Functional Outcomes After Endovascular Thrombectomy Among Patients with Acute Large Vessel Infarct: A Philippine Single Center Experience

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ABSTRACT

Background

Endovascular thrombectomy (EVT) is the gold standard of care for large vessel occlusion strokes, but is underutilized in developing countries.

Methodology

This single-center retrospective study included patients who underwent EVT during the period of September 2018 to April 2023. Data collected were demographics, underlying co-morbidities, use of anti-thrombotics/coagulants, CT or MR ASPECTS, thrombolysis prior to EVT, technique, timing, TICI score, occlusion site, discharge and 90-day MRS.

Results

Of the 1,595 stroke patients, 57 (3%) cases underwent EVT. The mean age was 65 with a male to female ratio of 6:5. Hypertension, atrial fibrillation, and diabetes were the common co-morbidities. Majority of patients (90%, n=54) presented with moderate to severe disability (MRS 3-5). Majority were in the anterior circulation (89%, n=51). Stentriever technique was mostly used (59% n=34) with a 77% (n=44) recanalization rate. Early neurologic improvement (ENI) was seen in 7% (n=4), 2 of which translated to a favorable outcome after 90-days. Mortality occurred in 24% (n=14) of cases, mostly from neurological complications. 24% (n=14) had favorable outcome of MRS 0-2 after 90 days. Among those grouped in the unfavorable outcome, 53% (n=23) were MRS 3, still showing marked improvement of quality of life.

Conclusion

EVT outcomes in this study is aligned with the landmark trials which exhibited a number needed to treat of 2.8-7.4. This local data highlights that EVT is a possible and effective treatment for large vessel strokes despite wide gap in accessibility and use in the country.

Keywords*: endovascular thrombectomy, large vessel occlusions, mechanical thrombectomy, thrombectomy, thrombolysis*

INTRODUCTION

Cerebrovascular disease or stroke remains to be the second most common cause of death worldwide at 11%,[1] and this applies locally in the Philippines, where roughly 43 thousand people were affected in the period of January to September 2022 alone.[2] Stroke also compromises quality of life, and is the third leading cause of disability worldwide where cerebrovascular disease patients would lose 10.27 quality adjusted life years (QALYs) due to this disease.[3,4] Ischemic stroke accounts for 87% of all strokes.[5] A popular notion on stroke, more specifically for ischemic stroke is “time is brain”, as acute and potentially disease-reversing interventions for this condition are

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time-dependent. Over the past 2 decades, novel treatments for ischemic stroke have emerged, including intravenous thrombolysis and endovascular thrombectomy (EVT) as standard of care, although the latter can be offered to large vessel strokes for up to 24 hours after symptom onset as seen in the DAWN trial.[6] Despite its known efficacy on outcomes for stroke, there is still a low utilization of EVT globally.[7,8] Locally, only a few tertiary hospitals are EVT capable centers, and almost all are located in Metro Manila. Hindrances for its use are identified as scarcity of neuro-interventionists, high cost, lack of infrastructures, inadequate awareness of its utilization for acute stroke.[9] A single center study in a tertiary hospital on endovascular thrombectomy (EVT) use in the Philippines showed that it is a possible treatment option for large vessel infarcts and compared the level of functional dependence upon admission and discharge.[10] Up to date, this is the only local study looking into the long-term functional outcomes of such patients. This study aimed to determine the functional outcomes after endovascular thrombectomy among patients with acute large vessel infarct admitted in a Philippine tertiary hospital from 2018 to 2023.

METHODOLOGY

Population and Sample

Patients included were all those who underwent endovascular thrombectomy from the period of September 2018 until April 2023. They were beyond the age of 18, private patients, diagnosed with acute ischemic infarct secondary to large vessel occlusion (occlusion of the Internal Carotid Artery, proximal segment of the Middle Cerebral Artery and/or Basilar Artery), as evidenced by neuroimaging using either contrast-enhanced cranial computed tomography (CT) Angiogram or cerebral magnetic resonance imaging (MRI) and MR angiogram. Patients excluded were those who underwent endovascular thrombectomy without available data at 90-day MRS or with unavailable charts.

Data Collection

The following variables were collected from medical charts: demographic data (age and sex), admitting MRS, National Instute of Health (NIHSS) score[11] upon admission, underlying co- morbidities (hypertension, diabetes, history of previous stroke), use of anti-thrombotics/anti-coagulants as maintenance medications, Alberta Stroke Program Early CT Score (ASPECTS) or MR ASPECTS,[12] history of recombinant Tissue Plasminogen Activator (rTPA) administration prior to EVT, technique, ictus to groin time, door to ictus, post-EVT recanalization score Thrombolysis in Cerebral Infarction (TICI),[13] site of occlusion, and discharge Modified Rankin Score (MRS).[14,15] The 90-day MRS were collected through phone call after obtaining proper consent from the patient or by reviewing the patient's outpatient or inpatient (if re-admitted) records at 3 months post stroke. Mortality was recorded as well as its primary cause, either during hospitalization or in the 90-day period post stroke. This study was approved by the institutional review board.

Analysis

Stata MP version 17 software was used for data processing and analysis. Continuous variables were presented as mean (standard deviation/SD) or median (interquartile range/IQR) depending on the data distribution. Shapiro Wilk's test was used to assess data normality. Categorical variables were expressed as frequencies and percentages. Comparison of MRS at admission, on discharge and 90-days post-intervention was done using Friedman test. Significant results were further analyzed using Wilcoxon signed-rank test with Bonferroni correction. P values ≤0.05 were considered statistically significant.

RESULTS

Patient Characteristics

Table 1 presents the characteristics of included patients. In 2018-2023, there were 1,595 patients admitted for acute ischemic strokes, 57 (3%) cases underwent EVT and 20 (1%) of which underwent combined EVT and IVT. Mean age was 65.96 years (range: 26-94 years), majority were ≥60 years old at the time of admission and more than half were males.

The most common underlying co-morbidities were hypertension (60%), type 2 diabetes mellitus (42%) and atrial fibrillation (39%). 15 patients had other co-morbidities which include chronic kidney disease (n=3), liver cirrhosis (n=2), benign prostate hypertrophy (n=1), duodenal cancer (n=1), hyperuricemia (n=1), hypothyroidism (n=1), invasive mucinous adenocarcinoma (n=1), MVA (n=1), obesity (n=1), ovarian cancer (n=1), post-stroke seizure (n=1) and previous history of pulmonary tuberculosis (n=1).

Stroke Severity

Median pre-treatment NIHSS was 16, range: 1 to 25 where majority were classified as moderate. The median post-treatment NIHSS was 15, range: 0 to 3 their majority were classified as moderate. Lastly, median discharge NIHSS was 7, range: 0 to 24 where most were still classified as moderate. On imaging, mean ASPECTS score was 7.51, range: 4-10 indicating that most patients had a small infarct core on initial assessment.

Pre EVT Anti-thrombotic/coagulant and rTPA Administration

Prior to EVT, 16% used anticoagulant while 30% used antiplatelet for the treatment of their existing co-morbidities. 35% had history of rTPA administration prior to EVT where they were given either 0.6mg/kg or the standard dose of 0.9mg/kg. Among those who received rTPA,17 out of the 20 patients (85%) received a dose of 0.9mg/kg.

Procedure Features

The median ictus to groin time was 7 hours (range: 4-336 hours) where most (61%) had an ictus to groin time of 6 to 16 hours. Median door to groin time was 4 hours (range: 1-10 hours). Majority underwent stent retriever technique (67%) where the rest were either aspiration or combination techniques. 7 (12%) of the procedures were terminated due to unfavorable anatomy or re- occlusion. Majority (78%) had a TICI score of 3. A third of the participants had multiple passes prior to recanalization. Specific number of passes were 2 (n=9), 3 (n=6), 4 (n=2), 5 (n=2). Most common sites of occlusion were M1 (39%) and ICA (39%). There were 4 cases of basilar artery occlusions.

Functional Outcomes

The median MRS significantly differ over time. Patient's MRS were identified in 3 different time frames, upon admission, discharge, and 90 days post-intervention. MRS were dichotomized into favorable and unfavorable outcomes as defined by MRS 0-2 and 3-5 respectively. Favorable outcome at 90 days post-intervention were see in 14 (25%) patients (Table 2). Further analysis revealed that the median MRS on admission was significantly higher than MRS 90-days post-intervention (p=0.0029), but not significantly different with MRS on discharge (p=0.0588) (Table 3). Median MRS on discharge was significantly higher than MRS 90-days post-intervention (p=0.0042) indicating further improvement in functional outcome during the follow-up at 90 days. Early neurologic improvement, defined as either a reduction of > 8 points in the NIHSS compared to baseline or NIHSS 0 at 24 hours post stroke were seen in 4 patients. MRS (0-2, 3-5, and 6), ictus to groin time (<6, 6-16, 17-24, >24 hours), association remained non-significant (p=0.857).

Combined rTPA and EVT did not show any significant association with better functional outcome at 90-days post treatment (p=1.000) (Table 4).

Table 1. Demographic and clinical characteristics of patients who underwent EVT (n=57)

CHARACTERISTICS	n(%)
Age (in years), mean	65.96 ± 14.19
<60 years old	14 (25)
≥60 years old	43 (75)
Sex	
Male	31 (54)
Female	26 (46)
Underlying comorbidities	
Hypertension	34 (60)
Type 2 Diabetes mellitus	24 (42)
Atrial fibrillation	22 (39)
Dyslipidemia	9 (16)
History of previous stroke	9 (16)
Valvular heart disease	4 (7)
CAD/ACS[a]	5 (9)
Heart failure	4 (7)
Bronchial asthma/COPD[b]	4 (7)
Others	15 (26)
Smoking history	
No	36 (63)
Yes	21 (37)
Pre-treatment NIHSS[c], median	16 [IQR[d]: 9-19]
Mild	6 (11)
Moderate	45 (79)
Severe	6 (11)
Post-treatment NIHSS, median	15 [IQR: 8-21]
Mild	5 (9)
Moderate	43 (75)
Severe	9 (16)
Discharge NIHSS, median	7 [IQR: 3-13]
Mild	14 (25)
Moderate	28 (49)
Severe	15 (26)
Use of anti-coagulant pre-treatment	
No	48 (84)
Yes	9 (16)
Use of antiplatelet pre-treatment	
No	40 (70)
Yes	17 (30)

CHARACTERISTICS	n(%)
Imaging performed	
MRI[e]	25 (44)
CT[f]	32 (56)
ASPECTSg score, mean	7.51 ± 1.42
History of rTPA[h] administration prior to EVT[i]	
No	37 (65)
Yes	20 (35)
Procedure features	
Technique	
Stent retriever only	38 (67)
Aspiration only	7 (12)
Combined stent retriever and aspiration	7 (12)
Stenting	2 (4)
IA-rTPA[j]	2 (4)
Terminated	7 (12)
mTICI[k] score [n=50]	
1	2 (4)
2	1 (2)
2B	8 (16)
3	39 (78)
Number of passes	
Unable to pass	9 (16)
Single pass	29 (51)
Multiple pass	19 (33)
Ictus to groin time (in hours), median	7 [IQR: 5-9]
<6 hours	15 (26)
6 to 16 hours	35 (61)
17 to 24 hours	5 (9)
>24 hours	2 (4)
Door to groin time (in hours), median	4 [IQR: 3-5]
Site of occlusion	22 (39)
M1	6 (11)
M2	1 (2)
M3	1 (2)
P1	22 (39)
ICA!	1 (2)
PCam	4 (7)
Basilar	
Hemorrhagic conversion	
No	36 (64)
Yes	20 (26)

a – Coronary Artery Disease/Acute Coronary Syndrome, b – Chronic Obstructive Pulmonary Disease, c - National Institute of Health Stroke Scale, d – Interquartile Range, e – Magnetic Resonance Imaging, f – Computed Tomography, g - Alberta Stroke Program Early CT Score, h – recombinant Tissue Plasminogen Activator, i – Endovascular Thrombectomy, j – Intra-arterial rTPA, k – Modified Thrombolysis in Cerebral Infarction, l – Internal Carotid Artery, m – Posterior Cerebral Artery

Table 2. Modified Rankin Scores on admission, discharge, and 90 days post-intervention

	MRS on admission n%	MRS at discharge n%	MRS at day 90 n%
0-2	3 (5)	10 (18)	14 (25)
3-5	54 (95)	33 (58)	28 (49)
6	0	14 (25)	15 (26

MRS – Modified Rankin Score

Table 3. Comparison of functional outcome based on MRS on admission, discharge and 90-days post-intervention (n=57)

	Admission Median [IQR]	Discharge Median [IQR]	90-day PostIntervention Median [IQR]	P-value
MRS	5 [IQR: 4-5]	5 [IQR: 3-5]	4 [IQR: 3-6]	0.0009*[a]

a- [a]Friedman test was used

Table 4. Comparison of 90-day MRS in relation with rTPA administration and ictus to groin time. (n=57)

	MRS at day 90		P value[a]
	0-2 (n=14) n%	3-6 (n-43) n%	
History of rTPA administration prior to EVT No Yes	 9 (64) 5 (36)	 28 (65) 15 (35)	1.000
Ictus to groin time (in hours) <6 hours 6 to 16 hours 17 to 24 hours >24 hours	 0 3 (21) 10 (71) 1 (7)	 12 (28) 25 (58) 4 (9) 2 (5)	0.937

Table 5. Mortality rates patients who underwent EVT (n=57)

	N	Incidence (95% CI)
In-hospital mortality	14	24.56 (14.13-37.76)
Total Mortalities	15	26.32 (15.54-39.66)

Safety Outcomes and Mortality

Hemorrhagic conversion occurred in 20 (36%) patients, with severity stratified as HI1 (n=2), HI2 (n=6), PH1 (n=9), PH2 (n=3). Among these patients, 12 (60%) were considered symptomatic ICH (Table 1). However, there was no significant association between the incidence of hemorrhagic conversion in those patients who received rTPA and those with pre-treatment anti-platelet/coagulant use ($p > 0.05$). In-hospital mortality occurred in 14 (25%) patients, where most of the causes were due to brain herniation (n=6), some were due to septic shock from nosocomial infections (n=3), acute coronary syndrome (n=1), hospital acquired pneumonia (n=3), and arrhythmia (n=1). During the 90-day follow up, 1 (1.6%) expired due to septic shock (Table 5).

DISCUSSION

In this single center retrospective study, there were 1,595 patients admitted for acute ischemic strokes in 2018-2023, 57 (3%) cases underwent EVT and 20 (1%) of which underwent combined EVT and IVT. The mean age was 65 with a male to female ratio of 6:5. Hypertension was a common co-morbidity in half of the population, also diabetes and atrial fibrillation were existing in 1/3 of cases. During their admission, majority of patients (90%, n=54) presented with moderate to severe disability (MRS 3-5) with a mean NIHSS of 16, indicating a moderate stroke severity. The identified site of occlusion is mainly in the anterior circulation (89%, n=51) and with 6 cases of posterior circulation strokes. Stentriever technique is primarily utilized in 59% (n=34), aspiration in 10% (n=6), and combined stentriever and aspiration in 17% (n=10) with a 77% (n=44) recanalization rate. Early neurologic improvement (ENI) defined as a difference of 8 points in NIHSS or a score of 0 at day 1 post-EVT were found in 7% (n=4), 2 of which translated to a favorable outcome using the 90-day MRS.[16] In-hospital mortality occurred in 24% (n=14) of cases, 6 from brain herniation and the rest were due to complications of prolonged hospitalization such as septic shock. On long term follow-up at 90 days post ictus, 24% (n=14) had favorable outcome of MRS 0-2. Among those grouped in the unfavorable outcome, 53% (n=23) were MRS 3, still showing marked improvement of quality of life.[17]

Endovascular thrombectomy has emerged in the last decade to be the gold standard of care for acute ischemic stroke. This was pioneered by the team that conducted the MR CLEAN clinical trial in 2015, where it showed that patients who underwent EVT had significantly higher rates of functional independence than those who received bed medical treatment.[18] Its effectivity was more highlighted by the low number needed to treat (NNT) in the landmark trials ranging 2.8 to 8,[19] with the EXTEND-IA trial showing the lowest NNT among all the others.[20] In the current study, favorable outcomes of MRS 0-2 were seen in 1 out 4 cases similar to the ESCAPE and SWIFT PRIME trials with an NNT of 4.[21,22] In these landmark trials, combination of EVT and IVT were seen to fair better in terms of long term functional outcomes compared to those who had IVT alone.[19] However, this did not reflect similarly in our study, where there was no significant difference in outcomes for those who had combined therapies. Same goes for the ictus to groin time, stratified according to different time windows used in the landmark trials. It also displayed no significant association with functional outcomes.

Its use in basilar artery occlusion remains to be inconsistent as evidenced by the meta-analysis on the 4 clinical trials on its utilization. Among these 4, 2 of them showed positive results (BAOCHE and ATTENTION clinical trials) but the other 2 (BEST and BASICS clinical trials) revealed negative results.[23] In this study, 4 patients presented with basilar artery occlusion, 2 had a 90- day MRS of 3 and the rest were in-patient mortalities due to brainstem failure. Comparing the 2 halves of this sub-group, patients with poorer outcomes were those with poorer revascularization.

In terms of safety, mortality rate was the same as the rate of favorable outcomes of 25%. Majority of the causes of death were related to brain herniation. Malignant brain edema post EVT leads to poorer outcome and mortality. Usual predictors of this complication were low ASPECTS, poor angiographic collateral scoring, absent hyperdense MCA sign, and poor re-vascularization score.[24] Mean ASPECTS of the patients in this study was 7.51, indicating a small infarct core at the time of intervention and less risk for malignant reperfusion injuries. However, the imaging done were not standardized and not all patients underwent angiographic collateral imaging, hence these were not included in the analysis of factors causing mortality. Hemorrhagic transformation occurred in 36% of patients and 60% of which were symptomatic ICH. 5 cases of mortalities were associated with higher severity of hemorrhagic transformation considered as PH1 and PH2, the same patients were also those with poor mTICI scores and underwent multiple passes.[25] One mortality with hemorrhagic transformation was that of a basilar artery occlusion with a punctate hemorrhage over the pons, but the patient succumbed due to brainstem failure from poor re-vascularization (mTICI 2).

CONCLUSIONS

This study has demonstrated that Endovascular thrombectomy significantly improves long-term functional outcomes in patients with large vessel occlusions. The favorable outcomes seen in 1 out of 4 patients is at par with the landmark trials which exhibited a number needed to treat of 2.8-7.4. This is the single local data on the long-term clinical outcomes of EVT in the Philippines and it aims to spread awareness that EVT is a possible and effective treatment for large vessel strokes despite wide gap in accessibility and use in the country.

Limitations

The limitations of this study is that only a single center was included and data was gathered retrospectively. Also, due to a small population of subjects available, the proper sample size was not achieved, hence generalizations and further analytical analysis such as those done in larger trials (ordinal/ shift analyses) were not appropriate.

Recommendations

Future researches on the cost-effectiveness of EVT in our setting is worth looking into, considering the current healthcare system in the country where treatments such as this are shouldered by the patients. Also, using a standardized neuroimaging for all EVT cases including their angiographic collateral scoring to analyze its association with functional outcomes and safety. We highly suggest that future EVT cases in this center be added to the collection of data such that future analyses may be done to improve case selection and EVT utilization.

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