



Research article

Predictors of delayed reocclusion after successful recanalization in acute basilar artery occlusion patients[☆]Xuan Sun^{a,1}, Huijun Zhang^{b,1}, Qiting Zhang^{b,1}, YiQiao Zheng^c, Feng Gao^a, Zhongrong Miao^{a,*}^a Department of Interventional Neuroradiology, Beijing Tiantan Hospital, Capital Medical University, China^b Department of Neurology, Tong Ren Hospital Shanghai Jiaotong University School of Medicine, China^c Goodwill Hessian Health Technology Co., Ltd., 100007, Beijing, China

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ABSTRACT

Background: Delayed reocclusion (DR) after successful recanalization in acute basilar artery occlusion (BAO) patients, which is associated with clinical deterioration and poor outcome, has not been well studied. The current study is aimed to predict DR after successful endovascular therapy in acute BAO patients.

Method: 187 consecutive patients presenting with acute BAO and undergoing endovascular treatment (EVT) were selected in Beijing Tiantan Hospital from January 2012 to July 2018. Computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) within 7 days of the thrombectomy was used to identify reocclusion of the target vessel. Multivariable logistic regression analysis was used to evaluate associated factors and clinical impact.

Results: DR was observed in 17 of 169 successfully reperfused patients (10.1%). Patients with DR had higher frequency of intracranial atherosclerotic stenosis (ICAS) (94.1% vs. 61.8%; $P = 0.01$), higher frequency of intracranial angioplasty during EVT (88.2% vs. 57.2%; $P = 0.02$), lower frequency of stent-retriever use during EVT (52.9% vs. 78.9%; $P = 0.03$) and a lower proportion of modified Thrombolysis In Cerebral Infarction (mTICI) 3 reperfusion (41.2% vs. 78.3%; $P < 0.01$). Suggestive predictors were mTICI3 reperfusion (aOR, 0.205; 95% CI, 0.061–0.686) and stent-retriever using (aOR, 0.29; 95% CI, 0.086–0.980). DR was an independent predictor of unfavorable outcome at 90 days (aOR for mTICI ≤ 3 , 5.205; 95% CI, 1.129–24.005).

Conclusions: DR within 7 days after successful mechanical thrombectomy in acute BAO patients is rare but associated with poor outcome. Patients without mTICI3 reperfusion and stent-retriever using are at high risk for DR.

1. Introduction

The basilar artery which is generally the primary artery supplies blood flow to the posterior circulation consisting of the brain stem,

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occipital lobes, and part of the cerebellum and thalami. A posterior circulation stroke caused by BAO has a devastating and extremely high mortality rate at 90 days (40–80%) [1–5]. EVT now has evidentiary support for cases with onset within 0–6 h and a specific subset of patient's with onset out to 24 h [6–9]. Unfortunately, even though patients with BAO have achieved good recanalization, the mortality rate at 90 days is still more than 35% [5,10,11].

Although prevalence and predictors of reocclusion (<48 h or < 24 h) for all arterial stroke distributions [12–14] and DR ((5–7) days) for middle cerebral artery occlusion [15] after an initially successful endovascular thrombectomy are studied, there is a lack of research on DR (within 7 days) in patients with posterior circulation infarction. For patients with posterior circulation acute occlusion, due to the lack of effective collateral circulation, the consequences will be serious, so the pursuit of complete recanalization has become the key to the quality of the surgery. However, if DR occurs, not only the prognosis of patients cannot be improved, but also the economic burden of patients will be increased. We aimed to identify the prevalence and predictors of reocclusion within 7 days after an initially successful endovascular thrombectomy within a cohort of consecutive patients with acute BAO.

2. Methods

2.1. Study cohort

A prospectively registered cohort of patients with acute BAO treated by EVT (including stent-retriever thrombectomy and/or intra-arterial thrombolysis and/or emergency angioplasty) in Beijing Tiantan Hospital between January 2012 and July 2018 were reviewed. The final study population (n = 169) were included. Patient selection and grouping are presented in Fig. 1. The prospective registry database contained patient's baseline characteristics, risk factors, time metrics and clinical follow-up data within 3 months. Informed consent was obtained from all patients, and all protocols were approved by the Institutional Review Board of Beijing Tiantan Hospital for this retrospective study.

2.2. Image analysis

The following angiographic variables were evaluated: occlusion site (proximal, middle or distal basilar artery), tandem lesion (defined as vertebral artery ostium occlusion/severe stenosis and BAO occlusion), intracranial artery stenosis (ICAS, including basilar artery and/or vertebral artery V4 segment), use of stent retriever, intracranial or extracranial angioplasty (balloon and/or stenting), final mTICI score and residual stenosis on the last angiographic run after EVT, and DR defined as mTICI score of (0–1) evaluated by CTA/MRA at follow-up within 7 days (Fig. 2). The complete set of angiographic images was analyzed by 2 independent

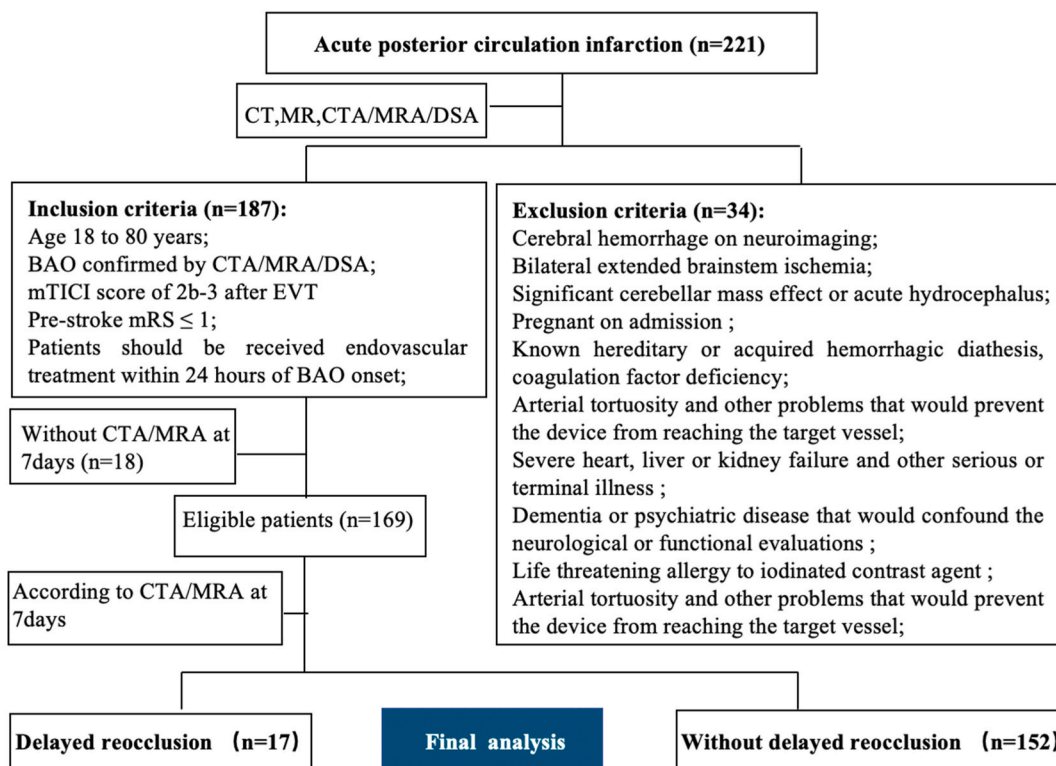


Fig. 1. Flowchart of the patients selection.

neuroradiologists (F.G. and X.S.). A third neuroradiologist (Z.M.) with 20 years of experience was involved to resolve any disagreement.

2.3. Endovascular therapy

All EVT were performed by a neurointerventionalist with more than 50 cases of experience in neurovascular intervention in mechanical thrombectomy for acute ischemic stroke. After evaluation by a dedicated anesthesiology team, cerebral angiography and EVT were performed under general anesthesia or conscious sedation. The thrombectomy technique was chosen at the interventionist's discretion, using either a stent retriever, aspiration or angioplasty first, with a possible switch toward another strategy in case of recanalization failure [mTICI grade 0-2a] with the first approach. Mechanical thrombectomy was performed with a stent-retriever (Solitaire, Covidien, Irvine, Calif; or Trevo stent, Stryker, Kalamazoo, Mich) or contact aspiration device (Penumbra, Alameda, Calif; or 5-F Navien intermediate catheter). If underlying intracranial atherosclerotic stenosis (ICAS) was revealed, intracranial angioplasty or stenting was performed when suitable. ICAS is considered in the following cases: (1) there is in situ stenosis according to the medical history and previous image data; (2) predicted by microcatheter "first-pass effect" during mechanical thrombectomy [16]; (3) during mechanical thrombectomy, if the stent-retriever is difficult to pass through the occlusion, consider it as local severe stenosis. Patients undergoing angioplasty and/or stenting received a loading dose of aspirin (300 mg) and clopidogrel (300 mg) orally or via nasogastric tube immediately after the intervention in patients who were antiplatelet naive. Intraoperative bridging with intravenous IIb/IIIa inhibitor was also allowed at the operator's discretion. Dual antiplatelet therapy was maintained for at least 3 months after the procedure followed by aspirin or clopidogrel monotherapy lifelong.

2.4. Statistical analysis

Study data were collected on standard forms, evaluated for completeness, and double keyed into an EpiData statistics data document. All data were presented as frequency or proportion for categorical variables, and mean or median for continuous variables. Univariate comparison was performed by Pearson's chi-square test or Fisher's exact test for categorical variables. Independent-samples *t*-test was used for normally distributed continuous variables, and Mann-Whitney *U* test for non-normally distributed continuous and ordinal scaled variables. Variables with $P < 0.1$ in univariate comparison entered a backward likelihood ratio multivariable binary logistic regression model. Finally, we performed a multivariable logistic regression to assess the association between DR and 3-month outcome. All statistical analyses were performed with SPSS software (Version 21.0; IBM, Armonk, New York). A *P* value 0.05 was significant.

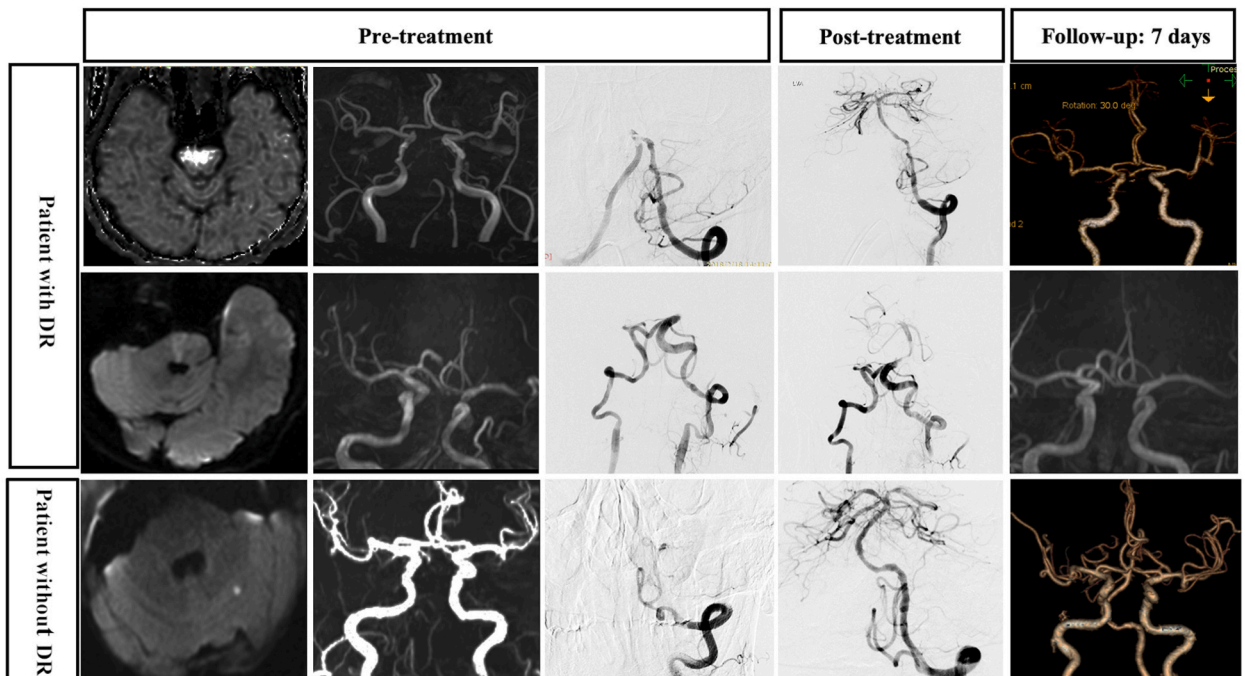


Fig. 2. Key pre-treatment, post-procedure, and follow-up images in patients who experienced DR and no DR.

3. Results

3.1. Prevalence and baseline factors of DR

Between January 2012 and July 2018, 187 consecutive patients with BAO underwent emergency EVT. Because of unsuccessful

Table 1

Univariate comparison of patient characteristics.

Variable names	Patient without DR (n = 152)	Patient with DR (n = 17)	P value
Demographic data			
Age, mean (SD), years	59 (10)	60 (13)	0.77
Male sex	126 (82.9)	15 (88.2)	0.74
Vascular risk factors			
Hypertension	107 (70.4)	12 (70.6)	>0.99
Diabetes mellitus	43 (28.3)	4 (23.5)	0.78
Dyslipidemia	24 (15.8)	4 (23.5)	0.49
Coronary heart disease	18 (11.8)	3 (17.6)	0.45
Prior stroke	29 (19.1)	5 (29.4)	0.34
Current smoking	58 (38.2)	7 (41.2)	0.80
Clinical features			
Presenting course			
Acute	74 (48.7)	11 (64.7)	
Progressive	72 (47.4)	5 (29.4)	
Fluctuating	6 (3.9)	1 (5.9)	
SBP, mean (SD), mmHg	160 (24)	156 (33)	0.49
NIHSS score, median (IQR)	23 (10–34)	20 (13–31)	0.82
WBCs, mean (SD), $\times 10^9/L$	11.1 (4.0)	10.9 (3.7)	0.90
Blood glucose, mean (SD), mmol/L	9.1 (3.6)	9.2 (4.4)	0.85
Creatinine, mean (SD), umol/L	70.6 (22.3)	67.3 (17.1)	0.55
pc-ASPECTS on DWI, median (IQR)	6.0 (5.0–8.0)	7.0 (6.0–8.0)	0.66
PMI on DWI, median (IQR)	2.0 (0.0–4.0)	3.0 (2.0–3.0)	0.62
Occlusion site			
Proximal BA	81 (53.3)	12 (70.6)	
Middle BA	43 (28.3)	5 (29.4)	
Distal BA	28 (18.4)	0 (0.0)	
Tandem lesion	18 (11.8)	0 (0.0)	0.22
Underlying ICAS	94 (61.8)	16 (94.1)	0.01
ASITN/SIR collateral system			
Grade 0-1	66 (43.4)	5 (29.4)	
Grade 2	67 (44.1)	9 (52.9)	
Grade 3-4	19 (12.5)	3 (17.6)	
Stroke subtype by TOAST criteria			
Large artery arteriosclerosis	119 (78.3)	17 (100.0)	0.10
Cardioembolic	29 (19.1)	0 (0.0)	
Other or unknown etiology	4 (2.6)	0 (0.0)	
Perioperative characteristics			
Prior use of intravenous tPA	32 (21.1)	1 (5.9)	0.20
General anesthesia	119 (78.3)	14 (82.4)	>0.99
Stent-retriever thrombectomy	120 (78.9)	9 (52.9)	0.03
Intra-arterial tPA or Urokinase	29 (19.1)	6 (35.3)	0.13
Infusion of Tirofiban	112 (73.7)	13 (76.5)	>0.99
Heparinization	61 (40.1)	8 (47.1)	0.61
Intracranial angioplasty (Balloon and/or stenting)	87 (57.2)	15 (88.2)	0.02
OTP, median (IQR), hours	6.8 (4.8–9.2)	7.0 (6.0–10.0)	0.47
PTR, median (IQR), hours	1.5 (1.0–2.0)	1.4 (1.0–2.0)	0.95
Complete recanalization (mTICI = 3)	119 (78.3)	7 (41.2)	<0.01
Residual stenosis rate >50%	13 (8.6)	4 (23.5)	0.07
Postoperative antithrombotic therapy			
Tirofiban within 24 h	92 (60.5)	13 (76.5)	0.29
Aspirin plus Clopidogrel within 24 h	88 (57.9)	11 (64.7)	0.80
LMWH within 24 h	36 (23.7)	4 (23.5)	>0.99
Tirofiban within 24 h to 7 days	33 (21.7)	6 (35.3)	0.23
Aspirin plus Clopidogrel within 24 h to 7 days	97 (63.8)	10 (58.8)	0.79
LMWH within 24 h to 7 days	18 (11.8)	4 (23.5)	0.24

Values are numbers with percentages in parentheses, unless indicated otherwise.

Abbreviations: DR = delayed reocclusion, BA = basilar artery, DWI = diffusion weighted imaging, ICAS = intracranial artery stenosis, IQR = interquartile range, LMWH = low-molecular-weight heparin, NIHSS=National Institutes of Health Stroke Scale, OTP = onset to puncture time, pc-ASPECTS = posterior circulation Acute Stroke Prognosis Early CT Score, PMI=Pons-Midbrain Index, PTR = puncture to recanalization time, SBP = systolic blood pressure, SD = standard deviation, mTICI = modified Thrombolysis in Cerebral Infarction, TOAST = Trial of Org 10,172 in Acute Stroke Treatment, tPA = tissue Plasminogen Activator, VA = vertebral artery, WBC = white blood cell.

recanalization and failure to obtain vessel imaging within 7-day follow-up, 18 patients were excluded. A total of 169 eligible patients were assessed in this study. Among them, average age was 59 years (range: 23–80 years); 141 cases (83.4%) were male, and median NIHSS score was 22 points (IQR: 10–34 points). A total of 129 cases (76.3%) were treated by stent retriever thrombectomy, and median onset-to-treatment time was 7 h (IQR: 5–10 h). In all, 17 cases (10.1%) suffered from DR within 7 days after EVT.

A univariate comparison of patients with and without DR is shown in Table 1. Patients with DR had significantly higher frequencies of ICAS (94.1% vs. 61.8%; $P = 0.01$) and intracranial angioplasty (88.2% vs. 57.2%; $P = 0.02$), but lower proportions of stent-retriever thrombectomy (52.9% vs. 78.9%; $P = 0.03$) and mTICI score of 3 on the last angiographic run after EVT (41.2% vs. 78.3%; $P < 0.01$). In addition, the severity of target arterial residual stenosis was unrelated to the occurrence of DR. In multivariable binary logistic regression analysis, mTICI score of 3 on the last angiographic run after EVT (aOR 0.205, 95% CI: 0.061–0.686, $p = 0.01$) and stent-retriever using (aOR 0.29, 95% CI: 0.09–0.98, $p = 0.05$) were factors significantly associated with DR within 7 days (Table 2).

18 of 187 patients (9.6%) were excluded from the study because of absent CTA or MRA within 7 days after operation. As this represents about 10% of the total sample, we provide details clinical Characteristics and Outcomes of these patients (see Table 1 in the online-only Data Supplement for details).

3.2. Clinical outcome

Distribution of Modified Rankin Scale Scores at Day 90 of patients with or without DR were presented in Fig. 3. Compared with patients with sustained recanalization those with DR had a worse clinical outcome at day 90 (modified Rankin Scale ≤ 3 , 48.68% vs 76.47%, $p = 0.03$). DR was an independent predictor of unfavorable outcome at 90 days after adjusting for age, sex, admission National Institutes of Health Stroke Scale, prestroke independence, TIC13 versus TIC12b, bridging IVT, time to admission, and site of occlusion (aOR for modified Rankin Scale ≤ 3 , 5.205; 95% CI, 1.129–24.005).

4. Discussion

In the current study among patients with acute BAO with available CTA/MRA follow-up imaging, we found that about 10% patients had DR. In patients with DR, the responsible vessels were still occluded at 90 days follow-up. DR was an independent predictor of unfavorable outcome at 90 days after adjusting for age, sex, admission National Institutes of Health Stroke Scale, prestroke independence, TIC13 versus TIC12b, bridging IVT, time to admission, and site of occlusion (aOR for modified Rankin Scale ≤ 3 , 5.205; 95% CI, 1.129–24.005). Reports on DR in the era of modern endovascular treatment for BAO are scarce. According to our results, unexpected DR within 7 days after successful mechanical thrombectomy occurs in 10.1% of cases, which compares unfavorably to the 1.1% reocclusion rate within (5–7) days in patients with acute middle cerebral artery (MCA) M1 occlusion after successful intravenous or intra-arterial thrombolysis [14]. The same phenomenon was found in the studies of early reocclusion ((24–48) h) of acute cerebral infarction in anterior (2.3% of cases within 48 h after successful mechanical thrombectomy and 3%–4% reocclusion rate within 24 h after successful intravenous or intra-arterial thrombolysis) [14,17,18] and posterior circulation (6.3% of cases within 48 h after successful mechanical thrombectomy) [14], which may be caused by the following factors: (1) the pathology of both anterior and posterior circulation are different, including the cause of stroke, the properties of the plaques, influence of blood flow and so on; (2) The vascular diameter and movement of posterior circulation are different from those of anterior circulation. Thus, the selection of devices and treatment strategy of posterior circulation thrombectomy may be different from that of anterior circulation thrombectomy [19, 20].

Our study showed that in the TIC1 2b reperfusion group 22.7% of patients had DR and in the TIC1 3 reperfusion group 5.6% of patients had DR, which meant TIC1 3 reperfusion was associated with a lower rate of DR (41.2% vs. 78.3%; $P < 0.01$). Previous studies have confirmed that reocclusion occurs more often in patients with partial recanalization, leading to neurologic deterioration and higher in-hospital mortality [11,21]. However, there is lack of study focused on the effect of complete recanalization (mTICI score of 3) on DR in patients with acute BAO after EVT. According to our study, after multivariable logistic regression analysis, mTICI score of 3 on the last angiographic run after EVT was one factor significantly associated with DR within 7 days (aOR 0.205, 95% CI: 0.061–0.686, $p = 0.01$).

Our results indicated that another factor of stent-retriever using is significantly associated with DR within 7 days (aOR 0.29, 95% CI: 0.09–0.98, $p = 0.05$). In our center, if underlying intracranial atherosclerotic stenosis (ICAS) was revealed, intracranial angioplasty or stenting was performed when suitable. ICAS is considered in the following cases: (1) there is in situ stenosis according to the medical history and previous image data; (2) predicted by microcatheter “first-pass effect” during mechanical thrombectomy [14]; (3) during

Table 2
Multivariable analysis for predictors of delayed reocclusion. Logistic Regression With $P < 0.2$ in Univariate Comparison.

Variable	Adjusted OR	95%CI	P Value
mTICI = 3	0.21	0.06–0.69	0.01
stent-retriever using	0.29	0.09–0.98	0.05
intracranial angioplasty	3.27	0.61–17.55	0.18
intracranial atherosclerotic stenosis	1.81	0.19–17.65	0.61
intravenous tPA	0.22	0.02–1.95	0.17
Intra-arterial tPA or Urokinase	1.31	0.39–4.38	0.67
Residual stenosis rate >50%	1.62	0.37–7.07	0.52

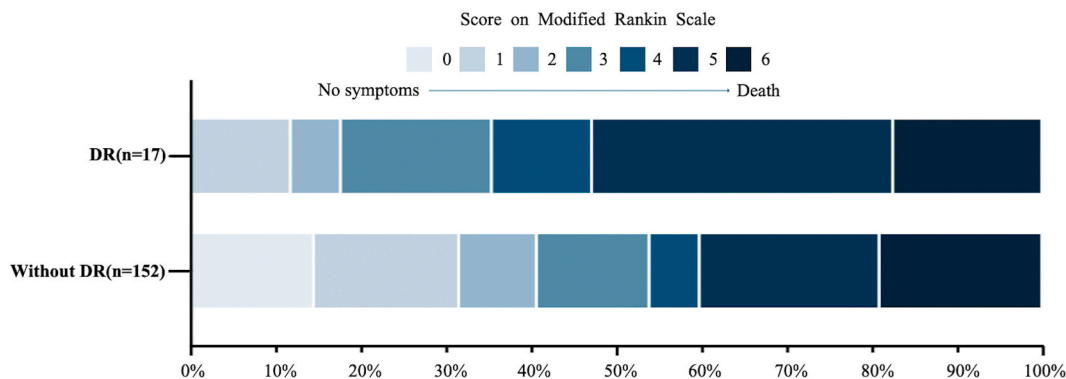


Fig. 3. Distribution of Modified Rankin Scale Scores at Day 90 of patients with or without DR.

mechanical thrombectomy, if the stent release catheter is difficult to pass through the occlusion, consider it as local severe stenosis. Many patients considered ICAS were treated with balloon dilatation or stent implantation directly instead of stent thrombectomy. In our study, univariate analysis showed that patients with DR had significantly higher frequencies of ICAS (94.1% vs. 61.8%; $P = 0.01$) and intracranial angioplasty (88.2% vs. 57.2%; $P = 0.02$) and most of these patients were treated with balloon dilatation or stent first which can damage the fibrous cap and lead to aggravation of in situ reocclusion [22,23]. Our further analysis showed that there was no significance related to in patients treated with remedial measures after stent thrombectomy. However, there is also one limitation in our current retrospective study, which is that there was a bias in the choice of treatment measure. Our ongoing multicenter randomized controlled study, angle reboot, may solve the above problems.

Different with previous study [15], our results didn't show that well-developed collaterals was associated with the occurrence of DR in patients with M1 occlusion after successful recanalization. The reason for this phenomenon might be speculated as the anatomical differences between anterior circulation and posterior circulation.

The strengths of this study are that it was the first to study the prevalence, baseline factors and clinical outcome of DR after successful endovascular therapy in acute BAO patients, which will assist clinicians in choosing treatment methods and in evaluating the prognosis of these patients. However, this study had limitations. Despite our best efforts, inherent bias because of the retrospective and monocentric design study was inevitable. Another limitation was that the data was derived from a single high-volume stroke center with the interventionalist being more experienced in the procedure, so the results may not be replicable in other lower volume stroke centers. Future multicenter studies are needed to validate the findings presented in our research.

5. Conclusions

In the current study among patients with acute BAO with available CTA/MRA follow-up imaging, we found that about 10% patients had DR. In patients with DR, the responsible vessels were still occluded at 90 days follow-up. DR was an independent predictor of unfavorable outcome at 90 days. After multivariable logistic regression analysis, we found that mTICI score of 3 on the last angiographic run after EVT and stent-retriever using were factors significantly associated with DR within 7 days.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Institutional Review Board of Beijing Tiantan Hospital. The appropriate permissions to access the patient database which provided the data for our study were granted by Beijing Tiantan Hospital.

Production notes

Author contribution statement

Xuan Sun, Feng Gao: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data.

Hui-Jun Zhang: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Qiting Zhang: Analyzed and interpreted the data; Wrote the paper.

YiQiao Zheng: Analyzed and interpreted the data.

Zhong-Rong Miao: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no competing interests.

Acknowledgments

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Abbreviations

DR	delayed reocclusion
BAO	basilar artery occlusion
EVT	endovascular treatment
CTA	computed tomography angiography
MRA	magnetic resonance angiography
mTICI	modified Thrombolysis in Cerebral Infarction
ICAS	intracranial atherosclerotic stenosis
OR	odds ratios
CI	confidence intervals
MCA	middle cerebral artery
LVO	Large vessel occlusion
NIHSS	National Institutes of Health Stroke Scale
pc-ASPECTS	Prognosis Early CT Score
IQ	Interquartile range
tPA	tissue plasminogen activator
PMI	Pons-Midbrain Index
PTR	puncture to recanalization time
OTP	onset to puncture time

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