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Outcome predictors of intravenous thrombolytic therapy in acute ischemic stroke patients: an Egyptian center experiences

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Abstract

Background: Intravenous thrombolytic therapy remains the guideline-recommended treatment to improve outcomes after acute ischemic stroke. However, the functional outcome among patients with acute ischemic stroke after receiving intravenous thrombolytic therapy is influenced by huge variety of factors, and this was the aim of our study to evaluate the outcome predictors of intravenous thrombolytic therapy in a sample of Egyptian patients with acute ischemic stroke.

Methods: We enrolled 183 acute ischemic stroke patients who were treated with intravenous recombinant tissue plasminogen activator (IV rtPA) according to the last updated guidelines of American Heart Association and American Stroke Association (AHA/ASA) from February 2018 to February 2020; however, only 150 patients of them completed our study plan till the end. Data of study variables were collected, analyzed statistically and correlated with the functional outcome 3 months after receiving IV rtPA using the modified Rankin Scale (mRS).

Results: Good functional outcome was seen in 98 (65.3%) patients and poor functional outcome was seen in 52 (34.7%) patients. Multivariate analysis of the study variables was done to detect the significant independent predictors of the functional outcome. Atrial fibrillation (AF) (*P* value < 0.001*OR 6.28* (95% C.I)), hypertension (*P* value 0.001*OR 3.65*(95% C.I)), diabetes mellitus (DM) (*P* value 0.009*OR 2.805*(95% C.I)), increased National Institute of Health Stroke Scale (NIHSS) score 24 h after receiving IV rtPA (*P* value 0.003* OR 8.039* (95% C.I)), increased pulsatility index (PI) value in cerebral vessels at the same side of stroke lesion (*P* value 0.038* OR 42.48*(95% C.I)) were the significant independent predictors of poor functional outcome. On the other hand decreased NIHSS score 24 h after receiving IV rtPA (*P* value 0.003* OR 0.124*(95% C.I)), Normal value of PI in cerebral vessels at the same side of stroke lesion (*P* value 0.038* OR 42.48*(95% C.I)) were the significant independent predictors of good functional outcome.

Conclusion: Intravenous thrombolytic therapy improves the functional outcome of acute ischemic stroke patients. Also, AF, hypertension, DM, NIHSS 24 h after receiving IV rtPA and PI could be used as independent predictors of the functional outcome.

Keywords: Acute ischemic stroke, Thrombolytic therapy, Pulsatility Index, Functional outcome predictors

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Introduction

Stroke is the second most common cause of death, and accounts for 11% of total deaths in 2015 and the fifth leading cause of death in the USA, also more than 80% of strokes are ischemic strokes [1, 2]. Stroke burden on families and society was projected to rise from approximately 38 million disability-adjusted life years (DALYs) lost globally in 1990 to 61 million DALYs in 2020 due to population ageing and is projected to further rise till 2030 [3]. In Egypt, the most populated nation in the Middle East, the overall crude prevalence rate of stroke is high (963/100,000 inhabitants) [4]. The official national statistics indicate that diseases of the circulatory system, including stroke, are the primary cause of death in Egypt [5].

Intravenous thrombolytic therapy remains the guideline-recommended treatment to improve outcomes after acute ischemic stroke, especially in patients without proximal arterial occlusion, and is associated with low complication rates [6]. Intravenous thrombolytic therapy improves functional outcome at three to six months when given within 4.5 h of ischemic stroke onset [7]. There has been an extensive investigation of prognostic indices of good outcomes that can be applied before, during, and after thrombolysis [8]. The benefit of intravenous thrombolysis for acute ischemic stroke decreases continuously over time from symptom onset, as shown in meta-analyses of randomized trials [9, 10].

It is well known that factors, such as age, initial NIHS S score, and systolic blood pressure, are of predictive value for clinical outcome and symptomatic intracerebral hemorrhage (sICH) [11]. Magnetic resonance imaging (MRI), computed tomography (CT), and transcranial doppler (TCD) have also been used as possible prognostic determinant tools. In particular, arterial occlusion, recanalization, and reocclusion, among other factors, have been investigated in terms of outcome prediction [12]. We aimed in this study to evaluate the functional outcome of intravenous thrombolytic therapy in a sample of Egyptian patients with acute ischemic stroke and correlate it with possible predictors.

Methods

We enrolled initially in this longitudinal cohort study 183 patients with acute ischemic stroke aged between 18 and 80 years old and who received IV rtPA in the first 4.5 h time window from the onset of stroke symptoms from February 2018 to February 2020. Fourteen patients did not accept to participate, 3 patients were lost during the first few days after admission who were discharged against medical advice, 9 patients were expired due to causes not related to thrombolytic therapy like cardiac and respiratory complications, 7 patients were lost during follow up at three months, and only 150 patients of them completed the study plan till the end who were subjected to statistical analysis.

All inclusion and exclusion criteria were based on AHA/ASA last updated guidelines. Additional exclusion criteria were applied to patients who had in-hospital complications or death due to causes other than that related to thrombolytic therapy, patients who were not available for follow up, discharged against medical advice and were not content for enrolling in this study. All patients were subjected upon hospital arrival to full general, vital, and neurological examinations, urgent routine laboratory sampling, and CT brain without contrast. All patients after receiving IV rtPA were transferred to stroke care units.

We analyzed patients demographic data (age and gender), baseline characteristics, location of stroke lesion based on brain and cerebral vessels imaging which included CT brain, computerized tomography angiography (CTA), MRI brain with diffusion, magnetic resonance angiography (MRA), and was classified into anterior circulation and posterior circulation ischemic stroke. Stroke severity was assessed at time of admission and 24 h after IV rtPA using NIHSS which is a tool used by healthcare providers to objectively quantify the impairment caused by a stroke [13, 14]. Door to needle time which is a parameter of efficiency of acute stroke care system was assessed. Also, we assessed timing of IV rtPA administration from onset of stroke symptoms which is a possible potential predictor of the functional outcome. Comorbidities which are potential stroke risk factors were included: hypertension, coronary artery disease (CAD), DM, AF, smoking and hyperlipidemia. We assessed the presence of intracranial ± extracranial atherosclerosis or stenosis using MRA, CTA, carotid, and vertebrobasilar duplex with 5–10 MHz linear probe, Esaote Mylab5-Italy. Also, transcranial color-coded duplex (TCCD) with phased array (2–4 MHz) probe, Esaote Mylab5-Italy, was done 24 h after receiving IV rtPA and the PI in the cerebral vessels at the same side of stroke lesion was measured. Major and minor complications of IV rtPA treatment after infusion and during hospital stay were analyzed especially intracerebral hemorrhage (ICH). Functional outcome 3 months after receiving IV rtPA was assessed using mRS which is a tool used to assess the functional status of the stroke survivors [15, 16].

All the previous data were collected, analyzed, and correlated with the mRS 3 months after receiving IV rtPA.

Stroke severity was categorized into mild stroke, when the NIHSS score was ≤ 8; moderate stroke when the NIHSS score was from 9 to 15; and severe stroke when the NIHSS score was ≥ 16 [17]. Patients with mRS score of 2 or less were considered to have a good functional

outcome and patients with score 3 or more were considered to have poor functional outcome [18]. Post-IV rtPA ICH was defined as any hemorrhage in the brain documented by CT or MRI within 36 h after thrombolysis. ICH was classified into symptomatic (sICH) and asymptomatic ICH.

sICH was defined as type 2 parenchymal hemorrhage (hemorrhage exceeding 30% in the infarcted area with significant space occupying effect) with deterioration in NIHSS score of ≥ 4 points or death [19, 20]. PI was evaluated as a derived flow parameter using pulsed wave doppler; it is derived from the difference in the peak systolic velocity (PSV) and end diastolic velocity (EDV) divided by the mean flow velocity (MFV); PI = (PSV–EDV)/MFV [21], and its normal value range from 0.5 to 1.2 [22].

Drug used and method

Actilyse 50 mg vial (IV rtPA) at a dose of 0.9 mg/kg to a maximum of 90 mg intravenously (10% bolus infused in 1 min, the remaining 90% infused in 1 h).

Statistical analysis of the data

Data were presented as qualitative data (number and percent), quantitative, range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Data was analyzed by chi-square test, Fisher's exact or Monte Carlo correction, Student's *t* test, Mann-Whitney test, and Regression test. Data were collected and analyzed by IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Significance of the obtained results was judged at the 5% level.

Results

Our study included 150 patients, male patients were 95 (63.3%) and female patients were 55 (36.7%), the age of our patients ranged between 24 and 80 years with median age 63 years. Other baseline characteristics in our study were detailed in Table 1.

Univariate analysis

The univariate analysis was done correlating the study variables (demographic, risk factors, and patients baseline characteristics) with the functional outcome and revealed significant correlations between the following variables and poor functional outcome; DM (*P* value 0.023*), hypertension (0.009*), AF (*P* value 0.004*), increased NIHSS score at time of admission (*P* value < 0.001*), increased NIHSS score 24 h after receiving IV rtPA (*P* value < 0.001*), stroke lesion in the posterior circulation territory (*P* value < 0.001*), Increased value of PI in the cerebral vessels at the same side of stroke lesion (*P* value < 0.001*), presence of post-IV rtPA ICH (symptomatic and asymptomatic) (*P* value 0.001*), other variables did not show significant correlations with poor functional outcome as seen in (Tables 3 and 4).

There were also significant correlations between the following variables and good functional outcome; decreased NIHSS score at time of admission (*P* value < 0.001*), decreased NIHSS score 24 h after receiving IV rtPA (*P* value < 0.001*), stroke lesion location in the anterior circulation territory (*P* value < 0.001*), normal range value of PI in the cerebral vessels at the same side of stroke lesion (*P* value < 0.001*), absence of post-IV rtPA ICH (*P* value 0.001*), and other variables did not show significant correlations with good functional outcome as seen in (Tables 5 and 6).

Multivariate analysis

The multivariate analysis of the study variables to detect the independent predictive factors of the functional outcome showed the following results: among study variables (demographic and risk factors), AF (*P* value < 0.001*OR 6.28* (95% C.I)), hypertension (*P* value 0.001*OR 3.65*(95% C.I)), DM (*P* value 0.009*OR 2.805*(95% C.I)), those were the significant independent predictive risk factors of poor functional outcome (Table 3).

Among study variables (stroke illness and ICH following IV rtPA), increased NIHSS score 24 h after receiving IV rtPA (*P* value 0.003* OR 8.039* (95% C.I)), increased value of PI in the cerebral vessels at the same side of stroke lesion (*P* value 0.038* OR 42.48*(95% C.I)), those were the significant independent predictive variables of poor functional outcome (Table 4).

On the other hand, decreased NIHSS score 24 h after receiving IV rtPA (*P* value 0.003* OR 0.124*(95% C.I)), normal value of PI in the cerebral vessels at the same side of stroke lesion (*P* value 0.038* OR 42.48*(95% C.I)), those were the significant independent predictive variables of good functional outcome (Table 6).

Discussion

Our study has demonstrated that use of intravenous thrombolytic therapy for acute stroke is associated with better functional and neurological outcomes and significantly reduce the effect of stroke morbidity and mortality; this was in agreement with several studies that supported the short- and long-term outcome benefits of IV rtPA like the large third international stroke trial [23], and the systematic review and meta-analysis study of real-world outcomes of acute ischemic stroke treatment with intravenous thrombolysis [24].

Our study 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 were found in the univariate analysis but

Table 1 Patients demographic data and their baseline characteristics (n = 150)

	No. (%)
Gender	
Male	95 (63.3)
Female	55 (36.7)
Age	
Min.–Max.	24.0–80.0
Mean ± SD.	62.23 ± 10.31
Median	63.0(55.0–70.0)
NIHSS score at time of admission	
Min.–Max.	4.0–21.0
Mean ± SD.	10.65 ± 3.91
Median (IQR)	10.0(7.0–14.0)
NIHSS score 24 h after IV rtPA	
Min.–Max.	0.0–21.0
Mean ± SD.	5.25 ± 4.99
Median (IQR)	3.0(2.0–9.0)
Categorical classification of stroke severity at time of admission	
Mild	39 (26.0)
Moderate	101 (67.3)
Severe	10 (6.7)
Stroke lesion location	
Posterior circulation territory	24 (16.0)
Anterior circulation territory	126 (84.0)
Pulsatility index at the same side of stroke lesion	
Within normal range	88 (58.7)
Increased	62 (41.3)
Door to needle time	
< 60 min	112 (74.7)
≥ 60 min	38 (25.3)
Time of receiving IV rtPA from stroke onset	
< 3 h	90 (60.0)
3–4.5 h	60 (40.0)
Risk factor	
Hyperlipidemia	58 (38.7)
Diabetes mellitus	51 (34.0)
Hypertension	70 (46.7)
Atrial fibrillation	27 (18.0)
Coronary artery disease	17 (11.3)
Smoking	50 (33.3)
Intracerebral hemorrhage following IV rtPA	
Asymptomatic intracerebral hemorrhage	9 (6.0)
Symptomatic intracerebral hemorrhage	4 (2.7)

Post-stroke functional outcome among patients in this study was assessed using mRS 3 months after receiving IV rtPA (Table 2) (Fig. 1 and 2).

Table 2 Functional outcome and mRS score 3 months after IV rtPA among the patients (n = 150)

	No. (%)
Functional outcome of IV rtPA	
Poor functional outcome (3–6)	52 (34.7)
Good functional outcome (0–2)	98 (65.3)
mRS score 3 months after IV rtPA	
From 0 to 2 (good)	98 (65.3)
From 3 to 6 (poor)	52 (34.7)
0	62 (41.3)
1	30 (20.0)
2	6 (4.0)
3	36 (24.0)
4	11 (7.3)
5	5 (3.3)
6	0 (0.0)
Min. – Max.	0.0–5.0
Mean ± SD.	1.46–1.55
Median (IQR)	1.0(0.0–3.0)

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, and this was in agreement with the study conducted by Alejandro et al. 2015 [25].

In our study, there were highly significant correlations between anterior circulation ischemic stroke and good functional outcome, posterior circulation ischemic stroke, and poor functional outcome; these correlations were present in the univariate analysis, but were not significantly independent predictors of the functional outcome. This result was in agreement with the study conducted by Faisal et al. 2018 [26] who related this to a delayed door to needle time in case of posterior circulation ischemic stroke patients compared to anterior circulation stroke as clinical recognition of posterior circulation stroke is challenging specially for physicians in emergency department (ED) settings, and this may delay diagnosis time and treatment with intravenous tissue plasminogen activator affecting patients outcome and prognosis so early clinical recognition is crucial. However, several studies had reported that risk of bleeding complications post IV rtPA is higher in the anterior circulation ischemic stroke than in the posterior circulation ischemic but functional outcome was similar in both territories [27].

It is known that vascular reactivity is impaired in acute stroke, transmission of the excessive pulsatile flow may overwhelm the autoregulatory reserve, causing further brain damage [28]. Our study showed highly significant correlations between the increased value of PI using TCCD and poor functional outcome in the univariate analysis, also the normal range value of PI and good functional outcome. Then, the multivariate analysis was done and revealed that the PI value is a strong independent predictor of functional outcome when increased it predicts a poor functional outcome, and when it is within normal range, it predicts a good functional outcome.

This was in agreement with previous studies like Nevzat et al. 2013 [29] Also, Kim et al. 2016 demonstrated that PI was an independent determinant of infarct volume in acute lacunar stroke and consequently the functional outcome [30].

Table 3 Univariate and multivariate analysis between study variable (demographic and risk factors) and poor functional outcome

	Univariate		#Multivariate	
	P	OR (95% C.I)	*P*	OR (95% C.I)
Age	**0.358**	1.016 (0.982–1.050)		
Male gender	**0.462**	1.304 (0.643–2.64)		
Hyperlipidemia	**0.309**	1.428 (0.719–2.834)		
Diabetes	**0.023***	2.254*(1.11–4.55)	**0.009***	2.805*(1.288–6.10)
Hypertension	**0.009***	2.526*(1.266–5.041)	**0.001***	3.65*(1.65–8.06)
Atrial Fibrillation	**0.004***	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)		
Smoking	**0.091**	1.833 (0.907–3.70)		

OR odd's ratio, *C.I* confidence interval
#All variables with $P < 0.05$ was included in the multivariate
R reference type
*Statistically significant at $P \leq 0.05$

Table 4 Univariate and multivariate analysis between study variable (stroke illness and ICH following IV rtPA) and poor functional outcome

	Univariate		#Multivariate	
	P	OR (95% C.I)	*P*	OR (95% C.I)
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	**0.001***	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)
Stroke lesion location in posterior circulation territory	**< 0.001***	6.314*(2.411–16.53)	**0.206**	13.36 (0.24–740.6)
Increased pulsatility index at the same side of stroke lesion	**< 0.001***	52.01*(17.77–152.17)	**0.038***	42.48* (1.24–1455.0)
Time of receiving IV rtPA from stroke onset (3–4.5 h)	**0.647**	0.864 (0.436–1.711)		
Intracerebral hemorrhage following IV rtPA (symptomatic +asymptomatic)	**0.001***	29.10* (3.66–231.9)	**0.570**	0.034 (0.0–3907.1)

OR odd's ratio, *C.I* confidence interval
All variables with $P < 0.05$ was included in the multivariate
R reference type
*Statistically significant at $P \leq 0.05$

Our study showed significant negative correlation between hypertension and the functional outcome in the univariate analysis and when tested as independent predictors of the functional outcome among risk factors using the multivariate analysis; it was a strong independent predictor of poor functional outcome. This was in agreement with previous studies which revealed association between presence of hypertension and poor functional outcome 3 months after IV rtPA [31, 32] and that result was in contrary to several studies which found non-significant correlation between history of hypertension and the functional outcome [33, 34]. It was hypothesized that patients with chronic hypertension have shifts in perfusion autoregulation parameters as well as changes in collateral blood supplies and this, in conjunction with other considerations such as carotid artery stenosis, put hypertensive stroke patients at a unique risk special consideration should be considered when determining rtPA eligibility in these patients [35, 36].

Our study showed significant negative correlation between DM and the functional outcome. This was present in the univariate analysis, and when tested as independent predictors of the functional outcome among risk factors using the multivariate analysis, it was a strong independent predictor of poor functional outcome. This was in agreement with many studies which had identified DM as a predictor of poor functional outcome after receiving IV rtPA among stroke patients like that conducted by Roquer and et al. 2014 and that was conducted by Gustavo et al. 2013 [32, 37]. However, other studies did not show significant correlations between DM and functional outcome after receiving IV rtPA, but had showed a significant correlation between admission hyperglycemia and poor functional outcome after receiving IV rtPA [31, 38].

The hypothesis was that DM increases the concentration of serum plasminogen activator inhibitor 1 and decreases fibrinolysis [39]. Also, there is a relationship between basal blood glucose and cerebral edema in IV thrombolytic patients, and this arise

Table 5 Univariate and multivariate analysis between study variable (demographic and risk factors) and good functional outcome

	Univariate		#Multivariate	
	P	OR (95% C.I)	*P*	OR (95% C.I)
Age	**0.358**	0.984 (0.952–1.018)		
Female gender	**0.462**	1.304 (0.643–2.64)		
Hyperlipidemia	**0.309**	0.700 (0.353–1.391)		
Diabetes	**0.023***	0.444*(0.22–0.89)	**0.009***	0.357* (0.164–0.776)
Hypertension	**0.009***	0.396*(0.198–0.790)	**0.001***	0.274*(0.124–0.60)
Atrial fibrillation	**0.004***	0.284*(0.120–0.673)	**< 0.001***	0.159*(0.059–0.431)
Coronary artery disease	**0.100**	0.425 (0.153–1.17)		
Smoking	**0.091**	0.545 (0.27–1.102)		

OR odd's ratio, *C.I* confidence interval
#All variables with $P < 0.05$ was included in the multivariate
R reference type
*Statistically significant at $P \leq 0.05$

Table 6 Univariate and multivariate analysis between study variable (stroke illness and intracerebral hemorrhage following IV rtPA) and good functional outcome

	Univariate		#Multivariate	
	P	OR (95% C.I)	*P*	OR (95% C.I)
NIHSS score 24 h after IV rtPA	**< 0.001***	0.275*(0.159–0.476)	**0.003***	0.124*(0.031–0.496)
Categorical classification of stroke severity at time of admission	**< 0.001***	0.107*(0.038–0.302)	**0.647**	0.230 (0.0–123.17)
NIHSS score at time of admission	**< 0.001***	0.677*(0.594–0.771)	**0.148**	1.95 (0.78–4.84)
Stroke lesion location in the anterior circulation territory	**< 0.001***	6.314*(2.411–16.53)	**0.206**	13.33 (0.24–740.6)
Normal range value of pulsatility index at the same side of stroke lesion	**< 0.001***	52.01*(17.77–152.17)	**0.038***	42.48*(1.24–1455.0)
Time of receiving IV rtPA from stroke onset (< 3 h)	**0.647**	0.864 (0.436–1.711)		
Absence of intracerebral Hemorrhage following IV rtPA	**0.001***	0.034*(0.004–0.273)	**0.570**	29.10 (0.0–3310707)

OR odd's ratio, *C.I* confidence interval
#All variables with $P < 0.05$ was included in the multivariate
R reference type
*Statistically significant at $P \leq 0.05$

from the fact that high glucose may impair the blood–brain barrier [40, 41].

Our study showed non-significant correlation between CAD and the functional outcome 3 months after receiving IV rtPA, and this was in agreement with various studies [33], and in contrary to several studies which had revealed significant correlations between CAD and the functional outcome 3 months after IV rtPA [31, 42].

Our study showed non-significant correlation between recent or current smoking and the functional outcome 3 months after receiving IV rtPA, and this was in agreement with previous studies [31, 42], and in contrary to other studies which revealed significant negative correlation between recent or current smoking and functional outcome 3 months after IV rtPA [43].

The exact mechanisms of AF on the outcomes of stroke patients were not clear, and stroke patients with AF may have large and old thrombi, which are not sensitive to the treatment of thrombolytic therapy [44]. Our study showed significant negative correlation between AF and the functional outcome in the univariate analysis. AF when was tested in this as an independent predictor of the functional outcome and the risk factors variables using the multivariate analysis, it was shown to be the strongest independent predictor of poor functional outcome. This was in agreement with many previous studies like that conducted by Wu et al. 2020 [45], and that study that was conducted by Yue et al. 2016 [46]. On the other hand, there were studies showed significant correlation between AF and favorable functional outcome after receiving IV rtPA [47, 48].

In our study, there was significant correlation between post-rtPA ICH (asymptomatic, symptomatic) and poor functional outcome in the univariate

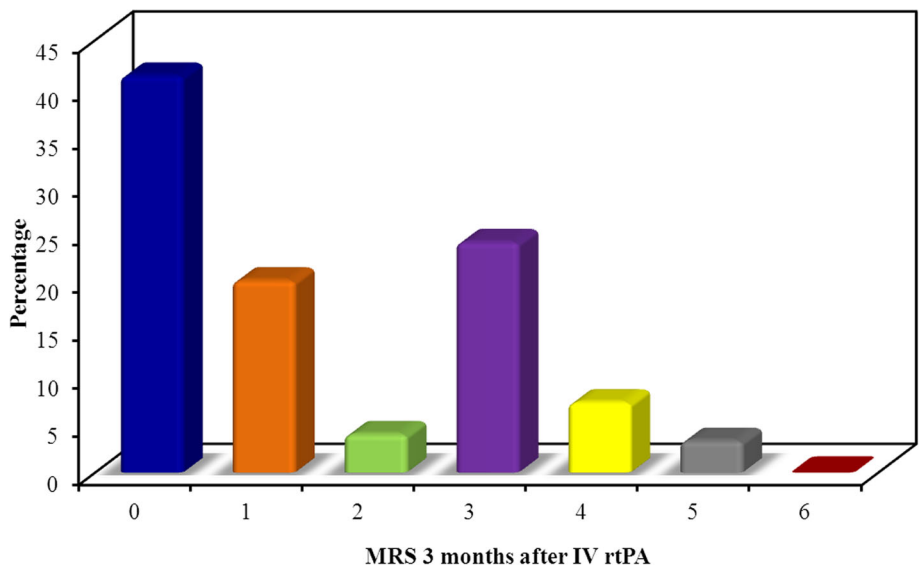

Fig. 1 mRS score 3 months after IV rtPA among the patients ($n = 150$).

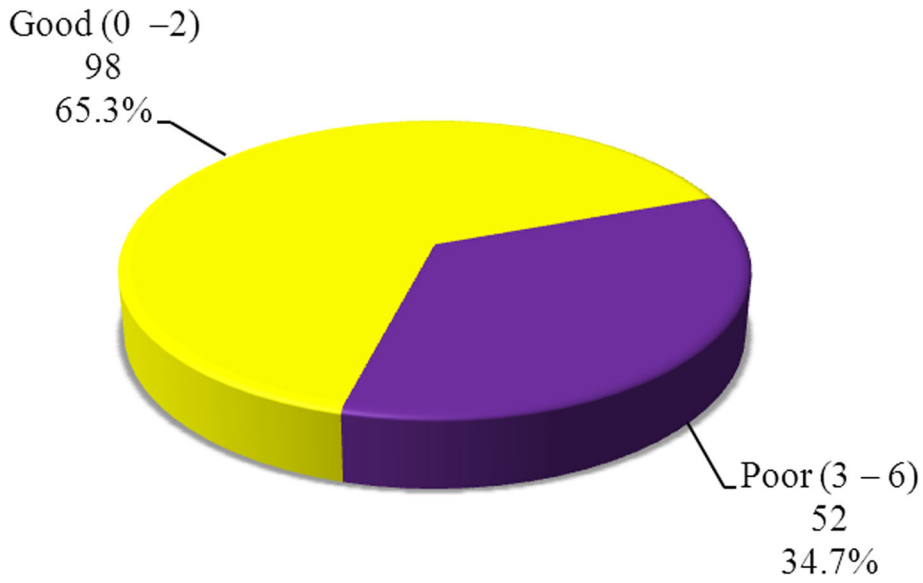

Fig. 2 Functional outcome 3 months after IV rtPA among the patients (n = 150).

analysis; however, it was non-significant independent predictor of the functional outcome among our study variables in the multivariate analysis. This was in agreement with the majority of studies exploring that issue and found poor functional outcome and increased mortality rates among patients who developed sICH after receiving IV rtPA [49, 50].

Conclusion

Intravenous thrombolytic therapy improves the functional outcome among acute ischemic stroke patients. Also, AF, hypertension, DM, NIHSS 24 h after receiving IV rtPA and PI value in the cerebral vessels at the same side of stroke lesion could be used as independent predictors of the functional outcome.

Limitations of the study

Our study was performed in a single center and included only those who completed the follow-up at 3 months after receiving IV rtPA. However, that follow-up period (3 months) is relatively short to some extent. Also, the study included the major potential variables affecting the functional outcome but, there are other variables could affect the outcomes like biomarkers, genetics, history of previous stroke, and infarction volume. These potential variables are recommended to be included in future studies with large number of patients sample and to be followed up over longer period.

Abbreviations

AF: Atrial fibrillation; AHA: American heart association; ASA: American stroke association; CAD: Coronary artery disease; CT: Computerized tomography; CTA: Computerized tomography angiography; DALYs: Disability Adjusted Life Years; DM: Diabetes mellitus; ED: Emergency Department; EDV: End diastolic velocity; ICH: Intracerebral hemorrhage; IV rtPA: Intravenous recombinant tissue plasminogen activator; MFV: Mean flow velocity; MRA: Magnetic resonance angiography; MRI: Magnetic resonance angiography; NIHS S: National institute of health stroke scale; PI: Pulsatility index; PSV: Peak systolic velocity; sICH: Symptomatic intracerebral hemorrhage; TCCD: Transcranial color coded duplex.

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Authors' contributions

MA: conceived of the study and participated in its design and coordination and helped to draft the manuscript (FG). HA: conceived of the study and participated in its design and coordination and helped to draft the manuscript (FG). HK: conceived of the study and participated in its design and coordination and helped to draft the manuscript (FG). MF: participated in the design of the study and performed the statistical analysis (ES). AS: conceived of the study and participated in its design and coordination and helped to draft the manuscript (FG). All authors have read and approved the manuscript.

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Availability of data and materials

All raw data will be available on the editor request through communication with the corresponding author.

Ethics approval and consent to participate

The study protocol was approved by the Ain Shams University, Faculty of Medicine Research Ethic Committee FWA 000017585 in February 2018. Participation was voluntary and all contributors or their first-degree relatives received detailed information about the aims of this research work and an informed consent was obtained prior to the commencement of the study.

Consent for publication
A written informed consent for the publication was obtained from all the participants (or their first degree relatives).

Competing interests
All authors declare that they have no competing interest.

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