

Glial Fibrillary Acidic Protein as a Potential Indicator for Symptomatic Intracranial Hemorrhage in Acute Ischemic Patients Undergoing Endovascular Thrombectomy

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Background: The correlation between glial fibrillary acidic protein (GFAP) and symptomatic intracranial hemorrhage (sICH) in acute ischemic stroke (AIS) patients undergoing endovascular thrombectomy (EVT) treatment remains uncertain. We aimed to assess the association between levels of GFAP in the bloodstream and the occurrence of sICH.

Methods: Between June 2019 and May 2023, 142 consecutive AIS patients undergoing EVT at Stroke Center and 35 controls from the Physical Examination Center were retrospectively included. The levels of GFAP in the bloodstream were quantified using enzyme-linked immunosorbent assay prior to endovascular treatment (T1) and 24 h after the procedure (T2). The identification of sICH was based on the Heidelberg Bleeding Classification.

Results: Serum GFAP levels at T1 in AIS patients were significantly higher than those in the controls (0.249 [0.150–0.576] versus 0.065 [0.041–0.110] ng/mL, $p = 0.001$), and there was a notably elevation in GFAP levels at T2 compared to T1 (3.813 [1.474, 5.876] versus 0.249 [0.150–0.576] ng/mL, $p = 0.001$). Of the 142 AIS patients, 18 (14.5%) had sICH after EVT. Serum GFAP levels at T2 showed significant associations with sICH in both the unadjusted model (OR 1.513, 95% CI 1.269–1.805, $p = 0.001$) and multivariable adjusted model (OR 1.518, 95% CI 1.153–2.000, $p = 0.003$). Furthermore, the addition of GFAP at T2 to conventional model resulted in a significant enhancement of risk reclassification for sICH (integrated discrimination improvement [IDI] 0.183, 95% CI 0.070–0.295, $p = 0.001$).

Conclusion: Serum GFAP levels were notably increased in AIS patients 24 h after EVT. Elevated GFAP levels were correlated to an elevated risk of sICH. GFAP could potentially serve as a dependable indicator for sICH in AIS individuals who treated with EVT.

Keywords: glial fibrillary acidic protein, stroke, symptomatic intracranial hemorrhage, indicator, endovascular thrombectomy

Introduction

Stroke has been identified as a standout cause of both mortality and morbidity in China, and it also contributes significantly to healthcare expenses.^{1,2} The implementation of endovascular thrombectomy (EVT) has led to notable enhancements in clinical outcomes for acute ischemic stroke (AIS) patients involving occlusion of large vessels.^{3,4}

Symptomatic intracranial hemorrhage (sICH) is a highly concerning complication following interventional procedures among AIS individuals, with reported incidence rates ranging from 4.4% to 16.0%.^{3,5} Previous studies have consistently demonstrated that sICH is associated with an elevated risk of unfavorable clinical outcomes and a diminished benefit-to-risk ratio of EVT accordingly.^{6–8} Hence, timely and precise identification of sICH following EVT holds importance for enhancing perioperative management and clinical prognosis.

Neuroinflammation is a pervasive phenomenon in the pathological progression of brain ischemic.⁹ Astrogliosis, a pivotal aspect of neuroinflammation, is distinguished by the substantial elevation of glial fibrillary acidic protein (GFAP) expression. The excessive expression of GFAP has been documented in diverse neurological disorders, including dementia, autoimmune encephalitis, multiple sclerosis (MS), traumatic brain injury, and malignant brain tumors.^{10–14} Recently, GFAP has been proposed as a reliable biomarker for distinguishing AIS from intracerebral hemorrhage.^{15,16} Moreover, elevated GFAP levels were intimately related to unfavorable prognosis at 90 days in patients after EVT for large vessel occlusion.¹⁷ Furthermore, patients with higher GFAP levels at 24 h after stroke had a 2.51-fold increased risk for parenchymal hemorrhage.¹⁸ Nevertheless, the relationship between GFAP and sICH in AIS patients undergoing EVT had not been investigated.

Herein, the study aimed to clarify whether GFAP is in relation to sICH in AIS patients undergoing EVT.

Materials and Methods

Study Participants

This was a retrospective cohort study based on prospectively collected data of AIS patients admitted to Taixing People's Hospital between June 2019 and May 2023. Inclusion criteria were patients who presented with large vessel occlusion in the anterior circulation and underwent EVT utilizing contemporary thrombectomy techniques. Conversely, patients diagnosed with concomitant conditions such as aneurysm, vasculitis, arterial dissection, arteriovenous malformation, Moyamoya syndrome, or hematological system diseases were excluded from the study. The control group consisted of participants without a history of stroke from the Physical Examination Center. Approval for this study was obtained from the Ethics Committee of Taixing People's Hospital (No. LS2021017). Based on a retrospective design of the study, the Ethics Committee of Taixing People's Hospital waived informed consent and de-identified patient information.

Data Collection

Demographics (age and gender), vascular risk factors, subtype of stroke, blood pressure, baseline National Institutes of Health Stroke Score (NIHSS), baseline Alberta Stroke Program Early CT Score (ASPECTS), procedural characteristics (occlusion site, interval time, collateral status, recanalization status, and passes with retriever) as well as laboratory data were collected as previously described.^{19,20} The subtype of stroke was classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, specifically as large-artery atherosclerosis, cardio-embolism or other subtypes.²¹ The collateral status was assessed using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading system.²² Recanalization status was categorized using the modified Thrombolysis in Cerebral Infarction (mTICI) score, wherein a score of mTICI 2b or 3 indicated successful reperfusion.²³ Age, gender, and vascular risk factors were collected as clinical characteristics from the control group.

Definition of sICH

The evaluation of any hemorrhagic transformation was conducted using a follow-up computed tomographic 24 h after EVT or whenever there was a deterioration in clinical condition. We defined sICH as any intracranial hemorrhage based on the Heidelberg Bleeding Classification with NIHSS score increase ≥ 4 points in the total score or ≥ 2 points in one category from baseline within 72 h after EVT.^{24,25} The diagnose of sICH was independently conducted by two certified neuroradiologists blinded to clinical data. When disagreement occurred, a third neuroradiologist was consulted to make a final judgment.

Measurement of Serum GFAP Levels

Blood samples were collected from both the control group and all patients with AIS prior to EVT (T1) and 24 h after the procedure (T2). The collected specimens were subjected to centrifugation at a speed of 1,000 times the force of gravity for a duration of 15 minutes at a temperature of 4°C. The resulting serum was then transferred to cryotubes and stored at a temperature of -80°C until further analysis. The levels of serum GFAP levels were quantified using an enzyme-linked immunosorbent assay kit (Catalog No. RK09302, ABclonal), following the instructions provided by the manufacturer. The minimum detectable level of GFAP was determined to be 0.1 ng/mL. The coefficients of variation for GFAP, both within and between assays, were found to be 10.0% and 15.0%, respectively.

Statistical Analysis

Statistical analyses were conducted by R 4.1.3 (<http://www.R-project.org/>) and GraphPad Prism 9.3.1 (GraphPad Software, San Diego, CA, USA). Categorical variables were represented as numbers accompanied by percentages, while continuous variables were expressed as means accompanied by standard deviations or medians accompanied by quartiles. Univariate analyses were performed utilizing the *t*-test or Mann–Whitney *U*-test for continuous variables, while the Pearson's chi-square test was employed for categorical variables, as deemed suitable. In order to assess the independent risk factors associated with sICH, multivariable logistic regression analyses were adjusted for age, gender and variables with a *p*-value < 0.1 in the univariate analysis. Furthermore, the C-statistic, net reclassification index (NRI) and integrated discrimination improvement (IDI) were computed to evaluate the discriminatory power as well as predictive value of GFAP when incorporated into conventional models.^{26,27} Statistical analyses were conducted with two-tailed testing, and *p*-values < 0.05 were deemed to be statistically significant.

Results

Baseline Characteristics

A total of 149 patients diagnosed with AIS and treated with endovascular therapy were initially screened for inclusion in this study. Seven patients were excluded for the following reasons: hematological system diseases (*n*=3), aneurysm (*n*=2), arterial dissection (*n*=1), and Moyamoya syndrome (*n*=1). Finally, 142 patients were recruited for analysis. The average age of the included patients was 70.9 ± 10.1 years, with 64.1% being male (Table 1). The baseline median NIHSS score was 15 (interquartile range [IQR], 12–18), and the baseline median ASPECTS was 9 (IQR 8–9). Poor collateral status was observed in 77 patients (54.2%), while successful recanalization was achieved in 118 patients (83.1%). The median GFAP at T1 and T2 were 0.249 (IQR 0.150–0.576) and 3.813 (IQR 1.474–5.876) ng/mL, respectively.

In addition, 35 control individuals were enrolled (24 males and 9 females), with an average age of 67.8 ± 7.2 years. The baseline characteristics of the control group and all patients with AIS were described in Table 2. Significant differences were found

Table 1 Clinical Characteristics of Participants According to with and without sICH in Patients Undergoing EVT

Variables	All Patients (n = 142)	With sICH (n = 18)	Without sICH (n = 124)	<i>p</i>
Demographic characteristics				
Age, years, mean ± SD	70.9 ± 10.1	73.9 ± 7.5	70.5 ± 10.4	0.179
Age, years, median (IQR)	73 (65, 78)	76 (70, 80)	73 (65, 77)	0.134
Male, n (%)	91 (64.1)	12 (66.7)	79 (63.7)	0.807
Vascular risk factors, n (%)				
Hypertension	94 (66.2)	13 (72.2)	81 (65.3)	0.563
Diabetes	30 (21.1)	4 (22.2)	26 (21.0)	0.904
Lipid metabolism disorders	22 (15.5)	2 (11.1)	20 (16.1)	0.568
Atrial fibrillation	69 (48.6)	9 (50.0)	60 (48.4)	0.898
Coronary artery disease	31 (21.8)	2 (11.1)	29 (23.4)	0.208
Previous stroke or TIA	31 (21.8)	5 (27.8)	26 (21.0)	0.524
Current smoker	42 (29.6)	7 (38.9)	35 (28.2)	0.354
Subtype of stroke, n (%)				0.660
Large-artery atherosclerosis	68 (47.9)	8 (44.4)	60 (48.4)	
Cardio-embolism	69 (48.6)	9 (50.0)	60 (48.4)	
Other subtypes	5 (3.5)	1 (5.6)	4 (3.2)	
Clinical assessment				
Systolic blood pressure, mmHg, mean ± SD	146.6 ± 30.7	153.4 ± 41.7	145.7 ± 29.0	0.473
Diastolic blood pressure, mmHg, mean ± SD	85.0 ± 18.1	87.8 ± 25.2	84.7 ± 17.0	0.502
Baseline NIHSS, score, median (IQR)	15 (12, 18)	17 (13, 22)	14 (12, 18)	0.045*
Baseline ASPECTS, score, median (IQR)	9 (8, 9)	7 (7, 8)	9 (8, 9)	0.001*
Intravenous thrombolysis, n (%)	50 (35.2)	8 (44.4)	42 (33.9)	0.380

(Continued)

Table 1 (Continued).

Variables	All Patients (n = 142)	With sICH (n = 18)	Without sICH (n = 124)	p
Interval time, min				
Door-to-needle, median (IQR)	45 (30, 53)	48 (33, 59)	45 (30, 52)	0.596
Onset-to-puncture, median (IQR)	220 (155, 260)	221 (168, 258)	210 (145, 260)	0.697
Onset-to-recanalized, median (IQR)	252 (310, 365)	326 (282, 396)	310 (245, 360)	0.206
Occlusion site, n (%)				0.204
ICA	44 (31.0)	8 (44.4)	36 (29.0)	
M1/M2	75 (52.8)	6 (33.3)	69 (55.6)	
ICA+M1/M2	23 (16.2)	4 (22.2)	19 (15.3)	
ASITN/SIR, n (%)				0.004*
0–1	65 (45.8)	14 (77.8)	51 (41.1)	
2–4	77 (54.2)	4 (22.2)	73 (58.9)	
mTICI, n (%)				0.214
0–2a	24 (16.9)	5 (27.8)	19 (15.3)	
2b–3	118 (83.1)	13 (72.2)	105 (84.7)	
Passes with retriever > 3, n (%)	17 (12.0)	5 (27.8)	12 (9.7)	0.047*
Laboratory data				
FBG, mmol/L, mean ± SD	7.2 ± 2.2	8.6 ± 2.8	6.9 ± 2.0	0.002*
Hs-CRP, mg/L, median (IQR)	3.63 (1.20, 7.57)	6.12 (1.58, 15.12)	3.47 (1.12, 7.11)	0.147
GFAP at T1, ng/mL, median (IQR)	0.249 (0.150, 0.576)	0.338 (0.139, 1.081)	0.248 (0.154, 0.489)	0.552
GFAP at T2, ng/mL, median (IQR)	3.813 (1.474, 5.876)	9.339 (5.385, 12.168)	3.571 (1.293, 5.232)	0.001*

Note: *p value < 0.05, statistical significance.

Abbreviations: sICH, symptomatic intracranial hemorrhage; EVT, endovascular thrombectomy; TIA, transient ischemic attack, NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; M1/M2, first or second segment of the middle cerebral artery; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; mTICI, Modified Thrombolysis in Cerebral Infarction; FBG, fasting blood glucose; hs-CRP, hyper-sensitive C-reactive protein; GFAP, glial fibrillary acidic protein; SD, standard deviation; IQR, interquartile range.

Table 2 Clinical Characteristics of the Control Group and Patients with AIS (at Baseline Before EVT)

Variables	Control (n = 35)	AIS (n = 142)	p
Age, years, mean ± SD	67.8 ± 7.2	70.9 ± 10.1	0.038*
Male, n (%)	24 (68.6)	91 (64.1)	0.618
Hypertension, n (%)	21 (60.0)	94 (66.2)	0.491
Diabetes, n (%)	12 (34.3)	30 (21.1)	0.101
Lipid metabolism disorders, n (%)	8 (22.9)	22 (15.5)	0.298
Atrial fibrillation, n (%)	13 (37.1)	69 (48.6)	0.224
Coronary artery disease, n (%)	10 (28.6)	31 (21.8)	0.397
Current smoker, n (%)	14 (40.0)	42 (29.6)	0.235
GFAP, ng/mL, median (IQR)	0.065 (0.041, 0.110)	0.249 (0.150, 0.576)	0.001*
Log GFAP, pg/mL, mean ± SD	4.2 ± 0.6	5.7 ± 1.0	0.001* ^a

Note: *p value < 0.05, statistical significance. ^aA t-test was used for the natural log-transformed GFAP, and the p value was adjusted for age.

Abbreviations: AIS, acute ischemic stroke; EVT, endovascular thrombectomy; GFAP, glial fibrillary acidic protein; SD, standard deviation; IQR, interquartile range.

between AIS patients and controls in respect of age (70.9 ± 10.1 versus 67.8 ± 7.2 , $p = 0.038$) and GFAP ($0.249 [0.150–0.576]$ versus $0.065 [0.041–0.110]$ ng/mL, $p = 0.001$). Although the controls were younger, similar results were obtained when GFAP levels were compared based on the age-adjusted model ($p = 0.001$).

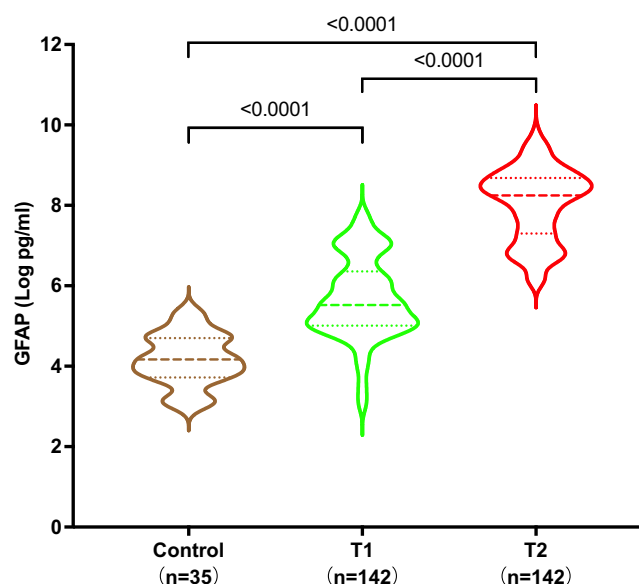


Figure 1 Violin plot of serum Log GFAP levels in AIS patients and controls. The violin plot was drawn through GraphPad Prism. Horizontal lines indicate the medians and interquartile ranges. *P*-values indicate differences between groups determined by Mann–Whitney *U*-test. It can be seen that serum GFAP levels at T1 (prior to endovascular treatment) in AIS patients were significantly higher than those in the controls (stroke-free participants), and there was a notably elevation in GFAP levels at T2 (24 h after endovascular treatment) compared to T1.

Abbreviation: GFAP, glial fibrillary acidic protein; AIS, acute ischemic stroke.

Figure 1 showed the violin plot of serum Log GFAP levels in AIS patients and controls. The average Log GFAP levels in controls were 4.2 ± 0.6 pg/mL. Compared to controls, a significant elevation was observed in patients with AIS at T1 (5.7 ± 1.0 pg/mL) or T2 (8.0 ± 0.9 pg/mL). Besides, Log GFAP levels were higher at T2 than at T1 ($p = 0.001$).

Correlation Between GFAP and sICH

Eighteen patients (14.5%) were diagnosed with sICH. As depicted in Table 1, patients with sICH exhibited higher baseline NIHSS ($p = 0.045$), lower baseline ASPECTS ($p = 0.001$), poorer collateral status ($p = 0.004$), more passes with retriever ($p = 0.047$), higher levels of FBG ($p = 0.002$) and GFAP at T2 ($p = 0.001$), compared to those without sICH.

After multivariable adjustment for age, gender, and potential confounders mentioned above in univariate analysis, patients with higher GFAP levels at T2 had an increased risk of sICH (OR 1.518, 95% CI 1.153–2.000, $p = 0.003$) (Table 3). Adding GFAP at T2 to models containing conventional risk factors did not significantly enhance the

Table 3 Logistic Regression Analyses for the Related Factors Associated with sICH in Patients Undergoing EVT

Variables	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Demographic characteristics				
Age	1.039 (0.983, 1.098)	0.179	1.082 (0.991, 1.181)	0.079
Male	1.139 (0.400, 3.243)	0.807	1.022 (0.174, 5.995)	0.981
Vascular risk factors				
Hypertension	1.380 (0.461, 4.129)	0.564		
Diabetes	1.077 (0.327, 3.548)	0.903		
Lipid metabolism disorders	0.650 (0.139, 3.050)	0.585		
Atrial fibrillation	1.067 (0.397, 2.867)	0.898		
Coronary artery disease	0.409 (0.089, 1.887)	0.252		
Previous stroke or TIA	1.450 (0.474, 4.436)	0.515		
Current smoker	1.618 (0.581, 4.511)	0.357		

(Continued)

Table 3 (Continued).

Variables	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Subtype of stroke				
Large-artery atherosclerosis	Reference			
Cardio-embolism	1.125 (0.407, 3.112)	0.820		
Other subtypes	1.875 (0.186, 18.930)	0.594		
Clinical assessment				
Systolic blood pressure	1.008 (0.992, 1.024)	0.336		
Diastolic blood pressure	1.009 (0.982, 1.037)	0.499		
Baseline NIHSS	1.055 (0.991, 1.123)	0.095	1.044 (0.942, 1.157)	0.412
Baseline ASPECTS	0.197 (0.093, 0.416)	0.001*	0.333 (0.111, 0.993)	0.049*
Intravenous thrombolysis	1.562 (0.574, 4.251)	0.383		
Interval time				
Door-to-needle	1.004 (0.962, 1.048)	0.858		
Onset-to-puncture	1.001 (0.995, 1.008)	0.662		
Onset-to-recanalized	1.003 (0.998, 1.008)	0.250		
Occlusion site				
ICA	Reference			
M1/M2	0.947 (0.252, 3.556)	0.936		
ICA+M1/M2	0.391 (0.126, 1.215)	0.104		
ASITN/SIR (0–1)	5.010 (1.559, 16.099)	0.007*	0.945 (0.156, 5.706)	0.950
mTICI 2b-3	0.470 (0.150, 1.473)	0.195		
Passes with retriever (>3)	3.590 (1.091, 11.810)	0.035*	5.747 (0.637, 51.894)	0.119
Laboratory data				
FBG	1.330 (1.088, 1.626)	0.005*	1.433 (1.055, 1.975)	0.022*
Hs-CRP	1.003 (0.987, 1.020)	0.673		
GFAP at T2	1.513 (1.269, 1.805)	0.001*	1.518 (1.153, 2.000)	0.003*

Note: *p value < 0.05, statistical significance.

Abbreviations: sICH, symptomatic intracranial hemorrhage; EVT, endovascular thrombectomy; TIA, transient ischemic attack, NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; M1/M2, first or second segment of the middle cerebral artery; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; mTICI, Modified Thrombolysis in Cerebral Infarction; FBG, fasting blood glucose; hs-CRP, hyper-sensitive C-reactive protein; GFAP, glial fibrillary acidic protein.

C-statistics ($p = 0.283$) for sICH. However, the risk reclassification for sICH was modestly improved by adding GFAP at T2 to convention models (IDI 0.183, 95% CI 0.070–0.295, $p = 0.001$, Table 4).

Discussion

To our knowledge, this study represents the initial investigation into the potential correlation between GFAP and sICH in AIS patients who underwent EVT. Our findings demonstrated a significant increase in serum GFAP levels 24 h after EVT, with higher levels correlating to an elevated risk of sICH. Furthermore, the inclusion of GFAP in conventional models resulted in improved risk reclassification for sICH. These results suggested that GFAP might serve as a dependable prognostic indicator for sICH following EVT in AIS patients.

In our cohort, the prevalence of sICH after EVT was 14.5%, which was in parallel with the rate reported in the ACTUAL registry (16.0%),⁵ but remarkably higher than that reported in the ESCAPE-NA1 trial (4.0%)²⁸ and MR CLEAN registry (5.9%).⁷ The inclusion criteria employed in the randomized controlled trials were more stringent compared to those applied in real-world clinical practices.^{5,7,28} In contrast to prior extensive randomized controlled trials,^{5,7,28} the expansion of clinical indications, less favorable treatment conditions, and inadequate experience among neurointerventionists were more prevalent in real-world clinical practices. These may be significant contributors to an increased risk of sICH in our study. Meanwhile, our research uncovered that sICH patients had higher baseline NIHSS score, lower initial ASPECTS score, poorer collateral status, more passes of retriever as well as higher levels of FBG,

Table 4 Reclassification of GFAP for sICH in Patients Undergoing EVT

Models	Discrimination		Reclassification			
	C-Statistic (95% CI)	p	NRI (95% CI)	p	IDI (95% CI)	p
Model 1	0.606 (0.474–0.739)		1.000 (reference)		1.000 (reference)	
+ GFAP at T2	0.854 (0.742–0.966)	0.005*	0.682 (0.467–0.896)	0.001*	0.343 (0.197–0.489)	0.001*
Model 2	0.893 (0.827–0.959)		1.000 (reference)		1.000 (reference)	
+ GFAP at T2	0.939 (0.888–0.991)	0.283	0.295 (–0.002–0.591)	0.051	0.183 (0.070–0.295)	0.001*

Note: *p value < 0.05, statistical significance. Model 1 included age and gender. Model 2 included age, gender, baseline NIHSS, baseline ASPECTS, ASITN/SIR, passes with retriever > 3, and FBG.

Abbreviations: GFAP, glial fibrillary acidic protein; sICH, symptomatic intracranial hemorrhage; EVT, endovascular thrombectomy; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination index; NIHSS, National Institute of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; FBG, fasting blood glucose.

which were coherent with literature data.^{25,29,30} Contrary to previously published findings, our study did not establish a substantial correlation between advanced age, elevated blood pressure, longer procedure duration and sICH.^{30,31} This discrepancy may be primarily caused by variations in study design, participants, regions, and the definition and timing of assessing sICH.

GFAP is a pivotal protein that specifically exists in astroglial intermediate filaments. When glial is damaged with astrocyte disintegration, this protein would be released from intracellular compartment into cerebrospinal fluid and bloodstream.³² In our cohort, the serum GFAP levels were elevated in AIS patients, and a subsequent continuous increase was observed 24 h after EVT in AIS patients. The findings indicated that GFAP levels reflect astrocytic dysfunction and blood-brain barrier disruption. Elevated GFAP levels have also been detected in neurodegenerative disorders.^{12–14} In a single-center cross-sectional study with 129 MS patients, serum GFAP was proposed as a potentially interesting marker to distinguish primary progressive MS and relapsing remitting MS.¹³ Another recent-published study with 282 Italian frontotemporal lobar degeneration patients observed a significant association between serum GFAP concentrations and disease intensity as well as severity.¹⁴ Moreover, the expression of GFAP is preferentially increased in intracerebral hemorrhage, which showed clinical significance in distinguishing between ischemic stroke and intracerebral hemorrhage, even during the initial stage.^{15,16} However, studies concerning the value of GFAP in EVT-treated AIS patients are relatively scarce. According to the study conducted in Sweden, serum GFAP predicted unfavorable functional outcome 3-month after EVT.¹⁷ In a recent clinical study involving 60 Taiwanese recanalized AIS patients, increased GFAP was linked to a greater risk of parenchymal hemorrhage.¹⁸ The present study found a strong association between elevated levels of GFAP at 24 h following EVT and an increased risk of sICH, alone or combined with other potential confounding factors. Our research built upon the prior discoveries by suggesting that serum GFAP could also serve as a promising predictor of sICH in AIS patients following EVT. In addition, our study also found that incorporation of GFAP alongside traditional risk factors resulted in a more accurate risk reclassification for sICH. This finding implies that GFAP has the potential to be integrated into existing factors to construct a predictive model for identifying EVT patients who are at a heightened risk of developing sICH.^{5,25,33} Consequently, this model could provide valuable clinical insights and help neurologists in identifying high-risk individuals.

Several limitations deserve comment. First, the presence of selection bias was unavoidable due to the retrospective nature of this study conducted in a single facility with a relatively limited number of participants, potentially diminishing the statistical strength. Second, the levels of GFAP might be influenced by a pre-existing neurological condition before the occurrence of a stroke, and the GFAP levels prior to the onset of stroke remained unknown. Third, several parameters, which may be potential confounders for sICH in previous study,^{34–38} were not measured, such as prior utilization of anticoagulants, early increase in body temperature, white matter hyperintensity, cerebral microbleeds, and fluctuations in blood pressure. Fourth, owing to the cross-sectional observational design of the study, it was challenging to establish a causal relationship between GFAP and sICH. In addition, the findings of our study were not corroborated in an external cohort. To further validate and expand the findings of our study, additional studies in external cohorts with larger sample sizes are necessary.

Conclusions

To summarize, this study indicated that higher levels of GFAP were independently linked to a higher risk of sICH in AIS patients following EVT. Despite its inherent limitations, our study presented preliminary evidence supporting the potential of serum GFAP as a valuable biomarker for diagnosing and predicting sICH. We cautiously proposed that incorporating GFAP into the sICH risk model for AIS patients undergoing EVT could enhance its reliability. Further prospective studies with larger sample sizes should be performed to comprehensively validate these preliminary results and to further explore the exact mechanism linking GFAP and sICH.

Data Sharing Statement

The data that support the findings of this study are available from Guomei Shi upon reasonable request.

Ethics Approval

The study was approved by the Ethics Committee of Taixing People's Hospital (No. LS2021017) and conducted according to the Declaration of Helsinki. The fully de-identified data on the participants enrolled in the study and its virtue of retrospective study design enables this study conducted under a waiver of informed consent by the Ethics Committee of Taixing People's Hospital.

Consent for Publication

No information or images that could lead to identification of a study participant were mentioned in our study.

Author Contributions

All authors made significant contributions to conception, study design, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflict of interest.

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