Endovascular therapy for acute vertebrobasilar occlusion (VERITAS): a systematic review and individual patient data meta-analysis

Raul G Nogueira, Tudor G Jovin*, Xinfeng Liu*, Wei Hu*, Lucianne C M Langezaal, Chuanhui Li*, Qiliang Dai, Chunrong Tao*, Francisco J A Mont'Alverne, Xunming Ji, Rui Liu, Rui Li, Diederik W J Dippel, Chuanjie Wu, Wusheng Zhu, Pengfei Xu, Wim H van Zwam, Longfei Wu, Chao Zhang, Patrik Michel, Jian Chen, Li Wang, Volker Puetz, Wenbo Zhao, Tianlong Liu, Heinrich J Audebert, Zhongjun Chen, Octavio M Pontes-Neto, Tingyu Yi, Timothy P Moran, Mohamed F Doheim, Wouter J Schonewille*, for the ATTENTION, BASICS, BAOCHE, and BEST Investigators*

Summary

Background Trials of endovascular therapy for basilar artery occlusion, including vertebral occlusion extending into the basilar artery, have shown inconsistent results. We aimed to pool data to estimate safety and efficacy and to explore the benefit across pre-specified subgroups through individual patient data meta-analysis.

Methods VERITAS was a systematic review and meta-analysis that pooled patient-level data from trials that recruited patients with vertebrobasilar ischaemic stroke who were randomly assigned to treatment with either endovascular therapy or standard medical treatment alone. We included studies done between Jan 1, 2010, and Sept 1, 2023. The primary outcome was 90-day favourable functional status (modified Rankin Scale [mRS] score 0–3, with a score of 3 indicating moderate disability). Safety outcomes were symptomatic intracranial haemorrhage and 90-day mortality.

Findings We screened 934 titles and abstracts. Of these, seven (<1%) full texts were screened. We included four trials (ATTENTION, BAOCHE, BASICS, and BEST). The pooled data included 988 patients (556 [56%] in the intervention groups and 432 [44%] in the control groups; median age 67 years [IQR 58–74]; 686 (69%) were male and 302 (31%) were female). 904 (91%) patients were randomly assigned within 12 h of estimated stroke onset. Three RCTs were done in a Chinese population and one included European and Brazilian patients. The proportion of patients achieving favourable functional status was higher in the endovascular therapy than control group (90-day mRS score 0–3 in 251 [45%] participants *vs* 128 [30%]; adjusted common odds ratio 2·41 [95% CI 1·78–3·26]; p<0·0001). Endovascular therapy led to an increase in functional independence (mRS score 0–2 in 194 [35%] participants *vs* 89 [21%]; 2·52 [1·82–3·48]; p<0·0001) as well as a reduction in both the degree of overall disability (2·09 [1·61–2·71]; p<0·0001) and mortality (198 [36%] of 556 patients *vs* 196 [45%] of 432; 0·60 [0·45–0·80]; p<0·0001) at 90 days, despite higher rates of symptomatic intracranial haemorrhage (30 [5%] of 548 *vs* two [<1%] of 413; 11·98 [2·82–50·81]; p<0·0001). Heterogeneity of treatment effect was noted for baseline stroke severity (uncertain effect in baseline National Institutes of Health Stroke Scale <10) and occlusion site (greater benefit with more proximal occlusions) but not across subgroups defined by age, sex, baseline posterior circulation Alberta Stroke Program Early CT Score, presence of atrial fibrillation or intracranial atherosclerotic disease, and time from onset to imaging.

Interpretation VERITAS supports the robust benefit of endovascular therapy in patients with vertebrobasilar artery occlusion with moderate to severe symptoms, with approximately 2·5-times increased likelihood of achieving a favourable functional outcome. Despite a significant increase in symptomatic intracranial haemorrhage risk, endovascular therapy for vertebrobasilar artery occlusion was associated with a significant reduction in both overall disability and mortality. Although the benefit of endovascular therapy remains uncertain for patients vertebrobasilar artery occlusion presenting with mild stroke severity and extensive infarcts on neuroimaging, we found a significant clinical benefit across a range of patients with vertebrobasilar artery occlusion.

Funding None.

Published **Online** December 11, 2024 https://doi.org/10.1016/S0140-6736(24)01820-8

See **Online/Comment** https://doi.org/10.1016/S0140-6736(24)02137-8

*Contributed equally

UPMC Stroke Institute, Departments of Neurology and Neurosurgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA (Prof R G Nogueira MD, M F Doheim MD); **Departments of Neurology, Cooper University Healthcare and Cooper Medical School of Rowan University, Camden, NJ, USA** (Prof T G Jovin MD); **Department of Neurology, The First Affiliated Hospital of USTC, Division of Life Science and Medicine, University of Science and Technology of China, Hefei, Anhui, China** (Prof X Liu MD, Prof W Hu MD, C Tao MD, R Li MD, P Xu MD, C Zhang MD, L Wang MD, T Liu MD); **Departments of Radiology, St Antonius Hospital, Nieuwegein, Netherlands** (L C M Langezaal MD); **Stroke Center and Department of Neurology, Xuanwu Hospital of Capital Medical University, China** (C Li MD, C Wu MD, L Wu MD, W Zhao MD); **Department of Neurology, Nanjing Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China** (Prof X Liu, Q Dai MD, R Liu MD, W Zhu MD); **Interventional Neuroradiology Service, Hospital Geral de Fortaleza, Fortaleza, Brazil** (F J A Mont'Alverne MD); **Department of Neurosurgery, Xuanwu Hospital of Capital Medical University, China** (X Ji MD, J Chen MD); **Departments of Neurology,**

Introduction

The overwhelming benefit of endovascular therapy for acute ischaemic stroke due to large vessel occlusion involving the anterior circulation has been shown in large, collaborative meta-analyses of individual patient data derived from randomised clinical trials (RCTs) in both the early and late treatment time windows.[1,2] Although vertebrobasilar artery occlusion (VBAO) accounts for only about 1% of all ischaemic strokes and 5–10% of all proximal intracranial occlusions, it

Erasmus University Medical Center, Rotterdam, Netherlands (Prof D W J Dippel MD); **Departments of Radiology and Nuclear Medicine, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center, Maastricht, Netherlands** (Prof W H van Zwam MD); **Stroke Center, Neurology Service, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland** (Prof P Michel MD); **Department of Neurology and Dresden Neurovascular Center, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, Dresden, Germany** (Prof V Puetz MD); **Department of Neurology and Center for Stroke Research, Charité Universitätsmedizin Berlin, Berlin, Germany** (Prof H J Audebert MD); **Department of Neurointervention, Dalian Municipal Central Hospital, Dalian, China** (Z Chen MD); **Stroke Service, Neurology Division, Department of Neuroscience and Behavioral Sciences, Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil** (Prof O M Pontes-Neto MD); **Department of Neurology, Zhangzhou Affiliated Hospital of Fujian Medical University, China** (T Yi MD); **Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA, USA** (T P Moran PhD); **Department of Neurology, St Antonius Hospital, Nieuwegein, Netherlands** (Prof W J Schonewille MD)

Correspondence to:
Prof Wei Hu, Department of Neurology, The First Affiliated Hospital of USTC Division of Life Science and Medicine, University of Science and Technology of China, Hefei, Anhui 230001, China
andinghu@ustc.edu.cn

or

Prof Wouter J. Schonewille, Department of Neurology, St Antonius Hospital, Koekoekslaan 1, 3435 CM, Nieuwegein, Netherlands
w.schonewille@antoniusziekenhuis.nl

Research in context

Evidence before this study

Endovascular therapy is the gold-standard treatment for eligible patients with acute ischaemic stroke due to large vessel occlusion involving the anterior circulation. However, whether endovascular therapy is beneficial for acute basilar artery occlusion or vertebral occlusion extending into the basilar artery is unclear. The results from two early randomised controlled trials (RCTs), BASICS and BEST, were inconclusive. Several limitations were encountered in these studies including slow recruitment, non-consecutive enrolment, and high crossover rates. Two other randomised trials, ATTENTION and BAOCHE, showed that endovascular therapy can lead to better functional outcomes compared with best medical treatment despite an increased risk of symptomatic intracerebral haemorrhage. In this systematic review and individual patient data meta-analysis, we searched PubMed, Web of Science, EMBASE, and ClincalTrials.gov, using the search terms "stroke", "endovascular", "basilar", "vertebrobasilar", "vertebral", and "posterior circulation" to identify relevant RCTs published between Jan 1,2010, and Sept 1, 2023, with no language restrictions, testing the efficacy of endovascular therapy using modern thrombectomy technology in patients presenting with vertebrobasilar artery occlusion. Although meta-analyses of observational studies and study level meta-analyses of RCTs have been published, we did not identify any patient-level meta-analyses in our search.

Added value of this study

We pooled data to assess the safety and efficacy endovascular therapy for vertebrobasilar artery occlusion and to explore the benefits across pre-specified subgroups through an individual patient-level meta-analysis. This analysis provided accurate overall estimates from all available evidence and showed the expected benefits across different subgroups. We found an approximately 2·5-times higher likelihood of achieving a favourable functional outcome (being able to walk independently) with endovascular therapy compared with standard medical management. Despite a significant increase in risk of symptomatic intracranial haemorrhage, endovascular therapy for vertebrobasilar artery occlusion was associated with a significant increase in functional independence as well as a reduction in both the degree of overall disability and mortality at 90 days. Although the benefit of endovascular therapy remained uncertain for patients presenting with mild stroke severity (baseline National Institutes of Health Stroke Scale score <10), we found a significant clinical benefit across a range of patients in terms of age, baseline infarct burden, level of vertebrobasilar artery occlusion, and time from vertebrobasilar artery occlusion to imaging, as well as for patients eligible and ineligible for intravenous thrombolytics. Because three of the four included trials were done in China and Asians are known to have higher incidence of intracranial atherosclerotic disease, the generalisability of our findings to Western countries needs to be considered. However, subgroup analysis showed significant benefit in patients with and without intracranial atherosclerotic disease as well as in those with and without atrial fibrillation suggesting a retained benefit across various causes of vertebrobasilar artery occlusion.

Implications of all the available evidence

Our study provides evidence to support endovascular therapy in a range of patients with vertebrobasilar artery occlusion. The observed benefit has important implications for clinical practice and health policies, and might result in changes to guidelines. Although the benefit of endovascular therapy remains uncertain for vertebrobasilar artery occlusion patients presenting with mild stroke severity and extensive infarcts on neuroimaging, we found a significant clinical benefit across a range of patients with vertebrobasilar artery occlusion. Most of the patients pooled in this study presented within 12 h of estimated stroke onset.

represents a devastating condition leading to high rates of severe disability and mortality that might exceed 70–80% without appropriate intervention.[3,4] Even though VBAO was one of the first targets for intra-arterial therapy with initial reports dating back to as early as 1983,[5] whether endovascular therapy is beneficial for acute VBAO remains uncertain.

The American Heart Association guidelines updated in 2019 considered endovascular therapy for patients with VBAO strokes to be a reasonable treatment option on the basis of evidence stemming from the observational studies available at the time (Class IIb; Level of Evidence C).[6] The results from two RCTs (Basilar Artery International Cooperation Study[7] [BASICS] and Acute Basilar Artery Occlusion: Endovascular Interventions Versus Standard Medical Treatment[8] [BEST]) for occlusions involving the vertebrobasilar circulation did not show significant differences between endovascular therapy versus best medical management alone. Although these studies had limitations including slow recruitment, lack of consecutive enrolment, high crossover rate, and limited sample size, they helped re-establishing equipoise and thus paved the way for two subsequent trials. The Endovascular Treatment For Acute Basilar Artery Occlusion (ATTENTION) and Basilar Artery Occlusion Chinese Endovascular Trial (BAOCHE) trials randomly assigned patients to endovascular therapy or medical treatment alone within 0–12 h (ATTENTION) and 6–24 h (BAOCHE) from time of estimated VBAO, and showed significantly better functional outcomes with endovascular therapy compared with best medical treatment despite an increased risk of symptomatic intracranial haemorrhage.[9,10]

To provide more precise, inclusive, and powered estimates from these ambiguous results, we—the main investigators from the ATTENTION, BAOCHE, BASICS, and BEST trials—formed the Vertebrobasilar Occlusion

Randomization to Endovascular Reperfusion versus Intravenous Thrombolysis or Medical Treatment Alone Systematic Evaluation (VERITAS) Collaboration. Herein, we report the results of a systematic review and meta-analysis of individual patient data derived from all published randomised controlled trials comparing the safety and efficacy of modern era endovascular therapy versus standard medical therapy in patients VBAO with while also exploring for potential heterogeneity of treatment effect across pre-specified patient subgroups.

Methods

Search strategy and selection criteria

In this systematic review and individual patient data meta-analysis, we searched PubMed, Web of Science, EMBASE, and ClincalTrials.gov, using the search terms "stroke", "endovascular", "basilar", "vertebrobasilar", "vertebral", and "posterior circulation" to identify relevant RCTs published between Jan 1, 2010, and Sept 1, 2023, with no language restrictions, which recruited patients with posterior circulation ischaemic stroke who were randomly assigned to treatment with either endovascular therapy or standard medical treatment alone.

We established the VERITAS collaboration to pool patient level data from included trials. RGN and MFD did the literature searches. MFD, RGN, and TM extracted the data from all individual datasets. MFD and TM cross-checked the data against previous publications. Any conflicts were resolved through consensus in coordination with the lead author (RGN).

Ethics approval for patient inclusion in the RCTs was obtained from each respective trial's participating centres or the central national ethical committees, as reported in the respective publications. All patients or proxies provided informed consent for data collection and usage in the original trials; all data were anonymised before pooling. This study followed a predefined protocol based on the PRISMA guidelines for individual patient data meta-analyses.

Outcomes

The pre-specified primary outcome in this meta-analysis was favourable functional status, defined as a modified Rankin Scale (mRS; ranging from 0 for no residual symptoms to 6 for death, with a score of 3 indicating moderate disability with the ability of walking independently) score of 0–3 at 90 days (–14 to +30 days). Pre-specified secondary outcomes included independent functional outcome, defined as a mRS score of 0–2 denotating functional independence, at 90 days; the distribution of mRS scores towards an improved outcome at 90 days; and stroke severity as measured with the National Institutes of Health Stroke Scale (NIHSS) at 24 h (–6 to +48 h) after stroke onset. We assessed technical efficacy by revascularisation at the end of the endovascular therapy using the modified Thrombolysis in Cerebral Infarction (mTICI) scale with successful revascularisation defined as a score of 2b or 3 (corresponding to reperfusion of at least 50% of the affected vascular territory) as adjudicated by the core laboratory of each individual trial.[14] Safety outcomes were symptomatic intracranial haemorrhage according to the modified Safe Implementation of Thrombolysis in Stroke–Monitoring Study criteria, defined as local or remote parenchymal haemorrhage type 2 (eg, haematoma occupying ≥30% of the infarcted tissue, with obvious mass effect), subarachnoid haemorrhage, or intraventricular haemorrhage on an imaging scan obtained 24–72 h after treatment, combined with a neurological deterioration of at least 4 points from baseline on the NIHSS or from the lowest NIHSS score between baseline and 24 h or leading to death that was deemed causative of the deterioration,[15] and death from any cause within 90 days (–14 to +30 days).

Statistical analysis

Details of the statistical analysis plan are available in the appendix (pp 5–10). The coordinating centre (University of Pittsburgh, PA, USA) established a core data set that includes common variables, definitions, and trial specifications in anticipation of the data merging for the pooled analysis. The team of each trial was contacted to provide the required data, and TM did the statistical analyses for the primary outcome, secondary efficacy outcomes, and safety outcomes. The primary analysis relied on the intention-to-treat (ITT) principle and secondary analyses included the results from the per protocol and the as-treated population. This analysis used a one-stage regression approach for meta-analyses of individual patient data to assess the primary and secondary efficacy outcomes as well as safety outcomes. We also planned to study the heterogeneity of the treatment effects across pre-specified subgroups. To account for between-trial differences, we used mixed-effects modelling for all analyses, with fixed effects for parameters of interest such as treatment assignment. The primary analyses used mixed-effects binary logistic regression to answer the following research question: "do patients with acute ischaemic stroke due to VBAO randomly assigned within 24 h of estimated time of VBAO to randomisation have higher rates of favourable functional status (mRS score 0–3) at 90 days when treated with endovascular therapy compared with standard medical management?" For analyses of the full mRS scores, we report unadjusted and adjusted treatment effects using common odds ratios (cORs) to indicate the odds that the intervention would lead to an improvement of at least 1 point on the mRS in a shift analysis. Missing data for relevant variables are described in the appendix (p 18). We imputed ten complete datasets using fully conditional specification provided multiple imputation by chained equations in R and Rubin's rules were used to pool the estimates across imputation sets.[16,17] The reported estimates were adjusted for age, baseline stroke severity on the NIHSS, baseline posterior circulation Acute Stroke Prognosis Early CT

See Online for appendix

Score (pc-ASPECTS), pre-morbid mRS score, use of intravenous thrombolytics, history of atrial fibrillation, and time from estimated stroke onset to imaging.

We also reported the number needed to treat (NNT) to estimate the overall treatment effect for both mRS scores of 0–3 using crude analysis of 1/absolute risk reduction and adjusted OR following previously described methods.[18] We additionally reported NNT according to the shift in the degree disability at 90 days by calculating the geometric mean of the values derived by the algorithmic joint outcome table method and the permutation test.[19,20]

	Control (n=432)	Endovascular treatment (n=556)	Total (n=988)
Median age, years	67 (58–74)	67 (57–74)	67 (58–74)
Sex			
Male	309/432 (712%)	377/556 (68%)	686/988 (69%)
Female	123/432 (28%)	179/556 (32%)	302/988 (31%)
Baseline NIHSS score	22 (12–35)	22 (14–35)	22 (13–35)
Pre-morbid mRS score	0 (0–0)	0 (0–0)	0 (0–0)
0	355/432 (82%)	469/555 (85%)	824/987 (83%)
1	50/432 (12%)	61/555 (11%)	111/987 (11%)
2	25/432 (6%)	22/555 (4%)	47/987 (5%)
3	2/432 (<1%)	3/555 (1%)	5/987 (1%)
Median pc-ASPECTS	9 (8–10)	9 (8–10)	9 (8–10)
4	1/426 (<1%)	2/544 (<1%)	3/970 (<1%)
5	4/426 (1%)	6/544 (1%)	10/970 (1%)
6	33/426 (8%)	42/544 (8%)	75/970 (8%)
7	51/426 (12%)	57/544 (10%)	108/970 (11%)
8	73/426 (17%)	107/544 (20%)	180/970 (19%)
9	55/426 (13%)	71/544 (13%)	126/970 (13%)
10	209/426 (49%)	259/544 (48%)	468/970 (48%)
Atrial fibrillation	71/432 (16%)	121/556 (22%)	192/988 (19%)
Coronary artery disease	59/431 (14%)	82/556 (15%)	141/987 (14%)
Time to imaging, h	3·81 (1·85–6·75)	3·80 (1·58–6·48)	3·81 (1·69–6·63)
Intravenous thrombolysis	199/432 (46%)	223/556 (40%)	422/988 (43%)
Hypertension	284/430 (66%)	390/556 (70%)	674/986 (68%)
Diabetes	95/432 (22%)	123/555 (22%)	218/987 (22%)
History of stroke	96/432 (22%)	116/556 (21%)	212/988 (21%)
Intracranial atherosclerosis	121/355 (34%)	220/461 (47%)	341/832 (41%)
Cause of stroke			
Cardioembolic	74/418 (18%)	122/548 (22%)	196/966 (20%)
Large artery atherosclerosis	186/418 (44%)	273/548 (50%)	459/966 (48%)
Other or undetermined	158/418 (38%)	153/548 (28%)	311/966 (32%)
Occlusion Site*			
Distal 1/3 BA	110/356 (31%)	137/477 (29%)	247/833 (30%)
Mid 1/3 BA	107/356 (30%)	151/477 (32%)	258/833 (31%)
None	0/356	1/477 (<1%)	1/833 (<1%)
Proximal 1/3 BA	125/356 (35%)	156/477 (33%)	281/833 (34%)
Vertebral	14/356 (4%)	32/477 (7%)	46/833 (6%)

Data are median (IQR), or n/N (%). IVT=intravenous thrombolysis. mRS= modified Rankin scale. NIHSS=National Institutes of Health Stroke Scale. pc-ASPECTS=posterior circulation Acute Stroke Prognosis Early CT Score. *The Acute Basilar Artery Occlusion: Endovascular Interventions Versus Standard Medical Treatment (BEST) trial was excluded as the relevant data were not available.

Table 1: **Baseline characteristics of participants in individual pooled patient data**

We examined the heterogeneity of treatment effect by pre-specified clinically relevant variables on the primary outcome (mRS score 0–3 at 90 days) and the three main secondary outcomes (functional independence and mRS score distribution at 90 days, and 90-day mortality) using a multiplicative interaction term (treatment × pre-specified variable) and mixed methods modelling. Pre-specified variables included age, sex, baseline stroke severity on NIHSS, baseline posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS), pre-morbid mRS, use of intravenous thrombolytics, history of atrial fibrillation, presence of intracranial atherosclerotic disease, level of vertebrobasilar occlusion, and time from estimated stroke onset to imaging. Stratum-specific treatment effects along with the p value for the interaction term were reported graphically using forest plots. Statistical analyses were done using SAS (version 9.4), STATA (version 17) and R (version 4.2.1).

Role of the funding source

There was no funding for this study.

Results

We screened 934 titles and abstracts. Of these, seven (<1%) full texts were screened. We included four studies in the systematic review and meta-analysis: BEST (n=131), BASICS (n=300), ATTENTION (n=340), and BAOCHE (n=217). All trials followed a 1:1 randomisation scheme, with the exception of the ATTENTION trial, which randomly assigned twice as many patients to endovascular therapy as to control (ie, 2:1 randomisation).[9] Notably, we excluded three RCTs that included combined VBAO and anterior circulation patients because of the small number of VBAOs (four patients in Mechanical Thrombectomy After Intravenous Alteplase versus Alteplase Alone After Stroke [THRACE],[11] four patients in Interventional Management of Stroke III [IMS II],[12] and ten patients in Endovascular Acute Stroke Intervention [EASI][13]). Summaries of the design of included RCTs are in the appendix (pp 16–17).

All included trials required imaging confirmation of basilar artery occlusion (with or without involvement of the intracranial vertebral artery). Specifically, patients with isolated vertebral artery occlusion (eg, patent basilar artery) were not included in any of the trials. The definition of time of estimated stroke onset was overall similar across the four trials (appendix pp 16–17), focusing on the onset of acute symptoms leading to the clinical diagnosis of VBAO or, if not known, the time the patient was last known to be at baseline. The BEST and ATTENTION trials did not consider the time of any preceding minor prodromal symptoms and the BAOCHE trial did not consider isolated vertigo as onset time.

The pooled data from the four included trials yielded a total of 988 patients (556 [56%] assigned to endovascular therapy and 432 [44%] assigned to standard medical

treatment alone). The median age of the participants was 67 years (IQR 58–74), 686 (69%) were male, 302 (31%) were female, and 422 (42%) received intravenous thrombolytics (table 1). The median baseline NIHSS score was 22 (13–35) and median pc-ASPECTS was 9 (8–10). The median time from estimated VBAO to imaging was 3·81 h (1·69–6·63), with 904 (91%) patients randomly assigned within 12 h of estimated stroke onset.

Large artery atherosclerosis was thought to be the cause of the VBAO in 459 (48%) of 966 patients, including intracranial atherosclerotic disease in 341 (41%) of 832, whereas 196 (20%) of 966 VBAOs were thought to be cardioembolic in nature, including atrial fibrillation in 192 (19%) of 988 patients (table 1). Baseline characteristics were largely balanced between the populations, but slightly more patients in the endovascular therapy group had atrial fibrillation than in the control group (table 1). Endovascular therapy patients also had lower rates of intravenous thrombolysis than those in the control group (table 1). In individuals assigned to endovascular therapy, successful revascularisation (mTICI scale score 2b or 3) was achieved in 405 (85%) of 475 patients in the ITT analysis and in 417 (84%) of 497 patients in the as-treated population.

In the ITT analysis, the rate of the primary outcome, the proportion of patients with favourable functional status defined as an mRS score of 0–3 at 90 days was higher in the endovascular therapy than in the control group (251 [45%] *vs* 128 [30%]; aOR 2·41 [95% CI 1·78–3·26]; p<0·0001). The NNT for one additional patient to have a favourable functional status was seven on crude estimation and six on adjusted estimation. Likewise, the proportion of patients with an independent functional outcome (mRS score 0–2) at 90 days was higher in the endovascular therapy than in the control group (194 [35%] *vs* 89 [21%]; aOR 2·52 [1·82–3·48]; p<0·0001). Endovascular therapy was associated with a significant reduction in the degree of overall disability at 90 days (adjusted cOR 2·09 [1·61–2·71]; p<0·0001), translating into an NNT for any functional status improvement of three (figure 1).

In the ITT analysis, despite higher rates of symptomatic intracranial haemorrhage at 24–72 h (30 [5%] of 548 *vs* two [<1%] of 413; aOR 11·98 [95% CI 2·82–50·81]; p<0·0001) in the intervention group, endovascular therapy was associated with a reduction in 90-day mortality (198 [36%] of 556 *vs* 196 [45%] of 432; aOR 0·60 [0·45–0·80]; p<0·0001). Details of all pre-specified efficacy and safety outcomes are shown in table 2. Complete case analysis and sensitivity analysis for crossover patients (per protocol and as treated) yielded similar significant results (appendix pp 19–21).

The results of the subgroup analyses for the primary outcome of ITT analysis (mRS score 0–3 at 90 days) are shown in figure 2. We assessed heterogeneity of treatment effect across the pre-specified variables including age, sex, baseline stroke severity on the NIHSS, baseline pc-ASPECTS, pre-morbid mRS score, use of intravenous thrombolytics, history of atrial fibrillation, presence of intracranial atherosclerotic disease, site of vertebrobasilar occlusion, and time from estimated stroke onset to imaging. The direction of effect favoured endovascular therapy across all strata except for NIHSS below 10, although the aORs for treatment were not significant for a pre-morbid mRS score of 2 or more, distal basilar artery occlusion, and those with time from onset to imaging 12 h or more (figure 2). Notably, effects favouring the intervention were significant in several subgroups of special interest,

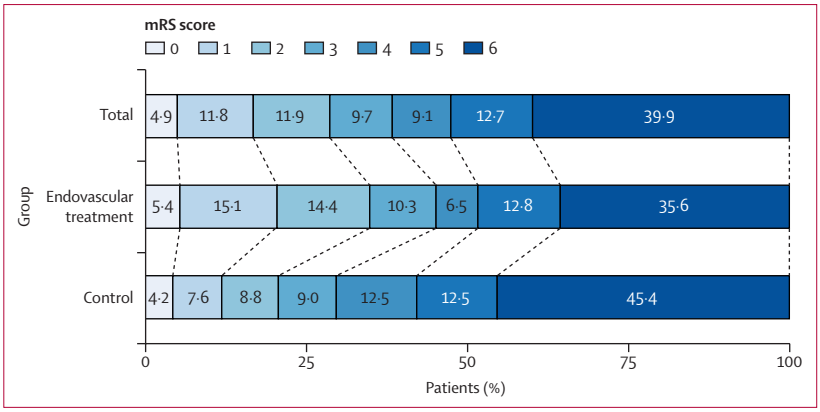

Figure 1: **Distribution of mRS scores at 90 days**
Adjusted for age (years), posterior circulation Acute Stroke Prognosis Early CT Score at baseline, atrial fibrillation, occlusion location based on angiographic imaging at baseline, National Institutes of Health Stroke Scale score at baseline, pre-stroke mRS score, and time from stroke onset to randomisation (minutes). EVT=endovascular treatment. mRS=modified Rankin Scale.

	Control (n=432)	Endovascular treatment (n=556)	Unadjusted odds ratio or mean difference (95% CI)	Adjusted odds ratio or mean difference (95% CI)
Favourable, mRS score ≤3	128/432 (30%)	251/556 (45%)	1·95 (1·50 to 2·55)	2·41 (1·78 to 3·26)
Independent, mRS score ≤2	89/432 (21%)	194/556 (35%)	2·13 (1·58 to 2·86)	2·52 (1·82 to 3·48)
90-day mRS score	..	..	1·65 (1·30 to 2·10)	2·09 (1·61 to 2·71)
0	18/432 (4%)	30/556 (5%)	..	..
1	33/432 (8%)	84/556 (15%)	..	..
2	38/432 (9%)	80/556 (14%)	..	..
3	39/432 (9%)	57/556 (10%)	..	..
4	54/432 (13%)	36/556 (6%)	..	..
5 or 6	250/432 (58%)	269/556 (48%)	..	..
NIHSS score at 24 h	22·0 (14%)	20·4 (14%)	−2·02 (−3·85 to −0·19)	−2·43 (−3·94 to −0·91)
Symptomatic intracranial haemorrhage	2/413 (<1%)	30/548 (5%)	11·90 (2·83 to 50·09)	11·98 (2·82 to 50·81)
90-day mortality	196/432 (45%)	198/556 (36%)	0·66 (0·51 to 0·86)	0·60 (0·45 to 0·80)

Data are n/N (%), unless otherwise indicated. mRS=modified Rankin scale. NIHSS=National Institutes of Health Stroke Scale.

Table 2: **Efficacy and safety outcomes in the pooled data, intention-to-treat population**

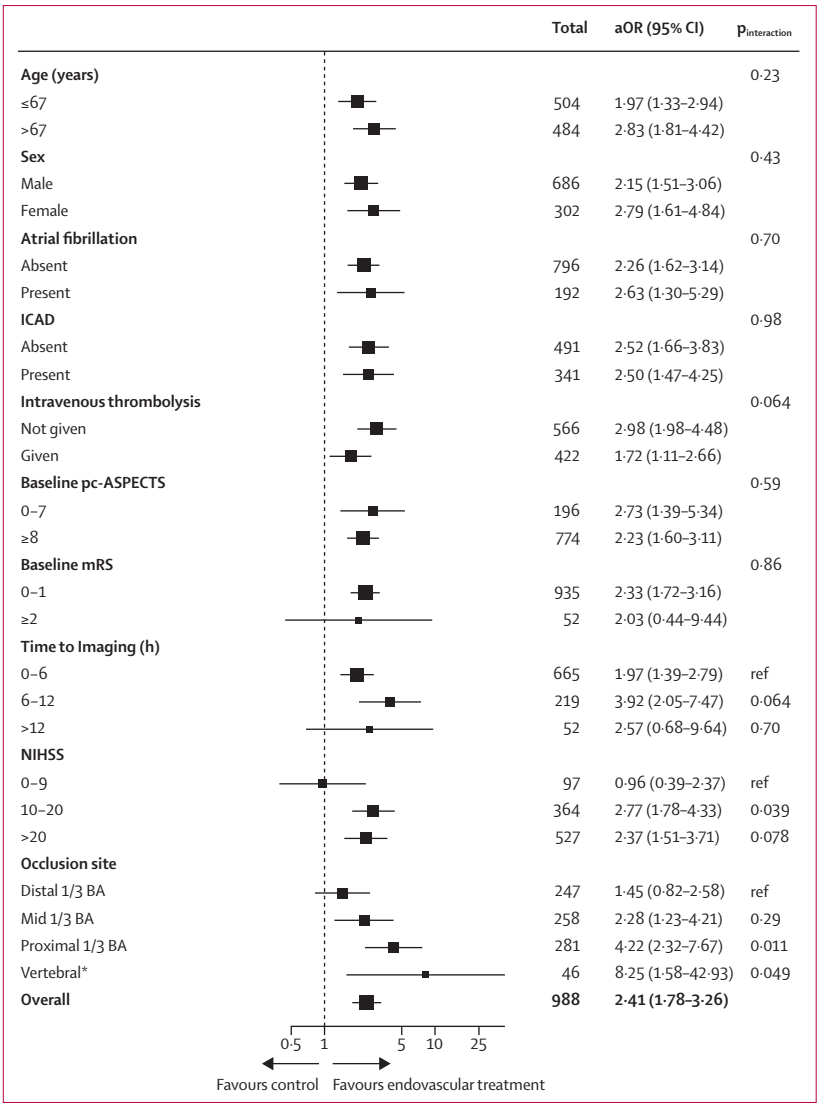

***Figure 2*: Forest plot showing adjusted treatment effect for the primary outcome of favourable functional status (mRS score 0–3) at 90 days in pre-specified subgroups**

Adjusted for age in years, baseline pc-ASPECTS, atrial fibrillation, occlusion location based on angiographic imaging at baseline, baseline NIHSS score, pre-stroke mRS score, and time from stroke onset to imaging (min). p values refer to results of interaction analyses. Time to randomisation was documented for all patients in the BEST, ATTENTION, and BAOCHE trials but was not available for BASICS trial. However, BASICS did not randomly assign any patients beyond 12 h. After the 12-h threshold, BAOCHE randomly assigned 82 patients, and ATTENTION randomly assigned an additional two patients, resulting in a total of 84 out of 988 patients (9%) randomly assigned beyond 12 h. Of these, 48 (9%) of 556 patients were in the endovascular therapy group and 36 (8%) of 432 patients were in the control group. The rates of mRS score 0–3 were 23 (48%) of 48 in the endovascular therapy group versus ten (28%) of 36 in the control group. Time to imaging data were available for 936 patients, with 52 cases missing. Most missing values (48) were from BASICS, and only four were from BAOCHE. Importantly, time to randomisation was recorded for all BAOCHE patients. Among the 936 patients with complete imaging data, 52 (6%) underwent imaging more than 12 h after symptom onset. Specifically for BAOCHE, time-to-imaging analysis revealed that 30 patients had imaging performed within (12 h), despite their time to randomisation being greater than 12 h. An additional two patients missing time to imaging data from BAOCHE had time to randomization greater than 12 h. aOR=adjusted common odds ratio. mRS=modified Rankin Scale. pc-ASPECTS=posterior circulation Acute Stroke Prognosis Early CT Score. NIHSS=National Institutes of Health Stroke Scale. *Vertebral artery occlusions extending into the basilar artery.

including patients with and without intracranial atherosclerotic disease as well as those with and without atrial fibrillation (appendix pp 22–24).

Discussion

This pooled analysis of patient-level data from all major published RCTs (BEST, BASICS, ATTENTION, and BAOCHE) that recruited patients with acute ischaemic strokes due to VBAO who were randomly assigned to receive either modern endovascular therapy or best medical treatment alone within 24 h from time of estimated time of VBAO showed a dramatic benefit of endovascular thrombectomy across various patient subgroups. We planned to only include trials that were published after 2010 to capture studies that incorporated the contemporaneous technology.[21–23] However, by doing so, we have only excluded one small previous randomised trial that used intra-arterial infusion urokinase and was terminated prematurely because of poor recruitment after enrolling only 16 participants.[24] The significant between-studies heterogeneity noted for the primary and secondary outcomes reflects the variation between the four trials in terms of inclusion criteria, number of patients, stroke severity thresholds, duration of the studies, and different treatment windows. Despite this heterogeneity, the benefit of endovascular therapy in acute VBAO was clearly shown. Specifically, we found that, compared with best medical therapy alone, endovascular therapy was associated with an improvement of approximately 2·5 times in the odds of both the primary outcome (mRS score 0–3) as well as functional independence (mRS score 0–2) at 90 days. The reduction in overall disability observed in the VERITAS meta-analysis (90-day mRS score ordinal shift analysis: adjusted cOR 2·09 [95% CI 1·61–2·71]) is within the same range as that observed in the meta-analyses involving patients with anterior circulation large vessel occlusion and small to moderate infarct sizes on presentation (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials [HERMES], which involved early window [0–12-h] patients: 2·49 [1·76–3·53]; and Analysis of Pooled Data from Randomized Studies of Thrombectomy More Than 6 Hours after Last Known Well [AURORA], which involved patients in the extended [6–24 h] window: 2·54 [1·83–3·54]).

Although the absolute risk of symptomatic intracranial haemorrhage with endovascular therapy was similar in the VERITAS (5·5%), HERMES (4·4%), and AURORA (5·3%) meta-analyses, the risk of symptomatic intracranial haemorrhage with medical treatment alone was lower in VERITAS (0·5%) than in HERMES (4·3%) and AURORA (3·3%), suggesting that, by contrast with the anterior circulation, there may be an increase in the likelihood of symptomatic intracranial haemorrhage with endovascular therapy in relation to medical treatment alone in the setting of VBAO. Nonetheless, despite this significant increase in the risk for symptomatic intracranial haemorrhage, endovascular therapy for VBAO was associated with a significant reduction in 90-day mortality, a finding that has not been previously observed with anterior circulation strokes in the HERMES and AURORA meta-analyses.

An important question that remains unanswered relates to the value of endovascular therapy for patients with VBAO in the extremes of severity spectrum. Although many patients with large vessel occlusions involving the posterior circulation present with low NIHSS scores,[25] ATTENTION did not include any patients while BEST only included 19 patients with an NIHSS score below 10. Patients with an NIHSS score below 10 were only added to the BASICS and BAOCHE trials after 91 (30%) of 300 (BASICS) and 61 (28%) of 218 (BOACHE) of their patients had been recruited. Moreover, BAOCHE only included patients with an NIHSS score of at least 6 and the time window in which patients were enrolled did not overlap across the BASICS (0–6 h) and BAOCHE (6–24 h) trials. Not surprisingly, our subgroup analysis for patients presenting with an NIHSS score below 10 was underpowered at only 97 (61 [63%] in BASICS, 17 [18%] in BAOCHE, and 19 [20%] in BEST) patients and showed inconclusive results. In alignment with these findings, the ATTENTION Registry[26] also showed that the effect of endovascular therapy is small in patients with an NIHSS score below 10 on presentation (adjusted risk ratio [aRR] 1·05 [95% CI 0·80–1·38]). There are several possible explanations why patients with milder symptoms might experience a lower treatment effect, including better collateral flow, a lower thrombus burden, non-occlusive thrombus, or more distal basilar thrombi, which might be more responsive to intravenous thrombolysis alone. Indeed, previous evidence suggests that many of these patients might respond reasonably well to acute anticoagulation.[27] Importantly, the NIHSS is strongly weighted toward motor and cortical deficits caused by anterior circulation lesions and thus might underestimate clinical severity in posterior circulation strokes. The Posterior-NIHSS scale adds extra points to the baseline NIHSS for abnormal cough, dysphagia, and gait or truncal ataxia, and might be useful to better identify patients with posterior circulation stroke with an NIHSS score below 10 at increased risk of poor outcome.[28] Of note, all four trials excluded patients with isolated vertebral artery occlusion with patent basilar artery flow through the contralateral vertebral artery. These patients presumably have a more favourable natural history than those included and might do better with medical treatment alone.[29] The optimal management of patients with VBAO with mild symptoms as well as those with isolated vertebral artery occlusions requires further investigation in a randomised controlled setting.

The four included trials differed in their upper age criteria. BEST and ATTENTION had no upper age limit, whereas BAOCHE excluded patients older than 80 years and BASICS excluded patients older than 85 years. In terms of baseline stroke burden, the BASICS and BEST trials only excluded patients with extensive bilateral brainstem infarction, cerebellar mass effect, or acute hydrocephalus on neuroimaging. By contrast, ATTENTION and BAOCHE only included patients with a pc-ASPECTS of at least 6 points among patients younger than 80 years, with ATTENTION also including patients aged 80 years or older with a pc-ASPECTS of at least 8 points. Nonetheless, most of the included patients had favourable neuroimaging with a median pc-ASPECTS of 9 (IQR 8–10) and only 13 (1%) of 970 presented with a pc-ASPECTS of 4–5. With the emerging results supporting endovascular therapy for large infarcts in the anterior circulation,[30–33] future studies should focus on assessing the effect of endovascular therapy in patients with VBAO with low (0–5) pc-ASPECTS.

Three of the four included trials were done in China, with Chinese patients comprising 690 (70%) of all 988 patients. As Asians are known to have increased rates of intracranial atherosclerotic disease, the generalisability of our findings to Western countries needs to be considered. In this context, stroke cause was thought to be related to intracranial atherosclerotic disease in 341 (41%) of 832 patients, with intracranial angioplasty or stenting done in 23 (30%) of 77 patients in BEST, 88 (40%) of 221 in ATTENTION, and 60 (55%) 110 in BAOCHE. In the BASICS trial, stroke cause was thought to be large artery atherosclerosis in 96 (35%) of 278 patients, with angioplasty done in 30 (22%) of 138 and stenting in 23 (17%) of 137. However, the higher prevalence of intracranial atherosclerotic disease is unlikely to have driven the superior results of endovascular therapy since, if anything, angioplasty and stenting are more technically demanding and presumably associated with higher complications than thrombectomy alone. Moreover, subgroup analysis showed no treatment effect modification on the basis of the presence of intracranial atherosclerotic disease and we found a statistically significant benefit in patients with non-intracranial atherosclerotic disease-related VBAOs (n=491; aOR 2·52 [95% CI 1·66–3·83]) as well as those with atrial fibrillation (n=192; 2·63 [1·30–5·29]), suggesting a retained benefit across various VBAO causes.

This meta-analysis has some additional limitations. Because the four trials were done by experienced operators at high-volume centres and higher procedural volumes are associated with better functional outcomes,[34] analyses from large population-based registries are needed to confirm the generalisability of our findings. Fortunately, an increasing number of such studies have been generated.[26,35,36] Even though procedural, imaging, and clinical outcome measures (eg, mTICI scale score, pc-ASPECTS, symptomatic intracranial haemorrhage, and mRS score) were ascertained in a blinded fashion, different core laboratories and interventional approaches were used across the four trials. Despite the large sample size (n=988), the ability to provide adjusted estimates of treatment effect for all the analysed subgroups was limited by the number of patients in each group. Although multiple comparisons inflate the risk of type I error, the analyses for the primary and key secondary outcomes

were all significant at an α level of 0·0001. Therefore, the resulting statistical inferences would be the same even with adjustments for multiple comparisons. Furthermore, the potential for bias was minimised by the pre-specification of the analysis, and the variance in resulting estimates was modelled appropriately by the inclusion of random effects in the statistical models. Some patient populations, particularly those with the largest infarcts at baseline, presenting beyond 24 h from estimated time of VBAO and with substantial pre-stroke disability (mRS score >2), were excluded from all participating trials. Accordingly, our findings cannot be extrapolated to these patient populations. As the study included some trials that were terminated prematurely, the possibility exists of over-estimation of the treatment effect. Conversely, because a high number of patients (28 [7%] controls) crossed over from medical treatment alone to endovascular therapy (14 [22%] of 65 in BEST, seven [5%] of 146 in BASICS, four [4%] of 107 in BAOCHE, and three [3%] of 114 in ATTENTION), a possibility also exists of under-estimation of the treatment effect. There was also a substantial under-representation of female participants (302 [31%] of 988) in our pooled analysis suggesting potential disparities in enrolment and limiting the power of generalisation. However, the subgroup analysis suggested that sex is not a modifier of the results from this analysis.

In conclusion, endovascular therapy within 24 h of VBAO is associated with a significant increase in mRS scores of 0–3 and functional independence as well as a reduction in both the degree of overall disability and mortality at 90 days, despite a significant increase in chances of symptomatic intracranial haemorrhage. Although the benefit of endovascular therapy remains uncertain for patients presenting with mild stroke severity and extensive infarcts on neuroimaging, we have shown a significant clinical benefit across a broad range of VBAO patients.

Contributors

The VERITAS collaboration was conceptualised by RGN, WH, WJS, TGJ, XJ, and XL. RGN prepared the first draft of the report after discussion with all authors on the results from the prespecified analyses. Data collection and study organisation were coordinated by RGN. The prespecified statistical analysis plan was written by MFD, TPM, and RGN, with input from all other authors. Data pooling and statistical analysis were conducted by TPM and MFD, with input from RGN. RGN, MFD, WH, WJS, TGJ, XJ, QD, TPM, and XL accessed and verified the underlying data reported in this manuscript. All authors participated in patient enrolment, data collection, curation of the pooled data, and critically reviewed the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

RGN reports consulting fees for advisory roles with Anaconda, Biogen, Cerenovus, Genentech, Philips, Hybernia, Hyperfine, Imperative Care, Medtronic, Phenox, Philips, Prolong Pharmaceuticals, Stryker Neurovascular, Shanghai Wallaby, and Synchron; and stock options for advisory roles with Astrocyte, Brainomix, Cerebrotech, Ceretrieve, Corindus Vascular Robotics, CrestecBio, Euphrates Vascular, Vesalio, Viz-AI, RapidPulse, and Perfuze. RGN is one of the Principal Investigators of the Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOLOW) trial. Funding for this project is provided by Cerenovus. RGN is the Principal Investigator of the Combined Thrombectomy for Distal Medium Vessel Occlusion Stroke (DUSK) trial. Funding for this project is provided by Stryker Neurovascular. RGN is an investor in Viz-AI, Perfuze, Cerebrotech, Reist/Q'Apel Medical, Truvic, Tulavi Therapeutics, Vastrax, Piraeus Medical, Brain4Care, Quantanosis AI, and Viseon. TGJ is advisor and investor for Anaconda, Route92, Viz.ai, FreeOx, Blockade Medical, and Methinks. He received personal fees in his role on the data and safety monitoring board (DSMB) and steering committee from Cerenovus and on the screening committee for Contego Medical. He received stock as an advisory board member for Corindus. He received grant support for Medtronic and from Stryker Neurovascular in his capacity as principal investigator for DAWN and AURORA. FJAM reports consulting fees from Stryker, Microvention, and Balt. DWJD reports funding from the Dutch Heart Foundation, Netherlands Brain Foundation, the Netherlands Organisation for Health Research and Development, Health Holland Top Sector Life Sciences & Health, Penumbra, Stryker, Medtronic, Thrombolytic Science, and Cerenovus (all unrestricted grants for research), paid to his institution. VP reports payment or honoraria for lectures, presentations or educational events from Boehringer Ingelheim, Daichii Sankyo, AstraZeneca, and Bristol Myers Squibb, and support for attending meetings or travel from NoNo (travel reimbursement). WHvZ reports speaker fees from Stryker, Cerenovus, Microvention, Medtronic, and Nicolab, and consulting fees from Philips, all paid to institution; chaired the DSMBs of WeTrust (Philips) and ANAIS (Anaconda), all paid to his institution. WHvZ chaired the DSMB of InExtremis (CHU Montpellier, Montpellier, France), for which no payment was received. PM reports consulting fees from Medtronic and steering committee fees from Penumbra, all paid to his institution. HJA reports consulting fees (speaker, Advisory Board, and Data Safety Board honoraria) from Boehringer Ingelheim, Roche, and Novo Nordisk. OMP-N reports fees from Bayer, Boehringer Ingelheim, Medtronic, and Pfizer. All other authors declare no competing interests.

Data sharing

Data from the VERITAS collaboration are currently not publicly available but are planned to be made available in the future. A deidentified dataset and data dictionary will be made accessible. The timing of this availability and criteria for gaining access have not yet been determined.

Acknowledgments

The VERITAS collaboration is self-funded. We acknowledge all the respective funding sources of each individual trial (ie, BEST, BASICS, ATTENTION, and BAOCHE) that contributed individual participant data for this study. The authors of the individual trials pooled in this meta-analysis disclosed their funding details in their respective publications.

References

1 Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016; **387:** 1723–31.

2 Jovin TG, Nogueira RG, Lansberg MG, et al. Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (AURORA): a systematic review and individual patient data meta-analysis. *Lancet* 2022; **399:** 249–58.

3 Alemseged F, Nguyen TN, Alverne FM, Liu X, Schonewille WJ, Nogueira RG. Endovascular therapy for basilar artery occlusion. *Stroke* 2023; **54:** 1127–37.

4 Haussen DC, Al-Bayati AR, Mohammaden MH, et al. The Society of Vascular and Interventional Neurology (SVIN) mechanical thrombectomy registry: methods and primary results. *Stroke Vasc Intervent Neurol* 2022; **2:** e000234.

5 Zeumer H, Hacke W, Ringelstein EB. Local intraarterial thrombolysis in vertebrobasilar thromboembolic disease. *AJNR Am J Neuroradiol* 1983; **4:** 401–04.

6 Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019; **50:** e344–418.

7 Langezaal LCM, van der Hoeven EJRJ, Mont'Alverne FJA, et al. Endovascular therapy for stroke due to basilar-artery occlusion. *N Engl J Med* 2021; **384:** 1910–20.

8 Liu X, Dai Q, Ye R, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. *Lancet Neurol* 2020; **19:** 115–22.

9 Tao C, Nogueira RG, Zhu Y, et al. Trial of endovascular treatment of acute basilar-artery occlusion. *N Engl J Med* 2022; **387:** 1361–72.

10 Jovin TG, Li C, Wu L, et al. Trial of thrombectomy 6 to 24 hours after stroke due to basilar-artery occlusion. *N Engl J Med* 2022; **387:** 1373–84.

11 Bracard S, Ducrocq X, Mas JL, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. *Lancet Neurol* 2016; **15:** 1138–47.

12 Broderick JP, Palesch YY, Demchuk AM, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med* 2013; **368:** 893–903.

13 Khoury NN, Darsaut TE, Ghostine J, et al. Endovascular thrombectomy and medical therapy versus medical therapy alone in acute stroke: a randomized care trial. *J Neuroradiol* 2017; **44:** 198–202.

14 Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. *Stroke* 2013; **44:** 2650–63.

15 Wahlgren N, Ahmed N, Dávalos A, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet* 2007; **369:** 275–82.

16 Van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in R. *J Stat Softw* 2011; **45:** 1–67.

17 Rubin DB. Multiple imputation for nonresponse in surveys. John Wiley & Sons, 2004.

18 Bender R, Kuss O, Hildebrandt M, Gehrmann U. Estimating adjusted NNT measures in logistic regression analysis. *Stat Med* 2007; **26:** 5586–95.

19 Howard G, Waller JL, Voeks JH, et al. A simple, assumption-free, and clinically interpretable approach for analysis of modified Rankin outcomes. *Stroke* 2012; **43:** 664–69.

20 Saver JL, Gornbein J, Grotta J, et al. Number needed to treat to benefit and to harm for intravenous tissue plasminogen activator therapy in the 3- to 4·5-hour window: joint outcome table analysis of the ECASS 3 trial. *Stroke* 2009; **40:** 2433–37.

21 Nogueira RG, Lutsep HL, Gupta R, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. *Lancet* 2012; **380:** 1231–40.

22 Saver JL, Jahan R, Levy EI, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet* 2012; **380:** 1241–49.

23 Pereira VM, Gralla J, Davalos A, et al. Prospective, multicenter, single-arm study of mechanical thrombectomy using Solitaire Flow Restoration in acute ischemic stroke. *Stroke* 2013; **44:** 2802–07.

24 Macleod MR, Davis SM, Mitchell PJ, et al. Results of a multicentre, randomised controlled trial of intra-arterial urokinase in the treatment of acute posterior circulation ischaemic stroke. *Cerebrovasc Dis* 2005; **20:** 12–17.

25 Heldner MR, Zubler C, Mattle HP, et al. National Institutes of Health stroke scale score and vessel occlusion in 2152 patients with acute ischemic stroke. *Stroke* 2013; **44:** 1153–57.

26 Tao C, Qureshi AI, Yin Y, et al. Endovascular treatment versus best medical management in acute basilar artery occlusion strokes: results from the ATTENTION multicenter registry. *Circulation* 2022; **146:** 6–17.

27 Schonewille WJ, Wijman CA, Michel P, 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:** 724–30.

28 Alemseged F, Rocco A, Arba F, et al. Posterior National Institutes of Health Stroke Scale improves prognostic accuracy in posterior circulation stroke. *Stroke* 2022; **53:** 1247–55.

29 Salerno A, Michel P, Strambo D. Revascularization of arterial occlusions in posterior circulation acute ischemic stroke. *Curr Opin Neurol* 2024; **37:** 26–31.

30 Yoshimura S, Sakai N, Yamagami H, et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med* 2022; **386:** 1303–13.

31 Sarraj A, Hassan AE, Abraham MG, et al. Trial of endovascular thrombectomy for large ischemic strokes. *N Engl J Med* 2023; **388:** 1259–71.

32 Huo X, Ma G, Tong X, et al. Trial of endovascular therapy for acute ischemic stroke with large infarct. *N Engl J Med* 2023; **388:** 1272–83.

33 Bendszus M, Fiehler J, Subtil F, et al. Endovascular thrombectomy for acute ischaemic stroke with established large infarct: multicentre, open-label, randomised trial. *Lancet* 2023; **402:** 1753–63.

34 Nogueira RG, Haussen DC, Smith EE, et al. Higher procedural volumes are associated with faster treatment times, better functional outcomes, and lower mortality in patients undergoing endovascular treatment for acute ischemic stroke. *Ann Neurol* 2024; **95:** 146–55.

35 Zi W, Qiu Z, Wu D, et al. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. *JAMA Neurol* 2020; **77:** 561–73.

36 Dicpinigaitis AJ, Dick-Godfrey R, Gellerson O, et al. Real-world outcomes of endovascular thrombectomy for basilar artery occlusion: results of the BArONIS study. *Ann Neurol* 2023; **94:** 55–60.