR, 29-53) minutes in the post-intervention group (p<0.001). In addition, significantly more patients in the post-intervention group received IV tPA within 60 minutes (81.6% versus 46.7%, p<0.001) and 45 minutes (64% versus 17.8%, p<0.001) than in the pre-intervention group. Of note, there was no significant difference in DNT between patients with minor (NIHSS £ 4) and major (NIHSS > 4) stroke (median 50, IQR 25-75 vs median 50, IQR 36-71; P = 0.317).

The rates of sICH and functional outcomes at hospital discharge are summarized in Table 2. There was no significant difference in the rates of sICH (1.5% vs 1.1%), functional independence (mRS 0-1, 29.4% vs 23.3), and hospital mortality (7.4% vs 6.7%) between the 2 groups. There was a trend of better functional outcome (more patients with mRS 0-1 and significantly less patients with mRS 5-6) in the post-intervention group (Table 2 and Figure 1). However, in the multi-variate regression models, there was insignificant difference between the 2 groups after adjusting for age, hypertension, hyperlipidemia, diabetes and NIHSS score at admission.

Discussion

With a simple and easily-implementable quality improvement initiative, we have increase IVT rate from 14.4% to 20% and reduced median DNT by 23 minutes to 40 minutes. Our results are better than recently reported benchmarks of 14.3% IVT rate and 52 minute DTN at the 134 CSCs in the U.S.[13]

Despite significant improvement, our results are still suboptimal compared with the benchmarks from centralized Hospital Systems in other developed countries.[4-8] For example, the hospital district of Helsinki and Uusimaa has a population of 1.6 million and a centralized regional emergency medical service (EMS).[4,14] All patients deemed as candidates for stroke therapies are transported with high priority and pre-notification to the Helsinki University Hospital, which is the only 24/7 neurology service to provide care for AIS. As a high volume and centralized Stroke center, the Helsinki University Hospital was very efficient due to thorough training for all EMS and ED staff, and long-standing experience.[4,14]

In contrast, our CSC, the only academic medical center in Orange County, California, is one of the 9 stroke receiving centers serving a population of 3.19 million.[15] In such decentralized healthcare system, it is very

challenging for all of the 9 stroke receiving centers to implement comprehensive protocols to achieve the fastest DNT for IVT.[4-10,13]

Our quality improvement initiative is easily-implementable, effective and safe. Uncontrolled hypertension is one of the most frequently reported factors causing delayed DNT.[5,8,16] In a single center study, uncontrolled hypertension was associated with more than 30 mins delay in DNT.[16] Per AHA/ASA guidelines, IV tPA should be held until blood pressure (BP) is less than 185/110 mmHg.[1] In the pre-intervention group, severe hypertension was managed by the ER physicians. During post-intervention period, stroke team was managing hypertension in the CT suite and ED without any delay as soon as patient was deemed to be eligible for IVT. This simple change effectively minimized hypertension-related delay for IVT.

Waiting for blood testing results is another common reason for delay up to 60 minutes in some eligible patients.[5,17] Previous studies reported extremely low rates of unidentified coagulopathies and thrombocytopenia that would have been a contraindication for IV tPA.[17-19] Therefore, we implemented the initiative for tPA administration without waiting for blood test results unless patients were taking anticoagulants or had history of severe thrombocytopenia. There was no significant difference in the rate of sICH between pre-intervention and post-intervention groups. No patient suffered sICH from IVT due to undiagnosed coagulopathy. In addition, the rates of sICH in our cohort were much lower than reported in clinical trials,[2] confirming the safety of our simple initiative.

Another change we made in practice in January 2015 was to give IV tPA in the CT suite. As CT imaging is an indispensable diagnostic tool for decision-making for IVT, shortening the CT imaging-to-needle time may significantly improve DNT.[4,5,20,21] Our data confirmed that giving tPA in the CT suite minimizes the delay from CT to needle time without significant risk of complications.

Of note, the initial NIHSS scores in the post-intervention group was significantly lower with more patients with non-disabling stroke (NIHSS £ 4) than in the pre-intervention group. There were numerous possibilities. Previous studies showed longer DNT in patients with minor stroke, possibly because of higher chance of atypical symptoms, misdiagnosis and delayed neurology notification.[22,23] The reduced DNT in the post-intervention group appeared to have helped some patients with minor strokes to receive IVT.

The strength of our study is the use of 3 easily-implementable changes to reduce DNT without additional infrastructure cost or undue burden on the stroke team and ED staff. This simple initiative is effective, safe and easily replicable at other CSCs and PSCs in the U.S. and other countries.

This study has some limitations. First, it is a single center retrospective study. We used pre-intervention period as historic control. Our post-intervention data could be affected by unmeasurable confounding factors and gradual improvement in stroke care due to better training and experience. Second, although we had a one-year transition period for full implementation of the 3 changes, there might be incomplete adherence during the post-intervention period. Since incomplete adherence to the changes would likely lead to prolonged DNT, it is possible that the simple changes could work better if the initiative was applied all the time effectively. Third, we have not addressed other hurdles in delaying DNT, such as point of care coagulation testing for patients taking anticoagulants, moving directly from the EMS stretcher to CT scanner.[4,7,14] Additional easily-implementable changes at decentralized healthcare system may significantly reduce DNT at CSCs and PSCs in the U.S..

Conclusions

We demonstrated that three easily-implementable changes increase IVT rate and reduce DNT for IV tPA significantly at our CSC. These changes are very safe with very low sICH rate and can be adopted at other stroke centers without any additional cost.

Abbreviations

AHA: American Heart Association; AIS: acute ischemic stroke; ASA: American Stroke Association; CSC: comprehensive stroke center: DNT: door-to-needle time; EMS: emergency medical service; ER: emergency room; IQR: interquartile range; IVT: intravenous thrombolysis; LKW: last-known-well; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; PSC: primary stroke center; SD: standard deviation; sICH: symptomatic intracranial hemorrhage; tPA: tissue-type plasminogen activator

Declarations

Funding

Not applicable.

Availability of data and materials

The data will be available from the corresponding author on reasonable request.

Authors' contribution

DT, ZZ: study design, data acquisition, analysis, interpretation, and drafting the manuscript.

MS, HA: data interpretation and critical revision.

DS: data acquisition.

WY: study concept, design, data analysis, interpretation, and manuscript revision.

Ethics approval and consent to participate

This study was approved by University of California Irvine Institutional Review Board, and informed consents were waived due to minimal risk of harm to the patients.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

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Tables

Table 1. Demographics and clinical features of patients in the pre-intervention and post-intervention groups

Variables	Pre-intervention	Post-intervention	OR (95% CI)	P value
IV tPA, n (%)	90 (14.4)	136 (20.0)	1.49 (1.11-1.20)	0.007
Age, mean ± SD	70 ± 16	71 ± 17	-	0.745
Male	44 (48.9)	68 (50.0)	1.04 (0.61-1.78)	0.870
Hypertension	62 (68.9)	107 (78.7)	1.67 (0.91-3.06)	0.097
Diabetes	22 (24.4)	46 (33.8)	1.58 (0.87-2.87)	0.132
hyperlipidemia	29 (32.2)	62 (45.6)	1.76 (1.01-3.07)	0.045
NIHSS, median (IQR)	14 (8-21)	7 (4-16)	-	<0.001
NIHSS £ 4	9 (10)	37 (27.2)	3.36 (1.53-7.38)	0.002
DTN time, median (IQR)	63 (53-81)	40 (29-53)	-	<0.001
DTN time < 60 min	42 (46.7%)	111 (81.6%)	5.08 (2.79-9.26)	<0.001
DTN time < 45 min	16 (17.8%)	87 (64.0%)	8.20 (4.31-15.3)	<0.001

Table 2. Outcomes in the pre- and post-intervention groups at discharge

Outcomes	Patients receiving tPA		OR	*P* value	Adjusted OR	*P* value*
	Pre-intervention (n=90)	Post-intervention (n=136)	(95% CI)		(95% CI)*	
sICH	1 (1.1)	2 (1.5)	1.33 (0.12-14.87)	0.817	1.15 (0.11-12.39)	0.911
mRS 0-1	21 (23.3)	40 (29.4)	1.37 (0.74-2.53)	0.314	1.01 (0.50-2.04)	0.983
mRS 5-6	39 (43.3)	34 (25.0)	0.44 (0.25-0.77)	0.004	0.53 (0.27-1.05)	0.068
mortality	6 (6.7)	10 (7.4)	1.11 (0.39-3.17)	0.844	1.33 (0.44-4.03)	0.619

***Adjusted for age, hypertension, diabetes, hyperlipidemia and baseline NIHSS.

sICH: symptomatic intracranial hemorrhage

Figures

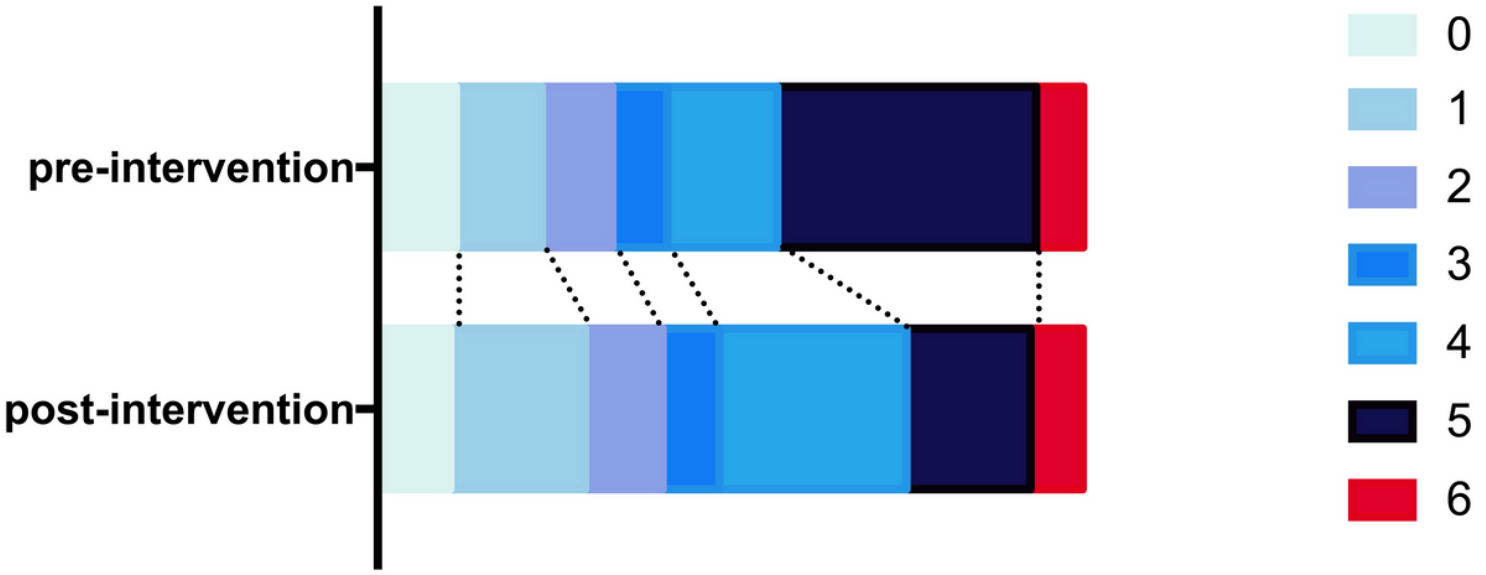

Figure 1

mRS at discharge in pre- and post- intervention groups (unadjusted P=0.054, adjusted P*=0.067)