Stroke: Vascular and Interventional Neurology

ORIGINAL RESEARCH

Endovascular Treatment for Basilar Artery Occlusion: Revisiting Evidence From Randomized Clinical Trials

Sherief Ghozy, MD; Amr Ehab El-Qushayri, MD; Mohamed Elfil, MD; Alis J. Dicpinigaitis, BA; Krishna Amuluru, MD; Mohammad El-Ghanem, MD; Chirag D. Gandhi, MD; Fawaz Al-Mufti, MD

BACKGROUND: Acute ischemic stroke attributed to basilar artery occlusion is known to be associated with high rates of mortality and disability. However, the previous clinical trials did not provide evidence to support the efficacy of endovascular treatment (EVT) in patients with basilar artery occlusion. The purpose of this study was to provide updated evidence about EVT's benefits and safety profile with the recent update from both the Endovascular Treatment for Acute Basilar Artery Occlusion (ATTENTION) and the Basilar Artery Occlusion Chinese Endovascular Trial (BAOCHE) trials.

METHODS: We searched for eligible articles from inception to November 1, 2022, in 5 databases and included all randomized controlled trials with no restrictions on the publication date or language. Meta-analysis statistics were performed using R software version 4.2.1.

RESULTS: The rate of modified Rankin scale score of 0 to 3 was significantly higher in the EVT group compared with best medical treatment (risk ratio [RR], 1.54 [95% CI, 1.16–2.04]; *P* value = 0.002), and the same was observed for the rate of modified Rankin scale score 0 to 2 (RR, 1.83 [95% CI, 1.08–3.08]; *P* value = 0.024). Moreover, there was a significant reduction in the 90-day mortality in the EVT group (RR, 0.76 [95% CI, 0.65–0.89]; *P* value = 0.002). However, there was a significantly higher rate of symptomatic intracerebral hemorrhage in the EVT group compared with best medical treatment (RR, 7.48 [95% CI, 2.27–24.61]; *P* value <0.001).

CONCLUSIONS: EVT may confer a clinical benefit to patients with acute ischemic stroke caused by basilar artery occlusion. Because of the small number of included studies and because all of them were conducted in the Chinese population, further trials might be needed to confirm and further investigate the generalizability of these results.

Key Words: basilar artery occlusion ■ mechanical thrombectomy ■ randomized controlled trials ■ stroke

Acute ischemic stroke attributed to basilar artery occlusion (BAO) is known to be associated with high rates of mortality and disability[1,2] and accounts for 1% of all strokes.[3] There has been a debate in the literature about the efficacy of endovascular treatment (EVT) in patients with posterior circulation strokes caused by acute BAO. On one hand, observational studies suggested that achieving successful recanalization in patients with BAO did not eventually lead to favorable outcomes, which led to the concept of futile recanalization.[2,4,5] On the other hand, other studies have investigated the outcome of EVT in acute BAO, and the results suggested that a considerable proportion of those patients treated with EVT achieved

Correspondence to: Sherief Ghozy, MD, Department of Radiology, Mayo Clinic Minnesota, Rochester, MN 55905.
Email: Ghozy.sherief@mayo.edu

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/SVIN.122.000655

S. Ghozy, A.E. El-Qushayri, and M. Elfil contributed equally.

Stroke: Vascular and Interventional Neurology is available at: www.ahajournals.org/journal/svin

good functional outcomes with an acceptable safety profile.[6–8] Some of these studies even suggested comparable outcomes between patients with anterior circulation stroke and patients with BAO undergoing EVT.[8] Given such conflicting results of observational studies, clinical trials were warranted to further investigate the efficacy of EVT in patients with acute ischemic stroke attributed to BAO. Recently, the results of both the Basilar Artery Occlusion Endovascular Intervention Versus Standard Medical Treatment (BEST) and the Basilar Artery International Cooperation Study (BASICS) trials were published,[9,10] and the overall conclusion from both trials was not encouraging about the benefits of EVT in patients with BAO. In contrast to these studies, the results of the Basilar Artery Occlusion Chinese Endovascular Trial (BAOCHE) and Endovascular Treatment for Acute Basilar Artery Occlusion (ATTENTION) trials pointed out EVT's clinical benefits in patients with BAO.[11,12] Using the data from the BEST and BASICS trials along with the updated evidence from the ATTENTION and BAOCHE trials, we conducted this meta-analysis to provide collective evidence about the benefits and the safety profile of EVT versus the best medical treatment (BMT) in patients with BAO, given the differing results of these trials.

Nonstandard Abbreviations and Acronyms

BAO	basilar artery occlusion
BMT	best medical treatment
EVT	endovascular treatment
PH	parenchymal hemorrhage
sICH	symptomatic intracerebral hemorrhage

CLINICAL PERSPECTIVE

- Using the newly published Endovascular Treatment for Acute Basilar Artery Occlusion (ATTENTION) and the Basilar Artery Occlusion Chinese Endovascular Trial (BAOCHE) trials, we conducted a meta-analysis to provide collective evidence about the efficacy of endovascular treatment for basilar artery occlusion.
- The results support endovascular treatment for basilar artery occlusion given the demonstrated advantages over the conservative approach in terms of functional outcomes and mortality.
- The generalizability of these results should be further investigated through larger trials with a more diverse population.

METHODS

Search Strategy and Study Selection

The data sets generated and analyzed during the current study are available from the corresponding author on reasonable request.

We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist in conducting the current systematic review and meta-analysis.[13] We searched for eligible articles until from inception to November 1, 2022, in the following 4 databases using key words or medical subject terms based on the population, intervention, comparator, and outcomes framework: PubMed, Web of Science, Scopus, and Embase. Eligible participants were those with acute BAO stroke, treated with EVT, who were then compared with BMT and all reported outcomes analyzed whenever possible. We tailored the search strategy based on each database, the search terms were the main components, and we also conducted a manual search of references in the included articles in order to avoid missing any other relevant studies.

We included all randomized controlled trials with no restrictions on the publication date or language of the included studies to avoid missing any relevant articles. We excluded nonhuman research and nonrandomized controlled trial studies. A total of 2 authors screened the title and abstracts of each record and then performed full-text screening for the inclusion of relevant articles. In each step, a third senior reviewer was consulted if disagreement occurred.

Data Extraction

We extracted the data using a predesigned Excel sheet. At least 2 authors extracted the necessary information from each article, which was revised by a third author for more accuracy.

Quality of Evidence

A total of 2 authors independently assessed the quality of the included studies using the revised Cochrane risk-of-bias tool for randomized trials.[14] If there were any disagreements, it was resolved by a third senior author. Furthermore, we assessed the quality of the evidence and the overall rating of confidence in effect estimates using the Grading of Recommendations, Assessment, Development and Evaluations guidelines.[15,16]

Statistical Analysis

All data were analyzed using R software version 4.2.1 using the "meta" package. We computed the pooled risk ratios (RRs) and their corresponding 95% CIs using a random-effects or fixed-effect model depending on heterogeneity among the included studies. Heterogeneity was assessed with Q statistics and the *I*2 test, and an I^2 value >50% or a *P* value <0.05 was considered significant. Because of the small number of included studies (<10 per the analysis), neither the Egger regression test for the assessment of publication bias nor meta-regression were applicable.[17,18]

RESULTS

Search Results and Study Characteristics

We initially retrieved 3774 records from all queried databases containing 732 duplicates to end up with 3042 records for screening. Of those, 3028 were excluded during the title and abstract screening for being irrelevant to observational retrospective studies, followed by excluding another 12 articles through full-text screening for the same reason. Finally, we manually added the ATTENTION and BAOCHE trials (were not database indexed yet), ending up with 4 included trials (Figure 1). A summary of the included trials is represented in Supplementary Table S1.

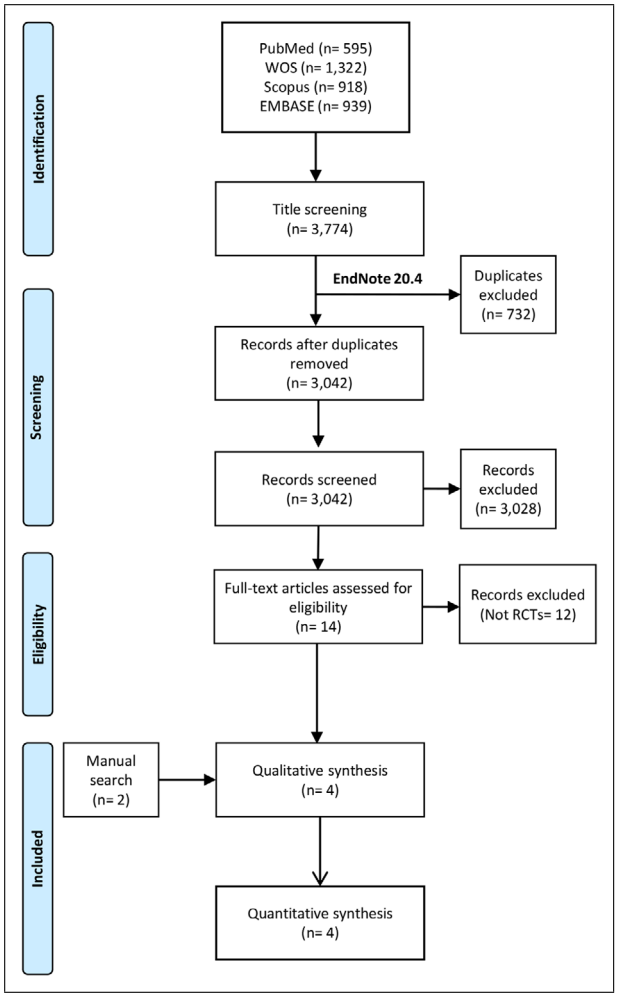

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the search and screening process. RCT indicates randomized controlled trial; and WOS, Web of Science.

Functional Outcome

The 4 included trials recruited a total of 988 patients and reported on functional outcomes. The rate of modified Rankin scale (mRS) score 0 to 3 was significantly higher in the EVT group compared with the BMT group (RR, 1.54 [95% CI, 1.16–2.04]; *P* value = 0.002), with moderate heterogeneity among the included studies (I^2=60%; *P* value = 0.059) (Figure 2A). The same was observed for the rate of mRS score 0 to 2, where the comparison favored the EVT group (RR, 1.83 [95% CI, 1.08–3.08]; *P* value = 0.024). However, the heterogeneity was more considerable (I^2=79%; *P* value = 0.002) (Figure 2B).

Intracranial Hemorrhage and Mortality

There was a significantly higher rate of symptomatic intracerebral (symptomatic intracerebral hemorrhage [sICH]) in the EVT group compared with the BMT group (RR, 7.48 [95% CI, 2.27–24.61]; *P* value <0.001), with no heterogeneity among the included studies (I^2=0%; *P* value <0.001) (Figure 3A). For parenchymal hemorrhage (PH), the overall PH and type I PH rates were comparable between both groups with an RR of 1.63 (95% CI, 0.61–4.37; *P* value = 0.438) and an RR of 0.37 (95% CI, 0.08–1.59; *P* value = 0.181), respectively, whereas type II PH was more prevalent in the EVT group compared with the BMT group (RR, 5.53 [95% CI, 1.47–20.84]; *P* value = 0.011). No significant heterogeneity was observed either overall or within the subgroups (Figure 3B). In terms of the 90-day mortality, the EVT group showed a significant reduction in mortality compared with the BMT group (RR, 0.76 [95% CI, 0.65–0.89]; *P* value = 0.002), with no heterogeneity observed (I^2=0%; *P* value = 0.442) (Figure 3C).

Quality of Evidence

The certainty of the evidence was high in all assessed outcomes except for the mRS score 0 to 2 outcome, mainly driven by the serious heterogeneity (Table 1).

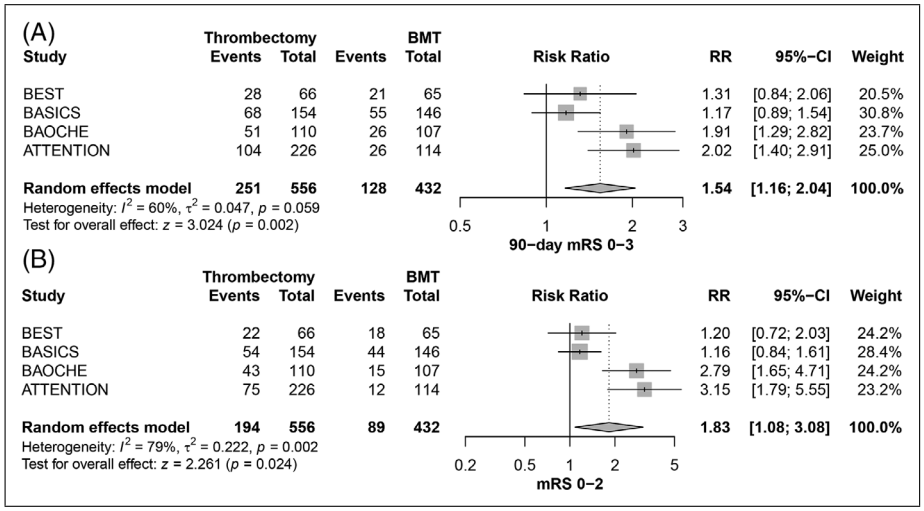

Figure 2. Forest plot showing the results of the meta-analysis for functional outcomes. **A**, The 90-day mRS score 0 to 3 and (**B**) the 90-day mRS score 0 to 2. BMT indicates best medical treatment; mRS, modified Rankin Scale; and RR, risk ratio.

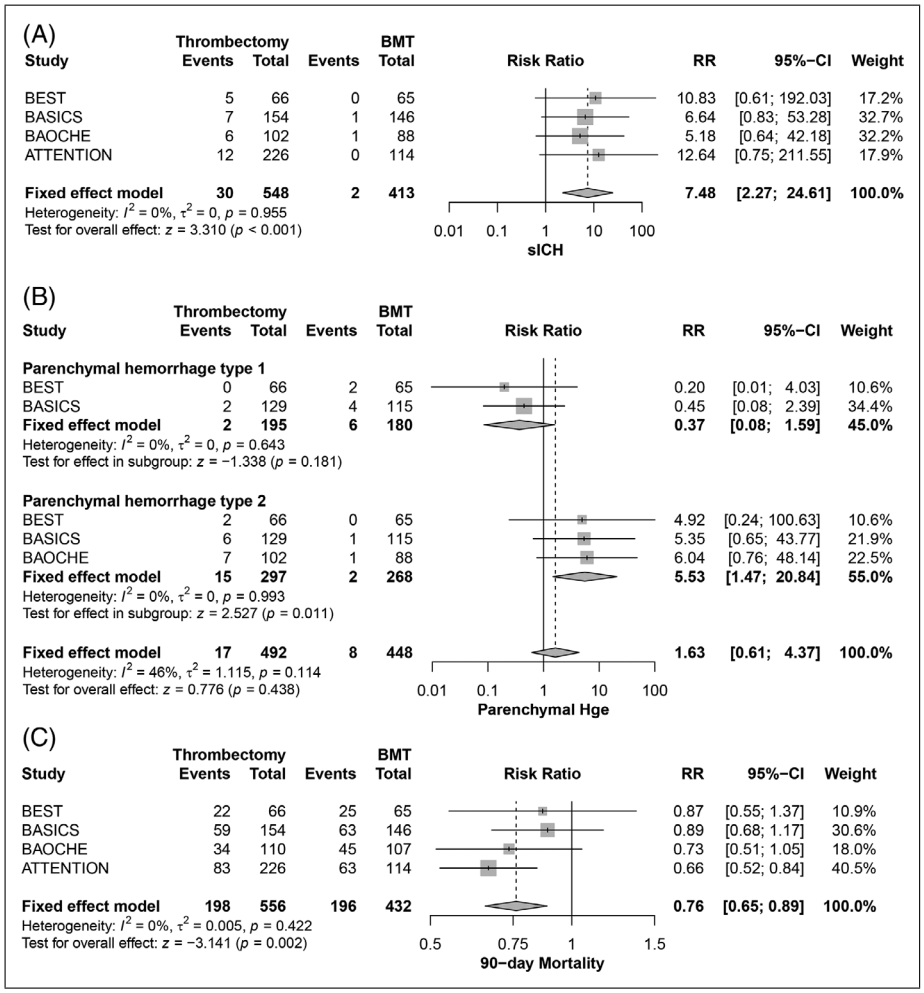

Figure 3. Forest plot showing the results of meta-analysis for safety outcomes. **A**, sICH, (**B**) parenchymal hemorrhage, and (**C**) 90-day mortality. BMT indicates best medical treatment; Hge, hemorrhage; RR, risk ratio; and sICH, symptomatic intracerebral hemorrhage.

Table. GRADE Assessment of Quality of Evidence

Certainty assessment							No. of patients (%)		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thrombectomy	BMT	Relative (95% CI)	Absolute (95% CI)		
90-D mRS 0–3												
4	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	251/556 (45.1)	128/432 (29.6)	RR, 1.54 (1.16–2.04)	160 More per 1000 (from 47 more to 308 more)	⊕⊕⊕⊕ High	Critical
90-D mRS 0–2												
4	Randomized trials	Not serious	Serious	Not serious	Not serious	None	194/556 (34.9)	89/432 (20.6)	RR, 1.83 (1.08–3.08)	171 More per 1000 (from 16 more to 429 more)	⊕⊕⊕◯ Moderate	Important
90-D mortality												
4	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	198/556 (35.6)	196/432 (45.4)	RR, 0.76 (0.65–0.89)	109 Fewer per 1000 (from 159 fewer to 50 fewer)	⊕⊕⊕⊕ High	Critical
sICH												
4	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	30/548 (5.5)	2/413 (0.5)	RR, 7.48 (2.27–24.61)	31 More per 1000 (from 6 more to 114 more)	⊕⊕⊕⊕ High	Important
Parenchymal hemorrhage												
3	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	17/492 (3.5)	8/448 (1.8)	RR, 1.63 (0.61–4.37)	11 More per 1000 (from 7 fewer to 60 more)	⊕⊕⊕⊕ High	Important

BMT indicates best medical treatment; GRADE, Grading of Recommendations, Assessment, Development, and Evaluations; mRS, modified Rankin scale; RR, risk ratio; and sICH, symptomatic intracerebral hemorrhage.

DISCUSSION

Our meta-analysis of 4 randomized controlled trials evaluating EVT in patients with BAO demonstrates that EVT achieved higher rates of favorable functional outcomes (mRS scores of either 0–2 or 0–3) in comparison with BMT. The safety profile included 2 outcomes: 90-day mortality and intracranial hemorrhage. EVT was found to be associated with a lower rate of 90-day mortality compared with BMT, but with a higher rate of sICH. There was no difference between EVT and BMT in rates of overall or type I PH, but EVT showed an increased risk for type II PH.

BAO stroke was associated with high mortality and long-term disability rates. A recent study estimated the 30-day fatality and functional disability to be 40% and 65% in patients with BAO with no reperfusion treatment.[19] Therefore, because EVT has been approved as the gold standard treatment for patients with acute ischemic stroke with large vessel occlusion in the anterior circulation, the efficacy of EVT for BAO has been an inevitable question to investigate. Many observational studies attempted to evaluate the benefit and safety of EVT for BAO without definitive conclusions. This created a necessity to conduct clinical trials to compare EVT with BMT for acute BAO given that the trial setting would be ideal for this type of question.

The BEST trial was the first to be conducted, and its results did not show any advantage of EVT over BMT in achieving favorable clinical outcomes, reducing mortality, or incidence of sICH.[9] The results of the BEST trial might have been confounded by the small sample size as well as the high crossover rate between the 2 treatment modalities, which might have led to the loss of balance between the 2 groups.[9] Following the BEST trial, the BASICS trial also demonstrated equipoise in these treatment modalities for patients with BAO in terms of favorable functional outcome, sICH, and morality.[10] There was a crossover rate of 5% from the BMT group to the EVT group, and the stratification in randomization in this study was done using the National Institute of Health Stroke Scale score, which is not the best tool to represent the clinical severity of the posterior circulation strokes.[10] Moreover, in both trials, advanced imaging such as computed tomography perfusion was not used for patient selection, which was associated with better functional outcomes in the early and late time windows compared with standard imaging.[20]

The results of the BAOCHE trial were recently published and demonstrated that EVT achieved a higher 90-day mild to moderate disabaility rates (mRS score of 0 to 3) than BMT, but there was no statistically significant difference between the 2 groups in mortality or sICH.[11] The BAOCHE trial included patients with BAO presenting within the time window of 6 to 24 hours, meaning that patients in the BMT group most likely did not receive intravenous thrombolysis, which was not the case in both the BEST trial, in which intravenous thrombolysis was used in 32% of BMT patients,[9] and in the BASIC trial, in which intravenous thrombolysis was used in 79.5% of BMT patients.[10] This factor might have contributed to the notable difference in results. The results of the ATTENTION trial were also recently published and revealed an advantage of EVT over BMT in achieving 90-mRS of 0 to 3 and mortality; however, EVT was also associated with a higher rate of sICH.[12] Of note, the ATTENTION trial included patients with BAO presenting in the time window of 0 to 12 hours, and patients in both groups received intravenous thrombolysis when eligible.

Our study provides collective evidence from all the available clinical trials that tested the efficacy and safety of EVT in patients with BAO. However, it is to be noted that our meta-analysis included a small number of studies that hindered the ideal exploration of heterogeneity or publication bias. Moreover, in some of the included trials, no advanced imaging was used for patient selection. Also, using the National Institute of Health Stroke Scale score for stratification of patients during randomization is a limitation given that it is less sensitive to posterior circulation stroke symptoms than it is to anterior circulation stroke symptoms. In addition, we could not perform subgroup analysis based on the type of arterial access used for EVT (transradial versus transfemoral) or the EVT technique used (stent retriever versus direct aspiration) as these data were not available in the included trials. Finally, it should be noted that, except for the BASICS trial, the studies were conducted in China (Asian population), which would limit the generalizability of the results to different populations.

CONCLUSIONS

The current evidence supports the use of EVT for BAO given the demonstrated advantages over the conservative approach in terms of functional outcomes and mortality. However, further large-scale trials of different populations are needed to validate these benefits and ensure generalizability.

ARTICLE INFORMATION

Received August 15, 2022; Accepted December 19, 2022

Affiliations

Department of Radiology, Mayo Clinic, Rochester, MN (S.G.); Nuffield Department of Primary Care Health Sciences and Department for Continuing Education (Evidence-Based Health Care Program), Oxford University, Oxford, UK

(S.G.); Nested Knowledge, St Paul, MN (A.E.E.-Q.); Department of Neurological Sciences, University of Nebraska Medical Center, Omaha, NE (M.E.); School of Medicine, New York Medical College, Valhalla, NY (A.J.D.); Division of Interventional Neuroradiology, Goodman Campbell Brain and Spine, Ascension St. Vincent Medical Center, Indianapolis, IN (K.A.); Neuroendovascular Surgery, HCA Houston Northwest/University of Houston College of Medicine, Houston, TX (M.E.-G.); Department of Neurosurgery, Westchester Medical Center, Valhalla, NY (C.D.G., F.A.-M.)

Acknowledgments

None.

Disclosures

None.

Sources of Funding

None.

Supplemental Materials

Supplementary Table 1: Characteristics of the included studies.

REFERENCES

1. Schonewille WJ, Wijman CA, Michel P, Rueckert CM, Weimar C, Mattle HP, Engelter ST, Tanne D, Muir KW, Molina CA, et al. Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. *Lancet Neurol*. 2009;8:724-730. https://doi.org/10.1016/S1474-4422(09)70173-5
2. Singer OC, Berkefeld J, Nolte CH, Bohner G, Haring HP, Trenkler J, Groschel K, Muller-Forell W, Niederkorn K, Deutschmann H, et al. Mechanical recanalization in basilar artery occlusion: the ENDOSTROKE study. *Ann Neurol*. 2015;77:415-424. https://doi.org/10.1002/ana.24336
3. Kwak HS, Park JS. Mechanical thrombectomy in basilar artery occlusion: clinical outcomes related to posterior circulation collateral score. *Stroke*. 2020;51:2045-2050. https://doi.org/10.1161/STROKEAHA.120.029861
4. Alonso de Lecinana M, Kawiorski MM, Ximenez-Carrillo A, Cruz-Culebras A, Garcia-Pastor A, Martinez-Sanchez P, Fernandez-Prieto A, Caniego JL, Mendez JC, Zapata-Wainberg G, et al. Mechanical thrombectomy for basilar artery thrombosis: a comparison of outcomes with anterior circulation occlusions. *J Neurointerv Surg*. 2017;9:1173-1178. https://doi.org/10.1136/neurintsurg-2016-012797
5. Gory B, Eldesouky I, Sivan-Hoffmann R, Rabilloud M, Ong E, Riva R, Gherasim DN, Turjman A, Nighoghossian N, Turjman F. Outcomes of stent retriever thrombectomy in basilar artery occlusion: an observational study and systematic review. *J Neurol Neurosurg Psychiatry*. 2016;87:520-525. https://doi.org/10.1136/jnnp-2014-310250
6. Werner M, Lopez-Rueda A, Zarco F, Roman LS, Blasco J, Amaro S, Carrero E, Fontanals J, Oleaga L, Macho J, et al. Mechanical thrombectomy in acute basilar artery occlusion: A safety and efficacy single centre study. *Interv Neuroradiol*. 2016;22:310-317. https://doi.org/10.1177/1591019916631145
7. Uno J, Kameda K, Otsuji R, Ren N, Nagaoka S, Maeda K, Ikai Y, Gi H. Mechanical thrombectomy for basilar artery occlusion compared with anterior circulation stroke. *World Neurosurg*. 2020;134:e469-e475. https://doi.org/10.1016/j.wneu.2019.10.097
8. Meinel TR, Kaesmacher J, Chaloulos-Iakovidis P, Panos L, Mordasini P, Mosimann PJ, Michel P, Hajdu S, Ribo M, Requena M, et al. Mechanical thrombectomy for basilar artery occlusion: efficacy, outcomes, and futile recanalization in comparison with the anterior circulation. *J Neurointerv Surg*. 2019;11:1174-1180. https://doi.org/10.1136/neurintsurg-2018-014516
9. Liu X, Dai Q, Ye R, Zi W, Liu Y, Wang H, Zhu W, Ma M, Yin Q, Li M, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. *Lancet Neurol*. 2020;19:115-122. https://doi.org/10.1016/S1474-4422(19)30395-3
10. Langezaal LCM, van der Hoeven E, Mont'Alverne FJA, de Carvalho JJF, Lima FO, Dippel DWJ, van der Lugt A, Lo RTH, Boiten J, Lycklama ANGJ, et al. Endovascular therapy for stroke due to basilar-artery occlusion. *N Engl J Med*. 2021;384:1910-1920. https://doi.org/10.1056/NEJMoa2030297
11. Jovin TG, Li C, Wu L, Wu C, Chen J, Jiang C, Shi Z, Gao Z, Song C, Chen W, et al. Trial of thrombectomy 6 to 24 hours after stroke due to basilar-artery occlusion. *N Engl J Med*. 2022;387:1373-1384. https://doi.org/10.1056/NEJMoa2207576
12. Tao C, Nogueira RG, Zhu Y, Sun J, Han H, Yuan G, Wen C, Zhou P, Chen W, Zeng G, et al. Trial of endovascular treatment of acute basilar-artery occlusion. *N Engl J Med*. 2022;387:1361-1372. https://doi.org/10.1056/NEJMoa2206317
13. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097. https://doi.org/10.1371/journal.pmed.1000097
14. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898
15. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401-406. https://doi.org/10.1016/j.jclinepi.2010.07.015
16. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, Atkins D, Kunz R, Montori V, Jaeschke R, et al. GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. *J Clin Epidemiol*. 2013;66:151-157. https://doi.org/10.1016/j.jclinepi.2012.01.006
17. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629-634.
18. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Comparison of two methods to detect publication bias in meta-analysis. *JAMA*. 2006;295:676-680.
19. Schonewille WJ, Algra A, Serena J, Molina CA, Kappelle LJ. Outcome in patients with basilar artery occlusion treated conventionally. *J Neurol Neurosurg Psychiatry*. 2005;76:1238-1241. https://doi.org/10.1136/jnnp.2004.049924
20. Dhillon PS, Butt W, Podlasek A, McConachie N, Lenthall R, Nair S, Malik L, Booth TC, Bhogal P, Makalanda HLD, et al. Perfusion imaging for endovascular thrombectomy in acute ischemic stroke is associated with improved functional outcomes in the early and late time windows. *Stroke*. 2022;53:2770-2778. https://doi.org/10.1161/strokeaha.121.038010