Invasive Management of Vertebrobasilar Artery Stenosis and Occlusion: A Meta-Analysis on Efficacy and Safety Endpoints

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Abstract

Vertebrobasilar angioplasty and stenting or mechanical thrombectomy (MT) using a stent retriever or suction thrombectomy are effective interventions in managing acute ischemic stroke caused by vertebrobasilar artery occlusion (VBAO). This study aims to investigate the safety and efficacy of self-expanding stents and balloon angioplasty in managing ischemic stroke. We reviewed the literature for relevant clinical trials and included those reporting the following primary outcomes: successful recanalization, favorable clinical outcome, and stenosis degree change. We included 24 studies (858 patients). In the subgroup analysis, participants were divided into three main subgroups based on the type of intervention: mechanical thrombectomy (MT), percutaneous transluminal angioplasty and stenting (PTAS), and MT+PTAS. Regarding overall mortality, the incidence was 34.5%, 9.9%, and 28.9% in the MT, PTAS, and MT+PTAS groups, respectively. The incidence of arterial dissection was 3.6% in the MT group, 3.1% in the PTAS group, and 1.3% in the MT+PTAS group. The incidence of intracranial hemorrhage was 5.2%, 4.5%, and 15.3% in the MT, PTAS, and MT+PTAS groups, respectively. Favorable clinical outcomes were reported in 42.8% of subjects in the MT+PTAS group, 64.7% in the PTAS group, and 39.2% in the MT group. The incidence of distal embolization, MT, PTAS, and MT+PTAS groups had 3.4%, 5.8%, and 9.5% incidence rates, respectively. Favorable clinical outcomes were reported in 42.8% of subjects in the MT+PTAS group, 64.7% in the PTAS group, and 39.2% in the MT group. The incidence of intracranial hemorrhage was 5.2%, 4.5%, and 15.3% in the MT, PTAS, and MT+PTAS groups, respectively. The incidence of successful recanalization was 85.3% in the MT group, 99.4% in the PTAS group, and 92.7% in the MT+PTAS group. Our analysis concludes that PTAS is the most effective intervention for VBAO and is associated with a lower rate of mortality compared to mechanical thrombectomy alone.

Categories: Cardiology, Medical Education, Neurology
Keywords: safety and efficacy, stroke, posterior circulation stroke, vertebrobasilar ischemia, vertebrobasilar circulation

Introduction And Background

Stroke is the leading cause of death and disability worldwide [1]. Ischemic stroke accounts for 87% of cerebrovascular accidents (CVAs) [2]. The vertebrobasilar artery supplies the brain stem, cerebellum, occipital lobe, posterior temporal lobe, and thalamus [3]. VBAO represents about 20% of all ischemic strokes occurring in the posterior circulation [4-6]. The most common causes of vertebrobasilar artery occlusion are embolism, atherosclerosis, penetrating-small artery diseases, and arterial dissection [4-6].

Many cases of VBAO are undiagnosed or misdiagnosed [9]. This is likely because the most common initial symptoms are nonspecific, including but not limited to vertigo, dizziness, vomiting, and head or neck pain [9, 10]. Further, CT or MR angiography reveals stenosis or occlusion of the affected artery in about 25% of posterior circulation strokes [11, 12]. Currently, the standard care varies depending on the location of the occlusion. Due to the lack of data from randomized clinical trials, decisions regarding extracranial occlusion are mostly dependent upon clinician judgment. In addition to risk factor modification, management options include single antplatelet therapy and PTAS [13]. Unfortunately, antithrombotic agents and intravenous thrombolytics have yielded poor results in achieving recanalization of affected vasculature [14-18]. Several studies suggest that mechanical thrombectomy (MT) using devices such as stent retriever or suction thrombectomy is a safe and effective treatment for acute ischemic stroke caused by vertebrobasilar artery occlusion [19-21].

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Vertebrobasilar angioplasty and stenting are effective options for patients with atherosclerotic vertebrobasilar disease [22]. There are various methods for achieving successful recanalization, including intra-arterial thrombolysis and percutaneous transluminal angioplasty (PTA) [23]. Although surgical management is a well-known and effective treatment option for intracranial vertebrobasilar atherosclerosis, there are high morbidity and mortality rates [24,25]. While the percutaneous management of vertebral artery occlusion was associated with lower morbidity than surgical repair [26], VBAO is generally associated with a relatively good prognosis. The only factor favoring better outcomes and prognosis is early recanalization of the occluded vessels [27-29].

A limited number of studies have been conducted regarding the safety and efficacy of self-expanding stents and balloon angioplasty in the management of ischemic stroke secondary to VBAO. Therefore, we conducted this systematic review and meta-analysis.

Methodology

We followed the criteria of preferred reporting items for systematic reviews and meta-analyses (PRISMA) in designing our systematic review and meta-analysis [30].

Literature Search

We searched the following databases for relevant articles published through November 2020: PubMed, Cochrane Central, Scopus, and Web of Science. We used the following keywords “basilar,” “vertebral,” “vertebra-basilar,” “recanalization,” “revascularization,” “occlusion,” “stenosis,” “thrombosis,” “stent,” “thrombectomy,” and “angioplasty.” All authors screened the titles and abstracts of the obtained records independently according to the eligibility criteria, followed by full-text screening, and when there was a conflict about the inclusion decision, it was solved by discussion.

Eligibility Criteria

We included one-arm retrospective and prospective observational cohort studies of patients with basilar, vertebral, or vertebral-basilar artery occlusion who had undergone an invasive intervention: mechanical thrombectomy or angioplasty with or without a stent. Our primary outcomes were successful recanalization, favorable clinical outcome, and stenosis degree change. Secondary outcomes included mortality, postoperative complications, NIHSS (National Institute of Health Stroke Scale) score change, need for retreatment, and Modified Rankin Scale (MRS) score change.

Data Extraction

We independently extracted data related to patient characteristics, procedure-related complications, and outcomes. Patient characteristics included age, gender, presenting symptoms, comorbidities, and site of occlusion. Procedure outcomes were post-procedure successful recanalization rate, favorable recanalization at three months, post-procedure NIHSS change, post-procedure MRS change, and post-procedural stenosis change. Post-procedure-related complications were the need for retreatment, infarction, intracranial hemorrhage (ICH), stent embolism, re-occlusion, restenosis, artery dissection, distal emboli, transient ischemic attack, and stroke. Successful recanalization was defined as a Modified Treatment in Cerebral Ischemia (mTICI) score of 2B or 3 measured after procedure performance or technical success. A favorable outcome was defined as the MRS between (0-2) at three months of follow-up.

Quality Assessment

We assessed the quality of the included studies by the Newcastle Ottawa scale (NOS). The NOS contains three main domains: selection, comparability, and ascertainment of the outcome. It is based on reviewer judgment by marking stars on specific items under each domain if matched in the included studies. A high number of total stars represents good quality.

Meta-Analysis

We calculated the qualitative outcomes by pooling each study’s proportions by the untransformed proportion equation, and the pooled proportion was presented with a 95% confidence interval (95% CI). Regarding quantitative outcomes, we calculated the change in MRS and NIHSS according to the Cochrane Handbook for Systematic Reviews of Interventions [31], then a meta-analysis was performed by pooling mean change values of each study using the inverse-variance method, and the pooled mean change value was presented with 95% CI. Results were considered significant when the p-value was less than 0.05. We used OpenMeta [Analyst] (an open source software available at http://www.cebm.brown.edu/openmeta/) to perform this meta-analysis.

Heterogeneity
We used the random-effects model as the existent difference between studies on patient characteristics, severity, site of occlusion, and various procedures. We tested heterogeneity by the chi-square test. Outcomes were considered homogenous if the P-value was more than 0.1 and I² was less than 50%. In the case of heterogeneous outcomes, we performed a sensitivity test and searched for the cause of heterogeneity.

**Review**

**Search results**

Our search of four databases revealed 1219 results. By Endnote software, 449 studies were excluded due to duplication. We performed title and abstract screening for the remaining 770 results. Study outcomes that were irrelevant to our study, posthoc analyses, non-English language studies, review articles, conference abstracts, editorials, or individual case reports were excluded. Only 29 of them were eligible for full-text screening. After the full-text screening, we included 24 studies according to our inclusion criteria. Twenty-two studies were retrospective cohort studies, and the two studies were prospective cohorts. We searched all references included in each study manually, but no further records were added to the included studies. We excluded five studies in the full-text screening for reasons including stenting of other cranial vessels. The PRISMA flow diagram is shown in Figure 1.

![PRISMA flow diagram of our literature search](image)

**TABLE 1:** Characteristics of included studies

The 22 cohort studies recruited 864 participants. The earliest of them was published in 1999 and the latest in 2019. Six studies were conducted in China, four in Germany, three in the USA, three in Australia, two in Japan, and one study in each of these countries: the UK, Turkey, Korea, and Spain. According to the type of treatment, three subgroups were defined: Percutaneous transluminal angioplasty with or without stenting (PTAS), Mechanical thrombectomy (MT), and combination PTAS+MT. A detailed summary of the characteristics of both included studies and the participants is illustrated in Table 1.
| Author and Year          | Country  | N     | Study design     | Male | Age: Mean (SD); range years | Baseline NIHSS score | Clinical presentation                                      | Site of occlusion | Follow-up period: mean (SD); range months |
|--------------------------|----------|-------|------------------|------|-----------------------------|----------------------|-----------------------------------------------------------|------------------|------------------------------------------|
| Barakate et al. 2001     | Australia| 11    | Retrospective cohort | 91%  | 66; 56-75                   | -                    | Dysarthria, vertigo, and visual disturbance               | 73% VA and 27% BA | 3                                       |
| Broussalis et al. 2011   | Austria  | 22    | Retrospective cohort | 64%  | 51-82                       | 0-12                 | Cerebellar infarction and brainstem infarction             | VA               | 12                                      |
| Canyigit et al. 2007     | Turkey   | 35    | Retrospective cohort | 87.50%| 60.3; 32-76                 | -                    | Diplopia, dysarthria, and vertigo                         | VA               | 6                                       |
| Chastain et al. 1999     | US       | 50    | Retrospective cohort | 74%  | 62.6 (9.1); 23-86           | -                    | TIA and stroke (94%) and asymptomatic (6%)                | VA               | 25 (10)                                 |
| Djurdjevic et al. 2019   | UK       | 24    | Retrospective cohort | 79.10%| 66; 33-85                   | 07-Nov               | TIA and stroke                                             | BA               | 18                                      |
| Elberhardt et al. 2006   | Germany  | 20    | Retrospective cohort | -    | 48-77                       | -                    | TIA and stroke (80%) and asymptomatic (20%)               | 80% VA and 20% BA | Jun-36                                   |
| Fiorella et al. 2007     | US       | 44    | Retrospective cohort | 79.50%| 64.8                        | -                    | Ischemic symptoms                                          | VBS              | 12                                      |
| Gao et al. 2015          | China    | 30    | Retrospective cohort | 84.60%| 56 (8.2); 19-34             | 6; 19-34             | Ischemic symptoms                                          | 76.9% BA and 13% VA | 3                                       |
| Gao et al. 2018          | China    | 14    | Retrospective cohort | 100% | 43-64                       | -                    | Dizziness, nausea, and vertigo                            | VA               | 3                                       |
| Huo et al. 2016          | China    | 36    | Prospective cohort  | 83.30%| 58.6 (8.1)                  | 25.5                 | Ischemic symptoms                                          | BA               | 3                                       |
| Karameshev et al. 2010   | Switzerland | 29  | Prospective cohort  | 59%  | 68 (8)                      | 1                   | TIA and stroke                                             | VA               | 33.6                                    |
| Kowri et al. 2013         | Germany  | 12    | Retrospective cohort | 66%  | 68; 45-83                   | 14.3                 | Cerebellar infarction                                      | 50% VA and 50% BA | 12                                      |
| Levy et al. 2001         | US       | 11    | Retrospective cohort | 100% | 43-77                       | -                    | TIA and stroke                                             | VBS              | 36                                      |
| Mohlenbruch et al. 2014  | Germany  | 24    | Retrospective cohort | 70%  | 70; 33-83                   | 24                  | Ischemic symptoms                                          | BA               | 3                                       |
| Parkhutik et al. 2010    | Spain    | 28    | Prospective cohort  | 75%  | 64 (9)                      | -                   | Symptomatic 50% and asymptomatic 50%                     | VA               | 32 (24)                                 |
| Quan et al. 2019         | China    | 43    | Retrospective cohort | 75%  | 62; 52-69                   | 17; 14–21           | Ischemic symptoms                                          | VBS              | 3                                       |
| Shore et al. 2019        | Australia| 28    | Retrospective cohort | 46%  | 65; 2; 20-89                | -                   | Weakness or sensory change                                 | BA               | -                                       |
| Tausumii et al. 2007     | Japan    | 12    | Retrospective cohort | 66%  | 58-81                       | -                   | Infarction and ischemic symptoms                          | VA               | 13                                      |
| Wajima et al. 2017       | Japan    | 8     | Retrospective cohort | 75%  | 69 (11); 54-80              | -                   | Vertigo, nausea, and dysarthria                           | VBS              | 10.3                                    |
| Wang et al. 2015         | China    | 88    | Retrospective cohort | 75%  | 62.6 (10.1); 41-82          | -                   | TIA 61%                                                   | VA               | 12                                      |
**Comorbidities**

Eighteen studies reported the presence of baseline comorbidities with the potential to influence the success of intervention or contribute to further complications. These comorbidities included hyperlipidemia/hypercholesterolemia, hypertension, diabetes mellitus, coronary artery disease, peripheral vascular disease, smoking, and alcohol consumption. This is summarized in Table 2.

| Study ID       | Hypertension | CAD, coronary artery disease | PVD, peripheral vascular disease | Tobacco / active smoker | DM, diabetes mellitus | Hyperlipidemia/hypercholesterolemia | Atrial fibrillation | History of previous TIA or stroke | Alcohol |
|----------------|--------------|------------------------------|----------------------------------|-------------------------|----------------------|--------------------------------------|---------------------|----------------------------------|---------|
|                | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event 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| total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total | event | total |event
TABLE 2: Comorbidity

| Study                  | TIA | CAD | PVD | DM | Stroke | TIA | All |
|------------------------|-----|-----|-----|----|--------|-----|-----|
| Quan et al. 2019       | 59  | 159 |     |    | 44     | 159 |    |
| Shore et al. 2018      | 19  | 28  | 6   | 28 | 28     | 28  | 28 |
| Tsutsumi et al. 2006   |     |     |     |    |        |     |    |
| Wajima et al. 2017     | 8   | 8   | 2   | 3  | 8      |     |    |
| Wang et al. 2015       | 68  | 88  | 22  | 88 | 88     |     |    |
| Weber et al. 2005      |     |     |     |    |        |     |    |
| Wahlman et al. 2004    |     |     |     |    |        |     |    |
| Zhang et al. 2019      | 54  | 88  | 14  | 88 | 25     | 31  |    |

TIA: Transient Ischemic Attack; CAD: Coronary Artery Disease; PVD: Peripheral Vascular Disease; DM: Diabetes Mellitus.

Risk of bias assessment

The quality of the included studies ranged from moderate to high, as shown in the risk of bias graph, and summary (Figure 2).
FIGURE 2: A summary and a graph showing the risk of bias in the included studies

Selection: Regarding the representativeness of the exposed cohort, all studies are of low risk of bias. The same was found to be true of the non-exposed cohort. Concerning the ascertainment of exposure, the presence of surgical records and follow-up interviews confer a low risk of bias. Finally, regarding the demonstration that the outcome of interest was not present at the start of the study, all studies are of low risk of bias.

Comparability: There was comprehensive matching for all plausible prognostic variables in 12 studies [31-42], so we considered them as low risk of bias. However, this item was not mentioned clearly in the remaining 10 studies [13,22,43-50], so we considered them of unclear risk of bias.

Outcome: Regarding confidence in assessing outcomes, all studies were of low risk of bias as an independent
blind assessment was conducted. As for follow-up, all studies are of low risk of bias. Regarding the adequacy of cohorts’ follow-up, 13 studies [13,22,32-34,37,40,42,44,45,47,48,50] reported adequate details suggesting no missing data or the missed data is not enough to have a significant impact on the intervention. Therefore, they were considered at low risk of bias. However, nine studies [31,35,36,39,41,45,46,49] did not report enough data about this outcome; thus, they were put at unclear risk of bias.

**Analysis of outcomes**

**Primary Endpoints**

Favorable clinical outcome was defined as an MRS score ≤2 at three months and/or improvement of ≥10 or ≤6 points in the NIHSS score. The incidence rate was 64.7% in the PTAS subgroup as reported by two studies [39,46], (95% CI [38.5%, 90.9%]). The analysis showed marked heterogeneity (p = 0.067; I² = 70.2 %). Regarding the MT subgroup, four studies reported this outcome [36-39], with incidence of 39.2% (95% CI [28.2%, 50.2%]). The analysis showed no significant heterogeneity (P= 0.135; I² = 46.05 %) In the PTAS+MT subgroup, two studies [35,39] reported this outcome, with an incidence of 42.8% (95% CI [29.9%, 55.8%]), the analysis showed no significant heterogeneity (P=.785; I² = 0 %) (Figure 3).

**Successful recanalization:** The PTAS subgroup included 12 studies [13, 22, 32, 34-39, 42, 44, 46, 47, 50] reporting this outcome, the incidence rate was 99.4% (95% [98.7%, 100%]), and the analysis of this subgroup was homogenous (P= 0.632; I² = 0 %). The MT subgroup included three studies [37-39], the incidence rate was 85.3% (95% CI [69.9%, 100%]), the analysis was heterogeneous (P= 0.029; I² = 71.65 %). In the PTAS+ MT subgroup three studies [35,39,49] reported this outcome, the incidence rate was 92.7% (95% CI [82.2%, 100%]), the analysis was heterogeneous (P= 0.016; I² = 75.85 %) (Figure 4).

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**FIGURE 3:** Forest plot for the analysis of favorable outcomes after three months

PTAS: percutaneous transluminal angioplasty and stenting, MT: mechanical thrombectomy.

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Successful recanalization: The PTAS subgroup included 12 studies [13, 22, 32, 34-39, 42, 44, 46, 47, 50] reporting this outcome, the incidence rate was 99.4% (95% [98.7%, 100%]), and the analysis of this subgroup was homogenous (P= 0.632; I² = 0 %). The MT subgroup included three studies [37-39], the incidence rate was 85.3% (95% CI [69.9%, 100%]), the analysis was heterogeneous (P= 0.029; I² = 71.65 %). In the PTAS+ MT subgroup three studies [35,39,49] reported this outcome, the incidence rate was 92.7% (95% CI [82.2%, 100%]), the analysis was heterogeneous (P= 0.016; I² = 75.85 %) (Figure 4).
Restenosis: This outcome was illustrated in seven studies in the PTAS subgroup [32-34,40-42,50]. Pooled estimate showed significant liability for restenosis (0.153 [0.091, 0.214]), (P value < 0.001). Pooled analysis was heterogeneous (P = 0.050; I² = 52.26%) as shown in Figure 5A. We solved the heterogeneity by the exclusion of Broussalis et al. 2011 study [33] (P = 0.262; I² = 22.87 %). The pooled analysis after exclusion of the study also showed significant increase in restenosis incidence as a complication of PTAS (study estimate =0.131 [0.084, 0.178]) (P < 0.01). Figure 5B illustrates the analysis after the exclusion of one study.

Re-occlusion: This outcome was represented in the PTAS subgroup in three studies [13,34,47] with an incidence rate of 7.8% (95% CI (1%, 14.7%)), the analysis showed no significant heterogeneity (P =0.791; I² = 0%) as shown in Figure 6.
FIGURE 6: Forest plot for the analysis of re-occlusion

PTAS: Percutaneous transluminal angioplasty, and stenting, MT: mechanical thrombectomy.

Stroke: This outcome was mentioned only in the PTAS subgroup in eight studies [22,31-34,42,47,48,50]. Pooled analysis showed that the incidence of stroke was 11.9% (95% CI [6.8%, 16.9%]); the analysis was heterogeneous (P = 0.047; I² = 50.77%) as shown in Figure 7A. We solved the heterogeneity by the exclusion of Broussalis et al. 2011 study [33] (P = 0.277; I² = 19.98%). Figure 7B illustrates the analysis after the exclusion of one study.

FIGURE 7: Forest plots for the analysis of stroke

(A) shows a forest plot for the analysis of stroke, and (B) shows a forest plot for the analysis of stroke after excluding one study.

Mortality: Eleven studies in the PTAS subgroup [13,22,33,34,39,41,44,45,47,48,50] reported this outcome, the incidence rate was 9.9% (95% CI [4.9%, 14.9%]), the analysis was heterogeneous (P < 0.001; I² = 72.01%). In the MT subgroup three studies were included [36,38,39] with an incidence rate of 34.5% (95% CI [17.3%, 51.7%]), the analysis was heterogeneous (P = 0.029; I² = 71.85%). In the PTAS+MT subgroup three studies [35,39,49] reported this outcome with an incidence rate of 28.9% (95% CI [16.8%, 41.1%]), (P value < 0.001) and the analysis showed no significant heterogeneity (P = 0.210; I² = 35.94%) (Figure 8).
Secondary Outcomes

Secondary outcomes included other complications of the procedure and methods of evaluation after it. Embolism or thrombus: this outcome was represented in the PTAS subgroup in two studies [32,45]. In the MT subgroup, it was mentioned in one study only, so it could not be analyzed. Concerning PTAS subgroup, the incidence rate was 2.9% (95% CI [2.9%, 8.6%]), the analysis showed no significant heterogeneity (P = 0.413; I² = 0%) as shown in Figure 9.

Distal emboli: In the PTAS subgroup, two studies [32,39] reported this outcome and the analysis revealed an incidence rate of 5.8% (95% CI [-0.098, 0.289]), the analysis was heterogenous (P=0.081; I² =67.06 %) (Figure 10).
Infarction: This outcome was represented in the PTAS subgroup by four studies [34,42,45,47]. The incidence of infarction was 11.8% (95% CI {-0.016, 0.252}). Pooled analysis was heterogeneous (P = 0.003; $I^2 = 78.51\%$), and this heterogeneity cannot be solved by study exclusion, as shown in Figure 11.

**FIGURE 11: Forest plot for the analysis of infarction**

PTAS: percutaneous transluminal angioplasty and stenting, MT: mechanical thrombectomy.

Transient ischemic attack: This outcome was mentioned in four studies [33,34,42,50] in the PTAS subgroup, and the result of the analysis revealed an incidence of 6.2% (95% CI {2.8%, 9.6%}). Pooled analysis showed no significant heterogeneity (P= 0.282; $I^2 = 21.37\%$) (Figure 12).

**FIGURE 12: Forest plot for the analysis of the transient ischemic attack**

Artery dissection: This outcome was represented in the PTAS subgroup in three studies [34,43,45]. The incidence of artery dissection was 3.1% (95% CI {-0.010, 0.071}). Pooled analysis showed no significant heterogeneity (P= 0.609; $I^2 = 0\%$) as shown in Figure 13.
ICH: In the MT subgroup three studies were included [37-39]. The incidence of ICH was 5.2% (95% CI [1.3%, 9%]), the analysis of this subgroup showed no significant heterogeneity (P= 0.78; I² = 0 %). In the PTAS subgroup three studies [39,41,47] reported this outcome. The incidence was 4.5% (-0.007, 0.097), the analysis of this subgroup showed no significant heterogeneity (P= 0.87; I² = 0 %). In the PTAS+MT subgroup two studies [39,49] reported this outcome with an incidence of 15.3% (95% CI [-0.080, 0.386]), the analysis was heterogeneous (P<0.001; I² = 85.46 %), this heterogeneity could not be solved by exclusion of one study (Figure 14).

Retreatment: This outcome was mentioned in the PTAS subgroup only by seven studies [22,31-33,40,42,44] with an incidence rate of 15.4% (95% CI [6%, 24.8%]). Pooled analysis was heterogeneous (P < 0.001; I² = 83.26 %); this heterogeneity could not be solved by excluding one study, as shown in Figure 15.

Ninety days mortality: In the PTAS subgroup, eight studies reported this outcome [22,33,34,39,44,47,48,50] with an incidence of 6.9% (95% CI [2%, 11.8%]) the analysis showed moderate heterogeneity (P = 0.027; I² = 55.81 %). In the MT subgroup three studies were included in the analysis [36,38,39] with an incidence of...
34.5% (95% CI [17.3%, 51.7%]), the analysis was heterogeneous (P=0.029; I² = 71.85 %). In the PTAS+MT subgroup two studies reported this outcome [35,39] with an incidence rate of 16.4% (95% CI [-0.097, 0.426]), the analysis was heterogeneous (P= 0.002; I² = 89.64 %) (Figure 16).

**FIGURE 16: Forest plot for the analysis of 90 days mortality**

PTAS: percutaneous transluminal angioplasty and stenting, MT: mechanical thrombectomy.

**Discussion**

Our analysis found that the use of mechanical thrombectomy alone is associated with the highest rates of adverse events and mortality. Percutaneous transluminal angioplasty with or without stenting is the most effective and least associated with mortality. Additionally, we found that the intervention led to a significant increase in NIHSS score but did not significantly increase the MRS score at discharge.

Endovascular therapy includes balloon-mounted stents, balloon angioplasty alone, and self-expandable stents with or without prior angioplasty [51]. Zhang et al. found that treatment with self-expanding stents has a higher risk of restenosis and longer operative time than treatment with balloon-mounted stents in patients with symptomatic intracranial vertebrobasilar arterial stenosis [50].

A review by Luo et al. suggested endovascular treatment as an effective and safe option for the management of intracranial athereosclerotic stenosis if it is used in selected patients and performed with an experienced team who could carefully manage the patients before, during, and after the procedure [51]. These results appear inconsistent with our results. Nevertheless, Goyal et al., in their review, presented challenges with the implementation of endovascular therapy that needed to be resolved. The first, viable implementation of the outcomes across a large number of people; the second, observing, empowering, and approving the new treatments that bring about additional improvements; and third, making a framework to permit induction of outcomes of trials on patients that were not previously tested. Finally, increasing the accessibility of endovascular therapy in developing countries [52].

Thrombolysis, either intravenous thrombolysis or local intra-arterial thrombolysis are among the treatments used to manage vertebrobasilar system stenosis or occlusion. They are considered the most treatment used for revascularization of acute vertebrobasilar artery occlusion. Intra-arterial thrombolysis (IAT) achieves a higher rate of revascularization than intravenous thrombolysis (IVT), but there is not much difference between the efficacy of both [53, 54]. Moreover, there is a strong relationship between the occlusion site and the efficacy of intravenous thrombolysis to achieve revascularization and earlier neurological recovery successfully. The chance for successful revascularization is least with terminal internal carotid artery occlusion, but a higher chance for revascularization is with smaller and more distal occlusion [55,56]. Lindeberg et al. revealed that the recanalization rate is higher in patients treated with intravenous thrombolysis than those treated with endovascular techniques [53].

**Endarterectomy and reconstruction are surgical treatments offered for the management of atherosclerotic stenosis of the vertebral artery. However, their performance has been diminished in recent years and replaced with endovascular interventions for refractory cases to medical treatment [57].**

Our analysis’s main strength is the inclusion of a large number of studies performed in different countries and the absence of any evidence of heterogeneity in the analysis. Conversely, cohort design, either retrospective or prospective with a moderate to high risk of bias, is considered the main limitation. We used subgroup analysis to overcome the inconsistency among the included studies. Further studies are...
recommended to compare the efficacy and safety of the medical treatment and endovascular therapy in managing vertebrobasilar system stenosis or occlusion.

Conclusions
With regard to VBAO, we conclude that PTA with or without stenting is associated with better outcomes and a lower rate of mortality when compared to MT alone.

Additional Information
Disclosures
Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors declare that there is no financial support received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References
1. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2018, 17:954-76. 10.1016/s1474-4422(18)30522-5
2. Lloyd-Jones D, Adams RJ, Brown TM, et al.: Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010, 121:948-54. 10.1161/CIRCULATIONAHA.109.192666
3. Kim JS: Stroke : Pathophysiology, Diagnosis, and Management . Grotta JC, Albers GW, Broderick JP et al. (ed): Elsevier Inc, 2015.
4. Baird TA, Muir KW, Bone I: Basilar artery occlusion. Neurocrit Care. 2004, 1:519-29. 10.1385/NEJMA00016068
5. Vennos KN, Takis CE, Georgilis K, et al.: The Athens stroke registry: results of a five-year hospital-based study. Cerebrovasc Dis. 2000, 10:153-41. 10.1159/000016042
6. Bogousslavsky J, Van Melle G, Regli F.: The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. Stroke. 1988, 19:1083-92. 10.1161/01.str.19.9.1083
7. Caplan LR, Wityk RJ, Glass TA, et al.: New England Medical Center Posterior Circulation Registry. Ann Neurol. 2004, 56:589-98. 10.1002/ana.20204
8. Moulin T, Tatu L, Vuiller F, Berger E, Chavot D, Rumbach L.: Role of a stroke data bank in evaluating cerebral infarction subtypes: patterns and outcome of 1,776 consecutive patients from the Besançon stroke registry. Cerebrovasc Dis. 2000, 10:261-71. 10.1159/000016068
9. Brandt T: Diagnosis and thrombolytic therapy of acute basilar artery occlusion: a review . Clin Exp Hypertens. 2002, 24:611-22. 10.1081/ceh-120015337
10. Savitz SI, Caplan LR: Vertebralbasilar disease. N Engl J Med. 2005, 352:2618-26. 10.1056/NEJMoa041544
11. Hass WK, Fields WS, North RR, Kircheff II, Chase NE, Bauer RB: Joint study of extracranial arterial occlusion. II. Arteriography, techniques, sites, and complications. JAMA. 1968, 203:961-8.
12. Wityk RJ, Chang HM, Rosenbarg A, Han WC, DeWitt LD, Pessin MS, Caplan LR.: Proximal extracranial vertebral artery disease in the New England Medical Center Posterior Circulation Registry. Arch Neurol. 1998, 55:470-8. 10.1001/archneur.55.4.470
13. Wajima D, Aketa S, Nakagawa I, et al.: Effectiveness of intracranial percutaneous transluminal angioplasty or stenting for athereosclerotic vertebrobasilar artery occlusion in the acute phase of ischemic stroke. World Neurosurg. 2017, 97:235-60. 10.1016/j.wneu.2016.09.106
14. Sarikaya H, Arnold M, Engelbert ST, et al.: Outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke. Stroke. 2011, 42:2496-502. 10.1161/STROKEAHA.110.607044
15. Saizanen T, Stebian D, Soine L, et al.: Intravenous thrombolysis of basilar artery occlusion: predictors of recanalization and outcome. Stroke. 2011, 42:2175-9. 10.1161/STROKEAHA.110.605584
16. Schulte-Altedorneburg G, Hamann GF, Mull M, et al.: Outcome of acute vertebralbasilar occlusions treated with intra-arterial fibrinolysis in 180 patients. AJNR Am J Neuroradiol. 2006, 27:2042-7.
17. Randomised controlled trial of streptokinase, aspirin, and combination of both in treatment of acute ischaemic stroke. Multicentre Acute Stroke Trial--Italy (MAST-I) Group. BMJ. 1995, 310:1509-14.
18. Hommel M, Cornu C, Boutitie F, Boissel JP: Ischemic stroke. Multicentre Acute Stroke Trial--Italy (MAST-I) Group. Lancet. 2006, 367:235-413. 10.1161/01.HTA.110.607044
19. Saizanen T, Stebian D, Soine L, et al.: Intravenous thrombolysis of basilar artery occlusion: predictors of recanalization and outcome. Stroke. 2011, 42:2175-9. 10.1161/STROKEAHA.110.605584
20. Weber R, Minnuperi J, Nordmeyer H, Eydinger J, Krogias C, Hadisurya J, Berger K: Thrombectomy in posterior circulation stroke: differences in procedures and outcome compared to anterior circulation stroke in the prospective multicentre REVASK registry. Eur J Neurol. 2019, 26:299-305. 10.1111/ene.13809
21. Kang DH, Jung C, Yoon W, et al.: Endovascular thrombectomy for acute basilar artery occlusion: a multicenter retrospective observational study. J Am Heart Assoc. 2018, 7:10.1161/JAHA.118.009419
22. Parkhutik V, Lago A, Tembl JJ, Aparici F, Vazquez V, Mainar E: Angioplasty and stenting of symptomatic and asymptomatic vertebral artery stenosis: to treat or not to treat. Eur J Neurol. 2010, 17:267-72. 10.1111/j.1468-1331.2009.02786.x
23. Kim SM, Sohn SI, Hong JH, Chang HW, Lee CY, Kim CH: The effectiveness of additional treatment modalities after the failure of recanalization by thrombectomy alone in acute vertebralbasilar arterial occlusion. J Korean Neurosurg Soc. 2015, 58:419-25. 10.3340/jkns.2015.58.5.419
24. Hopkins LN, Martin NA, Hadley MN, Spetzler RF, Budny J, Carter LP: Vertebralbasilar insufficiency. Part 2. Microsurgical treatment of intracranial vertebrobasilar disease. J Neurosurg. 1987, 66:662-74. 10.3171/jn.1987.66.5.0662

25. Spetzler RF, Hadley MN, Martin NA, Hopkins LN, Carter LP, Budny J: Vertebralbasilar insufficiency. Part 1: microsurgical treatment of extracranial vertebrobasilar disease. J Neurosurg. 1987, 66:648-61. 10.3171/jn.1987.66.5.0648

26. Jenkins JS, White CJ, Ramee SR, Collins TJ, Chilakamarri VK, McKinley KJ, Jain SP: Vertebral artery stenting. Catheter Cardiovasc Interv. 2001, 54:1-5. 10.1002/cdi.1228

27. Kim HY, Chung CS, Moon SY, Lee KH, Han SH: Complete nonvisualization of basilar artery on MR angiography in patients with vertebrobasilar ischemic stroke: favorable outcome factors. Cerebrovasc Dis. 2004, 18:269-76. 10.1055/s-0028-1085551

28. Archer CR, Horenstein S: Basilar artery occlusion: clinical and radiological correlation. Stroke. 1977, 8:385-90. 10.1161/01.str.8.3.385

29. Davis SM, Donnan GA: Basilar artery thrombosis: recanalization is the key. Stroke. 2006, 37:2440. 10.1161/01.STR.0000257669.89458.a9

30. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010, 8:536-41. 10.1016/j.ijsu.2010.02.007

31. Cochrane Training: Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (ed): John Wiley & Sons, Chichester, England; 2019. https://training.cochrane.org/handbook.

32. Barakate MS, Snook JL, Harrington TJ, Sorby W, Pik J, Morgan MK: Angioplasty and stenting in the posterior cerebral circulation. J Endovasc Ther. 2001, 8:538-65. 10.1177/152665370100800401

33. Broussalitis E, Kunz AB, Luthringhaus G, Klein S, McCoy MR, Trinka E, Koller-Oberpfalzer M: Treatment of vertebro artery origin stenosis with a Pharos stent device: a single center experience. Interv Neuroradiol. 2011, 17:516-22. 10.1510/19911017100506

34. Djurdjevic T, Cunha A, Schulz U, Briley D, Rothwell P, Küker W: Endovascular treatment of patients with high-risk symptomatic intracranial vertebrobasilar stenoses: long-term outcomes. Stroke. 2019, 50:1135-41. 10.1161/STROKEAHA.118.022822

35. Fiorella D, Chow MM, Anderon M, Woo H, Rasmussen PA, Masaryk TJ: A 7-year experience with balloon-mounted coronary stents for the treatment of symptomatic vertebrobasilar intracranial atheromatous disease. Neurosurgery. 2007, 61:236-42; discussion 242-3. 10.1227/01.NEU.0000255251.42579.31

36. Gao F, Lo WT, Sun X, Mo DP, Ma N, Miao ZR: Combined use of mechanical thrombectomy with angioplasty and stenting for acute basilar occlusions with underlying severe intracranial vertebrobasilar stenosis: preliminary experience from a single Chinese center. AJNR Am J Neuroradiol. 2015, 36:1947-52. 10.3174/ajnr.A4364

37. Hu X, Gao F, Sun X, et al.: Endovascular mechanical thrombectomy with the solitaire device for the treatment of acute basilar artery occlusion. World Neurosurg. 2016, 89:501-8. 10.1016/j.wneu.2016.02.017

38. Möhlenbruch M, Stampfl S, Behrens I, et al.: Mechanical thrombectomy with stent retrievers in acute basilar artery occlusion. AJNR Am J Neuroradiol. 2014, 35:959-64. 10.3174/ajnr.A5796

39. Quan T, Hou H, Xue W, et al.: Endovascular treatment of acute intracranial vertebrobasilar artery occlusion: a multicenter retrospective observational study. Neuroendovascular. 2019, 61:1477-84. 10.1007/s00234-019-0282-1

40. Tsuetsumi M, Kakekawa K, Onizuka M, et al.: Stent fracture in recanalization for symptomatic ostial vertebral artery stenosis. Neuroendovascular. 2007, 49:235-7. 10.1007/s00234-006-0185-x

41. Weber W, Mayer TE, Henkes H, et al.: Stent-angioplasty of intracranial vertebal and basilar artery stenoses in posterior cerebral syndromes. Eur J Radiol. 2005, 55:231-6. 10.1016/j.ejrad.2004.11.010

42. Wang ZL, Gao BL, Li TX, et al.: Symptomatic extracranial vertebrobasilar artery atherosclerotic stenosis (≥70%) with concurrent contralateral vertebral arteriosclerotic diseases in 88 patients treated with the intracranial vertebrobasilar stenting. J Vasc Surg. 2007, 46:510-6. 10.1016/j.jvs.2006.02.027

43. Caniżygi M, Arat A, Cel BE, Turkbey B, Saatci I, Cekirge S, Balkanci F: Stenting with concurrent contralateral vertebral atherosclerotic diseases in 88 patients treated with the intracranial vertebrobasilar stenting. J Vasc Surg. 2007, 46:510-6. 10.1016/j.jvs.2006.02.027

44. Chastain HD, Campbell MS, Iyer S, et al.: Extracranial vertebral artery stent placement: in-hospital and follow-up results. J Neurosurg. 1999, 91:547-52. 10.3171/jn.1999.91.4.0547

45. Eberhardt O, Neugele R, Haygrotzki S, Weller M, Ennemann U: Stenting of vertebralbasilar arteries in symptomatic atherosclerotic disease and acute occlusion: case series and review of the literature. J Vasc Surg. 2006, 43:1145-54. 10.1016/j.vjs.2006.02.027

46. Gao P, Wang Y, Ma Y, et al.: Endovascular recanalization for chronic symptomatic intracranial vertebal artery total occlusion: Experience of a single center and review of literature. J Neuroendovascular. 2018, 45:295-304. 10.1016/j.neurad.2017.12.025

47. Kowill CM, Moelker-Hartmann W, Fink GR, Haupt WF, Sobesky J: Acute interventional recanalisation of vertebralbasilar stenoses by angioplasty: complications and 12 months follow up. Neuroendovascular. 2015, 55:1135-41. 10.1007/s00234-015-1241-4

48. Levy EI, Horowitz MB, Koebbe CJ, Jungreis CC, Pride GL, Dutton K, Purdy PD: Transluminal stent-assisted angioplasty of the intracranial vertebrobasilar system for medically refractory, posterior circulation ischemia: early results. Neurosurgery. 2001, 48:1215-21; discussion 1221-3. 10.1097/00006123-200106000-00002

49. Shohe TH, Harrington TJ, Faulder K, Steinfort B: Endovascular therapy in acute basilar artery occlusion: a retrospective single-centre Australian analysis. J Med Imaging Radiat Oncol. 2019, 63:55-9. 10.1111/jmri.1285

50. Zhang Y, Rajah X, Liu P, et al.: Balloon-mounted versus self-expanding stents for symptomatic intracranial vertebrobasilar artery stenosis combined with poor collaterals. Neurosurg Res. 2019, 41:704-15. 10.1007/s00061-019-16085

51. Luo J, Wang T, Gao F, Kruings T, Jiao L: Endovascular treatment of intracranial atherosclerotic stenosis:
current debates and future prospects. Front Neurol. 2018, 9:666. 10.3389/fneur.2018.00666
52. Goyal M, Yu AY, Menon BK, et al.: Endovascular therapy in acute ischemic stroke: challenges and transition from trials to bedside. Stroke. 2016, 47:548-53. 10.1161/STROKEAHA.115.011426
53. Lindsberg Pj, Soine L, Tatlisumak T, Roine RO, Kallela M, Häppölä O, Kaste M: Long-term outcome after intravenous thrombolysis of basilar artery occlusion. JAMA. 2004, 292:1862-6. 10.1001/jama.292.15.1862
54. Schoen JC, Boysen MM, Warren CR, Chakravarthy B, Lotfipour S: Vertebrobasilar artery occlusion. West J Emerg Med. 2011, 12:233-9.
55. Saqqur M, Uchino K, Demchuk AM, et al.: Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. Stroke. 2007, 38:948-54. 10.1161/01.STR.0000257304.21967.bx
56. Sillanpää N, Saarinen JT, Rusunen H, Elovaara I, Dastidar P, Soimakallio S: Location of the clot and outcome of perfusion defects in acute anterior circulation stroke treated with intravenous thrombolysis. AJNR Am J Neuroradiol. 2015, 34:100-6. 10.3174/ajnr.A3149
57. Cloud GC, Markus HS: Diagnosis and management of vertebral artery stenosis. QJM. 2003, 96:27-54. 10.1093/qjmed/hcg003
58. Karameshev A, Schroth G, Mordasini P, et al.: Long-term outcome of symptomatic severe ostial vertebral artery stenosis (OVAS). Neuroradiology. 2010, 52:571-9. 10.1007/s00234-010-0662-0
59. Wehman JC, Hanel RA, Guidot CA, Guterman LR, Hopkins LN: Atherosclerotic occlusive extracranial vertebral artery disease: indications for intervention, endovascular techniques, short-term and long-term results. J Interv Cardiol. 2004, 17:219-32. 10.1111/j.1540-8183.2004.04055.x