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REVIEW

Percutaneous transluminal angioplasty and/or stenting for the treatment of basilar artery stenosis: a systematic review and meta-analysis

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Abstract

Purpose Basilar artery stenosis (BAS) carries high morbidity and mortality, with variable outcomes after endovascular treatments. We systematically reviewed the literature on percutaneous transluminal angioplasty and/or stenting (PTAS) for BAS.

Methods PubMed, EMBASE, Web-of-Science, Scopus, and Cochrane were searched upon the PRISMA guidelines to include prospective/retrospective cohort studies describing PTAS for BAS. Pooled rates of intervention-related complications and outcomes were analyzed with random-effect model meta-analyses.

Results We included 25 retrospective cohort studies comprising 1016 patients. All patients were symptomatic, presenting with transient ischemic attack or ischemic stroke. BAS frequently involved the middle basilar artery (51.4%), mostly classified as Mori-B (57.4%). PTAS for BAS was indicated in severe (≥ 50–70%), symptomatic BAS refractory to dual antiplatelet therapy. Patients underwent angioplasty (95.5%) and/or stenting (92.2%), preferably using Wingspan or Apollo stents. Median baseline BAS was 81% (range, 53–99%), while median post-intervention BAS was 13% (0–75%). Actuarial rates of successful intervention and "good" final outcome were 100% (95% CI: 100–100%) and 89% (95% CI: 85–93%). Intervention-related recurrent ischemic stroke occurred in 85 patients (8.3%) with actuarial rates of 5% (95% CI: 4–7%), differentiated into perforator (5.4%), in-stent (2.6%), and embolic (0.4%). Actuarial rates of intervention-related dissection, restenosis, and death were 0% (95% CI: 0–0%), 1% (95% CI: 0–1%), and 0% (95% CI: 0–2%).

Conclusion Elective PTAS appears to be safe and effective in selected patients with medically refractory, severe, symptomatic, and non-acute BAS. Different stent types and angioplasty-assisted procedures should be considered based on specific clinico-radiological characteristics of the lesions. Future randomized controlled trials are required to corroborate these findings.

Keywords Basilar artery stenosis · Intracranial atherosclerosis · Percutaneous angioplasty and stenting · Posterior circulation ischemia · Stroke

Introduction

Posterior circulation ischemia (PCI) comprises approximately the 20–25% of all ischemic strokes, with estimated 1-month death rates of 3.6–11% [1–3]. Intracranial atherosclerosis (ICAS) represents one leading cause, with higher risks of recurrent PCIs in vertebrobasilar stenosis compared to the risks of recurrent anterior circulation infarction in carotid stenosis [4]. The increasing incidence of risk factors and ICAS occurrence, coupled with the significant economic and social impact of ICAS-related complications, demands standardized prevention protocols [5].

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While endarterectomy and intracranial-extracranial bypass may be considered for anterior circulation ICAS, their implementation in vertebrobasilar stenosis is deterred by the major technical difficulties and high complication rates [6]. Current management for basilar artery stenosis (BAS) consists of aggressive medical therapy, combining dual antiplatelet therapy with risk factor control, and percutaneous transluminal angioplasty and/or stenting (PTAS). The SAMMPRIS [7] and VISSIT [8] trials observed higher-than-expected rates of recurrent 30-day strokes after PTAS compared to aggressive medical therapy, but they did not report distinct post hoc analyses for BAS. Despite the high risks of PTAS-related peri-interventional complications, the poor natural history of BAS frequently necessitates PTAS for medical-refractory cases to prevent long-term recurrent strokes.

Rates of outcomes and complications after PTAS for BAS largely vary across published series, preventing a clear definition of optimal indications and impact on prognoses [9–11]. We comprehensively summarized the literature on PTAS for BAS, focusing on indications, protocols, outcomes, and complications.

Methods

Literature search

A systematic review was performed upon the PRISMA guidelines [12]. PubMed, EMBASE, Scopus, Web-of-Science, and Cochrane were searched from database inception to April 30, 2022, using the search query: [(basilar OR vertebrobasilar) AND (stenting OR stent OR endovascular OR angioplasty) AND (occlusion OR stenosis OR atherosclerosis OR insufficiency)]. Studies were exported to Mendeley, and duplicates were removed.

Study selection

Pre-defined inclusion and exclusion criteria were set. Retrospective or prospective cohort studies written in English were included if they (1) involved ≥ 5 patients diagnosed with non-acute ICAS-related BAS (i.e., ≥ 24 h following the ischemic event) and treated with PTAS, as reported by the authors and (2) reported data on intervention protocols and post-intervention outcomes. Studies were excluded if they (1) were reviews, letters, editorials, or conference abstracts; (2) involved patients with BAS from different etiologies; (3) involved patients with basilar artery occlusion; and (4) did not differentiate patients with BAS from patients with vertebral artery stenosis (VAS) or with anterior circulation stenosis.

Two reviewers independently screened titles and abstracts of all collected articles, and then evaluated full-texts of studies meeting the inclusion criteria. Any disagreements at both stages of screening were resolved by discussion between the reviewers. Eligible articles were included and references were searched to retrieve additional relevant studies.

Data extraction

Data were extracted by one reviewer and then confirmed by one additional reviewer. Missing data from the included studies were not reported by the authors. Extracted data included authors, year, cohort size, age, gender, risk factors, clinical presentation (i.e., transient ischemic attack (TIA) or stroke), stenosis location, Mori classification, intervention protocol (i.e., access, angioplasty and/or stenting, angioplasty-assisted stenting protocol, and type of stent), degree of BAS at baseline and post-intervention, intervention-related complications, follow-up, restenosis, final outcome at last follow-up, and survival status. Based on location at angiography, lesions involved the distal third, middle third, or proximal third of the basilar artery (BA), or the vertebrobasilar junction. Based on the Mori classification, lesions were categorized as type-A, if ≤ 5 mm in length, concentric, or moderately eccentric; type-B, if 5–10 mm in length, tubular, and extremely eccentric; and type-C, if ≥ 10 mm in length, diffuse, and extremely angulated (> 90°) with excessive tortuosity of the proximal segment (Fig. 1) [13]. Post-intervention ischemic strokes are defined as PCI events occurring within 30 days after the intervention. Successful intervention defined angiographically confirmed post-intervention reduction of BAS by ≥ 30% or ≥ 50%, as explicitly pre-determined by the authors. In patients with successful intervention, restenosis was defined as ≥ 50% BAS diagnosed at last available follow-up. In patients with successful intervention, final outcomes were collected as reported across the included studies and differentiated as (1) "good," in case of improvement or complete return to patient's normal neurological status as before the ischemic event, with full functional independence in activities of daily living (ADL); (2) "stable," in case of persisting neurological deficits and no worsening of patients' neurological status compared to their initial hospitalization, with partial dependence in ADLs; (3) "poor," in case of worsening of patients' neurological status compared to their initial hospitalization, with full dependence in ADLs; and (4) "dead," in case of death related to post-intervention complications. Data on post-intervention outcomes and complications were collected at last available follow-up after a minimum of 6-month post-intervention follow-up.

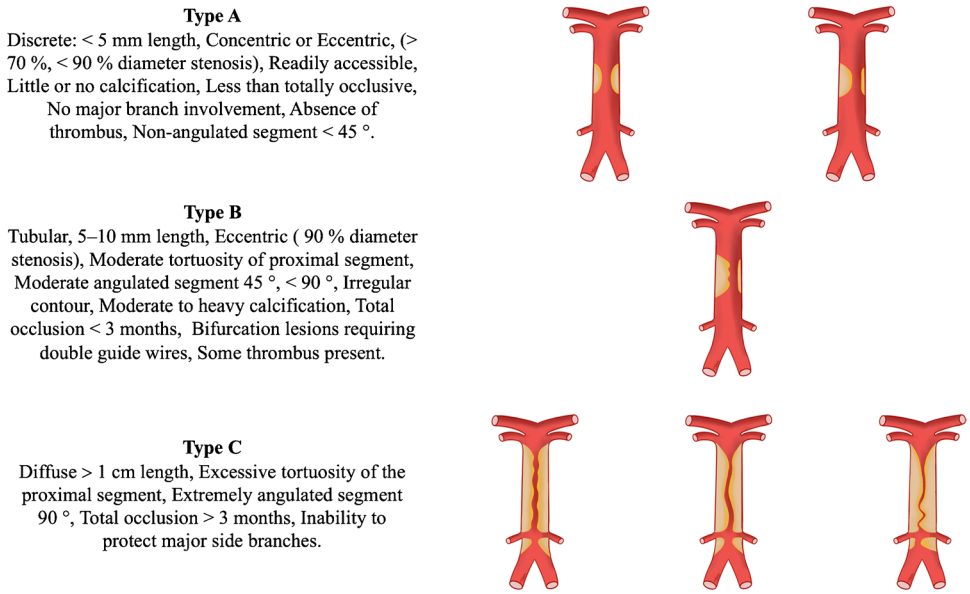


Fig. 1 Modified Mori classification [13] of atherosclerotic stenotic lesions involving the basilar artery, selectively excluding complete basilar artery occlusion

Data synthesis and quality assessment

The objective of this review was to comprehensively summarize and describe the role of PTAS in BAS. The primary outcomes of interest were intervention-related outcomes and complications after PTAS for BAS. For each article, level of evidence was independently evaluated by two reviewers upon the 2011 Oxford Centre For Evidence-Based Medicine guidelines, and risk of bias was assessed using the JBI checklists [14, 15]. This review's overall risk of bias was appraised by considering the risk of bias of all included studies in aggregate.

Statistical analysis

STATA 17.0 (StataCorp LLC, College Station, TX, USA) was used, and bilateral p-values < 0.05 were considered statistically significant. Continuous variables are summarized as medians and ranges, while categorical variables as frequencies and percentages based on the number of patients with available information and weighted to the number of cases presented in each included study. Indirect meta-analyses were conducted for rates of intervention-related success, ischemic stroke, dissection, restenosis, death, and good final outcome. Separate meta-analyses were conducted only for studies published after 2006, which marks the introduction of important patents of stent-delivery balloon catheters with improved stent retention [16]. Forest plots were computed to present outcomes reported with pooled proportions of events (effect size (ES) or actuarial rates) and 95% confidence intervals (CI), estimated using the Wilson score method [17]. Actuarial rates were calculated in proportion to the weight of each study's cohort size, differing from pooled "numerical rates" [18]. The Freeman-Tukey transformation was used to include studies with 0 or 1 event rate and to stabilize variance [19]. The random-effect model was operated based on the DerSimonian and Laird approach to account for between-study variability [20]. While the fixed-effect models assume that all studies share the same true effect, the random-effect models assume that each study estimates different underlying true effects due to various potential between-study differences. The Higgins I-square (I^2) test was used to evaluate between-study heterogeneity, with $I^2 > 75\%$ considered statistically significant [21]. Funnel plots were generated to evaluate publication bias, defined by any evident visual asymmetry. The Mann–Whitney test was used to appraise between-study differences in outcomes and complication rates based on their different cohort sizes.

Results

Study selection

Figure 2 illustrates the literature screening. Twenty-five retrospective cohort studies were included, categorized as level IIB of evidence (Table 1) [9–11, 22–43]. Most studies were conducted in China (9, 36%) or in the USA (8, 32%). Quality assessment returned low risk of bias for all studies (Supplementary File 1), predisposing this review to an overall low risk of bias. No evident visual asymmetry could be detected on the generated funnel plots, excluding publication bias (Supplementary Files 2 and 3).

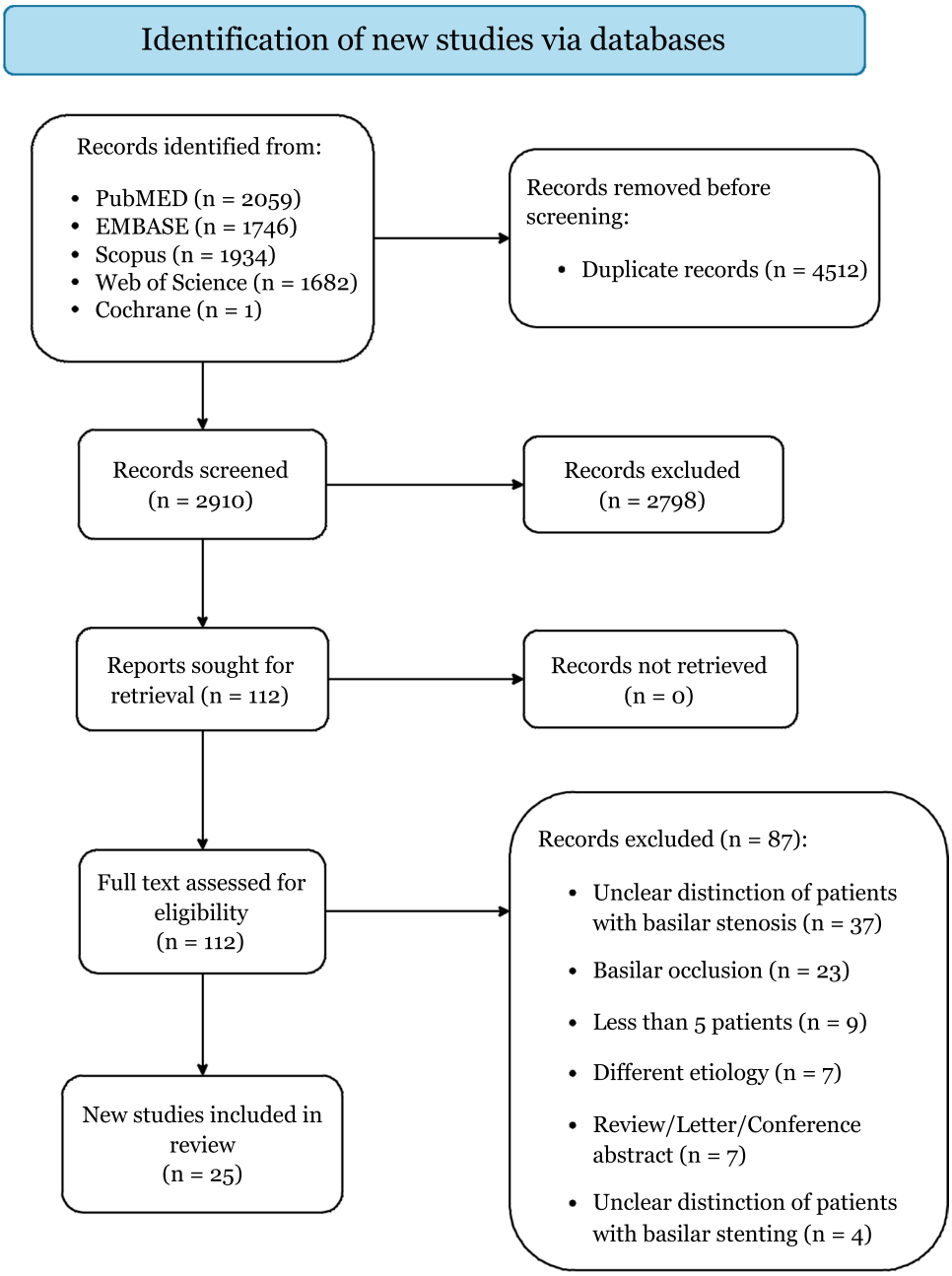


Fig. 2 PRISMA 2020 flow diagram

Clinical and radiological characteristics

A total of 1016 patients were included (Table 2). Across patients with available data on atherosclerosis risk factors ($n = 716$), hypertension was the most common ICAS-related risk factor (81.1%), followed by dyslipidemia (56.4%) and tobacco smoking (50.6%). All patients were symptomatic, presenting with TIA or ischemic stroke. Lesions most frequently involved the BA (98%) in the middle (111/216 cases, 51.4%) or proximal (98/216 cases, 45.4%) segments, and occurred in the vertebrobasilar junction only in 20 cases (2%). In patients with available data ($n = 204$), BAS were mostly classified as Mori type-B (57.4%).

Intervention protocols

All included studies reported that PTAS was performed 48–72 h after the occurrence of BAS-related ischemic events and patients' clinical manifestation of posterior cerebral circulation-related neurological deficits. The most common eligibility criteria for PTAS in BAS were (1) clinical presentation referred to PCIs and (2) severe symptomatic BA stenosis (≥ 50%) refractory to dual antiplatelet therapy. Patients

Table 1 Overview of all included studies

Authors–year (country)	Journal	Patient no./male	Age years Median (range)	Location No. of patients (percentage)	Stenosis at baseline Median (range)	Angioplasty/stenting No. of patients (percentage)	Type of stent No. of patients (percentage)	Success No. of patients (percentage)	Stenosis after treatment Median (range)	Post-intervention Ischemic stroke No. of patients (percentage)	Post-intervention Dissection No. of patients (percentage)	Re-stenosis No. of patients (percentage)	Other complications No. of patients (percentage)	Final outcome No. of patients (percentage)	Follow-up months Median (range)	Alive No. of patients (percentage)
Gomez et al.–2000 [22] (USA)	Stroke	12/10 (83.3%)	66 (40–82)	BA 10 (83.3%) VBJ 2 (16.7%)	74% (53–90%)	12 (100%)/12 (100%)	Duet 9 (75%) GFX 2 (16.7%) Microstent-II 1 (8.3%)	12 (100%)	7% (0–36%)	In-stent 1 (8.3%)	0 (0%)	1 (8.3%)	TIA 2 (16.7%)	Good 12 (100%)	4.5 (0.5–16)	12 (100%)
Sheikh et al.–2000 [23] (Saudi Arabia)	Interventional Neuroradiology	15/13 (86.7%)	N/A	BA 15 (100%)	≥ 70%	15 (100%)/0 (0%)	N/A	14 (93.3%)	25% (0–30%)	0 (0%)	2 (13.3%)	2 (13.3%)	SAH 1 (6.7%)	Good 14 (93.3%) Poor 1 (6.7%)	6	15 (100%)
Woolfenden et al.–2000 [24] (USA)	Journal of Stroke and Cerebrovascular Diseases	6/4 (66.7%)	71.5 (51–82)	BA 5 (83.3%) VBJ 1 (16.7%)	92.5% (77–99%)	6 (100%)/0 (0%)	N/A	6 (100%)	55% (15–75%)	0 (0%)	0 (0%)	0 (0%)	SAH 1 (6.7%) Death 1 (6.7%)	Good 4 (66.7%) Poor 1 (16.7%) Dead 1 (16.7%)	16 (0.1–59)	5 (83.3%)
Levy et al.–2001 [25] (USA)	Neurosurgery	8/8 (100%)	63.5 (43–77)	BA 8 (100%)	N/A	8 (100%)/8 (100%)	AVE 4 (50%), ACS 2 (25%), NIR 2 (25%)	5 (62.5%)	N/A	Perforator 1 (12.5%)	1 (12.5%)	1 (12.5%)	Death 3 (37.5%)	Good 5 (62.5%) Dead 3 (37.5%)	4.5 (0.5–8)	5 (62.5%)
Gress et al.–2002 [26] (USA)	Neurosurgery	15/N/A	62 (50–87)	VBJ 9 (60%) BA 6 (40%)	N/A	15 (100%)/0 (0%)	N/A	15 (100%)	N/A	Perforator 2 (13.3%)	1 (6.7%)	0 (0%)	Death 1 (6.7%)	Good 13 (86.7%) Poor 1 (6.7%) Dead 1 (6.7%)	6	14 (93.3%)
Levy et al.–2002 [27] (USA)	Journal of Neurosurgery	7/7 (100%)	69 (52–90)	BA 4 (57.1%) VBJ 3 (42.9%)	77% (65–90%)	7 (100%)/7 (100%)	N/A	6 (85.7%)	30% (20–60%)	0 (0%)	1 (14.3%)	0 (0%)	RPH 1 (14.3%)	Good 5 (71.4%) Poor 2 (28.6%)	24 (0.1–37)	5 (71.4%)
Levy et al.–2003 [29] (USA)	Journal of Neurosurgery	10/7 (70%)	77 (52–82)	BA 8 (80%) VBJ 2 (20%)	72% (58–83%)	10 (100%)/10 (100%)	Velocity (3), AVE INR, GFX, Maverick, S7, Neurolink, S540, S670,	10 (100%)	20% (10–30%)	Perforator 2 (20%)	0 (0%)	0 (0%)	TIA 1 (10%)	Good 6 (60%) Poor 4 (40%)	11.5 (2–42)	8 (80%)

Table 1 (continued)

Authors–year (country)	Journal	Patient no./male	Age years Median (range)	Location No. of patients (percentage)	Stenosis at baseline Median (range)	Angioplasty/stenting No. of patients (percentage)	Type of stent No. of patients (percentage)	Success No. of patients (percentage)	Stenosis after treatment Median (range)	Post-intervention Ischemic stroke No. of patients (percentage)	Post-intervention Dissection No. of patients (percentage)	Re-stenosis No. of patients (percentage)	Other complications No. of patients (percentage)	Final outcome No. of patients (percentage)	Follow-up months Median (range)	Alive No. of patients (percentage)
Tsuura et al.–2004 [30] (Japan)	Interventional Neuroradiology	6/3 (50%)	64 (57–74)	BA 6 (100%)	85% (70–90%)	6 (100%)/2 (33.3%)	N/A	6 (100%)	10% (10–50%)	0 (0%)	0 (0%)	1 (16.7%)	0 (0%)	Good 5 (83.3%) Poor 1 (16.7%)	12	6 (100%)
Guimaraens et al.–2005 [28] (Spain)	Rivista di Neuroradiologia	8/7 (87.5%)	69 (54–75)	BA 8 (100%)	80%	8 (100%)/8 (100%)	Velocity or INX	8 (100%)	7.5% (5–10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	Good 8 (100%)	6	8 (100%)
Kim et al.–2005 [31] (Korea)	American Journal of Neuroradiology	6/4 (66.7%)	61.5 (58–69)	BA 6 (100%)	82% (59–90%)	6 (100%)/6 (100%)	S670 2 (33.3%), Jo flex 2 (33.3%), Cypher 1 (16.7%), S660 1 (16.7%)	6 (100%)	0% (0–5%)	In-stent 1 (16.7%)	0 (0%)	2 (33.3%)	TIA 1 (16.7%)	Good 5 (83.3%) Poor 1 (16.7%)	17 (6–45)	6 (100%)
Weber et al.–2005 [32] (Germany)	European Journal of Radiology	9/8 (88.9%)	70 (36–78)	BA 9 (100%)	95% (90–95%)	9 (100%)/9 (100%)	INX 9 (100%)	9 (100%)	0% (0–20%)	In-stent 2 (22.2%)	0 (0%)	0 (0%)	0 (0%)	Stable 7 (77.8%) Dead 2 (22.2%)	9 (3–17)	7 (77.8%)
Yu et al.–2005 [33] (USA)	Neurology	18/15 (83.3%)	69 (54–82)	BA 18 (100%)	80% (65–95%)	18 (100%)/18 (100%)	N/A	18 (100%)	0% (0–30%)	Perforator 2 (11.1%)	1 (5.6%)	1 (5.6%)	TIA 3 (16.7%)	Good 17 (94.4%) Poor 1 (5.6%)	27 (12–40)	16 (88.9%)
Abruzzo et al.–2007 [34] (USA)	American Journal of Neuroradiology	10/8 (80%)	68 (50–83)	BA 10 (100%)	80% (67–95%)	10 (100%)/10 (100%)	PRIMO, Tristar, GFX, S670, S7	10 (100%)	22% (0–43%)	Perforator 4 (40%)	1 (10%)	1 (10%)	P-BA 1 (10%)	Good 3 (30%) Stable 5 (50%) Poor 1 (10%) Dead 1 (10%)	33 (0.5–46)	9 (90%)
Jiang et al.–2007 [35] (China)	Neurology	38/30 (78.9%)	60 (48–73)	BA 38 (100%)	75% (60–90%)	38 (100%)/38 (100%)	BiodivYsio or Apollo	35 (92.1%)	23% (0–60%)	In-stent 5 (13.2%)	0 (0%)	N/A	0 (0%)	Good 33 (86.8%) Poor 3 (7.9%) Dead 2 (5.3%)	27 (6–48)	36 (94.7%)
Steinfort et al.–2007 [36] (Australia)	Journal of Neurosurgery	5/5 (100%)	55 (44–72)	BA 5 (100%)	60% (60–85%)	5 (100%)/5 (100%)	Taxus (paclitaxel) 5 (100%)	5 (100%)	0% (0–10%)	Embolic 1 (20%) Perforator 1 (20%)	1 (20%)	0 (0%)	0 (0%)	Good 4 (80%) Poor 1 (20%)	6 (3–16)	5 (100%)

Table 1 (continued)

Authors–year (country)	Journal	Patient no./male	Age years Median (range)	Location No. of patients (percentage)	Stenosis at baseline Median (range)	Angioplasty/stenting No. of patients (percentage)	Type of stent No. of patients (percentage)	Success No. of patients (percentage)	Stenosis after treatment Median (range)	Post-intervention Ischemic stroke No. of patients (percentage)	Post-intervention Dissection No. of patients (percentage)	Re-stenosis No. of patients (percentage)	Other complications No. of patients (percentage)	Final outcome No. of patients (percentage)	Follow-up months Median (range)	Alive No. of patients (percentage)
Ralea et al.–2008 [37] (France)	European Neurology	7/5 (71.4%)	66 (57–73)	BA 7 (100%)	80% (70–90%)	7 (100%)/7 (100%)	Tsunami, INX, Cérébrence	7 (100%)	N/A	0 (0%)	0 (0%)	0 (0%)	ICH 1 (14.3%)	Good 7 (100%)	15 (6–18)	7 (100%)
Jiang et al.–2010 [38] (China)	Journal of NeuroInterventional Surgery	69/64 (92.8%)	59	BA 69 (100%)	81%	69 (100%)/69 (100%)	Wingspan or Apollo	65 (94.2%)	21%	Perforator 9 (13%) In-stent 4 (5.8%)	0 (0%)	4 (5.8%)	ICH 2 (2.9%)	N/A	23 (1–48)	66 (95.6%)
Li et al.–2012 [39] (China)	Cardiovascular Interventional Radiology	17/13 (76.5%)	59 (40–68)	BA 14 (82.3%) VBJ 3 (17.7%)	85% (73–99%)	17 (100%)/17 (100%)	Wingspan 17 (100%)	17 (100%)	10% (0–25%)	Perforator 2 (11.8%)	3 (17.6%)	2 (11.8%)	0 (0%)	Good 15 (88.2%) Poor 2 (11.8%)	18 (5–40)	17 (100%)
Bai et al.–2016 [40] (China)	Interventional Neuroradiology	91/66 (72.5%)	61 (41–82)	BA 91 (100%)	82%	91 (100%)/91 (100%)	Wingspan 91 (100%)	91 (100%)	16%	Perforator 8 (8.8%) In-stent 4 (4.4%)	0 (0%)	6 (6.6%)	0 (0%)	Good 83 (91.2%) Poor 7 (7.7%) Dead 1 (1.1%)	31 (7–60)	90 (95.7%)
Liu et al.–2016 [41] (China)	Clinical Neurology and Neurosurgery	52/42 (80.8%)	59	BA 52 (100%)	84%	52 (100%)/52 (100%)	Apollo 30 (57.7%) Wingspan 22 (42.3%)	49 (94.2%)	7%	Perforator 3 (5.8%)	0 (0%)	0 (0%)	N/A	N/A	1	52 (100%)
Jia et al.–2017 [9] (China)	Journal of NeuroInterventional Surgery	255/208 (81.6%)	60	BA 255 (100%)	N/A	255 (100%)/216 (100%)	Wingspan 123 (56.9%) Apollo 93 (43.1%)	255 (100%)	N/A	Perforator 13 (5.1%) In-stent 2 (0.8%)	6 (2.3%)	0 (0%)	ICH 3 (1.2%) SAH 2 (0.8%)	N/A	3	N/A
Maier et al.–2018 [10] (Germany)	Clinical Neuroradiology	79/60 (75.9%)	70	BA 79 (100%)	N/A	79 (100%)/79 (100%)	Apollo 63 (79.7%) Wingspan 16 (20.3%)	79 (100%)	N/A	Embolic 3 (3.8%) Perforator 3 (3.8%)	0 (0%)	8 (10.1%)	ICH + GH 2 (2.5%) SAH 1 (1.3%)	N/A	21 (12–36)	74 (93.7%)

Table 1 (continued)

Authors–year (country)	Journal	Patient no./male	Age years Median (range)	Location No. of patients (percentage)	Stenosis at baseline Median (range)	Angioplasty/stenting No. of patients (percentage)	Type of stent No. of patients (percentage)	Success No. of patients (percentage)	Stenosis after treatment Median (range)	Post-intervention Ischemic stroke No. of patients (percentage)	Post-intervention Dissection No. of patients (percentage)	Re-stenosis No. of patients (percentage)	Other complications No. of patients (percentage)	Final outcome No. of patients (percentage)	Follow-up months Median (range)	Alive No. of patients (percentage)
Zhou et al.–2019 [42] (China)	Journal of Clinical Neuroscience	118/N/A	58	BA 118 (100%)	86%	118 (100%)/118 (100%)	Wingspan 76 (64.4%) Apollo 42 (35.6%)	116 (98.3%)	9%	Perforator 3 (2.5%)	0 (0%)	0 (0%)	GH 4 (3.4%) Death 1 (0.8%)	N/A	12	117 (99.2%)
Liu et al.–2020 [43] (China)	Clinical Neurology and Neurosurgery	94/69 (73.4%)	60	BA 94 (100%)	84%	48 (100%)/94 (100%)	Apollo 48 (51.1%) Wingspan 46 (48.9%)	94 (100%)	10%	In-stent 5 (5.3%)	1 (1.1%)	6 (6.4%)	N/A	N/A	12	94 (100%)
Tang et al.–2021 [11] (China)	Acta Neurologica Belgica	61/45 (73.8%)	62 (44–75)	BA 61 (100%)	83% (70–90%)	61 (100%)/61 (100%)	Apollo 61 (100%)	61 (100%)	11% (0–30%)	Perforator 2 (3.2%) In-stent 2 (3.2%)	0 (0%)	5 (8.2%)	Vasospasm 1 (1.6%)	Good 58 (95.1%) Poor 1 (1.6%) Dead 2 (3.2%)	24 (6–60)	59 (96.7%)

ACS, advanced cardiovascular system; *AVE*, arterial vascular engineering-Medtronic; *BA*, basilar artery; *GH*, groin hematoma; *ICH*, intracerebral parenchymal hemorrhage; *N/A*, not available; *NIR*, NIR Medinol; *P-BA*, pseudoaneurysm brachial artery; *RPH*, retroperitoneal hematoma; *SAH*, subarachnoid hemorrhage; *TIA*, transient ischemic attack; *VBJ*, vertebro-basilar junction

Table 2 Summary of clinico-radiological characteristics, intervention protocols, and outcomes

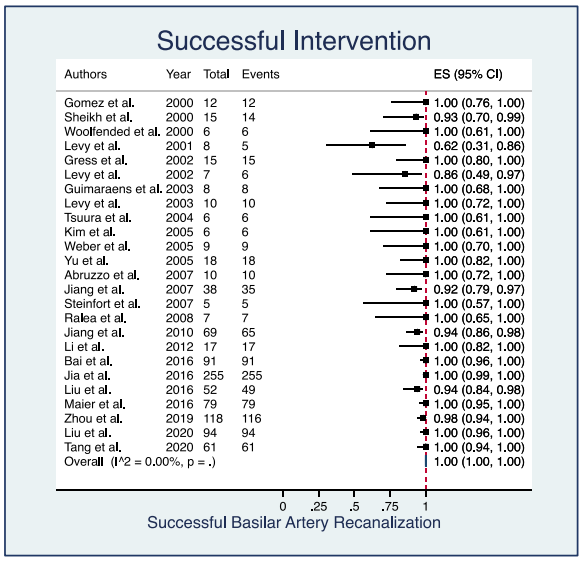
Characteristics	Value
Cohort size (no.)	1016
Demographics	
Age (years), median (range)	62 (36–90)
Gender (male) ($n=882$)	701 (79.5%)
Atherosclerosis risk factors ($n=762$)	No. (%)
Hypertension	618 (81.1%)
Dyslipidemia	430 (56.4%)
Tobacco smoking	386 (50.6%)
Diabetes mellitus	262 (34.4%)
Coronary artery disease	36 (4.7%)
Clinical presentation	No. (%)
Transient ischemic attack	297 (54.4%)
Stroke	249 (45.6%)
Location	No. (%)
Basilar artery	996 (98%)
Vertebrobasilar junction	20 (2%)
Basilar artery segment ($n=216$)	No. (%)
Proximal	98 (45.4%)
Middle	111 (51.4%)
Distal	7 (3.2%)
Mori classification ($n=204$)	No. (%)
A	50 (24.5%)
B	117 (57.4%)
C	37 (18.1%)
Intervention	No. (%)
Angioplasty	970 (95.5%)
Without stenting	79 (7.8%)
Stenting	937 (92.2%)
Conventional (stenting after angioplasty)	586 (62.5%)
Direct (in-stent angioplasty)	295 (31.5%)
Self-expandable stenting without angioplasty	46 (4.5%)
Staged (angioplasty followed by stenting after angioplasty)	10 (1.1%)
Access	
Femoral	1008 (99.2%)
Radial	7 (0.7%)
Brachial	1 (0.1%)
Outcomes	
Successful intervention	1001 (98.5%)
Stenosis at baseline, median (range) ($n=659$)	81% (53–99%)
Stenosis after intervention, median (range) ($n=652$)	13% (0–75%)
Intervention-related complications	No. (%)
Ischemic stroke	85 (8.3%)
Perforator	55 (5.4%)
In-stent thrombosis	26 (2.6%)
Embolic (posterior circulation)	4 (0.4%)
Dissection	18 (1.8%)
Intracerebral parenchymal hemorrhage	8 (0.8%)
Transient ischemic attack	7 (0.7%)
Groin hematoma	6 (0.6%)
Subarachnoid hemorrhage	5 (0.5%)
Pseudoaneurysm of the brachial artery	1 (0.1%)
Retroperitoneal hematoma	1 (0.1%)
Vasospasm	1 (0.1%)
Death	13 (1.3%)
Follow-up (months), mean (range)	14 (0.1–60)
Restenosis ($n=978$)	40 (4.1%)
Final Intervention-related outcomes ($n=349$)	No. (%)
Good	297 (85.1%)
Stable	12 (3.4%)
Poor	27 (7.7%)
Dead	13 (3.7%)
Survival ($n=761$)	No. (%)
Alive	733 (96.3%)
Dead	28 (3.7%)

underwent angioplasty (970; 95.5%) and/or stenting (937; 92.2%) mostly though the femoral access (99.2%) (Table 2). Of the patients, 79/970 (8.1%) underwent angioplasty without stenting and 46/937 (4.9%) received self-expandable stenting without angioplasty. For the 8 cases where the transfemoral approach was not pursuable, the radial and brachial accesses were used, respectively, by Liu et al. [34] in 7 patients (0.7%) and by Abruzzo et al. [27] in 1 (0.1%). The mostly used stents were the Wingspan (Boston Scientific, Fremont, CA, USA) or the Apollo (MicroPort Neuro Tech, Shanghai, China). The angioplasty-assisted stenting protocols were divided into (1) conventional (62.5%), where the stent was deployed after balloon-assisted dilatation of the target BAS; (2) direct (31.5%), where the stent was first placed through the target lesion and then followed by in-stent angioplasty; and (3) staged (1.1%), where conventional stenting placement was preceded by one angioplasty-only procedure performed within the previous month. Liu et al. [36] reported the use of stenting without angioplasty in 46 cases (4.9%). Data on post-intervention medical management were not granular, with most studies reporting the continuation of dual antiplatelet therapy management in all patients who underwent stenting and in the majority of patients who underwent angioplasty without stenting.

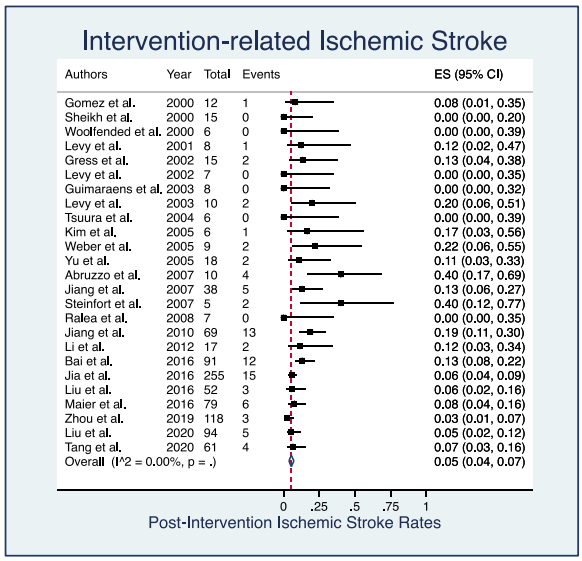
Post-intervention outcomes and complications

Median BAS at baseline was 81% (range, 53–99%) (data available in 659 cases), while median BAS post-intervention was 13% (0–75%) (data available in 652 cases) (Table 2). Median follow-up time was 14 months (range, 0.1–60). Successful intervention was reported in 1001 patients (98.5%),

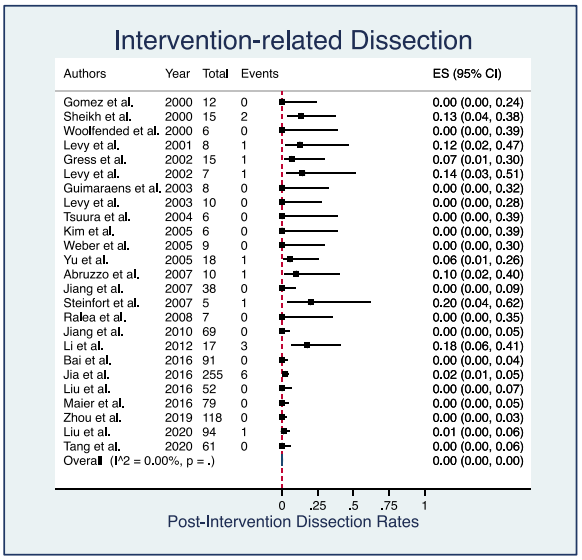
A


Successful Intervention
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 12 1.00 (0.76, 1.00)
Sheikh et al. 2000 15 14 0.93 (0.70, 0.99)
Woolfended et al. 2000 6 6 1.00 (0.61, 1.00)
Levy et al. 2001 8 5 0.62 (0.31, 0.86)
Gress et al. 2002 15 15 1.00 (0.80, 1.00)
Levy et al. 2002 7 6 0.86 (0.49, 0.97)
Guimaraens et al. 2003 8 8 1.00 (0.68, 1.00)
Levy et al. 2003 10 10 1.00 (0.72, 1.00)
Tsuura et al. 2004 6 6 1.00 (0.61, 1.00)
Kim et al. 2005 6 6 1.00 (0.61, 1.00)
Weber et al. 2005 9 9 1.00 (0.70, 1.00)
Yu et al. 2005 18 18 1.00 (0.82, 1.00)
Abruzzo et al. 2007 10 10 1.00 (0.72, 1.00)
Jiang et al. 2007 38 35 0.92 (0.79, 0.97)
Steinfort et al. 2007 5 5 1.00 (0.57, 1.00)
Ralea et al. 2008 7 7 1.00 (0.65, 1.00)
Jiang et al. 2010 69 65 0.94 (0.86, 0.98)
Li et al. 2012 17 17 1.00 (0.82, 1.00)
Bai et al. 2016 91 91 1.00 (0.96, 1.00)
Jia et al. 2016 255 255 1.00 (0.99, 1.00)
Liu et al. 2016 52 49 0.94 (0.84, 0.98)
Maier et al. 2016 79 79 1.00 (0.95, 1.00)
Zhou et al. 2019 118 116 0.98 (0.94, 1.00)
Liu et al. 2020 94 94 1.00 (0.96, 1.00)
Tang et al. 2020 61 61 1.00 (0.94, 1.00)
Overall (I^2 = 0.00%, p = .) 1.00 (1.00, 1.00)
0 .25 .5 .75 1
Successful Basilar Artery Recanalization

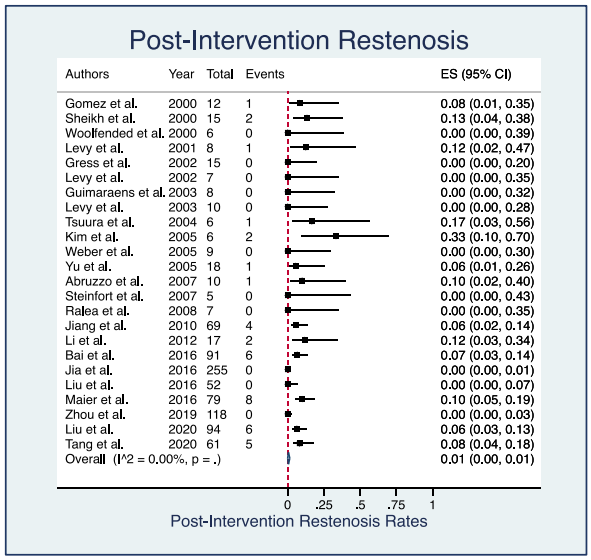
B


Intervention-related Ischemic Stroke
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 1 0.08 (0.01, 0.35)
Sheikh et al. 2000 15 0 0.00 (0.00, 0.20)
Woolfended et al. 2000 6 0 0.00 (0.00, 0.39)
Levy et al. 2001 8 1 0.12 (0.02, 0.47)
Gress et al. 2002 15 2 0.13 (0.04, 0.38)
Levy et al. 2002 7 0 0.00 (0.00, 0.35)
Guimaraens et al. 2003 8 0 0.00 (0.00, 0.32)
Levy et al. 2003 10 2 0.20 (0.06, 0.51)
Tsuura et al. 2004 6 0 0.00 (0.00, 0.39)
Kim et al. 2005 6 1 0.17 (0.03, 0.56)
Weber et al. 2005 9 2 0.22 (0.06, 0.55)
Yu et al. 2005 18 2 0.11 (0.03, 0.33)
Abruzzo et al. 2007 10 4 0.40 (0.17, 0.69)
Jiang et al. 2007 38 5 0.13 (0.06, 0.27)
Steinfort et al. 2007 5 2 0.40 (0.12, 0.77)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 13 0.19 (0.11, 0.30)
Li et al. 2012 17 2 0.12 (0.03, 0.34)
Bai et al. 2016 91 12 0.13 (0.08, 0.22)
Jia et al. 2016 255 15 0.06 (0.04, 0.09)
Liu et al. 2016 52 3 0.06 (0.02, 0.16)
Maier et al. 2016 79 6 0.08 (0.04, 0.16)
Zhou et al. 2019 118 3 0.03 (0.01, 0.07)
Liu et al. 2020 94 5 0.05 (0.02, 0.12)
Tang et al. 2020 61 4 0.07 (0.03, 0.16)
Overall (I^2 = 0.00%, p = .) 0.05 (0.04, 0.07)
0 .25 .5 .75 1
Post-Intervention Ischemic Stroke Rates

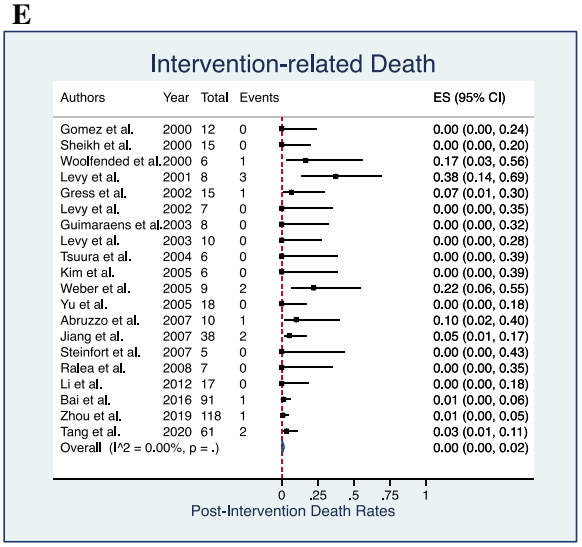
C


Intervention-related Dissection
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 0 0.00 (0.00, 0.24)
Sheikh et al. 2000 15 2 0.13 (0.04, 0.38)
Woolfended et al. 2000 6 0 0.00 (0.00, 0.39)
Levy et al. 2001 8 1 0.12 (0.02, 0.47)
Gress et al. 2002 15 1 0.07 (0.01, 0.30)
Levy et al. 2002 7 1 0.14 (0.03, 0.51)
Guimaraens et al. 2003 8 0 0.00 (0.00, 0.32)
Levy et al. 2003 10 0 0.00 (0.00, 0.28)
Tsuura et al. 2004 6 0 0.00 (0.00, 0.39)
Kim et al. 2005 6 0 0.00 (0.00, 0.39)
Weber et al. 2005 9 0 0.00 (0.00, 0.30)
Yu et al. 2005 18 1 0.06 (0.01, 0.26)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Jiang et al. 2007 38 0 0.00 (0.00, 0.09)
Steinfort et al. 2007 5 1 0.20 (0.04, 0.62)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 0 0.00 (0.00, 0.05)
Li et al. 2012 17 3 0.18 (0.06, 0.41)
Bai et al. 2016 91 0 0.00 (0.00, 0.04)
Jia et al. 2016 255 6 0.02 (0.01, 0.05)
Liu et al. 2016 52 0 0.00 (0.00, 0.07)
Maier et al. 2016 79 0 0.00 (0.00, 0.05)
Zhou et al. 2019 118 0 0.00 (0.00, 0.03)
Liu et al. 2020 94 1 0.01 (0.00, 0.06)
Tang et al. 2020 61 0 0.00 (0.00, 0.06)
Overall (I^2 = 0.00%, p = .) 0.00 (0.00, 0.00)
0 .25 .5 .75 1
Post-Intervention Dissection Rates

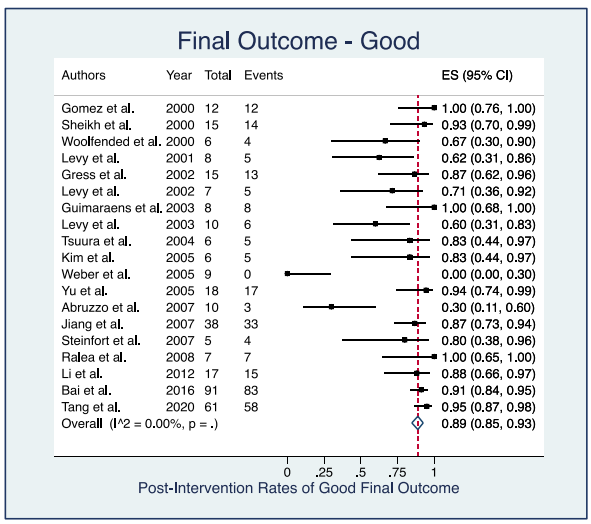
D


Post-Intervention Restenosis
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 1 0.08 (0.01, 0.35)
Sheikh et al. 2000 15 2 0.13 (0.04, 0.38)
Woolfended et al. 2000 6 0 0.00 (0.00, 0.39)
Levy et al. 2001 8 1 0.12 (0.02, 0.47)
Gress et al. 2002 15 0 0.00 (0.00, 0.20)
Levy et al. 2002 7 0 0.00 (0.00, 0.35)
Guimaraens et al. 2003 8 0 0.00 (0.00, 0.32)
Levy et al. 2003 10 0 0.00 (0.00, 0.28)
Tsuura et al. 2004 6 1 0.17 (0.03, 0.56)
Kim et al. 2005 6 2 0.33 (0.10, 0.70)
Weber et al. 2005 9 0 0.00 (0.00, 0.30)
Yu et al. 2005 18 1 0.06 (0.01, 0.26)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Steinfort et al. 2007 5 0 0.00 (0.00, 0.43)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 4 0.06 (0.02, 0.14)
Li et al. 2012 17 2 0.12 (0.03, 0.34)
Bai et al. 2016 91 6 0.07 (0.03, 0.14)
Jia et al. 2016 255 0 0.00 (0.00, 0.01)
Liu et al. 2016 52 0 0.00 (0.00, 0.07)
Maier et al. 2016 79 8 0.10 (0.05, 0.19)
Zhou et al. 2019 118 0 0.00 (0.00, 0.03)
Liu et al. 2020 94 6 0.06 (0.03, 0.13)
Tang et al. 2020 61 5 0.08 (0.04, 0.18)
Overall (I^2 = 0.00%, p = .) 0.01 (0.00, 0.01)
0 .25 .5 .75 1
Post-Intervention Restenosis Rates

E


Intervention-related Death
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 0 0.00 (0.00, 0.24)
Sheikh et al. 2000 15 0 0.00 (0.00, 0.20)
Woolfended et al. 2000 6 1 0.17 (0.03, 0.56)
Levy et al. 2001 8 3 0.38 (0.14, 0.69)
Gress et al. 2002 15 1 0.07 (0.01, 0.30)
Levy et al. 2002 7 0 0.00 (0.00, 0.35)
Guimaraens et al. 2003 8 0 0.00 (0.00, 0.32)
Levy et al. 2003 10 0 0.00 (0.00, 0.28)
Tsuura et al. 2004 6 0 0.00 (0.00, 0.39)
Kim et al. 2005 6 0 0.00 (0.00, 0.39)
Weber et al. 2005 9 2 0.22 (0.06, 0.55)
Yu et al. 2005 18 0 0.00 (0.00, 0.18)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Jiang et al. 2007 38 2 0.05 (0.01, 0.17)
Steinfort et al. 2007 5 0 0.00 (0.00, 0.43)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Li et al. 2012 17 0 0.00 (0.00, 0.18)
Bai et al. 2016 91 1 0.01 (0.00, 0.06)
Zhou et al. 2019 118 1 0.01 (0.00, 0.05)
Tang et al. 2020 61 2 0.03 (0.01, 0.11)
Overall (I^2 = 0.00%, p = .) 0.00 (0.00, 0.02)
0 .25 .5 .75 1
Post-Intervention Death Rates

F


Final Outcome - Good
Authors Year Total Events ES (95% CI)
Gomez et al. 2000 12 12 1.00 (0.76, 1.00)
Sheikh et al. 2000 15 14 0.93 (0.70, 0.99)
Woolfended et al. 2000 6 4 0.67 (0.30, 0.90)
Levy et al. 2001 8 5 0.62 (0.31, 0.86)
Gress et al. 2002 15 13 0.87 (0.62, 0.96)
Levy et al. 2002 7 5 0.71 (0.36, 0.92)
Guimaraens et al. 2003 8 8 1.00 (0.68, 1.00)
Levy et al. 2003 10 6 0.60 (0.31, 0.83)
Tsuura et al. 2004 6 5 0.83 (0.44, 0.97)
Kim et al. 2005 6 5 0.83 (0.44, 0.97)
Weber et al. 2005 9 0 0.00 (0.00, 0.30)
Yu et al. 2005 18 17 0.94 (0.74, 0.99)
Abruzzo et al. 2007 10 3 0.30 (0.11, 0.60)
Jiang et al. 2007 38 33 0.87 (0.73, 0.94)
Steinfort et al. 2007 5 4 0.80 (0.38, 0.96)
Ralea et al. 2008 7 7 1.00 (0.65, 1.00)
Li et al. 2012 17 15 0.88 (0.66, 0.97)
Bai et al. 2016 91 83 0.91 (0.84, 0.95)
Tang et al. 2020 61 58 0.95 (0.87, 0.98)
Overall (I^2 = 0.00%, p = .) 0.89 (0.85, 0.93)
0 .25 .5 .75 1
Post-Intervention Rates of Good Final Outcome

◂**Fig. 3** Forest plots of **A** successful intervention, **B** intervention-related ischemic stroke, and **C** intervention-related dissection, **D** intervention-related restenosis, **E** post-intervention death, and **F** post-intervention good final outcomes. Squares define the proportions (effect size (ES)) of individual studies and horizontal lines mark the 95% confidence intervals (CI). Diamonds indicate the pooled ES with 95% CI using the random-effect model meta-analyses

with actuarial rates of 100% (95% CI: 100–100%) both in the total cohort (Fig. 3A) and in more recent studies (Fig. 4A). Intervention-related recurrent ischemic stroke occurred in 85 patients (8.3%), with actuarial rates of 5% (95% CI: 4–7%) in the total cohort (Fig. 3B) and 6% (95% CI: 5–8%) in more recent studies (Fig. 4B), differentiated into perforator stroke (5.4%), in-stent thrombosis (2.6%), and embolic PCI (0.4%). Intervention-related dissection and restenosis ($n = 978$ of cases with available data) occurred in 18 (1.8%) and 40 patients (4.1%), respectively, with actuarial rates of 0% (95% CI: 0–0%) and 1% (95% CI: 0–1%) in the total cohort (Fig. 3C, D), and 0% (95% CI: 0–0%) and 1% (95% CI: 0–2%) in more recent studies (Fig. 4C, D). Post-intervention intracerebral parenchymal hemorrhages (ICH) and subarachnoid hemorrhage (SAH), both non-related to BA dissection, were diagnosed in 8 (0.8%) and 5 (0.5%) patients, respectively. Intervention-related deaths occurred in 13 cases (1.3%, among 761 cases with available data), with actuarial rates of 0% (95% CI: 0–2%) both in the total cohort (Fig. 3E) and in more recent studies (Fig. 4E). Among patients with available data ($n = 349$), post-intervention good final outcome was identified in 297 cases (85.1%), with actuarial rates of 89% (95% CI: 85–93%) in the total cohort (Fig. 3F) and 92% (95% CI: 87–96%) in more recent studies (Fig. 4F). No significant between-study differences in outcomes ($p = 0.378$) or complication rates ($p = 0.119$) were found related to each study's cohort sizes.

Discussion

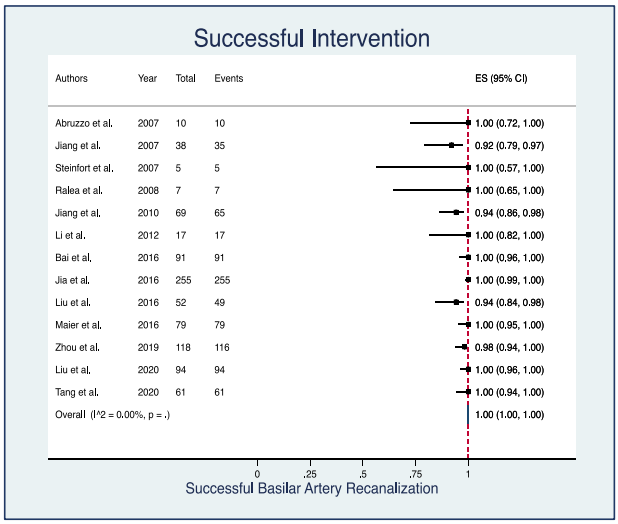
Symptomatic BAS represents a strong predictor for PCI recurrence and poor prognosis, with current management frequently being suboptimal in the long term [44]. Second-line PTAS may be considered in severe, symptomatic BAS refractory to aggressive first-line medical therapy, but the technical complexity and the variability in outcomes constitute major obstacles [7, 8, 45]. In this review, we found that elective PTAS may be effective and safe in selected patients with medically refractory, severe, non-acute BAS. Our meta-analysis showed high pooled rates of technical success and good clinical outcomes with minimal peri-interventional risks and mortality; however, an in-depth evaluation of the limitations and biases of all included studies is required to ascertain such results within the real context of routine clinical practice. Overall, careful patient selection and elective non-acute treatment planning proved to be critical for achieving favorable outcomes.

Posterior circulation ICAS merits to be considered as a unique entity compared to anterior circulation ICAS, estimated to account for approximately 60% of all PCI strokes [2, 46]. The large number of perforators and their blood supply to eloquent brain regions correlate with significant risks of debilitating neurological and functional impairments occurring as part of the disease's natural history or after therapeutic interventions. The middle BA segment is the most involved, probably because it gives origin to the highest number of perforators, leading to clinically manifest neurological deficits and contributing to higher risks of post-treatment adverse events [24, 33]. The interest for devising best BAS management strategies derives from the significant risks of intervention-related complications related to the greater tortuosity and smaller caliber of posterior circulation vessels, which is responsible for increasing the technical challenges [31].

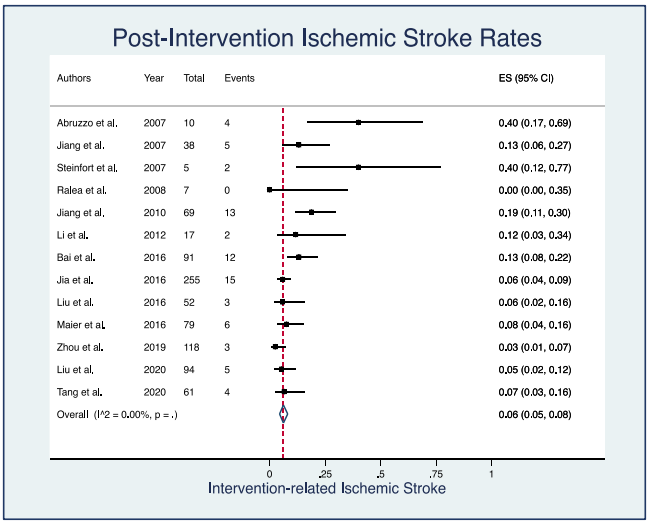
The first-line option for BAS consists of aggressive antiplatelet therapy with intensive risk factor control. The increasing incidence of symptomatic, refractory BAS has led to devising second-line treatments, especially balloon angioplasty [47] and stenting [48], as intracranial-extracranial bypass surgery is extremely challenging and high-risk. Among our included studies, PTAS was considered electively only in non-acute recurrent symptomatic PCI (i.e., TIA or stroke) despite treatment with dual antiplatelet therapy. The common choice to treat non-acute cases likely derived from early experiences showing lower complications related to stable plaques and symptoms [40]. BAS cutoffs varied across institutions, some treating lesions with stenosis $\geq 50\%$ [22, 24] and other treating lesions with stenosis $\geq 70\%$ [9, 33, 34]. We ascribe these differences to the between-center variability in expertise and related caution. Some institutions may have preferred to perform PTAS only for lesions with a high risk of recurrent ischemic stroke as per the WASID 2006 post hoc analyses, which reported almost twice the risk (19%) of recurrent stroke for ICAS with $> 70\%$ stenosis compared to the 10% risk for ICAS with $< 70\%$ stenosis. However, a recent meta-analysis found no significant correlation between $> 70\%$ stenosis and higher risks of recurrent stroke after PTAS for vertebrobasilar stenosis [45]. This lack of standardized inclusion criteria may have led the involved institutions to select only patients expected to obtain the most favorable outcomes, reducing the likelihood to replicate such positive findings in routine, "real-word" settings. The design and conduction of prospective multi-institutional studies with standardized eligibility criteria and randomized controlled methodologies are necessary to obtain uniform, reliable, and clinically replicable outcomes.

Although 2 early series used angioplasty alone for BAS [38, 39], all remaining studies performed

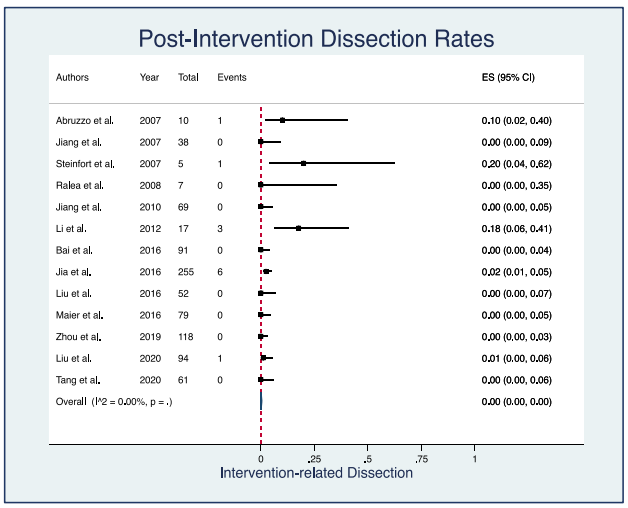
A


Successful Intervention
Authors Year Total Events ES (95% CI)
Abruzzo et al. 2007 10 10 1.00 (0.72, 1.00)
Jiang et al. 2007 38 35 0.92 (0.79, 0.97)
Steinfort et al. 2007 5 5 1.00 (0.57, 1.00)
Ralea et al. 2008 7 7 1.00 (0.65, 1.00)
Jiang et al. 2010 69 65 0.94 (0.86, 0.98)
Li et al. 2012 17 17 1.00 (0.82, 1.00)
Bai et al. 2016 91 91 1.00 (0.96, 1.00)
Jia et al. 2016 255 255 1.00 (0.99, 1.00)
Liu et al. 2016 52 49 0.94 (0.84, 0.98)
Maier et al. 2016 79 79 1.00 (0.95, 1.00)
Zhou et al. 2019 118 116 0.98 (0.94, 1.00)
Liu et al. 2020 94 94 1.00 (0.96, 1.00)
Tang et al. 2020 61 61 1.00 (0.94, 1.00)
Overall (I^2 = 0.00%, p = .) 1.00 (1.00, 1.00)
0 .25 .5 .75 1
Successful Basilar Artery Recanalization

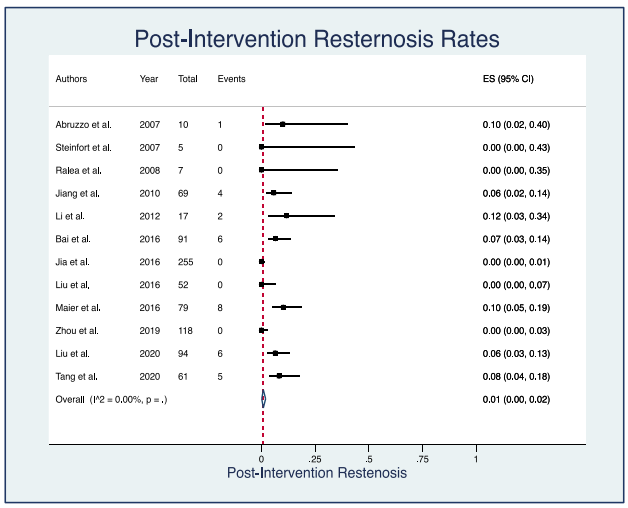
B


Post-Intervention Ischemic Stroke Rates
Authors Year Total Events ES (95% CI)
Abruzzo et al. 2007 10 4 0.40 (0.17, 0.69)
Jiang et al. 2007 38 5 0.13 (0.06, 0.27)
Steinfort et al. 2007 5 2 0.40 (0.12, 0.77)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 13 0.19 (0.11, 0.30)
Li et al. 2012 17 2 0.12 (0.03, 0.34)
Bai et al. 2016 91 12 0.13 (0.08, 0.22)
Jia et al. 2016 255 15 0.06 (0.04, 0.09)
Liu et al. 2016 52 3 0.06 (0.02, 0.16)
Maier et al. 2016 79 6 0.08 (0.04, 0.16)
Zhou et al. 2019 118 3 0.03 (0.01, 0.07)
Liu et al. 2020 94 5 0.05 (0.02, 0.12)
Tang et al. 2020 61 4 0.07 (0.03, 0.16)
Overall (I^2 = 0.00%, p = .) 0.06 (0.05, 0.08)
0 .25 .5 .75 1
Intervention-related Ischemic Stroke

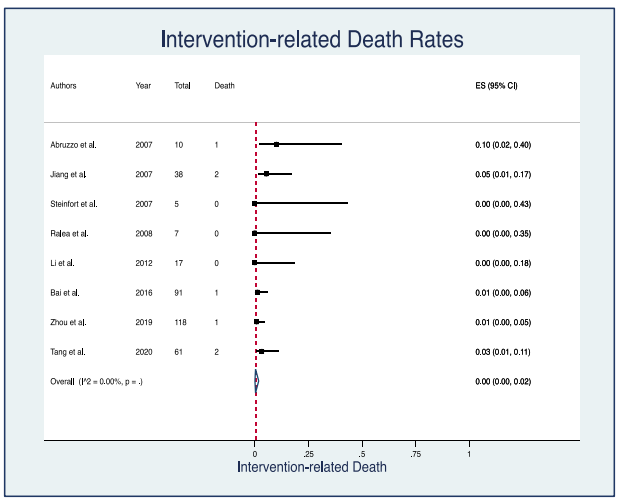
C


Post-Intervention Dissection Rates
Authors Year Total Events ES (95% CI)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Jiang et al. 2007 38 0 0.00 (0.00, 0.09)
Steinfort et al. 2007 5 1 0.20 (0.04, 0.62)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 0 0.00 (0.00, 0.05)
Li et al. 2012 17 3 0.18 (0.06, 0.41)
Bai et al. 2016 91 0 0.00 (0.00, 0.04)
Jia et al. 2016 255 6 0.02 (0.01, 0.05)
Liu et al. 2016 52 0 0.00 (0.00, 0.07)
Maier et al. 2016 79 0 0.00 (0.00, 0.05)
Zhou et al. 2019 118 0 0.00 (0.00, 0.03)
Liu et al. 2020 94 1 0.01 (0.00, 0.06)
Tang et al. 2020 61 0 0.00 (0.00, 0.06)
Overall (I^2 = 0.00%, p = .) 0.00 (0.00, 0.00)
0 .25 .5 .75 1
Intervention-related Dissection

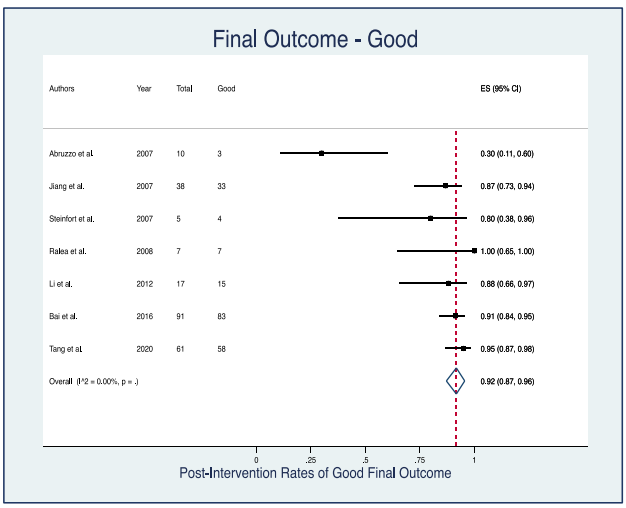
D


Post-Intervention Resternosis Rates
Authors Year Total Events ES (95% CI)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Steinfort et al. 2007 5 0 0.00 (0.00, 0.43)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Jiang et al. 2010 69 4 0.06 (0.02, 0.14)
Li et al. 2012 17 2 0.12 (0.03, 0.34)
Bai et al. 2016 91 6 0.07 (0.03, 0.14)
Jia et al. 2016 255 0 0.00 (0.00, 0.01)
Liu et al. 2016 52 0 0.00 (0.00, 0.07)
Maier et al. 2016 79 8 0.10 (0.05, 0.19)
Zhou et al. 2019 118 0 0.00 (0.00, 0.03)
Liu et al. 2020 94 6 0.06 (0.03, 0.13)
Tang et al. 2020 61 5 0.08 (0.04, 0.18)
Overall (I^2 = 0.00%, p = .) 0.01 (0.00, 0.02)
0 .25 .5 .75 1
Post-Intervention Restenosis

E


Intervention-related Death Rates
Authors Year Total Death ES (95% CI)
Abruzzo et al. 2007 10 1 0.10 (0.02, 0.40)
Jiang et al. 2007 38 2 0.05 (0.01, 0.17)
Steinfort et al. 2007 5 0 0.00 (0.00, 0.43)
Ralea et al. 2008 7 0 0.00 (0.00, 0.35)
Li et al. 2012 17 0 0.00 (0.00, 0.18)
Bai et al. 2016 91 1 0.01 (0.00, 0.06)
Zhou et al. 2019 118 1 0.01 (0.00, 0.05)
Tang et al. 2020 61 2 0.03 (0.01, 0.11)
Overall (I^2 = 0.00%, p = .) 0.00 (0.00, 0.02)
0 .25 .5 .75 1
Intervention-related Death

F


Final Outcome - Good
Authors Year Total Good ES (95% CI)
Abruzzo et al. 2007 10 3 0.30 (0.11, 0.60)
Jiang et al. 2007 38 33 0.87 (0.73, 0.94)
Steinfort et al. 2007 5 4 0.80 (0.38, 0.96)
Ralea et al. 2008 7 7 1.00 (0.65, 1.00)
Li et al. 2012 17 15 0.88 (0.66, 0.97)
Bai et al. 2016 91 83 0.91 (0.84, 0.95)
Tang et al. 2020 61 58 0.95 (0.87, 0.98)
Overall (I^2 = 0.00%, p = .) 0.92 (0.87, 0.96)
0 .25 .5 .75 1
Post-Intervention Rates of Good Final Outcome

◂**Fig. 4** Forest plots including only studies published after 2006 on **A** successful intervention, **B** intervention-related ischemic stroke, **C** intervention-related dissection, **D** intervention-related restenosis, **E** post-intervention death, and **F** post-intervention good final outcomes. Squares define the proportions (effect size (ES)) of individual studies and horizontal lines mark the 95% confidence intervals (CI). Diamonds indicate the pooled ES with 95% CI using the random-effect model meta-analyses (All figures are original to this submission so no credit or license is needed.)

angioplasty-assisted stenting procedures, owing to the proven lower rates of residual post-intervention stenosis [49]. Initial experience with coronary balloon-expandable stents showed higher stenosis reduction compared to angioplasty alone [37, 40, 42]. However, their limited flexibility and need for high-pressure inflation for deployment posed some difficulties in navigating the tortuous posterior circulation while increasing the risks of iatrogenic vessel injuries. The later introduction of the balloon-mounted Apollo stent and the self-expanding Wingspan stent have led to some improvement in peri-procedural outcomes, mainly second to the selection of stent types and angioplasty-assisted procedures on a case-by-case basis [9, 34, 36]. The literature suggests that the Apollo stent may be preferred for straight Mori type-A lesions, as it is stiffer and more difficult to pass through tortuous vessels, but also has better radial support, which may be optimal for heavily calcified lesions even without predilation angioplasty (i.e., direct stenting) [36, 50]. Contrarily, the Wingspan stent may be best suited for tortuous and longer Mori type-B and type-C lesions, especially when preceded by submaximal angioplasty inflation (i.e., conventional stenting) [9, 51]. The use of pre- and post-intervention antithrombotic therapy, coupled with intra-procedural heparin, may be critical to minimize the risks of in-stent thrombosis, but needs to be balanced with the potential occurrence of hemorrhagic complications.

The interim results from the SAMMPRIS [7] and VISSIT [8] trials discouraged PTAS for ICAS, demonstrating higher rates of peri-procedural complications (14.7% and 23.7%) compared to aggressive medical management (5.8% and 9.4%). The development of optimal patient-specific indications, coupled with the growing operator expertise, has led to a progressive reduction in intervention-related complications. Indeed, the more recent WEAVE [52] and CASSISS [53] trials have, respectively, shown the low periprocedural complication rate and excellent safety profile of the Wingspan stent for PTAS in ICAS [52] and the lack of significant differences in 30-day risk of stroke or death between medical therapy alone versus medical therapy plus stenting in the treatment of severe symptomatic ICAS [53]. Additionally, a recent meta-analysis found no significant differences in stroke recurrence or death comparing PTAS (14.8%) and medical (8.9%) strategies for treating vertebrobasilar stenosis [54]. Similarly, we found low actuarial rates of recurrent ischemic stroke and intervention-related deaths in patients with BAS undergoing PTAS, both in the total cohort and only in patients treated after 2006. In parallel, despite the dismal natural history and prognosis of BAS, high actuarial rates of successful intervention and good final outcomes were found in both groups. Although these findings may support the effectiveness and safety of elective PTAS in highly selected patients with non-acute BAS, they derived from non-standardized, subjectively reported measures collected at institutions with a high-load of cases. In addition, since early suboptimal experiences with PTAS for BAS may have been underreported, we note that these strongly positive results should be viewed with some caution as they may not reflect the clinical outcomes obtained at other institutions.

The risk of perforator strokes needs to be considered when counselling selected patients for interventional approaches. Jia et al. [9] found that patients with diabetes ($p=0.005$), pre-procedure stenosis < 88.4% ($p=0.012$), and/or < 18 days from last symptom to procedure ($p=0.031$) had higher risks, presumably because of the underlying presence of unstable plaques favoring the displacement of atheromatous debris over the perforators' ostia during the procedure (i.e., "snowplow effect"). Our pooled analyses also demonstrated low actuarial rates of intervention-related BA dissection both in the total cohort and only in patients treated after 2006, coupled with negligible occurrence of post-procedural ICH (0.8%) and SAH (0.5%). We associate these findings with the better operator expertise and device maneuverability observed in recent series, which may have favored superior intra-procedural caution during stent placement and deployment, minimizing the iatrogenic shift of the BA and preventing the avulsion of perforators [11, 36]. Objective assessments of operators' learning curves and between-operator rates of post-interventional outcomes should be further obtained to confirm the replicability of these pooled findings.

Limitations

Our review has important limitations. Most articles were retrospective series likely exposed to inherent selection bias. Although no publication bias was found in the funnel plots, the likelihood of institutional reporting bias must be considered, favoring the publication of series with good outcomes contrarily to series with high complication rates. We excluded studies with unclear distinction between BAS and VAS, limiting our pooled number of patients. However, as VAS may carry distinct prognosis compared to BAS, our selective inclusion criteria were set to calculate with high-accuracy intervention-related outcomes and complications specific for PTAS in BAS. The between-study heterogeneity in indications, definition of successful intervention, outcome assessments, and follow-up may have introduced

some confounding variables. Due to the lack of granular patient-level data, heterogeneously reported across studies, we could not perform multivariate analyses to evaluate the impact of distinct clinico-radiological and interventional characteristics on post-procedural outcomes and complications. The between-study variability in follow-up times and the limited availability of outcome data based on different follow-up time points prevented the conduction of separate meta-analyses based on post-intervention outcomes collected at different time points. However, as all included studies reported their outcomes after a minimum of 6 months at post-intervention follow-up, our analyses of pooled outcomes were performed using the findings obtained at last available follow-ups for each included study. The short median follow-up (14 months) may have prevented the evaluation of long-term outcomes and the detection of accurate rates of re-stenosis, whose incidence was found to be lower than previous reports. This also may have limited the availability of pertinent data and prevented accurate analysis of the need for re-treatment after PTAS in BAS. Finally, due to the limited availability of published studies directly comparing PTAS with standard medical management for BAS, comparative analyses between the two treatment strategies could not be performed. Despite these limitations, we provide the first methodologically rigorous, reproducible meta-analysis on post-procedural outcomes and complications following PTAS for BAS. These pooled data should be considered encouraging enough to systematically evaluate patients with BAS for PTAS, especially in light of their very poor natural history.

Conclusion

Although the tortuous and complex anatomy of the posterior cerebral circulation may pose some challenges for endovascular approaches, the literature reports that PTAS may be feasible, safe, and effective in selected patients with BAS. Elective PTAS may be considered in medically refractory, severe (≥ 50–70%), symptomatic BAS in non-acute stages. The used approaches and devices need to be tailored to the clinico-radiological characteristics of each lesion. Considering the likelihood of institutional reporting biases and the variability of reported parameters/outcomes across the literature, our pooled findings should be judged with some caution, warranting a standardization of reporting methods and treatment guidelines [55]. Though not generalizable, this meta-analysis supports the demand to design future prospective trials and/or multi-institutional registries targeting the management of BAS.

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Author contribution Paolo Palmisciano: conceptualization, methodology, formal analysis, writing — original draft preparation; Samer S. Hoz: validation, writing — reviewing and editing, visualization; Hagar A. Algburi: methodology, validation, formal analysis, investigation, writing — reviewing and editing; Giancarlo Ventre: methodology, validation, writing — reviewing and editing; Seth Street: methodology, validation, writing — reviewing and editing; Nana Agyeman: methodology, validation, writing — reviewing and editing; Michael W. Robinson: methodology, validation, writing — reviewing and editing; Matthew S. Smith: methodology, validation, writing — reviewing and editing; Peyman Shirani: methodology, validation, writing — reviewing and editing; Aaron W. Grossman: resources, writing — reviewing and editing; Charles J. Prestigiacomo: methodology, supervision, validation, writing — reviewing and editing.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval Ethical approval was waived by the IRB because this study is a review of the literature and does not involve institutional data.

Informed consent Informed consent was not required because this study is a review of the literature and no patients from the authors' institution were enrolled in this study.

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