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Door to needle time and functional outcome for mild ischemic stroke over telestroke

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Abstract

Introduction: Faster intravenous alteplase (tPA) administration from time of symptom onset is associated with better functional outcome. Lack of recognition of mild ischemic stroke (MIS) might result in delay in treatment with tPA. We hypothesise that patients with MIS have a longer door to needle (DTN) time when compared to patients with severe stroke symptoms.

Methods: Data on all patients who received tPA at spoke hospitals through the Medical University of South Carolina (MUSC) telestroke network were analysed. Collected data included baseline characteristics, stroke severity on presentation measured by the National Institute of Health Stroke Scale (NIHSS), the rate of symptomatic intracerebral haemorrhage, discharge location, and discharge functional outcome measured by the modified Rankin scale.

Results and Discussion: Of the 454 patients treated with tPA through the MUSC telestroke network in the period from January 2013 to April 2017, 98 (22%) had MIS defined as NIHSS $\leqslant 5$ on presentation; the remaining 356 (78%) patients were found to have severe stroke defined as NIHSS > 5 on presentation. Patients presenting with MIS were found to have a delay in receiving intravenous tPA by $\sim$10 min ($p = 0.007$) and approximately 15% of them had poor functional outcome at discharge. Patients with a MIS on presentation have significantly more prolonged DTN time. Nearly 15% of low severity strokes had poor outcome even after receiving tPA.

Keywords

Ischemic stroke, telestroke, telemedicine, alteplase, teleneurology, emergency care

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Introduction

Administration of alteplase (tPA) has been shown to reduce long-term disability in patients with acute ischemic stroke within 4.5 h of symptom onset.[1,2] The benefit of tPA is time dependent, and previous studies have shown that faster tPA administration time is associated with better long-term functional outcome and lower rate of complications,[3–6] leading to the current guidelines recommendations of door to needle (DTN) time of less than 60 min of patient arrival to the hospital.[7–9] However, studies have shown that less than 30% of patients are treated within this time window.[10,11]

The implementation of tele stroke programs allows patients living in rural areas, who otherwise may have to travel significant distances to seek stroke expert opinion, to be immediately evaluated by a stroke expert through this network.[12,13] However, barriers remain for rural patients as DTN time has been reported to be longer than for patients who go directly to a primary stroke center.[13–15] Among the main reasons for delay in DTN is the inability of patients and healthcare providers to recognise stroke symptoms, as well as delay in presentation to a stroke center.[16]

Previous studies have shown that patients with mild ischemic stroke (MIS) have substantial disability rates at hospital discharge.[17] In this study, we aim to evaluate DTN over telestroke for patients with mild stroke symptoms in comparison to patients with severe symptoms. We also aim to evaluate the discharge location, and functional outcome for patients with MIS on presentation.

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Methods

The Institutional Review Board of Medical University of South Carolina (MUSC) approved the study (approval number 00008381). The overall design, clinical and operational outcomes of the MUSC telestroke program have been described previously.[12,13,18] In brief, the MUSC telestroke program was established in 2008 to provide expert stroke care to patients in rural South Carolina. The number of participating sites covered by the MUSC telestroke network has increased from 6 sites in 2008 to 26 sites in April 2017.

Data source

MUSC telestroke network works in a hub (MUSC main hospital – the comprehensive stroke center) and spoke (primary stroke center) paradigm. The MUSC hub maintains a registry of all patients evaluated within the telestroke consultation network. The registry includes information on patient characteristics (age, race, sex) and process measures such as DTN times. In 2013, the hub began collecting patient stroke severity measured by the National Institute of Health Stroke Scale (NIHSS) on admission and on discharge, as well as symptomatic intracerebral hemorrhage rate (sICH). sICH was defined as Parenchymal Hemorrhage 2 (PH2) as defined by European Cooperative Acute Stroke Study (ECAS) III criteria.[3]

Our primary outcome of interest was patient DTN time in minutes at the spoke hospital. The primary explanatory variable is the patient's stroke severity. We classified patients across two categories of stroke severity. Patients with a severe stroke were coded as 1 and those with a MIS were coded as 0.

Statistical analysis

Descriptive statistics were used to describe patient demographic and clinical characteristics. We compared the differences between mild and severe stroke severity groups using t-tests. Chi-square was used to analyse categorical variables. To examine the relationship between stroke severity and our outcome of interest we estimated a generalised linear regression model using gamma distribution and a log link, adjusting for patient sex, age, race (white/non-white), and receipt of a thrombectomy. Analysis was conducted in Stata 14.2.

Results

Between January 2013 and April 2017, a total of 9960 telestroke consults were performed. The majority of the consultations were not eligible for tPA. A total of 8832 patients were excluded due to a diagnosis other than stroke, being out of window for tPA or having a contraindication to tPA. Due to lack of reliable discharge NIHSS data, telestroke patients who did not transfer to the hub were excluded as well (674 patients). Our final sample included 454 patients that received tPA via the telestroke program at the spoke hospital and were transferred to MUSC for further management.

Most patients in this study experienced a severe stroke (78%) (Table 1). Patients in the severe stroke group were older (66.9 versus 63.02 years, $p = 0.0248$) and had a higher percentage of non-whites (43.54% versus 29.59%, $p = 0.0021$) compared to the MIS group. One patient in the MIS group experienced symptomatic intracerebral hemorrhage compared to 15 patients in the severe symptom group ($p = 0.13$). Four of the MIS patients received thrombectomy in addition to tPA. A higher percentage of patients in the MIS group were discharged home compared to the severe symptom group (84 (85.7%) versus 178 (50%), $p = <0.0001$). Mean DTN for both groups was 65.2 min. Mean DTN in the MIS group was 73.3 min versus 63 min in the high NIHSS group ($p = 0.0021$).

For patients with a severe stroke, the predicted DTN time was 9.9 min shorter than for MIS, adjusting for sex, age, race, thrombectomy and year ($p = 0.007$) (Table 2).

Discussion

Our study shows that patients presenting with MIS symptoms experience a significant delay in receiving tPA. While most patients with MIS were discharged home, nearly 15% of patients presenting with MIS were discharged to rehab or had poor discharge functional outcome.

Few previous studies have evaluated functional outcome for patients with MIS treated with tPA.[5,17] A study by Romano et al. reported treatment complications and short-term outcome in patients with MIS who have received tPA.[17] This latter study evaluated 33,995 patients who received tPA within a 4.5-h window; of those, 22.4% had NIHSS of $\leqslant 5$. The authors found that, despite tPA administration, approximately 30% of these patients were unable to return home or ambulate interpedently at discharge.[17] Our findings are consistent with these study findings; additionally, our study evaluates DTN between the two groups, which has not been evaluated in prior studies.

Previous studies evaluated the impact of stroke location, race, and age on DTN times.[19,20] A study by Sarraj et al. evaluated door to needle times in patients with anterior circulation stroke to those with posterior circulation stroke.[19] This latter study showed that posterior circulation stroke is associated with a delay in diagnosis and therefore delayed tPA treatment. Another study by Moore et al. evaluated the presence of disparities in DTN times by age, race and gender.[20] The authors found no disparities in DTN time for age, race and gender. Our study is the first to evaluate DTN in patients with MIS and compare it to those with severe strokes.

In our study, patients presenting with MIS had approximately 10 min delay in tPA administration. The clinical significance of this delay has been evaluated in prior studies.[4] A study by Saver et al. evaluated the degree to which onset to treatment time influences outcome.[4] A total of 58,353 patients treated with tPA were

Table 1. Baseline characteristics.

	Mild ischemic stroke ($n = 98$)	Severe stroke ($n = 356$)	Total ($n = 454$)	p-value
Mean age (SD)	63.02 (15.6)	66.9 (15.01)	66.07	0.0248
Sex n (%)				
Female	47 (47.96)	195 (55)	242	0.231
Male	51 (52.04)	161 (45)	212	
Race n (%)				0.013
White	69 (70.41)	201 (56)	270 (59.47)	
Non-white	29 (29.59)	155 (44)	184 (40.53)	
Mean DTN time in minutes (SD)	73.3 (31.46)	63 (28.83)	65.2	0.0021
Mean admission NIHSS (SD)	3.7 (1.37)	14.4 (6.13)	12.1	0.0001
sICH	1 (1.03)	15 (4.25)		0.13
Mean discharge NIHSS (SD)	1.7 (3.01)	7 (8.56)	5.9	0.0001
Discharge mRS $\geqslant 3$ n(%)[a]	14 (14.3)	173 (48.6)	187 (43.9)	0.0001
Discharge location n(%)				0.0001
Death	0	9 (2.5)	9 (2)	
Rehab	13 (13.3)	107 (30.1)	120 (26.4)	
Home	84 (85.7)	178 (50.0)	262 (57.7)	
Hospice	0	23 (6.5)	23 (5.1)	
Nursing	1 (1.0)	24 (6.7)	25 (5.5)	
Other	0	9 (2.5)	9 (2)	

[a]Smaller n due to missing values

NIHSS: National Institute of Health Stroke Scale; DTN Door to needle time; MIS Mild ischemic stroke, mRS modified Rankin scale.

Table 2. Logistic regression.

Variable	Estimate	SE	p-value	95% CI	
Severe stroke	–9.9	3.7	0.007	–17.14	–2.66
Female	4.99	2.77	0.071	–0.42	10.42
Age	–0.09	0.09	0.337	–0.27	0.09
Race					
White	–4.86	2.93	0.097	–10.6	0.87
Thrombectomy	–8.33	3.51	0.018	–15.23	–1.44
Year	–4.05	1.18	0.001	–6.36	–1.74

enrolled in this latter study. The authors found that, for every 100 patients treated with tPA, with every 10 min delay in the start of rtPA within a 4.5-h window, 1.2 fewer patients had better ambulation at discharge. Additionally, the study showed that for every 15 min acceleration in start of tPA after onset was associated with patients having a 4% greater odds of walking independently at discharge.[4]

There are a few possible explanations for the delay in DTN in this group of patients. One of the most important factors determining DTN time is stroke recognition; previous studies have shown diagnostic accuracy of emergency physicians of acute ischemic stroke varies widely from 22% to 69%.[21–24] We hypothesise that severe strokes are more easily recognised than MIS, which could explain our finding of a faster DTN times in patients with higher NIHSS on presentation. Another possible explanation is the misconception that the MIS is a benign entity. Previous studies have shown that patients suffering from acute ischemic stroke commonly present with MIS, and that treatment with intravenous tPA or mechanical thrombectomy are often withheld as these patients are felt to be too well to treat.[25–28] A study by Willey et al. showed that almost one-third of patients presenting within 3 h of symptoms onset had 'too good to treat' listed as the only reason for not receiving thrombolysis.[29] At discharge, 5.5% of these patients were discharged with NIHSS > 4.[29]

The wisdom of this approach has been questioned in recent studies. A study recently published by Ali et al. examines the baseline clinical and imaging predictors of poor outcome in patients deemed to 'be too good to treat' with intravenous thrombolysis.[3] Approximately one-third of those patients not treated with tPA were unable to be discharged directly to home, suggesting that many of these patients deteriorate over time and eventually require significant rehabilitation.[30] The number of patients in our study that had poor functional outcome is lower than that reported in the study by Ali et al., possibly because those patients received tPA. We hypothesise that poor outcome in patients with MIS despite receiving tPA may be related to prolonged DTN time.

Our study has some limitations; the main limitation is the retrospective nature of the study as we were unable to

randomise patients into telestroke treatment or into different stroke severity categories. Another limitation is the fact that we did not include patients who did not transfer to the comprehensive stroke center in our analysis. In addition, there is the potential for miscalculation of NIHSS given the differences in competency in evaluating stroke patients across health care providers involved in the telehealth program. However, this limitation is less likely to affect the results given the reliability of NIHSS even for non-neurologist providers.[31]

Conclusions

Telestroke is a feasible way to provide tPA to patients living in rural areas. Through the telestroke service, patients with MIS received tPA slower than patients with severe stroke, and approximately 15% of those patients had poor functional outcome at discharge. Further prospective studies are warranted to confirm our findings.

Declaration of Conflicting Interests

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