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ORIGINAL RESEARCH

Transluminal Angioplasty and Stenting for Intracranial Vertebrobasilar Occlusive Lesions in Acute Stroke Patients

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BACKGROUND AND PURPOSE: The clinical outcome is often poor in acute stroke patients with a serious neurological status due to occlusive lesions of the intracranial vertebral and/or basilar artery (IVBA). The purpose of this study was to investigate retrospectively the clinical features and outcome of acute stroke patients who underwent transluminal angioplasty and/or stenting (TAS) for occlusive lesions of the IVBA and to clarify the prerequisites for improvement of outcome.

MATERIALS AND METHODS: Of 1690 consecutive acute ischemic stroke patients admitted to our institution, TAS for occlusive lesions of the IVBA was performed within 7 days after stroke onset in 28 patients. We classified these patients into 2 groups, those with total occlusion (occlusion group) and those with a high-grade stenosis (stenosis group), and compared the preprocedural neurologic status (severe: National Institutes of Health Stroke Scale >20), the rate of technical success, major procedure-related complications, subacute occlusion of the treated vessel, and favorable clinical outcome (0-2 points on a 3-month modified Rankin Scale) between the 2 groups.

RESULTS: In the occlusion group (n = 16) and stenosis group (n = 12), a severe preprocedural neurologic status was seen in 13 and 1 patients, respectively (81% versus 8%; $P = .0001$); technical success was achieved in 13 and 11 patients, respectively (81% versus 92%; P value not significant [NS]); complications occurred in 6 and 0 patients, respectively (38% versus 0%; $P < .05$); subacute occlusion was seen in 4 and 1 patients, respectively (25% versus 8%; P = NS); and a favorable clinical outcome was obtained in 3 and 9 patients, respectively (19% versus 75%; $P < .01$).

CONCLUSION: The clinical outcome of patients who underwent TAS for total occlusion of the IVBA was poor. Improvement of outcome requires reduction of procedure-related complications and subacute occlusion.

The clinical outcome is often severe disability or death in acute ischemic stroke patients with a serious neurologic status due to occlusive lesions of the intracranial vertebral artery and/or the proximal to midportion of the basilar artery (IVBA). Angioplasty and/or stent placement for the IVBA are becoming increasingly common,[1-10] and recanalization therapy with angioplasty and/or stent placement has been reported anecdotally for the IVBA, even in the acute stroke stage.[4,10] However, most case series have included patients of varied background: patients in acute and chronic stroke stages[4] or acute stroke patients with lesions of the anterior circulation.[10] Therefore, the clinical features and outcome in acute ischemic stroke patients who underwent transluminal angioplasty and/or stent placement (TAS) performed within 7 days after stroke onset for occlusive lesions of the IVBA are not well established, and the problems associated with TAS in clinical practice have not been determined. Intravenous administration of recombinant tissue plasminogen activator was unavailable for clinical use in Japan until October 2005. Before that time, we used primary angioplasty for total occlusion of the IVBA in acute stroke patients, because drug therapy or localized intra-arterial fibrinolysis alone has a low success rate in acute ischemic stroke patients with such an occlusion.[11,12]

The purpose of the current study was to investigate retrospectively the clinical features and outcome of acute stroke patients who underwent TAS for occlusive lesions of the IVBA and to clarify the prerequisites for improvement of outcome of this procedure.

Methods

Patient Population

Of 1690 consecutive acute ischemic stroke patients admitted to our institution (Shonan Kamakura General Hospital) from October 2000 to September 2005, 28 patients (1.7%) fulfilled the following criteria for TAS and received TAS for symptom-related occlusive lesions of the IVBA within 7 days after stroke onset. A retrospective review of these patients was conducted with institutional committee approval.

Criteria for TAS for the IVBA

Our criteria for TAS for the IVBA included the following patients: 1) those who were admitted to our institution within 7 days of stroke onset; 2) those who presented with serious neurologic symptoms defined as a moderate disturbance of consciousness and a National Institutes of Health Stroke Scale (NIHSS) score $\geq$10 at admission, who presented with serious neurologic symptoms that worsened in the setting of moderate neurologic symptoms (NIHSS score of $\leq$9), or who presented with moderate neurologic symptoms in the course of fluctuating stroke or crescendo transient ischemic attacks; 3) those whose neurologic symptoms included at least 1 that indicated posterior circulation ischemia, such as ophthalmoplegia, bulbar palsy, quadriparesis, or drop attack; 4) those who had neither cerebral hem-

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orrhage nor extensive bilateral pontine infarction on cranial CT; and 5) those who were angiographically proven to have symptom-related total occlusion or high-grade stenosis (≥70%) of the IVBA. Before the procedure, each patient was also examined by diffusion-weighted MR imaging (DWI), but the results of this examination did not influence the decision regarding performance of TAS.

Patients were excluded from the procedure if they had total occlusion of the basilar top alone, extracranial occlusive lesions of the bilateral vertebral artery alone, or both; if a medical contraindication for angiography was present; or if the patient or a family member did not provide informed consent for diagnostic angiography or endovascular procedures. There was no restriction regarding the time period from onset of symptoms until the decision to perform TAS.

TAS Procedure

Two antiplatelet agents, aspirin (100 mg/day) and ticlopidine (100 mg/day), were administered orally or through a gastrointestinal tube immediately after admission as preparation for TAS, as required. Once the decision to perform TAS was made, systemic anticoagulation was initiated by intravenous administration of a bolus of heparin to maintain an activated clotting time of more than 250 seconds during the procedure. TAS was performed under local anesthesia when possible. After a diagnostic angiogram was obtained by using a transfemoral approach, a 6F guiding catheter was placed in the foraminal segment of the dominant vertebral artery. A 0.016-inch microguidewire was carefully inserted into the stenotic/occluded portion and advanced up to the distal segment of the posterior cerebral artery. A microcatheter was then navigated over the wire across the stenotic/occluded segment. After the 180-cm microguidewire was exchanged for a 300-cm, 0.014-inch long microguidewire, the microcatheter was replaced by a low-profile 2.0- to 2.5-mm balloon catheter (Maverick or Gateway; Boston Scientific, Natick, Mass), which was generally undersized by at least 0.5 mm and slowly inflated under direct fluoroscopic visualization for 60–120 seconds. Maximal inflation at 4–6 atm was maintained for 15–30 seconds. Occasionally, a second or third inflation was performed in an identical fashion to achieve anatomic dilation of the stenotic vessel. The lengths of occlusive lesions were determined by a lack of opacification by using contrast material injected from a microcatheter, and the length of the balloon was chosen such that it was long enough to cover the distance from the normal vessels on the bilateral sides of the lesion. In a case of total occlusion in which the length of the lesion was unclear, a balloon of 20 mm, the longest available, was used to avoid inflating the edge of the balloon close to an unstable plaque or intraluminal thrombi. If recanalization was not achieved after several inflations, localized intra-arterial fibrinolysis was subsequently performed, and if the balloon had an initial diameter that was smaller than that of the vessel to be treated, it was replaced by a balloon with a larger diameter to ensure sufficient dilation of the lesion. When postangioplasty angiography showed haziness in the dilated segment, suggesting either a flow-limiting intimal dissection or an intraluminal thrombus, a balloon-expandable 2.5- to 3.5-mm coronary stent (S660, S670, or Driver; Medtronic, Minneapolis, Minn) was deployed across the lesion to minimize the risk of an acute occlusion. If repeat angiography revealed residual stenosis of an acceptable degree (<50%) and no distal embolism of the peripheral branches, the procedure was considered to be complete. On the other hand, if distal embolism of the basilar top occurred, recanalization was attempted with additional angioplasty and/or localized intra-arterial fibrinolysis. Neither embolic protection nor clot retrieval devices were used in any of the patients.

Management After TAS

After the procedure, each patient was monitored closely in the intensive care unit for 24 hours with strict blood pressure control because of the concern of hyperperfusion in the region of the treated vessel; systolic blood pressure was maintained at <140 mm Hg by intravenous administration of antihypertensive and sedative agents. Therapy with heparin (10,000 U per day) was continued for 7 days after the procedure. In addition, all of the patients undergoing the procedure since June 2001 received intravenous edaravone,[13] a free-radical scavenger, at a dose of 30 mg twice daily. Every patient received 2 antiplatelet agents orally or through a gastrointestinal tube: aspirin (100 mg/day), which was continued indefinitely, and ticlopidine (100 mg/day), which was continued for 90 days after the procedure. Cranial CT was performed immediately, after 24 hours, and 7 days after the procedure or immediately after neurologic deterioration during hospitalization.

Outcome Measures and Statistical Analysis

Pertinent medical records and imaging studies were reviewed for the 28 patients in the study. It was thought probable that procedural success in TAS and achieving a favorable clinical outcome in cases with total occlusion would be difficult, compared with cases with stenotic lesions, and, therefore, we classified the 28 patients into 2 groups for analysis: the occlusion group, composed of patients who underwent TAS for total occlusion of the IVBA, and the stenosis group, composed of patients who underwent TAS for a high-grade stenosis (≥70%) of the IVBA. The preprocedural neurologic status, technical success, incidence of major procedure-related complications, incidence of subacute occlusion of the treated vessel, and favorable clinical outcome (modified Rankin Scale score [mRS]) after 90 days were compared between the 2 groups. Neurologic outcome (NIHSS score) after 7 days and death within 90 days were also examined in subanalyses. The preprocedural neurologic status was considered severe if the NIHSS score was more than 20 points. Technical success was defined based on angiography performed immediately after the procedure as complete recanalization of the basilar artery without flow delay in the case of total occlusion and residual stenosis of the IVBA of 50% or less in the case of stenosis. The degree of stenosis was calculated by using the warfarin-aspirin symptomatic intracranial disease method.[14] Each preprocedural and postprocedural angiogram was also evaluated for stenoses by categorization according to the Thrombolysis in Myocardial Infarction (TIMI) Scale.[15] Major procedure-related complications were defined as disabling ischemic or hemorrhagic stroke, resulting in neurologic deterioration after the procedure or extracerebral hemorrhage requiring a blood transfusion or surgical intervention. Subacute occlusion of the treated vessel was defined as an occlusion occurring from 1 to 7 days after the procedure that was first suspected in screening by MR angiography or transcranial color duplex sonography and eventually diagnosed by angiography. Neurologic outcome after 7 days and clinical outcome after 90 days were considered favorable if the NIHSS score was 5 or less and the mRS was 0–2, respectively. Clinical outcome after 90 days was evaluated independently by doctors from another institution.

The numbers of patients with a severe preprocedural neurologic status, major procedure-related complications, subacute occlusion; the number of patients for whom technical success was achieved;

Table 1: OTDT/OTPT, preprocedural neurologic symptoms, and DWI/angiographic findings in the occlusion group

Patient/Sex/ Age (y)	OTDT/OTPT (h)	Preprocedural Neurologic Symptoms	A-NIHSS/P-NIHSS	High Signal Intensity on DWI	Occluded Vessels*
1/M/57	68/72	Deep coma, AR, OP, BP, QP	12/34	M, P, CER	lt.V4-pBA, rt.V1
2/M/72	31/48	Stupor, OP, BP, HP	8/21	M, CER, OL	lt.V4, rt.V1
3/M/63	1/3	Coma, AR, OP, BP, QP	29/29	P, CER	lt.V4, rt.V3
4/M/75	5/7	Somnolence, OP, BP, QP	17/17	P	lt.V4, rt.V3, pBA
5/F/62	8/10	Somnolence, BP, HP	12/12	P, CER	mBA
6/F/73	4/6	Deep coma, AR, OP, BP, QP	34/34	M, P, MB, CER	lt.V3, rt.V1
7/M/74	1/3	Deep coma, AR, OP, BP, QP	34/34	MB, CER	pBA
8/M/77	5/7	Stupor, AR, OP, BP, QP	22/22	P, CER, OL	lt.V4-pBA, rt.V2
9/M/84	9/11	Somnolence, BP, HP	3/15	P	mBA, lt.V4
10/F/74	3/5	Coma, AR, OP, BP, QP	30/30	P, OL	mBA
11/M/74	2/17	Deep coma, AR, OP, BP, QP	4/30	CER	lt.V4-pBA, rt.V2
12/M/63	7/9	Deep coma, AR, OP, BP, QP	35/35	P, CER	rt.V4, lt.V3
13/F/76	24/47	Stupor, AR, OP, BP, QP	6/27	P, CER, OL	lt.V4, rt.V4
14/F/81	12/36	Coma, AR, OP, BP, QP	4/32	P, MB, OL	mBA
15/F/71	4/47	Stupor, OP, BP, HP	7/20	P, CER	lt.V3, rt.V3
16/F/60	4/6	Deep coma, AR, OP, BP, QP	34/34	P	pBA

Note:—OTDT indicates onset-to-door time; OTPT, onset-to-the-procedure time; A-NIHSS, National Institutes of Health Stroke Scale score on admission; P-NIHSS, preprocedural National Institutes of Health Stroke Scale score; M (column 1), male; F, female; DWI, diffusion-weighted MR imaging performed immediately before the procedure; AR, ataxic respiration; OP, ophthalmoplegia; BP, bulbar palsy; QP, quadriparesis; HP, hemiparesis; M (column 5), medulla oblongata; P, pons; MB, midbrain; CER, cerebellum; OL, occipital lobe; lt., left-sided; rt., right-sided; V1, proximal extraosseous segment of the vertebral artery; V2, foraminal segment of the vertebral artery; V3, intra-extraspinal segment of the vertebral artery; V4, intradural segment of the VA; pBA, proximal basilar artery; mBA, middle basilar artery; dBA, distal basilar artery.
* This was diagnosed by angiography.

Table 2: OTDT/OTPT, preprocedural neurologic symptoms, and DWI/angiographic findings in the stenosis group

Patient/Sex/ Age (y)	OTDT/OTPT	Preprocedural Neurologic Symptoms	A-NIHSS/P-NIHSS	High Signal Intensity on DWI	Stenotic Vessels*	Occluded Vessels*
17/M/77	24/27	Somnolence, OP, BP, HP	15/15	CER	lt.V4-pBA, rt.V4	None
18/M/65	2/96	BP, frequent drop attacks	2/1	OL	rt.V4-pBA	lt.V4
19/M/78	2/4	Deep coma, AR, OP, BP, QP	33/33	CER	dBA	rt.V2
20/M/59	4/72	Frequent drop attacks	4/0	None	lt.V1, lt.V3, mBA	None
21/M/75	6/120	OP, BP, frequent syncopal attacks	2/2	OL	pBA	lt.V3
22/M/70	2/168	OP, BP, frequent drop attacks	6/2	P	Lt.V4, rt.V4, mBA	None
23/F/82	24/140	BP, HP, frequent syncopal attacks	3/3	P	mBA	rt.V3
24/M/64	48/168	OP, frequent syncopal attacks	2/1	P	pBA	None
25/M/60	51/98	Stupor, OP, BP, QP	8/17	MB, CER	mBA	None
26/M/74	10/96	BP, frequent drop attacks	1/1	None	mBA	rt.V1
27/M/78	12/144	Stupor, OP, BP, HP	8/18	CER	lt. V1, mBA	rt.V1
28/M/66	2/168	OP, BP, HP	10/7	P	rt.V4-pBA	lt.V3

Note:—OTDT indicates onset-to-door time; OTPT, onset-to-the-procedure time; A-NIHSS, National Institutes of Health Stroke Scale score on admission; P-NIHSS, preprocedural National Institutes of Health Stroke Scale score; M (column 1), male; F, female; DWI, diffusion-weighted MR imaging performed immediately before the procedure; AR, ataxic respiration; OP, ophthalmoplegia; BP, bulbar palsy; QP, quadriparesis; HP, hemiparesis; P, pons; MB, midbrain; CER, cerebellum; OL, occipital lobe; lt., left-sided; rt., right-sided; V1, proximal extraosseous segment of the vertebral artery; V2, foraminal segment of the vertebral artery; V3, intraextraspinal segment of the vertebral artery; V4, intradural segment of the vertebral artery; pBA, proximal basilar artery; mBA, middle basilar artery; dBA, distal basilar artery.
* This was diagnosed by angiography.

favorable neurologic and clinical outcomes; and the number of deaths were compared between the 2 groups, using a χ^2 test for independence or a Fisher exact test. A value of P below 0.05 was considered to indicate statistical significance, and SPSS software was used to perform the statistical analysis.

Results

Of the 28 patients who underwent TAS, 16 and 12 were assigned to the occlusion and stenosis groups, respectively. The baseline characteristics for these groups are shown in Tables 1 and 2, respectively. The onset-to-door time was 5.5 hours (range, 1–51 hours) in all of the patients and 5.0 and 8.0 hours in the occlusion and stenosis groups, respectively (P value not significant [NS]). The onset-to-procedure time was 41.5 hours (range, 3.0–168.0 hours) in all of the patients and 9.5 and 109.0 hours in the respective groups ($P < .01$). The median NIHSS on admission was 8 (range, 1–35) in all of the patients and 14.5 and 5.0 in the occlusion and stenosis groups, respectively ($P < .05$). Regarding the preprocedural neurologic status, the median preprocedural NIHSS score was 18.0 (range, 0.0–35.0) in all of the patients and 29.5 and 2.5 in the occlusion and stenosis groups, respectively ($P < .01$). Therefore, a severe preprocedural neurologic status was seen significantly more frequently in the occlusion group compared with the stenosis group, with rates of 81% (13 of 16) and 8% (1 of 12), respectively ($P = .0001$). Regarding the MR imaging findings, 4 and 1 patients had extensive DWI abnormalities of the pons in the occlusion (patients 3, 4, 9, and 16) and stenosis (patient 28) groups, respectively (P value NS). Four patients in the stenosis group had no or minimal deficits (NIHSS 0 or 1), and 2 of these patients had no DWI abnormalities (patients 20 and 26).

The technical success rate was 86% (24 of 28) in all of the patients and 81% (13 of 16) and 92% (11 of 12) in the occlu-

Table 3: Methods of TAS and angiographic results in the occlusion group

Patient/Sex/ Age (y)	No. of Used Stents	Dose of Urokinase*	Preprocedure/Postprocedure TIMI†	Prestenosis/Poststenosis (%)‡	Technical Success	Procedural Dissections or Clots
1/M/57	3	0	0/3	100/10	Success	Yes
2/M/72	1	0	0/3	100/5	Success	Yes
3/M/63	3	0	0/3	100/30	Success	Yes
4/M/75	0	12	0/3	100/40	Success	No
5/F/62	0	24	0/0	100/100	Failure	NE
6/F/73	0	42	0/0	100/100	Failure	NE
7/M/74	0	0	0/3	100/45	Success	No
8/M/77	0	12	0/3	100/20	Success	No
9/M/84	1	0	0/3	100/10	Success	Yes
10/F/74	0	0	0/3	100/40	Success	No
11/M/74	1	0	0/0	100/100	Failure	Yes
12/M/63	0	0	0/3	100/10	Success	No
13/F/76	3	0	0/3	100/8	Success	Yes
14/F/81	0	0	0/3	100/10	Success	No
15/F/71	1	0	0/3	100/25	Success	Yes
16/F/60	0	0	0/3	100/20	Success	No

Note:—TAS indicates transluminal angioplasty and/or stenting; NE, no evaluation; M, male; F, female; TIMI, Thrombolysis in Myocardial Infarction.
* Data are $\times 10^4$ units.
† Grading with the TIMI definitions, 0 indicates no perfusion; 1, penetration without perfusion; 2, partial perfusion; and 3, complete perfusion.
‡ Preprocedural and postprocedural stenotic ratio was measured with the warfarin-aspirin symptomatic intracranial disease method.

Table 4: Methods of TAS and angiographic results in the stenosis group

Patient/Sex/ Age (y)	No. of Used Stents	Dose of Urokinase*	Preprocedure/Postprocedure TIMI†	Prestenosis/Poststenosis (%)‡	Technical Success	Procedural Dissections or Clots
17/M/77	3	0	2/3	95/10	Success	Yes
18/M/65	0	0	2/3	90/22	Success	No
19/M/78	1	0	2/3	82/0	Success	Yes
20/M/59	0	0	1/3	94/30	Success	No
21/M/75	1	0	2/3	90/12	Success	Yes
22/M/70	0	0	2/3	80/20	Success	No
23/F/82	0	0	2/2	90/90	Failure	NE
24/M/64	0	0	1/3	90/30	Success	No
25/M/60	1	0	2/3	90/6	Success	Yes
26/M/74	1	0	2/3	80/10	Success	Yes
27/M/78	0	0	2/3	84/8	Success	No
28/M/66	1	0	1/3	95/10	Success	Yes

Note:—TAS, transluminal angioplasty and/or stenting; M, male; F, female; TIMI, Thrombolysis in Myocardial Infarction; NE, no evaluation.
* Data are 10^4 units.
† Grading with the TIMI definitions, 0 indicates no perfusion; 1, penetration without perfusion; 2, partial perfusion; and 3, complete perfusion.
‡ Preprocedural and postprocedural stenotic ratio was measured with the warfarin-aspirin symptomatic intracranial disease method.

sion and stenosis groups, respectively (*P* value NS; Tables 3 and 4). In 2 patients of the occlusion group (patients 4 and 8), technical success was achieved with TAS alone, but additional localized intra-arterial fibrinolysis by using urokinase was performed to delete an intraluminal thrombus seen just after recanalization of the basilar artery without distal embolism. TAS was unsuccessful in 4 patients. In the occlusion group, 2 patients (patients 5 and 6) underwent unsuccessful intracranial angioplasty, because the microguidewire could not be passed across the lesion, and additional localized intra-arterial fibrinolysis failed to recanalize the lesions. Vessel rupture occurred in another patient (patient 11) due to overdilation of the vertebrobasilar junction by stent placement. In the stenosis group, severe nausea and vomiting occurred in 1 patient (patient 23) just after injection of the contrast medium with the microcatheter; this was suspected to be a side effect of the contrast medium. The patient and family members refused continuation of the procedure under general anesthesia, resulting in discontinuation.

Major procedural complications occurred in 6 (21%) of the 28 patients (Tables 5 and 6). These events occurred for 6 (38%) of 16 patients in the occlusion group: distal embolism in 3 patients, intracranial hemorrhage in 2 patients, and vessel rupture in 1 patient. There were no major procedural complications in the stenosis group ($P < .05$). Minor procedure-related complications, such as nausea, vomiting, or headache, occurred after TAS in 3 patients. No patients developed extracerebral hemorrhage requiring a blood transfusion, and no surgical intervention was necessary. Of 3 patients with distal embolism to the basilar top, 2 (patients 2 and 3) underwent additional balloon angioplasty for the basilar top, which was completely recanalized; the other patient (patient 5) did not receive additional angioplasty, because we were unable to get the microguidewire to penetrate the clot embedded in the basilar top. Intracranial hemorrhage occurred in patients 12 and 15 of the occlusion group, as found in cranial CT performed just after and 3 hours after the procedure, respectively, and was regarded as a major complication because of acute neurologic deterioration; both patients died within 7 days after the procedure. These patients had not received urokinase, and patient 12 did not receive postprocedural antithrombotic

Table 5: Complications, subacute occlusion, and neurologic/clinical outcome in the occlusion group

Patient/Sex/ Age (y)	Procedure-Related Complications	Major Complications	Subacute Occlusion of the Treated Vessel	NIHSS Score at 7 Days after Procedure	mRS Score at 90 Days after Procedure
1/M/57	None	No	Yes	34	6
2/M/72	Distal embolism	Yes	Yes	28	5
3/M/63	Distal embolism	Yes	Yes	33	5
4/M/75	Hemorrhagic transformation	No	No	10	3
5/F/62	Distal embolism	Yes	No	20	6
6/F/73	None	No	No	42	6
7/M/74	None	No	No	3	1
8/M/77	None	No	No	14	3
9/M/84	None	No	Yes	14	6
10/F/74	None	No	No	7	1
11/M/74	Vessel rupture	Yes	No	42	6
12/M/63	Intracranial hemorrhage	Yes	No	42	6
13/F/76	Subarachnoid hemorrhage	No	No	11	2
14/F/81	None	No	No	17	3
15/F/71	Intracranial hemorrhage	Yes	No	42	6
16/F/60	Distal embolism	No	No	22	5

Note:—NIHSS indicates National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; M, male; F, female.

Table 6: Complications, subacute occlusion, and neurologic/clinical outcome in the stenosis group

Patient/Sex/ Age (y)	Procedure-Related Complications	Major Complications	Subacute Occlusion of the Treated Vessel	NIHSS Score at 7 Days after Procedure	mRS Score at 90 Days after Procedure
17/M/77	None	No	Yes	31	6
18/M/65	None	No	No	0	0
19/M/78	None	No	No	42	6
20/M/59	None	No	No	0	0
21/M/75	None	No	No	0	0
22/M/70	None	No	No	0	0
23/F/82	Nausea and vomiting	No	No	2	1
24/M/64	None	No	No	0	0
25/M/60	Headache and vomiting	No	No	8	2
26/M/74	None	No	No	0	0
27/M/78	None	No	No	12	6
28/M/66	Headache and vomiting	No	No	4	1

Note:—NIHSS indicates National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; M, male; F, female.

treatment; the other (patient 15) had received continuous intravenous heparin for more than 3 hours after TAS until a diagnosis of intracranial hemorrhage. One patient (patient 11) experienced catastrophic and fatal vessel rupture of the vertebrobasilar junction due to overdilation by a stent.

Subacute occlusion of the treated vessel occurred in 5 (18%) of 28 patients: 4 (25%) of 16 and 1 (8%) of 12 patients in the occlusion and stenosis groups, respectively (*P* value NS). All were related to deterioration in clinical symptoms, especially in consciousness disturbance. All of the subacute occlusions occurred in patients treated by using multiple stents or a small stent (2.5 mm).

After 7 days, 8 (29%) of the 28 patients had a favorable outcome, with this number increasing to 12 patients (43%) after 90 days (Tables 5 and 6). In the occlusion and stenosis groups, a favorable clinical outcome was observed after 7 days in 1 (6%) and 7 patients (58%), respectively ($P < .01$), and after 90 days in 3 (19%) and 9 patients (75%), respectively ($P < .01$). Ten of the 28 patients (36%) died within 90 days after the procedure. These deaths included 7 patients in the occlusion group (43.8%), of whom 5 died of stroke and 2 of pneumonia, and 3 patients in the stenosis group (25%; *P* value NS), of whom 2 died of stroke and 1 of pneumonia.

Discussion

The main finding of the present study is that TAS for occlusive lesions of the IVBA involving total occlusion is technically feasible and may be performed successfully; however, there is a high risk of complications during TAS, and subacute occlusion of the treated vessel after TAS should be anticipated, especially in patients with total occlusion. To our knowledge, this study is the first comparison of clinical features and outcome between patients who underwent TAS for total occlusion and for high-grade stenosis of the IVBA. Improvement of clinical outcome in the former patients will require the reduction of procedural complications and careful postprocedural management involving prevention of subacute occlusion of the treated vessel.

In the present study, the technical success rate was a little lower than the reported rates in previous patient series in which intracranial angioplasty was performed mainly for stenotic lesions.[2-10] In the present study, TAS for occluded lesions was shown to be technically feasible with a high success rate, similar to treatment of stenotic lesions. Technical success in treating the occluded lesion depends on the freshness of the occluded clots and the occluded segment being short enough for the microguidewire to pass through it; such conditions are frequently encountered in the acute stroke stage. The stents

used for TAS in the present study were all coronary balloon-expandable stents, and newer self-expandable stents for intracranial atherosclerotic disease (ie, Wingspan, Boston Scientific), which are designed to facilitate access to the lesion and to minimize vessel recoil after angioplasty, may increase the technical success rate of TAS.

The procedure-related complication rate in the present study was higher than the reported rates in previous studies performed mainly for stenotic lesions and in the chronic stroke stage.[2-10] This may be because TAS for occluded lesions tends to induce distal embolism, intracranial hemorrhage involving hemorrhagic transformation and cerebral hyperperfusion syndrome, and vessel injury or rupture in comparison with the treatment of stenotic lesions. Because distal embolism tends to occur for a lesion crossed by a microguidewire, balloon catheter, or stent and is especially common with occluded lesions, the use of an embolic protection device with proximal flow control may reduce the incidence of this complication.[16] Hemorrhagic complication also tends to occur in the acute stroke stage and is especially common with occluded lesions. In the acute stroke stage, damage to cerebral autoregulation and injury to the blood-brain barrier may promote both hemorrhagic transformation and cerebral hyperperfusion syndrome of the infracted region. Regarding extracranial carotid lesions, cerebral hyperperfusion syndrome or phenomenon after endovascular recanalization is uncommon in the chronic stroke stage (5%)[17] but may occur more frequently in the acute stroke stage (29%).[18] Vessel rupture is a catastrophic complication that results directly in patient death,[3,9] and we note that self-expandable stents for intracranial vessels are safer than coronary balloon-expandable stents and the use of these devices may reduce such a complication rate in TAS.

In the present study, subacute occlusion of the treated vessel always aggravated the neurologic condition of patients undergoing TAS. Therefore, aggressive periprocedural antithrombotic therapy is important to prevent such complications, though strong antithrombotic therapy after intervention may also carry a risk of hemorrhagic complications.[19] Intravenous antiplatelet agents that block the GP IIb/IIIa receptor are currently unavailable for clinical use in Japan, and clopidogrel has only been authorized for use since April 2006; therefore, we administered 2 antiplatelet agents, aspirin and ticlopidine, to every patient immediately after admission to prepare for TAS and continued these drugs for at least 90 days after the procedure. We also administered intravenous heparin (10,000 U/mL per day) for 7 days after the procedure. However, the dose of heparin and the period of continuation of this agent are chosen empirically in our institution and, similar to coronary intervention, adjunctive anti-GP IIb/IIIa[20] or a new regimen such as cilostazol[21] may decrease the occurrence of subacute occlusion of the treated vessel. Therefore, further studies are needed to determine the optimal antithrombotic therapy after TAS in acute stroke patients. In retrospect, we also note that all of the subacute occlusion occurred in patients treated by using multiple stents or a small stent (2.5 mm). The use of multiple stents and treatment of vessels of 3.0-mm or smaller diameter may also induce subacute occlusion of stented vessels, which is similar to the effect reported in coronary intervention.[22] Therefore, other strategies may be necessary to decrease subacute occlusion. Simple angioplasty without stent placement to restore the minimal vessel lumen to ensure sufficient blood flow to the brain region and staged stent placement on occurrence of restenosis[8,23] may be such strategies, unless flow-limiting intimal dissection occurs, though it has been reported that coronary stent placement constitutes an effective therapeutic strategy for patients with thrombus-containing lesions and results in a low incidence of subacute thrombosis.[24] The nature of the treated lesions that required stent placement may also promote high activation of platelet cells through attachment to the deployed stents. These include long-segment lesions or lesions accompanied with intraluminal thrombus or dissection, which are often seen in an occluded lesion. Such lesions may also induce the presence of many clots and occlusion at the deployed stents, and preprocedural angiographic morphologic features of total occlusion are likely to remain as predictors of subacute occlusion of a vessel treated with TAS.

Patients with total occlusion of the basilar top alone were excluded from the study because the probable stroke mechanism of these patients was embolization from a source other than the IVBA. However, even after excluding these patients, various etiologies of occlusion may be included in the occlusion group: acute atherosclerotic occlusion due to plaque rupture likely to cause acute coronary syndrome, cardiogenic embolism, artery-to-artery embolism from the origin of the vertebral artery or the aortic arch, arterial dissection, or even chronic occlusion causing hemodynamic ischemia of the posterior circulation. These etiologies of total occlusion of the IVBA will contribute to differences in clinical outcome after intervention, both between occlusion and stenosis of the IVBA and between total occlusion of the symptom-related vessel in acute stroke and of the culprit vessel in acute coronary syndrome, the main etiology of which is plaque rupture at the occluded site.[25] In acute stroke patients, it is impossible to diagnose an exact etiology of occlusion of the IVBA before the procedure and to determine a uniform strategy for such lesions. Therefore, in some cases, the possibility of various etiologies of occlusion may require other forms of revascularization therapy, such as primary localized intra-arterial fibrinolysis or intravenous thrombolytic agents before angioplasty or application of protective devices with proximal flow control before TAS.

In the present study, the preprocedural neurologic status of patients with total occlusion of the IVBA was severe, and TAS in these patients was not frequently associated with a favorable clinical outcome. The poor clinical outcome may be due not only to the high rate of complications and subacute occlusion of the vessel but also to the severity of the baseline neurologic status in patients with total occlusion (Table 7). The relatively poor outcome of TAS for total occlusion of the IVBA does not suggest that early initiation of TAS is useful before deterioration of the NIHSS score to more than 10 points. Although it is possible that the stroke mechanisms of patients with total occlusion might be essentially different from those with a severe stenosis, the occluded lesions must originate partly from stenotic lesions, and, therefore, early prophylactic TAS for high-grade stenotic lesions of the IVBA before progression to total occlusion may be critical in neurologically unstable patients who are refractory to drug treatment. However, our results do

Table 7: Comparison of baseline characteristics, procedure, and outcome between the groups

Variable	Data	Subgroup (n = 28)		P
		Occlusion Group (n = 16)	Stenosis Group (n = 12)	
Age, median (range), y	73.5 (57.0–84.0)	73.5 (57.0–84.0)	72 (59–82)	NS*
A-NIHSS, median (range), point	8 (1–35)	14.5 (3.0–35.0)	5 (1–33)	<.05*
P-NIHSS, median (range), point	18 (0–35)	29.5 (12.0–35.0)	2.5 (0.0–33.0)	<.001*
20 ≤P-NIHSS, *n* (%)	14 (50)	13 (81)	1 (8)	.0001‡
OTD time, median (range), h	5.5 (1.0–51.0)	5 (1-48)	8 (2–51)	NS*
OTP time, median (range), h	41.5 (3.0–168.0)	9.5 (3.0–72.0)	109 (4–168)	<.01*
Stenting, *n* (%)	13 (46)	7 (44)	6 (50)	.74†
LIF, *n* (%)	4 (14)	4 (25)	0 (0)	.09‡
Technical success, *n* (%)	24 (86)	13 (81)	11 (92)	.42‡
Major complication, *n* (%)	6 (21)	6 (38)	0 (0)	.02‡
Subacute occlusion, *n* (%)	5 (18)	4 (25)	1 (8)	.27‡
7-NIHSS ≤5 at 7 days, *n* (%)	8 (29)	1 (6)	7 (58)	.004‡
mRS ≤2 at 90 days, *n* (%)	12 (43)	3 (19)	9 (75)	.004†
Death within 90 days, *n* (%)	10 (36)	7 (44)	3 (25)	.27‡

Note:—A-NIHSS indicates National Institutes of Health Stroke Scale score on admission; P-NIHSS, preprocedural National Institutes of Health Stroke Scale score; OTD time, onset-to-door time; OTP time, onset-to-procedure time; LIF, localized intra-arterial fibrinolysis; 7-NIHSS, National Institutes of Health Stroke Scale score at 7 days; mRS, modified Rankin Scale; NS, not significant.
* Data are from Mann-Whitney *U* test.
† Data are from χ^2 test for independence.
‡ Data are from Fisher exact test.

not allow a definitive indication and timing for TAS based on the results for patients with a severe stenosis.

There was no significant difference in the number of deaths from pneumonia after the procedure in our patient groups (a total of 3 patients [10.7%] died of pneumonia: 2 with total occlusion and 1 with a severe stenosis); however, this disease was seen frequently during hospitalization, in 11 (68.8%) and 4 (33%) patients in the occlusion and stenosis groups, respectively, and necessitated clinical management involving administration of an adequate dose of antibiotics. Therefore, careful postprocedural management may also be important for the improvement of clinical outcome of patients who undergo TAS,[10] and it is also of importance to prevent subacute occlusion of the treated vessel by avoiding probable risk factors, such as infection and dehydration.

Our study has several limitations. First, the study design was retrospective in nature, and an inherent selection bias of patients indicated for TAS was present in our cohort. Second, the number of patients is too small and the recruitment period is too short for the investigation of the exact features of clinical practice in TAS for total occlusion of IVBA. Finally, knowledge of the exact natural history of acute ischemic patients with atherosclerotic occlusive lesions of the IVBA receiving conservative treatment alone is limited, though recently several studies have analyzed the long-term outcome in patients with such lesions.[26] Although the risks and benefits of TAS in the treatment of acute ischemic stroke patients with occlusive lesions of the IVBA were not completely established in this small retrospective study, our results suggest that TAS for such patients is feasible, and this warrants further clinical research in larger numbers of patients.

Conclusion

TAS for occlusive lesions of the IVBA in acute stroke patients appears to be technically feasible, but the preprocedural neurologic status and the 3-month clinical outcome in patients with total occlusion were poor compared with those with a severe stenosis. Improvement of outcome in patients with total occlusion of the IVBA requires a reduction of procedural complications and careful postprocedural management involving prevention of subacute occlusion of the treated vessel.

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