Predictors of Favorable Outcomes for Vertebrobasilar Artery Occlusion after Endovascular Therapy within 24 Hours of Symptom Onset

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Abstract

Objective

The aim of the present study was to describe our results of endovascular therapy (EVT) for vertebrobasilar artery occlusion (VBAO) within 24 h of symptom onset, and to evaluate prognostic factors associated with favorable outcomes.

Methods

The present study enrolled patients who underwent EVT for acute ischemic stroke (AIS) caused by VBAO. Inclusion criteria for EVT to treat VBAO were as follows: (1) computed tomography angiography (CTA) or magnetic resonance angiography (MRA) confirmed acute VBAO; (2) baseline National Institutes of Health Stroke Scale (NIHSS) score ≥ 2 ; (3) premorbid modified Rankin scale (mRS) score ≤ 2 ; (4) onset or last known time to puncture within 24 h; and (5) posterior-circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS) ≥ 6 . Favorable outcomes were defined as mRS scores of 0–3 at three months following EVT. The associations among baseline parameters, procedural parameters, and favorable outcomes were assessed.

Results

A total of 67 patients were recruited in this study, of which 40 patients (59.7%) had favorable outcomes. Of the 50 patients with a late-window (6–24 h), 29 patients (58%) had favorable outcomes. Univariate analysis revealed significant associations of the following parameters with favorable outcomes in the enrolled patients: age, sex, smoking status, baseline NIHSS score, baseline Glasgow coma scale (GCS) score, Pons-midbrain index (PMI), and intracranial atherosclerosis (ICAS). Multivariate logistic regression indicated that only age (OR 0.914, 95% CI: 0.849 to 0.984; $p = 0.017$), baseline GCS score (OR 1.234, 95% CI: 1.061 to 1.435; $p = 0.006$), and PMI (OR 0.448, 95% CI: 0.252 to 0.798; $p = 0.006$) were independently correlated with favorable outcomes at three months following EVT. After adjustments for confounding factors in patients with a late-window, only age (OR 0.879, 95% CI: 0.799 to 0.967; $p = 0.008$) was associated with favorable outcomes.

Conclusions

Younger age, lower PMI, and higher GCS scores in patients with VBAO-induced AIS were associated with more favorable outcomes. In late-window (6–24 h) patients, younger age correlated to favorable outcomes, and lower NIHSS scores and lower PMI each also had a tendency to correlate with favorable outcomes.

Introduction

Acute ischemic stroke (AIS) caused by vertebrobasilar artery occlusion (VBAO) is a devastating subtype of stroke with high disability and mortality rates.¹ Endovascular therapy (EVT) for selected patients with AIS caused by large-vessel occlusions of the anterior circulation within 24 h of onset has been proved safe and effective by multiple randomized controlled studies.^{2,3} However, the benefit of EVT for VBAO is unknown due to a lack of effective evidence from randomized controlled trials. The Basilar Artery International Cooperation Study (BASICS) registry showed that 68% of the analyzed patients had a poor outcome and there was no difference between intravenous thrombolysis (IVT) and EVT in the treatment of patients with mild-to-moderate deficits.⁴ However, a lack of effective recanalization methods—such as stent-retriever and direct-aspiration first-pass techniques—may have affected these results. The recent ENDOSTROKE study suggested that the use of a stent retriever was associated with high recanalization rates, and collateral status and stroke severity significantly predicted clinical outcomes.⁵ Similarly, many clinical and imaging factors have been found to be associated with outcomes after EVT for VBAO.^{6,7} However, few studies have focused on prognostic factors of EVT for VBAO within 24 h of the onset of symptoms. Hence, the present study provides our results of EVT for VBAO within 24 h of symptom onset. Additionally, we evaluated prognostic factors associated with favorable outcomes of EVT in the VBAO patients in our present study.

Methods

Patients

The present study was a single-center retrospective study that enrolled patients who underwent EVT for VBAO between January 2012 and December 2017. The Ethics Committee of the Baotou Central Hospital approved the research protocol. The informed consent was signed by the subjects or their legal representatives prior to endovascular therapy. EVT were performed following the current guidelines and approved equipment. Clinical characteristics, brain imaging features, and procedures for EVT were added into the EVT database. Trained and qualified neurologists recorded the National Institutes of Health Stroke Scale (NIHSS) scores and premorbid modified Rankin scale (mRS) scores at baseline, 24 h, and 90 days after EVT. Brain computed tomography (CT), CT angiography (CTA), CT perfusion (CTP), and/or magnetic resonance imaging (MRI) were performed at baseline and at 24 h after EVT. The imaging data were interpreted by two experienced radiologists. The posterior-circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS)⁸ and Pons-midbrain index (PMI)⁹ on non-contrast CT or diffusion-weighted MRI were evaluated and analyzed. All eligible patients received IVT with recombinant tissue plasminogen activator (rt-PA) within 4.5 h after the onset of symptoms.

Procedure for endovascular therapy

Routine inclusion criteria for EVT due to VBAO were as follows: (1) computed tomography angiography (CTA) or magnetic resonance angiography (MRA) confirmed acute vertebrobasilar occlusion; (2) baseline

NIHSS score ≥ 2 ; (3) premorbid mRS score ≤ 2 ; (4) onset or last known time to puncture within 24 h; and (5) pc-ASPECTS ≥ 6 . Patients with progressive neurological deficits despite aggressive medical therapy and with pc-ASPECTS < 6 were also treated with EVT. Local anesthesia or conscious sedation were the main methods of anesthesia in the present study. Patients with abnormalities in vital signs underwent general anesthesia and were intubated before the procedure. A diagnostic cerebral angiography was performed for all patients before EVT. The collateral grade was evaluated with the American Society of Interventional and Therapeutic Neuroradiology and Society of Interventional Radiology (ASITN/SIR), and vertebrobasilar occlusion was defined as modified Thrombolysis in Cerebral Infarction (mTICI) scales 0–1. Stent-retriever thrombectomy with a Solitaire stent AB or FR (Covidien, Irvine, California, USA), combined with local aspiration, were performed as the primary EVT method. Rescue-therapy strategies included balloon angioplasty, Solitaire detachment, other stent placements, intra-arterial thrombolysis (IAT), or a combination of the above-mentioned therapies. The degree of vertebrobasilar stenosis was calculated by the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) criteria.¹⁰ Successful recanalization was defined as achieving mTICI grades of 2b or 3¹¹ on the delayed angiogram at least 10 min after recanalization.

Outcome assessments

Favorable outcomes were defined as mRS scores of 0–3 at three months after EVT.¹² The safety outcomes included symptomatic intracranial hemorrhage (SICH) and all intracranial hemorrhages within seven days of EVT. SICH was defined by the Heidelberg criteria, which consisted of new intracranial hemorrhages detected by brain imaging associated with an increase by ≥ 4 points or an increase by ≥ 2 points of an NIHSS subcategory as a relevant change in neurological status.¹³

Statistical analysis

Continuous variables and medians were analyzed using the Mann–Whitney U test. The χ^2 method and Fisher exact test were used to evaluate significant differences among proportions. A multivariate logistic regression model by the forward LR method calculated odds ratios (ORs) and 95% confidence intervals (CIs). The baseline variables that showed possible associations among the confounding factors following univariate analysis ($p < 0.05$) were entered into the multivariate model. Statistical significance was defined as $p < 0.05$. SPSS software was employed for all analyses (version 22.0, IBM, Armonk, New York, USA).

Results

Between January 2012 and December 2017, 239 consecutive subjects were enrolled in the prospective endovascular-treatment database for AIS. AIS was caused by posterior-circulation occlusion in 72 (31.0%) patients; three subjects were excluded due to a lack of data, and another two subjects were excluded due to having arterial dissections. Following these exclusions, 67 patients were ultimately recruited in the present study, of which 40 patients (59.7%) had favorable outcomes and 27 patients

(40.3%) had poor outcomes. Fifty patients with onsets or last-known times to puncture greater than 6 h were defined as late-window patients; among them, 29 patients (58%) achieved favorable outcomes (Fig. 1).

The median age of all including patients was 63 years (interquartile range [IQR], 57–68 years), and the median NIHSS score was 13 (IQR, 10–22). Successful recanalization was achieved in 60/67 patients (89.6%), SIH occurred in 3/67 patients (4.5%), and mortality occurred in 20/67 patients (29.9%) at 90 days following EVT (Fig. 2). Analysis of all enrolled patients (Table 1) showed that the favorable-outcome group had a prevalence of smoking (42.5% vs. 18.5%; $p = 0.04$) and intracranial atherosclerosis (ICAS, 62.5% vs. 37%; $p = 0.041$) compared to those of the poor-outcome group. There was a lower NIHSS score ($p = 0.003$), lower PMI ($p = 0.003$), and higher GCS score ($p = 0.000$) at the time of admission in the favorable-outcome group. However, there were no significant differences in any other risk factors, including stroke, the location of the occlusion, collateral status, anesthesia, rescue therapies, procedural complications, revascularization, or SIH ($p > 0.05$). In univariate analysis of late-window patients, younger age, lower NIHSS, lower PMI, higher GCS, and complications with ICAS were associated with favorable outcomes (Table 2).

Table 1
Baseline, Procedural, and Outcome Parameters in All Patients

Variables	Total	Favorable outcome (mRS, 0–3)	Poor outcome (mRS, 4–6)	P Value
N	67	40(59.7)	27(40.3)	
Age (IQR)	63(57–68)	61(53.25–65.75)	65(58–72)	0.029
Male (%)	44(65.7)	30(75)	14(51.9)	0.050
Prior or current smoking (%)	22(32.8)	17(42.5)	5(18.5)	0.040
Hypertension (%)	39(58.2)	23(57.5)	16(59.3)	0.886
Diabetes (%)	12(17.9)	7(17.5)	5(18.5)	0.915
Hyperlipidemia (%)	13(19.4)	6(15)	7(25.9)	0.267
Coronary heart disease (%)	9(13.4)	5(12.5)	4(14.8)	0.785
Atrial fibrillation (%)	11(16.4)	7(17.5)	4(14.8)	0.771
Previous stroke or TIA (%)	19(28.4)	10(25)	9(33.3)	0.458
Baseline NIHSS (IQR)	13(10–22)	12.5(8.25-17)	19(13–29)	0.003
Baseline GCS (IQR)	14(7–15)	15(13–15)	10(6–13)	0.000
Pc-ASPECTS (IQR)	8(6–8)	8(6–8)	7(6–8)	0.319
Pons midbrain index (IQR)	2(1–3)	1(0–2)	2(1–3)	0.003
Pretreatment IV tPA (%)	11(16.4)	7(17.5)	4(14.8)	0.771
Anesthetic (%)				0.061
Local anesthesia	64(95.5)	40(100)	24(88.9)	
General anesthesia	3(4.5)	0(0)	3(11.1)	
Location of occlusion				0.119
BA (%)	29(43.3)	16(40)	13(48.1)	
VA (%)	6(9)	6(15)	0(0)	
Tandem (%)	32(47.8)	18(45)	14(51.9)	
ASITN/SIR (IQR)	0(0–1)	0(0-1.75)	0(0–1)	0.375
Rescue therapy (%)	40(59.7)	26(65)	14(51.9)	0.282
Stent retriever detachment	9(13.4)	6(15)	3(11.1)	0.647
Other stents	24(35.8)	17(42.5)	7(25.9)	0.165

Variables	Total	Favorable outcome (mRS, 0–3)	Poor outcome (mRS, 4–6)	P Value
Balloon expansion	29(43.3)	20(50)	9(33)	0.177
Intra-arterial thrombolysis	11(16.4)			
With ICAS (%)	35(52.2)	25(62.5)	10(37)	0.041
Successful recanalization (mTICI 2b-3, %)	60(89.6)	37(92.5)	23(85.2)	0.427
Number of Stent retriever passes (IQR)	1(1–2)	1(1–2)	2(1–2)	0.396
Procedural complications (%)	15(22.4)	8(20)	7(25.9)	0.568
Distal embolism	5(7.5)	3(7.7)	2(7.4)	
Vessel perforation	3(4.5)	0(0)	3(10.7)	
Stent thrombosis	4(5.9)	2(5.1)	2(7.1)	
Dissection	3(4.5)	2(5.1)	1(3.6)	
Vasospasm	1(1.5)	0(0)	1(3.6)	
Onset to door time (IQR)	390(215–669)	355.5(174–660)	410(231–744)	0.462
Late-window (6–24 h, IQR)	50(74.6)	29(72.5)	21(77.8)	0.626
Door to puncture time (IQR)	142(90–233)	145(89–239)	131(87–208)	0.483
Puncture to first reperfusion time (IQR)	55(41-80.5)	55(42–81)	55(40.5–81.5)	0.794
Puncture to final reperfusion time (IQR)	96.5(63- 137.75)	88(71–127)	116(58-158.5)	0.596
Onset to first reperfusion time (IQR)	582.5(392.25- 1082.25)	575(391–1035)	652(424.5– 1150)	0.858
Onset to final reperfusion time (IQR)	649.5(462.25- 1103.75)	643(446–1100)	668(473–1159)	0.810
sICH (%)	3(4.5)	1(2.5)	2(7.4)	0.560
ICH (%)	7(10.4)	2(5)	5(18.5)	0.108

Table 2
Baseline, Procedural, and Outcome Parameters in late-window

Variables	Total	Favorable outcome (mRS, 0–3)	Poor outcome (mRS, 4–6)	P Value
N	50	29(58)	21(42)	
Age (IQR)	61(54.75-67)	59(51–65)	65(59-72.5)	0.005
Male (%)	33(66)	22(75.9)	11(52.4)	0.084
Prior or current smoking (%)	17(34)	12(41.4)	5(23.8)	0.196
Hypertension (%)	28(56)	15(51.7)	13(61.9)	0.474
Diabetes (%)	7(14)	4(13.8)	3(14.3)	1.000
Hyperlipidemia (%)	11(22)	6(20.7)	5(23.8)	0.793
Coronary heart disease (%)	6(12)	2(6.9)	4(19)	0.223
Atrial fibrillation (%)	9(18)	5(17.2)	4(19)	0.870
Previous stroke or TIA (%)	11(22)	6(20.7)	5(23.8)	0.793
Baseline NIHSS (IQR)	13(9-19.25)	12(7.5–17)	18(10.5–23)	0.015
Baseline GCS (IQR)	14(7–15)	15(13.5–15)	10(6.5–14)	0.004
Pc-ASPECTS (IQR)	7(6–8)	7(6–8)	7(6–8)	0.984
Pons midbrain index (IQR)	2(1–3)	1(0–2)	2(1–3)	0.019
Pretreatment IV tPA (%)	8(16)	4(13.8)	4(19)	0.706
Anesthetic (%)				0.068
Local anesthesia	47(94)	29(100)	18(85.7)	
General anesthesia	3(6)	0	3(14.3)	
Location of occlusion				0.145
BA (%)	21(42)	10(34.5)	11(52.4)	
VA (%)	4(8)	4(13.8)	0	
Tandem (%)	25(50)	15(51.7)	10(47.6)	
ASITN/SIR (IQR)	0(0–1)	0(0–2)	0(0–1)	
Rescue therapy (%)	30(60)	19(65.5)	11(52.4)	0.349
Stent retriever detachment	7(14)	5(17.2)	2(9.5)	
Other stents	19(38)	15(51.7)	4(19)	

Variables	Total	Favorable outcome (mRS, 0–3)	Poor outcome (mRS, 4–6)	P Value
Balloon expansion	23(46)	14(48.3)	9(42.9)	
Intra-arterial thrombolysis				
With ICAS (%)	26(52)	19(65.5)	7(33.3)	0.025
Successful recanalization (mTICI 2b-3, %)	45(90)	27(93.1)	18(85.7)	0.638
Number of Stent retriever passes (IQR)	1.5(1–2)	1(1–2)	2(1–2)	0.544
Procedural complications (%)	12(24)	6(20.7)	6(28.6)	0.520
Distal embolism	3(6)	1(3.4)	2(9.5)	
Vessel perforation	2(4)	0(0)	2(9.5)	
Stent thrombosis	2(4)	2(6.9)	0(0)	
Dissection	3(6)	3(10.3)	0(0)	
Vasospasm	1(2)	0	1(4.8)	
Onset to door time (IQR)	450(313– 950.75)	420(309–865)	470(318–997.50)	0.680
Door to puncture time (IQR)	177(107– 240)	195(107.5–296.5)	176(94–213)	0.487
Puncture to first reperfusion time (IQR)	56(42–84)	60.5(42–83.5)	55(40–99)	0.803
Puncture to final reperfusion time (IQR)	89(63– 137)	84(73.5–116.25)	124(59–158)	0.448
Onset to first reperfusion time (IQR)	756(565– 1307)	756(565.5–1318.25)	753(564–1299)	0.914
Onset to final reperfusion time (IQR)	781(598– 1336)	784(607.25–1372)	781(593–1299)	0.965
sICH (%)	3(6)	1(3.4)	2(9.5)	0.565
ICH (%)	6(12)	2(6.9)	4(19)	0.223

In the multivariate logistic regression analysis adjusted for males, smoking, NIHSS, and underlying ICAS among all patients, the following three factors were independently correlated with favorable outcomes at three months following EVT: age (OR 0.914, 95% CI: 0.849 to 0.984; $p = 0.017$), baseline GCS score (OR 1.234, 95% CI: 1.061 to 1.435; $p = 0.006$) and PMI (OR 0.448, 95% CI: 0.252 to 0.798; $p = 0.006$). After adjustments for confounding factors in late-window patients, only age (OR 0.879, 95% CI: 0.799 to 0.967; $p = 0.008$) was associated with favorable outcomes following EVT. Additionally, NIHSS score (OR 0.914,

95% CI: 0.835 to 1.001; $p = 0.054$) and PMI (OR 0.533, 95% CI: 0.277 to 1.023; $p = 0.0059$) each independently correlated with favorable outcomes in late-window patients (Table 3).

Table 3
Logistic regression analysis for favorable outcome

	All patients (n = 67)			Late window (n = 50)		
	OR	95% CI	P Value	OR	95% CI	P Value
Age	0.914	0.849–0.984	0.017	0.879	0.799–0.967	0.008
Baseline GCS	1.234	1.061–1.435	0.006			
Pons midbrain index	0.448	0.252–0.798	0.006	0.533	0.277–1.023	0.059
Baseline NIHSS				0.914	0.835–1.001	0.054

Discussion

The present study analyzed factors associated with favorable outcomes of EVT for VBAO-induced AIS. The main findings were that younger age, lower PMI, and higher GCS scores were associated with more favorable EVT outcomes in patients with VBAO-induced AIS. In late-window (6–24 h) patients, young age was also closely related to favorable outcomes, and lower NIHSS scores and lower PMI each correlated with favorable EVT outcomes. This study found a good outcome in 47.8% of the patients and a favorable outcome in 59.7% as consistent with recent studies using the new generation of stent retrievers and aspiration device.⁷ These percentages of favorable outcomes were higher than those of in the ENDOSTROKE registry and from another study that stent retrievers were fewer used.^{5,14} We also obtained similar findings for three-month mortality rates compared with those reported in previous studies. The recanalization rate was 89.6% across all patients, which is similar to findings from two case-series studies from China.⁷ Although the recanalization rate in the favorable-outcome group (92.5%) was higher than that in the poor-outcome group (85.2%), there was no significant difference between the two groups ($p = 0.427$). A systematic review on outcomes of stent-retriever thrombectomy in basilar artery occlusion showed that successful recanalization does not systematically yield a favorable functional outcome.¹⁵ In the present study, we found that severe neurological conditions on admission may lessen the benefits of recanalization. Additionally, patients with favorable functional outcomes had lower baseline NIHSS scores, as indicated via univariate analysis, but did not show this trend via multivariate analysis. In late-window patients, lower NIHSS scores (OR 0.914, 95% CI: 0.835 to 1.001; $p = 0.054$) correlated with favorable outcomes. These results of our present study are not exactly the same as those of previous studies.^{14,16} This discrepancy may be due to successful recanalization at the early window being helpful to the prognosis regardless of the severity of neurological symptoms, whereas—at the late-window—baseline NIHSS scores may be related to clinical outcomes.

Unlike acute anterior-circulation infarction, which often results in focal nervous system dysfunction, the hallmark of VBAO is reduced consciousness or comatose. The current study found that baseline GCS scores and PMI were independent predictors for favorable outcomes at 90 days for all enrolled patients. Consistent with our study, Huo et al.¹⁷ also found that low pre-thrombectomy GCS scores were associated with poor clinical outcomes. Lower PMI was also a predictor for favorable outcomes in late-window patients in the present study. Schaefer et al.⁹ found that PMI was highly predictive of clinical outcomes in patients with acute VBO treated with angioplasty or first-generation thrombectomy devices. To the best of our knowledge, this study represents the first demonstration that PMI was associated with favorable clinical outcomes in VBAO patients treated with second-generation thrombectomy devices. Previous studies^{15,18,19} have reported that pc-ASPECTS before treatment is an independent predictor of functional outcomes in patients with acute basilar artery occlusion (BAO). However, Mourand et al.²⁰ and our present study found that pc-ASPECTS was not associated with a favorable prognosis. Possible reasons for this discrepancy may be due to different imaging methods and/or different definitions of the time of symptom onset. Another reason for this discrepancy may be due to PMI being more responsive than pc-ASPECTS to brainstem dysfunction. Similar to the BASICS analysis¹⁶, the current study demonstrated in a series of 67 patients with VBAO that age was highly associated with favorable outcomes. Nevertheless, the HERMES study²¹ of EVT for anterior circulation larger artery occlusion, as well as the ENDOSTROKE study⁵, suggest that selected elderly patients may also benefit from EVT. This may be a selection bias in screening patients for EVT, and further randomized controlled trials are needed to clarify this phenomenon. The present study showed that patients with ICAS had a more favorable outcome than non-ICAS patients via univariable analysis, which may be due to better collateral circulation and/or ischemic conditioning during the progression of ICAS. However, this trend did not show a statistical difference in multivariate analysis. Alemseged et al.⁶ found that revascularization is associated with good outcome in BAO with good collaterals and less extensive occlusion, even at > 6 h after onset. Our present study suggests that collateral circulation was not associated with a favorable outcome, which may be due to different evaluation methods between our study and previous studies. Similarly, we did not find a relationship between an effective therapeutic time window and a favorable outcome.

The present study had several limitations. The current study was a single-center retrospective study with a non-controlled study design, due to which some selection bias may have existed. The relatively small sample size of our present study may have reduced the power of our statistical tests. Also, this study was conducted in a Chinese population, so our results may be affected by ethnic-specific factors. We anticipate that three currently ongoing randomized controlled trials—BEST (NCT02441556), BAOCHÉ (NCT02737189) and BASICS (NCT01717755)—will provide more information on endovascular treatment for posterior circulation.

Conclusions

EVT with stent-retriever thrombectomy followed by rescue treatment can achieve high rates of successful revascularization and favorable outcomes in the treatment of VBAO. Younger age, lower PMI, and higher GCS scores in patients with VBAO-induced AIS were associated with more favorable outcomes. In late-window (6–24 h) patients, younger age was also associated with favorable outcomes, and lower NIHSS scores and lower PMI each correlated with favorable outcomes as well.

Declarations

Contributors

Changchun Jiang contributed to the conception and design of the work, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved. Yu Fan drafted the work and analyzed of data for the work. Junmei Zhao, Fei Hao, Junfeng Yang acquired the data. Yuechun Li, Baojun Wang revised it critically for important intellectual content.

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Declaration of interests

All authors declare no competing interests.

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Figures

Figure 1

Flow chart of eligible patients.

Figure 2

Functional outcome at 90 days according to the score on the modified Rankin Scale (mRS).