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Original Article

Initial Results of Percutaneous Transluminal Angioplasty/Stenting for Vertebrobasilar Occlusion due to Atherothrombotic Disease during Acute Phase

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Objective: The efficacy and safety of acute percutaneous transluminal angioplasty or stenting (PTA/PTAS) for vertebrobasilar artery occlusion with atherothrombotic brain infarction (ATBI) have not been confirmed despite the resistance to medical therapy alone. There are few reports about this disease and its treatment. Therefore, the treatment outcomes at our hospital were summarized to evaluate the efficacy and safety.

Methods: This was a retrospective study of acute PTA/PTAS for vertebrobasilar artery occlusion due to atherosclerotic change in 19 consecutive patients with a modified Rankin Scale (mRS) score of 0-2 before stroke between March 2010 and December 2018. The factors related to prognosis were investigated. Outcomes were assessed at 90 days of follow-up.

Results: Of 19 patients with acute vertebrobasilar artery occlusion treated by PTA/PTAS, 8 had good outcomes (mRS 0–2) and 11 had poor outcomes (mRS 3–6). There were no differences in the clinical or patient background except for the National Institutes of Health Stroke Scale (NIHSS) score between groups. The good outcome group had a lower NIHSS score than the poor outcome group (median: 9.5 vs 35, $p < 0.001$). The Thrombolysis in Cerebral Ischemia (TICI) 2b-3 group had a slightly more favorable outcome than the TICI0-2a group ($p = 0.10$). There were no differences in outcome between PTA and PTAS groups ($p = 0.65$).

Conclusion: Reperfusion of the posterior circulation by PTA/PTAS may be necessary for a good outcome. Although acute stenting must be performed under careful observation, a stent can be placed when recurrence in the early phase is estimated with high probability.

Keywords ▶ vertebrobasilar occlusion, atherosclerotic change, ATBI, acute phase, PTA/PTAS

Introduction

In the Japanese Guidelines for the Management of Stroke 2015 (Supplement 2017), mechanical thrombectomy for major artery occlusion in the acute phase, within 6 hours after onset, is recommended as grade A. However, acute-phase percutaneous transluminal angioplasty/stenting (PTA/PTAS) are still based on Level 4 evidence and their grade of recommendation is C1, which is similar to that in 2009. There was a change in wording of the guidelines from "no sufficient scientific evidence" in 2009 to "may be considered" in 2015, but evidence is being established.[1,2] Currently, evidence is primarily obtained from observational studies, but the number of reports on posterior circulation occlusion remains small.[3–8] However, the results of medical treatment in atherothrombotic brain infarction (ATBI) patients with vertebrobasilar artery occlusion are not always favorable. At our hospital, acute-phase PTA/PTAS are actively performed. We report the prognostic factors, as well as the efficacy and safety of these procedures by examining the previous results of treatment.

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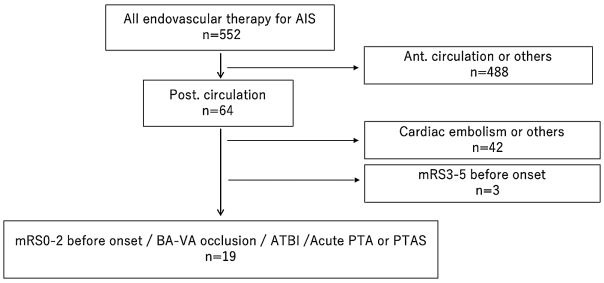

Fig. 1 Flowchart

Materials and Methods

We retrospectively investigated 19 patients with vertebrobasilar artery occlusion due to atherosclerotic disease and a modified Rankin Scale (mRS) score of 0 to 2 before onset in whom acute-phase PTA/PTAS were performed at our hospital between March 2010 and December 2018.

At our hospital, DSA is basically performed on all patients in whom acute occlusion is suspected based on CTA or MRA findings. Concerning anterior circulation, when there is no clinical-diffusion-weighted image (DWI) or perfusion- weighted image (PWI)-DWI mismatch, conservative treatment is routinely selected without performing recanalization therapy. However, concerning posterior circulation, it is often difficult to evaluate a mismatch using images and recanalization is tried, excluding patients with markedly mild symptoms. In those in whom a definitive diagnosis of ATBI cannot be made, a procedure with a stent retriever is initially performed for recanalization therapy. Under a diagnosis of ATBI, the basic acute-phase procedure is PTA alone, but stenting, which is off-label use, is performed after loading with two antiplatelet drugs (aspirin at 200 mg and clopidogrel at 300 mg) in patients with repeated re-occlusion during treatment or those in whom dissection is suspected. After intervention, the administration of the two antiplatelet drugs is continued, excluding patients with hemorrhagic infarction as a complication. Immediately after intervention, argatroban (60 mg/day) is administered intravenously for 2 days. For postoperative assessment, DSA is performed within 1 week after surgery. Subsequently, follow-up MRA is conducted at appropriate times. After 6 months, additional DSA is performed.

In this study, we examined the prognoses of all patients, assigned patients with a mRS score of 0–2 to the favorable outcome group and those with a mRS score of 3–6 to the poor outcome group and compared medical history, posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) before intervention, preoperative National Institutes of Health Stroke Scale (NIHSS) score, time from onset to puncture, site of occlusion, treatment methods, and results of treatment between two groups. When the basilar artery was occluded, site of occlusion was defined three divided areas: distal, middle, and proximal. In patients with slow progression, such as over ≥3 days, the time from onset to puncture was regarded as 3 days (72 hours). For statistical analysis, we used JMP software (ver. 10; SAS Institute). To compare the sex, previous diseases, treatment methods, and the results of treatment between the two groups, Fisher's exact test was used. The age, NIHSS score, pc-ASPECTS, and time from onset to puncture were compared using univariable logistic regression analysis. A p value of 0.05 was regarded as significant.

Results

The 19 subjects accounted for 3% of 552 patients who underwent acute-phase recanalization therapy during the study period, accounting for 30% of 64 patients with posterior circulation disorder (**Fig. 1**). They consisted of 15 males and 4 females, with a mean age of 67.2 years (median: 70 years, 42–85 years) (**Table 1**). On assessment 90 days after treatment, the outcome was favorable (mRS score: 0–2) in eight patients, whereas it was poor (mRS score: 3–6) in 11 (**Fig. 2**). Concerning medical history, hypertension was most frequently noted (89%). Furthermore, the mean time from onset to puncture was approximately 23 hours. Treatment was started within 6 hours after onset in 6 (31%) of the 19 patients. The sites of occlusion with significant stenosis included the vertebral artery in 10 patients and basilar artery in 9. However, there was no such occlusion of the distal basilar artery. For treatment, PTA alone was performed in 10 patients and PTAS in 9. Thrombolysis in Cerebral Infarction (TICI) 2b or higher recanalization was achieved in 15 patients (79%). The TICI grade was 2a or lower in 4 patients (**Table 2**). In most patients

Table 1 Baseline of the study population

	All (n = 19)	mRS 0–2 (n = 8)	mRS 3–6 (n = 11)	p value
Male sex	15 (79%)	6 (75%)	9 (82%)	1.0
Age (year)	67.2 (70, 42–85)	65.5 (66, 42–85)	68.5 (73, 45–85)	0.62
Diabetes mellitus	5 (26%)	2 (25%)	3 (27%)	1.0
Hypertension	17 (89%)	8 (100%)	9 (82%)	0.49
Hyperlipidemia	10 (59%)	6 (75%)	4 (36%)	0.17
Chronic renal failure	4 (21%)	0 (0%)	4 (36%)	0.10
Hemodialysis	3 (17%)	2 (25%)	1 (9.0%)	0.55
NIHSS score	23.6 (29, 4–40)	12.6 (9.5, 4–29)	31.5 (35, 11–40)	<0.001
pc-ASPECTS	6.4 (6, 3–10)	6.1 (6, 4–9)	6.5 (7.5, 3–10)	0.67
O to P (hr.)	23.1 (8.3, 1.4–72)	35.9(29.6, 1.4–72)	13.6 (7, 1.6–72)	0.07
Underlying site of stenosis				
Mid. BA	4 (21%)	2 (25%)	2 (18%)	
Pro. BA	5 (26%)	2 (25%)	3 (27%)	
V4 portion	4 (21%)	2 (25%)	2 (18%)	
V1-3 portion	6 (32%)	2 (25%)	4 (36%)	

Data are mean (median, range) or No. of cases (%). Mid. BA: middle basilar artery; NIHSS: National Institute of Health Stroke Scale; O to P: onset to puncture time; pc-ASPECTS: posterior circulation Alberta stroke program early CT score; Pro. BA: proximal basilar artery

requiring stenting, recanalization was not achieved despite PTA or PTA-related dissection developed. For PTA, Gateway balloons (Stryker, Kalamazoo, MI, USA) were used in all patients. For stenting, coronary stents were used in many patients (**Fig. 3**), although they were not applicable. As a post-treatment hemorrhagic complication, hemorrhagic infarction (HI) 2, which was evaluated using the SIST-MOST classification, was observed in two patients. In 2 of 10 patients in whom acute-phase PTA was performed, re-stenosis-related symptoms developed, and a Wingspan was placed 3 and 7 months after PTA treatment, respectively, leading to favorable outcomes, with mRS scores of 1 and 2, respectively (**Fig. 4**).

There was no significant difference in any background factor between the favorable and poor outcome groups. However, chronic renal failure tended to correlate with a poor outcome (p = 0.10). There was no significant difference in the baseline pc-ASPECTS between the two groups. The baseline NIHSS score was significantly lower in the favorable outcome group (median: 9.5 vs. 35, respectively, p <0.001); the preoperative NIHSS score was a prognosis- associated factor. Furthermore, there was no specific tendency in the distribution of occlusion sites with significant stenosis in either group. There was no significant correlation between the time from onset to puncture and prognosis, but the onset to puncture time was in a tendency to be longer in the favorable outcome group (p = 0.07) (**Table 1**). There was no difference in the outcome between PTA and PTAS (p = 0.65), but TICI 2b or higher tended to correlate with the favorable outcome (p = 0.10) (**Table 2**).

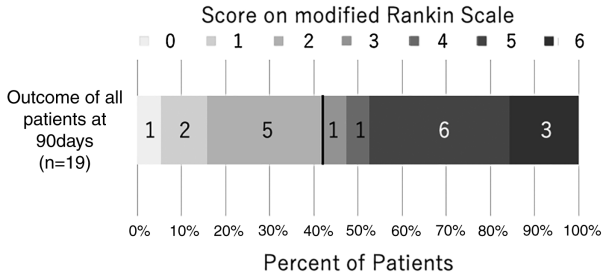

Fig. 2 Modified Rankin Scale scores at 90 days

Table 2 Procedures and TICI grades

	All (n = 19)	mRS 0-2 (n = 8)	mRS 3-6 (n = 11)	p value
PTA	10 (53%)	5 (63%)	5 (45%)	0.65
PTAS	9 (47%)	3 (38%)	6 (55%)	
TICI 0–2a	4 (21%)	0 (0%)	4 (36%)	0.10
2b–3	15 (79%)	8 (100%)	7 (64%)	

Data are No. of cases (%). PTA: percutaneous transluminal angioplasty; PTAS: percutaneous transluminal angioplasty with stent; TICI: thrombolysis in cerebral ischemia

Discussion

In this study, we examined whether risk factors for arteriosclerosis are associated with the prognosis after treatment, but there was no significant item. However, there was a correlation between chronic renal failure and prognosis. This may have been related to the influence of contrast medium use during treatment or poor control of renal failure by drugs after admission, differing from the blood pressure, blood glucose level, and cholesterol level throughout the recovery process after treatment. There was no correlation

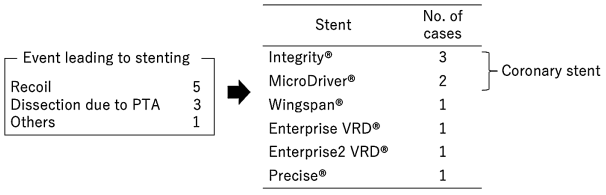

Fig. 3 The reasons for stenting and details of the stent

between the site of occlusion and prognosis, but the site of occlusion was located at an area proximal to the middle segment of the basilar artery in all patients. Lee et al.[9] reported a similar finding, with significantly more proximal cerebral basilar artery occlusions in the ATBI group and significantly more distal basilar artery occlusions in the embolic infarction group. A high preoperative NIHSS score was associated with a poor outcome, but there was no difference in the preoperative pc-ASPECTS between the favorable and poor outcome groups. This suggests that the NIHSS score more markedly reflects extensive brainstem or thalamus disturbance in the presence of gradually progressing irreversible changes of the brain compared with changes on imaging. In the favorable outcome group, the onset to puncture time was in a tendency to be longer. In many patients with ATBI in the posterior circulation, symptoms slowly deteriorate and the time from onset until arrival may be slightly prolonged overall. Considering the above correlation between the NIHSS score and prognosis, the NIHSS score on arrival was low in the favorable outcome group, with slow progression, whereas the condition may have rapidly deteriorated in the poor outcome group.

Efficacy and safety

The favorable outcome group accounted for 42% (8/19). This was similar to that (favorable outcome group: 46%) in an observational study reported by Gao et al.,[5] which was similar to our study design. A randomized controlled trial (RCT) of vertebrobasilar artery occlusion, including embolism, the BEST study, revealed that patients with a mRS score of 0–2 accounted for 39% in the intervention group, being similar to the above results.[10] However, in the BEST study, the median preoperative pc-ASPECTS was 8, being higher than that in this study (median: 6). Lee et al.[9] reported that the rate of patients with a mRS score of 0–2 after 90 days in the ATBI group was higher than that in the embolic infarction group (no significant), while the incidences of distal basilar artery occlusion and bilateral thalamus infarction were significantly higher in the embolic infarction group. Thus, the BEST study results, which were similar to those of this study despite a high preoperative pc-ASPECTS, may have resulted from the influence of embolism patients. In 8 (53%) of 15 patients in whom TICI 2b or higher recanalization was achieved, the mRS score after 90 days was 0–2; recanalization led to a favorable outcome (**Table 2**). On the other hand, all four patients with TICI 2a or lower recanalization had a poor outcome. The prognosis tended to be dependent on the presence of recanalization ($p = 0.10$). Recanalization achievement by endovascular therapy may be a requirement for improving the outcome in patients with vertebrobasilar artery occlusion related to ATBI, although the number of patients was small.

Overall, three patients (15%) died (Fig. 2). The mortality rate was similar to those reported by Gao et al. (15%) and Lee et al. (13% in the ATBI group).[5,9] Regarding treatment procedures, there was no difference in the prognosis between PTA and PTAS. Based on our experience, the safety of acute-phase PTAS was not inferior to that of PTA (**Table 2**). However, of nine patients in whom acute-phase PTAS was performed, additional imaging after ≥6 months was conducted in only 4 with a mRS score of ≤3; the long-term patency cannot be mentioned because sequelae were often serious in patients with posterior circulation ATBI, making follow-up difficult. The results of this study are based on initial assessment (after 90 days). The results of long-term assessment must be accumulated to evaluate the efficacy and recurrence rate.

Therapeutic strategies

For acute-phase PTAS, no stents are applicable. However, at our hospital, to obtain accurate vasodilation, coronary stents as balloon expandable stents were frequently used (**Fig. 3**). In our series, bare metal stents were used, but in the future, it may be difficult to obtain bare metal stents due to advances in drug-eluting stents (DESs) in the field of cardiology. According to a systematic review reported by Ye et al.,[11] DES insertion to the site of intracranial stenosis is relatively safe, but evidence has not been established; it should be established early. Although a Wingspan was used in the acute phase only in one patient in this study, on a post-marketing survey on Wingspan (JAPAN PMS), 305 patients were registered between June 2014 and July

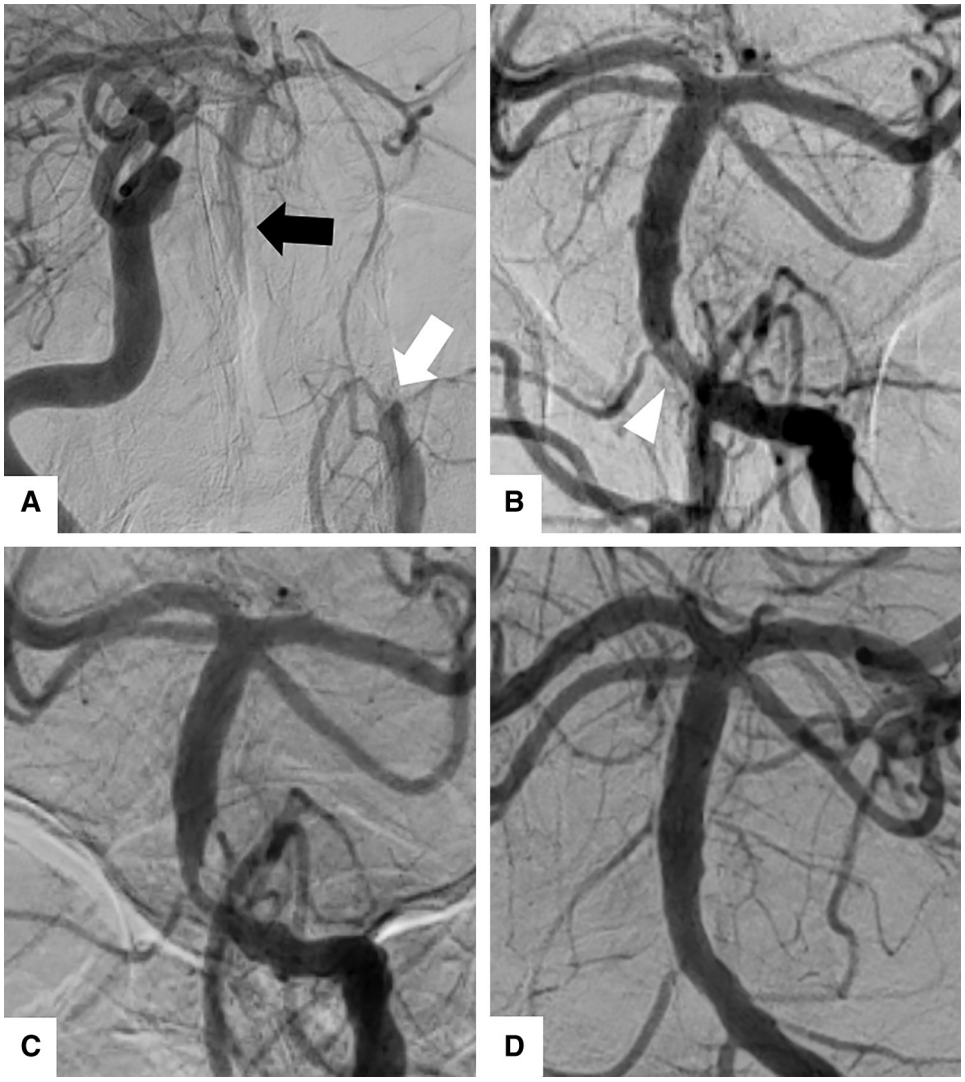

Fig. 4 Representative case. The case of a 49-year-old woman in a state of agitation with a NIHSS score of 5. (**A**) Initial angiography performed synchronously from the right internal artery and left vertebral artery demonstrated left vertebral artery occlusion (white arrow) and retrograde flow in the basilar artery (black arrow) via the posterior communicating artery. (**B**) The image after PTA. Note that the true occlusion site was the proximal basilar artery where PTA was performed (white arrowhead). (**C**) Cerebral angiography at 3 months after the first procedure demonstrated re-stenosis in the proximal basilar artery. The patient noted dizziness at that time. (**D**) The image just after PTAS. There has been no re-stenosis for 2 years after PTAS. NIHSS: National Institutes of Health Stroke Scale; PTA: percutaneous transluminal angioplasty; PTAS: percutaneous transluminal angioplasty stenting

2016, and 26.7% had vertebrobasilar artery occlusion. The overall perioperative (within 30 days) total stroke/mortality rate was 7.2%; however, it was 3.3% among patients meeting the recommendation criteria: resistance to medical treatment, a percent stenosis of ≥50%, and an interval of ≥7 days from onset, whereas it was 31% among those in whom a Wingspan was used even though it was not applicable. Furthermore, in the WEAVE trial, the perioperative (within 3 days) overall stroke/mortality rate in the Wingspan-adopted group was 2.6%; the result was more favorable than those of the SAMMPRIS and VISSIT trials,[12–14] this was achieved through strict compliance with indication criteria. On the other hand, the perioperative (within 3 days) overall stroke/mortality rate among off-label-use patients was 23.9%. Based on these results and this study, recanalization is important in patients with ATBI due to major artery occlusion or near-occlusion in the posterior circulation, but acute-phase PTAS should be limited to patients in whom the risk of early re-occlusion is markedly high such as those with repeated occlusion after PTA or PTA-related arterial dissection. As a basic strategy, PTA alone should be selected and strict medical management

and careful follow-up should be conducted after PTA. If necessary, stenting should be performed in accordance with the criteria adopted in the WEAVE trial. This may minimize treatment-related risks. Of our patients, two patients requiring Wingspan insertion in the chronic phase met the criteria employed in the WEAVE trial.

Conclusion

As previously reported, our treatment results revealed that recanalization therapy by acute-phase PTA/PTAS was effective in ATBI patients with vertebrobasilar artery occlusion, and a requirement for improving the outcome. Based on such evidence, the indication of acute-phase PTAS should be carefully examined, but our study suggested that there was no significant difference in the outcome between the PTA and PTAS groups; PTAS may be considered in high-risk patients for early re-occlusion. However, to evaluate the safety, long-term follow-up should be conducted involving a larger number of patients.

Disclosure Statement

Hirotoshi Imamura received rewards as lecture fees from Stryker Japan and Medtronic Japan.

Nobuyuki Sakai received research funds from Terumo Corporation, and rewards as lecture fees from Biomedical Solutions, Johnson & Johnson, Medtronic Japan, Penumbra, Stryker Japan, and Terumo Corporation. The remaining authors declare no conflicts of interest regarding the publication of this article.

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