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Predictors of 90-Day Functional Outcome Following Direct Mechanical Thrombectomy for Anterior Circulation Large Vessel Occlusion: A Prospective Study

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Abstract

Background: Mechanical thrombectomy (MT) is becoming a growing trend in the management of large vessel occlusion (LVO) during the past few decades, although data on the predictors of outcome following MT are scarce. We aimed to study the predictors of 90-day outcome in a cohort of patients with ischemic stroke with large-vessel occlusion.

Methods: This was a three-month prospective study of 40 patients with anterior circulation LVO who underwent MT and were followed up for three months with modified Rankin Score (mRS).

Results: Of the 40 patients recruited, 55% were men. M1 was the most common vessel occluded (32.5%) followed by internal carotid artery (ICA) and carotid trunk (20%). Tandem occlusion occurred in 25% of the cases. Among the demographic, clinical, radiological, and procedural variables studied, the factors that had a significant impact on the mRS at 3 months were age, diabetes mellitus (DM), hyperlipidemia, stroke mechanism, blood glucose level during procedure, post-procedural National Institutes of Health Stroke Scale (NIHSS), baseline Alberta stroke program early CT score (ASPECT) score, collaterals grade, and procedural thrombolysis in cerebral infarction (TICI) score ($P<0.05$). On multivariate regression, patients' age (B: 0.025, 95% CI: 0.001- 0.049, $P=0.038$), post-procedural NIHSS (B: 0.192, 95% CI: 0.101–0.283, $P<0.001$), and baseline ASPECT score (B: -0.442, 95% CI: -0.838- -0.046, $P=0.03$) were the most independent factors to affect the mRS at 3 months.

Conclusion: Patients' age, baseline ASPECT score and post-procedural NIHSS are significant predictors of 90-day outcome of large-vessel occlusion following MT.

Keywords: Mechanical thrombectomy; Large vessel occlusion; Predictors.

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Introduction

Mechanical thrombectomy (MT) has proven its efficacy in large vessel occlusion in a number of clinical trials during the past few decades.[1-5] It is a well-established innovative modality for recanalization in patients with acute ischemic stroke (AIS) caused by anterior circulation large vessel occlusion (LVO) up to 24 hours after stroke onset.[6,7] The benefit of MT was consistent across a wide range of demographic and stroke parameters, including age, stroke severity, time to groin, imaging modality, and the location of the occlusion in the anterior circulation.[8]

Although MT has become a standard care for AIS presented with LVO in the anterior circulation within 24 hours of onset,[9] a significant number of patients had experienced futile recanalization.[10] The rate of futile recanalization, defined as failure of clinical improvement despite successful recanalization (modified treatment in cerebral ischemia [mTICI] 2c/3), reached 54% in a meta-analysis of five major randomized clinical trials.[11]

Clinical explanations for futile recanalization are still unclear and the studies discussing this issue are scanty in the literature. Insufficient collateral circulation, large hypoperfusion volumes, microvascular impairment, and poor cerebral autoregulation are the key pathological mechanisms now being discussed.[12]

Yet, there is discrepancy between recanalization and functional outcome indicating that recanalization is not the only factor to be considered.[13] The reason for the noted gap between recanalization and clinical improvement still needs to be explored. Thus, we aimed to study the predictors of functional outcome three months following MT done within 24 hours of symptoms onset in a cohort of patients with LVO.

Methods

Participants and Procedures

This was a prospective study of patients diagnosed with AIS with anterior circulation LVO who underwent MT within 24 hours of symptoms in Alexandria University stroke unit during July 2019 and January 2020. Only patients who accepted to use their anonymous data for research purposes were recruited.

Pre-procedural Imaging

All patients indicated for MT underwent non-contrast brain computer tomography (CT), CT perfusion and CT angiography to detect the extent of early ischemic changes and to document the site of LVO, the clot burden score (CBS)[14] and the clot perviousness (64 slices Siemens, Erlangen, Germany). Clot perviousness was measured by subtracting the mean attenuation values of the thrombus on non-contrast CT from CT angiography (CTA). Patients who had artifact or poor contrast opacification on CTA were excluded. Regions with Hounsfield unit (HU) values of more than 100, which represented calcifications, were also excluded. CT perfusion was performed via intravenous injection of a bolus of contrast material (40-50 mL of Ultravist 370; Bayer Healthcare, Berlin, Germany) at a rate of 4-6 mL/s, with 45 time points acquired each 1.33 seconds. Each perfusion series covered a 24–40-mm section acquired as four adjacent 6-mm sections. The first section was at the level of the basal ganglia and/or internal capsule, and the second was placed 6 mm toward the vertex to avoid overlap. CTA was performed after perfusion CT, with acquisition from the aortic arch to the top of the lateral ventricles.[15] The CTA data were automatically processed including multiplanar 7-mm maximum intensity projection reconstructions and 4-mm axial reformats of CTA source images. Parenchymal hemorrhages were assessed and classified according to the European Cooperative Acute Stroke Study II (ECASS II) classification.[16]

Procedural Details

Adult patients (≥ 18 years) with National Institutes of Health Stroke Scale (NIHSS)[17] of ≥ 6, pre-stroke modified Rankin Scale (mRS)[18] of 0 to 1, anterior circulation LVO,[19] acute neurological deficit of less than 24 hours of duration, and diffusion/perfusion mismatch of ≥ 20% were eligible for MT. MT was conducted via either stent retrievers,[20] thrombus aspiration,[21] or a combination of both approaches, depending on the specialized vascular team's discretion. The vascular team who performed MT for all cases has a long experience (more than twenty years) in the field of vascular neuro-intervention. Mapping of the patients' specific vasculature and MT was done in real time operation of Siemens ARTIS-ZEE (Siemens, Erlangen, Germany). The acquisition time for this system is 6 seconds, with 5 ms exposure per image.

Follow up After 90 Days

Three months postoperatively, all patients were reassessed and the mRS[18] was evaluated. The mRS is a validated score developed to assess the functional outcome following cerebrovascular stroke and the impact of the stroke on the daily activities and dependence state.[18] It is a 6-point score ranging from zero (indicating no symptoms) to 6 (indicating severe disability and maximum functional dependence).

Data Collected

Data collected for the research were demographic, clinical, radiological, and procedural variables. Demographic variables included age, sex, and smoking state. Clinical variables included risk factors for stroke (diabetes mellitus [DM], hypertension [HTN], dyslipidemia, cardiac disease, atrial fibrillation [AF], history of previous transient ischemic attack [TIA], and history of previous stroke), stroke onset witnessing (wake-up, witnessed, unwitnessed), time since stroke onset at clinical presentation to the hospital, stroke mechanism, stroke classification according to the trial of ORG 10172 in acute stroke treatment (TOAST), systolic blood pressure (SBP) at presentation, diastolic blood pressure at presentation (DBP), and NIHSS at presentation. Radiological variables included occlusion site, baseline Alberta stroke program early CT score (ASPECT), collaterals status,[14] Clot perviousness, and CBS. Procedural and postprocedural variables included time to groin, procedure technique, procedural blood glucose level, procedural SBP, procedural DBP, procedural heart rate, procedural thrombolysis in cerebral infarction (TICI), modified TICI (mTICI), post-procedural NIHSS, and complications. Three months after MT, all patients were reevaluated and modified Rankin Score (mRS) was assessed.

Statistics and data analysis

Collected data were analyzed using IBM Statistical Package for the Social Sciences (SPSS), software version 22.0. Qualitative data were presented as numbers and percentages. The Kolmogorov-Smirnov test was used for verification of the normality of distribution of variables. Non-parametric continuous variables were expressed using median and interquartile range (IQR). Parametric continuous variables were expressed using mean and standard deviation (SD). Mann-Whitney and Kruskal-Wallis tests were used to compare non-parametric continuous variables among two and more than two groups, respectively. Spearman's coefficient was used for correlation analysis. Linear regression analysis was used to identify the most independent variable affecting the mRS at 3 months. Significant variables on univariate regression were chosen for subsequent multivariate regression. Significance of the obtained results was judged at the 5% level.

Results

Descriptive Analysis

Of 40 patients recruited, 22 (55%) were men. The median age of the patients was 66.5 (IQR 57-72.75) years. HTN, DM, and dyslipidemia occurred in 25 (62.5%), 21 (52.5/%), 20 (50%) of all cases, respectively. Approximately 37.5% of recruited patients (n = 15) were smokers, and 10 (25%) of them had AF. The mean ± SD initial NIHSS among the studied patients was 15.53 ± 4.64. The mean ± SD onset to presentation time was 6.91 ± 4.13 hours. M1 was the most common vessel occluded (n = 13, 32.5%) followed by the internal carotid artery (ICA) (n = 9, 22.5%) and the carotid trunk (n = 8, 20%). Tandem occlusion occurred in 10 (25%) patients.

The Relation Between Qualitative Baseline Characteristics and mRS

Table 1 depicts the relation between qualitative baseline characteristics and the mRS at 3 months. Of note, the mRS was significantly higher among patients with dM (median (IQR) 2 (1-4) versus 1 (1-2), *P* = 0.009) and those with dyslipidemia (median (IQR) 2 (1-4) versus 1 (1-2), P = 0.02). Patients with multiple stroke mechanisms (hypoperfusion, embolic and large vessel atherosclerosis) had the highest mRS (*P* = 0.021). Patients who had complete revascularization as assessed by procedural TICI and those who did not experience procedural related complications had lower mRS scores (*P* = 0.004 and *P* = 0.026, respectively).

The Correlation Between Quantitative Baseline Characteristics and mRS

On studying the correlation between the mRS and baseline quantitative characteristics (Table 2), it was noted that age

Table 1. Relation Between Baseline Characteristics and mRS Scores 3 Months Following MT (n = 40)

Patients' Characteristics	mRS (Median-IQR)	Test of Significance	*P* Value
Gender			
Male	1.50 (1-3.25)	Z = 169.5	0.424
Female	2.00 (0-3.25)		
DM			
No	1 (1-2)	Z = 106.5	0.009*
Yes	2 (1-4)		
HTN			
No	1 (1-2)	Z = 144	0.210
Yes	2 (1-4)		
Smoking			
No	2 (1-3)	Z = 168.5	0.584
Yes	1 (1-4)		
Dyslipidemia			
No	1 (1-2)	Z = 116.5	0.020*
Yes	2 (1-4)		
Cardiac			
No	2 (1-4)	Z = 193.5	0.955
Yes	2 (1-3)		

Table 1. Continued

Patients' Characteristics	mRS (Median-IQR)	Test of Significance	*P* Value
AF			
No	2 (1-4)	Z = 104.5	0.143
Yes	1 (0.75-2)		
Thrombophilia			
No	2 (1-3)	Z = 10.5	0.422
Yes	1 (1-1)		
previous TIA			
No	1 (1-3)	Z = 128	0.114
Yes	2 (1-4)		
Previous stroke			
No	2 (1-3)	Z = 75	0.137
Yes	3 (1-4)		
Onset of stroke			
Wakeup	1 (0.75-3)	K = 1.097	0.578
Witnessed	2 (1-4)		
Unwitnessed	2 (1-4)		
Stroke mechanism			
Artery to artery embolism	1 (1-2)	K = 7.760	0.021*
Hypoperfusion	2 (2-2)		
Multiple mechanisms	3 (1-4)		
TOAST classification			
Cardioembolic	1 (0.0-2)	K = 4.503	0.034*
Large artery ATH	2 (1-4)		
Multiple	3 (1.5-4)		
Cryptogenic	1 (1-1)		
Occlusion site			
M1	1 (1-2.5)	K = 5.198	0.158
ICA	2 (1-2.5)		
Tandem	3.5 (1.75-4)		
Carotid trunk	1 (1-3.5)		
MT technique			
Aspiration	1 (1-1)	K = 0.708	0.702
Stent retrieval	2 (2-2)		
Both	2 (1-3.75)		
mTICI			
2B	3 (2-4)	Z = 74	0.004*
3	1 (1-2)		
Complications			
No	1 (0.75-2.25)	Z = 118.5	0.026*
Yes	2 (1-4)		

AF: atrial fibrillation, ATH: atherosclerosis, DM: diabetes mellitus, HTN: hypertension, ICA: internal carotid artery, K = Kruskal Wallis, M1: First segment of middle meningeal artery, mRS: modified Rankin score, MT: mechanical thrombectomy, TIA: transient ischemic attack, TOAST: trial of ORG 10172 in acute stroke treatment, Z: Mann Whitney test.
*Statistically significant.

had a significant positive correlation with mRS (r = 0.346, P = 0.02). The higher the procedural blood glucose levels, the higher the mRS reached at 3 months after MT (r = 0.481, P = 0.002). Additionally, the collateral status and the initial ASPECT score had a significant negative correlation with mRS (r = -0.463, P = 0.003 and r = -0.560, P < 0.001, respectively).

Table 2. Correlation Between Baseline Characteristics and mRS Scores 3 Months Following MT (n = 40)

Baseline Characteristics	r	*P* Value
Age	0.346	0.02*
Presentation SBP	0.048	0.769
Presentation DBP	0.135	0.406
Procedural SBP	0.015	0.928
Procedural DBP	0.119	0.466
Procedural heart rate	-0.018	0.914
Procedural blood glucose	0.481	0.002*
Time to presentation	0.061	0.707
time to procedure	-0.054	0.742
NIHSS prior to procedure	0.323	0.042*
NIHSS post procedure	0.670	< 0.001*
NIHSS change	-0.214	0.186
ASPECT score	-0.560	< 0.001*
CBS	-0.237	0.140
Collaterals status	-0.463	0.003*
Procedure TICI	-0.508	0.001*

ASPECT: Alberta stroke program early CT score, CBS: Clot Burden Score, DBP: diastolic blood pressure, NIHSS: The National Institutes of Health Stroke Scale, r: Spearman coefficient, TICI: thrombolysis in cerebral infarction.
*Clinically significant.

Regression Analysis of Factors Affecting mRS at 3 Months

Univariate and multivariate regression analysis were performed on the significant findings from relation and correlation analysis to identify their independent effect on mRS (Table 3). We found a significant association between the mRS at 3 months and most of the analyzed variables including age, DM, hyperlipidemia, the stroke mechanism, blood glucose level during procedure, post-procedural NIHSS, baseline ASPECT score, collaterals grade, and procedural TICI score (P < 0.05). On multivariate regression, patients' age (B: 0.025, 95% CI: 0.001-0.049, P = 0.038) (Figure 1), post-procedural NIHSS (B: 0.192, 95% CI: 0.101–0.283, P < 0.001, Figure 2), and baseline ASPECT score (B: -0.442, 95% CI: -0.838- -0.046, P = 0.03, Figure 3) were the most independent factors to affect the mRS at 3 months.

Discussion

In this study, we evaluated the predictors of functional outcome at 3 months following MT in a cohort of patients with anterior circulation LVO. The main findings of this research were that the patient's age, ASPECT score at time of presentation, and post-procedural NIHSS were the most significant independent predictors of functional outcome following MT.

Age had a negative impact on mRS. Older patients were less likely to have a good functional outcome than younger patients. This is in line with the data reported from most of the literature study.[22-26] For instance, Yoon et al, in their study of 335 patients reported that younger patients had a favorable outcome after MT compared with older patients, and age was an independent factor for good outcome (odds ratio [OR], 0.965; 95% CI, 0.944-

Table 3. Regression Analysis of Factors Affecting DASS-21 Scores

	Univariate Regression			Multivariate Regression[a]		
	B	95% CI	*P* Value	B	95% CI	*P* Value
Age[a]	0.348	0.004-0.064	0.028*	0.025	0.001- 0.049	0.038*
DM[a]	1.341	0.408- 2.273	0.006*	0.070	-0.980- 1.121	0.892
Smoking	-0.200	-1.262- 0.862	0.705			
Dyslipidemia	1.040	0.067- 2.013	0.037*	0.363	-0.600- 1.325	0.447
Stroke mechanism[a]	0.741	0.279- 1.202	0.002*	0.104	-0.350- 0.557	0.644
TOAST	0.527	-0.093- 1.147	0.093			
Procedural blood glucose[a]	0.002	0.000- 0.003	0.030*	0.002	-0.004- 0.007	0.533
Presentation NIHSS	0.102	-0.006- 0.209	0.062			
Post procedural NIHSS[a]	0.243	0.161- 0.325	< 0.001*	0.192	0.101-0.283	< 0.001*
ASPECT[a]	-0.801	-1.233- -0.368	0.001	-0.442	-0.838- -0.046	0.030*
Collateral status[a]	-0.868	-1.470- -0.266	0.006*	0.103	-0.463- 0.670	0.711
Procedural TICI[a]	-1.558	-2.605- -0.512	0.005*	-.051-	-1.032- 0.930	0.916
Complications	0.187	-0.116- 0.490	0.002			

ASPECT: Alberta stroke program early CT score, B: Unstandardized Coefficients, CBS: Clot Burden Score C.I: Confidence interval, NIHSS: The National Institutes of Health Stroke Scale, r: Spearman coefficient, TICI: thrombolysis in cerebral infarction.
[a]All variables with P < 0.05 was included in the multivariate analysis.
*Statistically significant at P ≤ 0.05.

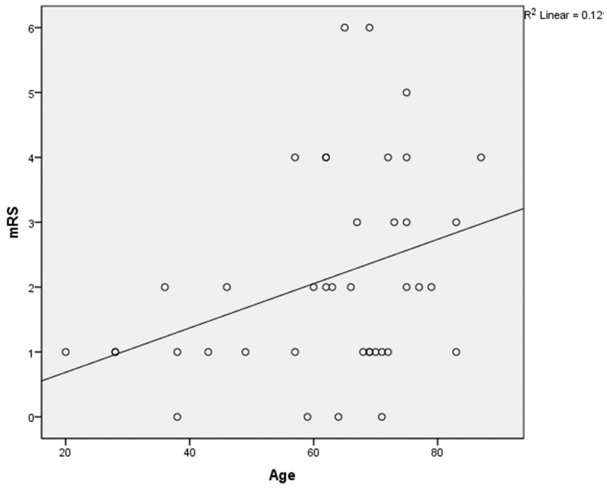

Figure 1. Correlation Between Patients' Age at Stroke Presentation and mRS at 3 Months After Direct Mechanical Thrombectomy.

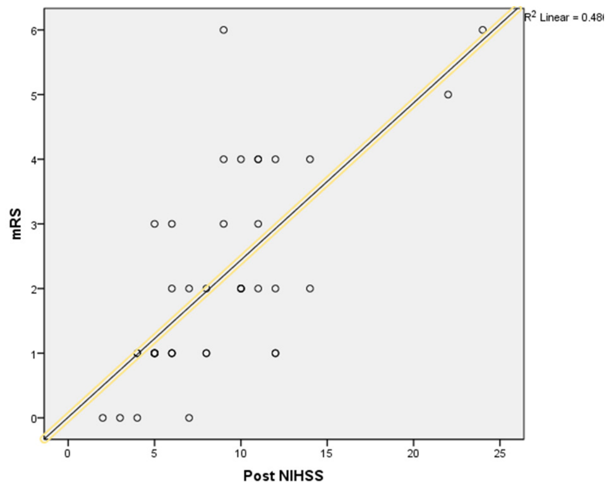

Figure 2. Correlation Between Post-procedural NIHSS and mRS at 3 Months After Direct Mechanical Thrombectomy.

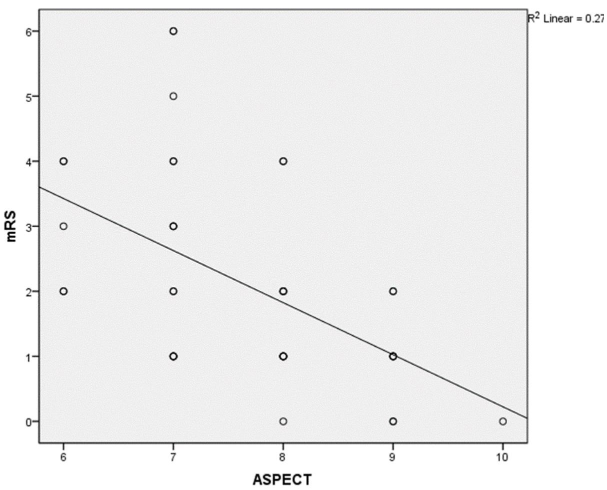

Figure 3. Correlation Between Baseline ASPECT Score and mRS at 3 Months After Direct Mechanical Thrombectomy.

0.986; $P=0.001$).[22] Similarly, age was reported to have a negative correlation with functional outcome in a study of patients with 305 with LVO (OR: 0.96; 95% CI: 0.95 to 0.98; $P=0.0004$).[26] These data do not imply that MT is not suitable for elderly as many literatures demonstrated efficacy of MT in that group of patients.[27,28]

With regards to ASPECT scores, our results revealed an inverse correlation between the ASPECT score and mRS. The lower the ASPECT score (represent more irreversible tissue damage), the higher the mRS (i.e., worse functional outcome) at 3 months. In agreement with our results, van Horn et al demonstrated that lower ASPECT score is linked to poor prognosis after MT in their study of 123 patients between July 2015 and April 2019 (OR: 0.6, 95% CI: 0.4 to 0.84; $P=0.007$).[23] Moreover, ASPECTS was frequently used to identify patients who are most likely to benefit from MT, hence improving clinical prognosis.[29-31]

The post-procedural NIHSS was also a significant independent determinant of mRS at 3 months postoperatively in this cohort. In accordance with this result, Wirtz et al demonstrated that the patients who had an NIHSS score of less than 11 immediately post operative achieved functional independency at 90 days follow-up.[32] Another study reported that a 24-hour NIHSS score of ≤ 7 was an independent predictor of good outcome after 3 months.[33] Previous studies reported an association between collateral circulation status and outcome after MT.[34] We, however, failed to prove this association in our cohort where good outcome had been achieved independently irrespective of the collateral circulation status. This can be explained by the different methodologies used and the presence of many scoring systems to assess the collateral status making the comparison between these studies and ours challenging. To date, a validated standardized score for outcome prediction is still lacking.[35]

The main limitation of our study was the small sample size of the study. The small sample size resulted in abnormally distributed data in most of the study variables. However, the results were significant even with this sample size.

Conclusion

Patients' age and ASPECT score at time of presentation and post-MT NIHSS were significant determinants of functional outcome 3 months following stroke onset.

Conflict of Interest Disclosures

The authors declare no conflicts of interest.

Data Availability

The data are available upon request.

Ethical Statement

Prior to conducting this research, ethical approval was obtained from the Ethics Committee of Alexandria University Faculty of Medicine. This committee has a federal wise assurance (FWA) for more than 20 years now.[36] It operates according to the International Conference of Harmonization Good Clinical Practice (ICH GCP) and applicable local and institutional regulations and guidelines.[37] An informed consent was obtained from all the patients to use their anonymous data for research purpose.

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