Functional Outcomes of Intravenous Thrombolysis in Octogenarians and Nonagenarians Through Telestroke: Single-Center Experience

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Abstract

Background: Patients aged ≥ 80 years are often underrepresented in stroke trials. Observational studies have shown that older patients have worse outcomes compared with younger patients, but outcomes in patients aged ≥ 80 years treated with intravenous (IV)-alteplase specifically through telestroke (TS) have not been studied.

Aim: To compare clinical and safety outcomes in stroke patients aged ≥ 80 and 60–79 years treated with IV-alteplase via TS.

Methods: The Medical University of South Carolina TS database was analyzed to identify IV-alteplase-treated patients aged 60–79 and ≥ 80 years between January 2015 and March 2018. Baseline demographics and TS-specific variables were compared. Clinical outcomes were assessed using the 90-day modified Rankin Scale (mRS). Safety outcomes were evaluated by comparing symptomatic intracranial hemorrhage (sICH). Multivariate logistic regression analysis was performed to determine odds ratio (OR) for good outcome (mRS 0–2) in the older age group at 90 days.

Results: IV-alteplase was used in 151 patients in ≥ 80 years age group and 273 patients in 60–79 years age group. The older age group had more women and a higher National Institutes of Health Stroke Scale. The mean “ED-door-to-TS-consultant-login” time was shorter (21.6 min vs. 25.6 min; $p=0.048$), but “TS-consultant-login-to-alteplase” time was longer (22.1 min vs. 19.3 min; $p=0.01$) in the older age group. No difference was noted in eventual “door-to-needle” time. The older age group had fewer good outcomes (39.1% vs. 74%; $p=0.001$) and more deaths (38% vs. 14%; $p=0.001$) at 90 days. The sICH rates were similar in the two groups. The OR

for good outcome in ≥ 80 years age group was 0.20 (95% CI: 0.12–0.34) after controlling for baseline variables.

Conclusions: Stroke patients aged ≥ 80 years treated via TS have similar post-thrombolysis hemorrhage rates but worse clinical outcomes compared with patients aged 60–79 years.

Keywords: teleneurology, telestroke, telemedicine, emergency medicine/teletrauma, cardiology/cardiovascular disease

Background

The incidence of stroke increases with age and is particularly high in octogenarians and nonagenarians.¹ Despite this, patients older than 80 years are often excluded or significantly underrepresented in randomized clinical trials studying the effects of various interventions for acute ischemic stroke treatment. We know that outcomes in octogenarians and nonagenarians are worse compared with younger age cohorts based on observational studies across the United States and Europe in which intravenous (IV)-alteplase was administered after a traditional face-to-face evaluation of the patients by a neurologist.^{2–4}

Telestroke (TS) has emerged as an essential modality to provide acute stroke care to patients in rural and small community hospitals.^{5–7} The overall safety profile of IV-alteplase administration via TS has been established, and the post-thrombolysis symptomatic hemorrhage rates are similar to the rates noted when patients are treated with IV-alteplase in the traditional setting.^{8,9} These studies, unfortunately, have underrepresented patients older than 80 years. There is even more dearth of data regarding functional outcomes in elderly patients treated with IV-alteplase after remote evaluation via TS. The elderly population is at higher risk of symptomatic intracranial hemorrhage (sICH) and hence poorer outcomes compared with younger patients; therefore, there is an urgent need to assess the safety and functional outcomes in elderly patients treated for acute stroke over TS.

The goal of this study was to assess the above-mentioned safety and functional outcomes in patients aged ≥ 80 years treated with IV-alteplase via TS at the Medical University of South Carolina (MUSC) Health TS program and compare these outcomes with patients aged between 60 and 79 years.

Methods

PATIENTS AND BASELINE VARIABLES

The MUSC Health TS program started in 2008 to provide expert stroke care to remote hospitals in South Carolina (SC).^{6,10,11} Over the past 10 years, the TS program has expanded and now covers 28 hospitals across the state of SC. The MUSC Health TS database is a prospectively collected quality improvement database. The database was retrospectively analyzed from January 2015 to March 2018 for patients aged ≥ 60 years and received IV-alteplase after evaluation by TS neurologist for stroke-like symptoms. The cohort was dichotomized to 60–79 and ≥ 80 years age groups. SC lies within the “stroke-belt” and has a higher proportion of the young and middle-aged population affected by stroke compared with national average.¹² To avoid potential bias by the inclusion of younger patients in our study, the population younger than 60 years was excluded from the analysis. Baseline variables including age, gender, National Institutes of Health Stroke Scale (NIHSS) on presentation, and TS-specific time variables were collected. The TS-specific time variables included “ED door to TS consult page,” “TS consult page to TS consultant login,” “TS consultant login to alteplase decision,” and “alteplase decision to administration” times. The eventual “door to needle” time and the final diagnosis of “stroke vs. stroke-mimic” were also obtained from the database.

OUTCOMES

Primary clinical outcome was assessed using the modified Rankin Scale (mRS) at 90 days. The mRS is a 7-point scale ranging from 0 (no symptoms) to 6 (death), with the score of 0–2 indicating functional independence (“good outcome”). Primary safety outcome included sICH post-IV-alteplase (defined per the National Institute of Neurological Disorders and Stroke [NINDS] criteria as any hemorrhage on computed tomography [CT] scan within 36 h of thrombolysis with NIHSS increase by at least 1 point) and asymptomatic intracranial hemorrhage (aICH) (defined as hemorrhage on CT scan without any neurological worsening). Discharge disposition was also analyzed from the database. The NINDS criteria for sICH were the standard and most commonly utilized definitions of post-thrombolysis sICH when the MUSC TS program was initiated in 2008. To ensure that spoke sites continue to provide consistent reports of sICH, the NINDS criteria continued to be used in the MUSC TS database for the definition of sICH.

The safety outcome data were collected by the MUSC Health TS program coordinators either by chart review of the patient admitted to the MUSC and its affiliated sites or by a telephonic conversation with the stroke coordinator of the treating hospital. All patients receiving IV-alteplase were called by the

MUSC Health TS coordinator 90 days after stroke to determine their functional status and to assign mRS. Three attempts were made to get in touch with each of the patients to determine their 90-day mRS.

STATISTICAL METHODS

Patient variables were described as means with standard deviation for continuous variables, and frequencies and percentages for categorical variables. All analyses were two-tailed and performed at a significance level of 0.05. Fisher’s exact test was used to compare categorical variables, and *t* test was used to compare continuous variables between the two groups. Multivariate logistic regression analysis was performed to determine odds ratio (OR) for good outcome and mortality in ≥ 80 years age group after controlling for baseline variables. All analyses were performed using SPSS v25 software (IBM Corporation, New York).

Results

Between January 2015 and March 2018, 151 patients aged ≥ 80 years and 273 patients aged 60–79 years received IV-alteplase via the MUSC Health TS program. The mean age was 86.6 years for the older age group (range 80–98 years) and 69.5 years for the younger age group (*Table 1*). The older age group had more women (70% in ≥ 80 years vs. 51% in 60–79 years; $p=0.0002$) and a higher mean NIHSS on presentation (11.9 in ≥ 80 years vs. 9.4 in 60–79 years; $p=0.0012$). The older age group had more aphasic patients compared with younger patients based on NIHSS score of ≥ 1 point for language (63.1% in ≥ 80 years vs. 43.7% in 60–79 years; $p=0.002$). The two groups did not differ in the percentage of patients with a normal level of awareness per the NIHSS score of LOC1a of 0 points on presentation (88% in ≥ 80 years vs. 89.3% in 60–79 years; $p=0.58$).

There was a nonsignificant trend toward earlier activation of TS alert in older patients (“ED-door-to-TS-consult-page” mean time of 17.4 min in ≥ 80 years vs. 20.8 min in 60–79 years; $p=0.058$). The TS consultant neurologists took more time to determine IV-alteplase candidacy in the older age group (“TS-consultant-login-to-alteplase-decision” time of 22.1 min in ≥ 80 years vs. 19.3 min in 60–79 years; $p=0.01$). The final door to needle times were similar in both groups (57.1 min in ≥ 80 years vs. 60.2 min in 60–79 years; $p=0.24$).

With regard to safety, both groups had similar rates of sICH and aICH post-IV-alteplase (*Table 2*). At the end of hospital stay, 22% of older patients were discharged home compared with 41% of younger patients ($p=0.001$) (*Table 2*). A more significant percentage of older patients died during the hospitalization (15% in ≥ 80 years vs. 6% in 60–79 years;

Table 1. Baseline Characteristics

BASILINE VARIABLE	≥80 YEARS	60–79 YEARS	p
Total number	151	273	
Age, mean (SD), years	86.6 (4.53)	69.5 (5.86)	<0.001
Females, n (%)	106 (70)	140 (51)	0.0002
NIHSS, mean (SD)	11.9 (7.4)	9.4 (7.7)	0.0012
NIHSS-LOC1a score, n (%)			
0	132 (88)	243 (89.3)	0.58
1	10 (6.7)	21 (7.7)	
2	5 (3.3)	6 (2.2)	
3	3 (2)	2 (0.7)	
Aphasia (based on NIHSS score), n (%)			
No	55 (36.9)	152 (56.3)	0.002
Yes	94 (63.1)	118 (43.7)	
Symptom onset to ED door time, mean (SD), min	75.3 (51.6)	77.3 (52.6)	0.71
ED door to TS consult page time, mean (SD), min	17.4 (16.5)	20.8 (18.1)	0.058
Consult page to TS consultant login time, mean (SD), min	4.3 (2.8)	4.3 (3.5)	0.97
ED door to TS consultant login time, mean (SD), min	21.6 (17.1)	25.6 (20.8)	0.0448
TS consultant login to alteplase decision time, mean (SD), min	22.1 (14.6)	19.3 (9.4)	0.01
Door to needle time, mean (SD), min	57.1 (26.9)	60.2 (27.3)	0.24
Symptom onset to needle time, mean (SD), min	131.6 (57.6)	137.4 (57.2)	0.32
Alteplase decision to alteplase administration time, mean (SD), min	15 (14.2)	16 (13.8)	0.53

ED, emergency department; LOC, level of consciousness; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; TS, telestroke.

$p=0.004$) or were discharged to hospice care (11% in ≥80 years vs. 1% in 60–79 years; $p=0.001$) compared with younger patients. At 90 days, the older age group had a significantly lower number of patients with a good functional outcome (39.1% in ≥80 years vs. 74% in 60–79 years; $p=0.001$) as well as higher mortality (38% in ≥80 years vs. 14% in 60–79 years; $p=0.001$) (Table 3). After controlling for gender, NIHSS, and door to needle times, the OR for good

Table 2. Outcomes

OUTCOME	≥80 YEARS	60–79 YEARS	p
Symptomatic ICH, n (%)			
Yes	6 (4)	13 (5)	0.81
No	103 (68)	174 (64)	
Missing	42 (28)	86 (31)	
Asymptomatic ICH, n (%)			
Yes	19 (13)	23 (9)	0.22
No	84 (58)	161 (62)	
Missing	42 (29)	76 (29)	
Confirmed diagnosis, n (%)			
Ischemic stroke	102 (68)	164 (60)	0.31
Stroke-mimic	10 (7)	24 (9)	
Missing	39 (25)	85 (31)	
Discharge disposition, n (%)			
Home	34 (22)	111 (41)	<0.001
Rehab	25 (17)	40 (15)	
Nursing home	12 (8)	12 (4)	
Hospice	16 (11)	4 (1)	
Death	23 (15)	17 (6)	
Missing	41 (27)	89 (33)	
ICH, intracranial hemorrhage.			

functional outcome was 0.20 (95% CI: 0.12–0.34; $p<0.001$) and the OR for mortality was 4.26 (95% CI: 2.42–7.49; $p<0.001$) in the older cohort.

Discussion

To the best of our knowledge, this is the largest cohort of octogenarians and nonagenarians who received IV-alteplase after remote evaluation by a neurologist via TS. The older age group was observed to have more women and higher NIHSS on presentation than the younger age group. These trends are similar to other studies, which compared ≥80-year-old acute ischemic stroke patients with <80-year-old patients in traditional setting.^{13–16}

There is a trend toward earlier TS consult request by the emergency departments, and the “ED-door-to-TS-consult-MD-login” time is significantly shorter for the older age group. This difference, however, is being balanced by the longer time taken by TS consultant to conclude candidacy for IV-alteplase leading to similar “door to needle” times in both groups.

Table 3. 90-Day Functional Outcomes

FUNCTIONAL OUTCOME	≥80 YEARS	60–79 YEARS	p
Good outcome (mRS 0–2), n (%)	59 (39.1)	202 (74)	0.001
Mortality (mRS 6), n (%)	58 (38)	39 (14)	0.001

mRS, modified Rankin Scale.

To our knowledge, no other study has highlighted such an observation. We believe that this noteworthy observation can be explained by increased awareness of the higher incidence of cerebrovascular diseases in elderly by the emergency department physicians and staff leading to sooner activation of TS consultation. The relatively longer time for evaluation is likely multifactorial and can include factors such as presence of more aphasic patients leading to delays in performance of neurological examination remotely via TS and higher prevalence of cognitive impairment in ≥80-year-old patients requiring inclusion of family members in obtaining

history and decision-making process to ensure that the time from symptom onset to treatment conforms to the current guidelines. Although our database does not include the stroke etiology, more aphasic patients in the older age group can be explained by greater prevalence of larger cortical strokes from cardioembolic etiology and lower prevalence of small vessel etiology in older patients compared with younger patients.^{17–19}

No significant difference was observed with regard to sICH between the two groups. This observation is consistent with studies comparing sICH in IV-alteplase-treated ≥80-year-old patients and <80-year-old patients in the traditional face-to-face evaluation setting.^{3,15} The percentage of patients with a good outcome at 90 days was significantly lower in the older age group compared with the younger age group. *Table 4* compares the outcomes of ≥80-year-old IV-alteplase-treated patients after going through traditional face-to-face evaluation by a neurologist in the emergency department. Most of these studies were published in early to mid-2000s. While the patients with good functional outcomes at 90 days are similar

Table 4. Outcomes in ≥80-Year-Old Patients Treated with IV-Alteplase After Traditional Evaluation

AUTHOR	SOURCE	N	MEAN AGE (YEARS)	WOMEN (%)	NIHSS (MEAN)	CLINICAL OUTCOME		SICH (%)
						GOOD, %	DEAD (MRS 6), %	
Ford et al. ¹⁵	SITS-ISTR	1,831	83	59.3	14	mRS 0–2, 35.2	30.2	9.5 (NINDS) 1.8 (SITS-MOST)
Purroy et al. ²¹	Multicenter registry	1,189	85	60.1	13	mRS 0–2, 38.7	23.2	4.7 (SITS MOST)
Sylaja et al. ³	Canadian Alteplase for Stroke Effectiveness Study (CASES)	270	84.7	63	16	mRS 0–1, 25.9	35.3	4.4 (NINDS)
Toni et al. ²²	Multicenter registry	41	83	63	13.5 (median)	mRS 0–2, 44	34.1	4.8 (ECASS II)
van Oostenbrugge et al. ²³	Single-center registry	45	85	60	NR	mRS 0–1, 27	40	11.1 (NINDS)
Engelter et al. ²⁴	Multicenter registry	38	84	63	14.1	mRS 0–1, 29	32	13 (NINDS)
Chen et al. ²⁵	Single-center registry	56	84	55	18	NR	20 at discharge	7.1 (ECASS II)
Ringleb et al. ²⁶	Single-center registry	90	83	62	13	mRS 0–1, 19	29	6.7 (NINDS)
Tanne et al. ²⁷	Multicenter survey	30	85	50	NR	NR	20 at discharge	3 (NINDS)
Berrouschot et al. ²⁸	Multicenter registry	38	83	60.5	16	mRS 0–2, 31.6	21.1	2.6 (ECASS II)
Our study	MUSC Health TS database	151	86.6	70	11.9	mRS 0–2, 39.1	38	4 (NINDS)

sICH definitions: NINDS (any hemorrhage on CT scan within 36 h of thrombolysis with NIHSS increase by at least 1 point); SITS-MOST (parenchymal hematoma-2 on CT scan within 36 h of thrombolysis with NIHSS increase by at least 4 points); ECASS II (any hemorrhage on CT scan within 36 h of thrombolysis with NIHSS increase by at least 1 point).

CT, computed tomography; ECASS, European Cooperative Acute Stroke Study; MUSC, Medical University of South Carolina; NINDS, National Institute of Neurological Disorders and Stroke; NR, not reported; sICH, symptomatic intracranial hemorrhage; SITS-ISTR, Safe Implementation of Treatment in Stroke International Stroke Treatment Registry; SITS-MOST, Safe Implementation of Treatment in Stroke-Monitoring Study.

in our cohort and those described in *Table 4*, the mortality at 90 days appears to be higher in our TS-treated patients than some of the reported outcomes in other studies. Higher utilization of hospice and palliative care in elderly patients with strokes in the U.S. over the recent years could attribute to some of the difference in the mortality rate in our study compared with most of the other studies, which were published over 10 years ago; however, further studies are encouraged to compare mortalities in elderly patients treated with IV-alteplase via TS to validate our observation.²⁰

LIMITATIONS

Our study has several limitations. The study is nonrandomized and retrospective. The etiology of the stroke, cause of death, and complications occurring during the hospital stay are not included in the database. Inherent limitations of obtaining mRS at 90 days over telephonic interview cannot be overstated. Approximately 20–30% of the missing 90-day mRS and hemorrhagic conversion rates are the most significant limitations in our study. Given that only 45% of patients were transferred to the MUSC, we have to rely on other primary and comprehensive stroke centers to obtain data on post-IV-alteplase complications, final diagnosis, and disposition status at discharge. Because of this, there is a sizable portion of data missing in these variables and underlines an important requirement of implementing quality controls to ensure spoke sites have acceptable training and resources to obtain various quality metrics at par to the national standards.

In conclusion, our findings suggest that ≥80-year-old patients treated with IV-alteplase after remote evaluation via TS have poorer outcomes than 60- to 79-year-old patients, but importantly, the rates of sICH and aICH are similar in the two groups. Compared with traditionally evaluated ≥80-year-old patients treated with IV-alteplase, our patients had similar rates of a good functional outcome, but a higher mortality rate.

Disclosure Statement

No competing financial interests exist.

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