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Clinical study

Comparison of thrombolytic agents in treatment of patients with acute ischemic stroke; findings from a single centre follow up study in real-life settings.

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ABSTRACT

Background and objectives: Health outcome data of thrombolysis in patients with acute ischemic stroke in real life-settings in India are scarce. We studied the clinical profile, risk factors and functional outcome of patients with acute ischemic stroke (AIS) who were thrombolysed.
Methods: In a single centre retrospective study from January 2017 to June 2020, we analysed the data of adult patients with AIS presented within 4.5 h of symptom onset. We included patients if they had NIHSS score ≥4, modified Rankin score of 2 or less before the stroke onset and without evidence of haemorrhage. Modified Rankin score of two or less at the end of three months was defined as the primary efficacy outcome. The development of symptomatic intracerebral haemorrhage was considered as the primary safety outcome. We tried to analyse the primary safety and efficacy outcomes between two thrombolytic agents.
Results: Ninety patients (Tenecteplase = 61; Alteplase, n = 29) underwent stroke thrombolysis during the study period. The mean age was 64.3 years in Tenecteplase group and 63.2 years in Alteplase group. Twenty patients were aged more than 75 years. Hypertension was the most common comorbidity in both the groups (72% and 72.4%). Median mRS score at 3-months was 1 in Tenecteplase group and 0.5 in Alteplase group ($p < 0.001$), however there was no statistically significant difference between both treatment groups in terms of NIHS score at 24 h (70.4% vs 51.7%, $p = 0.08$), functional recovery calculated with mRS at 3-month (83.6% vs 79.3%, $p = 0.62$) or in terms of symptomatic ICH (9.8% and 17.2% $p = 0.36$).
Conclusion: Tenecteplase appears to have similar clinical outcomes as Alteplase for stroke thrombolysis. Given the relatively low-cost and ease of administration, Tenecteplase may be better than Alteplase for management of acute ischemic stroke.

1. Introduction

Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range, 84–262/100,000 in rural and 334–424/100,000 in urban areas [1]. Arterial ischemic stroke (AIS) is a leading cause of lifelong disability with high negative impact on quality of life [2]. Treatment of AIS aims at minimizing neurologic injury by reducing clot burden and restoring adequate blood flow to the brain. Current standard of care for the treatment of AIS includes treatment with intravenous fibrinolytic therapy, directed intra-arterial fibrinolytic therapy, and/or mechanical thrombectomy. However, only 5–10% of all AIS patients presenting to emergency departments could receive thrombolytic therapy [2]. Thrombolytic treatment with Alteplase, a second generation recombinant tissue plasminogen activator (rTPA), within 4.5 h of symptom onset for acute ischemic stroke is of proven benefit [3] Currently, only Alteplase is FDA approved for thrombolytic treatment of AIS [4]. Despite many advantages, some adverse effects such as short half-life requiring continuous infusion, relatively low recanalization rate and the risk of intracranial haemorrhage occurs with Alteplase [5]. In the National Institute of Neurologic Disorders (NINDS) trial, risk of symptomatic intracerebral haemorrhage (SICH) was 6% higher (6.0% vs 0.0%, $p = 0.0001$) for Alteplase as compared to placebo [6]. Tenecteplase is a fibrinolytic protein bioengineered from human tissue plasminogen activator (Alteplase) with 15-fold higher fibrin specificity and 6-fold prolonged plasma half-life. Tenecteplase can be given as single intravenous bolus infusion[7]. Although Tenecteplase is

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approved for use in India for thrombolytic treatment of AIS, only limited Indian data from real-life settings comparing the outcomes of Alteplase and Tenecteplase are available. We aim to describe the clinical profile and risk factors in patients admitted with acute ischemic stroke and to compare the clinical outcomes of thrombolysis with Tenecteplase vs Alteplase.

2. Methods

2.1. Study settings

Our study was a single centre, retrospective, comparative study in a cohort of patients who received Alteplase or Tenecteplase for acute ischemic stroke. The study was done in Renai Medicity Multi Super Specialty Hospital with a bed capacity of 294 with about 5stroke admissions per day. As part of the hospital protocol, the treating physician obtained a written informed consent from a close relative of the patient, which included a detailed explanation of the benefits and risks including haemorrhage. We retrospectively reviewed the charts of all stroke patients admitted to our hospital during the study period and gathered the data. The ethics committee of Renai Medicity (HR/RIMS/217/2021) reviewed and approved the study protocol.

2.2. Inclusion and exclusion criteria

We included all adult patients 18 years or older with acute ischemic stroke who presented within 4.5 h of symptom onset with a functional deficit (National Institute of Health Stroke Scale (NIHSS) score $\geq$4) and no evidence of haemorrhage on non-contrast computed tomography (NECT) imaging of brain. Patients with contraindications for thrombolysis were excluded.

2.3. Acute ischemic stroke management protocol

For all patients with acute stroke coming in the window period ($\leq$4.5 h), after initial assessment including NIHSS score, the treating team obtain an urgent NECT brain with CT contrast angiogram of brain and neck vessels. ASPECTS based on the initial computed tomography (CT) scan was calculated. The Alberta Stroke Program Early (non contrast) CT score (ASPECT) is a scoring system used to assess the extent of early ischaemic changes in the middle cerebral artery territory on non-contrast computed tomography. The clinician/radiologist studies the appearance at two different axial slices corresponding with two different anatomical levels (lentiform nucleus level/centrum semiovale level) and subtracts 1 from total maximum score of 10 for each area affected. A score of 0 suggests extensive MCA infarction and correlates inversely with NIHSS. A score of 10 is normal [8]. The patients without any evidence of intracranial bleed in CT Brain and those with ASPECTS score of seven or more were given IV thrombolysis. Patients were administered either Tenecteplase or Alteplase based on treating Neurophysicians discretion. Tenecteplase was preferred in Emergency department where it is done due to ease of administration (single bolus injection) as well as the lower cost of the drug (rT-PA cost 560 USD and Tenecteplase cost 390 USD). The dose of Tenecteplase was 0·2 mg/kg (maximum of 20 mg) as a single bolus intravenously and that of alteplase was 0·9 mg/kg (maximum of 90 mg −10% of the dose as initial bolus, followed by 90% as intravenous infusion over 1 h). Those with evidence of large vessel occlusion on CT angiogram was referred to another centre for mechanical thrombectomy. The treating team shift the patients to intensive care unit after initial observation for one-hour. The NIHSS score, Glasgow coma scale (GCS) and vital parameters were monitored on an hourly basis. A follow up NECT brain was done after 24 h or earlier in case of any neurological worsening. Antithrombotic agents were added and patients were managed accordingly. NIHSS score reduction was documented on discharge. After discharge from hospital, the patients were followed-up initially after 1-week, then fortnightly and monthly in initial months. On follow-up visits, the treating neuro-physician record the functional status of the patient including mRS score.

3. Design of study and outcome measures

We compared the characteristics of patients who underwent thrombolysis in both study groups. Mean age of thrombolysis, Risk factors including Hypertension, Diabetes Mellitus, Dyslipedemia, Atrial fibrillation. Hypertension was diagnosed based on ISH guidelines [9]. Diabetes was categorized using ADA 2021 guideline [10] and dyslipidemia using ESC guidelines [11]. The association of these risk factors (Table 3) with efficacy outcome was studied. There were 20 patients aged more than 75 years and characteristics in them were also studied. The primary efficacy outcome and primary functional outcome were also compared.

The following functional outcomes were included in the study; the NIHS score at 24 h and at discharge, (reduction of NIHS score of 4 from the baseline status is considered as clinically meaningful reduction), and functional recovery assessed at 3-month using mRS score and categorized in to favourable (score $\leq$ 2) and unfavourable (score 3 or more). A good functional recovery (mRS of 0–2) at three-month was considered as the primary efficacy outcome.

Symptomatic ICH as per the European Cooperative Acute Stroke Study (ECASS) II definition is any type of intracerebral haemorrhage on any post treatment imaging after the start of thrombolysis and increase of $\geq$4 NIHSS points from baseline, or from the lowest value within 7 days, or leading to death [11,13]. All patients underwent a follow-up brain imaging after 24 h of receiving thrombolytic therapy as per the institutional protocol and before discharge in case of any neurological worsening.

3.1. Statistical analysis

We analysed data using SPSS 20 trial version. Continuous data were assessed for normality using Kolmogorov-Smirnov test. Data with normal distribution were analysed using parametric test, while we employed non-parametric tests for skewed data. Descriptive statistics used were frequency, mean, median, standard deviation and interquartile range (IQR) which is taken as difference between 75th quartile (Q3) and 25th quartile (Q1). Inferential statistics used were independent sample *t* test and Man Whitney *U* test for continuous variables and Chi-square test for categorical variables. After performing univariate analysis, multiple logistic regression analysis using enter method was performed to assess the predictors of outcomes of stroke.

4. Results

A total of 1650 patients presented to Emergency department with stroke during the study period. Out of this one hunderd and sixty four patients were in the window period. Fifty two patients who were high risk were excluded from the study. Of the remaining one hundered and twelve patients, ninety gave conscent for thrombolysis. Out of them29 received Alteplase, while 61 received Tenecteplase. The results of the study are depicted in the (Figure 1). The mean age at the time of presentation in Tenecteplase group was 64.3 ± 11.3 years, while it was 63.2 ± 12.0 years in Alteplase group (Table 1). Twenty patients were aged more than 75 years. Most of the study subjects were males (Tenecteplase, 60.6%; Alte-

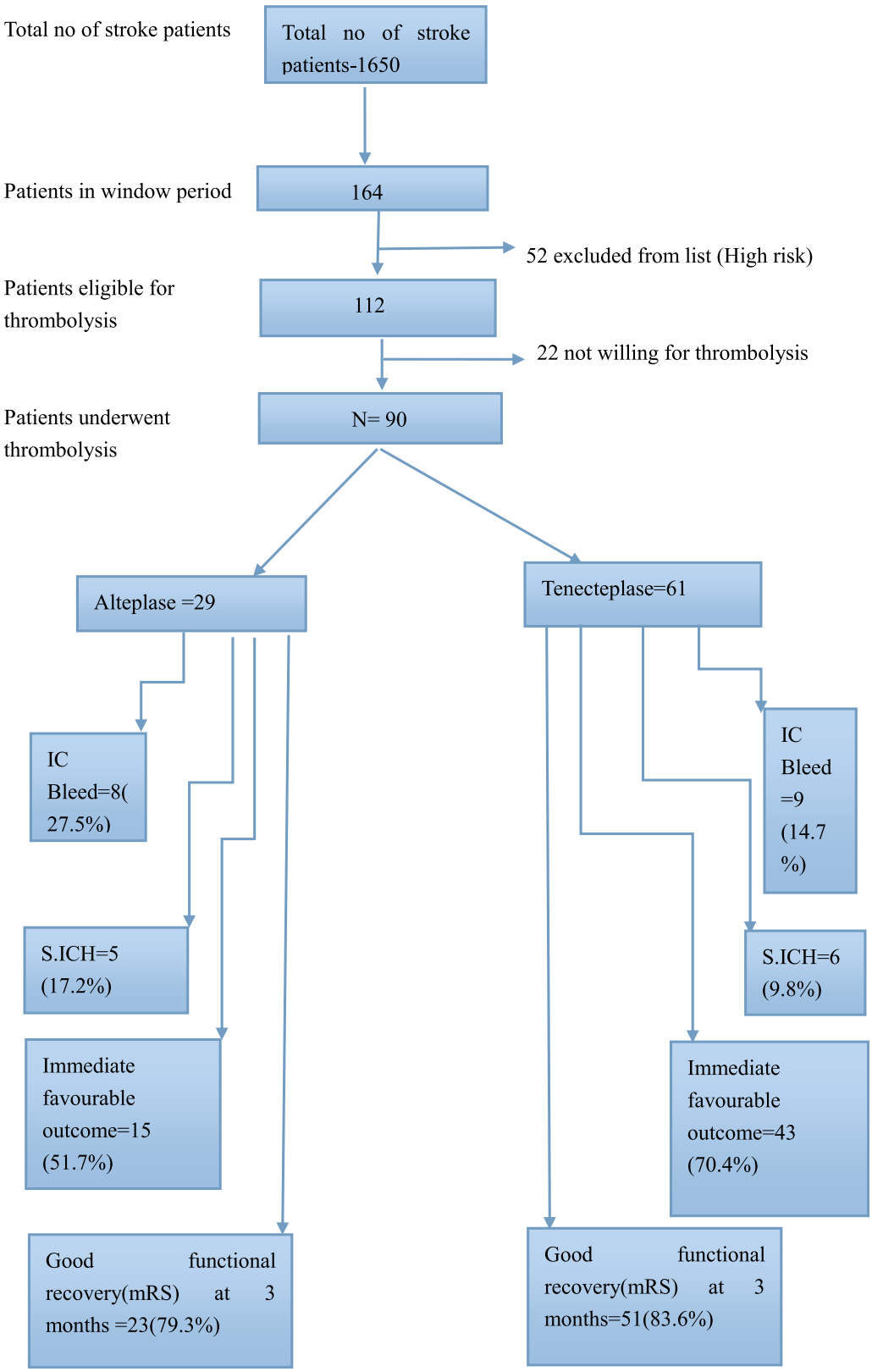

Fig. 1. Flow chart depicting outcome of study.

plase, 65.5%). Hypertension was the most common comorbidity in both the groups (Tenecteplase, 72%; alteplase, 72.4%), followed by Type 2 Diabetes (39.3% vs 41.3%). Mean arterial blood pressure was comparable in both groups (118 and 115 mmHg in Tenecteplase and Alteplase groups, respectively). Further, the median random blood sugar was 134 mg/dl with IQR 120, 198 in Tenecteplase group and 130 mg/dl with an IQR of 118,180 in Alteplase group. On assessing the ASPECTS, fourteen patients had a score of seven

Table 1
Baseline characteristics of patient receiving thrombolytic therapy.

Characteristics	Tenecteplase (n-61)	Alteplase (n-29)	p-value
Age in years, mean ± SD	64.3 ± 11.3	63.2 ± 12.01	0.67[€]
Gender, n (%)			0.63[#]
Male	37 (60.6)	19 (65.5)	
Female	24 (39.3)	10 (34.4)	
Risk factors, n (%)			
HTN	44 (72)	21 (72.4)	0.93[#]
DM	24 (39.3)	12 (41.3)	0.82[#]
CAD	9 (14.7)	4 (13.7)	0.74[#]
AF	8 (13.1)	6 (20.6)	0.51[#]
DLP	10 (16.3)	5 (17.24)	0.32[#]
CKD	(4.9)	(6.8)	0.74[#]
Hyperhomocystinemia	(3.2)	(6.8)	0.42[#]
Time of onset to arrival			
<1 hour	29 (47.5)	19 (65.5)	0.26[#]
1–4 h	24 (39.3)	8 (27.6)	
>4 h	8 (13.1)	2 (6.9)	
MABP(mm of Hg), mean ± SD	118.7 ± 18.5	115.4 ± 19.4	0.16[€]
GRBS, median(IQR-Q1,Q3)	134 (120,198)	130 (118,180)	0.42[¥]
ASPECTS			
7	10 (16)	9 (31.3)	0.23[#]
8-9	41 (67.2)	18 (62)	
10	10 (16)	2 (6.8)	
Localization			0.63[#]
Anterior territory	50 (81.9)	25 (86.2)	
Posterior territory	10 (16)	3 (10.9)	
Referred for mechanical thrombectomy	1 (1.6)	1 (3.4)	
NIHS score on arrival			0.34[¥]
Median (IQR)	8(5,12)	8(4.5,12)	
NIHSS on Arrival			0.64[#]
< 6	30 (49.1)	12 (41.3)	
6-15	22 (36.1)	12 (41.3)	
> 15	9 (14.7)	5 (17.2)	

SD-Standard deviation; HTN-Hypertension; DM-Diabetes Mellitus; CAD-Coronary artery disease; AF-Atrial fibrillation; DLP-Dyslipidemia; CKD-Chronic kidney disease; MABP-mean arterial blood pressure; GRBS-general random blood sugar; GCS-Glasgow coma scale; ASPECTS-Alberta Stroke programme early CT score; NIHSS-National Institute of heath stroke scale; IQR-inter quantile range.
[¥] Mann Whitney *U* test, [#]chi-square test [€]t = independent *t* test level of significance p < 0.05.

Table 2
Comparison of the outcome of stroke and safety among Tenecteplase and alteplase group.

Outcome parameters	Tenecteplase (n-61)	Alteplase (n-29)	P value
NIHSS at 24 h			0.04[#]
<6	43 (70.4%)	18 (62%)	
6–15	17 (27.8%)	7 (24.1%)	
>15	1 (1.6%)	4 (13.75)	
Immediate favourable outcome (NIHS reduction >4 at 24 h)			0.08[#]
Favourable, n (%)	43 (70.4)	15 (51.7)	
Unfavourable, n (%)	18 (29.5)	14 (48.3)	
Recanalization of LVO			0.06[#]
Yes	0	2 (6.8%)	
No	9 (14.8%)	7 (24.1%)	
Not applicable	52 (85.2%)	20 (68.9%)	
NIHSS at discharge			0.08[#]
<6	51 (83.6%)	19 (65.5%)	
6–15	9 (14.7%)	8 (27.5%)	
>15	1 (1.6%)	2 (6.8%)	
IC bleed			0.16[#]
Yes	9 (14.7%)	8 (27.5%)	
No	52 (85.2%)	21 (72.4%)	
Symptomatic ICH			0.36[#]
Yes	6 (9.8%)	5 (17.2%)	
No	55 (90.1%)	24 (82.75%)	
Symptomatic ICH with >4 worsening of NIHS score	1 (1.6%)	2 (6%)	0.38[#]
Prolonged Hospital stay			0.61[#]
<7 days	40 (65.57%)	17 (58.6%)	
8–14 days	13 (21.3%)	6 (20.6%)	
>2weeks	7 (11.4%)	4 (13.79%)	
died	1 (1.6%)	2 (6.8%)	
Median mRS score at 3-month (IQR; Q1,Q3)	1 (0,2)	0.5 (0,1)	<0.001[¥]
Good functional recovery at 3 months			0.62[#]
Favourable (mRS 0–2)	51 (83.6%)	23 (79.3%)	
Unfavourable (mRS > 2)	10 (16.3%)	6 (20.7%)	

NIHSS-National Institute of heath stroke scale; IQR-inter quantile range which means 75th quartile(Q3)-25th quartile (Q1); LVO-large vessel occlusion; mRSmodofied Rankin score.
[#] Chi-square test [¥]Mann Whitney *U* test, level of significance p < 0.05.

and 11 patients had a score of 10. In total, nine patients had ICA occlusion. Further, seven and one patient had MCA and basilar occlusion, respectively. Only two patients were referred for thrombectomy.

4.1. Efficacy and safety

The median NIHSS at arrival was eight in both the groups with IQR (5,12) in tenecteplase group and 4.5,12 in alteplase group (p = 0.08). Immediate favourable outcome in terms of reduction of >4 NIHS score at 24 h was seen in 70.4% of patients in Tenecteplase group and 51.7% in Alteplase group (p = 0.08) (Table 2). Median mRS at 3-month follow-up was 1, interquantile range of 0,2 in Tenecteplase group and 0.5 with an IQR of 0,1 in Alteplase group. On calculating mRS at 3 months, 83.6% of patients in Tenecteplase group had good functional recovery at 3 months compared to 79.3% of patients in Alteplase group, however the data was not statistically significant (p = 0.62). The total number of patients with intracranial haemorrhage was 17(14.7% in Tenecteplase group and 27.5% in Alteplase group). Eleven of 17 patients with haemorrhage reported symptomatic ICH (9.8% in Tenecteplase group and 17.2% in Alteplase group p = 0.36). Thirteen patients had prolonged hospital stay for more than 2-weeks. The most observed complications during extended hospital stay were aspiration pneumonia (n = 9), urinary tract Infection (n = 6) followed by acute kidney injury (n = 4). Further, four patients died, out of these three were due to large vessel occlusion and extension of the infarct and one had symptomatic ICH, who received Alteplase. Three of four patients who died received Alteplase as thrombolytic agent. Three patients died during hospital stay and one during follow-up. Of the 17 patients with large vessel occlusion, two were referred for mechanical thrombectomy, and others were given option of mechanical thrombectomy, but refused due to financial issues (6000 USD).

4.2. Recanalization rates

Recanalization was assessed by repeat imaging after 24 hrs. One patient with basilar thrombus had recanalization with Alteplase with near total improvement in NIHS. Another patient with right M2 occlusion had recanalization following Alteplase (Table 2).

4.3. Predictors of outcomes after thrombolysis

Patients with atrial fibrillation had 9.15times higher propensity for unfavourable outcome at three-month as compared to patients without atrial fibrillation (95% CI:1.7–49.2,p- 0.01). Those with low ASPECTS score (<8) had 6.4 times higher propensity for unfavourable outcome as compared to patients with ASPECTS score of 9–10 (95%CI: 1.2–31.1,p = 0.024).None other variables were found

Table 3
Predictors of stroke outcome based on MRS and NIHS score.

Predicted outcome	Variables	OR	95% CI	P value
mRS score unfavourable vs favourable outcome	Age	0.97	0.86–1.09	0.64
	Gender(male)(1) vs female	0.29	0.02–3.37	0.32
	Tenecteplase(1)/Alteplase	0.65	0.12–3.54	0.62
	Risk factor (hypertension yes(1)/no)	0.242	0.057–1.039	0.056
	Atrial fibrillation (yes(1)/no)	**9.152**	**1.701–49.250**	**0.010**
	Symptomatic ICH (yes(1)/no)	2.090	0.189–23.090	0.548
	Large vessel occlusion (yes (1)/No)	0.200	0.048-0.837	0.028
	GCS < 8 (1) vs >8	2.681	0.160–44.984	0.493
	ASPECTS 7–8 (1) vs 9–10	**6.364**	**1.2–31.1**	**0.024**
	GRBS >250 (1) vs <250	1.010	1–1.02	0.010
NIHSS score unfavourable vs favourable outcome	Gender (male) (1) vs female	0.266	0.09–0.7	0.009
	Tenecteplase (1)/alteplase	0.290	0.1–0.8	0.020
	GRBS > 250 (1) vs < 250	1.007	1–1.03	0.045
	Hypertension yes (1)/no)	2.390	0.49–11.58	0.279
	Dyslipidaemia yes (1)/no)	1.583	0.26–9.59	0.618
	History of CAD) (yes(1)vs No	1.186	0.23–5.9	0.835
	Risk factor (AF) yes (1) vs no	2.114	0.42–10.4	0.359

Multiple binary logistic regression(forward), OR-odds ratio, CI-confidence interval, level of significance p < 0.05. Adjusted R2 for mRS score (0.39) and for NIHSS score (0.21) mRS-modified Rankin score; ICH-intra cranial haemorrhage; GCS-Glasgow coma scale; ASPECTS-Alberta Stroke programme early CT score; GRBS-general random blood sugar; NIHSS-National Institute of heath stroke scale; CAD-Coronary artery disease; AF-Atrial fibrillation.

to be significant predictors of stroke outcome based on NIHSS score (Table 3).

4.4. Thrombolysis in patients aged more than 75 years

In our study 20 patients were more than 75 years (Table 4). Among them 70% were females. Hypertension (90%) was most common risk factor. Fifteen patients received Tenecteplase and 5 received Alteplase. Immediate favourable outcome (>4reduction in NIHSS) was seen in 65% of patients aged more than 75 years (p = 0.95). Favourable mRS score at 3 months was seen in 80% of old stroke (p = 0.76). Symptomatic ICH was seen in 20% of patients aged more than 75 years compared to those less than 75 years (10%), but was not statistically significant (p = 0.31).

5. Discussion

We assessed the clinical and functional outcomes of stroke patients after fibrinolysis in real-life settings. Most common comorbid conditions associated with stroke in our study were Hypertension followed by Diabetes mellitus and Dyslipidaemia. There was no significant difference in immediate functional outcome at 24-hour and functional recovery at 3-month between the Tenecteplase and Alteplase groups. Patients with atrial fibrillation and those with low ASPECTS score were found to have poor functional outcomes calculated with mRS score at 3-month. There was no significant difference between two groups in safety outcome in the form of symptomatic ICH.

Hypertension was the most common comorbid condition observed in our study. Hypertension was observed as an established risk factor for both stroke incidence and mortality in many studies [13,15]. Diabetes has also been recognized as a risk factor for stroke incidence and mortality in many studies [16].

In our study, immediate favourable outcome with >4 NIHSS reduction was seen in 70.4% of patients in Tenecteplase group and 51.7% of patients in Alteplase group. Good functional outcome was found in 83.6% of patients in Tenecteplase group and 79.3% of patients in Alteplase group. However, the primary efficacy outcome was comparable between both the groups in terms in NIHSS at 24 h (p = 0.08) and functional recovery at 3 months (p = 0.62) as there was no statistically significant difference. Our study showed similar results as the NORTEST trial, which showed no significant difference between Tenecteplase and alteplase arms in terms of NIHS score at 24 h, good functional outcome at

Table 4
Comparison of sample characteristics based of age categories below and above 75 years.

Characteristics	<75 years (n = 70)f(%)	>75years (n = 20) (%)	p-value
Gender, n (%)			***P < 0.001*** [#]
Male	50 (71.4)	6 (30)	
Female	20 (28.6)	14 (70)	
Risk factors, n (%)			
HTN	47 (67.1)	18 (90)	p **= 0.04** [#]
DM	26 (37.1)	10 (50)	p = 0.30[#]
CAD	10 (14.3)	3 (15)	p = 0.93[#]
AF	9 (12.9)	5 (25)	p = 0.18[#]
DLP	12 (17.1)	3 (15)	p = 0.82[#]
CKD	4 (5.7)	1 (5%)	p = 0.90[#]
Smoking	2 (2.9)	1 (5)	p = 0.63[#]
MABP(mm of Hg)	116.7 ± 17.6	120.35 ± 22.4	p = 0.16^
GRBS	163.9 ± 71.1	147.4 ± 48.1	p = 0.41^
GCS			p = 0.54[#]
< 8	4 (5.7)	0	
8-12	7 (10)	2 (10)	
12-15	59 (84.3)	18 (90)	
NIHSS on Arrival			p = 0.42[#]
< 6	34 (48.6)	8 (40)	
6-15	24 (34.3)	10 (50)	
> 15	12 (17.1)	2 (10)	
NIHSS at discharge			p = 0.23[#]
< 6	53 (75.7)	19 (90)	
6-15	15 (21.4)	1 (5)	
> 15	2 (2.9)	1 (5)	
ASPECTS score			
7,8	45 (64.3)	11 (55)	p = 0.81[#]
9-10	25(35.7)	9 (45)	
Tenecteplase	46 (65.7)	15 (75)	p = 0.43[#]
Alteplase	24 (34.3)	5 (25)	
Intra cranial bleed			p = 0.42[#]
Yes	12 (17.1)	5 (25)	
No	58 (82.9)	15 (75)	
Symptomatic ICH			p = 0.31[#]
Yes	7 (10)	4 (20)	
No	63 (90)	16 (80)	
NIHS outcome- Favourable	45 (64.3)	13 (65)	p = 0.95[#]
Unfavourable	25 (35.7)	7 (35)	
mRS outcome - Favourable	58 (82.9)	16 (80)	p = 0.76[#]
Unfavourable	12 (17.1)	4 (20)	

^independent sample *t* test, #chi square test level of significance p < 0.05.
HTN-Hypertension; DM-Diabetes Mellitus; CAD-Coronary artery disease; AF-Atrial fibrillation; DLP-Dyslipidemia; CKD-Chronic kidney disease; MABP-mean arterial blood pressure; GRBS-general random blood sugar; GCS-Glasgow coma scale; ASPECTS-Alberta Stroke programme early CT score; NIHSS-National Institute of heath stroke scale; IQR-inter quantile range; ICA-internal carotid artery; MCA-middle cerebral artery; ICH-intracerebral haemorrhage; mRS-modified Rankin score.

90 days, any ICH or SICH and mortality at 90 days [17]. However our data contrast with the results of some Western studies, which reported lower mRS at 3-months in Tenecteplase as compared to alteplase [17,19].

Symptomatic ICH was seen in 9.8% of patients in Tenecteplase group and 17.2% of patients in Alteplase group. Primary safety outcome defined as symptomatic intracerebral bleed with worsening of NIHSS > 4 in the first 24 h after admission was seen in 1.6% of patients in Tenecteplase group and 6% of patients in Alteplase group with no statistically significant difference. Previous studies on Tenecteplase had conflicting reports on safety outcomes. Parsons et al. compared two Tenecteplase doses (0.1 and 0.25 mg/kg) while Huang et al. used a dose of 0.25 mg/kg [20]. In both these studies the safety profile was comparable with alteplase; but in a trial by Haley et al. Tenecteplase at a dose of 0.4 mg/ kg was compared with 0.9 mg/kg alteplase and was observed to significantly increase the risk of SICH [16%] patients [21]. There are many studies which are similar to our study which showed similar efficacy and safety profiles in both the groups [5,22,23].

In our study it was found that low ASPECTS score was associated with less favourable outcome (p-0.024). These results are similar to studies done by Demchuk et al who concluded that high ASPECTS, high GCS and low NIHSS is associated with good functional recovery at 3 months (mRS $\leq$ 3) [8,22,24]. It was further proved that large strokes are associated with more severe initial NIHSS and lower ASPECTS and has unfavourable outcomes compared to smaller strokes which are associated less severe NIHSS score and higher ASPECTS score [25].

In our study, we used Tenecteplase 0.2 mg/kg (max dose 20 mg) and the primary safety outcome was comparable between the two groups. Considering the results of the previous studies, the Tenecteplase dose of 0.2 mg/kg appears optimal for safety and efficacy [24]. In EXTEND-IA trial, among patients with acute ischemic stroke from major vessel occlusion within 4.5 h after the onset of symptoms, intravenous Tenecteplase resulted in a significantly higher incidence of reperfusion of the occluded vascular territory than did intravenous alteplase (22% vs 10%; P = 0.02) [20]. However in our study, two patients had recanalization following thrombolysis, of which both received Alteplase as thrombolytic agent.

We had twenty patients aged more than 75 years. There were six males and 14 females in the study group. Hypertension (90%) was observed as most common risk factor. There was no statistically significant difference in terms of NIHS score at 24 h(p-0.95) and mRS score at 3 months (p-0.76). The risk of SICH was found to be more in older age group (20%) compared to those less than 70 years (10%), however there was no statistically significant difference (p-0.31). This finding is similar to study done by Chen et al. [26] and Pundik et al [27] reported a higher risk of symptomatic ICH in elderly cohorts compared with the younger population (7.1% vs 6.3%; 12.8% vs 10.4%); however, the difference were not statistically significant. There were other studies which was contradictory to our case reports which showed risk of symptomatic ICH was more in elderly compared to young people post thrombolysis [27,29].

There are a few limitations in our study. Firstly, it was a non-randomized single centre retrospective study. Secondly, the number of patients were more in Tenecteplase arm (61 vs 29) mainly due to ease of administration. Third, the number of patients enrolled in the two arms were relatively small and underpowered to detect meaningful clinical differences. Finally, we had only 20 patients who were aged more than 70 years. We therefore recommend a large-scale multi-centric prospective study in real-life settings to confirm the findings of our study.

6. Conclusion

Tenecteplase appear to have similar clinical outcomes as Alteplase for stroke thrombolysis. In view of the lower cost and ease of administration, Tenecteplase have a great potential as a stroke thrombolytic agent especially in the resource-limited settings in low and middle-income countries.

Author contributions

MG: Study design, concept, data acquisition, literature search, manuscript drafting, critical review and will act as guarantor of the article. NB: Design, concept, data collection, literature search, manuscript editing and critical review. RP: Concept, design, data and critical review. CT: Data acquisition, concept, study design and literature search. MZ-Data acquisition, concept and critical review.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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