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Endovascular therapy for acute vertebrobasilar occlusion underlying atherosclerosis: A single institution experience

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ABSTRACT

Objective: To compare the safety and efficacy of endovascular therapy in acute ischemic stroke (AIS) caused by large artery occlusion (LAO) in the posterior circulation with or without intracranial atherosclerosis (ICAS).
Patient and methods: The study enrolled patients who underwent endovascular therapy for AIS caused by posterior circulation LAO. Inclusion criteria for endovascular therapy of vertebrobasilar occlusion were as follows: (1) CTA or MRA confirmed acute vertebrobasilar occlusion; (2) baseline NIHSS score ≥2; (3) premorbid mRS score ≤2; (4) onset or last known well time to puncture within 24 h; (5) pc-ASPECTS ≥6. Outcomes were compared between the ICAS group and the non-ICAS group.
Results: A total of 67 patients were recruited in this study, of which 35 (52.2%) had underlying ICAS, while 32 (47.8%) did not. Rescue therapies were more commonly performed in the ICAS group (82.9% vs. 34.4%; p = 0.000). The proportion of favorable outcome at 90 days was higher in the ICAS group than in the non-ICAS group (71.4% vs. 46.9%; p = 0.041). There was no significant difference in symptomatic ICH (2.9% vs. 6.3%, p = 0.603) or death within 90 days (22.9% vs. 37.5%, p = 0.191) between the two groups. The baseline GCS score (OR 1.281, 95% CI: 1.085–1.513; p = 0.004) and PMI (OR 0.402, 95% CI: 0.233 to 0.693; p = 0.001) were independently associated with favorable outcome at 90 days.
Conclusions: Endovascular therapy with stent-retriever thrombectomy followed by rescue treatment can achieve high rates of successful revascularization and favorable outcome in the treatment of AIS caused by posterior circulation LAO.

1. Introduction

Intracranial atherosclerosis (ICAS) is the most common cause of ischemic stroke in Asia, and is associated with a higher rate of recurrent stroke and mortality. [1] A prospective study [2] in China found that the prevalence of ICAS was 46.6%. Endovascular thrombectomy has been proven by several clinical trials [3,4] to be an effective and safe therapy for selected intracranial large artery occlusion (LAO) patients, but these studies were mainly aimed at anterior circulation occlusions. Acute ischemic stroke (AIS) caused by LAO with underlying ICAS can be refractory to endovascular therapy, with lower rate of recanalization and frequent instant reocclusion [5,6]. Recent studies reported that thrombectomy and suitable rescue therapies such as angioplasty or stenting are safe and effective in AIS with underlying ICAS [6–8]. However, majority of these studies involved anterior circulation or very few cases of posterior circulation. The basilar artery and intracranial vertebral arteries are the most common sites of ICAS. [1] Very few studies have focused the outcomes after endovascular therapy in patients with acute vertebrobasilar occlusion and underlying atherosclerosis [9,10]. This study aimed to compare the safety and efficacy of endovascular therapy in AIS caused by posterior circulation LAO with or without ICAS.

2. Patient and methods

2.1. Patients

The present study enrolled patients who underwent endovascular therapy for AIS caused by posterior circulation LAO between January 2012 and December 2017. Demographic features, past medical history, clinical characteristics, neuroimaging, therapy and process times were prospectively added into the database. The Ethics Committee of Baotou Central Hospital approved the research protocol. The informed consent was signed by the subjects or their legal representatives prior to

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endovascular therapy. The Glasgow coma scale (GCS) and the National Institutes of Health Stroke Scale (NIHSS) were measured at baseline and 24 h. The modified Rankin scale (mRS) was measured at 90 days. Trained neurologists, who were qualified to use NIHSS and mRS, recorded the scores. The brain computed tomography (CT), CT angiography (CTA), CT perfusion (CTP) or magnetic resonance imaging (MRI) were performed at baseline and 24 h. The imaging findings were interpreted by at least two experienced radiologists. The posterior circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS) [11] and Pons-midbrain-index (PMI) [12] on non-contrast CT or diffusion-weighted MRI were evaluated and analyzed. Pc-ASPECTS is range, 0–10, subtracted for any evidence of early ischemic change in each defined region on the CT scan, with one point for hypoattenuation in the left or right thalamus, cerebellum, or posterior cerebral artery territory, respectively, and two points each for hypoattenuation in any part of the midbrain or pons. For the PMI, each side of pons and midbrain was graded as follows: 0, no hypoattenuation; 1, ≤ 50% hypoattenuation; or 2, > 50% hypoattenuation. A PMI of 0 indicates absence of hypoattenuation in the midbrain and pons, and a score of 8 indicates > 50% hypoattenuation bilaterally in these brain stem territories. All eligible patients received IVT with rt-PA within 4.5 h.

2.2. Endovascular therapy procedure

Routine inclusion criteria for endovascular therapy of vertebrobasilar occlusion were as follows: (1) CTA or MRA confirmed acute vertebrobasilar occlusion; (2) baseline NIHSS score ≥2; (3) premorbid mRS score ≤2; (4) onset or last known well time to puncture within 24 h; (5) pc-ASPECTS ≥6. Anesthetic methods were selected based on individual differences in patients. The vast majority of patients underwent treatment with local anesthesia. Patients with abnormalities in vital signs underwent general anesthesia, and were intubated before the procedure. The diagnostic cerebral angiography was performed for all patients before endovascular therapy. 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 endovascular therapy method. The definition of underlying ICAS was stenosis degree > 50% or repeated reocclusion on the follow-up angiography after one pass of stent-retriever. The degree of vertebrobasilar stenosis was calculated by the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) criteria. [13] When underlying ICAS was suspected, the number of stent-retriever passes or rescue therapy was decided by the operator. Rescue therapy strategies included balloon angioplasty, Solitaire detachment, other stent placement, intra-arterial thrombolysis (IAT), or a combination of the above-mentioned therapies. Other stent angioplasty was performed with APOLLO Intracranial Stent System (MicroPort Medical, Shanghai, China) or Enterprise stent (Codman, Miami Lakes, FL, USA) off-label. Patients received local intra-arterial 50,000–300,000 unit urokinase infusion for IAT. Patients undergoing angioplasty received bridging approach of intravenous infusion of glycoprotein IIb/IIIa inhibitor (tirofiban), which was followed by clopidogrel bisulfate (75 mg/day) combined with aspirin (100 mg/day) for three months. Successful recanalization was defined as achieving mTICI grades 2b or 3 [14] on the delay angiogram at least 10 min after recanalization.

2.3. Outcome assessment

The efficacy outcome was satisfactory outcome at 90 days, which was defined as an mRS score of 0–2. Favorable outcome was defined as mRS score of 0–3. [15] The safety outcomes included symptomatic intracranial hemorrhage (sICH) and all intracranial hemorrhage within seven days and mortality within 90 days after the endovascular therapy. SICH was defined by the Heidelberg criteria, which were new intracranial hemorrhage 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. [16]

2.4. Statistical analysis

This study compared the baseline data between the ICAS group and the non-ICAS group. The continuous variables and medians were analyzed using the Mann–Whitney U test. The χ^2method and Fisher exact test were used to evaluate significant differences among the proportions. For comparing the outcomes between the two groups, the multivariate logistic regression model calculated the odds ratios (ORs) and 95% confidence intervals (CIs). The baseline variables that showed possible associations among the confounding factors with the consequences from univariate analysis ($p < 0.1$) were entered into the multivariate model, and $p < 0.05$ was defined as statistical significance. SPSS software was employed for all analyses (version 22.0, IBM-Armonk, New York, USA).

3. 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 lack of data and two subjects had arterial dissection. Finally, 67 patients were recruited in this study, of which 35 (52.2%) had underlying ICAS, while 32 (47.8%) did not (Fig. 1).

3.1. Baseline characteristics

Table 1 demonstrates the baseline clinical information of subjects and Table 2 lists the periprocedural characteristics. Of the 67 patients enrolled in the analysis, the median age was 63 years (interquartile range [IQR], 57–68 years), and 44 (65.7%) were males. The non-ICAS group had a higher prevalence of coronary heart disease (25% vs. 2.9%; $p = 0.008$) and atrial fibrillation (28.1% vs. 5.7%; $p = 0.013$) than the ICAS group. However, there were no obvious differences in the other risk factors for stroke (such as smoking, hypertension, hyperlipidemia, and diabetes) among the two groups ($p > 0.05$). All patients presented with median baseline NIHSS score of 13 (IQR, 10–22) and median GCS score of 14 (IQR, 7–15). Median pc-ASPECTS was 8 (IQR, 6–8) and PMI was 2 (IQR, 1–2). There was no difference between the two groups in the location of occlusion and anesthesia ($p > 0.05$). Rescue therapies were performed more often in the ICAS group (82.9% vs. 34.4%; $p = 0.000$), and included stent-retriever detachment in nine (25.7%) patients, balloon angioplasty in 19 (54.3%) patients, other stent angioplasty in 18 (51.4%) patients, and intra-arterial thrombolysis in five (14.3%) patients. Procedural complications occurred in 22.4% of the patients, and no significant difference was found between the two groups. The procedure time (from puncture to final reperfusion) of the ICAS group was longer than that of the non-ICAS group (median, 120 vs. 83; $p = 0.048$).

3.2. Recanalization outcomes

Table 3 demonstrates the safety consequences and outcomes. Successful recanalization was achieved in 60 patients (89.6%), of which 31 (88.6%) were in the ICAS group and 29 (90.6%) in the non-ICAS group, respectively. Satisfactory outcome was seen in 32 (47.8%) patients, while 39 (58.2%) patients had favorable outcome at 90 days. The proportion of favorable outcome at 90 days was higher in the ICAS group than in the non-ICAS group (71.4% vs. 46.9%; $p = 0.041$). There was no significant difference in symptomatic ICH (2.9% vs. 6.3%,

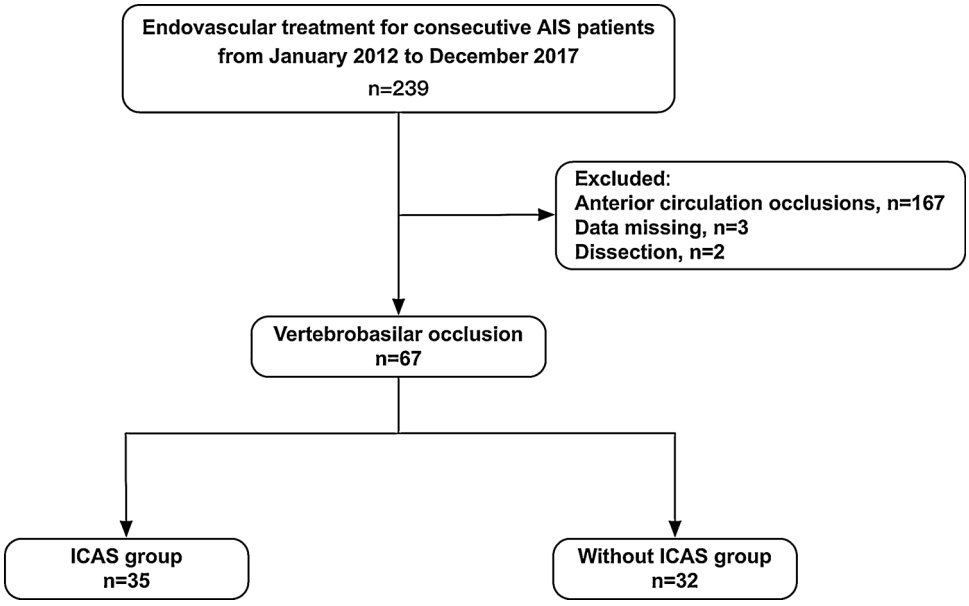

Fig. 1. Flow chart of eligible patients.

p = 0.603) or death within 90 days (22.9% vs. 37.5%, p = 0.191) between the two groups. ICH was more frequently observed in the non-ICAS group (18.8% vs. 2.9%, p = 0.048). Multivariate logistic regression analysis showed that the baseline GCS score (OR 1.281, 95% CI: 1.085–1.513; p = 0.004) and PMI (OR 0.402, 95% CI: 0.233 to 0.693; p = 0.001) were independently associated with favorable outcome at 90 days.

4. Discussion

This study examined patients who underwent endovascular therapy for AIS caused by posterior circulation LAO, and compared the outcomes between patients with or without underlying ICAS. The main findings were as follows: 1) ICAS was identified in 52.2% AIS patients caused by vertebrobasilar occlusion; 2) endovascular therapy with stent-retriever thrombectomy followed by rescue treatment could achieve high rates of successful revascularization, favorable outcome, and lower ICH in AIS patients with underlying ICAS; 3) baseline GCS and PMI were independent predictors of favorable outcome after endovascular therapy in vertebrobasilar occlusion patients.

Patients with AIS caused by vertebrobasilar occlusion were not enrolled in recent randomized controlled trials of endovascular treatments. [4,17–20] Hence, the current American Heart Association/American Stroke Association (AHA/ASA) guidelines has a relatively low level of recommendation (IIb, C-EO) [21]. In this study, we analyzed endovascular therapy for acute vertebrobasilar occlusion and found favorable functional outcome in 59.7% of the patients as compared to 25.7% in the intra-arterial group of the BASICS registry [22] and 42% in ENDOSTROKE registry [23]. A possible explanation might be that the new generation of thrombectomy devices was used in this study and a higher recanalization rate was achieved. The proportion of patients with favorable functional outcome was relatively lower as compared to 62.9% in the HERMES meta-analysis [3] of endovascular thrombectomy for anterior circulation stroke, which could be because acute vertebrobasilar occlusion patients have severe symptoms, and more disorders of consciousness. The current study also found that baseline GCS and PMI were independent predictors for favorable outcomes at 90 days. Patients with higher GCS (OR 1.281, 95% CI: 1.085–1.513; p = 0.004) and lower PMI (OR 0.402, 95% CI: 0.233 to 0.693; p = 0.001) could achieve better clinical prognosis.

Underlying ICAS tends to be refractory to thrombectomy treatment, which might be linked to poor outcomes [24]. The proportion of underlying ICAS was 14.2–37.3% in Asian populations [7,9,10,25,26], which appears to be higher than in western countries. Only 5.5% of

Table 1
Demographic and baseline clinical characteristics of two groups.

Characteristics	Total(n = 67)	ICAS(n = 35)	Without ICAS(n = 32)	P Value
Age (IQR)	63(57-68)	60(55-67)	64.5(58-69.5)	0.130
Male (%)	44(65.7)	26(74.3)	18(56.3)	0.120
Prior or current smoking (%)	22(32.8)	13(37.1)	9(28.1)	0.432
Hypertension (%)	39(58.2)	22(62.9)	17(53.1)	0.420
Diabetes (%)	12(17.9)	6(17.1)	6(18.8)	0.864
Hyperlipidemia (%)	13(19.4)	6(17.1)	7(21.9)	0.625
Coronary heart disease (%)	9(13.4)	1(2.9)	8(25)	0.008
Atrial fibrillation (%)	11(16.4)	2(5.7)	9(28.1)	0.013
Previous stroke or TIA (%)	19(28.4)	9(25.7)	10(31.3)	0.616
Baseline NIHSS (IQR)	13(10-22)	13(11-22)	17(9-23)	0.593
Baseline GCS (IQR)	14(7-15)	14(10-15)	13(6.25-15)	0.270
Pc-ASPECTS (IQR)	8(6-8)	7(6-8)	8(6-8)	0.195
Pons midbrain index (IQR)	2(1-3)	1(1-2)	2(0.25-3)	0.709
Pretreatment IV tPA (%)	11(16.4)	7(20)	4(12.5)	0.408
Anesthetic (%)				0.603
Local anesthesia	64(95.5)	34(97.1)	30(93.8)	
General anesthesia	3(4.5)	1(2.9)	2(6.3)	

Table 2
Periprocedural characteristics of two groups.

Characteristics	Total(n = 67)	ICAS(n = 35)	Without ICAS(n = 32)	P Value
Location of occlusion				0.117
BA (%)	29(43.3)	11(31.4)	18(56.3)	
VA (%)	6(9)	4(11.4)	2(6.3)	
Tandem (%)	32(47.8)	20(57.1)	12(37.5)	
ASITN/SIR (IQR)	0(0-1)	0(0-1)	0(0-1)	0.565
Rescue therapy (%)	40(59.7)	29(82.9)	11(34.4)	0.000
Stent retriever detachment	9(13.4)	9(25.7)	0(0)	
Other stents	25(37.3)	18(51.4)	7(21.9)	
Balloon expansion	25(37.3)	19(54.3)	6(18.8)	
Intra-arterial thrombolysis	11(16.4)	5(14.3)	6(18.8)	
Number of Stent retriever passes	1(1-2)	1(1-2)	2(1-2)	0.397
Procedural complications (%)	15(22.4)	9(25.7)	6(18.8)	0.495
Distal embolism	5(7.5)	2(5.7)	3(9.4)	
Vessel perforation	3(4.5)	1(2.9)	2(6.3)	
Stent thrombosis	4(6)	3(8.6)	1(3.1)	
Dissection	3(4.5)	3(8.6)	0(0)	
Vasospasm	1(1.5)	1(2.9)	0(0)	
Onset-to-door time (IQR)	390(215-669)	390(223-633)	365(204.5-706.5)	0.816
Door-to-puncture time (IQR)	142(90-233)	131(95-206)	176(70-240)	0.712
Puncture-to-first reperfusion time (IQR)	55(41-80.5)	60(42-97)	50(41-74)	0.122
Puncture-to-final reperfusion time (IQR)	96.5(63-137.75)	120(74.5-158.5)	83(59-118)	0.048
Onset-to-first reperfusion time (IQR)	582.5(392.25-1082.25)	575(393-1314.5)	652(360-1033)	0.682
Onset-to-final reperfusion time (IQR)	649.5(462.25-1103.75)	620(463-1360)	668(446-1065)	0.643

patients treated with stent-retriever showed intracranial stenosis in a French study [27], and 13.7% in a USA study [6]. In this study, ICAS was identified in 52.2% (35/67) patients, which was higher than in previous reports, perhaps due to the different definitions of ICAS used in various studies. In this study, the definition of underlying ICAS was as follows: 1) stenosis degree > 50%; 2) repeated reocclusion on the follow-up angiography after one pass of stent-retriever. The definition of the degree of stenosis was the same as WASID [13] and CICAS [2] studies, which led to higher rate of underlying ICAS.

In this study, patients with underlying ICAS had a lower prevalence of coronary heart disease and atrial fibrillation, which were in line with previous studies [8,26]. There was no difference in stroke severity at the time of admission between the ICAS and non-ICAS groups in posterior circulation strokes, which was consistent with other reports [9,10], while in a similar study, anterior circulation patients with underlying ICAS had relatively mild symptoms [8]. Possible reasons might be that good collaterals were developed during the progression of ICAS, and better collaterals in the posterior than in the anterior circulation [28].

In this study, the successful recanalization rate and satisfactory outcome at 90 days were similar in the ICAS group and the non-ICAS group. Similar results were seen by Lee et al. [9] and Kim et al. [10] in acute vertebrobasilar occlusion underlying atherosclerosis. Since 82.9% of patients with underlying ICAS required rescue treatment, revascularization time in the ICAS group was longer than that of the non-ICAS group. The rescue therapy included angioplasty with or without placement of a stent or intra-arterial thrombolysis. Underlying ICAS follow-up rescue therapy was performed by one or two passes of stent-retriever, with angioplasty and intravenous infusion of tirofiban. The main cause of LAO underlying ICAS was in situ thrombosis in a stenotic lesion. Therefore, first stent-retriever thrombectomy is an appropriate treatment choice, and the first pass of stent-retriever achieving partial recanalization would improve patient outcomes because the blood supply can be more rapidly restored to the ischemic brain [29]. Then, the rescue treatment can be determined according to follow-up angiography results. This endovascular treatment strategy for LAO with underlying ICAS was confirmed by the recent research recommendations [30]. In this study, there was no significant difference in procedural complications and sICH between the two groups. This means that rescue therapy and the use of antiplatelet medication did not increase the risk of endovascular treatment for vertebrobasilar occlusion with underlying atherosclerosis. The ICAS group had a more favorable outcome than the non-ICAS group, perhaps due to better collateral circulation and ischemic conditioning during the progression of ICAS.

The present study had several limitations. First, it was a single center retrospective study with noncontrolled study design, due to which some selection bias may exist. Second, there may be confounding factors, including the choice of inclusion criteria, rescue treatment, and periprocedural strategies. Third, the relatively small sample size might reduce the significant power of the tests. Fourth, this study was conducted in Chinese population; thus, the results may be affected by ethnic discrepancies. Future prospective controlled trials are needed to confirm the efficacy and safety of endovascular therapy for acute vertebrobasilar occlusion with underlying atherosclerosis.

5. Conclusions

Endovascular therapy with stent-retriever thrombectomy followed by rescue treatment can achieve high rates of successful revascularization and favorable outcome in the treatment of AIS caused by

Table 3
Safety consequences and clinical outcomes of two groups.

Characteristics	Total(n = 67)	ICAS(n = 35)	Without ICAS(n = 32)	P Value
Successful recanalization (mTICI, 2b or 3, %)	60(89.6)	31(88.6)	29(90.6)	1.000
Good outcome (mRS, 0-2, %)	32(47.8)	18(51.4)	14(43.8)	0.530
Favorable outcome (mRS, 0-3, %)	40(59.7)	25(71.4)	15(46.9)	0.041
Mortality within 90 days (%)	20(29.9)	8(22.9)	12(37.5)	0.191
sICH (%)	4(5.9)	1(2.9)	2(6.3)	0.603
ICH (%)	7(10.4)	1(2.9)	6(18.8)	0.048

posterior circulation LAO. Angioplasty with or without the stent is effective, and does not increase sICH and ICH rates even while using antiplatelet drugs during the procedure. In addition, baseline GCS and PMI were independent predictors of favorable outcome after endovascular therapy in vertebrobasilar occlusion patients.

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. Tianyou Zhang, Xia Li, Junfeng Yang acquired the data. Yuechun Li, Baojun Wang revised it critically for important intellectual content. Yuechun Li approved of the version to be published;

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Declaration of interests

All authors declare no competing interests.

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