

Predictors of Acute Ischemic Stroke Outcome in Young Adult in Assiut University Hospitals

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Abstract

Background: Predictors of prognosis and recurrence of ischemic stroke in young adults are remaining unclear. The main goal of the present study was to identify acute ischemic stroke outcome predictors in young adult patients based on imaging and clinical data.

Methodology: A sample of 54 patients with acute ischemic stroke recruited from one of the university hospitals in Egypt were included in this prospective cross sectional descriptive study. Data were gathered from January 1st 2020 to December 31st 2020. Eligible participants were underwent full history collection, systematic clinical examination, routine laboratory data, and radiological assessment. TOAST and Bamford classification were used to classify studied cases with stroke. The modified Rankin Scale (mRS) and the National Institute of Health Stroke Scale (NIHSS) were used, respectively, to assess the severity and disability of the stroke. The frequency (%), mean, and standard deviation (SD) were used to represent our data. Student t-test was used to compare means of quantitative data, Chi square or Fisher's exact test was used to compare categorical data, and logistic regression analysis was done to identify different risk factors of the outcome.

Results: Older aged patients had substantially higher mRS scores ($P = 0.036$), hypertensive ($P = 0.024$), and higher baseline NIHSS ($P < 0.001$), while no significant relation was observed between etiology, occluded system, other studied risk factors and mRS score ($P > 0.05$, for all).

Conclusion: The most common risk factor for stroke among young adult was smoking status followed by dyslipidemia, rheumatic heart disease and valvular lesion then obesity. Age, hypertension, and higher baseline NIHSS have negative impact on stroke disability with poor outcome.

Keywords: Acute Ischemic Stroke; Predictive Factors; Young Adult; Outcome

Abbreviations

TOAST: Trial of ORG 10172 in Acute Stroke Treatment; SD: Standard Deviation; OR: Odds Ratio; NIHSS: National Institute of Health Stroke Scale; mRS: Modified Rankin Scale; MRI: Magnetic Resonance Imaging; ECG: Electrocardiography Monitoring; CVS: Cerebrovascular Stroke; CT: Computed Tomography

Introduction

Cerebrovascular Stroke (CVS) is one of the major causes of death and disability in all societies irrespective of the community's nature (industrial, agricultural, urban or rural). A stroke can affect all ages but certainly it is more prevalent among older aged individuals. The

risk of incident stroke is known to increase with age and is the strongest non-modifiable risk factor, this risk was doubled for every ten years after the fifty-five years old [1].

The incidence rate of ischemic stroke in young people has been rising recently as a result of lifestyle changes. More focus must be given on early detection of stroke in this age range because it has a significant impact on the lives and jobs of young patients and even cause changes in their family's structure. However, the TOAST classification system is still utilized to categorize young stroke affected patients, leading to some young stroke affected patients being categorized as unknown [2]. Stroke mortality and morbidity vary greatly among countries, but populations in low-income countries are more affected [3].

Prevalence of stroke in younger aged patients account for around 10 to 15 percent of all strokes in the US [4]. It has been demonstrated that the prevalence of stroke among people 20 to 44 years old has increased, from 17/100,000 US adults in 1993 up to 28/100,000 US adults in 2015 [5]. In Europe, the incidence rate of ischemic stroke had increased for adults under the age of 55 from 10.7/100,000 in 1994 - 2002 up to 18.1/100,000 in 2003 - 2011 [6].

Currently no active national registry for stroke in Egypt, the most reliable data on stroke incidence and case fatality come from community based incidence studies. Many community based studies have been done in different regions in the world [7]. One of these studies is epidemiological study of stroke and its risk factors at Assiut governorate, Egypt by Khedr, *et al* [8]. In this study the crude prevalence rate of ischemic stroke was 895/100000, the prevalence and incidence rates were higher among males than females [8]. The populations in these governorates, however, may not be representative of the rest of Egypt, and thus the rising incidence of stroke cannot be confirmed [7].

Different stroke risk factors, both modifiable and non-modifiable, have been identified. The risk variables that were non-modifiable are race, ethnicity, age, gender, and ethnicity. A few examples of modifiable risk factors are diabetes mellitus, hypertension, dyslipidemia, atrial fibrillation, smoking, drug use, and alcohol consumption [9].

Aim of the Study

The aim of the present study was to identify predictors of the acute ischemic stroke outcome in young adult and possible relation between such risk factors and the disease outcome "based on mRS" after 3 months of follow up.

Materials and Methods

This prospective cross-sectional descriptive analysis included all cases of acute ischemic stroke aged 18 to 48 who presented to our hospital within 72 hours of the stroke's beginning (registered at Clinical trial.gov; NCT03700879) starting from January 1st 2020 to December 31th 2020. In all patients, the diagnosis of ischemic stroke was made using clinical signs and imaging. Each patient had a thorough medical history taken, a comprehensive neurological examination that included the NIHSS scores, standard laboratory blood tests following routine evaluation, and a stroke workup that included magnetic resonance imaging (MRI), computed tomography (CT), Doppler ultrasound of the major neck arteries, echocardiography, electrocardiography monitoring (ECG) and collection of coagulation and vasculitis profiles.

Standard protocol was followed for recording patient characteristics, known risk factors (diabetes mellitus, smoking, family history of stroke, hyperlipidemia, obesity, hypertension, coronary artery, peripheral vascular disease, or autoimmune disease), as well as medical history, laboratory testing, and technical examinations and assessing severity according to NIHSS scores. TOAST classification system was applied in order to classify strokes based on its etiology [10], also Bamford classification [11] classifies according to the vascular territory involved. After discharge, all cases were monitored for a minimum of 3 months to evaluate and document outcomes. Significant disability

(mRS > 2) was used to characterize poor outcomes. The study protocol was approved by the Assiut University Medical Ethical Review Board (IRB: 17100600).

Data was analyzed using SPSS program. Quantitative variables were described in the form of mean ± SD. Qualitative variables were described as number (%). Student t test was used to compare quantitative variables. Chi square (χ^2) test was used for comparing categorical data. Exact test was used instead when the expected frequency is < 5. To determine the various risk variables for poor outcome in patients with acute ischemic stroke, odds ratios (OR) with 95 percent confidence intervals (CI) and logistic regression were calculated. Significance defined by $p < 0.05$.

Results

Fifty four young aged patients with acute ischemic stroke were enrolled in this descriptive cross-sectional study. Their mean age was 37.94 ± 6.64 years and ranged from 21 to 48 years. Out of 54 studied cases; 29 (53.7%) were males and 25 (46.3%) were females with male to female ratio of 1.2:1. Based on TOAST classification we observed that; atherosclerotic strokes were recorded in ten patients (18.5%), cardio-embolic strokes were observed in 17 patients (31.5%) and small vessel occlusion were observed in 7 patients (13.0%), a total of 5 patients (9.3%) had a stroke of other etiology. Among these patients, different etiologies identified; 2 patients (3.7%) had antiphospholipid antibody syndrome, however Behcet’s disease, polycythemia and leukemia caused stroke in three patients. Moreover, the rest, 15 patients (27.8%), diagnosed as a stroke of undetermined origin. According to Bamford classification we found that; most of our patients (59.3%) had partial anterior circulation stroke, 11 patients (20.4%) had total anterior circulation stroke, 9 patients (16.7%) had lacunar anterior circulation stroke, while only two patients (3.7%) had posterior circulation stroke. The mean of NIHSS score was 13.33 ± 4.81 (range 12-28). Assessment of stroke disability after 3 months of follow up was carried out using modified Rankin Scale (mRS). According to mRS we classify our studied cases into two groups; patients with favorable outcome (mRS 0 - 2, n = 31) and patients with unfavorable outcome (mRS 3 - 6, n = 23). Table 1 summarizes the incidence of risk variables in patients with acute ischemic stroke.

By assessing the relation between different studied risk factors and stroke disability based on mRS we observed that; older aged patients, who suffered from hypertension, and those with higher NIHSS at baseline were suffered from unfavorable mRS (3 - 6) ($P < 0.05$, for all) (Table 1).

Variable name	Modified Ranking Scale (mRS) after 3 months						P value
	mRS (0 - 2), n = 31		mRS (3 - 6), n = 23		Total		
Age							0.036*
Mean ± SD	36.32 ± 7.02		40.13 ± 5.51		37.94 ± 6.64		
Median (range)	36 (21 - 48)		39 (30 - 48)		38 (21 - 48)		
Sex							0.363
Male	15	(48.4)	14	(60.9)	29	(53.7)	
Female	16	(51.6)	9	(39.1)	25	(46.3)	
Etiology “according to TOAST classification”							0.602
Large artery atherosclerosis	4	(12.9)	6	(26.1)	10	(18.5)	
Cardio-embolism	9	(29.0)	8	(34.8)	17	(31.5)	
Small-vessel occlusion	5	(16.1)	2	(8.7)	7	(13.0)	
Stroke of other determined etiology	4	(12.9)	1	(4.3)	5	(9.3)	

Stroke of undetermined etiology	9	(29.0)	6	(26.1)	15	(27.8)	
Occluded system "according to Bamford classification"							0.812
Total anterior circulation	5	(16.1)	6	(26.1)	11	(20.4)	
Partial anterior circulation stroke	19	(61.3)	13	(56.5)	32	(59.3)	
Lacunar anterior circulation stroke	6	(19.4)	3	(13.0)	9	(16.7)	
Posterior circulation stroke	1	(3.2)	1	(4.3)	2	(3.7)	
NIHSS at baseline							0.000*
Mild (1 - 4)	0	(0.0)	0	(0.0)	0	(0.0)	
Moderate (5 - 15)	29	(93.5)	11	(47.8)	40	(74.1)	
Moderate to severe (16 - 20)	2	(6.5)	7	(30.4)	9	(16.7)	
Severe (21 - 42)	0	(0.0)	5	(21.7)	5	(9.3)	
Risk factors							
Hypertension							0.024*
No	28	(90.3)	15	(65.2)	43	(79.6)	
Yes	3	(9.7)	8	(34.8)	11	(20.4)	
Diabetes mellitus							0.556
No	25	(80.6)	17	(73.9)	42	(77.8)	
Yes	6	(19.4)	6	(26.1)	12	(22.2)	
Dyslipidemia							0.653
No	22	(71.0)	15	(65.2)	37	(68.5)	
Yes	9	(29.0)	8	(34.8)	17	(31.5)	
Ischemic heart disease							0.098
No	29	(93.5)	18	(78.3)	47	(87.0)	
Yes	2	(6.5)	5	(21.7)	7	(13.0)	
Rheumatic heart disease							0.887
No	21	(67.7)	16	(69.6)	37	(68.5)	
Yes	10	(32.3)	7	(30.4)	17	(31.5)	
Atrial fibrillation							0.346
No	25	(80.6)	16	(69.6)	41	(75.9)	
Yes	6	(19.4)	7	(30.4)	13	(24.1)	
Obesity							0.911
No	22	(71.0)	16	(69.6)	38	(70.4)	
Yes	9	(29.0)	7	(30.4)	16	(29.6)	
Smoking status							0.784
No	20	(64.5)	14	(60.9)	34	(63.0)	
Yes	11	(35.5)	9	(39.1)	20	(37.0)	
Migraine with aura							1
No	27	(87.1)	21	(91.3)	48	(88.9)	
Yes	4	(12.9)	2	(8.7)	6	(11.1)	

Autoimmune disease							0.125
No	28	(90.3)	23	(100.0)	51	(94.4)	
Yes	3	(9.7)	0	(0.0)	3	(5.6)	
Family history							0.902
No	26	(83.9)	19	(82.6)	45	(83.3)	
Yes	5	(16.1)	4	(17.4)	9	(16.7)	
History of previous stroke							0.556
No	25	(80.6)	17	(73.9)	42	(77.8)	
Yes	6	(19.4)	6	(26.1)	12	(22.2)	
History of transient ischemic attack							0.443
No	28	(90.3)	19	(82.6)	47	(87.0)	
Yes	3	(9.7)	4	(17.4)	7	(13.0)	
Female risk factors							
Contraceptive pills							0.509
No	11	(68.8)	5	(55.6)	16	(64.0)	
Yes	5	(31.3)	4	(44.4)	9	(36.0)	
Abortion							0.280
No	13	(81.3)	9	(100.0)	22	(88.0)	
Yes	3	(18.8)	0	(0.0)	3	(12.0)	
No. of risk factors							0.162
Single	9	(29.0)	3	(13.0)	12	(22.2)	
Multiple	22	(71.0)	20	(87.0)	42	(77.8)	

Table 1: Association between different risk factors and mRS after 3 months of FU.

DWI: Diffusion-Weighted Image. Quantitative data are presented as mean ± SD and median (range), qualitative data are presented as number (percentage). *p value is significant ≤ 0.05.

This finding was confirmed on univariate logistic regression analysis (Table 2), but in multivariate model, only patients with moderate to severe NIHSS (16 - 20) at baseline were ten times more likely to developed poor outcome as defined by mRS (3 - 6) (OR = 10.347, 95%CI = 1.685 - 63.528, P = 0.012).

Variables	n	Univariate analysis			Multivariate analysis		
		OR	P value	95% CI	OR	P value	95% CI
Age (years)	54	1.102	0.042*	1.003 - 1.210	1.108	0.126	0.971 - 1.264
Hypertension							
No	43	ref			ref		
Yes	11	4.978	0.032*	1.147 - 21.598	2.897	0.250	0.406 - 18.049
NIHSS at baseline							
Moderate (5 - 15)	40	ref					
Moderate to severe (16 - 20)	9	9.227	0.011*	1.656 - 51.422	10.347	0.012*	1.685 - 63.528
Severe (21 - 42)	5	NA	0.999	0.00 - NA	NA	0.999	0.00 - NA

Table 2: Univariate and multivariate logistic regression analysis for prediction of unfavorable outcome “according to mRS” based on patients characteristics (n = 54).
CI: Confidence Interval; OR: Odds Ratio; NA: Not Achieved. *p value is significant ≤ 0.05.

Discussion

Stroke has turned to be a significant illness that poses a threat to people's lives and health on a global scale and must be managed. Recent epidemiological researches indicate an increase in age-specific stroke incidence in younger aged people, particularly in low- and middle-income nations [12].

Younger people have a considerably better prognosis for ischemic stroke than older people do, with reduced death, recurrence rates, and better functional recovery [2,13]. Thus, most of the series have reported that prognosis of stroke in young people as being favorable [13-21], but compared to the general population of the same age, the long-term prognosis is noticeably worse, with a greater death rate, a higher risk of cardiovascular events, and substantial limitations in quality of life [13]. However, in our series (with a mean follow up of almost 3 months), only 57.4% of the studied patients were monitored for > 3 months are still alive, without substantial impairment, a recurrence of a stroke, or another vascular event, while 42.3% have unfavorable outcome as defined by mRS > 2, among them three cases were died (5.6%) which considered high mortality rate in this young age. This come in agreement with Varona, *et al.* (2011) [22] study who reported that only 57% of patients who were followed for > 3 years are still living, without substantial disability, a recurrence of their stroke, or have experienced another vascular incident. Similar finding was reported by the Chinese study of Yang (2013) who stated that the prognosis of stroke in young patients with low income and low education level is poor [23].

This could be due to patients factors as different age range included in these studies, educational level, environmental and socioeconomic difference and difference in the available diagnostic modalities used for earlier diagnosis and proper management. So caution must be taken for prevention of modifiable risk factors by comprehensive widespread health education system, early detection and prompt management of such patients in our country.

Aging is a known risk factor for ischemic stroke [24]; among our studied cases we noticed that patients with unfavorable outcome (mRS 3 - 6) were older than patients with more favorable outcome (mRS ≤ 2), P = 0.036. This finding supported by the literature of Knoflach, *et al.* (2012) [25] as the author reported that aging has a significant detrimental effect on stroke morbidity. Also aging is known as non-modifiable risk factor for AIS [1].

Evaluation of the current study and earlier research has revealed that one of the most common cardiovascular risk factors is hypertension. In the present study, hypertension was documented in 11/54 (20.4%) and detected to be associated with poorer stroke outcome as defined by mRS 3 - 6, P = 0.024.

The findings of previous observational research were contradictory. Numerous studies indicate that high blood pressure is a poor predictor of outcome following an acute ischemic stroke (AIS) [26-28], Yang, 2013 [23] reported that young patients with high systolic blood pressure upon admission have a bad prognosis. On the other hand, data from the International Stroke Trial (IST) revealed that, in 17 398 patients, rising systolic blood pressure was independently linked to an increased risk of both early and late death or dependency [29].

However, some authors have even shown that patients with high baseline blood pressure have better outcomes [30,31].

Recent research from both the United States and Europe have also revealed that the classic stroke risk factors (diabetes mellitus, hypertension, dyslipidemia, obesity, and cigarette use) that are generally prevalent in older persons are also prevalent in younger acute stroke patients [6,32-36]. Similar results was documented by Wu, *et al.* (2022) [2] who reported that, hypertension is among the risk factors for ischemic stroke in young patients, while other studies could not find any association between them [37,38].

According to the NIHSS; we observed that the severity of stroke score was recorded as moderate in 40 (74.1%), moderate to severe in nine cases (9.3%), and severe in five cases (9.3%). Also we noted that higher baseline NIHSS associated with poorer outcome (mRS

3 - 6). In agreement with our finding Hand, *et al.* 2014 [39] reported that higher NIHSS score is associated with a higher incidence of complications.

Few studies have examined the ability of clinical, laboratory, or imaging variables to predict the clinical outcome of ischemic stroke in young adults. Predicting prognosis and outcome in acute ischemic stroke is crucial, especially when determining which patients might benefit from reperfusion therapies and which ones would be hazardous or ineffective [40].

Young stroke patients' short-term prognosis has been extensively assessed, but there have been few studies on their long-term functional recovery. Our study supported by the previous literature of Varona, 2011 [22] who reported that increasing age (> 35 years) associated with higher risk of death (relative risk [RR] of 2.0 and hazard ratio [HR] of 2.5).

Also in concordance with our study Shihmanter, *et al.* (2021) [41] reported poorer outcome with higher age but the finding didn't achieved statistical significance difference. The author reported that according to multivariate analysis, the following four factors are significantly associated with severe impairment and the inability to return to the work: hypertension (OR = 0.37, 95% CI: 0.16 - 0.85, $p = 0.007$), recurrent stroke (by mRS) (OR = 3.54, 95% CI: 1.65 - 7.6, $p = .0005$), Coronary artery diseases (OR = 1.15, 95% CI: 0.04 - 0.55, $p = .0009$), and large artery disease (by TOAST classification) (OR = 0.08, 95% CI: 0.02 - 0.29, $p = .0001$).

Rajbhandari, *et al.* (2019) [42] reported that having a history of hypertension was substantially correlated with having a poor stroke outcome in the form of significant impairment (mRS > 2) ($p = 0.024$), diabetes mellitus ($p = 0.003$), dyslipidemia ($p = 0.023$) and a sedentary lifestyle ($p = 0.001$). The same authors reported a positive correlation between bad outcomes (disability mRS > 2) and cardio-embolic stroke and the unclassified stroke subtypes, although this correlation did not reach statistical significance. In the current study we were failed to find such association that may be attributed to small sample size. This highlights the need for larger multicenter studies on larger sample size to evaluate TOAST classification in such younger age, to determine the most beneficial classification for AIS in young adult, as this may benefit in management of those patients.

The US NIHSS score is widely used to describe the severity of stroke and also can be used to predict its outcomes [39]. In line with our study Nedeltchev, *et al.* (2005) [43] and Rajbhandari, *et al.* (2019) [42] reported that high NIHSS score, was independent predictor of unfavourable outcome or death, Li, *et al.* (2017) [44] found that baseline NIHSS score was associated with increased recurrence rate of ischemic stroke in young adults. And in 2022 Wu, *et al.* stated that high baseline NIHSS score have associated with poor outcome [2].

Conclusion

Based on our finding we could be concluded that stroke in young adults is not as benign as previously suggested as only 57.4% of the studied cases have favorable outcome. Predictors of an unfavorable outcome were older age, hypertension, and a severe neurological deficit at presentation; however higher NIHSS at baseline was superior to other risk factors.

Conflict of Interest

The authors declare that they have no competing interests.

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