Factors predicting poor functional outcome in patient with acute ischemic stroke treated with recombinant tissue plasminogen activator

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Abstract

Background: Ischemic stroke may account for about 85% of all strokes. Recombinant tissue plasminogen activator (rTPA) remains the main standard medical treatment of acute ischemic stroke (AIS). It has the ability to restore brain circulation due to its thrombolytic effect. Narrow therapeutic window is usually responsible for low treatment rate of rTPA. Many researchers believe that many stroke risk factors have an impact on development of ischemic stroke, but they do not contribute to permanent functional disability after rTPA. **Objectives:** to study clinical predictors of poor functional outcome in AIS patients treated with rTPA. **Methods:** a hospital-based study in Minia University Hospital over period of one year duration on patients who having AIS and treated with rTPA. **Results:** 32 patients fulfilled the inclusion criteria over the period of the study. There was significant relation between outcome and Age, hypertension (HTN) and National institute of Health stroke scale (NIHSS) at admission, in which their higher values related to poor outcome. **Conclusion:** Age & HTN and NIHSS at admission were the factors in which higher value related to poor outcome.

Key words: Acute ischemic stroke, outcome, rTPA.

Introduction

Acute ischemic stroke is a prominent cause of morbidity and mortality globally and is a time sensitive medical emergency[1]. rTPA remains the gold standard medical treatment of AIS[2]. rTPA is useful within 4.5 hours of symptom onset in proper patients[3]. Low treatment rate is mainly due to limited time window for rTPA[4]. However, not all patients experience a good functional outcome with rTPA. The presence of stroke risk factors may influence the outcome[5]. some studies[6, 7] demonstrate that Diabetes mellitus (DM), HTN, Atrial fibrillation (AF), hyperlipidemia and Coronary heart disease (CHD) are not prognostic factors for outcome. In other researches[8, 9] AF, CHD and dyslipidemia are related to outcome. This study aimed to study clinical predictors of poor functional outcome in patients treated with rTPA.

Patients and methods:

This is a hospital-based study which was carried out in stroke unit, Neurology department, Minia University Hospital, in the period from1st of October 2022 to 30 th of September 2023. The inclusion criteria include both sex aged 18

years or more and diagnosed as having AIS and treated with rTPA. The exclusion criteria include patients who did not receive full dose of rTPA, patients did not complete rTPA administration due to occurrence of complication or refusal of patients or their caregivers to participate in the study.

All patients underwent complete assessment included complete history taking from the patients or their caregivers, complete general examination and full neurological examination including, NIHSS at baseline before rTPA administration. For outcome evaluation we used the modified rankin scale (mRS) at 90 days after rTPA administration. The outcome classified according to mRS into good(favorable) outcome (mRS:0-2) and poor(unfavorable) outcome (mRS:3-6). Contraindications for rTPA administration and laboratory tests were checked before rTPA include CBC and coagulation profile to exclude any risk of bleeding. Radiological assessment by non-contrast computed tomograghy (NNCT) before rTPA and after 24 hours.

Ethical consideration:

The protocol of the thesis got the approval of the ethical committee at Minia University.

All subjects have given their consent as regard participation in the study or their caregivers.

Approval number: 840:7/2023.

Statistical analysis:

Data analysis was done by the Statistical Package for Social Sciences (SPSS) IBM Inc., Chicago, Illinois, USA Version 24.0 for Windows. Descriptive statistics: Frequencies and percentages were calculated for categorical variables, while means and standard deviations were calculated for continuous variables. The level of statistical significance was established at $p \leq 0.05$.

Results:

Thirty-two patients fulfilled the inclusion criteria during the study period.

The outcome after rTPA based on modified rankin scale (mRS) in relation to demographic and clinical data find that there was significant relation between outcome and Age and HTN, in which their higher value related with Poor outcome. **Table (1)**

The outcome of stroke in relation to stroke severity as measured by NIHSS at admission and find that there is significant relation between outcome and NIHSS at admission, in which higher NIHSS at admission related to poor outcome with P value <0.001. **Table (2) & Figure (1)**

Univariate and multivariate binary logistic regression analysis for predictors of poor outcome demonstrate that presence of HTN, older age and higher baseline NIHSS were associated with poor outcome after rTPA, but on multivariate analysis only HTN and higher baseline NIHSS were significant (OR=3.4; 95%CI=1.8 – 10.9, P=0.03, and OR=1.7; 95%CI=1.06 – 2.7, P=0.02) respectively. **Table (3)**

Table (1) Comparison between demographic and clinical data and outcome after rTPA based on Modified Rankin Scale (mRS)

Baseline data		Good outcome (n=19)	Poor outcome (n=13)	P value
Age	Mean ± SD	53.3±13	61.3±11.9	0.05*
	Range	30:73	39:75	
Sex	Male	10(52.6%)	7(53.8%)	0.94
	Female	9(47.4%)	6(46.2%)	

Smoking	Non-smoker	14(73.7%)	9(69.2%)	0.78
	Smoker	5(26.3%)	4(30.8%)	
Comorbidities	HTN	8(42.1%)	10(76.9%)	0.05*
	DM	7(36.8%)	8(61.5%)	0.16
	Hyperlipidemia	10(52.6%)	5(38.5%)	0.43
	VHD	3(15.8%)	0(0%)	0.13
	Coronary artery disease	3(31.6%)	3(23.1%)	0.59
	AF	6(31.6%)	5(38.5%)	0.68
Past history of stroke or TIA		3(15.8%)	2(15.4%)	0.97

* Significant at p value <0.05, IV rTPA; intravenous recombinant tissue plasminogen activator, SD; standard deviation, HTN; hypertension, DM; diabetes mellitus, VHD; valvular heart disease, AF; atrial fibrillation, TIA; transient ischemic attack.

Table (2) comparison between cases with good outcome and poor outcome regarding NIHSS at admission

NIHSS at admission	Good outcome (n=19)	Poor outcome (n=13)	P value
Mean ± SD	9.2±4.6	14.4±4	
Median (Range)	8(3:18)	16(7:20)	<0.001*

* Significant at p value <0.05, SD; standard deviation, NIHSS; national institute of health stroke scale.
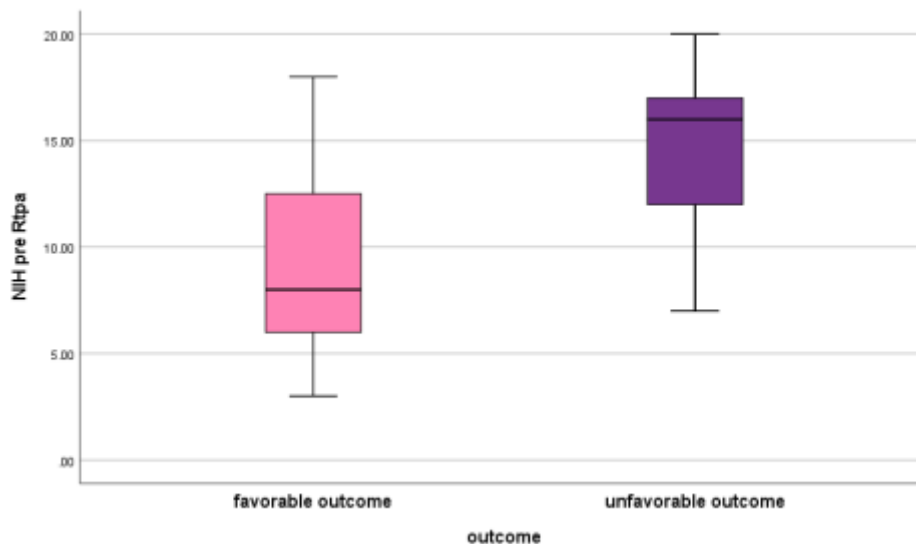

Figure (1): box plot represent comparison between cases with good outcome and poor outcome regarding NIHSS at admission

Table (3) Univariate and Multivariate binary logistic regression analysis for predictors of unfavorable outcome

Independent variables	Dependent variable (unfavorable outcome)					
	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.05	1.01-1.09	**0.006***	1.02	0.97-1.07	0.29
Gender(male)	0.57	0.23-1.4	0.22			
Smoker	1.2	0.42-3.4	0.72			
HTN	3.4	1.3-9.4	**0.02***	3.4	1.8-10.9	**0.03***
DM	1.5	0.62-3.7	0.35			
Hyperlipidemia	1.36	0.55-3.3	0.49			
Past history of stroke	0.46	0.11-1.9	0.29			
NIHSS baseline	1.26	1.12-1.42	**<0.001***	1.7	1.06-2.7	**0.02***

OR odd ratio, CI; confidence interval, * significant at p value <0.05,

HTN; hypertension, DM; diabetes milletus, NIHSS; national institute of health stroke scale

Discussion:

This is a hospital-based study that included 32 patients who were diagnosed as having AIS and received rTPA and aimed to study clinical predictors of poor functional outcome.

The study revealed that there was significant relation between outcome and age and HTN, in which their higher value related with poor outcome.

While there was no significant relation between outcome and sex, smoking, DM, Hyperlipidemia, VHD, coronary artery disease, AF, past history of stroke or TIA. While there was no significant relation between outcome and sex, smoking, DM, Hyperlipidemia, VHD, coronary artery disease, AF, past history of stroke or TIA.

In accordance with Elsayed et al., 2019 who found that advanced age correlated significantly with poor outcome at 3 month in AIS patients who received rTPA[10].

Also, agreed with Bhardwaj et al., 2017 who demonstrate that in AIS patients, advanced age is an independent predictor of a poor prognosis following rTPA. He also found that

51.6% of patients with a median age of 75 years had a poor outcome and 48.4% of patients with a median age of 60 years had a favorable outcome which was statistically significant [11].

As well, Hamed et al., 2024 found that the demographics associated with poor outcomes were AF, high blood pressure upon presentation, a history of stroke, and dyslipidemia[12].

Furthermore, Mehrpour et al., 2019 reported that advanced age, higher SBP on admission, AF and history of CAD could be the independent predictors of outcome after rTPA in AIS patients[13].

Additionally, Abdel-Monem et al., 2020 found that age≥ 60 years is independent predictors of poor outcome in AIS patients with P value =0.012[14].

Also, satumanatpan et al., 2022 showed that older age, HTN, DM and AF were linked to poor outcomes following rTPA and acted as good predictors of patient functional outcomes[15].

As Regard the comparison between cases with good outcome and poor outcome measured by NIHSS at admission, this study revealed that there was significant relation

between outcome and NIHSS at admission, in which higher NIHSS at admission related to poor outcome.

In agreement with Mehrpour et al., 2019 who investigated whether the outcome of intravenous thrombolytic therapy after three months in AIS patients who are candidates for rTPA can be predicted based on their risk factors prior to rTPA administration and the result showed a highly significant relationship, with a higher NIHSS at admission being associated with a poorer outcome[13].

According to Elsayed et al., 2019, individuals with AIS receiving rTPA had a strong correlation between their functional outcome at three months and their clinical assessment upon admission using NIHSS. Thus, it is a powerful and reliable predictor of the outcome of an early stroke[10].

Conclusion:

Age, HTN, and NIHSS at admission all showed significant relationships with outcome in the current study; a greater value was associated with a poorer outcome. This conclusion was supported by the logistic regression analysis, which revealed that higher baseline NIHSS, older age, and the presence of HTN were linked to unfavorable outcomes following rTPA.

Our data will help medical practitioners to expect outcome after rTPA administration and may explain why sometimes thrombolysis failed even if the patients came in the therapeutic window for rTPA, but still more researches are needed to determine other clinical predictors that could affect the outcome of rTPA.

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Limitations of study:

The limitations of the current study were that it was performed in a single center, in which small number of AIS patients had received rTPA. The inclusion criteria were limited to research of standard dose of rTPA (0.9 mg/kg) only. Also, relatively short period of time of patient follows up (3 months).

Funding:

Conflict of interest:

The authors have no conflicts of interest to declare.

List of abbreviations:

rTPA: Recombinant tissue plasminogen activator
AIS: Acute ischemic stroke
NIHSS: National institute of Health stroke scale
DM: Diabetes mellitus
HTN: Hypertension
AF: Atrial fibrillation
CHD: Coronary heart disease
mRS: Modified Rankin scale
NNCT: Non-contrast computed tomograghy
SPSS: Statistical Package for SocialSciences

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