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Clinical efficacy of collateral circulation in the evaluation of endovascular treatment for acute internal carotid artery occlusion

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Abstract

Objectives: Despite successful recanalization, there remain many patients suffering bad outcome after endovascular treatment, especially for occlusion at the distal portion of internal carotid artery. The goal of the current study was to investigate the value of collateral circulation in predicting malignant events after endovascular treatment in acute ischemic stroke-terminal internal carotid artery (AIS-TICA) patients.

Methods: The records of forty-one patients with AIS-TICA as confirmed by digital subtraction angiography and subjected to mechanical thrombectomy were reviewed. On the basis of the collateral circulation grading system (ACG) from the American Society of Interventional and Therapeutic Neuroradiology/American Society of Interventional Radiology (ASITN/SIR), class of leptomeningeal compensation were evaluated as grade 0 to 4. Factors for

malignant events were evaluated by retrospectively univariate analysis. Moreover, analysis of correlation was performed between collateral circulation and malignant events. Malignant events were defined as a malignant middle cerebral artery infarction or parenchymal hemorrhage 2.

Results: Of the 41 subjects, 13 (31.71%) had postoperative malignant events. Though 36 (87.80%) of the patients had a complete recanalization, only 17 patients (41.46%) showed good outcomes with modified Rankin score ≤ 2 at 3 months. 9 (21.95%) deaths occurred in the hospital. Besides, patients in the malignant group had significantly higher scores on the National Institute of Health stroke scale ($P = 0.032$) and lower anterior circulation compensation ($P = 0.000$). Furthermore, correlation analysis showed that probability of malignant events was negatively correlated with anterior circulation compensation ($r_s = -0.534$, $P = 0.000$).

Conclusions: The leptomeningeal compensation of anterior circulation can be predicted whether a malignant event will occur after endovascular treatment in AIS-TICA patients. The probability of malignant events is significantly increased if the anterior circulation collateral compensation score is 0–1.

Keywords: Neurology, Surgery

1. Introduction

Recent results as obtained from five randomized controlled trial (RCT) studies have demonstrated the efficacy and safety of endovascular therapy for acute anterior circulation large vessel occlusions [1]. However, in cases of terminal internal carotid artery (TICA) occlusion, a malignant middle cerebral artery infarction (mMCAI) may likely result, in part, due to the presence of a large thrombus burden followed by a low successful rate of recanalization with application of intravenous thrombolysis [2, 3, 4]. Even though revolution of endovascular therapy fundamentally improved the probability of complete recanalization, some patients still suffered from failed clinical benefit such as intracranial hemorrhagic transformation (ICH), mMCAI and so on, possibly ascribed to those patients with lower Alberta stroke program early computed tomography scores (ASPECTS) [1]. Furthermore, lesion of TICA usually implied the bigger ischemic region and lower ASPECTS than middle cerebral artery (MCA) or anterior cerebral artery (ACA) occlusion alone. Presently, it remains inconclusive as to whether immediate mechanical thrombectomy is beneficial for those with lower ASPECTS that TICA occlusion represented [1]. Therefore, the goal of our current study was to investigate the potential benefits of endovascular therapy in patients with acute ischemic stroke-TICA (AIS-TICA).

2. Methods

This was a retrospective study involving the records of 41 AIS-TICA patients who underwent endovascular therapy in the Department of Neurology of our hospital. The records covered the period from March 2016 to March 2018 and the following criteria were required for inclusion in our analysis. 1) Endovascular therapy was implemented within 6 hours after AIS symptom onset. 2) For those cases that exceeded this 6 hour period after AIS symptom onset, multimodal imaging screening was performed to verify that patients met the DEFUSE3 or DAWN study criteria [5, 6]. 3) T or L-typed occlusion of TICA was confirmed by digital subtraction angiography (DSA). If lesion of ICA simultaneously extended to both ipsilateral A1 and M1 segments, it was categorized as T-typed occlusion, whereas L-typed occlusion escaped the involvement of A1 segment and neither A1 nor M1 being involved were defined as I-typed occlusion [7]. and 4) A National Institute of Health stroke scale (NIHSS) score of >8 was present on admission. Exclusion criteria included: 1) I-typed occlusion of TICA ascribed to its without affection of the circle of Willis, 2) history of previous cerebral infarction with a modified Rankin Scale (mRS) score > 2 prior to surgery, 3) patients with major organ failure, such as severe renal insufficiency, cardiac insufficiency or chronic obstructive pulmonary disease and 4) patients with intracranial hemorrhage, subarachnoid hemorrhage or other obvious space-occupying lesions as confirmed by computed tomography (CT).

According to guidelines from the American Heart Association (AHA/American Stroke Association, ASA) published in 2018 and the China's "Expert Consensus on Early Intravascular Interventional Therapy Process and Norm for Acute Ischemic Stroke 2017", AIS patients were recommended for treatment with intravenous thrombolysis followed by intra-arterial thrombectomy [8, 9].

Intravenous thrombolysis treatment consisted of administration of a recombinant tissue plasminogen activator (rt-PA) (Germany Boehringer Ingelheim Pharmaceutical Co., Ltd., National Pharmaceutical Standard S20020034, trade name: Ai Tong Li) at a dose of 0.90 mg/kg. The maximum dose administered did not exceed 90 mg, even for patients whose dose based on body weight would have exceeded 90mg. The preferred method was an initial intravenous bolus of 10%, with the remaining 90% administered within 1 hour.

Prior to endovascular therapy, anterior and posterior circulation compensation levels were evaluated by DSA. As based on the collateral circulation grading system (ACG) from the American Society of Interventional and Therapeutic Neuro-radiology/American Society of Interventional Radiology (ASITN/SIR), Grade 0: No collaterals visible to the ischemic site, Grade 1: Slow collaterals to the periphery of the ischemic site with persistence of some of the defect, Grade 2: Rapid collaterals to the periphery of ischemic site with persistence of some of the defect and to only a

portion of the ischemic territory Grade, 3: Collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase, Grade 4: Complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion, a Grade of 0–1 indicates poor collateral circulation, Grade 2 indicates moderate collateral circulation while Grades of 3–4 indicate good collateral circulation [10]. All the DSA images of 41 cases were sent to three different senior interventional neuroradiologists in order to assess collateral score. Interobserver agreement by anterior circulation compensation grades was excellent (Kendall W = 0.917, P = 0.000), so was the posterior circulation (Kendall W = 0.903, P = 0.000).

Endovascular therapy consisted mainly of thrombectomy through the stent-like device, combined with arterial thrombolysis, thrombus aspiration, balloon dilation and stent placement.

Safety evaluations included: 1) Performance of the European Cooperative Acute Stroke (ECASS) II standard classification of intracranial hemorrhagic transformation (ICH) [11] within 72 hours and 2) Definition of a malignant event defined as a malignant middle cerebral artery infarction (mMCAI) or parenchymal hemorrhage (PH) 2.

Effectiveness evaluations included: 1) The degree of recanalization as assessed by modified Thrombolysis in Cerebral Infarction (mTICI) with a complete recanalization being mTICI = 2b or 3 and 2) Documentation of mRS grading as provided by telephone interview or clinic follow up at 90 ± 7 days after the surgery, with mRS ≤ 2 indicating the good outcome, mRS > 2 indicating the bad and mRS = 6 indicating death.

Statistical analysis was conducted using SPSS 21.0 software. Quantitative data with a normal distribution were expressed as mean \pm standard deviation (SD) and an independent samples t-test was used. Quantitative data with a skewed distribution were expressed as the median. Mann–Whitney U-tests were used for comparisons between groups with skewed distributions. Qualitative data as described by frequency were analyzed with use of the χ^2 or Fisher exact probability method. The Spearman test was used to analyze the correlation between collateral circulation gradings and the probability of occurrence of malignant events. P < 0.05 was required for results to be considered statistically significant (2 sides).

3. Results

3.1. Basic information on AIS-TICA patients with endovascular therapy

The records from 41 AIS-TICA patients who underwent endovascular therapy were included in this study, including 17 patients (41.46%) with good outcomes at 3

months ($mRS \leq 2$), 5 patients (12.20%) who experienced a severe disability ($mRS = 4$ or 5), and 9 patients (21.95%) who died in the hospital. Regardless of 36 patients (87.80%) who achieved complete recanalization, there were 13 (31.71%) patients had malignant events and 23 patients (56.10%) developed ICH, including 4 patients (9.76%) with PH2 after revascularization. 12 (29.27%) patients emerged complication of distal embolization and the average number of thrombectomies was 2.29 ± 1.81 .

3.2. Potential factors related with malignant events in AIS-TICA patients with endovascular treatment

Univariate analysis showed that the National Institutes of Health Stroke Scale (NIHSS) score of the patients in the malignant event group (21 score) was significantly greater than that in the non-malignant event group (17.5 score) ($Z = -2.149$, $P = 0.032$). Additionally, anterior circulation collateral compensatory grading and anterior circulation + post-circulation collateral circulations were apparently worse as compared with the non-malignant event group ($t = -4.744$, $P = 0.000$ and $t = -3.795$, $P = 0.001$, respectively). Within the malignant event group, more ICH patients were present ($\chi^2 = 6.286$, $P = 0.012$), fewer patients showed good outcomes ($\chi^2 = 5.334$, $P = 0.021$), and significantly greater numbers of patients died in the hospital ($\chi^2 = 14.193$, $P = 0.000$) (See Table 1 and Fig. 1 for details).

3.3. Correlations between collateral circulation grade and malignant events in AIS-TICA patients with endovascular therapy

Results of the Spearman correlation test revealed that the probability of malignant events was negatively correlated with both the anterior circulation collateral circulation grade ($r_s = -0.534$, $P = 0.000$) and anterior circulation + posterior circulation collateral circulation ($r_s = -0.563$, $P = 0.000$) (as shown in Fig. 2). The probability of malignant events was not related to the posterior circulation collateral circulation ($r_s = -0.257$, $P = 0.105$).

4. Discussion

In this study, 41.46% of patients experience a good functional outcome, which was slightly lower than the 46% reported within the five previous RCT studies. These differences may be attributable to a greater prevalence of middle cerebral artery occlusion in patients within the RCT studies, whereas patients in our current study mainly experienced TICA occlusion with cerebral infarction localized within a larger region [1]. However, compared with Liebeskind et al reported 28% of patients ($mRS \leq 2$) aiming at TICA occlusion in 2014, our results made better

Table 1. Factors influencing malignant events in AIS-TICA patients after endovascular treatment.

	Malignant event (n = 13)	Non-malignant event (n = 28)	Test value	P value
Age, year (median)	66 (37–78)	61.5 (34–84)	-0.421a	0.674
Female, n (%)	6 (46.2)	10 (35.7)	0.407	0.524
Hypertension, n (%)	8 (61.5)	12 (50.0)	1.240	0.265
Diabetes, n (%)	2 (15.4)	6 (21.4)	0.001	0.975
Hypercholesterolemia, n (%)	1 (7.7)	8 (28.6)	1.205	0.272
Smoking, n (%)	3 (23.1)	10 (35.7)	0.201	0.654
Atrial fibrillation, n (%)	8 (61.5)	12 (42.9)	1.240	0.265
NIHSS on admission, (median)	21 (15–27)	17.5 (6–26)	-2.149a	0.032
Intravenous thrombolysis, n (%)	8 (61.5)	15 (53.6)	0.229	0.632
General anesthesia, n (%)	5 (38.5)	10 (35.7)	0.000	1.000
OTP, min (median)	258 (190–420)	213 (120–600)	-1.990a	0.047
OTR, min (median)	333 (260–530)	305.5 (172–660)	-1.149a	0.250
Anterior circulation compensation score, ($\bar{x}\pm s$)	0.2 \pm 0.4	1.4 \pm 1.2	-4.744b	0.000
Posterior circulation compensation score, ($\bar{x}\pm s$)	1.0 \pm 0.9	1.8 \pm 1.4	-1.817b	0.077
Anterior and posterior circulation compensation score, ($\bar{x}\pm s$)	1.2 \pm 1.1	3.1 \pm 1.7	-3.795b	0.001
Number of embolization removal, ($\bar{x}\pm s$)	2.3 \pm 1.4	2.3 \pm 2.0	0.036b	0.972
Complete recanalization mTICI \geq 2b, n (%)	11 (84.6)	25 (89.3)	0.000	1.000
Distal embolization, n (%)	5 (38.5)	7 (25.0)	0.263	0.608
ICH, n (%)	11 (84.6)	12 (42.9)	6.286	0.012
PH2-type ICH	4 (30.8)	0 (0.0)	6.372	0.012
mRS (0–2), n (%)	2 (15.4)	15 (53.6)	5.334	0.021
mRS (4–5), n (%)	2 (15.4)	3 (10.7)	0.000	1.000
mRA (6), n (%)	8 (61.5)	1 (3.6)	14.193	0.000

^aZ value; ^bt value; else χ^2 value or adjusted χ^2 value; NIHSS, National Institutes of Health Stroke Scale; OTP, onset to groin puncture; OTR, onset to recanalization.

prognosis owing to the newest thrombectomy materials and progressively skilled operation technology other than their pooled dataset originating from MERCI and MERCI trials with the first thrombectomy apparatus [7]. Although 87.80% of the patients had a complete recanalization, 58.54% of these patients manifested bad outcomes and nearly 31.71% of these patients experiencing a malignant event after revascularization. The 21.95% mortality was substantially greater than the 15.3% as reported in previous studies [1]. Given these findings, we further assessed the influencing factors that may affect malignant events after endovascular treatment in TICA patients.

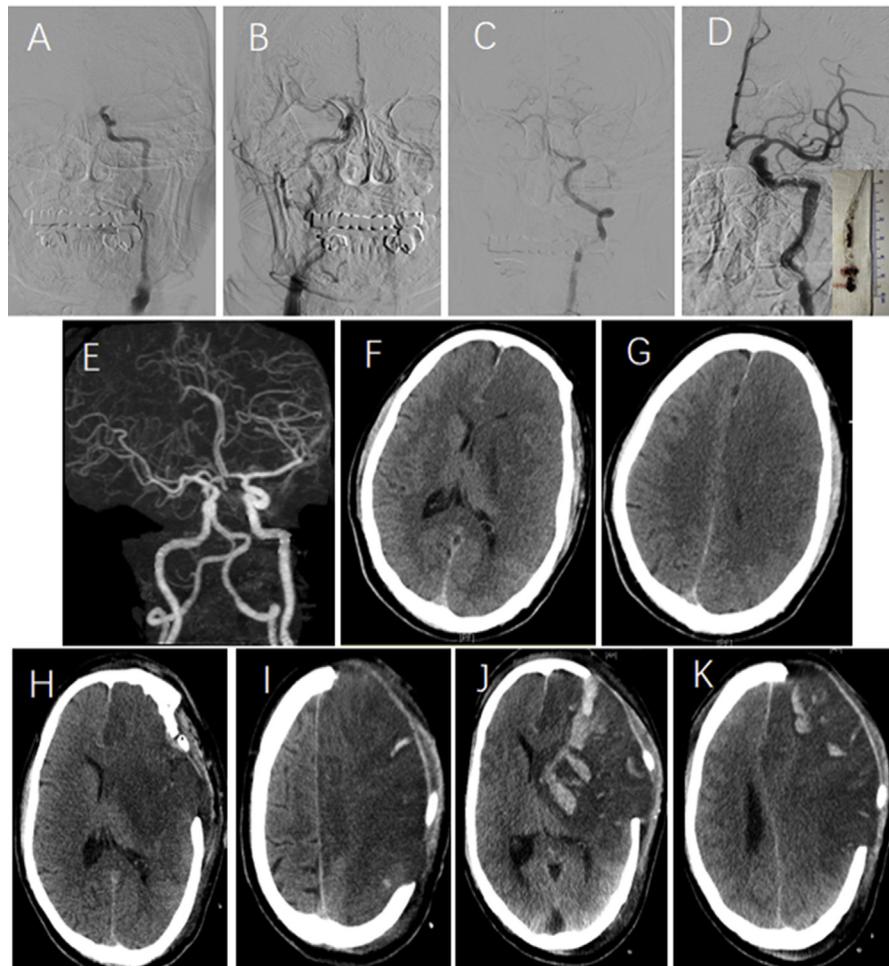


Fig. 1. An AIS-TICA patient with poor collateral circulation compensation, complete recanalization after endovascular treatment followed by a malignant event. One middle-aged patient admitted at 3 hours after onset, OTP: 257 min, OTR: 350 min. (A) DSA showed left TICA occlusion. (B) ACA collateral compensation score = 0. (C) PCA collateral compensation score = 1. (D) mTICI level 3. (E, F and G) CT angiography of the brain at 6 hours after surgery demonstrating smooth blood flow within responsive blood vessels. Edema was present in the left cerebral hemisphere and the midline was shifted right. (H and I) 13 hours after surgery, the bone flap was decompressed. Reexamination of the brain with CT at 30 hours after surgery continued to show swelling in the left cerebral hemisphere. (J and K) 48 hours after surgery, the patient showed respiratory and heart arrhythmia disorders, brain CT showed PH2 type ICH in the edema region, and the patient died.

Although the window of time for thrombectomy can be extended to 24 hours following strict imaging screening criteria, results of our current study suggests that the longer the duration between onset and intravascular treatment, the higher the probability of malignant events. Such findings emphasize the importance of this time variable for effective endovascular treatment in AIS. Additionally, we also found that the average number of thrombectomies in our study was 2.29 ± 1.81 , which was higher than that of the recommended 3 times as proposed previously [12]. This difference may be due to the large thrombus burden and high

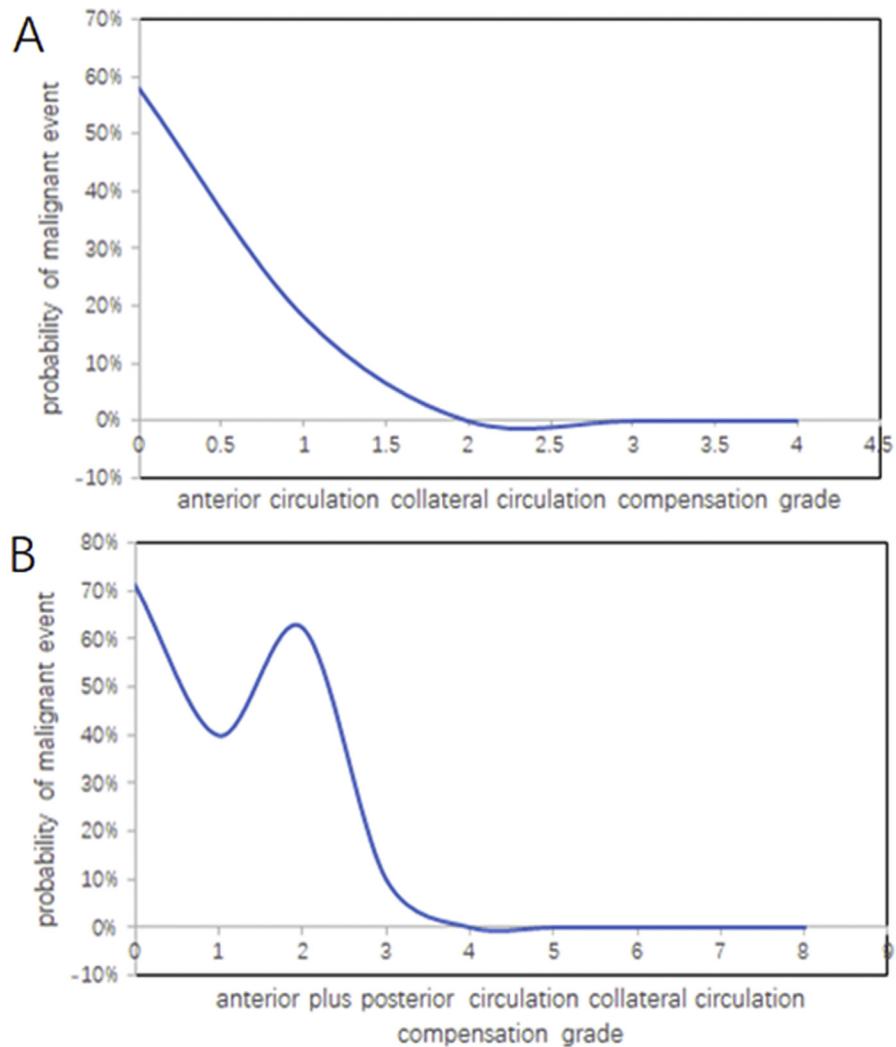


Fig. 2. Correlations between collateral circulation grade and malignant events in AIS-TICA patients with endovascular therapy. (A) Correlations between anterior collateral circulation grade and malignant events. (B) Correlations between anterior plus posterior collateral circulation grade and malignant events.

incidence of distal embolization in our TICA patients, which suggest that multiple intravascular therapy methods, such as double stent thrombectomy, thrombus aspiration and balloon occlusion, may be required for high-load thrombus cases. The application of multiple methods has the potential to diminish vascular endothelial cell damage caused by the stent, reduce the risk of distal embolization and increase vascular recanalization rates for high-load thrombi at the distal portion of the internal carotid artery. A more detailed evaluation of the endovascular treatment strategy for occlusion of TICA is planned for a future study within our institution.

In recent years, collateral circulation has attracted a considerable amount of interest in this field, but many issues remain unresolved. For example, whether it is

considered a non-invasive or invasive procedure, whether the assessment of collateral circulation before treatment will delay treatment and whether it can guide clinical decision-making through evaluations of baseline collateral circulation represent some of the more salient issues to be addressed [13]. Differing from previous reported method based on shape of TICA clot, in this study, we directed exploring the predictive value of leptomenigeal compensation of collateral circulation for L- or T-typed occlusion patients [7]. And we found that anterior circulation collateral compensatory grade can affect whether a malignant event will occur after endovascular treatment in AIS-TICA patients. Further evidences continually revealed that a negative correlation was present between collateral circulation of the anterior circulation and occurrence of malignant events; The probability of malignant events increases dramatically, if anterior circulation collateral circulation scores are 0–1. For those patients with poor compensation for TICA collateral circulation, it is necessary to look before you leap whether to perform endovascular treatment. While the relatively small sample size of our current retrospective study as performed at a single medical center limits such an analysis, it does provide the foundation and direction for future, large-sample, randomized controlled trials in this decision-making process for use in clinical treatment.

Declarations

Author contribution statement

Wang Chen: Conceived and designed the experiments; Wrote the paper.

Xiaojie Song: Analyzed and interpreted the data; Wrote the paper.

Dachen Tian, Xin Hui: Contributed reagents, materials, analysis tools or data.

Hongyang Sun: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Lijun Zhang: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Bonaventure YM Ip: Conceived and designed the experiments.

Xianjun Wang: Conceived and designed the experiments; Performed the experiments.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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