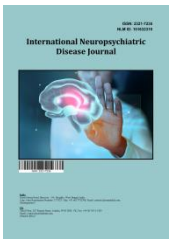

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Primary Endovascular Thrombectomy in Acute Ischemic Stroke in Patients Ineligible for Intravenous Thrombolysis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Endovascular treatment (EVT) of acute ischemic stroke (AIS) is the main treatment of large vessel occlusion (LVO). Nonetheless, access to EVT is limited specially in developing countries. It is not uncommon in these regions to miss the time window for intravenous thrombolysis (IVT) or to arrive within the IVT window but with a contraindication for it. Hence, a lot of patients with LVO face a situation where either they receive EVT only or conservative management according to available logistics.

Aim: To study the outcome of EVT vs best medical treatment (BMT) in two Egyptian stroke centres (Tanta and Alexandria) in AIS patients ineligible for IVT.

Results: 390 patients with AIS and LVO were included in the study. 74 underwent EVT while 316 underwent BMT. There were no statistical differences in age, sex, time of onset, initial severity, or imaging scores in both groups. The EVT group had more diabetes mellitus (DM) patients, more

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smokers and more systolic and diastolic blood pressure (BP) while the BMT had more anticoagulated patients. The EVT group had better functional outcome but more symptomatic intracerebral haemorrhage with no difference in mortality.
Conclusion: Endovascular treatment doubles the good functional outcome of AIS in LVO patients but ICH is more with no effect on mortality.

Keywords: Acute ischemic stroke; EVT; mechanical thrombectomy; access to treatment; functional disability.

1. INTRODUCTION

Acute ischemic stroke (AIS) is the leading cause of disability and the second cause of mortality worldwide [1]. Medical treatment by IVT is established treatment for AIS but restricted by the tight time window of 4.5 hours and by many contraindications like anticoagulation treatment, recent surgery, or trauma beside others [2]. More hope emerged for LVO patients with the HERMES meta-analysis confirmed a benefit of EVT in the first 6 hours [3]. Despite the more time allowed for intervention it was still relatively narrow. A breakthrough in 2018 proved the possibility of a good outcome of AIS due to LVO with EVT as late as 18 or 24 hours from onset according to DEFUSE-3 [4] and DAWN [5] studies respectively. Both American and European AIS guidelines rapidly adopted the recommendation.

Despite the new hope, it was demanding as it needs a proof of tissue viability or penumbra by advanced imaging like Magnetic resonance imaging (MRI) with clinical-diffusion mismatch or MRI-perfusion or CT-perfusion with the need for more time, contrast, and expensive software to decipher the perfusion maps [6]. In ideal conditions the recanalization rates can reach between 75%-85% [7]. This translates to only 40%-50% of patients with good functional outcomes. It is of note that the access to EVT within 15 minutes in United States (US) is <20% [8]. In some developed countries like United kingdoms the service of EVT is not available on 24/7 basis due to lack of sufficient numbers of well-trained staff [9].

In some developing countries in Asia, Africa, or Latin America access to EVT may be less than 25% within 3 hours and much lower within 1 hour [10]. Time from onset is detrimental factor for the outcome of EVT. Different reasons exist for such a disparity. Lack of good transportation roads and efficient paramedics are among the top causes. Other reasons include lack of awareness of AIS recognition or available treatment [11]. In Egypt where a universal insurance cannot cover all the country, the service is limited to certain lightly populated regions. Economic problems with the high cost of the procedure causes periodic shortage of used materials. Limited training centres caused insufficient numbers of qualified staff with impossibility to cover the service on a 24/7 basis. Lack of financial compensations for the operating staff caused an indirect shift of EVT to private hospitals causing a class disparity in access to treatment with more privilege to wealthy societies.

1.1 Aim

Aim to study the outcome of EVT vs BMT in LVO in a poorly resourced regions in Egypt in situations where IVT is not available or contraindicated.

2. METHODS

We made a retrospective analysis of prospectively collected registries in two regions of Egypt, Tanta and Alexandria, from 2015 to 2020. We identified 2213 patients with AIS from which 390 with anterior circulation LVO. We defined LVO as internal carotid artery (ICA) occlusion, middle cerebral artery (MCA) M1 or M2 according to CTA, MRA or CT hyperdense artery sign. For each patient, we collected age, sex, medical comorbidities, time metrics, initial examination vital signs and initial national institute of health stroke scales (NIHSS) [12]. Contraindications for IVT were noted for each case. Relevant imaging data included site of arterial occlusion, Alberta Stroke Program Early CT Scale (ASPECTs) [13]. Relevant available laboratory data and possible aetiologies as shown in Table 1. We compared two groups based on modality to treatment either EVT or BMT. Late onset was defined as >6 hours. We sought the functional disability scale outcome by 3-months modified Rankin scale (m-Rs) [14] on both ordinal and dichotomised points where m-Rs (0-2) represents good outcome. Intracerebral haemorrhage ICH was classified according to

ECASS-3 classification into HI-1, HI-2, PH-1, PH-2. Symptomatic ICH was defined as any ICH with 4 points of decline in NIHSS in the first 48 hours [15].

Mortality was recorded as m-Rs [6]. Two qualified doctors (R.A and O.Y) reviewed the imaging for site of occlusion and ASPECTs. In case of disagreement, it was resolved by (A.B). We classified aetiologies according to TOAST classification. We collected m-Rs outcomes by personal interviews if possible and by phone-call in case of no show up to follow up.

2.1 Statistics

Statistics were done by SPSS V.21. Data were examined for normality by the Shapiro-Wilk test. We used the Chi-square test for categorical data and in case of expected cells less than 5 we used fisher exact test. In case of numerical data we used the Mann-Whitney test for nonparametric data. Categorical data were represented as percentages while numerical data were represented as medians (m) and interquartile ranges (IQR). Threshold for significance was 0.05. For independent predictors we used logistic regression with a forward likelihood ratio method after correction for age and sex. The model was built in layers where block one included age, sex and modality of treatment and block two included comorbidities and block three included other variables. Independent predictors of good outcome were represented by adjusted odds ratio (AOR) and 95% confidence interval (CI).

3. RESULTS

Table 1 shows the difference between the two studied groups. There was no statistical difference in age within BMT and EVT groups [median (65) years vs. (62)] respectively. Males represented 34.2% in BMT vs 43.2% in EVT. No differences were noted in hypertension (HTN), dyslipidaemia or atrial fibrillation (AF) but the EVT group had statistically significant more patients with DM [54% vs 35%, (p=0.004)] and more smokers [35% vs. 5%, (p=0.000)]. We noted more elevated systolic and diastolic BP in EVT group [systolic m=155 mmHg vs. m=140 mmHg, (p= 0.000)] while diastolic BP was [m=100 mmHg vs. m=90mmHg, (p=0.000)]. stroke severity by NIHSS was comparable in the two groups [m=11 in EVT vs. m=12 in BMT, (p=0.77)]. We noted no difference in initial lab data regarding random blood sugar (RBS). A statistically higher initial WBCs in BMT against a significant elevated platelet count and international normalized ration (INR) in EVT group. On the level of imaging most of the patients had CT scans. Median ASPECTs was 10 in both groups. The group of EVT had more ICA [9.5% vs 1.6%, (p= 0.002)] and M1[63% vs. 24%,(p=0.000)] occlusion. On the other side BMT group had more M2 occlusion [51% vs. 28%, (p=0.000)]. Regarding aetiology, embolic stroke with unspecified source (ESUS) was more prevalent in BMT [70.6% vs 51.4%, (p=0.002)] while atherosclerosis was more prevalent in EVT group [20% vs. 3.5%, (p=0.000)]. The outcomes were better in the EVT group with more patients achieving an m-Rs (0-2) [23% vs. 11.1%%, (p=0.012)]. The median was 4 in both groups with better IQR in EVT group (3-5). The group of EVT had more ICH in both forms (any-ICH and symptomatic-ICH). Despite less complications in BMT group mortality was numerically higher but with no statistically significant difference. Logistic regression was done for the dichotomised m-Rs outcome with the results shown in Table 2. The most significant predictor of good functional outcome was initial NIHSS [AOR(0.784), CI (0.696:0.884), p=(0.000)] with every additional point on NIHSS decreasing the odds of good outcome by 0.784. this was followed by EVT which increased the odds of good outcome by 5.2, [CI (1.9:14.3), p=0.001]. Being female was independent predictors of bad outcome while being a male comparatively increased the odds of good outcome by 5.9. each one point of INR increased the odds of good outcome by 2.8 [CI (1.226- 6.537), p= 0.015].

4. DISCUSSION

In this study we tried to through the light on the missed opportunity and the results of the lack or limited access to EVT in Egypt. Our results shows that despite public reimbursement of the procedure, the service is largely underutilised-at least in the two represented regions- with only 74 (about 19%) of the study group undergoing EVT. Possible barriers to access are mostly related to not available materials on the public level due to economic problems [16]. This results in a greater number of cases to be done on a private basis to afford for the extra-cost. The lack of sufficient numbers of trained staff on the level of neuro-interventionists or qualified nursing is another factor. Less numbers means inability to cover the totality of the time on emergency basis. Risk of

radiation and compromised life-style can cause a significant drop-out of trained staff to other subspecialities. This is a worldwide problem that resulted in the search for trained staff in other specialities like vascular surgery and sometimes cardiology [11].

Table 1. Bivariate analysis between the BMT and EVT groups

	Best medical treatment group (N=316)	Interventional group (N=74)	P value
Demographics			
Age [median (IQR)] years	65 (55-75)	62(56-72)	0.642
Sex (male/female)	108/208 (34.2%/65.8%)	32/42 (43.2%/56.8%)	0.178
Vascular risk factors			
HTN	189 (59.8%)	50 (67.6%)	0.235
DM	112 (35.4%)	40 (54.1%)	0.004*
smoking	15 (4.7%)	26 (35.1%)	0.000*
Dyslipidaemia	84 (26.6%)	26 (35.1%)	0.152
AF	91(28.8%)	21(28.4%)	1.000
Anticoagulation	41(13%)	3(4.1%)	0.026*
Onset to presentation			
Early vs late window	226 (71.5%)	46(62.2%)	0.123
Initial Eamination data			
BP SYS [median (IQR)] mmHg	140(130-150)	155(145-175)	0.000*
BP DIA [median (IQR)] mmHg	90(80-100)	100(90-110)	0.000*
Initial NIHSS [median (IQR)]	12(7-16)	11(7-17)	0.774
Initial lab data			
RBS (mg/dl) [median (IQR)]	134.5 (116-156)	130(112.75-159.75)	0.677
WBCs (1000/dl) [median (IQR)]	7.2(6-8.9)	6.1(5.1-8)	0.005*
Platelets (1000/dl) [median (IQR)]	256(193-281)	304.5(256.2-350.5)	0.000*
INR [median (IQR)]	1.02(1-1.2)	1.06(1.05-1.33)	0.000*
Imaging			
ASPECT [median (IQR)]	10(5-10)	10(10-10)	0.000*
Modality of imaging (CT vs MRI)	258 (81.6%)	66(89.2%)	0.204
Site of occlusion			
ICA	5(1.6%)	7(9.5%)	0.002*
M1	75 (23.7%)	47(63.5%)	0.000*
M2	162 (51.3%)	21 (28.4%)	0.000*
TOAST-classification			
cardioembolic	82(25.9%)	21(28.4%)	0.663
atherosclerotic	11(3.5%)	15(20.3%)	0.000*
ESUS	223(70.6%)	38(51.4%)	0.002*
Outcomes			
M-Rs (0-6) [median (IQR)]	4(4-5)	4(3-5)	0.009*
M-Rs (good vs bad)	35 (11.1%)	17(23%)	0.012*
Any-ICH	0(0%)	8(10.8%)	0.000*
Symptomatic ICH	0(0%)	5(6.8%)	0.000*
Mortality	50(15.8%)	9(12.2%)	0.477

AF; atrial fibrillation, ASPECTS; Alberta stroke program early CT score, BP; blood pressure, CT; computerized tomography, DIA; diastolic, DM; diabetes mellitus, ESUS; embolic stroke of unspecified source, HTN; Hypertension, ICA; internal carotid artery, ICH, intracerebral haemorrhage, INR; international normalized ratio, IQR; interquartile range, M1; 1st part of MCA, M2; 2nd part of MCA, MRI; magnetic resonance imaging, M-Rs; modified Rankin score, NIHSS; national institute of health stroke scale, RBS; random blood sugar, Sys; systolic, WBC; white blood cell

Table 2. Logistic regression for good outcome in the EVT group corrected for centre

Variable	AOR (95% interval)	P value
EVT	5.2 (1.895-14.298)	0.001
Age	0.983 (0.954-1.014)	0.284
Male sex	5.981 (2.083-17.175)	0.001
Initial NIHSS	0.784 (0.696-0.884)	0.000
INR	2.831 (1.226-6.537)	0.015
ICH	0.000	0.998

AOR; adjusted odds ratio, EVT; endovascular treatment, ICH; intracerebral haemorrhage, INR; international normalized ratio, NIHSS; national institute of health stroke sacle

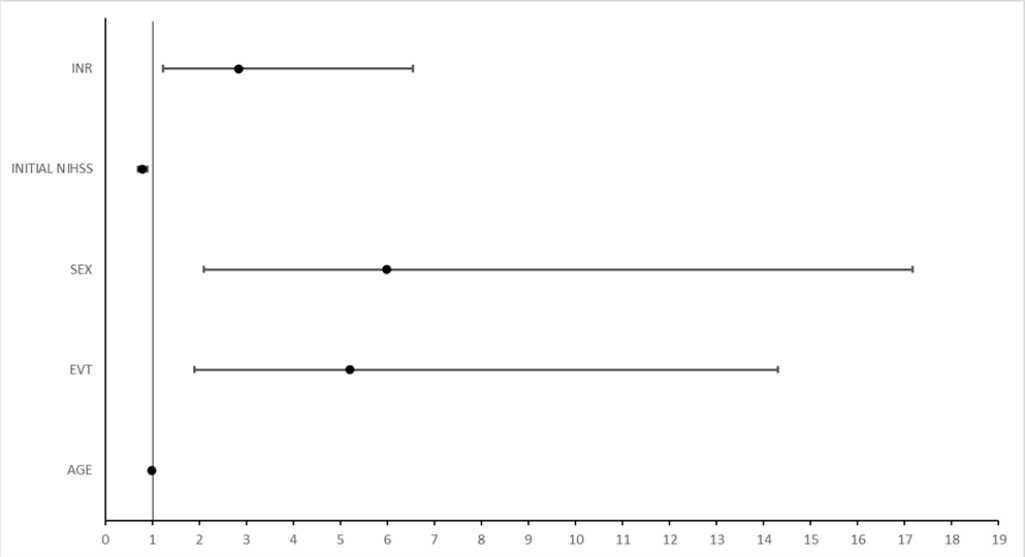

Fig. 1. Forest plot of independent predictors of good functional outcome by m-Rs

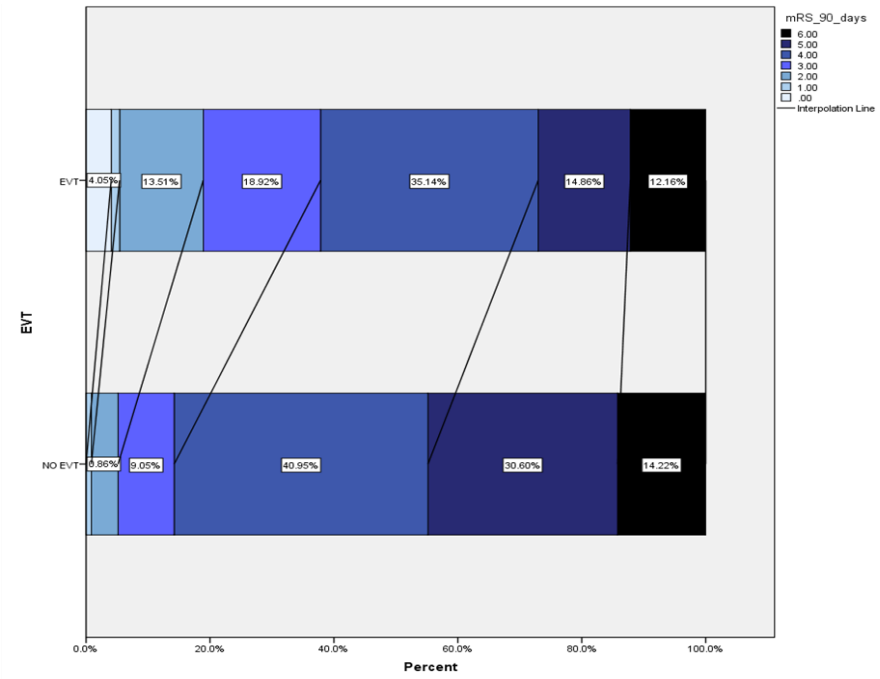

Fig. 2. Modified Rankin scale ordinal distribution in the two groups

Other factors that may contribute to the limited access is the delayed presentation of a lot of patients either due to lack of awareness or limited transportation. This could have resulted in a lot of candidate patients presented beyond the 6 hours window of EVT. With the lack of advanced imaging like MRI diffusion volumetry or perfusion imaging, many potentially treated patients are left with conservative treatment.

In our study, independent predictors of good outcome included lower stroke severity by NIHSS, EVT, increased INR and not being of female sex. Stroke severity by NIHSS is one of the detrimental factors in most studies. More NIHSS may signify more affected tissue. In our study ASPECTS was similar in the two groups. The fact that most of the patients were imaged with CT rather than MRI may contribute to the discordance between NIHSS and ASPECTS. Another possible explanation is damage of a strategic areas like area 4 with more motor disability on a modified Rankin scale [17].

Endovascular treatment is another independent factor of good outcome in our study. It resulted in improved odds by about five times. This is reproducible in many other studies but the rate in Egypt is about 20% [18]. Despite the better outcome compared with the BMT, this is much lower than observed results in international studies. Causes may be due to over selection of AIS patients (younger patients with less NIHSS) or the condensation of the service in private sector leaving a potential part with conservative treatment only. Another cause may be the lack of specialized neurological intensive care units.

In our study, female sex was independently associated with worse functional outcome. This was similar to the findings of other studies in UK with a suggestion of reduced mortality and increased fragility with older age and comorbid depression and anxiety. Also, females were more represented in the BMT group. This may signify less access of females to better health care [19].

Increased INR proportionally increased the odds of good outcome. This wasn't observed in previous study as Huanwen Chen et al. [20] observed the inverse in EVT. With possible explanation of increased rates of ICH. Older research noted less severity and better outcomes in anticoagulated patients treated conservatively. Explanations may be improved rheology and lower rates of re-occlusion or extension of thrombus [21].

5. CONCLUSION

Conclusion despite the lower rates of access to EVT it is still of substantial benefit to AIS patients. Improved access and studying the barriers to better service could establish a service that may decrease the extra-cost of disabled patients with special attention to female sex.

Our study has limitations regarding the lower number of patients treated with thrombectomy in comparison to developed countries which may reduce generalization of the results.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Saini V, Guada L, Yavagal DR. Global Epidemiology of stroke and access to acute ischemic stroke interventions. 2021;97(20 Supplement 2):S6-S16.
2. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American stroke association. 2021;52(7):e364-e467.
3. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials. The Lancet. 2016;387 (10029):1723-31.
4. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 Hours with Selection by perfusion imaging. 2018;378(8):708-18.
5. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al.

Thrombectomy 6 to 24 hours after stroke with a mismatch between Deficit and Infarct. 2017;378(1):11-21.
6. Stanton RJ, Wang LL, Smith MS, Aziz Y, Zhang B, Grossman AW, et al. Differences in automated perfusion software: Do they matter clinically? 2022; 2(6):e000424.
7. Bai X, Zhang X, Wang J, Zhang Y, Dmytriw AA, Wang T, et al. Factors influencing recanalization after mechanical thrombectomy with first-pass effect for acute ischemic stroke: A Systematic Review and Meta-Analysis. 2021;12.
8. Sarraj A, Savitz S, Pujara D, Kamal H, Carroll K, Shaker F, et al. Endovascular Thrombectomy for acute ischemic strokes: Current US access paradigms and optimization methodology. Stroke. 2020; 51(4):1207-17.
9. Weddell J, Parr E, Knight S, Muddegowda G, Natarajan I, Chembala J, et al. Mechanical thrombectomy: Can it be safely delivered out of hours in the UK? BMC Neurology. 2020;20(1):326.
10. Roa JA, Martins SCO, Montalverne FJJASMitEoT. Stroke Care and Mechanical Thrombectomy in Developing Countries; 2019.
11. Gongora-Rivera F, Gonzalez-Aquines A, Marquez-Romero JM. Identification of Barriers to Access Endovascular Treatment for Acute Ischemic Stroke in the Health Care System of Mexico: Results From a National Survey Among Endovascular Neurologists. Frontiers in Neurology. 2021;12:601328.
12. Lyden P. Using the National Institutes of Health Stroke Scale. 2017;48(2):513-9.
13. Mokin M, Primiani CT, Siddiqui AH, Turk AS. ASPECTS (Alberta Stroke Program Early CT Score) Measurement Using Hounsfield Unit Values When Selecting Patients for Stroke Thrombectomy. 2017; 48(6):1574-9.
14. Pożarowszczyk N, Kurkowska-Jastrzębska I, Sarzyńska-Długosz I, Nowak M, Karliński M. Reliability of the modified Rankin Scale in clinical practice of stroke units and rehabilitation wards. 2023;14.
15. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke. 2008;359 (13):1317-29.
16. Aref H, Zakaria M, Shokri H, Roushdy T, El Basiouny A, El Nahas N. Changing the Landscape of Stroke in Egypt. Cerebrovascular Diseases Extra. 2021; 11(3):155-9.
17. Wouters A, Nysten C, Thijs V, Lemmens R. Prediction of Outcome in Patients With Acute Ischemic Stroke Based on Initial Severity and Improvement in the First 24 h. Frontiers in Neurology. 2018;9:308.
18. Farghaly WM, Ahmed MA, El-Bassiouny A, Hamed AA, Shehata GA. Predictors of three months mortality after endovascular mechanical thrombectomy for acute ischemic stroke. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2022;58(1):96.
19. Xu M, Vallejo AA, Calvete CC, Rudd A, Wolfe C, O'Connell MDL, et al. Stroke outcomes in women: A population-based cohort study. 2022;53(10):3072-81.
20. Chen H, Ahmad G, Colasurdo M, Yarbrough K, Schrier C, Phipps MS, Cronin CA, Mehndiratta P, Cole JW, Wozniak M, Miller TR. Mildly elevated INR is associated with worse outcomes following mechanical thrombectomy for acute ischemic stroke. Journal of NeuroInterventional Surgery; 2022.
21. Hylek EM, Go AS, Chang Y, Jensvold NG, Henault LE, Selby JV, Singer DE. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. New England Journal of Medicine. 2003; 349(11):1019-26.

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