

Type of the Paper (Systemic review)

Prognostic Factors Affecting the Clinical Course and Short-term Outcome of Acute Ischemic Stroke Patients Receiving Thrombolytic Therapy

Mohamed E. El-Khatib¹, Sayed Sobhy¹, Mahmoud I. Aboelnor², Asmaa Mohammed³,
Mohammed Gomaa^{1*}

¹Department of Neurology, Faculty of Medicine, Fayoum University, Fayoum 63511, Egypt.

²Department of Radiology, Faculty of Medicine, Fayoum University, Fayoum 63511, Egypt.

³Department of Medical Biochemistry & Molecular Biology, Faculty of Medicine, Fayoum University, Fayoum 63511, Egypt.

*Correspondence: Mohammed Gomaa, mgd00@fayoum.edu.eg, Tel: (002) 01010509700.

Received: 24 March, 2024

Accepted: 15 May, 2024

Reviewed: 1 May, 2024

Published online: 30 Sep, 2024

Abstract:

Introduction: There is limited data on prognostic factors of acute ischemic stroke (AIS) patients treated with thrombolytic therapy.

Aim of the study: This study aimed to illustrate the prognostic parameters of AIS individuals who received intravenous recombinant tissue plasminogen activator (IV rt-PA).

Subjects and Methods: Forty-five AIS patients eligible for receiving IV rt-PA underwent a complete neurological examination, CT brain, extra-cranial carotid duplex, stroke severity utilizing National Institutes of Health Stroke Scale (NIHSS), disability evaluation using modified Rankin Scale(mRS) 3 months post-stroke and routine lab tests.

Results: 18 patients (40%) had unfavorable outcomes (mRS >2), while 27 patients (60%) had favorable outcomes (mRS 0-2). unfavorable outcome was observed among patients with abnormal mean common carotid intima-media thickness (CIMT > 8 mm), dyslipidemia, obesity, old age, diabetes mellitus (DM), and increased NIHSS score at admission and 24 h after IV rt-PA. while a favorable outcome was identified in patients with hypertension and atrial fibrillation (AF). DM, common CIMT And NIHSS at admission and 24 h following IV rt-PA were all significant independent predictors of functional outcome at three months post-stroke according to multivariable linear regression analysis ($p < 0.05, 0.01, 0.02, 0.04, \text{ and } 0.000$, respectively).

Conclusions: Abnormal common CIMT, DM, stroke severity, dyslipidemia, obesity, and increased patient age demonstrated a relationship with an unfavorable outcome. At the same time, AF and hypertension were correlated with a favorable outcome. NIHSS at admission and 24 h following IV rt-PA, DM, and common CIMT can be employed as independent predictors of functional outcome

Keywords: Functional outcome; Acute ischemic stroke; carotid intima media thickness; Thrombolytic therapy.

1. Introduction

Stroke is a commonly occurring neurological disorder that is associated with unfavorable consequences. This disorder is widely acknowledged as the primary factor contributing to acquired disability and is the second most common cause of illness globally [1]. The most efficacious therapy for persons with acute ischemic stroke (AIS) is recombinant tissue plasminogen activator (rt-PA) [2]. Previous research has shown that rt-PA has beneficial independent effects in addition to its thrombolytic effect on the functional recovery of individuals with acute ischemic stroke (AIS), which may be associated with neuroplasticity

[3]. Conducting a comprehensive evaluation of stroke is crucial in assessing the prognosis of patients and identifying the most appropriate treatment strategies to improve patient outcomes [4].

The objective of this study was to assess the predictive significance of vascular risk factors and functional outcome indicators in individuals undergoing intravenous thrombolytic treatment. This research was motivated by the limited availability of data regarding prognostic variables for acute ischemic stroke patients who have received thrombolytic therapy.

2. Subjects and Methods

2.1. Subjects

The present research is a prospective observational longitudinal study that was carried out from February 2019 to March 2022. A cohort of 54 consecutive eligible patients presented with acute ischemic stroke within the therapeutic range for rt-PA therapy (during the first 4.5 hours), with no contraindication for rt-PA injection and ≥ 18 years old were included in our study. The selection of these patients was conducted according to the standards set out by The

American Heart Association/American Stroke Association [10]. Three patients refused to share in the current study, five patients lost throughout the follow-up period and a solitary patient passed away following the occurrence of a myocardial infarction leading to a cumulative count of 45 individuals (ranging in age from 29 to 78 years) who successfully adhered to the study protocol and underwent statistical analysis. The participants in this study were selected from the stroke care unit at Fayoum

University Hospital. The patients who satisfied the established criteria were subjected to intravenous administration of rt-PA at the prescribed dose of 0.9 mg/kg.

Inclusion and Exclusion criteria

criteria patients presented with acute ischemic stroke within the therapeutic range for rt-PA therapy (during the first 4.5 hours), with no contraindication for rt-PA injection and ≥ 18 years old were included in our study. The selection of these patients was conducted following the standards set out by The American Heart Association/American Stroke Association [10]

2.2. Study design

Participants were divided into two groups based on their assessment using a modified Rankin Scale (mRS) after a 3-month follow-up period. Group 1 consisted of 27 patients who had favorable outcomes ($mRS \geq 2$), whereas Group 2 consisted of 18 patients who had unfavorable outcomes ($mRS > 2$).

2.3. Methods

Upon arriving at the hospital, all participants were subjected to a collection of demographic information related to their age and sex, along with a medical background including risk factors such as diabetes mellitus (DM), hypertension, dyslipidemia,

body mass index, smoking, and previous strokes. These data were gathered at the start of the study. During the course of the experiment, participants had an assessment of their cerebrovascular risk factors.

The diagnosis of diabetes mellitus was established for a person by considering the following criteria: fasting blood glucose (FBG) levels above 126 mg/dL, 2-hour postprandial plasma glucose levels above 200 mg/dL, and HbA1c values falling above 6.5%. Participants who have provided self-reported information on a medical background of diabetes mellitus diagnosed by a physician or a self-reported history of using antihyperglycemic medication. The diagnosis of individuals with hypertension was conducted following the guidelines set out by The American College of Cardiology/American Heart Association/American Public Health Association [7]. The study included two categories: self-reported use of antihypertensive medicine and a clinically determined history of hypertension. Indicators of dyslipidemia encompass a previous occurrence of hyperlipidemia within the previous year, self-reported utilization of lipid-lowering medication, a self-reported background of physician-diagnosed hypercholesterolemia, elevated

levels of high-density lipoprotein (HDL-C) below 1.04 mmol/L, elevated levels of low-density lipoprotein (LDL-C) above 3.37 mmol/L, elevated levels of triglycerides (TG) above 1.70 mmol/L, or elevated levels of total cholesterol (TC) exceeding 5.18 mmol/L [8]. The participants in our study were categorized into three groups: persons with a normal weight and a body mass index (BMI) ranging from 18.5 to 24 kg/m², individuals who were overweight with a BMI ranging from 24 to 30 kg/m², and those who were obese with a BMI of 30 kg/m² or higher [9]. The National Survey on Drug Use and Health defined "current smoking" as the act of using tobacco or cigarettes during the last 30 days [10].

The National Institutes of Health Stroke Scale (NIHSS) was used to perform a thorough evaluation of stroke severity upon hospital admission and 24 hours following intravenous (IV) r-TPA [11,12].

A battery of routine laboratory testing is performed, including a lipid profile, renal function assessments, random blood glucose levels, uric acid levels, glycosylated hemoglobin levels, international normalized ratio (INR) measurements, complete blood count, and liver function tests. All patients had a computed tomography (CT) scan of the

brain without contrast using the Canon Aquilion Prime SP technology from Japan to assess the extent of the ischemia infarction and exclude any structural abnormalities or bleeding. The assessment was conducted in a supine position without the administration of contrast agents. The procedure included the acquisition of axial images spanning from the base of the skull to the vertex, subsequently followed by sagittal and coronal reconstruction.

During the patient's hospitalization, the Neurology Department at Fayoum University used the Philips HD 11 XE ultrasound equipment, manufactured in Germany, to perform duplex ultrasonography on the extra-cranial arteries. The carotid arteries were scanned using a linear array transducer within a high-frequency range of 3-12 MHz. The measurements chosen for examination were denoted as common carotid intima-media thickness (CIMT). A plaque-free site on the distal wall of the common carotid artery, situated at a distance more than 1.5 cm from the bifurcation, was used to quantify the intima-media thickness. The typical intima-media thickness was determined using a cut value of 0.8 mm. Furthermore, a comprehensive assessment was performed on the common carotid and internal carotid

arteries to assess the presence of plaque, while also examining its surface characteristics and reduction in diameter. The pulsed duplex examination was used in the research to assess the waveform and flow pattern inside the carotid arteries. Furthermore, an assessment was conducted on the vertebral arteries to ascertain their patency and validate the existence of antegrade flow. To exclude the existence of ischemic heart disease and atrial fibrillation (AF), cardiac examinations have used either a 12-lead electrocardiogram (ECG) or a 24-hour Holter test. At the end of the third month, the functional status and impairment were evaluated using a modified version of the Rankin Scale (mRS) [13,14]. The individuals underwent daily surveillance for a period of one week after the first incident, followed by weekly surveillance for a maximum length of three months.

2.4. Statistical Methods

Before being input into Microsoft Access and analyzed using SPSS V22

(SPSS Inc., Chicago, Illinois, USA), the data were gathered and coded to enhance data processing. The qualitative data was subjected to a basic descriptive analysis, using percentages and numerical values. The p-value has a statistical significance of 0.05. The standard deviation was used to quantify the quantitative parametric data, whereas the dispersion arithmetic mean was utilized to assess the central tendency. Before undertaking inferential statistical analysis, the researchers used the one-sample Kolmogorov-Smirnov test to evaluate the normality of the quantitative data within each study group. To compare two or more qualitative groups, the chi-square test was used. The t-test was used to compare quantitative variables between two separate groups in the setting of independent samples. The researchers used the bivariate Pearson correlation test to assess the relationship between the variables.

3. Results

This research was carried out on 45 individuals aged between 29 and 78. Their mean age range was 55.3 ± 14.9 years. Their

sex distribution was 64.4% males and 35.6% females (**Table 1**).

Table 1: Demographics and baseline characteristics.

	Variables	n = 45 (%)
Age	Range	29-78
	Mean \pm SD	55.3 \pm 14.9
Gender	Male	29 (64.4%)
	Female	16 (35.6%)
Comorbidities	HTN ^a	25 (55.6%)
	DM ^b	16 (35.6%)
	AF ^c	11 (24.4%)
	Dyslipidemia	17 (37.8%)
	Smoking	15 (33.3%)
BMI ^d	Normal	15 (33.3%)
	Overweight	17 (37.8%)
	Obese	13 (28.9%)
Mean carotid IMT ^e	Range (mm)	0.6-1.25
	Mean \pm SD	0.94 \pm 0.17
	Normal (< 8 mm)	10 (22.2%)
	Abnormal (> 8 mm)	35 (77.8%)
NIHSS ^f score at the time of admission	Minor stroke (1-4)	0 (0%)
	Moderate stroke (5-15)	39 (86.7%)
	Moderate to severe (16-20)	6 (13.3%)
	Severe stroke (21-42)	0 (0%)
NIHSS score 24h after IV rt-PA	Minor stroke (1-4)	8 (17.8%)
	Moderate stroke (5-15)	35 (77.8%)
	Moderate to severe (16-20)	2 (4.4%)
Intracerebral hemorrhage following IV rt-PA	Asymptomatic intracerebral hemorrhage	5 (11.1%)
	symptomatic intracerebral hemorrhage	0 (0%)
mRS ^g 3 months post-stroke	Favorable(mRS<2)	27 (60%)
	Unfavorable(mRS>2)	18 (40%)

^aHTN: hypertension; ^bDM: diabetes mellitus; ^cAF: atrial fibrillation; ^dBMI: body mass index; ^eCIMT: Carotid Intima-Media Thickness; ^fNIHSS: National institutes of health stroke scale; ^gmRS: modified Rankin score

Comparing NIHSS scores before IV rt-PA in different risk factors of stroke

demonstrated a statistically significant correlation between NIHSS score and

common CIMT, DM, and level of obesity, with higher scores among patients with abnormal common CIMT, DM, and obesity ($p < 0.05$). In contrast, there were no significant differences concerning sex, hypertension, atrial fibrillation (AF), dyslipidemia, or smoking ($p > 0.05$). Moreover, AF patients were associated with a lower NIHSS (Table 2).

Comparisons of NIHSS scores 24 h following IV rt-PA in different risk factors of stroke revealed a significant association

between NIHSS score after intervention and common CIMT, DM, dyslipidemia, smoking, and level of obesity, with higher scores among patients with abnormal common CIMT, DM, dyslipidemia, smoking and obesity ($p < 0.05$)

Unlikely, there were no significant differences concerning hypertension, sex, and AF ($p > 0.05$). Lower NIHSS was found among patients with AF and hypertension (Table 2).

Table 2: Comparisons of NIHSS score before and after IV rt-PA in different stroke risk factors.

Variables		Before IV rt-PA	P-value	24 h after IV rt-PA	P-value
Gender	Male	11 ±3.2	0.13	8.5 ±2.4	0.36
	Female	12.4 ±2.7		9.7 ±3.8	
Mean CIMT	Normal (< 8mm)	9.3 ±2.9	0.009*	6.1 ±3.8	0.01*
	Abnormal (≥ 8)	12.1 ±2.9		9.7 ±3.8	
HTN	No	11.3 ±3.2	0.69	9.15 ±4.1	0.75
	Yes	11.7 ±3.03		8.76 ±4.1	
DM	No	10.1 ±2.5	0.001*	7.2 ±3.8	<0.001*
	Yes	14.1 ±2.5		12.1 ±2.2	
AF	No	11.9 ±3.2	0.19	9.1 ±4.1	0.72
	Yes	10.5 ±2.6		8.6 ±4.3	
Dyslipidemia	No	11 ±3.1	0.15	8 ±4.1	0.04*
	Yes	12.4 ±2.9		10.5 ±3.6	
Smoking	No	11.04 ±2.9	0.14	8.1 ±3.9	0.04*
	Yes	12.5 ±3.2		10.7 ±3.8	
BMI groups	Normal	10.1 ±2.8	0.01*	5.2 ±4.2	0.001*
	Overweight	11.2 ±2.5		10.1 ±1.8	
	Obese	13.5 ±3.3		11.8 ±2.8	

HTN: hypertension; DM: diabetes mellitus; AF: atrial fibrillation; BMI: body mass index; CIMT: Carotid Intima-Media Thickness; NIHSS: National Institutes of Health stroke scale.

Comparisons of the mRS score after three months of stroke and different stroke risk factors illustrated significant associations between the mRS score and common CIMT, DM, dyslipidemia, and obesity with unfavorable outcomes among patients with abnormal common CIMT,

DM, dyslipidemia, and obesity ($p < 0.05$). Although there were no significant differences concerning sex, hypertension, AF, or smoking, a more favorable outcome was found among patients with AF and hypertension (**Table 3**).

Table 3: Comparisons of the mRS score after three months and different stroke risk factors.

Variables	Before IV rt-PA		P-value	
	Favorable	Unfavorable		
Gender	Male	19 (70.4%)	10 (55.6%)	0.35
	Female	8 (29.6%)	8 (44.4%)	
Mean CIMT	Normal (< 8mm)	10 (37%)	0 (0%)	<0.003*
	Abnormal (≥ 8)	17 (63%)	18 (100%)	
HTN	No	12 (44.4%)	8 (44.4%)	0.99
	Yes	15 (55.6%)	10 (55.6%)	
DM	No	26 (96.3%)	3 (16.7%)	< 0.001*
	Yes	1 (3.7%)	15 (83.3%)	
AF	No	18 (66.7%)	16 (88.9%)	0.16
	Yes	9 (33.3%)	2 (11.1%)	
Dyslipidemia	No	21 (77.8%)	7 (38.9%)	0.01*
	Yes	6 (22.2%)	11 (61.1%)	
Smoking	No	20 (74.1%)	10 (55.6%)	0.22
	Yes	7 (25.9%)	8 (44.4%)	
BMI groups	Normal	14 (51.9%)	1 (5.6%)	0.005*
	Overweight	8 (29.6%)	9 (50%)	
	Obese	5 (18.5%)	8 (44.4%)	

HTN: hypertension; DM: diabetes mellitus; AF: atrial fibrillation; BMI: body mass index; CIMT: Carotid Intima-Media Thickness; NIHSS: National Institutes of Health stroke scale.

The correlation between disease severity and functional outcome determined via the NIHSS and mRS, respectively on one hand and the patient's age, BMI, and common CIMT on the other hand illustrated a significant positive correlation between the

NIHSS score at admission and (BMI, IMT, NIHSS following 24 h and mRS three months post-stroke), which indicated an increase in BMI and IMT would be associated with an increase in the NIHSS scores at admission ($p < 0.05$). In addition,

an increase in NIHSS scores at admission will be associated with an increase in NIHSS and mRS scores after intervention. Unlikely, no significant correlation was determined between NIHSS level at admission and patient age ($p >0.05$). Moreover, it illustrates a significant positive correlation between NIHSS level after 24 h

and mRS score after three months of follow-up with patient variables such as age, BMI, CIMT, and NIHSS at admission, which indicated an increase in all these variables would be associated with an increase in NIHSS scores after 24 h IV rt-PA and mRS scores after three months post-stroke follow-up ($p <0.05$) (Table 4).

Table 4: Correlation between disease severity and disability scores and patient variables.

	Stroke severity and disability scores					
	NIHSS Before intervention		NIHSS After intervention		mRS after three months	
	r	P-value	r	P-value	R	P-value
Age (years)	0.21	0.16	0.43	0.003*	0.52	0.001*
BMI (kg/m²)	0.38	0.01*	0.55	0.001*	0.58	0.001*
Mean CIMT (mm)	0.56	0.001*	0.59	0.001*	0.72	0.001*

BMI: body mass index; CIMT: Carotid Intima-Media Thickness; NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin score

Using a multivariate linear regression model for investigating the explanatory power of various risk factors in the prediction of the functional outcome as determined by the mRS score after three months of follow-up ($R^2 =0.929$, $p < 0.001$)

revealed significant predictors for DM, common CIMT and NIHSS scores at admission and after 24 h of IV rt-PA injection with p -values < 0.05 (0.01, 0.02, 0.04, and 0.000, respectively) (Table 5).

Table 5: Multivariate linear regression analysis to assess different risk factors' power in predicting MRS outcomes.

Model	Unstandardized coefficients		Standardized coefficients	T	Sig.
	B	Std. Error	Beta		
(Constant)	-0.515-	0.631		-0.816-	0.420
Age	-0.002-	0.006	-0.027-	-0.328-	0.745
DM	0.574	0.219	0.247	2.619	0.013*
Dyslipidemia	0.095	0.165	0.041	0.576	0.568
BMI	0.001	0.018	0.003	0.036	0.971
CIMT on admission	1.610	0.680	0.239	2.370	0.023*
NIHSS on admission	-0.074-	0.036	-0.204-	-2.084-	0.044*
NIHSS after 24 h	0.200	0.027	0.727	7.454	0.000*

DM: diabetes mellitus; BMI: body mass index; CIMT: Carotid Intima-Media Thickness; NIHSS: National Institutes of Health Stroke Scale; mRS: modified Rankin score.

4. Discussion

Acute ischemic stroke (AIS) is a well-known catastrophic neurological illness that has been associated with significant consequences for people afflicted by it, their caregivers, and the whole economy of the country. Recent breakthroughs in treatment have had an impact on the prognosis and outcome. Thrombolytic therapy with IV rt-PA is the predominant therapeutic approach for individuals diagnosed with AIS within the designated timeframe. [15]

The present study revealed a significant association between the mean CIMT and stroke severity assessed by the NIHSS score (at the time of admission and

24 hours after the administration of intravenous rt-PA) and functional outcomes (by the mRS score) after three months of intravenous rt-PA indicated that individuals with increased common CIMT were correlated with a more severe stroke and a more unfavorable prognosis. Furthermore, applying the multivariate linear regression model analysis to examine the explanatory power of different risk variables on the outcome prediction evaluated by the mRS, after a three-month period demonstrated that the common CIMT had a noteworthy and autonomous prediction capacity for unfavorable functional outcome ($p < 0.05$).

The potential effectiveness of the stroke outcome prediction model may be enhanced by using common CIMT as a predictor for functional outcomes. These findings of this study agreed with the research conducted by Heliopoulos et al., which demonstrated a positive association between the median CIMT and stroke severity as evaluated by the NIHSS upon admission, as well as unfavorable functional outcome three months post-stroke determined by the mRS. Hence the higher the common CIMT, the more severe the neurological impairment at the beginning of the stroke and the worse the functional outcome at short-term follow-up. According to other researchers, high common CIMT and NIHSS values at admission highly indicated short-term functional impairment and mortality after three months of AIS. The aforementioned results highlight the considerable significance of these indicators in predicting clinical outcomes of AIS [16,17]. On the other hand, Ellul et al. provided evidence indicating that there was no correlation between increased common CIMT and worse functional outcomes in both short and long follow-up periods after an AIS [18]. The disagreement that has been noticed may be explained by differences in mean age and sample size.

This research found no significant correlations between hypertension and NIHSS at admission, NIHSS 24 hours after IV rt-PA, and mRS three months following stroke. However, it revealed that hypertension was linked to decreased stroke severity and more favorable outcome. This finding supports previous studies that have shown that the reduction of blood pressure in the first phase of stroke is either ineffective or detrimental [19-21]. The results of our study differ from those of Cisse et al., who reported a negative correlation between the likelihood of a favorable stroke outcome and the mean arterial blood pressure [22]. Research has shown that the variability in systolic and diastolic blood pressure experienced by patients with AIS throughout their hospital stay hurts their functional results following their discharge. Nevertheless, the precise etiology of this observation in medical therapies remains unclear. Hence, it is crucial to provide individualized patient treatment, since the reduction of blood pressure levels results in heightened fluctuations in blood pressure [23]. Following current recommendations, those considered suitable for reperfusion should demonstrate permissive blood pressure <

185/110 mmHg and up to 220/120 mmHg to provide sufficient cerebral perfusion [24].

Significant associations were seen between NIHSS at admission, 24 hours after intravenous rt-PA, and mRS three months following AIS about diabetes mellitus (DM). The results of this study indicate that persons diagnosed with diabetes exhibit elevated levels of stroke severity and encounter worse functional outcomes. The use of multivariate linear regression analysis demonstrated that DM had a strong and independent predictive association with worse functional outcomes after a stroke. The results were consistent with previous research, which showed that increased blood glucose levels at admission hurt functional outcomes [25,26]. In addition, the stroke-monitoring study experiment demonstrated that individuals diagnosed with DM had higher levels of impairment, a more unfavorable clinical course, and increased rates of mortality [27]. Furthermore, a study conducted by Thoren et al. revealed a significant association between cerebral edema and blood glucose levels at admission in individuals undergoing intravenous thrombolytic therapy (28). The results may be attributed to the observed decrease in fibrinolysis and increase in serum plasminogen activator inhibitor 1

concentration. In addition, it has been shown that increased levels of glucose might hinder the integrity of the blood-brain barrier [29,30].

Although there was no significant correlation between AF and NIHSS (at admission and 24 h post IV rt-PA) or mRS three months post-stroke, patients with AF had lower NIHSS and better outcomes. These findings agreed with those in earlier studies, where cardiac-originating embolisms were richer in fibrin than those originating from atherosclerotic plaques, which were rich in platelets. The embolic thrombus was more soluble when interacting with rt-PA, which might explain why AF patients demonstrated better functional outcomes (31,32). Similar to the results of this study, Frank and his colleagues discovered that AF was not a reliable indicator of poor outcomes (33). Other researchers found that those with AF had a worse outcome than those without (34-37) and discovered an association between AF and poor outcomes. AF with stroke increases the possibility of hemorrhagic transformation because of old or large thrombi, poor collateral circulation, and large infarct size, and some AF patients might be administered an anticoagulant medication before IVT, which could

increase the possibility of bleeding (37). Moreover, Molina and Montaner showed earlier proximal middle cerebral artery recanalization in individuals suffering from cardiac embolic stroke compared to other stroke subtypes following treatment with rt-PA (38). These contradictions may be explained by differences in sample size and duration of follow-up periods in these researches.

In addition, there were significant correlations seen between NIHSS scores 24 hours after intravenous rt-PA, mRS scores three months following stroke, and dyslipidemia. Individuals with dyslipidemia exhibited higher NIHSS scores and had worse functional outcomes. The findings of this study are consistent with other research, which indicated that people diagnosed with dyslipidemia had inferior results after intravenous rt-PA treatment [26,32]. It is thought to originate from a lipid-rich thrombus that is not soluble due to a high level of platelet, potentially leading to hemorrhagic transformation and worse outcomes [39].

A significant correlation was seen between stroke severity measured by NIHSS scores after IV rt-PA and smoking, with smoker patients exhibiting higher NIHSS

scores. The findings of this study align with the research conducted by Matsuo et al., which indicated that those who had smoked in the past or continue to smoke are more prone to experiencing poor functional results after undergoing AIS. Daily cigarette usage seems to increase the likelihood of experiencing a negative functional result [40].

In the current study, there were significant associations between (NIHSS at admission, NIHSS 24 h post IV rt-PA, and mRS three months post-stroke) and level of obesity (BMI) with more severe stroke and unfavorable outcomes among overweight and obese patients.

In contrast, Peng Zhang et al. demonstrated that there was no observed survival benefit associated with obesity or overweight status after an AIS, as compared to individuals with a normal weight. There was no statistically significant difference seen in the likelihood of mortality and functional impairment between people classified as obese and overweight. After experiencing a stroke, being underweight was shown to be associated with an increased likelihood of mortality and functional disability [41]. Furthermore, a study conducted by Doehner et al. revealed

that individuals who were classified as obese or overweight had a stroke and exhibited enhanced non-fatal functional status and overall survival. These inconsistent results were explained by the limited inclusion of AIS patients without either TIA or hemorrhagic stroke in this study. Furthermore, Doehner et al. performed a further investigation of outcome factors using telephone interviews and questionnaires. Moreover, research showcasing the beneficial impacts of obesity often assessed the functional result over extended periods (years) and disregarded the influence and documentation of comorbidities. [42].

In our study, we observed notable positive associations between NIHSS (pre and post-rt-PA administration) and mRS score three months later. These findings suggest that an elevation in admission NIHSS scores are linked to heightened stroke severity 24 hours after IV rt-PA and

5. Conclusion

Intravenous r-TPA has emerged as a reliable treatment in the setting of acute ischemic strokes. Stroke severity at admission, abnormal common CIMT, DM, dyslipidemia, obesity and rising patient age were associated with unfavorable functional

unfavorable functional outcomes three months later. Functional prognosis among patients receiving rt-PA is highly predicted by NIHSS scores at admission or 24 hours post-IV rt-PA. The findings aligned with the study conducted by Cetiner and colleagues., who said that NIHSS is a reliable and reputable measure that researchers acknowledge for evaluating AIS patients who are suitable for rt-PA [32].

The present study is subject to the following constraints: Given the limited sample size of patients at a single site, it is imperative to do future research with a larger number of patients from other stroke centers. The duration of the 3-month follow-up period using the mRS score was rather brief to a certain degree. Consequently, extending the follow-up time and including other scales to assess patient outcomes might provide more reliable and comparable findings on patients' functional status.

outcomes, while AF and hypertension were associated with favorable functional outcomes. NIHSS at admission and 24 h after receiving IV rt-PA, DM, and common CIMT may be employed as an independent predictor of functional outcome.

Ethics approval and consent to participate:

The Research Ethical Committee approved the study and informed consent at the Faculty of Medicine, Fayoum University, Egypt (February 17, 2019; session number: D192).

Funding: This study is not funded.

Conflicts of Interest: All authors declare they have no conflicts of interest.

References

1. Alawieh A, Zhao J, Feng W. Factors affecting post-stroke motor recovery: implications on neurotherapy after brain injury. *Behav Brain Res.* 2018;340:94-101. doi:10.1016/j.bbr.2016.09.002
2. Satumanatpan N, Tonpho W, Thiraratnanukulchai N, Chaichanamongkol P, Lekcharoen P, Thiankhaw K. Factors Associated with Unfavorable Functional Outcomes After Intravenous Thrombolysis in Patients with Acute Ischemic Stroke. *Int J Gen Med.* 2022;15:3363-3373. doi: 10.2147/IJGM.S362116.
3. Meiner Z, Sajin A, Schwartz I, Tsenter J, Yovchev I, Eichel R, et al. Rehabilitation outcomes of stroke patients treated with tissue plasminogen activator. *PM R.* 2010;2:698-702. doi:10.1016/j.pmrj.2010.03.015.
4. Chang YJ, Lin CM, Ou YH, Liu CK, Chen WL, Chang SL. Carotid duplex parameters to predict long term outcomes of ischemic stroke patients receiving intra-arterial thrombectomy treatment. *Medicine (Baltimore).* 2019;98(20):e15734. doi: 10.1097/MD.00000000000015734.
5. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 50:e344–e418. doi:10.1161/STR.0000000000000211
6. American Diabetes Association (2011) Diagnosis and classification of diabetes mellitus. *Diabetes Care* 34(Suppl 1):S62–S69. doi:10.2337/dc11-S062.
7. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018 Jun. 71(6):e13-e115. Doi:10.1161/HYP.000000000000006.
8. Rao W, Su Y, Yang G, Ma Y, Liu R, Zhang S, Wang S, Fu Y, Kou C, Yu Y, Yu Q. Cross-Sectional Associations between Body Mass Index and Hyperlipidemia among Adults in Northeastern China. *Int J Environ Res Public Health.* 2016;13(5):516. doi: 10.3390/ijerph13050516.
9. World Health Organization. Global Database on Body Mass Index: BMI Classification. 2006 [cited 2022 July 27]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

10. Ryan H, Trosclair A, Gfroerer J. Adult current smoking: differences in definitions and prevalence estimates—NHIS and NSDUH. *Int J Environ Res Public Health*. 2012;9(7):1481-1491. doi:10.3390/ijerph9071481.
11. Lyden P, Brott T, Tilley B, Welch KM, Mascha EJ, Levine S, Haley EC, Grotta J, Marler J. Improved reliability of the NIH Stroke Scale using video training. NINDS TPA Stroke Study Group. *Stroke*. 1994;25(11):2220-2226. doi:10.1161/01.str.25.11.2220.
12. Lyden P, Lu M, Jackson C, Marler J, Kothari R, Brott T, Zivin J. Underlying structure of the National Institutes of Health Stroke Scale: results of a factor analysis. NINDS tPA Stroke Trial Investigators. *Stroke*. 1999;30(11):2347-2354. doi:10.1161/01.STR.30.11.2347.
13. Bonita R, Beaglehole R. Modification of Rankin Scale: recovery of motor function after stroke. *Stroke*. 1988;19(12):1497-1500. doi:10.1161/01.STR.19.12.1497.
14. Van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, Van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*. 1988;19(5):604-607. doi:10.1161/01.STR.19.5.604.
15. Lloyd-Sherlock P. Stroke in developing countries: epidemiology, impact and policy implications. *Dev Policy Rev*. 2010;28(6):693-709. doi:10.1111/j.1467-7679.2010.00503.x.
16. Lehmann ALCF, Alfieri DF, de Araújo MCM, Trevisani ER, Nagao MR, Pesente FS, Gelinski JR, de Freitas LB, Flauzino T, Lehmann MF, Lozovoy MAB, Breganó JW, Simão ANC, Maes M, Reiche EMV. Carotid intima media thickness measurements coupled with stroke severity strongly predict short-term outcome in patients with acute ischemic stroke: a machine learning study. *Metab Brain Dis*. 2021;36(7):1747-1761. doi:10.1007/s11011-021-00784-7.
17. Guo X-J, Wu M, Pei S-F, Xie P, Wu M-Y. Influence of carotid intima-media thickness levels at bifurcation on short-term functional outcomes among non-cardiogenic ischemic stroke patients with and without type 2 diabetes mellitus. *Diabet Metab Syndr Obes*. 2022;15:897-905. doi:10.2147/DMSO.S352258.
18. Ellul J, Talelli P, Terzis G, Chrysanthopoulou A, Gioldasis G, Papapetropoulos T. Is the common carotid artery intima-media thickness associated with functional outcome after acute ischaemic stroke? *J Neurol Neurosurg Psychiatry*. 2004;75(8):1197-1199. doi:10.1136/jnnp.2003.017558.
19. Nasi LA, Martins SCO, Gus M, Weiss G, de Almeida AG, Brondani R, Rebello LC, DalPizzol A, Fuchs FD, Valença MJM, Wirth LF, Nunes G, Anderson CS. Early Manipulation of Arterial Blood Pressure in Acute Ischemic Stroke (MAPAS): Results of a Randomized Controlled Trial. *Neurocrit Care*. 2019;30(2):372-379. doi:10.1007/s12028-018-0642-5.
20. Wang H, Tang Y, Rong X, Li H, Pan R, Wang Y, Peng Y. Effects of early blood pressure lowering on early and long-term outcomes after acute stroke: an updated meta-analysis. *PLoS One*. 2014;9(5):e97917. doi:10.1371/journal.pone.0097917.
21. Oliveira-Filho J, Silva S, Trabuco C, Pedreira BB, Sousa EU, Bacellaret A, Carvalho EM. Detrimental effect of blood pressure reduction in the first 24 hours of acute stroke onset. *Neurology*. 2003;61(8):1047-1051. doi:10.1212/01.WNL.0000086813.69709.E1.

22. Cisse FA, Ligot N, Conde K, Barry DS, Toure LM, Konate M, Minga CA, Balde MD, Diallo MB, Barry MS, Diallo MS, Boiro D, Cisse AA, Balde MJ. Predictors of stroke favorable functional outcome in Guinea, results from the Conakry stroke registry. *Sci Rep.* 2022;12(1):1-7. doi:10.1038/s41598-022-08128-2.
23. Pedro T, Pereira P, Costa AS, Almeida F, Loureiro ML, Alfaiate T, Carvalho P, Rodrigues B, Fonseca C, Faria C. Systolic blood pressure variability within 120 hours of admission predicts the functional outcomes at discharge of patients with acute ischemic stroke. *J Neurocrit Care.* 2022;15:32-38. doi:10.18700/jnc.210020.
24. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brunger JW, Cushman M, Demaerschalk BM, Hoh BL, Jauch EC, Leira EC, Levitt AJ, Likosky DJ, Lloyd-Jones D, Matsumoto J, Mckenna P, Qureshi AI, Ross MA, Saver JL, Schneck MJ, Summers DV, Tirschwell DL. 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.* 2019;50:e344-e418. doi:10.1161/STR.0000000000000211.
25. Bruno A, Levine SR, Frankel MR, Brott TG, Lin Y, Tilley BC, Lyden PD, Broderick JP, Kwiatkowski T, Koroshetz WJ. Admission glucose level and clinical outcomes in the NINDS rt-PA Stroke Trial. *Neurology.* 2002;59:669-674. doi:10.1212/WNL.59.5.669.
26. Mehta A, Mahale R, Buddaraju K, Majeed A, Sharma S, Javali M, Acharya P, Rajalingappa R. Intravenous thrombolysis for acute ischemic stroke: review of 97 patients. *J Neurosci Rural Pract.* 2017;8:38-43. doi:10.4103/0976-3147.196442.
27. Trost S, Pratley RE, Sobel BE. Impaired fibrinolysis and risk for cardiovascular disease in the metabolic syndrome and type 2 diabetes. *Curr Diabetes Rep.* 2006;6:47-54. doi:10.1007/s11892-006-0037-3.
28. Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, Hennerici MG, Kaste M, Kuelkens S, Larrue V, Lees KR, Roine RO, Soenne L, Toni D, Vanhooren G. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet.* 2007;369:275-282. doi:10.1016/S0140-6736(07)60149-4.
29. Krzyt ND, Biessels GJ, DeVries JH, Roos YB. Hyperglycemia in acute ischemic stroke: pathophysiology and clinical management. *Nat Rev Neurol.* 2010;6:145-155. doi:10.1038/nrneuro.2010.17.
30. Thorén M, Azevedo E, Dawson J, Egidio JA, Falcou A, Ford GA, Grond M, Hennerici MG, Launhardt H, Lees KR, Toni D, Wahlgren N, Ahmed N. Predictors for cerebral edema in acute ischemic stroke treated with intravenous thrombolysis. *Stroke.* 2017;48:2464-2471. doi:10.1161/STROKEAHA.117.017564.
31. Zhao Q, Li X, Dong W, Ye M, Cao Y, Zhang M, Yuan R, Liu Z, Zhang W, Zhang Y. Factors associated with thrombolysis outcome in ischemic stroke patients with atrial fibrillation. *Neurosci Bull.* 2016;32:145-152. doi:10.1007/s12264-016-0004-x.
32. Çetiner M, Aydın HE, Güler M, Kabay SC, Zorlu YA, Aytar H, Bekar A, Alagöz F. Predictive

- factors for functional outcomes after intravenous thrombolytic therapy in acute ischemic stroke. *Turk J Cerebrovasc Dis.* 2018;24:171S-177S. doi:10.5505/tbdhd.2018.19088.
33. Frank B, Fulton R, Weimar C, Shuaib A, Lees KR, VISTA Collaborators. Impact of atrial fibrillation on outcome in thrombolized patients with stroke: evidence from the Virtual International Stroke Trials Archive (VISTA). *Stroke.* 2012;43:1872-1877. doi:10.1161/STROKEAHA.111.648725.
34. Saposnik G, Gladstone DJ, Raptis R, Zhou L, Hart RG. Atrial fibrillation in ischemic stroke: predicting response to thrombolysis and clinical outcomes. *Stroke.* 2013;44:99-104. doi:10.1161/STROKEAHA.112.668574.
35. Findler M, Molad J, Bornstein NM, Auriel E. Worse outcome in patients with acute stroke and atrial fibrillation following thrombolysis. *Neurol Res.* 2017;19:293-295. doi:10.1080/17431343.2017.1290484.
36. Padjen V, Bodenat M, Jovanovic DR, Ponchelle-Dequatre N, Novakovic N, Cordonnier C, Bracard S, Leys D, Hénon H. Outcome of patients with atrial fibrillation after intravenous thrombolysis for cerebral ischaemia. *J Neurol.* 2013;260:3049-3054. doi:10.1007/s00415-013-7101-7.
37. Hu Y, Ji C. Efficacy and safety of thrombolysis for acute ischemic stroke with atrial fibrillation: a meta-analysis. *BMC Neurol.* 2021;21:1-11. doi:10.1186/s12883-021-02137-4.
38. Molina CA, Montaner J, Arenillas JF, Ribo M, Rubiera M, Alvarez-Sabín J, Romero F, Codina A. Differential pattern of tissue plasminogen activator-induced proximal middle cerebral artery recanalization among stroke subtypes. *Stroke.* 2004;35:486-490. doi:10.1161/01.STR.0000110317.25547.0E
39. Urbach H, Hartmann A, Pohl C, Omran H, Wilhelm W, Schild HH. Local intra-arterial thrombolysis in the carotid territory: does recanalization depend on the thromboembolus type? *Neuroradiology.* 2002;44:695-699. doi:10.1007/s00234-002-0783-8.
40. Matsuo R, Ago T, Kiyuna F, Sato N, Nakamura K, Kuroda J, Wakisaka Y, Kitazono T. Smoking status and functional outcomes after acute ischemic stroke. *Stroke.* 2020;51:846-852. doi:10.1161/STROKEAHA.119.028172.
41. Zhang P, Yan XL, Qu Y, Guo ZN, Yang Y. Association between abnormal body weight and stroke outcome: a meta-analysis and systematic review. *Eur J Neurol.* 2021;28(8):2552-2564. doi:10.1111/ene.14881.