Han et al. BMC Neurology (2025) 25:92
https://doi.org/10.1186/s12883-025-04111-w

BMC Neurology

RESEARCH Open Access

Early venous filling is associated with unfavorable outcomes in acute ischemic stroke with large vessel occlusion after mechanical thrombectomy: a real-world analysis

Jiaxin Han[1], Yixuan Wu[1], Zihan Wang[1], Jianfeng Han[1], Guogang Luo[1,2*] and Kang Huo[1,2*]

Abstract

Background The presence of early venous filling (EVF) post-mechanical thrombectomy (MT) in acute ischemic stroke (AIS) patients has been observed, yet its prognostic value for clinical outcomes remains underexplored. This study aimed to assess the correlation between EVF and poor clinical outcomes in AIS patients who underwent MT.

Materials and methods This retrospective analysis included AIS patients with large vessel occlusions treated with MT at the First Affiliated Hospital of Xi'an Jiaotong University from January 2018 to June 2023. The primary outcome was mRS at 90 days, secondary outcomes included hemorrhagic transformation, symptomatic intracranial hemorrhage, and malignant brain edema. The study used inverse probability weighting for balancing baseline characteristics and employed univariate and multivariate logistic regression analyses to explore the association between EVF and clinical outcomes. G*Power was used to calculate the sample size.

Results Among 307 patients, 75 (24.4%) presented with EVF. Patients with EVF had significantly higher rates of unfavorable outcomes at 90 days (76.00% vs. 46.12%, $P<0.001$). Multivariate analysis revealed significant associations between EVF and unfavorable outcome (odds ratio [OR] = 2.69, 95%CI [1.37–5.26], $P=0.004$), hemorrhagic transformation (OR = 3.11, 95%CI [1.73–5.62], $P<0.001$), symptomatic intracranial hemorrhage (OR = 3.24, 95%CI 1.42 to 7.37, $P=0.005$), and malignant brain edema (OR = 3.06, 95%CI [1.56–6.01], $P=0.001$). Stratified analysis showed EVF group with a baseline Alberta Stroke Program Early CT (ASPECT) score of ≤ 8 exhibited a higher risk of unfavorable outcomes compared with patients in the non-EVF group (OR = 2.64, 95%CI [1.03–6.73], $P=0.042$). Mediation analysis indicated that malignant brain edema accounted for 35.42% of the correlation between EVF and unfavorable outcomes.

Conclusions This study establishes EVF as an independent risk factor for unfavorable outcomes after MT in AIS. Therefore, EVF in conjunction with a low ASPECT score provides essential insights for identifying patients at high risk for unfavorable outcomes.

Keywords Acute ischemic stroke, Clinical outcomes, Early venous filling, Mechanical thrombectomy, Risk factor

*Correspondence:
Guogang Luo
lguogang@163.com
Kang Huo
huokang@xjtufh.edu.cn
Full list of author information is available at the end of the article

Background

Mechanical thrombectomy (MT) has demonstrated superiority to intravenous thrombolytics as a treatment for patients with acute ischemic stroke (AIS) due to large-vessel occlusion [1]. Previous randomised trials have shown an overwhelming benefit of mechanical thrombectomy for treating acute ischaemic stroke due to large vessel occlusion [2]. Despite the success of second-generation thrombectomy devices, a meta-analysis revealed that 54% of patients do not achieve favorable clinical outcomes following endovascular thrombectomy. This was called futile recanalization, defined as a 90-day modified Rankin Scale score > 2 [3]. Malignant brain edema and symptomatic intracranial hemorrhage were common devastating complications following MT for AIS. Both conditions can lead to neurological deterioration and diminish the efficacy of MT, ultimately impacting long-term clinical outcomes [4, 5].

Early venous filling (EVF) is identified through digital subtraction angiography (DSA) following revascularization procedures, such as MT in AIS [6]. This imaging phenomenon, initially described by E. J. Ferris et al., is characterized by the premature appearance of venous structures during the arterial phase of DSA, suggesting a deviation from the normal sequential flow of blood from arteries through capillaries to veins [7]. It was described that EVF is associated with vascular responses of cerebral ischemia—leading to vasodilation in the ischemic region and rapid contrast transit, reflecting a local state of hyper-perfusion [8]. It was also demonstrated that EVF indicates a higher circulating blood flow, representing local cerebral congestion known as "luxury perfusion" defined as a state of cerebral increased venous saturation when cerebral blood-flow exceeded the demands of cerebral metabolism [9, 10]. Such events can escalate the disruption of the blood–brain barrier, potentially leading to hemorrhagic transformation and malignant brain edema [11–13].

Further studies indicated that the presence of EVF following MT serves as a predictor for postoperative reperfusion hemorrhage [8, 14]. Li et al. demonstrated an independent association between EVF and adverse clinical outcomes, including hemorrhagic transformation and malignant brain edema [15]. However, previous studies exhibited considerable variability in the baseline National Institutes of Health Stroke Scale (NIHSS) score and applied overly stringent inclusion criteria, such as requiring NIHSS score greater than 6 [8, 15]. Numerous studies have investigated the efficacy of MT in patients with minor strokes (NIHSS score < 6) due to large vessel occlusion, indicating that approximately 20% of these patients may deteriorate without recanalization therapy [16, 17]. Consequently, in the real world, operators often employ revascularization in this patient group. Studies that associate EVF with poor clinical outcomes after EVT in a real-world setting are lacking. Therefore, this study included patients who underwent EVT under real-world conditions and aimed to elucidate the association between EVF and unfavorable clinical outcomes following MT in a real-world setting.

Material and methods

Study design and patient selection

We retrospectively reviewed the data of patients diagnosed with AIS caused by large artery occlusion who underwent MT at the First Affiliated Hospital of Xi'an Jiaotong University from January 2018 to December 2022. All data were collected retrospectively, so informed consent was not required by the ethics committee by the Medical Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University. The research was approved by the Medical Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University (XJTU-1AF2023LSK-443). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Inclusion criteria were as follows: 1) Treatment with EVT within 24 h of symptom onset; 2) Diagnosis of AIS from imaging-confirmed intracranial occlusion, specifically in the internal carotid or middle cerebral artery (M1/M2); 3) Successful reperfusion post-EVT, indicated by a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b or higher on DSA; 4) A baseline mRS score of ≤ 2 prior to stroke onset; 5) A baseline Alberta Stroke Program Early CT (ASPECT) score ≥ 6. Exclusion criteria included: 1) Loss of CT images within 72 h or DSA films post-MT; 2) Detection of hemorrhage in immediate postoperative CT scans post-EVT; 3) Loss to follow-up during the 90-day visit; 4) Presence of arteriovenous malformations.

Data collection

Baseline data were categorized into three main groups for analysis: demographics (age, gender), patient characteristics (hypertension, diabetes, coronary artery disease, atrial fibrillation), and specific metrics related to thrombectomy procedures (door-to-puncture time and stroke onset-to-puncture time). The NIHSS scores at admission were obtained through a standardized chart review [18]. The ASPECT scores were collected based on baseline CT images [19]. Assessment of ASPECT scores was independently conducted by two experienced neurointerventionalists and interobserver agreement between the two physicians was assessed using the Kappa statistic.

Stroke subtypes were classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. Laboratory tests encompassed neutrophils, lymphocytes, platelets, low-density lipoprotein, and glucose levels. Surgical factors included the administration of intravenous thrombolysis, number of device passes, and balloon dilation.

Definition of EVF

We collected digital subtraction angiography (DSA) images of all patients from the venous to the arterial phase in every frame. EVF was defined as the angiographic early appearance of any cerebral vein before the late arterial phase on post-reperfusion DSA, which was categorized dichotomously (i.e., present or absent) for functional outcomes [20]. This encompassed EVF in cortical and thalamostriate veins. The arterial phase was delineated from the initial appearance of contrast in the cervical internal carotid artery to its appearance in the M4 segment of the middle cerebral artery (MCA) [21]. Assessment of EVF was independently conducted by two experienced neurointerventionalists, with 13 years and 8 years of experience, respectively, without prior knowledge of the clinical findings. The interobserver agreement between the two neurointerventionalists was assessed using the Kappa statistic.

Outcome assessment

Neurological function recovery was assessed using mRS at 90 days after symptom onset. The primary outcome was defined as an mRS score of >2, indicating an unfavorable outcome. Secondary unfavorable outcomes included hemorrhagic transformation (defined as any hemorrhage verified by follow-up CT scans within 72 h after MT), symptomatic intracranial hemorrhage (confirmed by CT images associated with a neurological decline of ≥ 4 points on the NIHSS scale), and malignant brain edema (characterized by parenchymal hypodensity in $\geq 50\%$ of the MCA territory and evidence of local swelling [e.g., sulcal effacement, lateral ventricle compression] or a ≥ 5 mm midline shift [septum pellucidum, cerebral falx, midbrain, pineal gland, or third ventricle], confirmed by CT within 72 h following MT) [4].

Sample size

The prevalence of EVF was elevated to approximately 25% based on previous studies. Assuming unfavorable outcomes in patients without EVF to be 40% and an odds ratio of 1.5 for unfavorable outcomes in patients with EVF we needed 295 samples with an 80% power and 5% significance.G*Power was used to calculate sample size.

Statistical analysis

Continuous variables (age, time from door to puncture, time from stroke onset to puncture, and laboratory measures) are presented as the median (IQR), and categorical variables (gender, occluded site, intravenous thrombolytic, medical history) are presented as proportions. Missing data were imputed using a machine learning algorithm, specifically random forest imputation. Baseline characteristics between groups were balanced using inverse probability weighting (IPTW).

Univariate and multivariate logistic regression were used to find the association between EVF and unfavorable outcomes. Univariate analysis was followed by multivariate logistic regression with stepwise variable selection. Significant confounders ($P \leq 0.1$) were included in the multivariate model through stepwise variable selection. Propensity scores based on these characteristics (age, gender, baseline glucose, occlusion site, baseline NIHSS score, and baseline ASPECT score) were calculated using a probit model. Multivariable logistic regression analysis adjusted for prespecified covariates mentioned above, and inverse probability treatment weighting (IPTW) was used to assess the association of the treatment approach with primary and secondary outcomes. Stratified multivariate logistic regression analyses were conducted based on infarct core sizes: small (ASPECT score >8) and large (ASPECT score ≤ 8). Mediation analysis was utilized to assess the mediation effect of EVF on the association between infarct core size and unfavorable outcome, employing the Baron and Kenny framework and the Vanderweele and Vansteelandt method in Stata statistical software. Sensitivity analyses were performed by stratifying data according to stroke severity, using NIHSS scores of 13 as thresholds. Some independent variables had missing values. Consequently, we utilized multiple imputation by chained equations (MICE) and conducted subsequent analyses to ascertain the robustness of the model. All statistical analyses were conducted using StataSE16 (StataCorp LP, College Station, TX, USA). A two-tailed value of $P \leq 0.05$ was considered significant.

Results

Patient baseline characteristics

Among the 375 patients with AIS in the anterior circulation who were admitted to the First Affiliated Hospital of Xi'an Jiaotong University between January 2018 and June 2023, a total of 307 who underwent MT were included in the study (Supplementary Fig. 1, Flowchart). In terms of assessment of imaging indicators, the interrater agreement demonstrated good consistency, with a kappa coefficient of 0.884 for the assessment of EVF, and a kappa coefficient of 0.846 for the assessment of ASPECT score. As shown in Table 1, A total of 75 patients (24.4%) presented with EVF. The EVF group exhibited a higher baseline NIHSS score (14 [11,18] vs. 12 [8,15], $P=0.003$), a higher age (69[63,77] vs. 67[57,73], $P=0.020$) and a lower ASPECT score (8 [7,9] vs. 9 [8,9], $P=0.003$) compared to the non-EVF group. No significant differences were observed between the EVF and non-EVF groups in terms of stroke cause or occlusion site, regardless of whether taking intravenous thrombolytic therapy, the number of device passes, or the time from stroke onset to puncture. Baseline characteristics between the two groups were balanced using IPTW. After inverse probability weighted matching, no significant differences were found in the baseline NIHSS scores (12 [9,17] vs. 13 [9,16], $P=0.534$), age (66[58,75] vs. 67[58,75], $P=0.851$) or ASPECT scores (8 [7,9] vs. 8 [8,9], $P=0.081$) between the EVF and non-EVF groups. Figure 1 shows the follow-up CT images of 2 cases who presented with EVF after MT.

Association between EVF and poor clinical outcomes after MT

Table 2 shows the results of the univariate and multivariate logistic regression used to investigate the association

Table 1 Baseline characteristics of EVF(+) and EVF(-)Cohorts before and after IPTW

	Original population			**IPTW adjusted population**		
	EVF + (*n* = 75)	**EVF- (*n* = 232)**	***P***	**EVF + (*n* = 151)**	**EVF- (*n* = 156)**	***P***
Demographic characteristics						
Age;years, median(IQR)	69(63,77)	67(57,73)	0.020	66(58,75)	67(58,75)	0.851
Male, n (%)	44(58.67)	143(61.64)	0.647	92(61.11)	95(61.21)	0.988
Risk factors, n (%)						
Atrial fibrillation	27(32.76)	76(36.00)	0.605	49(32.29)	53(33.66)	0.824
Hypertension	39(52.00)	120(51.72)	0.967	80(53.57)	81(51.55)	0.767
Diabetes	19(25.33)	45(19.40)	0.271	46(30.71)	30(18.94)	0.067
Coronary artery disease	20(26.67)	51(21.98)	0.403	37(24.75)	36(22.89)	0.746
NIHSS score, median(IQR)	14(11,18)	12(8,15)	0.003	12(9,17)	13(9,16)	0.534
ASPECT score, median(IQR)	8(7,9)	9(8,9)	0.003	8(7, 9)	8(8, 9)	0.081
Intravenous hrombolytic, n (%)	25(33.33)	65(28.02)	0.379	41(32.95)	35(26.63)	0.373
Stroke cause, n (%)			0.252			0.897
LAA	95(44.00)	33(40.95)		67(53.06)	51(39.05)	
CE	38(50.67)	109(46.98)		51(40.23)	63(47.97)	
Undetermined or others	4(5.33)	28(12.07)		8(6.71)	17(12.98)	
Occlusion site, n (%)			0.187			0.338
ICA	17(22.67)	73(31.47)		33(26.56)	42(31.96)	
MCA	44(58.67)	131(56.47)		69(55.11)	71(54.45)	
ICA + MCA	28(18.67)	14(12.07)		23(18.33)	18(13.60)	
Laboratory index						
Platelets*10^9/L, median(IQR)	196(152,230)	195(168,230)	0.670	196(161,224)	195(166,230)	0.749
Neutrophil*10^9/L, median(IQR)	6.9(5.7,9.4)	7.3(5.7.8.5)	0.678	6.8(5.5,9.5)	7.3(5.7,9.1)	0.416
Lymphocyte*10^9/L, median(IQR)	1.0(0.8,1.4)	1.1(0.8,1.5)	0.172	1.0(0.7,1.2)	1.1(0.6,1.4)	0.704
Glu;mmol/L, median(IQR)	6.9(6.1,8.3)	6.6(5.6,8.2)	0.148	6.8(5.7,8.5)	6.7(5.5,8.1)	0.629
LDL;mmol/L, median(IQR)	2.1(1.6,2.7)	2.1(1.7,2.6)	0.956	2.1(1.8,2.8)	2.0(1.6,2.4)	0.067
Operation-related indicators						
OPT;min, median(IQR)	390(285,505)	465(311,567)	0.287	422(289,505)	468(311,570)	0.530
DPT;min, median(IQR)	130(81,225)	130(96,191)	0.965	131(80,162)	126(92,146)	0.921
Balloon dilation, n (%)	19(25.33)	64(27.59)	0.703	37(29.49)	39(30.04)	0.939
Endovascular stents, n (%)	16(21.33)	55(23.71)	0.672	33(25.07)	35(28.04)	0.668
mTICI > 2b; n(%)	175(64.00)	48(75.43)	0.054	78(62.10)	94(72.24)	0.159
Number of device passes, median(IQR)	2(1,3)	2(1,3)	0.059	2(1,3)	2(1,3)	0.118

CE Cardioembolic, *DNT* time from door to puncture, *ICA* Internal carotid artery, *LAA* Large artery atherosclerosis, *LDL* Low-density lipoprotein, *MCA* Middle cerebral artery, *mTICI* modified thrombolysis in cerebral infarction score, *OPT* time from stroke onset to puncture

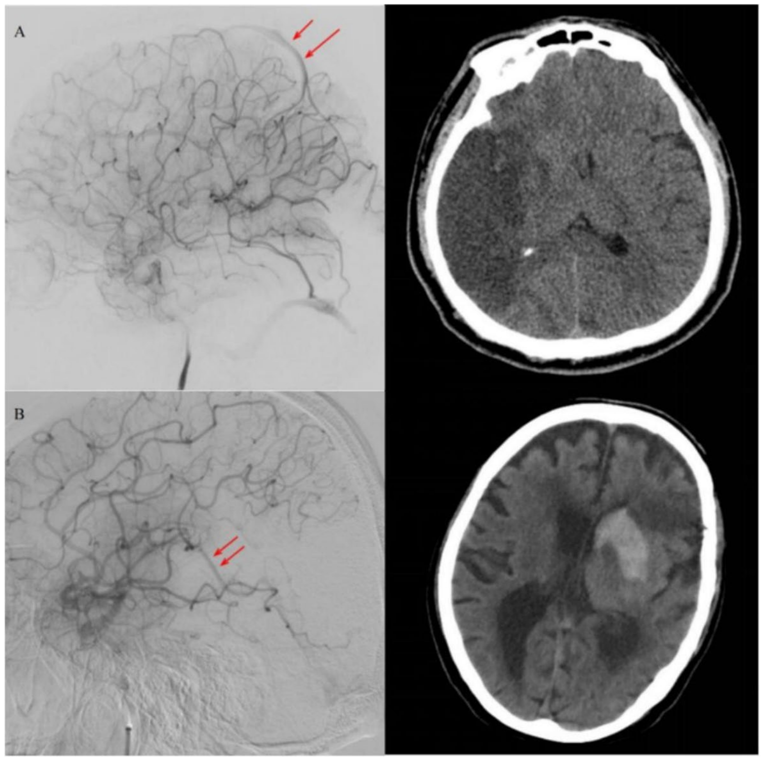

Fig. 1 Outcomes of EVF during MT. **A** Patient 1 presents with EVF on DSA during MT (indicated by red arrows), and follow-up CT images suggest malignant brain edema; **B** Patient 2 presents with EVF on DSA during MT (indicated by red arrows), and follow-up CT images suggest hemorrhagic transformation. CT, computed tomography; DSA, digital subtraction angiography; EVF, early venous filling; MT, mechanical thrombectomy

between EVF and poor clinical outcomes. The overall incidence rates of unfavorable outcome, hemorrhagic transformation, symptomatic intracranial hemorrhage, and malignant brain edema were 53.42%, 34.85%, 10.10%, and 19.21%, respectively. The distribution of the mRS score on the 90th day between the EVF group and non-EVF group is displayed in Fig. 2. The incidence of unfavorable outcomes was significantly higher in the EVF group compared with the non-EVF group (76.00% vs. 46.12%, $P<0.001$). Univariate analysis revealed a significant association between EVF and unfavorable outcomes (OR = 3.69, 95% CI [2.05–6.99], $P<0.001$). Multivariate regression analysis, after adjusting for factors such as age, gender, baseline glucose, atrial fibrillation, coronary artery disease, baseline NIHSS score and baseline ASPECT score (Model 1), showed EVF was significantly associated with unfavorable outcomes (OR = 2.96, 95% CI [1.53–5.71], $P=0.001$). Even upon further adjustment for factors including an mTICI score > 2b and the number of device passes (Model 2), EVF was still significantly associated with unfavorable outcomes (OR = 2.69, 95% CI[1.37–5.26], $P=0.004$). Similarly, the incidence rates of hemorrhagic transformation (57.33% vs. 27.59%, $P<0.001$), symptomatic intracranial hemorrhage (21.33% vs. 6.47%, $P<0.001$), and malignant brain edema (37.33% vs. 13.36%, $P<0.001$) were significantly higher in the EVF group compared with the non-EVF group. In univariate analysis, EVF was significantly associated with hemorrhagic transformation (OR = 3.52, 95% CI [2.05–6.05], $P<0.001$), symptomatic intracranial hemorrhage (OR = 3.92, 95% CI [1.83–8.39], $P<0.001$), and malignant brain edema (OR = 3.86, 95% CI [2.11–7.04], $P<0.001$). Multivariate analysis suggested that EVF was significantly associated with hemorrhagic transformation (OR = 3.06, 95% CI [1.72–5.46], $P<0.001$), symptomatic intracranial hemorrhage (OR = 3.42, 95% CI [1.51–7.74], $P=0.003$) after adjusting for age, gender, baseline glucose, occlusion site, baseline NIHSS score, and baseline ASPECT score (Model 1). This association remained significant upon further adjustment for variables such as the number of device passes and the use of endovascular stents (Model 2). Likewise, when adjusting for age, gender, baseline NIHSS score, baseline ASPECT score, baseline glucose, baseline neutrophil, and coronary artery disease (Model 1), EVF was significantly associated with malignant brain edema (OR = 3.16, 95% CI [1.62–6.18], $P=0.001$). Upon further adjustment for stroke onset-to-puncture time(OPT) and number of device passes (Model 2), the

Table 2 Univariate and multivariate regression analysis for comparison of EVF by clinical outcome

	Total	EVF +	EVF-	OR(95%CI)	*P*	IPTW adjusted	
	n = 307	*n* = 75	*n* = 232			OR(95%CI)	*P*
Unfavorable outcome	164(53.42%)	57(76.00%)	107(46.12%)				
Univariate analysis				3.69(2.05–6.99)	< 0.001	2.35(1.25–4.40)	0.008
Model 1				2.96(1.53–5.71)	0.001	2.88(1.49–5.59)	0.002
Model 2				2.69(1.37–5.26)	0.004	2.70(1.39–5.25)	0.003
MBE	59(19.21%)	28(37.33%)	31(13.36%)				
Univariate analysis				3.86(2.11–7.04)	< 0.001	2.52(1.33–4.76)	0.004
Model 1				3.16(1.62–6.18)	0.001	3.02(1.56–5.84)	0.001
Model 2				3.06(1.56–6.01)	0.001	3.01(1.55–5.84)	0.001
SICH	31(10.10%)	16(21.33%)	15(6.47%)				
Univariate analysis				3.92(1.83–8.39)	< 0.001	2.59(1.15–5.79)	0.021
Model 1				3.42(1.51–7.74)	0.003	3.14(1.37–7.16)	0.006
Model 2				3.24(1.42–7.37)	0.005	3.25(1.38–7.62)	0.007
HT	107(34.85%)	43(57.33%)	64(27.59%)				
Univariate analysis				3.52(2.05–6.05)	< 0.001	2.73(1.53–4.84)	0.001
Model 1				3.06(1.72–5.46)	< 0.001	2.94(1.64–5.29)	< 0.001
Model 2				3.11(1.73–5.62)	< 0.001	3.26(1.81–5.88)	< 0.001

Notes: For unfavorable outcome: Model 1 included age, gender, baseline glucose, atrial fibrillation, coronary artery disease, baseline NIHSS score, baseline ASPECT score; Model 2 included age, gender, baseline glucose, atrial fibrillation, coronary artery disease, baseline NIHSS score, baseline ASPECT score, mTICI score > 2b, number of device passes

For malignant brain edema: Model 1 included age, gender, baseline NIHSS score, baseline ASPECT score, baseline glucose, baseline neutrophil, coronary artery disease; Model 2 included age, gender, baseline NIHSS score, baseline ASPECT score, baseline glucose, baseline neutrophil, coronary artery disease, OPT, number of device passes

For hemorrhagic transformation and symptomatic intracranial hemorrhage: Model 1 included age, gender, baseline glucose, occlusion site, baseline NIHSS score, baseline ASPECT score; Model 2 included age, gender, baseline glucose, occlusion site, baseline NIHSS score, baseline ASPECT score, number of device passes, endovascular stents

ASPECT Alberta Stroke Program Early CT, *EVF* Early venous filling, *HT* Hemorrhagic transformation, *MBE* Malignant brain edema, *mTICI* modified thrombolysis in cerebral infarction, *NIHSS* National Institutes of Health Stroke Scale, *OPT* time from stroke onset to puncture, *SICH* Symptomatic intracranial hemorrhage

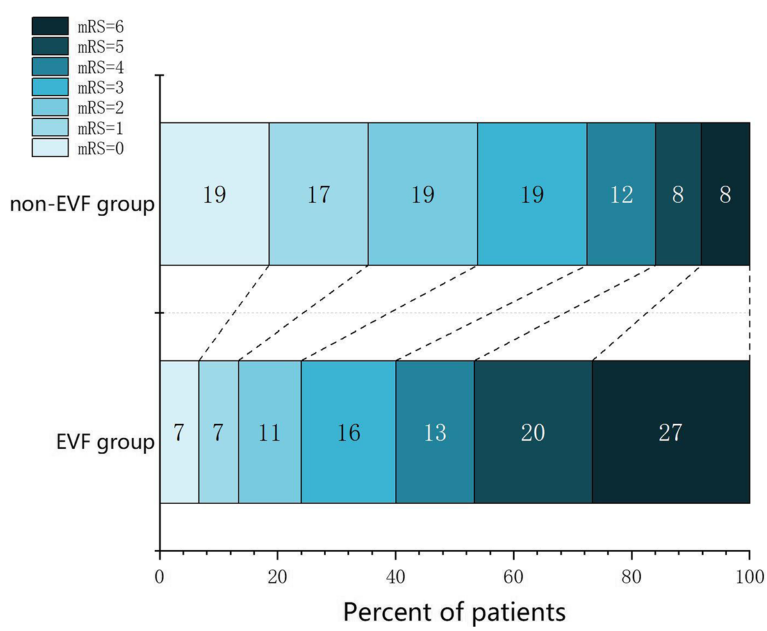

Fig. 2 Distribution of modified Rankin scale scores at 90 days in patients grouped by EVF. EVF, early venous filling

result remained consistent (OR = 3.06, 95% CI [1.56–6.01], $P = 0.001$) Supplementary Fig. 2-5 shows forest plot for multivariate analyses.

These findings were also validated in the dataset with covariates balanced by PSW. In all three IPTW-weighted regression models, the ORs ranged from 2.35 to 2.70 in estimating unfavorable outcome, 2.73 to 3.26 in estimating hemorrhagic transformation, 2.52 to 3.01 in estimating malignant edema, and 2.59 to 3.25 in estimating symptomatic intracranial hemorrhage (Table 2).

Stratified analysis of EVF association with poor clinical outcomes

In the subgroup stratified analysis, patients in the EVF group with a baseline ASPECT score ≤ 8 exhibited a significantly higher risk of unfavorable outcome (OR = 2.64, 95% CI [1.03–6.73], $P = 0.042$), malignant brain edema (OR = 4.59, 95% CI [1.94–10.83], $P < 0.001$), symptomatic intracranial hemorrhage (OR = 4.10, 95% CI [1.55–10.86], $P = 0.004$) and hemorrhagic transformation (OR = 3.56, 95% CI [1.59–7.95], $P = 0.002$) than patients in the non-EVF group, whereas this association was not observed in patients with a baseline ASPECT score > 8 (Table 3.). Sensitivity analyses were performed by stratifying data according to stroke severity, EVT time windows, occlusion sites we found that association between EVF and poor clinical outcomes remained consistent (Supplementary Table 1–3).

Mediation analysis between EVF and unfavorable outcome

To further investigate whether the impact of EVF on unfavorable outcome is mediated through increased rates of malignant brain edema, symptomatic intracranial hemorrhage, or hemorrhagic transformation, a mediation analysis was conducted. The results revealed malignant brain edema as a significant mediator, contributing to 35.42% of the relationship between EVF and unfavorable outcomes. Conversely, no significant mediation effects were detected for symptomatic intracranial hemorrhage or hemorrhagic transformation in relation to unfavorable outcomes (Supplementary Table 4).

Discussion

This study identified EVF as an independent risk factor for unfavorable outcomes, including malignant brain edema, symptomatic intracranial hemorrhage, hemorrhagic transformation, and 90-day mRS > 2 following MT in AIS patients with large vessel occlusions. Further

Table 3 Association between poor clinical outcomes and EVF after mechanical thrombectomy in ASPECT score stratified analyses

	Total *n* = 307	**EVF +** *n* = 75	**EVF-** *n* = 232	**OR(95%CI)**	***P***
Unfavorable outcome					
Total	164(53.42%)	57(76.00%)	107(46.12%)	2.69(1.37–5.26)	0.004
ASPECT score > 8	70(46.36%)	21(72.41%)	49(40.16%)	2.73(0.96–7.70)	0.058
ASPECT score ≤ 8	94(60.26%)	36(78.26%)	58(52.73%)	2.64(1.03–6.73)	0.042
MBE					
Total	59(19.21%)	28(37.33%)	31(13.36%)	3.06(1.56–6.01)	0.001
ASPECT score > 8	17(11.26%)	5(17.24%)	12(9.83%)	1.28(0.36–4.54)	0.699
ASPECT score ≤ 8	42(26.92%)	23(50.00%)	19(17.27%)	4.59(1.94–10.83)	< 0.001
HT					
Total	107(34.85%)	43(57.33%)	64(27.59%)	2.98(1.64–5.42)	< 0.001
ASPECT score > 8	41(27.15%)	14(48.28%)	27(22.13%)	2.38(0.93–6.09)	0.070
ASPECT score ≤ 8	66(42.31%)	29(63.04%)	37(33.64%)	3.56(1.59–7.95)	0.002
SICH					
Total	31(10.10%)	16(21.33%)	15(6.47%)	2.86(1.23–6.66)	0.041
ASPECT score > 8	6(3.97%)	2(6.90%)	4(3.28%)	1.67(0.26–10.72)	0.591
ASPECT score ≤ 8	25(16.02%)	14(30.43%)	11(10.00%)	4.10(1.55–10.86)	0.004

For unfavorable outcome: Adjusted for age, gender, baseline glucose, atrial fibrillation, coronary artery disease, baseline NIHSS score, baseline ASPECT score, mTICI score > 2b, number of device passes

For malignant brain edema: Adjusted for age, gender, baseline NIHSS score, baseline ASPECT score, baseline glucose, baseline neutrophil, coronary artery disease, OPT, number of device passes

For hemorrhagic transformation and symptomatic intracranial hemorrhage: Adjusted for age, gender, baseline glucose, occlusion site, baseline NIHSS score, baseline ASPECT score, number of device passes, endovascular stents

ASPECT Alberta Stroke Program Early CT, *EVF* Early venous filling, *HT* Hemorrhagic transformation, *MBE* Malignant brain edema, *mTICI* modified thrombolysis in cerebral infarction, *NIHSS* National Institutes of Health Stroke Scale, *OPT* time from stroke onset to puncture, *SICH* Symptomatic intracranial hemorrhage stratified analysis showed that patients in the EVF group with a baseline ASPECT score ≤ 8 exhibited a higher risk of unfavorable outcomes compared with patients in the non-EVF group. Additionally, it was found that malignant brain edema fully mediated the impact of EVF on 90-day unfavorable outcomes.

The pathophysiological mechanisms of EVF have not been fully understood. Previous studies have suggested an association with local hyperperfusion and also proposed the possibility of intracranial venous autoregulation failure after ischemic reperfusion therapy. The sudden increase in blood flow floods the venous system with consequent widespread vasodilatation, leading to premature venous manifestation. Venous dilatation may lead to blood retention, thereby impairing cerebral venous return [22]. Yu et al. suggested that abnormal cerebral venous drainage in large infarcts accelerates and exacerbates cerebral edema [23]. Song K et al. demonstrated that blocking the bilateral external jugular veins in animal models impaired cerebral venous return. They also found that this blockage did not reduce neurological function in normal mice. However, in the case of middle cerebral artery occlusion, a blockade of bilateral external jugular veins can significantly exacerbate neurological impairment [24]. In addition, tight junctions consisting of proteins located between endothelial cells play an important role in the formation of continuous vascular structures and help to maintain the integrity of the blood–brain barrier. In a study by Song K et al., crucial tight junction proteins, such as ZO-1 and occludin, significantly decreased in mice with blocked bilateral external jugular veins, which was accompanied by more severe brain edema [25]. Therefore, it is speculated that venous malformations resulting from impaired cerebral venous return post-ischemia further exacerbate blood–brain barrier disruption, leading to hemorrhagic transformation or malignant brain edema.

Previous studies have investigated the association between EVF and poor clinical outcomes after MT for AIS. Li et al. associated EVF with a higher likelihood of intracranial hemorrhage and malignant brain edema but not with mortality or favorable outcomes, emphasizing its predictive value for post-procedural complications [15]. Similarly, Faisal et al. found significant associations between EVF and worse hemorrhagic outcomes, including symptomatic intracranial hemorrhage and hemorrhagic transformation, underscoring the need for vigilant patient management. Recent studies by Elands et al. and Shuai et al. have linked EVF to an increased risk of reperfusion hemorrhage after MT for AIS [26, 27], although these findings were sometimes constrained by limitations like small sample sizes and imbalanced baseline NIHSS scores [28, 29]. What's more, our study included a population with EVF under real-world conditions, and employed IPTW to more accurately control for potential confounders, thereby offering a refined analysis that aligns with the nuanced understanding brought forth by recent investigations. It was demonstrated that EVF remains an important predictor of poor outcomes in the broader EVT population.

Our findings further underscore EVF as a significant predictor for both short-term and long-term adverse outcomes post-MT, notably malignant brain edema and overall unfavorable outcome. Unlike Li Y et al.'s study, EVF was independently associated with hemorrhagic transformation, malignant brain edema, and symptomatic intracranial hemorrhage, but not with unfavorable long-term outcomes [15]. To explore possible causes, we performed a mediation analysis and found that malignant brain edema accounted for 35.42% of the EVF effect on unfavorable long-term outcomes. This suggested a significant pathway through which EVF contributes to poor long-term outcomes, primarily by elevating the risk of malignant brain edema. Notably, the occurrence rate of malignant brain edema in our cohort was 19.21%, which was considerably higher than the 8.60% reported by Li Y et al., which may be attributed to differences in stroke severity and infarct size among the enrolled patients.

Our stratified analysis revealed that EVF is an independent risk factor for malignant brain edema, symptomatic intracranial hemorrhage, and hemorrhagic transformation after MT, but only in patients with an ASPECT score of ≤ 8 points. Therefore, the predictive value of EVF for malignant brain edema and hemorrhagic transformation is limited in patients with small infarct cores (ASPECT score > 8). This conclusion needs to be further explored in studies with larger sample sizes. It could be interpreted that ASPECT scores are indicative of the size of the infarct core and quality of collateral circulation [30]. Patients with relatively high ASPECT scores upon admission may have smaller infarct cores and better collateral circulation, and they may be more tolerant of the local hyperperfusion induced by EVF [31–33]. This underscores the practical relevance of our findings: EVF may be considered a risk factor for predicting poor clinical outcomes after MT for patients with severe ischemic stroke in the real world. The EVF and ASPECT scores offer accessible imaging data, enabling neurointerventionalists to rapidly identify patients at high risk for poor short-term clinical outcomes through CT and DSA imaging interpretation. Patients with EVF and a low ASPECT score might require a more robust surgical strategy and careful post-operative management. At the same time, EVF can serve as a novel independent predictor, combined with other known predictors such as blood glucose levels, to assess poor prognosis after EVT and enhance predictive performance.

There were limitations in our study. Firstly, this was a retrospective study, and the sample may not be fully representative. The study exclusively included Asian populations from northwestern China, which imposes limitations on the generalizability and extrapolation of the findings to other demographic or geographic groups. Secondly, the limited sample size precluded a detailed exploration of the two subtypes of EVF, including Type I (from cortical arterioles to cortical veins) and Type II (from lenticulostriate arteries to the thalamostriate vein). Currently, the mechanism of EVF is thought to involve local hyperperfusion. However, in this study, we were unable to obtain perfusion imaging data from patients to investigate the correlation between EVF and local hyperperfusion status after EVT. The association between EVF and localized intracranial hyperperfusion can be further investigated through a prospective cohort study design. This would involve the systematic collection of postoperative neuroimaging data, including CT perfusion imaging (CTP), as well as other advanced imaging modalities. Quantitative assessment of intracranial hemodynamic parameters, such as cerebral blood volume (CBV) and cerebral blood flow (CBF), following EVT, would be conducted to elucidate the underlying mechanisms linking EVF and localized intracranial hyperperfusion.

Conclusion

This study establishes EVF as an independent risk factor for unfavorable outcomes after MT in AIS patients with large vessel occlusions. EVF in conjunction with a low ASPECT score can provide essential insights for identifying patients with severe AIS who are at a higher risk for unfavorable outcomes, indicating a need for tailored surgical strategies and careful post-operative management.

Abbreviations

AIS	Acuteischemic stroke
ASPECT	Alberta Stroke Program Early CT
DSA	Digital subtraction angiography
EVF	Early venous filling
MT	Post-mechanical thrombectomy
Mrs	Modified Rankin Scale
MCA	Middle cerebral artery
NIHSS	National Institutes of Health Stroke Scale
TOAST	Trial of Org 10172 in Acute Stroke Treatment
OR	Odds ratio
PSW	Propensity score weighting
IPTW	Inverse probability weighting

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-025-04111-w.

Supplementary Material 1.

Acknowledgements

We thank the Clinical Centre of the First Affiliated Hospital of Xi'an Jiaotong University for providing statistical advice.We thank Medjaden Inc. for its assistance in the preparation of this manuscript.

Authors' contributions

JH, HK and GL conceived, designed, and drafted the manuscript. YW and ZW collected the data and edited the figures. JH provided imaging data. All authors revised the article and approved the submitted version.

Funding

This work was supported by grants from Key Research and Development Program of Shaanxi (Program No. 2023-YBSF-413,S2024-YF-YBSF-0882) and Shaanxi Provincial Basic Research Program for Natural Sciences (Program No. 2023-JC-YB-736).

Data availability

The datasets generated and analyzed during the present study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The research was approved by the Medical Ethics Committee of the First Affiliated Hospital of Xi 'an Jiaotong University (XJTU1AF2023LSK-443). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was waived by the ethics committee by the the Medical Ethics Committee of the First Affiliated Hospital of Xi 'an Jiaotong University.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Neurology, First Affiliated Hospital of Xi'an Jiaotong University, No. 277, Yanta West Road, Xi'an, Shaanxi 710061, China. [2]Center for Brain Science, First Affiliated Hospital of Xi'an Jiaotong University, No. 277, Yanta West Road, Xi'an, Shaanxi 710061, China.

Received: 30 October 2024 Accepted: 26 February 2025
Published online: 06 March 2025

References

1. Powers WJ, Rabinstein AA, Ackerson T. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association [published correction appears in Stroke. Stroke. 2019;50(12):e440–1.
2. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387(10029):1723–31.
3. Hussein HM, Georgiadis AL, Vazquez G, et al. Occurrence and predictors of futile recanalization following endovascular treatment among patients

with acute ischemic stroke: a multicenter study. AJNR Am J Neuroradiol. 2010;31(3):454–8.
4. van Kranendonk KR, Treurniet KM, Boers AMM, Berkhemer OA, van den Berg LA, Chalos V, et al. Hemorrhagic transformation is associated with poor functional outcome in patients with acute ischemic stroke due to a large vessel occlusion. J Neurointerv Surg. 2019;11(5):464–8.
5. Wu S, Yuan R, Wang Y, Wei C, Zhang S, Yang X, et al. Early prediction of malignant brain edema after ischemic stroke. Stroke. 2018;49(12):2918–27.
6. Liang W, Wang Y, Du Z, Mang J, Wang J. Intraprocedural angiographic signs observed during endovascular thrombectomy in patients with acute ischemic stroke: a systematic review. Neurology. 2021;96(23):1080–90.
7. Ferris EJ, Gabriele OF, Hipona FA, Shapiro JH. Early venous filling in cranial angiography. Radiology. 1968;90(3):553–7.
8. Shimonaga K, Matsushige T, Takahashi H, Hashimoto Y, Mizoue T, Ono C, et al. Early venous filling after reperfusion therapy in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2020;29(8):104926.
9. Marchal G, Furlan M, Beaudouin V, Rioux P, Hauttement JL, Serrati C, et al. Early spontaneous hyperperfusion after stroke. A marker of favourable tissue outcome? Brain. 1996;119(Pt 2):409–19.
10. Lassen NA. The luxury-perfusion syndrome and its possible relation to acute metabolic acidosis localised within the brain. Lancet. 1966;2(7473):1113–5.
11. Arba F, Rinaldi C, Caimano D, Vit F, Busto G, Fainardi E. Blood-brain barrier disruption and hemorrhagic transformation in acute ischemic stroke: systematic review and meta-analysis. Front Neurol. 2020;11:594613.
12. Thorén M, Dixit A, Escudero-Martínez I, Gdovinová Z, Klecka L, Rand VM, et al. Effect of recanalization on cerebral edema in ischemic stroke treated with thrombolysis and/or endovascular therapy. Stroke. 2020;51(1):216–23.
13. Simard JM, Kent TA, Chen M, Tarasov KV, Gerzanich V. Brain oedema in focal ischaemia: molecular pathophysiology and theoretical implications. Lancet Neurol. 2007;6(3):258–68.
14. Cartmell SCD, Ball RL, Kaimal R, Telischak NA, Marks MP, Do HM, et al. Early cerebral vein after endovascular ischemic stroke treatment predicts symptomatic reperfusion hemorrhage. Stroke. 2018;49(7):1741–6.
15. Li Y, Cao W, Xu X, Li T, Chen Y, Wang Y, et al. Early venous filling after mechanical thrombectomy in acute ischemic stroke due to large vessel occlusion in anterior circulation. J Neurointerv Surg. 2024;16(3):248–52.
16. Goyal N, Tsivgoulis G, Malhotra K, Ishfaq MF, Pandhi A, Frohler MT, et al. Medical management vs mechanical thrombectomy for mild strokes: an international multicenter study and systematic review and meta-analysis. JAMA Neurol. 2020;77(1):16–24.
17. Safouris A, Palaiodimou L, Nardai S, Kargiotis O, Magoufis G, Psychogios K, et al. Medical management versus endovascular treatment for large-vessel occlusion anterior circulation stroke with low NIHSS. Stroke. 2023;54(9):2265–75.
18. Kwah LK, Diong J. National institutes of health stroke scale (nihss). J Physiother. 2014;60(1):61.
19. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet. 2000;355(9216):1670–4.
20. Ohta H, Nakano S, Yokogami K, Iseda T, Yoneyama T, Wakisaka S. Appearance of early venous filling during intra-arterial reperfusion therapy for acute middle cerebral artery occlusion: a predictive sign for hemorrhagic complications. Stroke. 2004;35(4):893–8.
21. Wu TH, Lin CJ, Lin YH, Guo WY, Huang TC. Quantitative analysis of digital subtraction angiography using optical flow method on occlusive cerebrovascular disease. Comput Methods Programs Biomed. 2013;111(3):693–700.
22. Budohoski KP, Czosnyka M, Kirkpatrick PJ, Smielewski P, Steiner LA, Pickard JD. Clinical relevance of cerebral autoregulation following subarachnoid haemorrhage. Nat Rev Neurol. 2013;9(3):152–63.
23. Yu W, Rives J, Welch B, White J, Stehel E, Samson D. Hypoplasia or occlusion of the ipsilateral cranial venous drainage is associated with early fatal edema of middle cerebral artery infarction. Stroke. 2009;40(12):3736–9.
24. Song K, Zeng X, Xie X, Zhu R, Liang J, Chen G, et al. Dl-3-n-butylphthalide attenuates brain injury caused by cortical infarction accompanied by cranial venous drainage disturbance. Stroke Vasc Neurol. 2022;7(3):222–36.
25. Pandit R, Chen L, Götz J. The blood-brain barrier: physiology and strategies for drug delivery. Adv Drug Deliv Rev. 2020;165–166:1–14.
26. Elands S, Casimir P, Bonnet T, Mine B, Lubicz B, Sjøgård M, et al. Early venous filling following thrombectomy: association with hemorrhagic transformation and functional outcome. Front Neurol. 2021;12:649079.
27. Yu S, Zhang H, Jiang QM, Hou J, Guo ZL, Xiao GD. Value of angiographic regional circulation signs in predicting hemorrhagic transformation after endovascular thrombectomy. J Neuroradiol. 2023;50(3):327–32.
28. Tian B, Tian X, Shi Z, Peng W, Zhang X, Yang P, et al. Clinical and imaging indicators of hemorrhagic transformation in acute ischemic stroke after endovascular thrombectomy. Stroke. 2022;53(5):1674–81.
29. Yamal JM, Grotta JC. National institutes of health stroke scale as an outcome measure for acute stroke trials. Stroke. 2021;52(1):142–3.
30. Zaidat OO, Liebeskind DS, Jadhav AP, Ortega-Gutierrez S, Nguyen TN, Haussen DC, et al. Impact of age and alberta stroke program early computed tomography score 0 to 5 on mechanical thrombectomy outcomes: analysis from the STRATIS registry. Stroke. 2021;52(7):2220–8.
31. Huo X, Ma G, Tong X, Zhang X, Pan Y, Nguyen TN, et al. Trial of endovascular therapy for acute ischemic stroke with large infarct. N Engl J Med. 2023;388(14):1272–83.
32. Sun D, Guo X, Nguyen TN, Pan Y, Ma G, Tong X, et al. Alberta stroke program early computed tomography score, infarct core volume, and endovascular therapy outcomes in patients with large infarct: a secondary analysis of the ANGEL-ASPECT trial. JAMA Neurol. 2024;81(1):30–8.
33. Nguyen TN, Abdalkader M, Nagel S, Qureshi MM, Ribo M, Caparros F, et al. Noncontrast computed tomography vs computed tomography perfusion or magnetic resonance imaging selection in late presentation of stroke with large-vessel occlusion. JAMA Neurol. 2022;79(1):22–31.

Publisher's Note