

Endovascular Treatment for Posterior Circulation Stroke: Ways to Maximize Therapeutic Efficacy

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The efficacy of endovascular treatment (EVT) in patients with posterior circulation stroke has not been proven. Two recent randomized controlled trials failed to show improved functional outcomes after EVT for posterior circulation stroke (PC-EVT). However, promising results for two additional randomized controlled trials have also been presented at a recent conference. Studies have shown that patients undergoing PC-EVT had a higher rate of futile recanalization than those undergoing EVT for anterior circulation stroke. These findings call for further identification of prognostic factors beyond recanalization. The significance of baseline clinical severity, infarct volume, collaterals, time metrics, core-penumbra mismatch, and methods to accurately measure these parameters are discussed. Furthermore, their interplay on EVT outcomes and the potential to individualize patient selection for PC-EVT are reviewed. We also discuss technical considerations for improving the treatment efficacy of PC-EVT.

Keywords Cerebral infarction; Posterior circulation; Endovascular treatment; Mechanical thrombectomy; Basilar artery occlusion; Vertebrobasilar artery occlusion

Introduction

Endovascular treatment (EVT) based on mechanical thrombectomy (MT) has become the gold standard for treatment of large-vessel occlusion (LVO) of the anterior circulation. In posterior circulation LVO, EVT was associated with improved functional outcomes in a large prospective multicenter registry,¹ and successful reperfusion was associated with favorable outcomes in multiple studies (Table 1)²⁻⁵ and a recent systematic review.⁶ While we wait for positive results of two recent randomized controlled trials (RCTs),⁷⁻¹⁰ two RCTs failed to show the therapeutic efficacy of EVT.^{11,12} A meta-analysis showed that compared with anterior circulation EVT (AC-EVT), outcomes of EVT for posterior circulation stroke (PC-EVT) were unfavorable, with higher rates of futile recanalization (poor outcomes despite successful recanalization).¹³ Such data highlight the issue

of patient selection, which may be key to the success of PC-EVT.

Moreover, efforts to expand EVT indications for patients who will benefit from this potentially powerful treatment should also be sought. For AC-EVT, these efforts have resulted in the success of late-window trials,^{14,15} based on the selection of patients through clinical-core mismatch or core-penumbra mismatch. A recent RCT also showed the benefit of AC-EVT for larger infarcts based on the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) 3–5.¹⁶ Efforts to expand EVT to patients with a low National Institutes of Health Stroke Scale (NIHSS) score are also under evaluation,^{17,18} along with efforts to expand to patients with distal vascular occlusion.¹⁹ All these efforts should eventually be pursued in PC-EVT.

In this paper, we first review recent RCTs on PC-EVT. We then discuss the prognostic factors of PC-EVT and how to apply

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Table 1. Studies evaluating the effect of reperfusion on outcomes

Author (published year) (study period)	Study design	No. of patient	Artery	Clinical outcomes	Significance of reperfusion
Mokin et al. (2016) ² (2011–2015)	Multicenter retrospective	100	VBAO	3-mo mRS 0–2	Successful recanalization is a predictor of good outcome.
Bouslama et al. (2017) ³ (2005–2015)	Two center retrospective	214	VBAO	3-mo mRS 0–2	Reperfusion predicts good outcomes (aOR, 10.80; 95% CI, 1.36–85.96).
Gory et al. (2018) ⁴ (2010–2016)	Multicenter ETIS registry	100	BAO	3-mo mRS 0–2	Reperfusion predicts good outcome (aOR, 5.64; 95% CI, 1.32–24.06).

VBAO, vertebrobasilar artery occlusion; mRS, modified Rankin Scale; aOR, adjusted odds ratio; CI, confidence interval; ETIS, Endovascular Treatment in Ischemic Stroke; BAO, basilar artery occlusion.

them to maximize clinical benefits and expand therapeutic indications. We also describe the technical aspects of PC-EVT.

RCTs of EVT for vertebrobasilar artery occlusion

Four RCTs have so far been published or presented regarding the efficacy and safety of EVT for acute stroke due to vertebrobasilar artery occlusion (VBAO) (Table 2). The Basilar Artery Occlusion Endovascular Intervention Versus Standard Medical Treatment (BEST)¹¹ was a multicenter randomized open-label trial with a blinded outcome assessment in patients presenting within 8 hours of VBAO at 28 centers in China between 2015 and 2017. The primary outcome was a modified Rankin Scale (mRS) score of ≤3 at 90 days, assessed on an intention-to-treat basis. The primary safety outcome was mortality at 90 days. While a sample size of 344 was originally calculated, only 131 (66 endovascular and 65 medical) patients were enrolled due to excessive crossovers and a progressive drop in per center recruitment. In the control group, 22% of the patients ended up receiving EVT, while 5% of the intervention group ended up receiving medical therapy only. The primary outcome was achieved in 42% of the patients in the EVT group and 32% in the medical care group, failing to reach statistical significance (adjusted odds ratio [aOR], 1.74; 95% confidence interval [CI], 0.81 to 3.74). The rates of symptomatic intracranial hemorrhage (sICH) and mortality did not differ between the groups. However, in secondary prespecified analyses, EVT compared to medical treatment alone was associated with a higher rate of mRS 0–3 at 90 days in both per-protocol (44% vs. 25%; aOR, 2.90; 95% CI, 1.20 to 7.03) and as-treated (47% vs. 24%; aOR, 3.02; 95% CI, 1.31 to 7.00) populations.

The Basilar Artery International Cooperation Study (BASICS) trial was performed at 23 centers in seven countries and enrolled patients presenting within 6 hours of stroke due to basilar artery occlusion (BAO).¹² The original inclusion criteria were

patients aged <85 years and NIHSS scores of ≥10. However, due to slow enrollment, the inclusion criteria were expanded to include patients aged >85 years, NIHSS score <10, and those with contraindications for intravenous thrombolysis. The primary outcome was a mRS score between 0 and 3 at 90 days. The primary safety outcomes were sICH and mortality at 90 days. A total of 300 patients were enrolled (154 in the EVT group and 146 in the medical care group). The primary outcome was achieved in 44.2% of the EVT group and 37.7% of the medical care group, failing to show a significant difference (risk ratio [RR], 1.18; 95% CI, 0.92 to 1.50). The sICH and mortality rates did not differ between the groups.

The results of two more RCTs are expected to be positive, and preliminary data presented at the 2022 European Stroke Organization Conference are promising (Table 2). The Basilar Artery Occlusion Chinese Endovascular (BAOCHE) trial enrolled VBAO patients who presented between 6 and 24 hours after onset between 2016 and 2022. In contrast to BEST and BASICS, the BAOCHÉ trial utilized a clinical severity criteria of NIHSS >6 and imaging-based inclusion criteria of Posterior Circulation Acute Stroke Prognosis Early Computed Tomography Score (PC-ASPECTS) ≥6, and a pons midbrain index of ≤2.⁷ In the interim analysis including 212 of the originally planned 318 patients, the rates of favorable outcomes (mRS score between 0 and 3 at 90 days) were significantly higher in the intervention arm (46.4% vs. 24.3%; aOR, 2.92; 95% CI, 1.56 to 5.47).⁹ The Endovascular Treatment for Acute Basilar Artery Occlusion (ATTENTION) was a prospective, open, blinded-endpoint RCT that enrolled 342 BAO patients who presented within 12 hours of onset in 36 Chinese stroke centers between 2021 and 2022. The ATTENTION trial had both a clinical severity criterion of NIHSS >10, and an imaging-based inclusion criterion using PC-ASPECTS.⁸ Successful reperfusion rates were as high as 93%, and favorable outcomes were achieved in 46% of the intervention arm and 22.8% of the control arm (adjusted risk ratio [aRR], 2.1; *P*<0.001).¹⁰

Table 2. Randomized clinical trials

	BEST	BASICS	BAOCHE	ATTENTION				
Protocols								
Inclusion period	2015–2017	2011–2019	2016 – 2022	2021–2022				
Onset to treatment	Within 8 hr	Within 6 hr	6–24 hr	Within 12 hr				
Occlusion location	Basilar artery Vertebral artery resulting in no flow to basilar artery	Basilar artery	Basilar artery or both intracranial vertebral artery	Basilar artery				
Clinical severity criteria	None	NIHSS ≥ 10 (later deleted)	NIHSS ≥ 6	NIHSS ≥ 10				
Imaging-based inclusion criteria	-	-	PC-ASPECTS ≥ 6 and pons midbrain index of ≤ 2	Age < 80 , PC-ASPECTS ≥ 6 ; age ≥ 80 , PC-ASPECTS ≥ 8				
Imaging-based exclusion criteria	ICH, significant cerebellar mass effect, acute hydrocephalus, or extensive bilateral brainstem ischemia	ICH, extensive bilateral brainstem infarction; cerebellar mass effect; or acute hydrocephalus		Complete bilateral thalami or brainstem infarction cerebellar mass effect				
IV thrombolysis	Within 4.5 hr of last seen well	Within 4.5 hr of estimated onset	Before randomization	Within 4.5 hr of last seen well				
Intracranial stenting	Allowed	Allowed	Allowed	Allowed				
Primary efficacy endpoint	Proportion of patients with mRS score of 0–3 at 3 months Intention-to-treat analysis							
Subjects								
Screened	288	424						
Enrolled/target sample size	131/344	300/300	212/318	340				
Crossover rate (%)	13	3	2.3					
Results								
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Number	66	65	154	146	110	107	226	114
Age (yr)	62 (50–74)	68 (57–74)	66.8 \pm 13.1	67.2 \pm 11.9	64 \pm 10	64 \pm 10	67	68
Atrial fibrillation	18 (27)	10 (15)	44 (29)	22 (15)				
NIHSS, median	32 (18–38)	26 (13–37)	21	22	20 (15–29)	19 (12–30)		
IV thrombolysis	18 (27)	21 (32)	121 (79)	116 (80)	15 (13.6)	23 (21.5)		
Atherosclerotic etiology	37 (56)	32 (49)						
Outcomes								
Time from onset-to-EVT	114 min (66–150)		4.4 hr (3.3–6.2)					
Successful reperfusion	45 (71)		63 (72)				93.3%	
3-mo mRS 0–3*	28 (42)	21 (32)	68 (44)	55 (38)	51 (46.4)	26 (24.3)	46%	22.8%
3-mo mRS 0–2	22 (33)	18 (28)	54 (35)	44 (30)			33.2%	10.5%
3-mo mortality [†]	22 (33)	25 (38)	59 (38)	63 (43)	34 (30.9)	45 (42.1)	36.7%	55.3%
PC-ASPECTS score at 24 hours	6 (4–7)	6 (4–8)	8 (6–9)	8 (6–9)				

Values are presented as median (interquartile range), number (%), or mean \pm standard deviation.

BEST, Basilar Artery Occlusion Endovascular Intervention Versus Standard Medical Treatment; BASICS, Basilar Artery International Cooperation Study; BAOCHHE, Basilar Artery Occlusion Chinese Endovascular; ATTENTION, Endovascular Treatment for Acute Basilar Artery Occlusion; NIHSS, National Institutes of Health Stroke Scale; ICH, intracranial hemorrhage; PC-ASPECTS, Posterior Circulation Acute Stroke Prognosis Early Computed Tomography Score; IV, intravenous; mRS, modified Rankin Scale; EVT, endovascular treatment.

*BEST trial, adjusted odds ratio, 1.74 (95% confidence interval [CI], 0.8–3.7) for the intervention arm; BASICS trial, relative risk, 1.2 (95% CI, 0.92–1.50); BAOCHHE trial, adjusted odds ratio, 2.92 (95% CI, 1.56–5.47); ATTENTION, adjusted risk ratio, 2.1 ($P < 0.001$); [†]BEST trial, odds ratio, 0.80 (95% CI, 0.37–1.64) for the intervention arm; BASICS trial, relative risk, 0.87 (95% CI, 0.68–1.12).

Several factors should be discussed regarding the failure of the BEST and BASICS. First, the inclusion criteria may not have been tailored to maximize EVT outcomes (it was also expanded in BASICS owing to slow recruitment). For the maximal effica-

cy of reperfusion therapy, there should be a large penumbral area relevant to clinical severity, while the extent of the infarct core should be limited.²⁰ The inclusion criteria of both studies seemed permissive to large infarct volumes only excluding in-

tracranial hemorrhage, extensive bilateral brainstem infarction, cerebellar mass effect, or acute hydrocephalus. Accordingly, the probability of futile recanalization may have increased.¹³ Furthermore, there were no clinical severity criteria for BEST, and NIHSS scores ≥ 10 in the BASICS criteria were later discarded.¹² Initially, the BASICS investigators assumed a primary outcome rate of 40% in the EVT group and 30% in the medical group, which was modified to 46% and 30%, respectively, taking into account the results of AC-EVT trials and slow recruitment. The observed primary outcome rate of 44.2% in the EVT group was largely comparable to the predicted rate; however, the rate of 37.7% in the medical group was higher than predicted. In a subgroup of patients with an NIHSS score of ≥ 10 , which was the initial severity criterion, the primary outcome rate was 39% (48/123) in the EVT group and 27% (31/119) in the medical group, with an absolute difference of 12%. However, in patients with an NIHSS score < 10 , the primary outcome rate was higher in the medical group (80%, 24/30) than in the EVT group (65%, 20/31), reaffirming the importance of clinical severity criteria.¹²

The second issue was the high crossover rate and drops in the average rate of valid recruitments per center. This occurred because of resistance to conservative treatment by family members in the BEST trial and perhaps in BASICS also. Therefore, a large number of patients were treated outside the trial (29% of screened patients in the BASICS and 55% of screened patients in the BEST trial),²¹ potentially causing bias.

The positive results of the ATTENTION and BAOCHÉ trials emphasize the importance of patient selection. Both trials applied specific patient selection criteria composed of baseline neurological severity and infarct volumes estimated by PC-ASPECTS and the pons midbrain index. These factors are discussed further in the following sections.

PC-EVT versus AC-EVT

Many studies have compared the outcomes of PC-EVT and AC-EVT.²²⁻²⁵ Overall, the reported clinical severity measured by the NIHSS was similar between the groups. However, a lower rate of IV thrombolysis and longer interval from stroke onset-to-recanalization were mostly observed in PC-EVT than in AC-EVT,¹³ likely due to delays in diagnosis or need for general anesthesia in real-world practice. Recanalization rates were comparable,^{13,22,23} while one study reported longer procedure duration for BAO and a trend toward more frequent procedural complications.²⁴ A meta-analysis comparing PC-EVT and AC-EVT including seven studies showed that PC-EVT was associated with a lower rate of functional independence at 90 days (odds ratio

[OR], 0.72; 95% CI, 0.57 to 0.90), higher rate of mortality (OR, 2.03; 95% CI, 1.30 to 3.18), and lower rate of sICH (OR, 0.54; 95% CI, 0.29 to 0.99).¹³ Rates of futile recanalization were higher for PC-EVT in multiple studies,^{24,26} with age, stroke severity, maneuver count, and intracranial stenting identified as predictors of futile recanalization.²⁶ Such differences between PC-EVT and AC-EVT urge us to closely consider the prognostic factors associated with PC-EVT as proper patient selection is essential to reduce futile recanalization.

Another neglected issue is the etiology (or pathogenesis) of stroke. LVO stroke patients undergoing EVT have different etiologies, such as cardiac embolism (CE-LVO), intracranial atherosclerotic (ICAS) thrombosis, and artery-to-artery embolism.²⁷ Upon comparison of the etiology-related outcomes between PC-EVT and AC-EVT, PC-EVT group tend to be younger, had CE-LVO less frequently, and had a longer onset-to-recanalization time.²³ The relatively longer onset-to-door time in the PC-EVT group may be attributed to symptoms including dizziness, diplopia, and visual dimness that were not considered as serious neurologic symptoms.²⁸

The relatively delayed onset-to-puncture time in the PC-EVT group was most striking in patients with CE-LVO. Although the NIHSS score was highest in CE-LVO patients in the AC-EVT group, it was similar among the three etiologies in the PC-EVT group. Although CE-LVO in the AC-EVT group produced abrupt and severe motor dysfunction associated with sudden middle cerebral artery or internal carotid occlusion, CE-LVO in the PC-EVT group typically occluded the distal basilar or posterior cerebral arteries. This is less likely to cause severe motor dysfunction, thereby delaying the initiation of the EVT decision.²⁹

Prognostic factors and EVT indications

As discussed above, the careful selection of optimal candidates for PC-EVT is important. In this regard, the prognostic factors of PC-EVT, which may generally be identifiable before the procedure, are discussed below as follows: baseline neurological severity, infarct volumes, collateral circulation, time from onset-to-EVT, and core-penumbra mismatch. In each section, discussions on wider or expanded indications are incorporated. Good clinical outcomes were defined as 3-month mRS 0-2 and favorable outcomes as mRS 0-3 in this review.

Baseline neurological severity

Baseline severity: can we treat the lower extreme?

Although an NIHSS score ≥ 6 has been recommended for AC-EVT, evidence regarding the clinical severity threshold for PC-

EVT has not been well studied. While BASICS failed to demonstrate the EVT efficacy in the overall participants, possible benefits were observed in patients who had an NIHSS score ≥ 10 , whereas the chances of achieving favorable outcomes in those with NIHSS score < 10 tended to be higher in the medical management group (65% vs. 80%).¹² The lower margin criterion for clinical severity in the BASICS is supported by the BASICS cohort, which showed that in patients with a mild-to-moderate deficit (vs. severe deficits, defined as coma, tetraplegia, or a locked-in state), direct comparison of intra-arterial therapy and intravenous thrombolysis showed an absolute increase in the risk of death or dependence by 20% with intra-arterial therapy.^{21,30} For patients with low NIHSS scores, EVT complications, such as distal thrombus migration resulting in Willisian collateral failure,³¹ may be devastating. In addition, these patients may have well-developed collaterals,³² and may be more responsive to intravenous thrombolysis.³³

Thus, EVT for patients with low NIHSS scores in the posterior circulation should be selectively performed, e.g., when early neurological deterioration (END) is expected. Patients who experience END are often treated with EVT beyond the traditional therapeutic time window, and they are likely to benefit the most from preemptive EVT before clinical deterioration. This issue is important because the END rate in patients with VBAO was over 30% in those with a low NIHSS score in a retrospective study.³⁴ However, data regarding predictors of END are limited, and potential factors predictive of END that need to be validated include high blood pressure, shorter onset-to-door times, incomplete occlusions, larger infarct cores, and poorer collaterals.³⁵

The second issue is the safety of EVT in VBAO patients with low NIHSS scores. The posterior circulation may be more prone to Willisian collateral failure during procedure,³⁶ resulting in critical END.³¹ In VBAO with low NIHSS, it is likely that the critical Willisian collateral flow involving the basilar top is partially spared, and manipulation of the thrombus may hamper this. The procedural issues for PC-EVT are discussed in detail in the following sections. It should be noted that the ATTENTION trial enrolled patients with NIHSS ≥ 10 , and BAOCHÉ a severity of NIHSS ≥ 6 .^{7,8}

Baseline severity: can we treat the higher extreme?

It is also an issue whether a very high NIHSS score or coma is an appropriate indication for PC-EVT. Higher NIHSS scores were consistently associated with worse PC-EVT outcomes (Table 3). However, a high NIHSS score is generally not considered a contraindication to EVT. The outcomes of comatose patients

undergoing EVT have not been reported uniformly. The data from the Endovascular Treatment in Ischemic Stroke (ETIS) cohort showed that comatose presentation was associated with worse long-term outcomes (mRS 0–3, 11% vs. 54%, $P < 0.0001$) and higher mortality (64% vs. 34%, $P < 0.0001$) than non-comatose presentation.³⁷ In contrast, in a single center study performed in Finland, 20.4% of comatose patients had a favorable outcome after EVT, contesting the futility of EVT in this population.³⁸ Furthermore, data from the Endovascular Treatment for Acute Basilar Artery Occlusion Study Registry (BASILAR) showed a more than 5-fold increase in the likelihood of achieving favorable functional outcome at 90 days with EVT for severe BAO classified as an NIHSS score ≥ 21 .³⁹ Accordingly, it is the authors' opinion that patients should not be deprived of treatment opportunity due to severe symptoms alone. Studies evaluating the effect of clinical severity on outcomes are summarized in Table 3.^{3,5,30,32,34,37–47}

Baseline infarct volumes

CT-based measurements

While a small baseline infarct core, for which the ASPECTS was most widely used, was emphasized in AC-EVT,⁴⁸ recent RCTs for PC-EVT did not have an infarct volume criterion.^{11,12} However, multiple studies have shown that baseline infarct volume was associated with outcomes and responsiveness to PC-EVT (Table 4).^{5,34,40,47,49–58}

PC-ASPECTS was developed as a tool to measure infarct volume based on noncontrast computed tomography (CT) or CT angiography source images (CTASI). Owing to the regional eloquence of the brainstem over the cerebellum, a weighted scale was applied. One point is subtracted for early ischemic changes on noncontrast CT or hypoattenuation on CTASI in the left or right thalamus, cerebellum, or posterior cerebral artery (PCA) territory, respectively, and 2 points each for early ischemic change (noncontrast CT) or hypoattenuation (CTASI) in any part of the midbrain or pons.⁴⁹ In the original report, PC-ASPECTS score on CTASI but not noncontrast CT predicted functional independence with a cutoff value of ≥ 8 in BAO patients.⁴⁹ Its utility was further confirmed in the BASICS registry that included patients with BAO, in which a point of ≥ 6 was associated with favorable outcomes (aRR, 3.1; 95% CI, 1.2 to 7.5) compared with those with PC-ASPECTS of < 6 .⁵⁰ The pons midbrain index is another scoring system that assesses the ischemic changes localized to the pons and midbrain in CTASI.⁵¹ From an early report, the index has been measured with hypoattenuation degrees in the medulla, pons, midbrain, thalami, cerebellum, occipital lobes, inferior parietal lobes, and mid-

Table 3. Studies evaluating the effect of clinical severity on outcomes

Author (year) (study period)	Study design	No. of patient	Vascular territory	Outcome definition	Main study findings
Overall severity					
Singer et al. (2015) ⁴¹ (2011–2013)	Multicenter ENDOSTROKE registry	148	BAO	3-mo mRS 0–2	NIHSS on functional outcomes (aOR, 0.92; 95% CI, 0.88–0.96)
Yoon et al. (2015) ⁴⁰ (2010–2015)	Single center retrospective	50	BAO	3-mo mRS 0–2	NIHSS on functional outcomes (aOR, 0.82; 95% CI, 0.71–0.95)
Bousslama et al. (2017) ³ (2005–2015)	Two center retrospective	214	VBAO	3-mo mRS 0–2	Lower NIHSS on functional outcomes (aOR, 1.09; 95% CI, 1.04–1.13)
Gory et al. (2018) ⁵ (2010–2017)	Multicenter ETIS registry	117	BAO	Mortality	NIHSS \geq 13 for mortality (aOR, 4.62; 95% CI 1.42–15.03)
Giorgianni et al. (2018) ⁴⁴ (2010–2015)	Multicenter retrospective RELOBA registry	102	BAO	3-mo mRS 0–2	Decrease in NIHSS on functional outcomes (aOR, 1.12, 95% CI, 1.01–1.13)
Kang et al. (2018) ⁴⁵ (2011–2017)	Multicenter retrospective	212	BAO	3-mo mRS 0–2	NIHSS on functional outcomes (aOR, 0.904; 95% CI, 0.875–0.935)
Li et al. (2018) ⁴⁶ (2014–2016)	Single center retrospective	50	BAO	3-mo mRS 0–3	NIHSS on functional outcomes (aOR, 0.832; 95% CI, 0.715–0.968)
Baek et al. (2019) ⁴³ (2010–2018)	Single center retrospective	77	VBAO	3-mo mRS 0–2	NIHSS on functional outcomes (aOR, 0.82; 95% CI, 0.74–0.91)
Choi et al. (2020) ⁴² (2016–2019)	Single center retrospective	50	BAO	3-mo mRS 0–2	NIHSS on functional outcomes (aOR, 0.893; 95% CI, 0.806–0.990)
Low NIHSS					
Schonewille et al. (2009) ³⁰ (2002–2007)	Multicenter prospective	All=592 IAT=288	BAO	1-mo mRS 4–6	Patients with mild-to-moderate deficit had higher risk of poor outcome (37% vs. 57%) when treated with IAT (aRR, 1.49, 95% CI, 1.00–2.23).
Raymond et al. (2018) ³⁴ (2004–2016)	Single center retrospective	89 Medical or EVT	VBAO	3-mo mRS 0–2	Patients with NIHSS >10 did better with EVT, NIHSS \leq 10 did well regardless of treatment type.
High NIHSS or coma					
Luo et al. (2018) ⁴⁷ (2012–2016)	Single center retrospective	69	VBAO	3-mo mRS 0–2	NIHSS \geq 22 for good outcomes (aOR, 0.157; 95% CI, 0.040–0.614)
Wu et al. (2021) ³² (2016–2020)	Multicenter retrospective	72	BAO	3-mo mRS 0–2	Minor to moderate stroke (NIHSS <21) had better collateral and had better outcomes than those patients with severe stroke.
Guenego et al. (2021) ³⁷ (2012–2019)	Multicenter ETIS registry	269	BAO	3-mo mRS 0–3	Comatose vs. non-comatose (11% vs. 54%, $P < 0.0001$)
Ritvonen et al. (2021) ³⁸ (1995–2019)	Single center retrospective	312 IV or EVT	BAO	3-mo mRS 0–3	One in five BAO patients with acute coma had still had favorable outcome.
Kong et al. (2021) ³⁹ (2014–2019)	Multicenter BASILAR registry	542 Medical or EVT	BAO	3-mo mRS 0–3	In BAO patients with severe symptoms (NIHSS \geq 21) EVT was associated with increased odds of favorable outcomes.

ENDOSTROKE, Endovascular Stroke Treatment; BAO, basilar artery occlusion; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; aOR, adjusted odds ratio; CI, confidence interval; VBAO, vertebrobasilar artery occlusion; ETIS, Endovascular Treatment in Ischemic Stroke; RELOBA, Registro Endovascolare Lombardo Occlusione Basilar Artery; IAT, intra-arterial therapy; aRR, adjusted risk ratio; EVT, endovascular treatment; BASILAR, Endovascular Treatment for Acute Basilar Artery Occlusion Study Registry.

dle temporal lobes: 0, no hypoattenuation; 1, <50% hypoattenuation; and 2, >50% hypoattenuation. Only the pons and midbrain scores were associated with death and disability. The authors proposed a combined pons midbrain index of ≥ 3 as a cutoff point.⁵¹

Magnetic resonance imaging-based measurements

Because CT evaluation of the brainstem is limited by bone artifacts or partial volume effect,⁵⁹ studies have used diffusion-weighted magnetic resonance imaging (DWI) for infarct volume measurements.⁵² PC-ASPECTS measured by DWI⁵³ has been used in various cohort data.^{40,52} In a retrospective study

Table 4. Studies evaluating the effect of infarct volume on outcomes

Author (year) (study period)	Study design	No. of patient	Modality	Evaluated index	Main study findings
CT-based measurements					
Puetz et al. (2008) ⁴⁹ (2001–2006)	Single center retrospective	130 Vertebrobasilar ischemia and 46 BAO	CTASI	PC-ASPECTS	PC-ASPECTS ≥ 8 associated with favorable outcome (RR, 12.1; 95% CI, 1.7 to 84.9)
Puetz et al. (2011) ⁵⁰ (2002–2007)	Multicenter BASICS registry	78 BAO	CTASI	PC-ASPECTS	PC-ASPECTS ≥ 6 associated with favorable outcome (RR, 3.1; 95% CI, 1.2–7.5)
Schaefer et al. (2008) ⁵¹ (2003–2006)	Single center retrospective	16 EVT	CTASI	Pons midbrain index	Combined pons/midbrain score of ≥ 3 associated with mortality
Pallesen et al. (2016) ⁵⁷ (2002–2007)	Multicenter BASICS registry	158 BAO	CTASI	Pons midbrain index PC-ASPECTS	Among comatose patients, a Pons midbrain index < 3 related to reduced mortality (aRR, 0.66; 95% CI, 0.46–0.96)
MRI-based measurements					
Tei et al. (2010) ⁵³ (1994–2008)	Single center retrospective	132 Posterior circulation infarction	DWI	PC-ASPECTS	PC-ASPECTS predictive of unfavorable functional outcomes (aOR, 0.40; 95% CI, 0.23–0.67)
Son et al. (2015) ⁵⁸ (2011–2014)	Single center retrospective	35 BAO EVT	DWI	PC-ASPECTS	Good vs. poor outcomes, mean PC-ASPECTS (7.8 ± 1.6 vs 5.4 ± 1.8 , $P=0.001$)
Yoon et al. (2015) ⁴⁰ (2010–2015)	Single center retrospective	50 BAO EVT	DWI	PC-ASPECTS	PC-ASPECTS predictive of good outcomes (aOR, 1.854; 95% CI, 1.012–3.397)
Gory et al. (2018) ⁵ (2010–2017)	Multicenter ETIS registry	117 BAO EVT	CT or DWI	PC-ASPECTS	Lower PC-ASPECTS predictive of mortality (aOR, 1.71; 95% CI, 1.19–2.44)
Luo et al. (2018) ⁴⁷ (2012–2016)	Single center retrospective	69 BAO EVT	DWI	PC-ASPECTS	PC-ASPECTS ≥ 6 associated with good clinical outcome (aOR, 7.335; 95% CI, 1.495–36.191)
Guillaume et al. (2019) ⁵⁶ (2010–2017)	Multicenter ETIS registry	95 BAO EVT	DWI	PC-ASPECTS	Association between imaging-to-reperfusion time and good outcomes for patients with PC-ASPECTS < 8 (aOR, 0.4 per 30 min; 95% CI, 0.18–0.85), compared with those with PC-ASPECTS ≥ 8
Mourand et al. (2014) ⁵⁴ (2009–2011)	Single center retrospective	31 BAO EVT	DWI	BSS	BSS < 3 associated with good outcomes (OR, 9.92; 95% CI, 1.75–56.30)
Yang et al. (2018) ⁵⁵ (2012–2016)	Single center retrospective	50 BAO EVT	DWI	BSS	DWI BSS ≤ 2 predictive of favorable outcome (aOR, 12.4; 95% CI, 2.5–61.2) and > 3 associated with mortality (aOR, 7.9; 95% CI, 1.4–45.8)
Raymond et al. (2018) ³⁴ (2004–2016)	Single center retrospective	89 Medical and EVT	DWI	Proposed MRI criteria for EVT exclusion	Bilateral thalamus $> 50\%$ brainstem > 20 cc of cerebellum
Lee et al. (2020) ⁵² (2011–2016)	Multicenter ASIAN KR registry	VBAO EVT Derivation: 71 Validation: 32	DWI	Infarct volume	DWI volume < 10 mL predictive of good outcomes (aOR, 19.3; 95% CI, 3.0–126.4)

CT, computed tomography; BAO, basilar artery occlusion; CTASI, computed tomography angiography source image; PC-ASPECTS, Posterior Circulation Alberta Stroke Prognosis Early Computed Tomography Score; RR, risk ratio; CI, confidence interval; BASICS, Basilar Artery International Cooperation Study; EVT, endovascular treatment; aRR, adjusted risk ratio; MRI, magnetic resonance imaging; DWI, diffusion-weighted MRI; aOR, adjusted odds ratio; ETIS, Endovascular Treatment in Ischemic Stroke; BSS, brainstem score; ASIAN KR, Acute Stroke due to Intracranial Atherosclerotic occlusion and Neurointervention Korean Retrospective; VBAO, vertebrobasilar artery.

involving 31 patients undergoing PC-EVT, DWI correlated well to outcomes with high inter-rater reliability, with a score of ≥ 8 resulting in a positive predictive value of 90% and negative predictive value of 100% for the prediction of favorable outcomes.⁶⁰ A similar score, the brainstem score (BSS), is a DWI-based semi-quantitative 12-point system in which each brainstem level (medulla, pons, and midbrain) is evaluated separately. One point was assigned for each unilateral high-intensity

lesion at the brainstem level (medulla, pons, and midbrain) that occupied less than half of the area; 2 points were given if the lesion occupied more than half of the area. The brainstem DWI lesion score ranges from 0 to 12.⁵⁴ In patients undergoing PC-EVT, DWI BSS ≤ 2 was an independent predictor of good outcomes, while DWI BSS > 3 was predictive of high mortality.⁵⁵ Currently, the PC-ASPECTS (DWI or CT) score is most widely used for the pre-procedural infarct volume assessment. It has

Table 5. Studies evaluating significance of collateral on outcomes

Author (year) (study period)	Design	No. of patients	Classification of collaterals	Main study results
Singer et al. (2015) ⁴¹ (2011–2013)	Multicenter ENDOSTROKE registry	148 BAO EVT	ASITN/SIR grade TFCA	Collaterals associated with good clinical outcome (aOR, 2.12; <i>P</i> =0.023) and recanalization (aOR, 3.087; <i>P</i> =0.002)
van Houwelingen et al. (2016) ⁶⁵ (2006–2015)	Single center retrospective	38 BAO EVT	Composite collateral score	No association between collateral score and outcomes
van der Hoeven et al. (2016) ⁶¹ (2002–2007)	BASICS registry	149 BAO	PC-CS	Lower risk of poor outcome for good PC-CS (6–10) than with poor PC-CS (0–3) (RR, 0.74; 95% CI, 0.58–0.96)
Alemseged et al. (2017) ⁶² (2005–2016)	Prospective multicenter 2005–2016	124 BAO	BATMAN	BATMAN score of <7 associated with poor outcomes (aOR, 5.5; 95% CI, 1.4–21)
Luo et al. (2018) ⁴⁷ (2012–2016)	Single center	69 BAO EVT	ASITN/SIR grade	≥2 points associated with mortality (aOR, 0.210; 95% CI, 0.059–0.752)
Alemseged et al. (2019) ⁶⁴ (2002–2017)	Multicenter BATMAN & BASICS registry	172 BAO EVT	BATMAN	Early (time-to-treatment ≤6 hours) but not late revascularization associated with improved outcome in patients with unfavorable collaterals
Lee et al. (2020) ⁵² (2011–2016)	Multicenter ASIAN KR registry	VBAO EVT Derivation: 71 Validation: 32	PC-CS, BATMAN	No association between collaterals and outcomes
Kwak et al. (2020) ⁶³ (2012–2019)	Single center retrospective	81 BAO EVT	BATMAN, PC-CS	PC-CS ≥6 associated with good functional outcome (aOR, 3.79; 95% CI, 1.05–13.66)
Yang et al. (2018) ⁶⁶ (2012–2016)	Single center prospective	63 BAO EVT	DSA BATMAN	BATMAN score >3 associated with good outcome (aOR, 5.214; 95% CI, 1.47–18.483)

ENDOSTROKE, Endovascular Stroke Treatment; BAO, basilar artery occlusion; EVT, endovascular treatment; ASITN/SIR, The American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; TFCA, transfemoral cerebral angiography; aOR, adjusted odds ratio; BASICS, Basilar Artery International Cooperation Study; PC-CS, posterior circulation collateral score; RR, risk ratio; CI, confidence interval; BATMAN, Basilar Artery on Computer Tomography Angiography; ASIAN KR, Acute Stroke due to Intracranial Atherosclerotic Occlusion and Neurointervention Korean Retrospective; VBAO, vertebrobasilar artery; DSA, digital subtraction angiography.

not been proven that eloquence-weighted methods of assessing infarct volume, such as PC-ASPECTS or BSS, are superior to simple infarct volume measurement. In the Acute Stroke due to Intracranial Atherosclerotic Occlusion and Neurointervention Korean Retrospective (ASIAN KR) multicenter registry, PC-ASPECTS or BSS was not superior to simple infarct volume measurement, and a DWI volume of <10 mL highly predicted good outcomes (OR, 57.5; 95% CI, 4.6 to 713.4).⁵²

It should be noted that the PC-ASPECTS, measured on non-contrast CT/CTASI/DWI, was used as one of the inclusion criteria in the ATTENTION trial. For patients aged <80 years, PC-ASPECTS ≥6 was included, while for those aged ≥80 years, PC-ASPECTS ≥8 was included.⁸ In the BAOCHÉ trial, patients had to have both PC-ASPECTS ≥6 and pons midbrain index ≤2.⁷

Collateral circulation

Good collateral circulation and better clinical outcomes

The collateral circulation of the posterior circulation has been

evaluated using catheter angiography or noninvasive methods (Table 5).^{41,47,52,61–66} The American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grade (range 0–4) could be applied to the posterior circulation. In the Endovascular Stroke Treatment (ENDOSTROKE) study, a 1 step increase in the ASITN/SIR grade was associated with an increased good outcome (OR, 2.12; 95% CI, 1.11 to 4.06) and successful reperfusion (OR, 3.09; 95% CI, 1.51 to 6.31) in BAO patients treated with EVT.⁴¹ The collateral scores can also be noninvasively evaluated using the posterior circulation collateral score (PC-CS) or Basilar Artery on Computer Tomography Angiography (BATMAN) score. The PC-CS is a 10-point grading system in which each patent posterior inferior cerebellar artery, anterior inferior cerebellar artery, and superior cerebellar artery is allocated 1 point. Identification of a posterior communicating artery (PCoA) was allocated 1 point if its diameter was smaller than the ipsilateral P1 segment and 2 points if its diameter was equal or larger than this segment. Fetal variants of PCA were not included in this score. This score was evaluated in the BASICS registry.⁶¹ When the PC-CS was trichotomized to poor (PC-CS, 0–3), intermediate (PC-CS, 4–5),

and good (PC-CS, 6–10) collaterals, patients with a good PC-CS compared to those with a poor PC-CS were less likely to have poor outcome (aRR, 0.74; 95% CI, 0.58 to 0.96).⁶¹ The BATMAN score is a 10-point computed tomographic angiography-based grading system that incorporates thrombus burden and presence of collaterals.⁶² For a patent segment of each P1 PCA, vertebral arteries (considered as 1 segment), proximal BA, middle BA, and distal BA, one point was allocated. For each patent PComA that had continuity with BA through P1 segment, two-point was given if the diameter was ≥ 1 mm and one point was assigned if it was < 1 mm. In case of patent fetal-type PComA, 3-point was allocated in each side. When tested in BAO patients presenting within 24 hours, the BATMAN score was significantly associated with outcomes, and it had greater accuracy than PC-CS.⁶²

Collateral status influenced by etiology

Some factors may influence the impact of collaterals on the outcomes. First, it may be influenced by occlusion etiology. In the analysis of the ASIAN KR registry, which included VBAO patients undergoing EVT, collateral scores were not predictive of outcomes.⁵² There was abundance of ICAS-related occlusions in this Asian cohort, which was associated with poor outcomes.^{67,68} Chronic longstanding ICAS may be associated with higher collaterals, diluting the impact of collaterals on outcomes.⁶⁹ Second, in proximal occlusions, the impact of collaterals seems less obvious.⁷⁰ In vertebral artery (VA) or proximal basilar occlusions causing critical perfusion failure, the basilar top may be more frequently spared, resulting in higher collateral scores. However, this does not seem to guarantee favorable outcomes for proximal occlusions.

In contrast, in another more recent Korean cohort in which underlying ICAS-related occlusion was not associated with outcomes, both the BATMAN score and PC-CS were associated with good outcomes in univariate analysis. PC-CS ≥ 6 was associated with good outcomes (OR, 3.79; 95% CI, 1.05 to 13.66) in multivariate analysis, while a BATMAN score ≥ 6 was not.⁶³ Thus, the two study results showed a possible interaction between collaterals and etiology on outcomes.

Collaterals via posterior communicating artery

The PComA collateral status is emphasized in both the PC-CS and BATMAN grades.^{61,62} The presence of PComA is generally considered to be associated with favorable clinical outcomes.^{61,71} However, the significance of fetal PComA is controversial. A positive association between the presence of fetal-type PComA and good outcomes has been reported,⁷² claiming that PComA acts as a safeguard against ischemic in-

sult. In contrast, when limited to the top of the basilar artery stroke, mostly caused by an embolism,⁷³ the presence of fetal-type PComA was associated with poorer outcomes, due to inaccessibility of retrograde flow from P1 segment to the basilar artery, and the thrombus to be lodged in the basilar top, causing downward thrombus extension.⁷⁴ From the perspective of EVT, there is a chance that fetal PComA may complicate EVT results by producing lower rates of reperfusion due to the absence of collateral flow and a smaller vertebrobasilar artery diameter.

Time from onset to treatment

In AC-EVT, the emphasis of onset-to-EVT time is diminishing with the recognition that the therapeutic time window can be modified by collateral status,⁷⁵ or selection of patients by clinical-core or core-penumbra mismatch.^{14,15} Once an EVT candidate is selected, interest is focused on the time from imaging-to-reperfusion.⁷⁶ However, in the analysis of real-world AC-EVT data in patients who presented within 8 hours, shorter onset-to-puncture time was associated with better functional outcomes, and its relationship slope was steeper in the 30 to 270 minutes than in the 271 to 480 minutes timeframe.⁷⁷

Despite the inconsistent results (Table 6),^{2,41-43,45,46,52,56,63,64,78} the onset-to-EVT time is intuitively correlated with infarct growth in PC-EVT. A recent multicenter study utilizing the Get With The Guidelines-Stroke nationwide United States registry, which included 3,015 BAO patients, showed that onset-to-EVT time < 6 hours was significantly associated with lower in-hospital mortality (aOR, 0.55; 95% CI, 0.45 to 0.68) and sICH (aOR, 0.52; 95% CI, 0.32 to 0.84) rates, and a higher rate of independence at discharge (aOR, 2.21; 95% CI, 1.66 to 2.95) than those with > 6 hours.⁷⁸ The fastest decline of good outcomes per hour occurred within 6 hours of symptom onset. Regarding late-window treatment, imaging-based patient selection utilizing the core-penumbra mismatch concept is currently less established in PC-EVT. However, recent literature has revealed that the significance of time to outcome may differ on an individual basis, and rapid and slow growers may be identified by infarct volume and collateral status, as shown in the anterior circulation.⁷⁹

Some studies have shown that time criteria may be modified by baseline infarct volumes. The multicenter ETIS registry showed that time dependent deteriorations in clinical outcomes was less significant in those with PC-ASPECTS ≥ 8 , compared with the decay in probability of good outcomes as time passed in medium to large stroke (PC-ASPECTS < 8).⁵⁶ A predictive model of good outcomes generated from the ASIAN KR

Table 6. Studies evaluating the effect of time to endovascular treatment on outcomes

Author (year) (study period)	Study design	No. of patients	Vascular bed	Inclusion time criteria	Main findings
Singer et al. (2015) ⁴¹ (2011–2013)	Multicenter ENDOSTROKE registry	148	BAO	Not specified	Onset to treatment time in 3 hr increments showed no association
Mokin et al. (2016) ² (2011–2015)	Multicenter retrospective	100	VBAO	<24 hr	Shorter time from onset-to-puncture associated with good outcomes
Li et al. (2018) ⁴⁶ (2014–2016)	Single center retrospective	50	BAO	<24 hr	No difference in outcomes between time to EVT <6 hr and ≥6 hr
Alemseged et al. (2019) ⁶⁴ (2002–2017)	Multicenter BATMAN Et BASICS registry	172	BAO	<24 hr	Early (time-to-treatment ≤6 hours) but not late revascularization associated with improved outcome in patients with unfavorable collaterals
Kang et al. (2018) ⁴⁵ (2011–2017)	Multicenter retrospective	212	BAO	<12 hr	Time from onset to reperfusion not associated with functional independence
Guillaume et al. (2019) ⁵⁶ (2010–2017)	Multicenter ETIS registry	95	BAO	Not specified	Negative association between imaging-to-reperfusion time for patients with PC-ASPECTS <8, compared with those with PC-ASPECTS ≥8
Baek et al. (2019) ⁴³ (2010–2018)	Single center retrospective	77	VBAO	<12 hr	Puncture-to-recanalization time associated with good outcomes (per 10 min, OR, 0.81; 95% CI, 0.65–0.99)
Lee et al. (2020) ⁵² (2011–2016)	Multicenter ASIAN KR registry	Derivation: 71 Validation: 32	VBAO	<24 hr	Onset-to-puncture time <8 hr associated with good outcomes (aOR, 8.7; 95% CI, 1.8–42.0)
Kwak et al. (2020) ⁶³ (2012–2019)	Single center retrospective	81	BAO	Not specified	Time from symptom onset-to-recanalization not correlated with good outcomes
Choi et al. (2020) ⁴² (2016–2019)	Single center retrospective	50	BAO	Not specified	Longer procedure time shows reverse association with favorable outcomes (aOR, 0.97; 95% CI, 0.95–0.99)
Joundi et al. (2022) ⁷⁸ (2015–2019)	Multicenter GWTG-stroke registry	3015	BAO	<24 hr	Onset-to-EVT time ≤6 hr (vs. >6 hr) associated with independence at discharge (aOR, 2.21, 95% CI, 1.66–2.95), ambulation at discharge, lower in-hospital mortality, and sICH

ENDOSTROKE, Endovascular Stroke Treatment; BAO, basilar artery occlusion; VBAO, vertebrobasilar artery; EVT, endovascular treatment; BATMAN, Basilar Artery on Computer Tomography Angiography; BASICS, Basilar Artery International Cooperation Study; ETIS, Endovascular Treatment in Ischemic Stroke; PC-ASPECTS, Posterior Circulation Alberta Stroke Prognosis Early Computed Tomography Score; OR, odds ratio; CI, confidence interval; ASIAN KR, Acute Stroke due to Intracranial Atherosclerotic occlusion and Neurointervention Korean Retrospective; aOR, adjusted odds ratio; GWTG, Get With The Guidelines; sICH, symptomatic intracranial hemorrhage.

registry also agrees with this finding.⁵² In the generated predictive model for good outcomes (BAO patients within 24 hours from onset-to-EVT), the three most important variables identified were baseline infarct volume (<10 mL), onset-to-puncture time (<8 hours), and embolic occlusions (compared with ICAS occlusions).⁵² If the patient suffered an embolic VBAO and the presenting infarct volume was small, the total score of the predictive model was sufficiently enough that good outcomes could be expected irrespective of time.

Similarly, several studies have shown that time criteria may be modified by collateral status. A pooled analysis of the multicenter BATMAN and BASICS registries showed that in patients with poor collaterals (unfavorable BATMAN collateral score), time-to-treatment of ≤6 hours was associated with improved outcomes, while this association was not shown in patients with good collaterals, concluding that revascularization

can be associated with favorable outcomes in BAO patients with good collaterals and less extensive occlusion, even >6 hours after onset.⁶⁴ This result was also replicated in another single center retrospective study that showed pronounced impact of collateral status on functional outcome and mortality, particularly in the subgroup of patients who experienced recanalization beyond 6 hours.⁸⁰

Core-penumbra mismatch for PC-EVT

Criteria of core and penumbra

An imminent challenge is to better understand the core-penumbra mismatch or clinical-core mismatch in the posterior circulation.^{14,15} The clinical-core mismatch concept is based on preliminary data that showed a mismatch between NIHSS score ≥8 and DWI volume ≤25 mL to strongly predict infarct

growth in patients with middle cerebral artery M1 occlusion.^{81,82} Similarly, it is important to generate an optimal mismatch criterion in the posterior circulation. First, the upper limit of the tolerable infarct volume must be identified. In VBAO, an overall infarct volume of 10 mL,⁵² or a volume of 10 mL localized to the brainstem, is considered a predictor of poor outcomes.^{83,84} If MRI is not feasible, PC-ASPECTS should be considered. A PC-ASPECTS score of ≥ 6 , predictive of favorable outcomes,⁵⁰ or a score of PC-ASPECTS ≥ 5 ,⁸⁵ which was identified as the lower limit for benefit of EVT, may be used as a core criterion. In the latter study, EVT was associated with favorable outcomes and lower mortality than medical therapy in both PC-ASPECTS 5–7 and 8–10 subgroups. Furthermore, the association of onset-to-puncture time and favorable outcome was not significant after adjustment for PC-ASPECTS, suggesting that the core criterion is more significant than time parameters.⁸⁵

Second, penumbral criteria for predicting infarct growth should be established. It may be generated clinically by utilizing NIHSS criteria of ≥ 10 , which showed promising results in BASICS.¹² Alternatively, alteration of mental status may be used as a criterion. In a retrospective study evaluating VBAO patients with acceptable infarct volumes (PC-ASPECTS ≥ 6), a decrease in the NIHSS consciousness subset scores of ≥ 1 was more strongly predictive of infarct growth than an NIHSS score of >10 .⁸⁶ Reduction in mental status may be indicative of global perfusion failure of the vertebrobasilar territory, resulting in infarct growth.

Mismatch studies with perfusion maps

Only recently studies utilizing perfusion imaging in VBAO have been published. In these studies, perfusion parameters were considered proxies for the infarct core and predictors of outcome, rather than to identify the core and penumbral mismatch. In 2019, the value of PC-ASPECTS manually measured in CT perfusion parameters was reported.⁸⁷ The cerebral blood volume (CBV) PC-ASPECTS was predictive of poor outcomes, with an area under the receiver operating characteristic curve (AUROC) of 0.83 (95% CI, 0.72 to 0.93), which was significantly higher than that of CTASI (AUROC, 0.64; 95% CI, 0.50 to 0.79). In the logistic regression analysis, CBV PC-ASPECTS ≤ 8 was independently associated with poor outcomes (aOR, 9.3; 95% CI, 2.2 to 41). Inter-rater agreement was substantial for the CBV PC-ASPECTS (intraclass correlation coefficient, 0.82; 95% CI, 0.71 to 0.90). Other CT perfusion parameters in BAO were also reported to be of prognostic significance.⁸⁸ In this study, perfusion deficit was defined as "the presence of a focal decrease of cerebral blood flow (CBF) or CBV, or focal increase

of mean transit time or time to drain compared with the contralateral side on at least two adjacent slices." Quantitative thresholds were not used in this study. In this analysis, early ischemic changes were measured using PC-ASPECTS on non-contrast CT, CTASI, and parametric whole-brain CT perfusion images. Perfusion deficit volumes on all CT perfusion maps (OR range, 0.77 to 0.98; 95% CI, 0.63 to 1.00) were independent outcome predictors in multivariable analysis adjusted for age and NIHSS. CBF deficit volume yielded the best performance for the classification of good clinical outcomes (AUROC, 0.92; 95% CI, 0.84 to 0.99). The predictive ability of the critical area perfusion score (CAPS, 0 to 6 points) on perfusion maps in BAO patients undergoing thrombectomy was also reported.⁸⁹ CAPS points were assigned based on the presence of Tmax >10 seconds, which involved adjacent axial image slices and had a minimum diameter of 6 mm on at least one slice within the following brain regions: cerebellum (1 point per hemisphere), pons (2 points), and midbrain and/or thalamus (2 points), for a total of 6 possible points. In this analysis, CAPS ≤ 3 was a robust independent predictor of favorable outcomes after adjustment for reperfusion, age, and NIHSS score (OR, 39.25; 95% CI, 1.34 to >999). Despite these significant results, successive studies focusing on cutoff values for the core and penumbra criteria are needed in the future. Using such criteria, fast/ultra-fast growers and slow growers,⁷⁹ which may potentially compose 19% and 14% of BAO strokes, respectively,⁹⁰ can be identified to provide individualized treatment.

Technical issues of EVT in posterior circulation stroke

Contact aspiration vs. stent retrieval

Comparison of contact aspiration and stent retrieval in AC-EVT has shown similar results in revascularization rate and clinical efficacy.⁹¹ While no clinical trials exist regarding this issue in PC-EVT, first-line contact aspiration may be more feasible. First, due to the blunt angle of the basilar bifurcation, microwire penetration inside the small thalamoperforating arteries may result in perforation or dissection of the arteries.^{92,93} Passing through the thrombus with a microwire and microcatheter is not required in contact aspiration methods, but it is necessary to deploy a stent retriever. Blind navigation of the microwire beyond the occlusive segment may increase the risk of perforation or dissection.⁴² Second, a large thrombus burden in both PCAs may result in a to-and-fro movement of the thrombus into the contralateral PCA without efficient thrombus removal if stent retrievers are deployed in only one PCA. Dual stent retrievers deployed to both PCAs have been utilized as a rescue

technique in some cases.⁹⁴ Contact aspiration may be superior to stent retrievers in this regard, as different forces are used. Furthermore, delivery of larger-bore catheters to the basilar artery is easier than to the anterior circulation because of the relatively straight vascular course; hence, the procedure time is reduced.⁴² Cohort data support such concerns. In the Multi-center Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in The Netherlands (MR CLEAN) registry data including 205 patients with posterior circulation stroke, contact aspiration was associated with better functional outcomes than stent retrieval (adjusted common OR for a 1-point improvement on the mRS, 1.94; 95% CI, 1.03 to 3.65), with higher rates of successful reperfusion and shorter procedure time when used as a first-line strategy.⁹⁵ Furthermore, in the ETIS prospective multicenter registry regarding BAO patients, contact aspiration was a strong predictor of the first pass effect.⁹⁶ In a meta-analysis including eight observational studies, compared with the stent retriever group, the direct aspiration group was associated with a higher thrombolysis in cerebral infarction 2b/3 reperfusion rate (OR, 1.85; 95% CI, 1.06 to 3.23). There was a tendency for higher rates of complication with stent retrievers, although statistical significance was not reached.⁹⁷ However, the findings may be attributed to selection bias inherent for observational studies. As a first-line treatment, direct aspiration with a large-bore aspiration catheter was likely used for patients with favorable vascular anatomy, while stent retriever thrombectomy might be provided to those in whom contact aspiration was not applicable.

A recent retrospective analysis including two prospectively maintained stroke registries showed higher odds of complete recanalization using combined stent retrievers plus direct aspiration than stent retrieval or direct aspiration alone or switching techniques.⁹⁸ Flow arrest with balloon guide catheters to reduce distal embolization⁹⁹ is not feasible in most cases of PC-EVT due to dual VA supplies.¹⁰⁰ Combined techniques may reduce antegrade blood flow due to the larger caliber and negative pressure, thus creating an environment similar to flow arrest.

Overcoming underlying atherosclerosis

ICAS LVO in the posterior circulation poses a greater therapeutic challenge given its higher proportion (40%) than that in the middle cerebral artery (23%) or internal carotid artery occlusions (6%) among patients treated with EVT.¹⁰¹ Different EVT results have been reported for ICAS-related VBAO. Some studies reported that the PC-EVT outcome was worse in patients with ICAS LVO than in those with embolic occlusions.^{5,52,67} However, others reported similar outcomes.^{43,102} Longer proce-

dures and complicated procedures may in part be accountable for the poor outcomes.³⁴ ICAS LVO may also be associated with involvement of the pontine perforators, as occlusion location tends to be lower than in embolic occlusions.^{103,104} Practically, it may be important to identify ICAS LVOs before the procedure.⁷³ If ICAS LVO can be identified before procedure, stent retrieval may be preferred over aspiration as the first-line treatment, as in some cases, *in situ* thrombus removal may be difficult due to lack of contact between catheter tip and thrombus during contact aspiration.¹⁰⁵ Furthermore, the operator may prepare for rescue therapy, which is needed in a large number of cases.⁷³

Overcoming tandem occlusions

Vertebrobasilar occlusion may have been caused by tandem occlusion. There may be a severe stenosis or occlusion at the proximal VA, limiting distal flow.¹⁰⁶ When compared with embolic occlusions without tandem lesion, tandem BAO was more frequently associated with longer procedural time, and poorer clinical outcome, despite a high rate of successful recanalization, with a marginally lower rate of good outcomes (53% vs. 29%, $P=0.05$), which was not significant in multivariable analysis.¹⁰⁶ This result was reproduced in another cohort data, in which tandem occlusions were associated with lower rates of successful reperfusion and good clinical outcomes, and higher rates of mortality.¹⁰⁷ However, in one study, EVT of tandem occlusions was reported to be safe and feasible.¹⁰⁸ The majority of the tandem occlusion patients were treated by the dirty-road-pathway (via the stenotic or occluded vertebral artery)¹⁰⁸ and treated by retrograde technique (thrombectomy performed first). In some cases, it is not possible to select and cross the vertebral stump using the femoral approach, and the contralateral VA is too thin for the clean-road pathway. In these cases, vascular access may be gained through exchange-length microwire access through the vertebrobasilar junction from the contralateral VA to the ipsilateral VA. The lesion is retrogradely crossed, and then the microwire can be snared out of the arm through the ipsilateral trans-brachial approach.¹⁰⁹ The microwire can then be used as a rail for angioplasty/stenting and further advancement of the brachial guide catheter.

Adjuvant treatment with balloon angioplasty with or without stent insertion can be performed on the tandem VA lesion.^{106,108} However, the decision to perform angioplasty of the tandem VA lesion may be controversial if the clean-road pathway is selected for intracranial thrombectomy, or due to concerns of hemorrhage.¹¹⁰ In a case series of 55 tandem VBAO patients, angioplasty of the tandem VA lesion was performed in 29% of the patients, and there were no procedure-related

complications. Two patients developed short-term reocclusion of the basilar artery after MT, and both had been treated with contralateral VA access without angioplasty of the tandem VA lesion.¹¹⁰ If angioplasty is planned, it may be assisted by a distal embolic protection device,¹⁰⁸ and both balloon-mounted and self-expanding stents may be used.^{106,108,111}

Conclusions

While two RCTs investigating the utility of PC-EVT have shown negative results, the results of following studies seem to be optimistic. These studies indicate that the therapeutic efficacy of PC-EVT may be maximized by reducing futile recanalization through the identification of prognostic factors and optimizing EVT procedures. Neurological severity, infarct volume, collateral circulation, and the time from onset-to-EVT were identified as prognostic variables. Research unveiling the interplay of these variables and the application of advanced imaging, such as perfusion maps, will generate the core-penumbra criteria for PC-EVT. Such advances will lead to the success of RCTs and improve patient outcomes through individualized patient selection.

Disclosure

The authors have no financial conflicts of interest.

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