

Endovascular treatment for basilar artery occlusion: a meta-analysis

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Acute basilar artery occlusion (BAO) may lead to severe disability or death in about 70% of patients.^{1 2} Previous studies have established endovascular treatment (EVT) as the standard treatment for patients with acute anterior circulation occlusions.^{3–9} However, the ideal effective treatment for acute BAO remains controversial.

Two previously published randomised control studies (RCTs), BEST (Basilar Artery Occlusion Endovascular Intervention versus Standard Medical Treatment) and BASICS (Basilar Artery International Cooperation Study), failed to achieve an advantage of EVT over standard medical treatment (SMT).^{10 11} Recently, two other RCTs from China, ATTENTION (Endovascular Treatment For Acute Basilar Artery Occlusion: A Multicentre Randomised Clinical Trial) and BAOCHE (Basilar Artery Occlusion Chinese Endovascular), were presented at the European Stroke Organisation Conference 2022.^{12 13} The ATTENTION trial showed that EVT was associated with the better functional outcomes at 90 days, achieving a higher rate of modified Rankin Scale (mRS) score of ≤ 3 (46.0% vs 22.8%; adjusted relative risk (aRR) 2.1, 95% CI 1.5 to 3.0, $p < 0.001$; number needed to treat (NNT)=4) and $mRS \leq 2$ (33.2% vs 10.5%; aRR 3.2, 95% CI 1.8 to 5.4, $p < 0.001$; NNT=4.4). There was also a significantly lower risk of 90-day mortality (36.7% vs 55.3%; aRR 0.7, 95% CI 0.5 to 0.8, $p < 0.001$; NNT=5.4) but a higher incidence of symptomatic intracranial haemorrhage (sICH, Safe Implementation of Thrombolysis in Stroke—Monitoring Study (SITS-MOST) criteria, EVT 5.3% vs SMT 0%, $p = 0.001$; NNT=19). Likewise, the BAOCHE trial demonstrated that patients receiving EVT had a higher rate of mRS 0–3 (46.4% vs 24.3%, adjusted OR 2.92, 95% CI 1.56 to 5.47, $p = 0.001$; NNT=4.5), trends towards lower mortality (EVT 30.9% vs SMT 42.1%, $p = 0.088$) and a higher risk of sICH (SITS-MOST criteria, EVT 5.9% vs SMT 1.1%, $p = 0.125$). These findings showed the efficacy

of EVT, which could be a turning point for the treatment of acute BAO.

Here, we provided a brief meta-analysis of the aggregate data from BASICS, BEST, ATTENTION and BAOCHE trials according to the intention-to-treat principle. Key features of the design of included trials are summarised in online supplemental table 1. We found that EVT for ischaemic stroke due to acute BAO was correlated with improved functional outcomes compared with SMT. The pooled RR for 90-day mRS 0–3 was 1.54 (95% CI 1.16 to 2.04; heterogeneity $I^2 = 60\%$) (figure 1A). The pooled RR for 90-day mRS 0 to 2 was 1.83 (95% CI 1.08 to 3.08; heterogeneity $I^2 = 79\%$). Although there was a higher risk of sICH (RR 7.77, 95% CI 2.36 to 25.59; heterogeneity $I^2 = 0\%$) (figure 1B), EVT significantly decreased the risk of 90-day mortality (RR 0.76, 95% CI 0.65 to 0.89; heterogeneity $I^2 = 0\%$) (figure 1C). We found no evidence of publication bias using Egger's test ($p > 0.05$).

MERITS AND SHORTCOMINGS

The BEST and BASICS trials had partially similar inclusion criteria and evaluated patients with acute BAO within 8 hours or 6 hours of symptom onset, respectively. The BEST and BASICS both revealed the trend towards favourable outcomes (mRS 0–3) with EVT, but without statistically significant differences. In the meanwhile, both trials had the limitations of poor enrollment and high cross-over rates. Nearly 29% of eligible patients in BASICS group and 55% of patients in BEST group were treated outside trials, which might introduce bias in the enrolled population.¹⁴ The BASICS also had two protocol changes in the midst of the trial due to slow enrollment. Considering these problems, an individual meta-analysis redefined the target population as patients with baseline NIHSS (National Institutes of Health Stroke Scale) score ≥ 10 and found EVT strongly associated

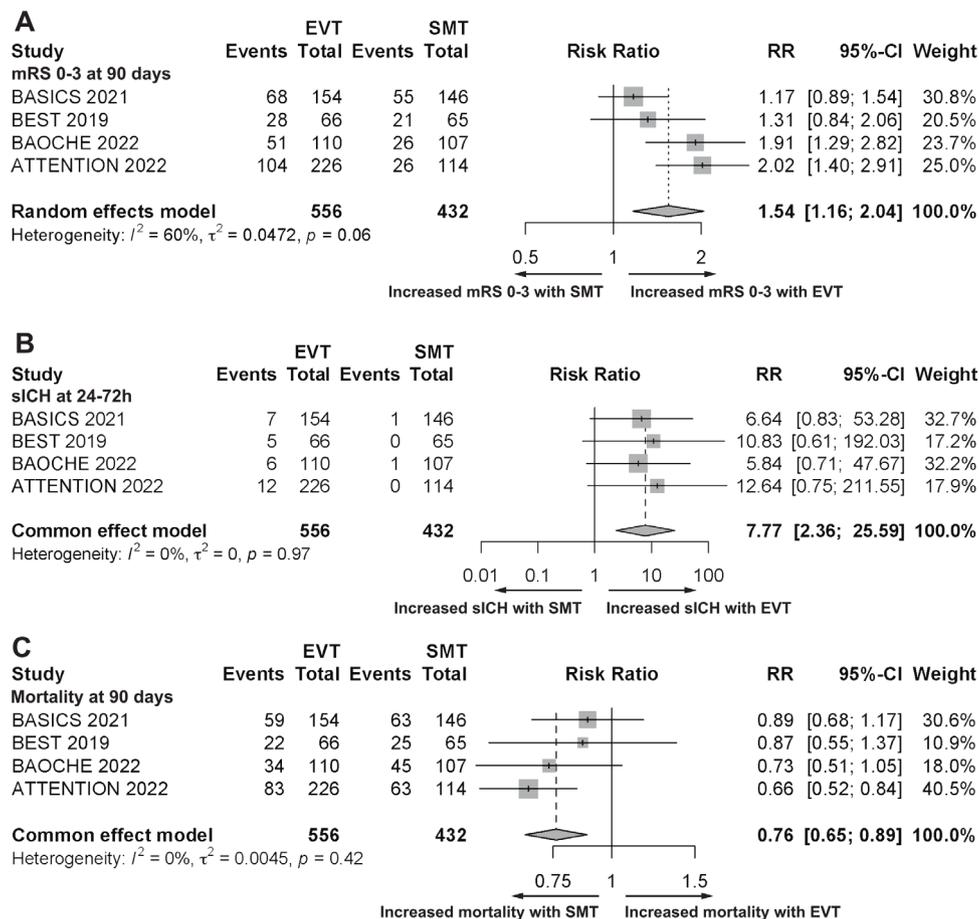


Figure 1 Meta-analysis of the efficacy and safety outcomes of four randomised trials. (A) Forest plot of mRS 0–3 at 90 days; (B) Forest plot of sICH (Heidelberg criteria in the BASICS; SITS-MOST criteria in the ATTENTION and BAOICHE; evidence of intracranial haemorrhage on imaging and an increase of 4 or more points on the NIHSS within 24 hours after randomisation in the BEST); (C) Forest plot of mortality at 90 days. ATTENTION, Endovascular Treatment For acute Basilar Artery Occlusion: A Multicentre Randomised Clinical Trial; BAOICHE, Basilar Artery Occlusion Chinese Endovascular; EVT, endovascular thrombectomy; mRS, modified Rankin Scale; SMT, standard medical treatment; sICH, symptomatic intracerebral haemorrhage.

with favourable clinical outcomes in both intention-to-treat and per-protocol analysis.¹⁵

Previous reports found that the efficacy of EVT might be related to the patients' clinical severity. The ATTENTION and BAOICHE trials, therefore, excluded patients with mild strokes. Both trials followed the protocol strictly so the crossover rates were effectively reduced. The ATTENTION selected 36 high-volume endovascular stroke centres as participating centres, which led to the completion of enrollment within almost 1 year. With the better-designed protocol and good follow-through, the results from ATTENTION and BAOICHE trials could be more persuasive.

Our analysis of the combined trial data further confirmed the benefit of EVT for BAO. Although there was a higher risk of sICH, the EVT might bring better functional outcomes and a lower risk of all-cause mortality at 90 days than the SMT group. These findings can provide more evidence to support EVT for BAO in real-world clinical practice.

However, several limitations in our analysis should be acknowledged. First, the results of two included

RCTs were unpublished and non-peer-reviewed, which may introduce the inherent risk of bias and lack more detailed results of RCTs. Second, high heterogeneity was found in the 90-day clinical outcome measured by mRS. This might be from the different therapeutic time windows defined in these four RCTs, which may affect the percentage of eligible patients for intravenous thrombolysis. Lastly, the BEST, ATTENTION and BAOICHE were restricted to Han Chinese patients, so caution should be exercised when generalising these findings to other ethnic groups.

FUTURE DIRECTIONS

The ATTENTION and BAOICHE trials showed a benefit of EVT for patients with severe symptoms from an acute BAO. However, the strong evidence about EVT for BAO was derived from Chinese Han patients, who had a higher rate of intracranial arterial stenosis than non-Asians. Hence, more RCTs are needed to study the effectiveness and safety in other ethnic groups with BAO.

Meanwhile, the radiographic assessment of posterior circulation stroke (PCS) is relatively poor in comparison with anterior circulation stroke (ACS). Non-contrast CT (NCCT) with CT perfusion (CTP) has been applied to identify ACS patients with salvageable tissue for EVT.⁷ However, the diagnostic utility of CTP and NCCT was limited in PCS due to the influence of blood flow velocity and bony structure of the posterior fossa.¹⁶ The diagnosis of PCS still depends on the diffusion-weighted MRI, which has a lower utilisation in emergency department due to availability issue and a longer scanning time.¹⁷ Therefore, exploring a rapid imaging assessment of PCS remains important.

Furthermore, BAOCHE and ATTENTION mainly enrolled patients with either a baseline NIHSS score ≥ 6 or ≥ 10 . For those outside of this range, EVT still needs more evidence. The subgroup analyses in BASICS and BAOCHE found that patients with a baseline NIHSS score of 10–20 benefited more from EVT.^{10,13} Recent evidence also found no benefit of EVT for patients with severe stroke (NIHSS score ≥ 35).¹⁸ Of note, the successful recanalisation in patients with mild BAO strokes could not guarantee good long-term clinical outcomes since these patients may have other poor predictors such as delay of treatment and other high-risk vascular factors.¹⁹ Therefore, it still remained uncertain for the effectiveness and safety of EVT in BAO patients with mild or severe symptoms. Selecting appropriate individuals for EVT should be implemented in clinical practice.

In summary, our findings demonstrated that EVT may be associated with improved clinical outcomes for selected acute BAO patients when compared with SMT.

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