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Predictors of Clinical Outcome in Post-Thrombolysis Among Sample of Egyptian Patients with Acute Ischemic Stroke

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Abstract

Acute ischemic stroke (AIS) is the second leading cause of death and a major cause of disability worldwide. Treatment for patients with AIS is guided by the time from the onset of stroke, the severity of neurologic deficit, and neuroimaging finding. The aim of this work was to investigate and identify factors affecting the functional outcome after using r-tPA in treatment of AIS in a sample of Egyptian patients. This prospective observational study was carried out on 60 AIS patients presented to emergency rooms and admitted to Neurology Departments at Badr University Hospital and Nasr City Hospital for Health Insurance. All patients were subjected to thorough history taking with complete general and neurological examination, laboratory assessment and neuroimaging. **Results:** The univariate analysis showed significant correlations between poor functional outcome and increased number of cardio-embolism subtype (p-value=0.009), large artery atherosclerosis subtype (p-value <0.001) and small artery occlusion (p-value<0.001). There were also significant correlation between good functional outcome 3 month after IV rtPA and higher number of small vessel occlusion subtype (p-value <0.02) and decreased number of large artery atherosclerosis (p-value <0.01) and cardio-embolism (p-value 0.02). Early administration of IV rtPA was associated with good outcome and decrease the mortality and morbidity, enhancement of modified risk factors improve the outcome of IV rtPA and decrease the incidence of recurrence of ischemic stroke. The study identified variations in functional outcomes based on stroke subtypes, with large artery atherosclerosis subtypes associated with worse outcomes compared to small artery occlusion subtypes.

Keywords: Clinical Outcome; Post-Thrombolysis; Acute Ischemic Stroke.

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1. Introduction

Acute ischemic stroke (AIS) is the second leading cause of death and a major cause of disability worldwide [1]. As the result of the widespread impact of stroke in patient's individual lives and financial cost on the economy, there are many efforts to improve acute ischemic stroke care aiming to decrease the morbidity and mortality [2]. The purpose in the first hours after the onset of AIS is to restore the blood flow so as to salvage the penumbra before it evolves into irreversibly damaged tissue, to prevent infarction and minimize the degree of permanent brain injury [3]. Treatment for patients with AIS is guided by the time from the onset of stroke, the severity of neurologic deficit, and neuroimaging finding. Recommended treatments in selected patients include intravenous (IV) thrombolysis recombinant tissue plasminogen activator (rtPA) and mechanical thrombectomy [4]. IV tissue-type plasminogen activator rtPA remains the guideline-recommended treatment to improve outcomes after AIS, especially in patients without proximal arterial occlusion, and is associated with low complication rates [5]. Up to 50% of all ischemic stroke patients initially present with mild or rapidly improving symptoms and a large proportion of these patients are not treated with IV rtPA, despite presenting within the 4.5hour time window [6].

Alteplase improves functional outcome at three to six months when given within 4.5 hours of ischemic stroke onset [7]. The benefit of rtPA for AIS decreases continuously over time from symptom onset, as shown in meta-analyses of randomized trials [8-9]. Also, in a registry that analyzed data from over 58,000 patients treated with rtPA within 4.5 hours of ischemic stroke symptom onset, each 15-minute reduction in the time to initiation of rtPA treatment was associated with improving morbidity and mortality [10]. However, this therapy is associated with an increased risk of hemorrhagic transformation (HT), which possibly worsens neurological deficit and leads to higher mortality but still the benefits will out weight the risks [10]. There has been an extensive investigation of prognostic indices of good outcomes that can be applied before, during, and after thrombolysis. known that factors, such as age, initial National Institutes of Health

Stroke Scale (NIHSS) score, and systolic blood pressure, are of predictive value for clinical outcome and symptomatic intracerebral hemorrhage [11]. The aim of this work was to investigate and identify factors affecting the functional outcome after using r-tPA in treatment of AIS in a sample of Egyptian patients.

2. Patients and Methods

This prospective observational study was carried out on 60 AIS patients presented to emergency rooms and admitted to Neurology Departments at Badr University Hospital and Nasr City Hospital for Health Insurance. Informed written consent was obtained from the patients. The study was done after approval from the Ethics Committee of the Faculty of Medicine, neurology Department from September 2022 to June 2023 (approval code:-117 2022). Inclusion criteria were AIS patients aged from 18 to 80 years old including both sexes presented within time window (first 4.5 hours from onset). Exclusion criteria were patient refuses giving consent or receiving r-tPA therapy, history of ischemic stroke, severe head trauma, intracranial or intra-spinal surgery in previous 3 months, gastrointestinal haemorrhage in last 3 weeks, major surgery or serious trauma other than CNS in previous 2 weeks, arterial puncture in non-compressible site or lumbar puncture in last week from onset, current use of DOAC in the last 48 hours.

Therapeutic doses of low molecular weight heparin received within 24 hours in addition to any neurological and/or psychiatric disorders interfere with outcome or functional assessment or pre-stroke mRS > 1, symptoms suggestive of subarachnoid haemorrhage or internal active bleeding, persistent elevated blood pressure (systolic ≥ 185 mmHg or diastolic ≥110 mmHg), stroke known or suspected to be associated with aortic arch dissection or presentation consistent with infective endocarditis, seizure at onset with postictal residual neurological impairments 22 ≤ or NIHSS < 4 or, platelet count <100.000/mm³, current anticoagulant use with an INR >1.7 or blood glucose concentration < 50 mg/dl or more then > 400 mg/dl and evidence of haemorrhage, multiple infarction (hypo density> 1/3 cerebral hemisphere) or extensive regions of obvious hypo density consistent with irreversible injury on head CT.

2.1. Clinical assessment

All patients were subjected to thorough history taking with complete general and neurological examination. Scoring on NIHSS (baseline on admission, after 24hours, and at 3 months (classified into mild NIHSS <8, moderate NIHSS ≤ 8 to ≤ 16 and severe NIHSS<16)), and scoring on mRS on admission, 24 hours and three months after receiving IV rtPA. The functional outcome among patients in this study was defined to be a good functional outcome (mRS 0 to 2 was) and poor functional outcome (mRS more than 3 to 6) [12]. Onset of door to needle (two groups: one group less than 60 minutes and the other group more the 60 minutes), major and minor complications after infusion of IV rtPA including symptomatic intra cerebral haemorrhage (sICH) which increases in NIHSS ≤ 4, decrease in consciousness level ≤1 or CT hyper dense area, and asymptomatic intra cerebral haemorrhage. All the studied patients underwent laboratory assessment including routine labs (random blood sugar, full chemistry, complete blood picture and INR) and neuroimaging including non-contrast CT brain at time of admission and after 24 hours or if any sign of deterioration of symptoms occurred, MRI brain with diffusion in some cases.

2.2. IV rtPA

Patient presented with AIS to emergency room, evaluated by stroke team using NIHSS scale, CT brain and laboratory investigation were performed for eligibility of IV rtPA, then start the IV rtPA thrombolytic therapy Actilyse® (Product Name) 50 mg 1 vial contains 50 mg Alteplase (Generic Name) and 1 vial of solvent contains 50 ml sterilized water for injections. The recommended total dose is 0.9 mg/kg body weight (maximum of 90 mg) infused starting with 10% of the total dose as an initial intravenous bolus immediately followed by the remainder of the total dose infused intravenously over 60 minutes.

2.3. Patient monitoring

Follow-up blood pressure every 15 minutes for 2 hours, every 30 minutes for 6 hours, and every hour for 16 hours and reassessment by NIHSS for any decline of consciousness or appearing of new neurological symptoms. Vital signs should be done every 30 minutes. The patient was transferred to ward after 24 hours with secondary preventive measures, assessment of swallowing and Nil Per Os (NPO) was performed and prophylaxis against DVT using intermittent stocking compression devices (SCDs) were conducted.

2.4. Statistical analysis

Data were analysed using Statistical Program for Social Science (SPSS) Version 20. Quantitative data were expressed as mean ±SD. Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used for comparing. Chi-square test for categorical variables to compare between different groups. Fisher's Exact or Monte Carlo correction: Correction for chi-square when more than 20% of the cells have expected < 5. Student t-test for normally distributed quantitative variables for comparing between two studied groups. Mann Whitney test used for abnormally distributed quantitative variables, to compare between two studied groups. Regression was used to detect the most independent/ affecting factor for good or poor outcome. P-value ≤ 0.05 was considered significant.

3. Results and discussion

3.1. Results

Regarding demographic data, age ranged from 25 to 80 years (Mean ± SD = 63.23 ± 11.50), predominant of male patients. The stroke severity measured by NIHSS at time of admission and 24 hours after receiving IV rtPA (median score 11 and 4 respectively), door to needle time 60 minutes or less was in 75 % of the cases while door to needle time more than 60 minutes was 25% of our patients. Post- IV rtPA symptomatic and asymptomatic intra cerebral haemorrhage occurred 10% of our patients (3.3% and 6.7% respectively) Table 1. NIHSS score at time of admission and 24 hours after receiving IV rtPA were found a high statistically significant association with the mRS score (p-value <0.001). This indicates that a higher NIHSS score at admission and 24 hours strongly associated with a poor functional outcome. Diabetes mellitus, hypertension and atrial fibrillation were significantly associated with poor out come when assessed with mRS at 3 months from IV rtPA therapy (p< 0.022, p=

0.008 and p=0.003 respectively). The mRS poor outcome after 3 months was statistically significant to presence of asymptomatic and symptomatic intra cerebral haemorrhage post IV rtPA (p-value= 0.001 and 0.013, respectively).

In terms of the TOAST classification of ischemic stroke, which categorizes strokes into five main subtypes based on etiology, statistically significant relationships were observed with large artery atherosclerosis towards poor outcomes(p-value <0.001), small artery occlusion and cardio-embolism toward a good outcomes (p-value <0.001 and p-value =007, respectively) Table 2. The results showed that the onset to needle less than 2 hours was associated with statistically significant improving in NIHSS score after 24 hours (p=0.02) with subsequent statistically improved in functional out come in this group when assessed by mRS score at 3 months after rtPA infusion (p-value= 0.03) when compared with patients with onset to needle>2hrs. While no significant difference was found between onset to needle and initial NIHSS Table 3. The univariate analysis showed the following variables were correlated with poor functional outcome: diabetes mellitus (p-value < 0.023), hypertension (p-value < 0.01), and atrial fibrillation (p-value = 0.04). The multivariate analysis of the study variables showed the following results: atrial fibrillation (p- value <0.001), hypertension (p-value= 0.001), diabetes mellitus (p-value =0.009) were the independent predictive risk factors of poor functional outcome.

However, no significant correlations were observed between poor functional outcome and other variables. The univariate analysis, the following variables exhibited significant correlations with poor functional outcome: increased NIHSS score at time of admission (p-value =0.01), increased NIHSS score 24 hours after receiving IV rtPA (p-value <0.001), and presence of post-IV rtPA intracerebral hemorrhage (symptomatic and asymptomatic) (p-value= 0.001). In the multivariate analysis, increased NIHSS score 24 hours after receiving IV rtPA (p-value =0.003) was the independent predictive risk factors of poor functional outcome. However, no significant correlations were observed between poor functional outcome and other variables Table 4. There were also significant correlations between the following variables and poor functional outcome; increased number of patients of diabetes (p-value= 0.03), hypertension (p-value= 0.009), atrial fibrillation (p-value= 0.004) and smoking (0.01) according to the univariate and multivariate analyses. Other variables did not show significant correlations with good functional outcome.

There were also significant correlations between the following variables and good functional outcome 3 months after IV rtPA; decreased NIHSS score at time of admission (P value <0.001), decreased NIHSS score 24 hours after receiving IV rtPA (P value <0.001), absence of post IV rtPA intracerebral hemorrhage (p value= 0.001). The multivariate analysis showed that decreased NIHSS score 24h after IV rtPA was the independent predictive risk factors of good functional outcome 3 months after IV rtPA Table 5. The univariate analysis showed significant correlations between poor functional outcome and increased number of cardio-embolism subtype (p-value=0.009), large artery atherosclerosis subtype (p-value <0.001) and small artery occlusion (p-value<0.001). There were also significant correlation between good functional outcome 3 month after IV rtPA and higher number of small vessel occlusion subtype (p-value <0.02) and decreased number of large artery atherosclerosis (p-value <0.01) and cardio-embolism (p-value 0.02). Other variables did not show significant correlations with good functional outcome Table 6.

3.2. Discussion

Acute ischemic stroke represents a significant global health concern, ranking as the second leading cause of mortality and the foremost specific cause of neurological disability worldwide [13]. The present study revealed that the mean age of studied cases was 63.23 ± 11.50 which was comparable to stroke studies by Dewan and Rana [14] (67.15±12.58 years). In contrast, privous studies in Nepal have reported lower mean ages [15]. This difference might be due to the difference in the sample size and the fact that patients included in these studies were younger than those included in our study. Regarding gender the present study showed predominant of male 35 (58.3%) patients and female 25 (41.7%) patients with no statistically significant difference between, gender disparities and the functional outcome three months following the administration of IV rtPA and that agree with Hametner and his colleagues [16], and disagree with Liu and his colleagues [17], that indicated women tend to exhibit less favorable functional outcomes after undergoing IV rtPA, as compared to men.

Our study showed that increased NIHSS score at the time of admission and 24 hours after receiving IV rtPA, was a significant predictors associated with poor outcome in univariate analysis. However, only increased NIHSS score 24 hours after receiving IV rtPA was the independent predictive risk factors of poor functional outcome. The multivariate analysis showed that decreased NIHSS score 24h after IV rtPA was the independent predictive risk factors of good functional outcome 3 months after IV rtPA. NIHSS score at the time of admission and 24 hours after receiving IV rtPA were found a high statistically significant association with the mRS score. This indicates that a higher NIHSS score at admission and 24 hours were strongly associated with a poor functional outcome. It was found that as the NIHSS score increased, there was a higher probability of poor functional outcome, and vice versa. In line with our findings, Tork and his colleagues [18] showed highly significant correlation between NIHSS score and the functional outcome, at time of admission, consequently categorical classification of stroke severity, and 24 h after receiving IV rtPA.

These correlations found in the univariate analysis but when multivariate analysis for the study variables was done, it showed that the NIHSS score 24 h after receiving IV rtPA was considered to be a strong independent predictor of the functional outcome, its increase was associated with poor functional outcome and vice versa, thus highly suggests that the initial clinical improvements in the first hours or 24 h after receiving IV rtPA is of great importance in determining the final degree of patient dependency in the future away from the degree of stroke severity at time of admission. Our study showed that the door to needle ≤ 60 minutes were in 45 (75%) patients while ≥ 60 minutes were in 15 (25%) patients, and onset to needle ≤ 2 hours was associated with a lower NIHSS after 24 hours (p-value=0.02) and favorable outcomes mRS score at 3 months after administration of IV rtPA (p-value= 0.03) and these was in agreement with Man et al. [19], while no significant difference found between onset to needle and initial NIHSS.

Table 1: Demographic data and baseline characteristics among patients in our study

		Statistic: n (%), Mean ± SD
Gender	**Male**	35(58.3%)
	Female	25(41.7%)
Age (Years)	**Min. – Max.**	25.0 – 80.0
	Mean ± SD.	63.23 ± 11.50
	Median (IQR)	63.0 (55.0 – 70.0)
NIHSS score at time of admission	**Min. – Max.**	4.0 – 22.0
	Mean ± SD.	11.55 ± 4.81
	Median (IQR)	11.0 (8.0 – 15.0)
NIHSS score 24 h after IV rtPA	**Min. – Max.**	0.0 – 22.0
	Mean ± SD.	6.25 ± 5.89
	Median (IQR)	4.0 (3.0 – 10.0)
Categorical classification of stroke (Severity classification)	**Mild**	12(20.0%)
	Moderate	40(66.7%)
	Severe	8(13.3%)
Door to needle time	**<60 min.**	45 (75.5%)
	≥60 min.	15(25.0%)
Time of receiving IV rtPA from stroke onset	**≤ 2 hr.**	5(8.33%)
	< 2hr –> 3 hr.	22(36.67%)
	3 hr.	13(21.67%)
	>3hr - ≤4.5hr.	20(33.33%)
Risk factor	**Hyperlipidemia**	28 (46.7%)
	Diabetes Mellitus	21(35.0%)
	Hypertension	35(58.3%)
	Atrial Fibrillation	12(20.0%)
	Coronary artery disease	15(25.0%)
	Smoking	28(46.7%)
Intra cerebral haemorrhage following IV rtPA	**Asymptomatic ICH**	4(6.7%)
	Symptomatic ICH	2(3.3%)
TOAST classification	**Large artery atherosclerosis**	19(31.7%)
	Small artery occlusion	20(33.3%)
	Cardio-embolism	14 (17.3%)
	Stroke of undetermined etiology	4 (23.3)
	Non atherosclerotic vasculopathy	2 (3.33%)
	Coagulopathy	1 (1.7%)
Functional outcome of IV rtPA	**Poor functional outcome (3 – 6)**	20 (33.3%)
	Good functional outcome (0–2)	40 (66.67%)
mRS score 3 months after IV rtPA	**0**	21(35%)
	1	10 (16.7%)
	2	9 (15.0%)
	3	9 (15.0%)
	4	8 (13.3%)
	5	3 (5.0%)
	6	0 (0.0%)

N, numbers; SD, standard deviation; IQR, Interquartile range; IV rtPA, intravenous Recombinant tissue plasminogen activator mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; TOAST, Trial of Org 10172 in Acute Stroke Treatment

Table 2: Relation between mRS and other variables

		mRS		Test	P-value
		≤2 (Good outcome) (n = 40)	**>2 (Poor outcome) (n = 20)**		
NIHSS score at time of admission	**Min. – Max.**	4.0 – 18.0	6.0 – 21.0	U= 827.50	**<0.001***
	Mean ± SD.	9.07 ± 3.43	13.62 ± 2.91		
NIHSS score 24 h after IV rtPA	**Min. – Max.**	0.0 – 9.0	5.0 – 21.0	U= 39.50*	**<0.001***
	Mean ± SD.	2.17 ± 1.95	11.04 ± 3.62		
Categorical classification of stroke severity at time of admission	**Mild**	11 (18.3%)	1 (1.7%)	χ^2= 15.35	**<0.001***
	Moderate	27 (45%)	13 (21.7%)		
	Severe	2 (3.3%)	6 (10.0%)		
Risk factors	**Hyperlipidemia**	18 (30%)	10 (16.7%)	χ2=1.039	0.308
	Diabetes	6 (10%)	15(25%)	**χ2=5.239***	**0.022***
	Hypertension	10 (16.7%)	25(41.7%)	**χ2=7.073***	**0.008***
	Atrial Fibrillation	4 (6.7%)	8 (13.3%)	**χ2=8.792***	**0.003***
	Coronary artery disease	7 (11.7%)	8 (13.3%)	χ2=2.827	0.093
	Smoking	15 (25%)	13 (21.7%)	χ^2=2.885	0.089
Intra cerebral haemorrhage following IV rtPA	**Asymptomatic intra cerebral haemorrhage**	1 (1.7%)	3 (5%)	χ^2=12.429*	**FEp=0.001***
	Symptomatic intra cerebral haemorrhage	0(0.0%)	2(3.3%)	χ^2=7.745*	**FEp=0.013***
TOAST classification	**Large artery atherosclerosis**	7 (17.5%)	12 (60%)	27.02*	**<0.001***
	Small artery occlusion	17 (42.5%)	3 (15%)	23.03*	**<0.001***
	Cardio-embolism	12 (30%)	2 (10%)	7.32*	**0.007***
	Stroke of undetermined etiology	3 (7.5%)	1 (5%)	3.38	0.068
Stroke of other determined etiology	**Non atherosclerotic vasculopathy**	1 (2.5%)	1 (5%)	0.20	FEp=1.000
	Coagulopathy	0 (0%)	1 (5%)	0.70	FEp=1.000

X2: Chi square test MC: Monte Carlo FE: Fisher Exact p: p value for comparing between the studied groups*: Statistically significant at $p \leq 0.05$, mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale, IV rtPA, intravenous Recombinant tissue plasminogen activator.

Table 3: Association between onset to needle and NIHSS score and mRS Score at 3 months

		Onset to needle		U-Test	P-value
		≤2 hrs.	**>2hrs.**		
NIHSS score at time of admission	**Min. – Max.**	5.0 – 22.0	4.0 – 22.0	U= 408.50	0.52
	Mean ± SD.	11.52 ± 4.59	12.28 ± 4.75		
NIHSS score after 24 hrs	**Min. – Max.**	4 – 20	2 – 22	U= 378.5	**0.02***
	Mean ± SD.	6.37 ± 4.43	8.65 ± 4.80		
MRS at 3 months	**Min. – Max.**	0.0 – 5.0	0.0 – 5.0	U= 415.0	**0.03***
	Mean ± SD.	1.56 ± 1.63	2.86 ± 1.61		

*: Statistically significant at $p \leq 0.05$, mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale

Table 4: Univariate and multivariate analysis between study variable and the poor functional outcome 3 months after IV rtPA

Variable type category	Univariate		Multivariate	
	P-value	OR (95% CI)	P-value	OR (95% CI)
Age	0.58	1.016 (0.982 – 1.050)	0.11	1.42(0.76-2.75
Male gender	0.42	1.304 (0.643 – 2.64)	0.37	2.5(0.85-3.6)
Hyperlipidemia	0.30	1.428 (0.719 – 2.834)	0.86	2.49(0.87-3.54
Diabetes	**<0.02***	2.254*(1.11 – 4.55)	**0.009***	2.805*(1.288–6.10)
Hypertension	**0.01***	2.526*(1.266 – 5.041)	**0.001***	3.65*(1.65 – 8.06)
Atrial Fibrillation	**0.04***	3.515*(1.48 – 8.31)	**<0.001***	6.28*(2.31 – 1.83)
Coronary artery disease	0.100	2.355 (0.850 – 6.526)	0.22	2.43(0.64-7.70)
Smoking	0.091	1.833 (0.907 – 3.70)	0,54	2.44(0.55-4.31)
NIHSS score 24 h after IV rtPA	**<0.001***	3.63*(2.10–6.27)	**0.003***	8.039*(2.01–32.07)
Categorical classification of stroke severity at time of admission	**0.01***	9.338*(3.31–26.32)	0.647	4.34 (0.008–2321.5)
NIHSS score at time of admission	**<0.001***	1.477*(1.297–1.68)	0.148	0.511 (0.206–1.26)
Time of receiving IV rtPA from stroke onset from (3–4.5 h)	0.647	0.864 (0.436–1.711)	0.87	0.67(0.54-2.34)
Intra cerebral haemorrhage following IV rtPA (symptomatic +asymptomatic)	**0.001***	29.10* (3.66–231.9)	0.570	0.034 (0.0–3907.1)

OR: Odds ratio, CI: Confidence interval, *: Statistically significant at $p \leq 0.05$; IV rtPA, intravenous Recombinant tissue plasminogen activator; mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale..

Table 5: Univariate and multivariate analysis between study variable and the good functional outcome 3 months after IV rtPA

Variable type category	Univariate		Multivariate	
	P-value	OR (95% CI)	P-value	OR (95% CI)
Age	0.35	0.88 (0.75 – 1.02)	0.21	0.96(0.98-1.65)
Female gender	0.462	1.30 (0.63 – 2.64)	0.63	2.13(0.51-2.96)
Hyperlipidemia	0.30	0.70 (0.35 – 1.39)	0.59	0.83(0.56-2.31)
Diabetes	**0.03***	0.54*(0.32 – 0.99)	**0.009***	0.35* (0.14 – 0.76)
Hypertension	**0.009***	0.39*(0.19 – 0.79)	**0.001***	0.27*(0.12 – 0.60)
Atrial Fibrillation	**0.004***	0.28*(0.12 – 0.67)	**<0.001***	0.15*(0.05 – 0.43)
Coronary artery disease	0.100	0.425 (0.153 – 1.17)	0.78	0.65 (0.15-2.31
Smoking	**0.01**	0.545 (0.27 –1.102)	0.54	0.87(0.51-1.68)
NIHSS score 24 h after IV rtPA	**<0.001***	0.275 (0.159–0.476)	**0.03***	0.124 (0.031 – 0.496)
Categorical classification of stroke severity at time of admission	**<0.001***	0.07 (0.03 – 0.50)	0.47	0.230 (0.0 – 123.17)
NIHSS score at time of admission	**<0.001***	0.67 (0.54 – 0.71)	0.48	1.95 (0.78 – 4.84)
Time of receiving IV rtPA from stroke onset (<3 hrs.)	0.647	0.86 (0.43 – 1.71)	0.34	0.99(0.78 - 2.67)
Absence of intra cerebral Haemorrhage following IV rtPA	**0.001***	0.03*(0.04 – 0.27)	0.57	26.10 (0.5– 451)

OR: Odds ratio, CI: Confidence interval, * Statistically significant at $p \leq 0.05$, IV rtPA, intravenous Recombinant tissue plasminogen activator; mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

Table 6: Univariate analysis between ischemic stroke etiological TOAST classification and the poor, good functional outcome 3 months after IV rtPA

Variable type category	Univariate	
	P-value	OR (95% CI)
Poor functional outcome		
Large artery atherosclerosis	**<0.001***	10.38*(3.84 – 28.07)
Small artery occlusion	**<0.001***	0.05*(0.01 – 0.25)
Cardio-embolism	**0.009***	3.20*(1.34– 7.63)
Stroke of undetermined etiology	0.07	2.02 (0.94 – 4.33)
Stroke of other determined etiology	0.94	1.06 (0.18 – 6.01)
Good functional outcome		
Large artery atherosclerosis	**<0.01***	0.03 (0.036 – 0.260)
Small artery occlusion	**<0.02***	5.35 (3.96 – 74.95)
Cardio-embolism	**0.02***	0.31 (0.13 – 0.74)
Stroke of undetermined etiology	0.07	0.49 (0.23 – 1.06)
Stroke of other determined etiology	0.84	0.24 (0.16 – 4.11)

OR: Odds ratio, CI: Confidence interval, * statistically significant at $p \leq 0.05$.

Despite dyslipidemia being recognized as a risk factor for ischemic stroke, the study showed no significant associations between dyslipidemia and functional outcomes observed three months following the administration of IV rtPA and this agree with Tai et al. [20]. While other studies revealed adversely affect correlation which based on formation of a non-soluble lipid-rich thrombus, which can lead to greater infarction and haemorrhagic transformation [21-22]. This study found no significant correlation between recent or current smoking and functional outcomes three months after receiving IV rtPA and this in agreement with Chiara et al. [23]. Our results revealed a significant negative correlation between hypertension (P value =0.008) and functional outcomes three months after IV rtPA treatment due to shift in perfusion auto regulation parameters as well as changes in collateral blood supplies. This correlation was evident not only in relation analysis but also in univariate (p value < 0.009) and multivariate analysis (p value= 0.001).this was agree with outcomes three months after receiving IV rtPA and this in agreement with Chiara et al. [23], while other studies did not found a significant correlation between a history of hypertension and functional outcomes due to both high blood pressure and low blood pressure were independent prognostic factors for poor outcome, relationships that appear to be mediated in part by increased rates of early recurrence and death resulting from presumed cerebral edema in patients with high blood pressure and increased coronary heart disease events in those with low blood pressure [20-24].

This study showed a significant negative correlation between diabetes mellitus (p value =0.022) and functional outcomes three months after receiving IV rtPA. This correlation was evident not only in relation analysis but also in univariate (p value 0.03) and multivariate analysis (p value 0.009) this was agree with Ali et al. [25]. Diabetes mellitus emerged as a potent and independent predictor factor of poor functional outcome in univariate and multivariate analysis. However, other studies did not show significant correlations between DM and functional outcome after receiving IV rtPA, but had showed a significant correlation between on admission hyperglycemia and poor functional outcome after receiving IV rtPA [23-26]. We showed a statically significant correlation between Atrial Fibrillation (P value=0.003) and poor functional outcomes 3 months after receiving IV rtPA. This correlation was evident not only in relation analysis but also in univariate (p value =0.04) and multivariate analysis (p value< 0.001) that was matched with Yue and colleagues [27] revealed that AF may amplify the risk of death and symptomatic intra cerebral haemorrhage while concurrently diminishing of favourable functional outcomes after stroke thrombolysis. Conversely, there a previoys study showed significant correlation between AF and favourable functional outcome after IV rtPA treatment [28]. The present study revealed that post- IV rtPA symptomatic and asymptomatic intra cerebral haemorrhage occurred 10% of our patients (3.3% and 6.7% respectively). This study showed significant negative correlations between post-rtPA (ICH) (asymptomatic and symptomatic) and the functional outcome 3 months following IV rtPA administration.

Furthermore, the univariate analysis revealed a significant correlation between post-rtPA (ICH) and poor functional outcomes at 3 months. However, in multivariate analysis failed to show a significant independent predictor of functional outcomes. This was comparable to previous study by Chen and his colleagues [29], they observed that 11% of sICH occurred within the first 12 hours. Our results revealed that a high statistically significant correlations between specific stroke subtypes and functional outcomes at 3 months following IV rtPA treatment. In relation analysis, a highly significant correlation was observed between large artery atherosclerosis (P value<0.001) subtypes associated with poor functional outcomes, these results were in agreement with Ong et al. [30], due to large core infarction and smaller penumbra, which associated with increase the risk of intra cerebral haemorrhage. Cardio-embolism (p value=0.007) and small artery occlusion (p value<0.001) subtypes associated with good functional outcome. Our study was in agreement with other studies that showed a good outcome of cardio embolic stroke and small artery occlusion after IV rtPA treatment [22]. Conversely, a highly significant correlation was observed between small artery occlusion and good functional outcomes in both relation and univariate analysis. These results agreement with Pan et al [31]. The current study had certail limitations, as relatively small sample size and a relatively short duration**.** Therefore, larger sample size is highly recommended and follow up time length is recommended to be longer.

4. Conclusions

Time is brain; early administration of IV rtPA was associated with good outcome and decrease the mortality and morbidity, enhancement of modified risk factors improve the outcome of IV rtPA and decrease the incidence of recurrence of ischemic stroke. Post-thrombolysis complications included asymptomatic, symptomatic intra cerebral haemorrhage and orolingual angioedema but still the benefits will out weight the risks. The study identified variations in functional outcomes based on stroke subtypes, with large artery atherosclerosis subtypes associated with worse outcomes compared to small artery occlusion subtypes.

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References

[1] M. Katan, A. Luft In *Global burden of stroke*, Seminars in neurology, 2018; Thieme Medical Publishers. 38: 208-211.

[2] V.L. Feigin, M. Brainin, B. Norrving, S. Martins, R.L. Sacco, W. Hacke, M. Fisher, J. Pandian, P. Lindsay. (2022). World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. Int J Stroke. 17(1): 18-29.

[3] J.C. Baron. (2019). Author Correction: Protecting the ischaemic penumbra as an adjunct to thrombectomy for acute stroke. Nat Rev Neurol. 15(3): 184.

[4] W.J. Powers, A.A. Rabinstein, T. Ackerson, O.M. Adeoye, N.C. Bambakidis, K. Becker, J. Biller, M. Brown, B.M. Demaerschalk, B. Hoh, E.C. Jauch, C.S. Kidwell, T.M. Leslie-Mazwi, B. Ovbiagele, P.A. Scott, K.N. Sheth, A.M. Southerland, D.V. Summers, D.L. Tirschwell. (2019). Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 50(12): e344-e418.

[5] M.G. Lansberg, E. Bluhmki, V.N. Thijs. (2009). Efficacy and safety of tissue plasminogen activator 3 to 4.5 hours after acute ischemic stroke: a metaanalysis. Stroke. 40(7): 2438-41.

[6] A.Y. Yu, M.D. Hill, S.B. Coutts. (2015). Should minor stroke patients be thrombolyzed? A focused review and future directions. Int J Stroke. 10(3): 292-7.

[7] K.R. Lees, J. Emberson, L. Blackwell, E. Bluhmki, S.M. Davis, G.A. Donnan, J.C. Grotta, M. Kaste, R. von Kummer, M.G. Lansberg, R.I. Lindley, P. Lyden, G.D. Murray, P.A. Sandercock, D. Toni, K. Toyoda, J.M. Wardlaw, W.N. Whiteley, C. Baigent, W. Hacke, G. Howard. (2016). Effects of Alteplase for Acute Stroke on the Distribution of Functional Outcomes: A Pooled Analysis of 9 Trials. Stroke. 47(9): 2373-9.

[8] J. Emberson, K.R. Lees, P. Lyden, L. Blackwell, G. Albers, E. Bluhmki, T. Brott, G. Cohen, S. Davis, G. Donnan, J. Grotta, G. Howard, M. Kaste, M. Koga, R. von Kummer, M. Lansberg, R.I. Lindley, G. Murray, J.M. Olivot, M. Parsons, B. Tilley, D. Toni, K. Toyoda, N. Wahlgren, J. Wardlaw, W. Whiteley, G.J. del Zoppo, C. Baigent, P. Sandercock, W. Hacke. (2014). Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 384(9958): 1929-1935.

[9] M. Goyal, M. Almekhlafi, D.W. Dippel, B.C.V. Campbell, K. Muir, A.M. Demchuk, S. Bracard, A. Davalos, F. Guillemin, T.G. Jovin, B.K. Menon, P.J. Mitchell, S. Brown, P. White, C. Majoie, J.L. Saver, M.D. Hill. (2019). Rapid Alteplase Administration Improves Functional Outcomes in Patients With Stroke due to Large Vessel Occlusions. Stroke. 50(3): 645-651.

[10] J.L. Saver, G.C. Fonarow, E.E. Smith, M.J. Reeves, M.V. Grau-Sepulveda, W. Pan, D.M. Olson, A.F. Hernandez, E.D. Peterson, L.H. Schwamm. (2013). Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. Jama. 309(23): 2480-2488.

[11] M.J. Molina, L.T. Molina. (2004). Megacities and atmospheric pollution. Journal of the Air & Waste Management Association. 54(6): 644-680.

[12] J.L. Banks, C.A. Marotta. (2007). Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke. 38(3): 1091-1096.

[13] V.L. Feigin, B. Norrving, G.A. Mensah. (2017). Global Burden of Stroke. Circ Res. 120(3): 439-448.

[14] K.R. Dewan, P.V. Rana. (2014). A study of seven day mortality in acute ischemic stroke in a teaching hospital in Chitwan. J Nepal Health Res Counc. 12(26): 33-38.

[15] V. Pathak, R. Kanth, H. Pant. (2006). Stroke: a case series study in Nepal Medical College Teaching Hospital. Nepal Med Coll J. 8(3): 180-181.

[16] C. Hametner, L. Kellert, P.A. Ringleb. (2015). Impact of sex in stroke thrombolysis: a coarsened exact matching study. BMC Neurol. 15: 10.

[17] M. Liu, G. Li, J. Tang, Y. Liao, L. Li, Y. Zheng, T. Guo, X. Kang, M. Yuan. (2018). The Influence of Sex in Stroke Thrombolysis: A Systematic Review and Meta-Analysis. J Clin Neurol. 14(2): 141-152.

[18] M.A. Tork, H.M. Aref, H.M. El-Khawas, M.F. Khalil, A. ElSadek. (2020). Outcome predictors of intravenous thrombolytic therapy in acute ischemic stroke patients: an Egyptian center experiences. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 56: 1-10.

[19] S. Man, Y. Xian, D.N. Holmes, R.A. Matsouaka, J.L. Saver, E.E. Smith, D.L. Bhatt, L.H. Schwamm, G.C. Fonarow. (2020). Association Between Thrombolytic Door-to-Needle Time and 1-Year Mortality and Readmission in Patients With Acute Ischemic Stroke. Jama. 323(21): 2170-2184.

[20] M.-L.S. Tai, K.J. Goh, K.A.A. Kadir, M.I. Zakaria, J.F. Yap, K.S. Tan. (2019). Predictors of functional outcome in patients with stroke thrombolysis in a

tertiary hospital in Malaysia. Singapore medical journal. 60(5): 236.

[21] A. Mehta, R. Mahale, K. Buddaraju, A. Majeed, S. Sharma, M. Javali, P. Acharya, R. Srinivasa. (2017). Intravenous Thrombolysis for Acute Ischemic Stroke: Review of 97 Patients. J Neurosci Rural Pract. 8(1): 38-43.

[22] M. Çetiner, H.E. Aydin, M. Güler, S. Canbaz Kabay, Y. Zorlu. (2018). Predictive Factors for Functional Outcomes After Intravenous Thrombolytic Therapy in Acute Ischemic Stroke. Clin Appl Thromb Hemost. 24(9_suppl): 171s-177s.

[23] B. Chiara, C. Guillaume, R. Gwendoline, M. Marie-Helene, S. Laurent. (2018). Predictors of clinical outcome after intravenous thrombolysis in ischemic stroke without large vessel occlusion: the role of admission glycemia. Mathews Journal of Emergency Medicine. 3(1): 1-6.

[24] M. Mehrpour, M. Afrakhte, S.F. Shojaei, A. Sohrabi, R. Ashayeri, S. Esmaeili, M. Bahadori. (2019). Factors predicting the outcome of intravenous thrombolysis in stroke patients before rt-PA administration. Caspian J Intern Med. 10(4): 424-430.

[25] S.F. Ali, K. Siddiqui, H. Ay, S. Silverman, A. Singhal, A. Viswanathan, N. Rost, M. Lev, L.H. Schwamm. (2016). Baseline predictors of poor outcome in patients too good to treat with intravenous thrombolysis. Stroke. 47(12): 2986-2992.

[26] H. El-Khawas, A. Nasef, A. Gaber. (2006). Department of Neurology, Ain Shams University. Admission Hyperglycemia in Acute Ischemic Stroke: Effects on Short Term Prognosis. Egypt J Neurol Psychiat Neurosurg. 43(1): 603-613.

[27] R. Yue, D. Li, J. Yu, S. Li, Y. Ma, S. Huang, Z. Zeng, R. Zeng, X. Sun. (2016). Atrial Fibrillation is Associated With Poor Outcomes in Thrombolyzed Patients With Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. Medicine (Baltimore). 95(10): e3054.

[28] S.-F. Sung, Y.-W. Chen, M.-C. Tseng, C.-T. Ong, H.-J. Lin. (2013). Atrial fibrillation predicts good functional outcome following intravenous tissue plasminogen activator in patients with severe stroke. Clinical Neurology and Neurosurgery. 115(7): 892-895.

[29] P.M. Chen, B. Lehmann, B.C. Meyer, K. Rapp, T. Hemmen, R. Modir, K. Agrawal, L. Hailey, M. Mortin, D.M. Meyer. (2019). Timing of symptomatic intracerebral hemorrhage after rt-PA treatment in ischemic stroke. Neurology: Clinical Practice. 9(4): 304-308.

[30] C.T. Ong, Y.S. Wong, C.S. Wu, Y.H. Su. (2017). Outcome of stroke patients receiving different doses of recombinant tissue plasminogen activator. Drug Des Devel Ther. 11: 1559-1566.

[31] Y.T. Pan, J.D. Lee, Y.H. Lin, Y.C. Huang, H.H. Weng, M. Lee, C.Y. Wu, H.L. Hsu, H.T. Yang, C.Y. Hsu, T.H. Lee, S.J. Liu, T.Y. Peng, C.W. Liou, K.C. Chang, Y.C. Huang. (2016). Comparisons of outcomes in stroke subtypes after intravenous thrombolysis. Springerplus. 5: 47.