Symptomatic Intracranial Stenosis: Cerebrovascular Complications from Elective Stent Placement[1]

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Purpose: To retrospectively evaluate the cerebrovascular complications from elective stent placement for symptomatic intracranial stenosis and to explore preliminarily which factors are associated with complications.

Materials and Methods: Institutional ethics committee approval was obtained, with waiver of informed consent. Records were reviewed of 181 consecutive elective stent placement procedures in 169 patients (mean age, 51.8 years; 142 male and 27 female patients) with symptomatic intracranial stenosis of more than 50% diameter reduction. Complications were evaluated. Fisher exact or χ^2 tests were used to assess statistical differences between rates for discrete variables. Stratification analysis was used to assess the significant relationship ($P < .05$) between a potential risk factor and a complication.

Results: Complications occurred in 20 patients (11.8%) of 169 patients: Ten patients (5.9%) had stroke (four patients had symptomatic intracranial hemorrhages [ICHs], and two of these patients died; six patients had ischemic strokes). Six patients had target-lesion thrombosis for which intrathrombus thrombolysis resulted in early complete patency without sequelae, two had asymptomatic ICHs, one had transient ischemic attack, and one had asymptomatic dissection. Perioperative noncompliance with antiplatelet therapy was found to be significantly associated with target-lesion thrombosis (two of eight patients [noncompliance] vs four of 161 patients [compliance], $P = .027$). Stratification analysis revealed a significant correlation between the use of double stents for a lesion and ICH ($P = .005$).

Conclusion: Cerebrovascular complications from elective stent placement for intracranial stenosis are diverse. The use of double stents for a lesion is an independent risk factor for ICH. Perioperative noncompliance with antiplatelet therapy is associated with a higher frequency of target-lesion thrombosis.

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The annual risk of ipsilateral ischemic stroke in patients with symptomatic intracranial atherosclerotic stenosis may reach 10%–24% despite optimal medical therapy (1–6). Angioplasty with or without stent placement may be a promising treatment option for symptomatic intracranial stenosis (7–18). Stent-assisted angioplasty can diminish the risks of dissection and elastic recoil associated with balloon angioplasty alone, but the procedural risks such as intraluminal thrombus, perforator stroke, and intracranial hemorrhage (ICH) remain a prime concern (7–20). Currently, the reports of cerebrovascular complications in stent placement for intracranial stenosis remain relatively few because of the small number of patients included in such reports or the lack of analysis of factors that might be associated with these complications (13–17,20). Thus, the purpose of our study was to retrospectively evaluate the cerebrovascular complications from elective stent placement for symptomatic intracranial stenosis and to explore preliminarily which factors are associated with complications.

Materials and Methods

Patients

Institutional ethics committee approval to perform stent placement for symptomatic intracranial stenosis was obtained. Each patient provided written informed consent for the procedure. Our institutional ethics committee approved this retrospective study and waived the need for informed consent.

Two neurologists who specialize in stroke treatment (T.W.L. and K.H.D.) in consensus reviewed the records for 181 consecutive elective stent placement procedures in 169 patients between September 5, 2001, and November 30, 2004. These records included data in 40 patients with symptomatic intracranial stenosis, and these data were published previously (14). There were 142 male and 27 female patients. The mean age was 51.8 years ± 12.76 (standard deviation) (range, 16–79 years; median, 52 years). The qualifying event was stroke in 69 (40.8%) patients and transient ischemic attacks (TIAs) in 100 (59.2%) patients. One hundred forty-three (84.6%) patients had a relevant regional infarct (ie, an infarct in the territory of the stenotic artery on a magnetic resonance image) and 26 (15.4%) did not. These ischemic events and relevant regional infarcts were attributed to 181 intracranial stenoses with a diameter reduction of 50% or more. The reference diameter was that of the normal vessel distal to the stenotic lesion; if the distal vessel was diseased, the diameter of the normal vessel proximal to the stenosis was used as the reference diameter.

Target Lesions

On the basis of the findings of cerebral angiography, 113 of 181 stenoses were located in the anterior circulation and 68 were located in the posterior circulation. Ninety-nine stenoses were at the M1 segment of the middle cerebral artery (MCA), one was at the M2 segment of the MCA, 13 were at the ophthalmic or communicating internal carotid artery, 31 were at the basilar artery, 31 were at the intracranial (fourth part) vertebral artery (VA), five were at the vertebrobasilar junction, and one was at the posterior inferior cerebellar artery. Eighty-two lesions involved bifurcation, and 99 did not. Fifty-nine stenoses were categorized as type A lesions (<5 mm in length, smooth, concentric or mildly eccentric stenosis); 100 stenoses, as type B lesions (5–10 mm in length, eccentric or angled [>45°] stenosis); and 22 stenoses, as type C lesions (>10 mm in length, angled [>90°] stenosis) (14). Forty-eight accesses between the target lesion and the end of the guiding catheter to be placed were categorized as type 1 (mild tortuosity and smooth vessel wall); 84 accesses, as type 2 (moderate tortuosity and irregular vessel wall); and 49 accesses, as type 3 (severe tortuosity) (14).

All except two patients had one or more atherosclerotic risk factors (arterial hypertension, diabetes mellitus, hyperlipidemia, hyperhomocysteinemia, and smoking). In two patients without risk factors, one who was 42 years old had eccentric plaques present in both the main right MCA (90% diameter reduction) and the right communicating internal carotid artery (50% diameter reduction), and these findings supported the idea that atherosclerosis was the likely cause. The other patient who was 16 years old had a spontaneous dissection and stenosis of the left MCA trunk that resulted in stroke and recurrent TIAs despite antithrombotic therapy. The lesion was presumed to be due to fibromuscular dysplasia. Thus, all intracranial stenoses but one were considered atherosclerotic.

Antiplatelet Therapy

The patients were pretreated with 300 mg of aspirin (Bayer, Leverkusen, Ger-

Advances in Knowledge

- We found that the use of double stents for a lesion is a significant ($P = .005$) independent risk factor for intracranial hemorrhage, and perioperative noncompliance with antiplatelet therapy is significantly ($P = .027$) associated with target-lesion thrombosis.
- Results of this study also indicate that aggressive endovascular and medical therapy for cerebrovascular complications (11.8%, 20 of 169) can reduce the stroke risk (5.9%, 10 of 169) and fatal or irreversible stroke rate (4.7%, eight of 169).

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Abbreviations:
ICH = intracranial hemorrhage
MCA = middle cerebral artery
NIHSS = National Institutes of Health Stroke Scale
TIA = transient ischemic attack
VA = vertebral artery

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many) daily plus 75 mg of clopidogrel (Sanofi, Paris, France) daily or 250 mg of ticlopidine (Sanofi) twice daily 7 days before surgery. Treatment was continued for at least 6 months after stent placement. Perioperative noncompliance with antiplatelet therapy was defined as no pretreatment with dual antiplatelet therapy or discontinuation of treatment within 30 days after stent placement.

Interventional Procedure

A low-dose nimodipine (Bayer) infusion was started 2 hours before surgery for prevention of vasospasm. Two anticoagulation regimens were employed. In the initial 68 patients, heparin was administered intravenously as a bolus of 3000 U (Shanghai No. 1 Biochemical and Pharmaceutical, Shanghai, China), followed by an infusion at 800 U/h to maintain an activated clotting time between 250 and 300 seconds. In the subsequent 101 patients, the heparin bolus and infusion were reduced to 2000 and 500 U/h, respectively, to maintain an activated clotting time between 160 and 220 seconds, which was the same as that for the protocol of the PROACT (Intra-arterial Pro-urokinase for Acute Ischemic Stroke) II study (21).

Procedures were performed by one of two interventional neuroradiologists (W.J.J. and B.D., who had 20 and 12 years of experience with endovascular therapy, respectively). With local (n = 113) or general (n = 56) anesthesia, a 6-F guiding catheter (Envoy; Cordis, Miami, Fla) was advanced to the distal cervical segment of the internal carotid artery or VA through a 6-F femoral (165 patients) or radial arterial sheath (four patients). A 0.014-inch microwire was carefully steered across the stenosis with road-map guidance and was anchored distally to support the delivery of the stent system. Assembly of a microcatheter and microwire was used in some cases when a single microwire navigation was difficult. Ioversol (Tyco Healthcare, Montreal, Quebec, Canada), 320 mg of iodine per milliliter, was used as a contrast agent during the procedure, and the total volume of ioversol we used ranged from 50 to 150 mL.

Eight types of balloon-expandable stents were used in this study (Table 1). These stents were classified into two categories: the coronary stent and the intracranial stent (Apollo; MicroPort Medical), which was specifically designed for treatment of intracranial stenosis. The coronary stent was used through 2003, after which the intracranial stent was used. The stent length was selected to completely cover the stenosis with an overhang of at least 1 mm on both sides. The diameter of the stent was the same as the diameter of a normal adjacent vessel on either side of the stenosis, whichever adjacent vessel was smaller or slightly smaller than that diameter. The stent was deployed by slow balloon inflation up to 6–8 atm, when the stent straddled the stenotic segment. The second stent was used when the lesion was not covered by the first stent completely. Double stents, which partially overlapped each other, were used in six patients (six lesions).

Technical success was achieved when a stent covered the target lesion completely and resulted in a 30% or smaller residual stenosis with good anterograde blood flow. After technical success (evaluated by W.J.J. and B.D. in consensus) was achieved, the balloon catheter was removed, and the microwire was left in the original site for a 10–30-minute observation. Simultaneously, the blood pressure was decreased to 100–120/60–80 mm Hg through titration of nimodipine or urapidil hydrochloride (Altana Pharma, Bad Homburg, Germany). After patency of the vessel treated with the stent was confirmed with angiography, the microwire and guiding catheter were then removed. Brain computed tomography (CT) was quickly performed to exclude ICH. The heparin infusion was discontinued 3 hours after surgery to allow removal of the arterial sheath 6 hours after surgery. The medication was then switched from a heparin infusion to subcutaneous nadroparin calcium (Fraxiparine; Sanofi Winthrop Industrie, Gentilly, France), which was administered at a dose of 0.4–0.6 mL (on the basis of the patient's body weight) every 12 hours for 3 days.

Complications

Cerebrovascular complications within 30 days of the procedure were considered perioperative and procedure related (22). ICHs included parenchymal hemorrhage and subarachnoid hemorrhage detected at brain CT. Target-lesion thrombosis was defined as intraluminal thrombus within the vessel treated with a stent or its side branch that was confirmed with cerebral angiography. TIA was defined as acute onset of a focal neurologic deficit that lasted 24 hours or less. Stroke was defined as acute onset of a focal neurologic deficit that lasted longer than 24 hours and that was specifically attributable to a cerebrovascular distribution (23,24). Stroke was further classified into minor stroke (National Institutes of Health Stroke Scale [NIHSS] score of <9) (23) and major stroke (NIHSS score of ≥9). Ischemic events consisted of TIAs and ischemic strokes. Stroke with the following characteristics was diagnosed as perforator stroke: *(a)* The onset was closely related to the procedure, and the deficits were referable to the perforator territory adjacent to the vessel treated with a stent (ie, stroke developed immediately or soon after stent placement, and the patient had a lacunar syndrome at presentation). *(b)* With cerebral angiography, occlusion or more than 50% diameter reduction in the stent or large artery (diameter of 1 mm or larger) had been excluded. *(c)* Brain CT 24 hours after stroke revealed a new infarct in the perforator territory, which was adjacent to the vessel treated with a stent, or no new lesion (25).

On the basis of the patient's syndrome, identified with clinical findings and neuroimaging findings (angiography, transcranial Doppler ultrasonography, brain CT, and perfusion CT), the probable cause of complication was determined with consensus in a multidisciplinary meeting of some authors (K.H.D., T.W.L., W.J.J., B.D., and M.J., all of whom had 5 years or more

of experience in neurologic evaluation in stroke).

Target-lesion thrombosis that manifested within 3 hours after stent placement was treated with intrathrombus thrombolysis with urokinase (Livzon Libao Biochemical & Pharmaceutical, Zhuhai, China). Currently, urokinase is a drug approved by the State Food and Drug Administration of our country. Spiral dissection was treated with additional stent placement. For perforator stroke and embolic stroke, the period of anticoagulation with nadroparin calcium was extended to 1 week. Vasospasm was treated with nimodipine infusion. In patients with ICH, antiplatelet therapy was withheld, heparin was neutralized by using protamine sulfate (Shanghai No. 1 Biochemical and Pharmaceutical), and blood pressure was controlled to be within 90–110/60–80 mm Hg.

Outcome of Stroke on Day 30

The patient's neurologic status at admission and at days 1 and 30 after surgery was assessed by an experienced neurologist (K.H.D., who had 20 years of experience in neurologic evaluation in stroke) with the NIHSS score. Stroke was considered "reversible" if the NIHSS score on day 30 was the same as or less than the preoperative NIHSS score, and stroke was considered "irreversible" if the NIHSS score on day 30 was greater than the baseline NIHSS score.

Statistical Analysis

All data were analyzed according to the intention-to-treat principle. The *t*

Table 1

Sites of Lesions and Types of Stents Deployed

	Stents with Technical Success*									
Site	Apollo†	AVE/ S-660‡	Biodiv Ysio§	BX Sonic‖	Coroflex#	Cypher Raptor‖	Express**	Multi-Link††	Total	No. of Stents with Failure and Reason
M1 segment of MCA	19 (19)	4 (4)	65 (69)	. . .	. . .	1 (1)	1 (1)	1 (1)	91 (95)	8; 2 with failure of microwire navigation through lesion, 6 with failed delivery of stent system
M2 segment of MCA	. . .	. . .	1 (1)	. . .	. . .	. . .	. . .	. . .	1 (1)	. . .
Ophthalmic or communicating internal carotid artery	7 (8)	. . .	2 (2)	1 (1)	1 (1)	. . .	. . .	. . .	11 (12)	2 with failed delivery of stent system
Intracranial VA	6 (6)	1 (1)	13 (13)	5 (5)	3 (3)‡‡	. . .	1 (1)	. . .	29 (29)	2; 1 with failure of guiding catheter positioning, 1 with failed delivery of stent system
Basilar artery	10 (11)	1 (1)	16 (16)	1 (1)	1 (1)	. . .	. . .	. . .	29 (30)	2; 1 with failure of guiding catheter positioning, 1 with failure of microwire navigation through lesion
Vertebrobasilar junction	. . .	. . .	3 (3)	. . .	2 (2)	. . .	. . .	. . .	5 (5)	
Posterior inferior cerebellar artery	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .	1 with failed delivery of stent system
Overall	42 (44)	6 (6)	100 (104)	7 (7)	7 (7)	1 (1)	2 (2)	1 (1)	166 (172)	15; 2 with failure of guiding catheter positioning, 3 with failure of microwire navigation through lesion, 10 with failed delivery of stent system

* Data are numbers of stenoses for which treatment with a stent was technically successful. Numbers in parentheses are numbers of stents used.

† MicroPort Medical Shanghai, Shanghai, China.

‡ Medtronic, Minneapolis, Minn.

§ Abbott Vascular Devices Ireland, Galway, Ireland.

‖ Cordis Europa N.V., Roden, the Netherlands.

B. Braun Melsungen, Melsungen, Germany.

** Boston Scientific Scimed, Maple Grove, Minn.

†† Guidant, Temecula, Calif.

‡‡ One case of proximal spiral dissection occurred after angioplasty with a Coroflex stent and it was treated with a Biodiv Ysio stent. This datum was not included in Table 1.

Table 2

Clinical Data in 20 Patients with Complications of Stent Placement

Patient No./ Sex/Age (y)	Lesion Site	Stent	Stent Diameter and Length (mm)	Stenosis (%)		Complication				
				Before Placement	After Placement	Event	Onset Time	Symptom	Probable Cause	Outcome on Day 30
1/M/40	Right M1 segment of MCA	Biodiv Ysio	2.25, 10	50	10	TIA	Day 2	Left hemiparesis	Vasospasm from early withdrawal of nimodipine	Reversible stroke
2/M/41	Left intracranial VA	Coroflex	4, 13	65	10	Spiral dissection	Intraoperative	Asymptomatic	Oversized stent	Reversible stroke
3/M/23	Left M1 segment of MCA	AVE/S-660	2.5, 9	80	10	Stent thrombosis	Intraoperative	Right hemiparesis	Noncompliance with preoperative antiplatelet therapy	Reversible stroke
4/M/68	Right intracranial VA	. . .	. . .	70	70	Right posterior inferior cerebellar artery thrombosis	Intraoperative	Left hemianesthesia, vertigo, nausea, nystagmus	Secondary to spasm of right VA during navigation of guiding catheter	Reversible stroke
5/M/53	Right communicating internal carotid artery	Apollo	3.0, 8	60	20	Stent thrombosis and distal thromboembolism	Intraoperative	Left hemiparesis	Unknown	Reversible stroke
6/M/45	Basilar artery	Coroflex	3.5, 13	70	20	Stent thrombosis	Day 3	Right cranial nerve III palsy, dysarthria, tetraparesis	Ticlopidine replaced with clopidogrel 1 day before stent placement	Reversible stroke
7/M/60	Left and right M1 segments of MCA	Biodiv Ysio for both	2.0, 10	75, both lesions	25, left lesion; 75, right lesion	Stent thrombosis of left M1 segment of MCA	Day 14	Right hemiparesis	Antithrombotic agents withheld because patient was suspected of having right ICH at CT	Reversible stroke
8/M/54	Right M1 segment of MCA	Biodiv Ysio	2.25, 7	70	10	Stent thrombosis	Day 2	Left hemiparesis, dysarthria	Unknown	Reversible stroke
9/M/68	Basilar artery	AVE/S-660	3.0, 9	70	15	Distal embolic stroke	Day 1	Left hemianopia, hemianesthesia	Repeated adjustment of stent position	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 4, and 4, respectively)
10/F/31	Left M1 segment of MCA	Biodiv Ysio	2.0, 7; 2.25, 7	98	15	Subarachnoid hemorrhage	Day 1	Headache, dizziness	Double stents, high-dose heparin	Died 36 h after onset of symptoms
11/M/16	Left M1 segment of MCA	Biodiv Ysio	2.25, 7; 2.5, 10	60	0	Subarachnoid and parenchymal hemorrhage	Day 1	Right hemiparesis	Double stents, high-dose heparin	Reversible stroke (NIHSS scores at baseline, and days 1 and 30 were 2, 10, and 2, respectively)

12/M/39	Right M1 segment of MCA	Biodiv Ysio	2.25, 7; 2.5, 7	70	0	Parenchymal hemorrhage	Day 1	Left hemiparesis	Double stents, high-dose heparin	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 5, and 2, respectively)
13/M/48	Vertebrobasilar junction	Coroflex	2.5, 9	95	15	Subarachnoid hemorrhage	Day 3	Sudden headache	Hyperperfusion syndrome	Died on day 10
14/M/41	Right communicating internal carotid artery, left M1 segment of MCA	Biodiv Ysio for both	4.0, 8 for right lesion; 2.0, 7 for left lesion	70, right lesion; 80, left lesion	20, right lesion; 0, left lesion	Right parenchymal hemorrhage	Day 1	Asymptomatic	High-dose heparin	Reversible stroke
15/M/44	Left M1 segment of MCA	Biodiv Ysio	2.0, 7	90	5	Subarachnoid hemorrhage	Day 1	Asymptomatic	High-dose heparin	Reversible stroke
16/M/74	Basilar artery	Biodiv Ysio	3.5, 11	80	20	Perforator stroke	10 h after stent placement	Dysarthria, right hemiparesis	Compromise of perforators	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 7, and 2, respectively)
17/M/47	Basilar artery	Biodiv Ysio, Apollo*	2.25, 10 for Biodiv Ysio; 2.5, 13 for Apollo	80	0	Perforator stroke	Intraoperative	Dysarthria, right hemiparesis	Compromise of perforators	Reversible stroke (NIHSS scores at baseline and days 1 and 30 were 4, 8, and 2, respectively)
18/M/45	Right M1 segment of MCA	Apollo	2.5, 8	70	0	Perforator stroke	Intraoperative	Left hemiparesis	Compromise of perforators	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 2, and 2, respectively)
19/M/59	Right intracranial VA	Biodiv Ysio	3.0, 11	70	0	Perforator stroke	Intraoperative	Right hemiparesis, anesthesia	Compromise of perforators	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 8, and 5, respectively)
20/M/69	Left M1 segment of MCA	Apollo	2.5, 8	60	20	Perforator stroke	Intraoperative	Right hemiparesis, aphasia	Compromise of perforators	Irreversible stroke (NIHSS scores at baseline and days 1 and 30 were 0, 6, and 4, respectively)

Note.—Patients 4, 5, 7, 8, 9, 13, 14, and 17 had stroke as the qualifying event; 12 patients had TIA as the qualifying event. Eighteen patients had a relevant regional infarct, and patients 1 and 15 did not. Nineteen patients had one or more risk factors, and patient 16 had dissection presumably related to fibromuscular dysplasia.

* Patient 17 had a long lesion involved in the proximal and distal areas of the basilar artery; the Biodiv Ysio stent was placed in an area from the distal to the middle segment of the basilar artery, and the Apollo stent was placed in an area from the middle to the proximal segment of the basilar artery.

test was used to assess the statistical difference between the age of patients with complications and the age of patients without complications. Fisher exact or χ^2 tests were used to assess statistical differences between rates for discrete variables. Stratification analysis with the Cochran-Mantel-Haenszel test was used to assess the significant relationship between the potential risk factor and complication, when there was a confounding effect of another factor. All reported probability values are two sided; differences with $P < .05$ were considered statistically significant.

Results

Interventional Procedure

The technical success rate (Table 1) was 91.7% (166 of 181 stent placement procedures). One hundred seventy-two stents were successfully placed in 166 lesions. Forty-four intracranial stents were placed in 42 lesions, and 128 coronary stents were placed in 124 lesions. Technical failure occurred in 15 stent placement procedures (15 of 181 procedures), and such failure included failure of the delivery of the stent system because of severe tortuous access despite an appropriate position of the guiding catheter and microwire ($n = 10$), failed microwire navigation through the stenosis ($n = 3$), and failed guiding catheter positioning ($n = 2$).

Antiplatelet Therapy

Perioperative noncompliance with antiplatelet therapy occurred in eight patients (patients 3, 7, and 10–15 in Table 2). These patients included one who inadvertently did not receive pretreatment with dual antiplatelet agents, six with ICH complications, and one who was suspected of having ICH (subsequently found to be contrast agent retention) who stopped the antiplatelet therapy immediately.

Complications

Complications (including those associated with perioperative noncompliance with antiplatelet therapy) occurred in 11.8% (20 of 169) of patients or 11.0% (20 of 181) of stent placement procedures. These complications included six ICHs, 13 ischemic events (six cases of stent thrombosis and posterior inferior cerebellar artery thrombosis, five minor perforator strokes, one embolic stroke, one TIA presumably from vasospasm), and one spiral dissection (Table 2).

In the six ICHs, four were symptomatic and two were asymptomatic. Five ICHs were detected immediately after stent placement, and one occurred on day 3, presumably from hyperperfusion syndrome (the blood pressure rebounded up to 150–160/90 mm Hg after withdrawal of nimodipine therapy on day 2).

In the six target-lesion thromboses, three were detected at surgery, one occurred on day 2, one occurred on day 3, and one occurred on day 14. Five target-lesion thromboses formed in the stent, and one formed within the side branch of the target lesion. The patient had a stenosis in the right intracranial VA across the stenotic ostium of the posterior inferior cerebellar artery and developed a right VA spasm during the delivery of the guiding catheter into the right VA. Although the VA spasm was resolved completely within 5 minutes with infusion of 0.2 mg nimodipine diluted with 10 mL of normal saline into

Table 3

Baseline Characteristics of Patients with and Patients without Complications

Characteristic	Patients with Complications ($n = 20$)	Patients without Complications ($n = 149$)	*P* Value
Clinical factor			
Age (y)*	48.3 ± 15.3	52.3 ± 12.4	.19
Male sex	95.0 (19)	82.6 (123)	.13
Risk factor			
Smoking	75.0 (15)	64.4 (96)	.35
Diabetes mellitus	25.0 (5)	17.4 (26)	.29
Hypertension	65.0 (13)	59.7 (89)	.65
Hyperlipidemia	75.0 (15)	81.9 (122)	.32
Hyperhomocysteinemia	25.0 (5)	27.5 (41)	.81
Other factors			
Qualifying stroke event	40 (8)	40.9 (61)	.94
Relevant regional infarct	90 (18)	83.9 (125)	.37
Patients with 2 intracranial stenoses	10.0 (2)	6.7 (10)	.43

Note.—Except where otherwise indicated, values are percentages, and data in parentheses are numbers of patients.

* Values are the mean ± standard deviation.

Table 4

Angiographic Characteristics of Lesions with and Lesions without Complications

Angiographic Characteristics	Lesions with Complications ($n = 20$)	Lesions without Complications ($n = 161$)	*P* Value
Stenosis of ≥70% diameter	70.0 (14)	67.1 (108)	.79
Bifurcation lesion	55.0 (11)	44.1 (71)	.36
Posterior circulation lesion	40.0 (8)	37.3 (60)	.81
Type C lesion	15.0 (3)	11.8 (19)	.45
Type 3 access	35.0 (7)	26.1 (42)	.40

Note.—Values are percentages, and data in parentheses are numbers of lesions.

the VA and withdrawal of the guiding catheter to the right subclavian artery, the patient had vertigo, nausea, nystagmus, and left hemianesthesia. Acute occlusion of the right posterior inferior cerebellar artery was considered as the cause and then was confirmed at angiography. A microcatheter was immediately advanced into this side branch, through which the 0.5 million units of urokinase (concentration, 40 000 U/mL of normal saline) was infused within 50 minutes. Complete recanalization was then obtained, followed by the complete disappearance of the syndrome. Intrathrombus thrombolysis with urokinase (total dose range, 0.2–1.0 million units) was immediately performed in the five other patients within several minutes to 1 hour from the onset of the syndrome, and complete patency was obtained in all within 2 hours from the onset, and patients returned entirely to the preprocedural status (ie, the postprocedural NIHSS score was the same as the preprocedural NIHSS score). No bleeding complications were documented at brain CT. These six events were all categorized as TIAs.

In the five perforator strokes, which had been described in detail previously (26), four occurred during the procedure, and one occurred 10 hours after stent placement. One patient developed right occipital and thalamic infarcts 12 hours after stent placement in the basilar artery. At angiography immediately after stent placement, one patient had asymptomatic spiral dissection of the VA proximal to the vessel treated with a stent; spiral dissection was treated with additional stent placement during the same procedure. The last patient with complications experienced five attacks of transient left hemiparesis on the next day after stent placement in the right MCA and 6 hours after withdrawal of nimodipine infusion. This event was presumably due to a vasospasm of a small artery, because repeated angiography revealed a widely patent vessel with a stent and good anterograde blood flow, and the patient had no further TIAs after resumption of treatment with the nimodipine infusion.

Thus, symptomatic and asymptomatic complications occurred in 17 and three patients (two ICHs, one dissection), respectively. Stroke occurred in 10 patients (5.9%, 10 of 169): five perforator strokes, one embolic stroke, and four symptomatic ICHs.

Table 5

Univariable Analysis of ICH and Ischemic Event

A: Variable 1—Use of Double Stents for a Single Lesion

Complication	Double Stent ($n = 6$)	No Double Stent ($n = 163$)	*P* Value
ICH	3 (50.0)	3 (1.8)	.005
Perforator stroke	1 (16.7)	4 (2.5)	.167
Target-lesion thrombosis	0 (0)	6 (3.7)	>.99
Ischemic events	1 (16.7)	12 (7.4)	.386

B: Variable 2—Intraoperative Heparin Dose

Complication	High Dose ($n = 68$)*	Low Dose ($n = 101$)†	*P* Value
ICH	5 (7.4)	1 (1.0)	.04
Perforator stroke	2 (2.9)	3 (3.0)	.68
Target-lesion thrombosis	2 (2.9)	4 (4.0)	.54
Ischemic events	6 (8.8)	7 (6.9)	.36

C: Variable 3—Perioperative Compliance with Antiplatelet Therapy

Complication	Complied ($n = 161$)	Did Not Comply ($n = 8$)	*P* Value
Perforator stroke	5 (3.1)	0 (0)	.76
Target-lesion thrombosis	4 (2.5)	2 (25.0)	.027
Ischemic events	10 (6.2)	3 (37.5)	.02

Note.—Data are number of patients, and numbers in parentheses are percentages.

* The dose was a 3000-U bolus, followed by administration of 800 U/h.

† The dose was a 2000-U bolus, followed by administration of 500 U/h.

Table 6

Analysis of Relationship between Stent Pattern and ICH with Stratification according to Intraoperative Heparin Dose

	High-Dose Heparin Therapy ($n = 68$)		Low-Dose Heparin Therapy ($n = 101$)	
ICH	Double Stents ($n = 4$)	Single Stent ($n = 64$)	Double Stents ($n = 2$)	Single stent ($n = 99$)
With ($n = 6$)	3	2	0	1
Without ($n = 163$)	1	62	2	98

Note.—Stent pattern is classified as two types: a single stent in one lesion and two (double) stents in one lesion. The results of the Cochran-Mantel-Haenszel test and the χ^2 value of 25.79 ($P < .001$) further verify a relationship between the placement of double stents for a lesion and ICH, after this association is verified in a univariable analysis (Table 5).

Outcome of Strokes on Day 30

In the four symptomatic ICHs, two were fatal strokes, one was a reversible minor stroke, and one was an irreversible minor stroke. In the six ischemic strokes, five were irreversible minor strokes and one was a reversible minor stroke. Thus, the frequency of irreversible minor stroke was 3.6% (six of 169), and the case fatality ratio was 1.2% (two of 169).

Statistical Analysis

Table 2 shows that complications in 19 patients occurred after the successful

placement of a stent, and one occurred during the delivery of a guiding catheter. In the 19 patients in whom complications occurred after stent placement, the complications occurred in four (9.5%) after intracranial stents were placed in 42 lesions, and they occurred in 15 (12.1%) after coronary stents were placed in 124 lesions. There was no significant difference in the complication rate between the use of intracranial stents and the use of coronary stents ($P = .268$). The baseline characteristics of patients with and patients without complications and the angiographic characteristics of lesions with and lesions without complications were comparable (Tables 3 and 4). The rates of complications in stent placement in anterior (10.6%, 12 of 113) and posterior (11.8%, eight of 68) circulation lesions were similar and not significantly different ($P = .81$). Univariable analysis (Table 5) showed that perioperative noncompliance with antiplatelet therapy was significantly associated with target-lesion thrombosis, and the use of double stents for a single lesion and high-dose intraoperative heparin therapy were significantly associated with ICH. Results of stratification analysis (Table 6) revealed a significant correlation between the use of double stents for a lesion and ICH ($P < .001$). No significant correlation between intraoperative heparin dose and ICH was observed after adjustment of the analysis for the potential confounding effect of the stent pattern (a single stent for a lesion vs two [double stents] for a lesion) ($P = .083$).

Discussion

Our study findings indicate that there is a spectrum of procedure-related cerebrovascular complications from stent placement; these complications consist of ICH, target-lesion thrombosis, perforator stroke, embolic stroke, TIA, and vessel dissection.

ICH could be fatal, and it caused two deaths in the series of patients in this study. ICH was detected immediately after stent placement in all but one of the six patients who had it, and these six patients included two with asymptomatic ICHs. These findings reiterate the importance of performing brain CT immediately after stent placement for intracranial stenosis. Hyperperfusion, vessel perforation, and vessel rupture are associated with ICH after stent placement in a cerebral artery (14,20,27). Currently, aggressive systemic blood pressure control remains the best available measure to prevent and treat hyperperfusion syndrome (14,28). Our study findings suggest that the use of double stents for treatment of a lesion is an independent risk factor for ICH. The most probable mechanisms include the following: The second (proximal) stent system may impinge onto the first (distal) stent during the procedure; the forward thrust of the distal end struts of the first stent may then perforate the arterial wall; and the eccentric advancement of the second stent system within the first expanded stent (advancement caused by the relatively tortuous course of the intracranial artery) may generate a forward drag on the major cerebral arteries, and this forward drag results in avulsion or rupture of the emanating fragile perforators. Although results of stratification analysis in this study revealed that high-dose intraoperative heparin (with which an activated clotting time of 250–300 seconds was obtained) was not an independent risk factor for ICH, interestingly, the low-dose intraoperative heparin regimen (with which a lower activated clotting time of 160–220 seconds was obtained) was not associated with increased target-lesion thrombosis. These data suggest that a randomized study may be warranted to investigate the optimal activated clotting time in stent placement for intracranial stenosis.

Target-lesion thrombosis is related to local intimal injury after angioplasty. Pretreatment with a combination of clopidogrel and aspirin before surgery has been recommended (19). Our results suggest the importance of periprocedural dual antiplatelet therapy because periprocedural noncompliance with antiplatelet therapy was associated with a higher frequency of target-lesion thrombosis.

About one-fourth of complications in our study were perforator strokes. Compromise of the perforators caused by angioplasty with or without stent placement may be associated with perforator stroke (29,30). Findings in our previous study indicated that patients with a preoperative perforator infarct adjacent to the stenotic segment have a higher frequency of perforator stroke after elective stent placement for intracranial stenosis (26). Thus, physicians should weigh carefully the risk against the benefit, when a patient with large-artery disease has a perforator event (TIA or stroke) and the pertinent perforators emanate from the target lesion. Currently, we only perform stent placement procedures in such patients when certain concurrent characteristics are present, as follows: *(a)* imminent main trunk occlusion (for example, a critical dissecting stenosis) or a high-grade symptomatic stenosis of the basilar artery without collateral vessels from bilateral posterior communicating arteries, *(b)* extensive perfusion failure referable to the stenosis evidenced at perfusion CT, and *(c)* failure of medical therapy.

Prudent patient selection, careful periprocedural medical treatment, and a highly skilled interventionist are all required to perform stent placement for intracranial stenosis with an acceptable stroke risk (18). Swift recognition and treatment of cerebrovascular complications are crucial for good patient outcomes. Our study results suggest that aggressive endovascular and medical therapy for cerebrovascular complications (11.8%, 20 of 169) can reduce the risk for stroke (5.9%, 10 of 169) or the fatal and irreversible stroke rate (4.7%, eight of 169).

Of note, there were some limitations of our study. First, the data are from a single center and may not be generalizable to other centers for reasons of selection bias, level of experience of the interventional neuroradiologist, and multidisciplinary care. Second, our study is not a randomized controlled trial in which stent placement with the best medical treatment or with balloon angioplasty alone were compared; therefore, we could not draw any conclusions about which option is better or worse.

Last, in our study, the number of patients in whom double stents were used for a lesion is small so that the observed difference in the sample ICH rates might be due to sampling uncertainty or error; therefore, further study is needed. We have not discussed the long-term outcomes and restenosis rate in this article, because the aim of this study was to focus on the procedure-related cerebrovascular complications.

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