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Association of CT perfusion parameters with outcomes in patients with medium vessel occlusion undergoing endovascular thrombectomy

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Abstract

Background: Imaging biomarkers obtained on computed tomography perfusion (CTP) have proven effective in predicting outcomes after endovascular thrombectomy (EVT) in patients with large vessel occlusion stroke. However, the association of CTP imaging biomarkers with outcomes in medium-size vessel occlusion (MeVO) stroke patients remains unknown.

Objectives: Therefore, we aimed to explore whether CTP parameters can be used for selection of a subset of MeVO patients that are more likely to benefit from EVT.

Methods: Consecutively enrolled acute MeVO stroke patients treated with EVT were included. All patients underwent CTP on admission and follow-up noncontrast CT 24 h post-EVT. CTP parameters including core and penumbra volumes were obtained. Excellent outcome, defined as a modified Rankin score of 0–1 at 90 days poststroke was the primary outcome, and survival at 90 days was the safety outcome. Regression analyses were performed to examine the associations between different CTP parameters and outcomes.

Results: Overall, 70 patients with MeVO were included (47% male, median age 75), and 66 (94%) had long-term follow-up data. Of those included, 26 patients (39%) had excellent outcomes and 2 (3%) had symptomatic intracerebral hemorrhage. On regression analysis, hypoperfused volumes on CTP were associated with excellent outcomes (adjusted odds ratio (aOR) 1.02, 95% confidence intervals (CI) 1.001–1.037), whereas core volume was not. Other factors associated with excellent outcome included admission National Institutes of Health Stroke Scale score (aOR 0.85, 95% CI 0.73–0.98) and lack of hypertension (aOR 0.07, 95% CI 0.07–0.62). Core or penumbral volumes were not associated with survival.

Conclusion: Higher volumes of hypoperfused tissue on CTP are associated with a higher likelihood of excellent outcome. Core and penumbral volumes are not associated with increased mortality in patients with MeVO that undergo EVT.

Keywords: CTP, MeVO, stroke

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Introduction

Medium diameter cerebral vessels are defined as vessels with luminal diameter of 0.75–2.0 mm. These typically include the nondominant branch of the M2 middle cerebral artery (MCA), M3 and M4 branches of the MCA, A1–A3 branches of the anterior cerebral artery (ACA), and P1–P3 branches of the posterior cerebral artery (PCA).[1] Categorization of M2 MCA, A1 ACA, and P1 PCA has been more challenging as the vessel architecture is highly heterogeneous across patients,[1] thus, in some patients, these vessels are considered medium-sized, but in others, they may defined as large vessels. Medium-diameter

vessel occlusion (MeVO) accounts for 25%–40% of all acute ischemic strokes.[1]

Although endovascular thrombectomy (EVT) has been established as safe in MeVO patients, the efficacy of EVT has not been well established, questioning the benefit of EVT over best medical management (BMT) including intravenous thrombolysis.[2–19] More recently, two of the randomized controlled studies exploring the efficacy of EVT in patients with MeVO failed to show the superiority of EVT over best medical care,[20,21] and the results of another large randomized controlled study are still pending (Distal Ischemic Stroke Treatment With Adjustable Low-profile Stentriever (DISTALS), NCT05152524).

This is somewhat surprising given that in patients presenting with large vessel occlusion (LVO), EVT has been proven to be efficacious over BMT in up to 24 h from symptoms onset despite the presence of large core.[22] One possible explanation to this discrepancy may be related to inadequate patient selection for EVT among patients with MeVO.

Computed tomography perfusion (CTP) imaging assessing tissue viability may increase diagnostic accuracy, in patients with LVO and MeVO.[23–28] However, whether CTP can aid in selecting treatment and provide prognostic information about functional outcomes among patients with MeVO remains controversial. Therefore, we aimed to study the usefulness of CTP as a prognostic tool in patients with MeVO that underwent EVT.

Patients and methods

Patients with MeVO were identified from two large cohorts of stroke patients admitted over the course of 5 years (January 2019–December 2023) to the stroke units at two tertiary academic centers. The study was approved by the institutional review board (HMO-0378-18) with an exemption to obtaining informed consent due to the retrospective use of anonymized data for this study.

Both centers maintain prospective all-inclusive registries of all patients undergoing EVT. Similar baseline demographics, risk factors, and clinical and radiographic data are documented prospectively at both centers. MeVO was diagnosed as an acute occlusion involving medium cerebral vessels (nondominant M2 branch to M4 MCA, A1–A3 ACA, and P1–P3 PCA) on CT angiography or MR angiography and confirmed at the time of EVT by digital subtraction angiography.

All included patients had an EVT procedure. The attending physician made the choice of EVT over medical treatment at the time of presentation and the reasons for choosing EVT over medical treatment were not available to us. The EVT technique was left to the discretion of the treating endovascular specialist, and all options including aspiration first or stentriever first were allowed. Recanalization of the occluded studies was classified with the modified thrombolysis in cerebral infarction (mTICI) score and mTICI 2b–3 was considered as successful recanalization.

All included patients also had CTP imaging upon presentation and were treated with EVT or BMT. CTP data were interpreted with automated software (RAPID; IschemaView Inc. Menlo Park CA USA at one institution and Philips IntelliSpace Portal, Amsterdam the Netherlands in the other) and data regarding cerebral blood flow (CBF), time to maximal contrast concentration (tMAX) delays, and presence of vessel occlusion were captured. The volume of tissue at tMAX delay of 6 s was used for hypoperfused tissue determination, and the volume of tissue showing CBF of $<30\%$ was used as the core volume. A stroke fellow, a stroke neurologist, and a neuroradiologist interpreted all CTP data. In cases of disagreement, the studies were seen by senior stroke neurologists (R.R.L., J.M.) and senior neuroradiologist (J.M.G.) for case adjudication.

The primary outcomes for this study included functional outcomes and survival, measured with the modified Rankin score (mRS) at 90 days after stroke. Excellent outcome was considered as mRS $\leqslant 1$. Secondary outcomes included the percentage of patients with symptomatic intracranial hemorrhage (sICH) defined according to ECASS 2 criteria.[29]

Statistical analysis

Statistical analysis was performed using the SPSS 29 software (IBM, Armrock, NY, USA). A $p < 0.05$ was considered significant. The χ^2 test was used to explore the link between qualitative variables. The Student's t test and Fisher exact test were used to compare continuous parametric

variables and the Median test with interquartile range (IQR) was used for nonparametric testing. Correlations between variables were measured with the Pearson's coefficient. We next performed multivariable logistic regression modeling to test for variables associated with the likelihood favorable outcome, mortality, and sICH. Variables entered in the regression analyses included only those variables yielding a p value of <0.05 on the univariate analyses with obligatory inclusion of core and hypoperfusion volumes. In addition, due to the relatively small number of included patients, we included in this regression only variables that were known to affect outcome such as age, the presence of sICH, and admission National Institutes of Health Stroke Scale (NIHSS).

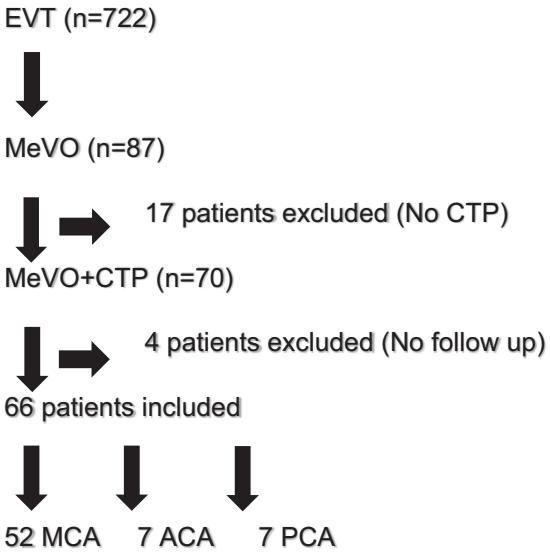

Figure 1. Flow chart for the study.
ACA, anterior cerebral artery; CTP, computerized tomography perfusion; EVT, endovascular thrombectomy; MCA, middle cerebral artery; MeVO, medium-size vessel occlusion; PCA, posterior cerebral artery.

Results

Overall, 722 patients underwent EVT during the study period. Among them, 87 patients had MeVO, and 70 patients underwent CTP imaging on admission (47 patients using RAPID, IschemaView Inc. and 23 patients using Philips IntelliSpace). For the outcomes analysis, we included 66 patients, and 4 patients were excluded due to lack of follow-up data on day 90 poststroke (Figure 1).

Among included patients, 26 (39%) achieved excellent outcomes (Table 1). Compared to those without excellent outcomes, patients with excellent outcomes were more often male (69% vs 37.5%, $p<0.01$), and less frequently had a history of hypertensions (69% vs 90%, $p<0.01$). They also had lower stroke severity at presentation ((NIHSS score (median, IQR 7 (5–8) vs 10.5 (8–16), $p<0.01$)). Patients with excellent outcomes showed a tendency toward younger age, but the difference between the groups did not reach statistical significance (median, IQR; 73 (55–80) vs 75 (67–81), $p=0.07$). Prestroke mRS was low and did not differ between the groups (median, IQR; 0 (0–0) vs 0 (0–2), $p=0.37$). The most common cause for MeVO was cardioembolism (Table 1). In both groups, the MCA was the most frequent blood vessel involved, and the M2 segment was occluded in 50% of all MeVO cases. Involvement of the M3 and M4 segments of the MCA were seen in 22% and 13% of the patients, whereas occlusions of the P1 segment occurred in 6% and in the P2, P3, A1, A2, and A3 in 2% each. Of note, involvement of the PCA was observed in one patient that had excellent outcomes and in six of those that did not. Similarly, none of the patients with ACA involvement had excellent outcomes and four had poor outcome. Individual vessel occlusion sites did not correlate with excellent outcome (Spearman's correlation, $p=0.114$). Both groups had excellent reperfusion rates post-EVT (mTICI 2b–3, 96% vs 87.5%, $p=0.23$), with low rate of any ICH (4% vs 17.5%, $p=0.09$) and sICH (0% vs 5%, $p=0.25$) post EVT (Table 1). On CTP imaging, hypoperfused tissue using tMAX delay of 6 s (mean, 64 ± 45 vs 63 ± 56, $p=0.68$) and core volume (mean $\pm$ SD, 9.67 ± 16.99 vs 14.68 ± 21.91, $p=0.33$) were similar. On further correlation testing, admission NIHSS was found to be correlated to hypoperfusion volumes ($p=0.002$), whereas the presence of hypertension was not ($p=0.583$).

In regression analysis that included variables that showed statistically significant differences between the groups (Table 2), factors that were negatively associated with excellent outcomes included hypertension (adjusted odds ratio (aOR), 0.07, 95% confidence intervals (CI), 0.01–0.62), and NIHSS score on admission (aOR 0.86, 95% CI 0.73–0.99). The volume of hypoperfused tissue on CTP was positively associated with excellent outcome (aOR 1.02, 95%, CI

Table 1. Characteristics of patients according to functional outcome.

Variable	Excellent outcome (*N* = 26)	Nonexcellent outcome (*N* = 40)	*p* Value
Sex (male %)	18 (69)	15 (37.5)	0.01
Age (median, IQR)	73 (55–80)	75 (67–81)	0.07
Hypertension (%)	18 (69)	38 (95)	<0.01
Diabetes mellitus (%)	9 (35)	13 (32.5)	0.86
Atrial fibrillation (%)	14 (54)	17 (42.5)	0.36
Ischemic heart disease (%)	13 (50)	16 (40)	0.42
Dyslipidemia (%)	16 (61.5)	25 (62.5)	0.94
Chronic heart failure (%)	3 (11.5)	5 (12.5)	0.91
Chronic kidney disease (%)	2 (8)	5 (12.5)	0.53
Smoking (%)	5 (19)	8 (20)	0.94
Old stroke (%)	6 (23)	8 (20)	0.76
Tissue plasminogen activator (%)	6 (24)	7 (17.5)	0.52
Vessel involved (%)			0.052
MCA (%)	25 (96)	27 (67)	
MCA M2 (%)	22 (84)	11 (27)	
MCA M3 (%)	2 (8)	10 (25)	
MCA M4 (%)	1 (4)	6 (15)	
PCA (%)	1 (4)	6 (15)	
PCA P1 (%)	1 (4)	3 (10)	
PCA P2 (%)	0 (0)	2 (2)	
PCA P3 (%)	0 (0)	1 (2)	
ACA (%)	0 (0)	7 (17)	
ACA A1 (%)	0 (0)	3 (7)	
ACA A2 (%)	0 (0)	2 (5)	
ACA A3 (%)	0 (0)	2 (5)	
TOAST (%)			0.30
Cardioembolism (%)	23 (88)	26 (65)	
Large artery atherosclerosis (%)	1 (4)	3 (7.5)	
Other known (%)	0 (0)	1 (2.5)	

(Continued)

Table 1. (Continued)

Variable	Excellent outcome (*N* = 26)	Nonexcellent outcome (*N* = 40)	*p* Value
Undetermined (%)	0 (0)	1 (2.5)	
Multiple	2 (8)	9 (22.5)	
mTICI 2b–3 (%)	25 (96)	35 (87.5)	0.23
Intra-cranial hemorrhage (%)	1(4)	7 (17.5)	0.09
Symptomatic ICH (%)	0 (0)	2 (5)	0.25
Number of passes (mean ± SD)	2.04 ± 1.62	2.97 ± 3.04	0.16
Admission NIHSS (median, IQR)	7 (5–8)	10.5 (8–16)	<0.01
Prestroke mRS (median, IQR)	0 (0)	0 (0–2)	0.37
OTD (minutes mean ± SD)	250 ± 249	318 ± 352	0.47
OTP (minutes mean ± SD)	414 ± 298	453 ± 386	0.74
ASPECT (median, IQR)	10 (8–10)	9 (7–10)	0.34
tMAX delay 6 s volume (cc, mean ± SD)	64 ± 45	63 ± 56	0.68
Core volume (cc, mean ± SD)	9.67 ± 16.99	14.68 ± 21.91	0.33

ACA, anterior cerebral artery; ASPECT, Alberta Stroke Program Early CT Score; ICH, intra-cranial hemorrhage; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin scale; mTICI, modified thrombolysis in cerebral infarction scale; NIHSS, National Institutes of Health Stroke Scale; OTD, onset to door (ED arrival); OTP, onset to groin puncture; PCA, posterior cerebral artery; tMAX, time to maximal contrast concentration; TOAST, trial of ORG 10172 in acute stroke treatment.

1.001–1.037). In contrast, core volume and male sex were not associated with excellent outcomes (Table 2).

Comparison of patients who survived ($N = 58$) to those that did not survive ($N = 8$) at 90 days from EVT (Table 3) showed that survivors were significantly younger (median, IQR, 74 (64–80) vs 81.5 (80.5–89), $p = 0.01$). However, survival was not associated with risk factors for stroke, lesion location, or stroke cause (Table 3). Prestroke mRS was significantly lower among survivors (median, IQR; 0 (0–0) vs 2 (0–3), $p < 0.01$). NIHSS scores on presentation were numerically lower in survivors but the difference between the groups did not reach statistical significance (median, IQR; 8 (6–12) vs 16.5 (11.75–18), $p = 0.06$). Analysis of radiological parameters showed that ASPECT scores were significantly higher among survivors (median, IQR; 9 (8–10) vs 6 (6–6.5), $p = 0.02$). CTP parameters showed that the volumes of hypoperfused tissue (mean ± sd, 60 ± 42 vs 102 ± 92, $p = 0.03$) and core (mean ± sd, 9.84 ± 16.58 vs 32.30 ± 11.17, $p < 0.01$) were lower among survivors. While onset of symptoms to presentation at the ER did not significantly differ between the groups (mean ± sd, 263 ± 292 vs 517 ± 388 min, $p = 0.16$), the time from symptoms onset to groin puncture was significantly shorter in survivors (mean ± sd, 394 ± 316 vs 892 ± 302, $p = 0.01$). Although sICH rates were numerically lower among patients that survived the difference between the groups did not reach significance (2% vs 12.5%, $p = 0.09$, Table 3). The causes of death among patients who did not survive were not directly related to the EVT procedure, except in one patient who had a sICH post EVT. Most commonly death was secondary to infectious complications or severe electrolyte imbalances causing cardiorespiratory arrest. Similarly, reperfusion status did not correlate with survival (Table 3).

In regression analysis exploring variables associated with survival, age (aOR 1, 95% CI

Table 2. Regression analysis for excellent outcomes among EVT-treated MeVO patients.

Variable	aOR	95% CI	*p* Value
Sex (male)	3.61	0.98–13.36	0.054
Hypertension	0.07	0.01–0.62	0.018
Admission NIHSS	0.85	0.73–0.99	0.035
tMAX delay 6 s volume	1.02	1.00–1.04	0.037
Core volume	0.96	0.92–1.01	0.092

aOR, adjusted odds ratio; CI, confidence interval; EVT, endovascular thrombectomy; MeVO, medium-size vessel occlusion; NIHSS, National Institutes of Health Stroke Scale; tMAX, time to maximal contrast concentration.

Table 3. Survival outcomes among patients with MeVO.

Variable	Survived (*N* = 58)	Deceased (*N* = 8)	*p* Value
Sex (male %)	30 (52)	3 (37.5)	0.47
Age (median, IQR)	74 (64–80)	81.5 (80.5–89)	0.01
Hypertension (%)	49 (83)	8 (100)	0.21
Diabetes mellitus (%)	21 (36)	1 (12.5)	0.19
Atrial fibrillation (%)	29 (49)	3 (37.5)	0.54
Ischemic heart disease (%)	25 (42)	4 (50)	0.68
Dyslipidemia (%)	37 (63)	5 (62.5)	0.99
Chronic heart failure (%)	6 (10)	2 (25)	0.22
Chronic kidney disease (%)	6 (10)	1 (12.5)	0.84
Smoking (%)	12 (20)	1 (12.5)	0.56
Old stroke (%)	13 (22)	1 (12.5)	0.53
Tissue plasminogen activator (%)	12 (21)	2 (25)	0.78
Vessel lesion (%)			0.41
MCA (%)	45 (77)	7 (87)	
MCA M2 (%)	28 (48)	5 (63)	
MCA M3 (%)	10 (17)	2 (25)	
MCA M4 (%)	7 (12)	0	
PCA (%)	6 (10)	1 (13)	
PCA P1 (%)	3 (5)	1 (13)	
PCA P2 (%)	2 (3)	0 (0)	
PCA P3 (%)	1 (2)	0 (0)	

(Continued)

Table 3. (Continued)

Variable	Survived (*N* = 58)	Deceased (*N* = 8)	*p* Value
ACA (%)	7 (12)	0 (0)	
ACA A1 (%)	3 (5)	0 (0)	
ACA A2 (%)	2 (3)	0 (0)	
ACA A3 (%)	2 (3)	0 (0)	
TOAST (%)			0.48
Cardioembolic	45 (76)	5 (63)	
Large artery atherosclerosis	4 (7)	0 (0)	
Other	1 (2)	0 (0)	
Undetermined	1 (2)	0 (0)	
Multiple etiology	8 (14)	3 (27)	
mTICI 2b–3 (%)	54 (91.5)	7 (87.5)	0.71
Intra-cranial hemorrhage (%)	6 (10)	2 (25)	0.22
sICH (%)	1 (2)	1 (12.5)	0.09
Number of passes (mean ± SD)	2.61 ± 2.63	2.29 ± 2.28	0.75
Admission NIHSS (median, IQR)	8 (6–12)	16.5 (11.75–18)	0.06
Prestroke mRS 0 (median, IQR)	0 (0–0)	2 (0–3)	<0.01
OTD (mean minutes ± SD)	263 ± 292	517 ± 388	0.16
OTP (mean minutes ± SD)	394 ± 316	892 ± 302	0.01
ASPECT (median, IQR)	9 (8–10)	6 (6–6.5)	0.02
tMAX 6 (mean ± SD)	60 ± 42	102 ± 92	0.03
CBF ± SD (mean ± SD)	9.84 ± 16.58	32.30 ± 11.17	<0.01

ACA, anterior cerebral artery; ASPECT, Alberta Stroke Program Early CT Score; CBF, cerebral blood flow; ICH, intra-cranial hemorrhage; IQR, interquartile range; MCA, middle cerebral artery; MeVO, medium-size vessel occlusion; mRS, modified Rankin scale; mTICI, modified thrombolysis in cerebral infarction scale; NIHSS, National Institutes of Health Stroke Scale; OTD, onset to door (ED arrival); OTP, onset to groin puncture; PCA, posterior cerebral artery; tMAX, time to maximal contrast concentration; TOAST, trial of ORG 10172 in acute stroke treatment.

0.75–1.00) and the presence of sICH (aOR 0.003, 95% CI 0.00–0.93) were associated with survival, whereas core or hypoperfused tissue volumes were not (Table 4).

Discussion

The main findings of the current study are that in MeVO patients that underwent EVT, higher volumes of hypoperfused tissue on CTP were associated with excellent outcome, whereas core volumes were not. Furthermore, core or hypoperfusion volumes were not associated with survival. Another finding that emerges from the current results is that EVT was relatively safe in this group of MeVO patients given the very low number of patients that experienced sICH in our cohort. It is important to note that the main objective of the

Table 4. Regression analysis for survival among EVT-treated MeVO patients.

Variable	aOR	95% CI	*p* Value
Admission NIHSS	0.89	0.69–1.03	0.342
Core volume	0.97	0.92–1.03	0.342
tMAX delay 6 s volume	1.00	0.98–1.03	0.98
Age (per year)	0.87	0.75–1.00	0.050
Prestroke mRS	0.48	0.20–1.11	0.085
Symptomatic ICH	0.003	0.00–0.93	0.047

aOR, adjusted odds ratio; CI, confidence interval; EVT, endovascular thrombectomy; ICH, intra-cranial hemorrhage; MeVO, medium-size vessel occlusion; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; tMAX, time to maximal contrast concentration.

current study was to test the prognostic value of CTP in patients with MeVO, and that the study was underpowered to provide evidence for the efficacy of EVT in these patients and did not include a control group.

Recently, two of the randomized controlled studies exploring the efficacy of EVT in patients with MeVO failed to show the superiority of EVT over best medical care,[20,21] and the results of another large randomized controlled study are still pending (DISTALS, NCT05152524). These neutral results highlight the need for better patient selection to enable better identification of a subset of MeVO patients that would benefit from EVT. Our study suggests that CTP may be a promising tool for such selection.

The baseline parameters of MeVO patients included in the current study are similar to those described before in terms of their age, lesion location, and comorbidities attesting to the potential generalizability of our results.[5,30]

Our results regarding the association between higher hypoperfusion volumes and excellent outcome are somewhat surprising given that recent published data found an association between, higher hypo-perfused volumes and poor outcomes in patients with LVO.[31,32]

Higher volumes of hypoperfused tissue likely correlate to a more proximal occlusion site and more akin to LVO. This could potentially make EVT simpler and more feasible due to less tortuosity and easier access.[1] Indeed, association of excellent outcomes to MCA lesion site were borderline significant ($p=0.052$). Moreover, lesions involving PCA or ACA territories were more commonly observed in patients who did not have excellent outcomes, and this is in line with the current literature showing that EVT in these types of strokes is likely less effective than for M2 MCA lesions.[4–11,33]

A recently published study also reported that higher hypoperfusion volumes were linked to better outcomes after EVT in patients with M2 MCA occlusions.[34] In that study, patient selection was limited to MCA M2 territory only, while our study included also more distal MCA lesions including M3 and M4, and other MeVO territories such as ACA and PCA, studying the use of CTP as a prognostic tool in a more heterogeneous group of patients, and thus better representing real world practice in patients with MeVO. Interestingly, the previous study[34] found core volume to be correlated with outcomes, whereas in our study, it was not. This discrepancy could potentially result from the wider inclusion criteria that allowed inclusion of patients with smaller cores involving more distal territories potentially diluting the effects of core size. Furthermore, the two studies used different automated software, and the previous study looked at mRS of 0–2 as favorable outcome, whereas in our mRS, outcome data was dichotomized to 0–1 versus 2 or larger. Moreover, favorable recanalization rates were much lower in the previous study ranging from 68% for those with favorable outcome to 50% in those with unfavorable outcome as compared to over 85% in both groups in the current study. All those represent factors which may have

impacted the results and could have led to the observed discrepancy in the results between the studies.

In the current analysis, core volumes were not associated with excellent outcomes. This is in contrast to findings among patients with LVO that underwent EVT[35,36] as well as in some studies in MeVO patients.[16,17] This discrepancy could result from the fact that in most MeVO cases core volumes were relatively small due to the more distal site of occlusion and would not be expected to lead to poor outcomes. Another potential explanation could be related to the perfusion scotoma phenomena, leading to underestimation of the core volume[37]; however, this phenomenon was not previously described in MeVO patients.

Other factors that were associated with lower rates of excellent outcomes in the current analysis included the presence of hypertension and more severe stroke symptoms and signs on admission outcome. The association of the former with lower rates of excellent outcome could be related to higher rates of atherosclerotic occlusion in patients with hypertension in contrast to cardioembolism secondary to heart failure or presence of left ventricular clots in some of the patients without hypertension. Atherosclerotic plaques in patients with MeVO may be more difficult to recanalize compared with embolic occlusions leading to this result.[38,39] This may be further complicated by the tendency for re-occlusion which is also more common in atherosclerotic disease. There is also association between intracranial atherosclerotic disease and smaller hypoperfused tissue on CTP comparing to LVO.[40] However, it should be noted that only a small fraction of our patients had large artery atherosclerosis as the cause of MeVO, and therefore, this could only partially explain the lack of efficacy of MeVO.

In contrast to previous studies, we could not show that older age was associated with poor outcomes in MeVO population treated with EVT despite a trend toward such an effect.[5,30]

On univariate analysis, MeVO patients that did not survive had larger hypoperfused tissue volumes and larger core volumes upon presentation. This is in line with the findings from recent studies, showing that larger hypo-perfused tissue and core volume are associated with poor outcomes.[31,32] However, in regression analysis, core or hypoperfusion volumes did not remain associated with survival. Large infarct cores were found to be associated with higher chances of poor outcome in LVO stroke.[35,36] As mentioned above, MeVO affects smaller volumes of brain tissue given the distal location of the occluded vessel, and this may explain at least in part the lack of association between core volumes and outcome in the current study.

Regarding the rates of recanalization and ICH, our patients had similar results to previously published data from case series, showing that EVT for MeVO is relatively safe, and that despite high recanalization rates, successful recanalization in itself does not predict outcome.[41,42] It should be noted that recanalization rates were lower in the published randomized controlled studies,[20,21] compared to our data and that obtained in prior case series, possibly due to inclusion of more distal occlusions and more ACA and PCA occlusions which may be less amenable to recanalization as compared to inclusion of higher proportion of M2 MCA occlusions in the current study.

Furthermore, while sICH was relatively rare in the current cohort, a relatively large number of patients did suffer from asymptomatic ICH mostly in the form of a mild hemorrhagic infraction type 1 or 2 that did not lead to neurological deterioration.

There are a number of limitations to our study, including its retrospective nature as well as the small number of included patients that could lead to a number of potential biases. Furthermore, ACA and PCA occlusions seemed to be underrepresented in the current study, but we believe that the frequency of these forms of strokes is much lower than those involving the MCA branches and therefore, the data are valid for real-life representation of MeVO strokes. In the current study, we used two different image processing software programs, and this may have caused sample heterogeneity and another potential form of bias. Given the use of different image processing systems, we could not compare further imaging data that could have important implications including Tmax rCBF mismatch, cerebral blood volume hypodensity index ratios, and indices of collateral perfusion estimates. Moreover, this study did not include a control group of non-EVT treatment and the reasons for choosing EVT over medical treatment for this study were not available

to us, which could have introduced selection bias as well. Nevertheless, the study did include consecutive patients treated with EVT, and the main characteristics of our patients are in line with those described in previous studies lending further credibility to our results. Furthermore, the current study was all-inclusive and not limited to one particular type of MeVO (e.g., M2 or PCA lesions) and therefore, it better portrays the everyday emergencies addressed in the emergency department.

In conclusion, MeVO patients treated with EVT have low rates of complications and mortality, but efficacy and excellent outcome remains unclear, and the results suggest that better outcomes could potentially be more frequent in selected patients including those patients with more proximal M2 MCA occlusion who are younger and have low NIHSS score upon presentation. CTP could guide for better selection of patients that would benefit from EVT treatment, and it could be used to predict outcomes in those with large hypo-perfused volumes. However, core volumes were not associated with excellent outcomes or with survival. Future larger-scale studies that include a control arm of patients that were not treated with EVT could reinform our findings and help us guide the correct treatment strategy for individual MeVO patients. Furthermore, we suggest that future studies should concentrate on more homogenous patient populations separately studying those with M2 MCA occlusions, PCA occlusions, and ACA occlusions in order to avoid dilution of the findings due to heterogeneity and different eloquence patterns.

Declarations

Ethics approval and consent to participate

The study was approved by the Hadassah Medical Organization institutional review board (HMO-0378-18) with an exemption to obtaining informed consent due to the retrospective use of anonymized data for this study.

Consent for publication

Not applicable.

Author contributions

Yoel Schwartzmann: Data curation; Formal analysis; Writing – original draft.

Hamza Joubran: Writing – review & editing.

Tamer Jubeh: Writing – review & editing.

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Aviva Alpernas: Data curation; Writing – review & editing.

Tali Jonas-Kimchi: Writing – review & editing.

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John M. Gomori: Writing – review & editing.

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Hen Hallevi: Writing – review & editing.

Jeremy Molad: Writing – review & editing.

Ronen R. Leker: Conceptualization; Formal analysis; Funding acquisition; Methodology; Supervision; Writing – review & editing.

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Competing interests

R.R.L. reports receiving speaker honoraria from IschemaView, Boehringer Ingelheim, Pfizer, Jansen, Biogen, Medtronic, and Abbott and advisory board honoraria from Jansen. All other authors have no disclosures.

Guarantor

As one of the main authors (R.R.L), I take full responsibility for the presented data, analyses, interpretation, and conduct of this study.

Availability of data and materials

Data can be available upon request of corresponding author.

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