



# Effect of endovascular treatment on patients with basilar artery occlusion presenting with different pathologic mechanisms: a systematic review and meta-analysis

Xianjin Shang<sup>1</sup> · Liying Pan<sup>2</sup> · Youqing Xu<sup>1</sup> · Yapeng Guo<sup>1</sup> · Ke Yang<sup>1</sup> · Qian Yang<sup>1</sup> · Zhiming Zhou<sup>1</sup>

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## Abstract

**Objective** This study aimed to summarize the clinical outcomes of endovascular treatment in patients with basilar artery occlusion (BAO) with different pathologic mechanisms.

**Methods** Two independent reviewers searched PubMed/MEDLINE, Embase and Cochrane Library database up to December 2022, patients with different BAO pathological mechanisms (BAO with in situ atherosclerosis vs. embolism alone without vertebral artery steno-occlusion vs. embolism from tandem vertebral artery steno-occlusion) were collected and analyzed. We calculated the odds ratios (ORs) and 95% confidence intervals (CIs) to assess the associations between clinical outcomes and BAO pathological mechanisms.

**Results** A total of 1163 participants from 12 studies were identified. Compared with embolism alone, patients with in situ atherosclerotic BAO had a lower favorable outcome rate (modified Rankin score [mRS] 0–2: 34.5% vs. 41.2%; OR 0.83, 95% CI 0.70–0.98;  $P=0.03$ ) and moderate outcome rate (mRS 0–3: 45.8% vs. 55.4%; OR 0.65, 95% CI 0.47–0.90;  $P=0.01$ ) at 3 months and a higher risk of mortality (29.9% vs. 27.2%; OR 1.31, 95% CI 0.96–1.79,  $P=0.09$ ; adjusted OR 1.46, 95% CI 1.08–1.96). Tandem BAO had a comparable mortality risk to that of in situ atherosclerotic BAO (OR 1.37, 95% CI 0.84–2.22;  $P=0.48$ ) or embolism alone (OR 1.44, 95% CI 0.65–3.21;  $P=0.43$ ), and there were no significant differences in favorable or moderate outcomes between tandem BAO and each of the other two BAO mechanisms.

**Conclusion** Among BAO patients with endovascular treatment, embolism mechanism had better clinical outcomes than in situ atherosclerosis, and atherosclerotic mechanism was associated with a higher mortality at 3 months. RCTs are needed to further confirm clinical outcomes of BAO by different mechanisms.

**Keywords** Basilar artery occlusion · Endovascular thrombectomy · Pathologic mechanism · Embolism · Atherosclerosis

## Introduction

Acute basilar artery occlusion (BAO) is an emergency neurological defect and has a very poor clinical prognosis if timely treatment is not received. More than one-third of

BAO patients do not survive, and the remaining patients often present functional dependence [1–3]. Recently, two randomized trials—ATTENTION (Endovascular Treatment for Acute Basilar Artery Occlusion) and BAOCH (Basilar Artery Occlusion Chinese Endovascular Trial)—found that endovascular thrombectomy led to better functional outcomes than best medical treatment but had a higher risk of intracerebral hemorrhage and procedural complications. Moreover, stroke subtype analyses revealed that large-artery atherosclerosis and cardioembolism generally responded best to thrombectomy treatment [4, 5].

We all know that cardiac embolism and artery atherosclerosis are the common causes of infarction in the basilar artery occlusion, atherosclerotic mechanisms leading to stroke include artery-to-artery embolism, in situ thrombosis,

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Xianjin Shang and Liying Pan have contributed equally to this work.

✉ Xianjin Shang  
shangxj2013@wnmc.edu.cn

<sup>1</sup> Department of Neurology, The First Affiliated Hospital (Yijishan Hospital) of Wannan Medical College, Wuhu, Anhui Province, China

<sup>2</sup> Department of Neurology, Longyan First Hospital of Fujian Medical University, Longyan, Fujian Province, China

hemodynamic impairment, perforator occlusion, and mixed causes. Nevertheless, posterior circulation occlusion and anterior circulation occlusion have inherent differences in vascular anatomy, clinical presentation, and clinical course. Furthermore, an underlying atherosclerotic lesion with/without tandem steno-occlusion is a confounding factor for thrombectomy outcomes. A better understanding of the underlying mechanisms may therefore help clinicians to select eligible patients, plan therapeutic strategies, and improve patient prognosis [6–8].

Recently, several studies have investigated the associations between the underlying mechanisms of posterior circulation occlusion, especially BAO, and endovascular treatment in stroke; however, they have reported inconsistent results, and their single-center designs and small sample sizes likely compromised their conclusions [9–14]. Here, we conducted a meta-analysis to compare the clinical outcomes of endovascular treatment in patients with BAO with different pathologic mechanisms.

## Materials and methods

The research and reporting methods of this review were according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [15].

### Search strategy

A comprehensive literature search of PubMed/MEDLINE databases, Cochrane Library database, and Embase was designed and carried out by two independent experienced reviewers with the study procedure. The key words ‘posterior circulation stroke’, ‘basilar artery occlusion’, ‘vertebral artery occlusion’, ‘endovascular thrombectomy’, ‘mechanical thrombectomy’, ‘intra-arterial thrombectomy’, ‘revascularization’, ‘pathologic mechanism’, ‘intracranial atherosclerotic disease’, ‘embolism’, ‘thromboembolism’, ‘cardioembolism’, ‘stroke etiology’ were used in both ‘AND’ and ‘OR’ combinations. The search was limited to articles published from beginning to December 2022 in the English language only. Furthermore, the reference lists of retrieved and recent reviews were also reviewed, we could contact with the authors if necessary.

### Study selection

The inclusion criteria were as follows: (1) included a series of > 50 patients; (2) comparison of BAO patients with different pathologic mechanisms, divided into two or three groups (in situ atherosclerotic thrombosis [Group A], embolism alone without vertebral artery [VA] steno-occlusion

[Group B], and/or tandem BAO with a proximal VA stenosis [Group C]); and (3) had available data on clinical and periprocedural evaluations and angiographic outcomes. When multiple studies were performed by the same center or authors, we selected the newest or largest sample article in the final analysis. Two reviewers (XJ Shang and LY Pan) independently screened the collected studies on the basis of the predetermined selection criteria, and any disagreements were resolved by discussion or consultation with a third reviewer (ZM Zhou).

### Data extraction and management

Two reviewers independently extract the following data for each eligible study: the last name of the first author, years of publication and recruitment, study design and populations, demographic data (age and sex), vascular risk factors, time intervals, intravenous thrombolysis rates, recanalization rates, 3-month clinical outcome and mortality. Recanalization rate was defined as a modified Thrombolysis in Myocardial Infarction (mTIMI) score of 2b or 3. Clinical outcome data included number of mortality and the modified Rankin Scale (mRS range: 0 [no symptoms] to 6 [death]) at 3 months. We resolved disagreements by consensus.

Primary outcomes were the rate of favorable clinical outcome (mRS: 0–2) and moderate outcome (mRS: 0–3) at 3 months. Secondary outcome measures mainly included 3-month mortality.

### Quality assessment in included studies

Quality assessment of case-control or cohort studies was according to the Newcastle-Ottawa scale. This scale assigns a maximum score of 4, 2 and 3 for subject selection, comparability, and exposure, respectively. A score of 9 is the best and reflects the highest quality. Independent reviewers evaluated the quality of the included study with the Newcastle-Ottawa scale for studies between groups. The third reviewer was consulted to address the discrepancies.

### Statistical analysis

This study calculated a pooled odds ratio (OR) and 95% confidence interval (CI) of clinical outcomes or mortality between different groups treated with endovascular treatment, and using RevMan software (Version 5.4, The Cochrane Collaboration, Oxford, United Kingdom). We chose  $P < 0.05$  as the level of significance. We used forest plots to determine whether there was a statistical association between the groups and to assess the heterogeneity of the collected studies. Heterogeneity was quantified using the  $I^2$  statistic, which yielded a range from 0 to 100%. We

considered a value greater than 50% as representing substantial heterogeneity [16], if heterogeneity existed, the random effects model was used; otherwise, the fixed model was used. The risk of publication bias was assessed by visual inspection of the funnel plots of included studies, and the Egger weighted linear regression test with the Comprehensive Meta-Analysis software (Version 3). If Egger's test shows significant difference suggesting small study bias existing, we would conduct a non-parametric analysis of 'trim and fill', which yields an effect adjusted for funnel plot asymmetry [17].

## Results

### Identification of eligible studies

Of the 29 articles identified initially, 12 studies—which included a total of 1163 participants—with available outcome data that met the inclusion criteria were collected (Fig. 1). Totally, there were 442 (38.0%) participants in Group A, 590 (50.7%) participants in Group B, and 131 (11.3%) participants in Group C.

### Characteristics of included studies

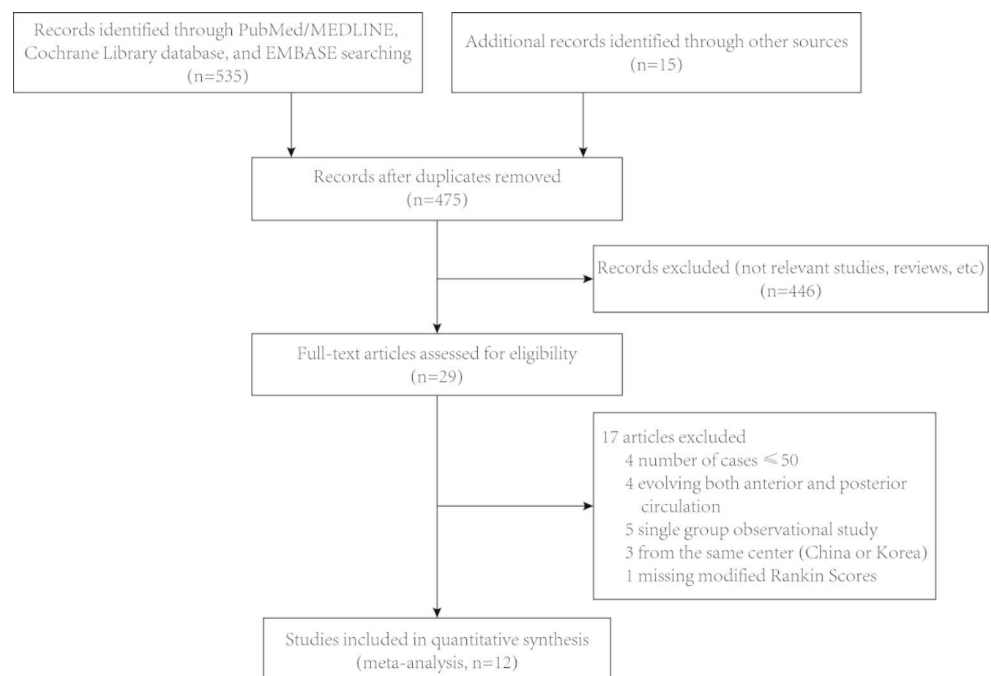
The details of the study design and the available data were summarized in the characteristics of the included studies (Table 1). Eight studies were performed in Asian population, four in South Korea [18–21], three in Chinese [11–13] and one in Japanese population [9], the remaining each in

Switzerland [22], American [23], Dutch [10] and French [14] population. All studies were designed as case-control studies, six of the studies were designed to compare in situ atherosclerotic thrombosis with embolism alone in BAO patients [9, 10, 19–21, 23], of note, the participants with embolism alone mechanism had those with tandem intracranial or extracranial VA lesion; and the remaining 6 studies were carried out to compare clinical outcomes and mortality between the three predisposed BAO groups [11–14, 18, 22]. All cases were defined as in situ atherosclerosis or embolism mechanism with/without tandem VA stenosis by radiographic manifestations and revascularization procedure. One study initially excluded patients with tandem lesion, and patients with atherosclerotic or embolic disease were defined by the revascularization procedure [23]. Another two study classified overall participants as large artery atherosclerosis, cardioembolism, dissection, and embolic stroke of undetermined source according to the TOAST criteria, we combined cardioembolism and embolic stroke of undetermined source as single embolic BAO in the pooled analysis [10, 14]. Additionally, six studies collected participants who received endovascular treatment during the last ten years, the other six studies recruited more earlier treated patients.

### Quality of included studies

The quality assessment of 12 published studies is shown in online supplemental Tables 1, two studies were rated at 5 stars (low quality), five studies at 6 stars (moderate quality), and five studies at 7 stars (high quality). The most common

**Fig. 1** Summary of the studies selection process



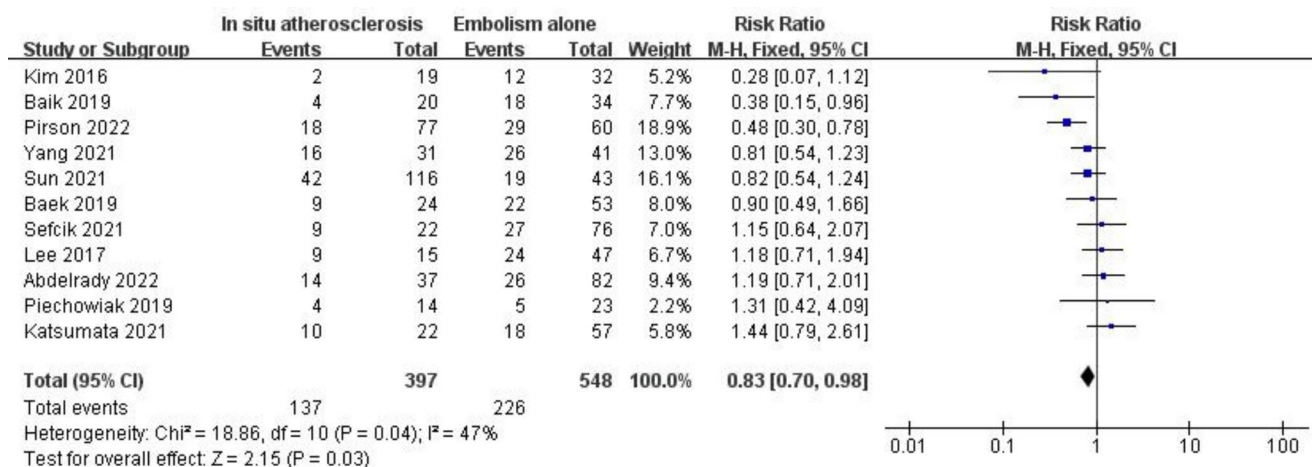
**Table 1** Characteristics of included studies

Characteristics		Collected studies										
		Kim 2016 <sup>21</sup>	Baek 2019 <sup>19</sup>	Baik 2019 <sup>18</sup>	Piechowiak 2019 <sup>22</sup>	Sun 2021 <sup>13</sup>	Jiang 2021 <sup>12</sup>	Katsumata 2021 <sup>9</sup>	Sefcik 2021 <sup>23</sup>	Yang 2021 <sup>11</sup>	Pirson 2022 <sup>10</sup>	Abdelrhady 2022 <sup>14</sup>
Population Groups		Korean A vs. B	Korean A vs. B	Korean A vs. B vs. C	Switzerland A vs. B vs. C	Chinese A vs. B vs. C	Chinese A vs. B vs. C	Japanese A vs. B	American A vs. B	Chinese A vs. B vs. C	Dutch A vs. B	French A vs. B
Onset time		OTP ≤ 12 h	BAO within 12 h	OTP ≤ 12 h vs. C	BAO within 24 h	OTP ≤ 24 h vs. C	BAO within 24 h	VBAO	Acute nontandem BAO	BAO within 24 h	Acute posterior circulation occlusion	Acute posterior circulation occlusion
Design		Retrospective, two centers	Retrospective, single-center	Prospective, single-center	Retrospective, single-center	Retrospective, single-center	Retrospective, two centers	Retrospective, multi-center	Retrospective, single-center	Retrospective, single-center	Retrospective, multi-center	Retrospective, two centers
No. of subjects		51	77	82	52	182	86	79	107	100	146	139
Study years		3/2009 to 3/2014	9/2010 to 6/2018	3/2010 to 12/2017	3/2010 to 9/2016	1/2012 to 7/2018	10/2015 to 7/2019	1/2015 to 3/2020	1/2013 to 12/2019	10/2013 to 12/2018	3/2014 to 12/2018	1/2015 to 12/2019
Age (yrs) <sup>§</sup>		67.48 ± 10.73	69.6 ± 11.9	73.2 ± 12.8	67(33.9–90)	59.5 ± 10.2	70.0 ± 10.9	77.0 (70.0–84.0)	64.5 ± 16.8	67 (58.3–73.8)	NA	69(61–76)
Gender (male)		34(66.7)	41 (53.2)	46(56)	32(61.5)	153(84.1)	64(74.4)	55 (69.6)	61(57)	77 (77)	86(58.9)	91(65)
NIHSS scores <sup>§</sup>		NA	12.4 ± 6.23 (7.0–24.0)	13 (7–24)	23(1–36)	NA	20.2 ± 9.2	24 (12–36)	18.7 ± 9.3	26.5 (15.0–31.0)	NA	15(9–24)
Onset to arrival/treatment <sup>¶</sup>		280.8 ± 143.2	321.0 ± 136.22	262.0(146.0–435.0)	211(12–634)	NA	524.3 ± 315.5	118.5 (44.7–255.7)	810 ± 1038	311.5(206.8–450.0)	NA	128(61–228)
Vascular risk factors												
Hypertension		38(74.5)	37 (59.7)	62(76)	35(67.3)	130(71.4)	65 (76)	59 (74.7)	80(77.7)	65 (65)	84(57.5)	88(62)
Diabetes mellitus		14(27.5)	14 (22.6)	25(30)	11(21.2)	50(27.5)	21 (24)	17 (21.5)	24(24.5)	20(20)	26(17.8)	24(17)
Atrial fibrillation		15(29.4)	NA	31(38)	16(30.8)	NA	34(39.5)	41 (51.9)	28(28.3)	31(31)	NA	29(20)
Hyperlipidemia		23(45.1)	16 (25.8)	9(11)	29(55.8)	30(16.5)	31 (36)	29 (36.7)	48(46.6)	11(11)	32(21.9)	32(23)
Smoking		NA	15 (24.2)	19(23)	11(21.2)	67(36.8)	37 (43)	NA	31(31)	29(29)	NA	46(33)
Intravenous tPA		24(47.1)	17(27.4)	19(23)	24(46.2)	35(19.2)	17(20)	32 (40.5)	18(18.2)	20(20)	62(42.5)	50(36)
mTICI: 2b-3		45(88.2)	60(96.8)	64(78.0)	50(96.2)	155(85.2)	82(95.3)	74 (93.6)	96(89.7)	99(99.0)	NA	110(79)

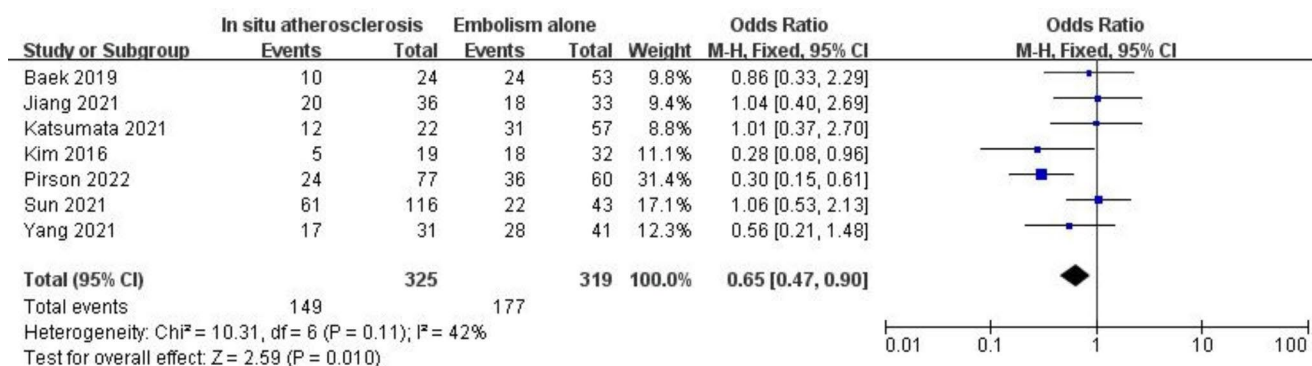
Group was divided into three subtypes: in situ atherosclerotic thrombosis (A), pure embolic BAO (B) and/or tandem BAO with a proximal vertebral artery stenosis (C)

Note. Data were shown as number(percentage); mTICI, modified Thrombolysis in Cerebral Infarction; NA, not available; NIHSS, National Institutes of Health Stroke Scale; OTP, onset to puncture; VBAO, vertebral basilar artery occlusion

§ Data shown as mean ± S.D. or mean/median (range or interquartile range)



**Fig. 2** mRS 0–2 outcome between group A and group B



**Fig. 3** mRS 0–3 outcome between group A and group B

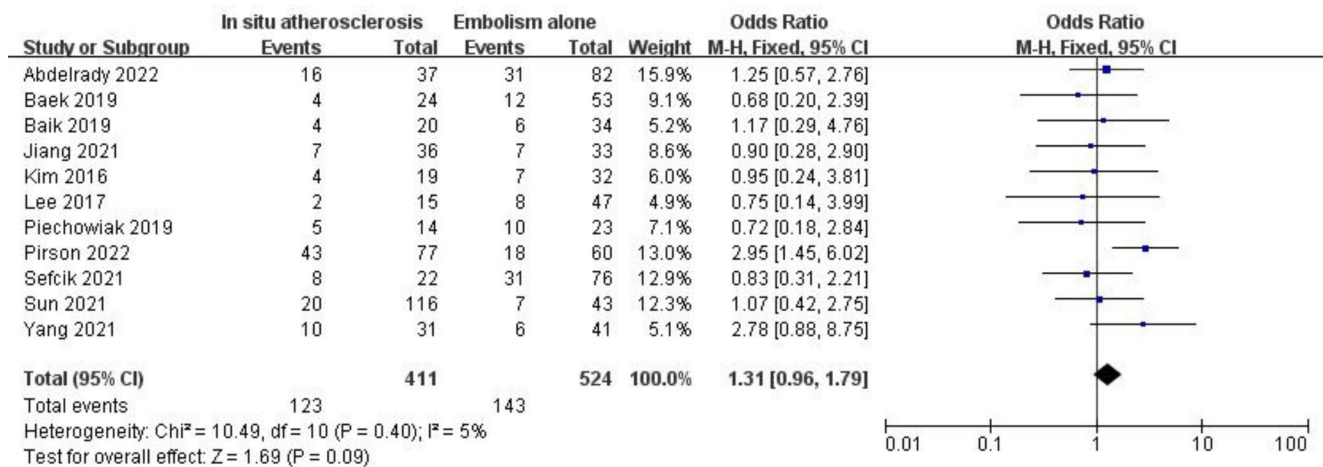
selection bias was the recruitment of participants from hospitalization. There was inadequate comparability between the studied groups of included studies on the basis of different design. Ascertainment of exposure was the most exposure bias in the studies.

### Comparison 1: in situ atherosclerotic BAO (group A) vs. embolism alone BAO (group B)

Figure 2 shows the estimated pooled OR of mRS 0–2 of group A compared with group B after endovascular treatment. Because there was no significant heterogeneity ( $I^2 = 47\%$ ), a fixed effects model was used. The pooled OR of the available data from 11 studies was 0.83 (95% CI: 0.70–0.98,  $P = 0.03$ ), and atherosclerotic BAO patients had a 34.5% (137/397) favorable outcome compared with 41.2% (226/548) for embolic causes. The funnel plot was symmetrical, indicating no publication bias existed, the Egger linear regression also detected no evidence of publication bias among the studies of pathologic mechanisms and favorable outcome benefits (Egger  $t = 0.038$ ,  $P = 0.97$ ).

The pooled OR of mRS 0–3 in Group A compared with Group B after endovascular treatment is shown in Fig. 3. Data from seven included studies were available, and the pooled OR was 0.65 (95% CI: 0.47–0.90,  $P = 0.01$ ), and atherosclerotic BAO patients had a 45.8% (149/325) moderate outcome compared with 55.4% (177/319) for embolic causes. The analysis had no heterogeneity ( $I^2 = 42\%$ ) and no publication bias (Egger  $t = 0.029$ ,  $P = 0.98$ ).

The pooled OR of mortality in Group A (29.9%) compared with Group B (27.2%) at 3-month follow-up was 1.31 (95% CI: 0.96–1.79,  $P = 0.09$ ), and there was no significant heterogeneity between them ( $I^2 = 5\%$ , Fig. 4). However, the funnel plot was unsymmetrical, suggesting that there was publication bias, and Egger linear regression also detected publication bias among the eleven included studies (Egger  $t = 2.238$ ,  $P = 0.05$ ). Then we found 3 possible missing studies with the ‘trim and fill’ method, the adjusted OR 1.46 (95% CI: 1.08–1.96) including the 3 missing studies was significantly different from our estimated pooled OR value.



**Fig. 4** mortality outcome between group A and group B

### Comparison 2: tandem BAO with a proximal VA stenosis (group C) vs. embolism alone BAO (group B)

The estimated pooled OR (95%CI) of mRS0-2, mRS0-3, and mortality of Group C compared with Group B were 0.87(0.38–1.98), 1.07(0.25–4.55) and 1.44(0.65–3.21), respectively. Due to the significant heterogeneity ( $I^2 > 50\%$ ), all three pooled analyses used the random-effect model. There were no publication biases for mRS0-2, mRS0-3 and mortality (Figs. 1, 2 and 3 in supplemental materials).

### Comparison 3: tandem BAO with a proximal VA stenosis (group C) vs. in situ atherosclerotic BAO (group A)

The estimated pooled OR (95%CI) of mRS0-2, mRS0-3, and mortality of Group C compared with Group A were 1.11(0.67–1.84), 1.08(0.28–4.22) and 1.37(0.84–2.22), respectively. Due to the significant heterogeneity ( $I^2 > 50\%$ ), the pooled analyses of mRS0-3 used the random-effect model. There were significant differences in publication biases, analysis of mRS0-2 (Egger  $t = 3.59$ ,  $P = 0.04$ ), when including the two missing studies by the ‘trim and fill’ method, their adjusted OR and 95% CI were changed to 1.11(0.69–1.76) (Figs. 4, 5 and 6 in supplemental materials).

## Discussion

Endovascular treatment for BAO patients is better than standard medical therapy, but increasing the risk of bleeding and procedural complications. Considering the differences in the etiology and mechanism of BAO, current studies have failed to further explicit the outcome differences of intravascular treatment for different mechanisms of BAO,

especially atherosclerosis and embolism. The present meta-analysis first found that in situ atherosclerotic BAO resulted in poorer clinical outcomes than embolism alone, with lower favorable and moderate outcome rates, and a higher mortality rate.

Most of the studies explored the associations between atherosclerotic and embolic mechanisms and clinical outcomes after thrombectomy. The intravenous thrombolysis rates ranged from 18.2 to 47.1% and successful reperfusion rates ranged from 78.0 to 99.0% (excluding one study with no reported data). All but one [22] study found that patients with atherosclerosis had poorer functional independence compared with those with an embolic mechanism at 3 months after thrombectomy. Furthermore, patients with tandem occlusion had the worst outcomes of the three groups despite the existence of variable conclusions between studies and having the smallest number of patients. However, there were substantial differences in mortality comparisons after treatment in all included studies; the inconsistent conclusions need to be further clarified in a meta-analysis.

There is evidence that in people with BAO with an in situ atherosclerotic mechanism, endovascular treatment is associated with a higher risk of death and/or unfavorable outcomes than in patients with embolic lesion [10, 18, 21]. There are many possible causes of this excess risk associated with in situ atherosclerotic thrombosis. First, there was a significant interaction between procedural length and the effects of treatment on 3-month outcomes among the published study data [14, 18, 21]. Atherosclerotic occlusion required a longer procedural time than embolism alone because it generally received more multimodal endovascular treatments—such as balloon angioplasty/permanent stenting and intra-artery thrombolysis—when existing remnant stenosis ( $\geq 70\%$ ) and stenotic lesions were repeatedly occluded or the flow was not rescued after thrombectomy

treatment. Second, embolism alone was associated with distal BAO, whereas in situ atherosclerotic BAO always had proximal and middle occlusion [10, 11]; this can be associated with extensive pons ischemia and lead to more severe conditions (such as locked-in syndrome). Third, in situ atherosclerotic BAO may have a lower recanalization rate than embolic BAO; recanalization is the most important prognostic factor and improves survival [18]. Finally, a higher number of passes during endovascular procedures in the atherosclerotic group may be associated with a higher risk of basilar artery reocclusion by inducing damage of the vessel wall and promoting local thrombosis, thus resulting in worse outcomes [11, 14, 24].

BAO combined with extracranial or intracranial vertebral artery stenosis—also known as a tandem BAO lesion—is a relatively less common mechanism of vertebral BAO [25, 26]. Higher thrombus load, challenging anatomical conditions, and related prolongation of procedural time were all associated with tandem BAO [12, 13, 18], ultimately leading to worse clinical outcomes. However, several studies have also reported that tandem BAO results in better outcomes than other pathologic mechanisms; this depends on minimizing the time to recanalization using retrograde techniques and reducing the risk of reocclusion in tandem lesions [22]. In the present meta-analysis, compared with atherosclerotic and embolic mechanisms, tandem BAO lesion had no differences in clinical outcomes or mortality. These findings indicate that the use of modern thrombectomy devices and advanced therapeutic strategies may achieve a better outcome.

This study had the following limitations. Although we included 12 eligible published studies, most were retrospective analysis in design, which carries a risk of selection bias for a meta-analysis. Furthermore, the pooled participant sample remained limited in size, especially for the tandem BAO group, possibly because some studies included these patients in the embolism alone stroke group. Moreover, the classification of pathologic mechanisms was not unified in the included studies. Atherosclerotic lesion is the most common cause of ischemic stroke in Asian populations but not Western populations; thus, the present conclusions cannot be generalized. Differences in endovascular strategies, first-line contact aspiration or stent-retriever thrombectomy, and even complex angioplasty procedures and intra-arterial tirofiban infusion among different studies also complicate the interpretation of the study outcomes. Furthermore, the recruitment period of study patients was wide (2010–2020) and likely led to differences in thrombectomy devices and surgeons' experiences, which may also bias the pooled results.

This study was to conduct a meta-analysis on the thrombectomy outcomes of BAO patients with different

mechanisms. Patients with atherosclerotic mechanism faced a higher risk of disability and short-term death, which had a suggestive significance for patients' treatment selection and clinical conversation in the future. Specific treatment measures would be taken to reduce the risk of disability and death for patients with atherosclerotic mechanism.

## Conclusion

Clinical outcomes in patients with BAO treated with endovascular strategies were significantly different among patients with different pathologic mechanisms. Embolic BAO without tandem VA steno-occlusion had better functional outcomes and safety than BAO with in situ atherosclerosis. Randomized studies with larger samples and comparative studies with tailored therapeutic strategies between in situ atherosclerotic and embolic BAO are necessary.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s11239-023-02884-w>.

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## Declarations

**Conflict of Interest** None.

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