Concomitant Multiple Revascularizations in Supra-Aortic Arteries: Short-Term Results in 50 Patients

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ORIGINAL RESEARCH

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BACKGROUND AND PURPOSE: The outcome for simultaneous revascularization of more than 1 supra-aortic arterial stenosis has not been evaluated because of concerns regarding the increased risk of additional procedures. We evaluated the feasibility and safety of concomitant multiple supra-aortic arterial revascularizations (CMSAR).

MATERIALS AND METHODS: We retrospectively evaluated 50 consecutive patients who underwent CMSARs with angioplasty and stent placement. The study included a separate lesion group (LG) ($n = 28$), ipsilateral LG ($n = 17$) including adjacent ($n = 6$) and remote ($n = 11$) tandem lesions, and triple LG ($n = 5$). We assessed the procedural success (defined as residual stenosis $<$30%) and periprocedural event rate (ER) (minor or major stroke, and death). We compared the ERs in the lesion (ipsilateral vs separate) and symptom (unstable vs stable) pattern groups with the Fisher exact test.

RESULTS: Procedural success was achieved in all patients (50/50). Periprocedural events within 30 days were noted in 5 (10%). ER within 2 days after the procedure was higher in the ipsilateral LG (4/17) than in the separate LG (0/28) ($P = .016$). Major events consisting of a major stroke and a death occurred in 2 patients in the unstable group (4%) and was more common in the unstable (2 of 7) than in the stable group (0/38) ($P = .029$). During the mean 11-month follow-up period, there was 1 symptomatic recurrence.

CONCLUSION: CMSARs are feasible with a high procedural success rate resulting in a favorable short-term outcome. However, they must be carefully performed in ipsilateral LG, especially in patients in the unstable group.

Carotid arterial stent placement is regarded as a safe and effective alternative option to carotid endarterectomy for the treatment of carotid arterial stenosis.[1-4] Although most atherosclerotic cerebral arterial stenoses might occur in 1 vascular territory, the coincidence of another stenosis in the same or a different artery is not infrequent.[5-7] The estimated prevalence of stroke varies from 20% to 50% in patients affected by carotid stenosis with intracranial carotid artery stenosis.[8-10] Rothwell et al[11] noted that the operative risk of carotid endarterectomy is significantly related to stenosis of the ipsilateral internal carotid siphon.

Concomitant supra-aortic arterial revascularizations are sometimes considered in patients with separate or ipsilateral multiple stenotic lesions and in patients with a fluctuating or deteriorating stroke with multiple stenotic lesions, especially those in the same vascular territory. However, concomitant revascularization must also be assumed to present the additional risks of procedural and periprocedural complications. The purposes of our study were to evaluate the feasibility and safety of 1-stage, multiple supra-aortic stenting and to discuss the possible complications of and a stepwise strategy for an endovascular treatment approach. We report our results for revascularization of 105 supra-aortic arterial lesions in 50 consecutive patients.

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Materials and Methods

Between June 2002 and January 2007, we treated 105 supra-aortic stenoses in 50 consecutive patients. We retrospectively reviewed multiple concomitant intracranial stent placements performed on 50 consecutive patients from a collected neurointerventional data registry. We included patients who were symptomatic as having 1) severe stenosis in 2 separate supra-aortic vessels ($n = 28$), 2) a remote tandem lesion when there were 2 stenotic lesions in different arterial segments in the same artery ($n = 11$), 3) an adjacent tandem lesion when there were 2 stenotic lesions in the same arterial segment ($n = 6$), 4) severe stenosis in 3 supra-aortic vessels ($n = 5$), and asymptomatic patients as having 5) multiple supra-aortic stenoses noted before coronary artery bypass surgery ($n = 5$). We excluded patients with 1) acute onset of symptoms within 6 hours of the onset of symptoms; 2) nonatherosclerotic arterial diseases such as Moyamoya disease, dissection, vasculitis, etc; 3) a history of significant hemorrhage within the past 6 weeks; 4) any bleeding tendency or a platelet count less than 100,000; 5) any contraindications to antiplatelet medication; 6) a significant neurologic deficit caused by a previous stroke (more than a 3 on the modified Rankin Scale [mRs]); 7) a cardiac source of embolism; and 8) any comorbid medical condition that limited the outlook for survival to less than 5 years.

Among 45 patients who were symptomatic, 38 had stable symptoms that had resolved, or improving or stationary symptoms before the stent placement, and 7 patients had progressive (gradually worsening) or fluctuating symptoms with a change of more than 4 on the National Institutes of Health Stroke Scale (NIHSS).

The clinical and lesion characteristics of these patients are shown in Tables 1 to 3. The patients' ages ranged from 45 to 87 years (mean

Table 1: Baseline characteristics of the fifty patients

Variables	Characteristics
Age*	66 ± 8.3
Male-to-female ratio	45:5
Presence of symptoms	45 (90%)
(Stroke:TIA)	(20:25)
(Stable:unstable)	(38:7)
Hypertension	37 (74%)
DM	17 (34%)
Hyperlipidemia	9 (18%)
History of previous stroke	20 (40%)
Coronary arterial disease	15 (30%)
Chronic renal failure	2 (4%)
C-reactive protein*	1.0 ± 1.8
Homocysteine (umol/L)*	16.5 ± 9.2

Note:—TIA indicates transient ischemic attack; DM, diabetes mellitus.
* Mean ± SD.

Table 2: Baseline lesion characteristics in the fifty patients

Variables	Characteristics
Degree of stenosis, mean ± SD	75.8 ± 9.2
Lesion length (mm), mean ± SD	12.0 ± 7.3
Location of lesion	
Anterior circulation	32/50 (64%)
Posterior circulation	5/50 (10%)
Combined circulation	13/50 (26%)
Separate lesion group	28/50 (56%)
Bilateral carotid lesions	15/50 (30%)
ICA lesion + other supra-aortic lesions	12/50 (24%)
Subclavian artery + VA ostium	1/50 (2%)
Ipsilateral lesion group	17/50 (36%)
Adjacent tandem	6/50 (12%)
Remote tandem	11/50 (22%)
Triple lesion	5/50 (10%)

Note:—ICA indicates internal carotid artery; VA, vertebral artery.

age, 65.5 ± 8.3 years), and the male-to-female ratio was 9:1 (male = 45, female = 5). Median initial NIHSS was 0 (0–7) in stable patients and 10 (6–14) in unstable patients. Median mRS at 6 months was 0 (0–6) in stable patients and 0 (0–6) in unstable patients.

Twenty patients had a stroke, and 25 had 1 or more transient ischemic attacks. Multiple lesions were detected in the 5 asymptomatic patients before coronary artery bypass graft (CABG). Two of these patients had a history of a previous stroke. Two of these 5 patients had bilateral carotid bulb lesions and 3 had ipsilateral remote tandem lesions; the carotid bulb lesions were associated with stenosis of the common carotid artery (CCA) or with the cavernous or petrous segments of the internal carotid artery (ICA). After discussion with the neurologist, cardiologist, and neurointerventional radiologist and after evaluating potential risks and benefits as well as cardiac function before ($n = 1$) or after ($n = 4$) CABG, we decided on revascularization.

Among these 50 patients, the lesions involved only the anterior circulation in 32, both the anterior and posterior circulations in 13, and only the posterior circulation in 5. Revascularization with angioplasty and stent placement was performed in the separate lesion group ($n = 28$) including 15 bilateral ICA bulb lesions, 12 ICA lesions (9 bulbar, 2 cavernous, and 1 petrous) associated with the other supra-aortic stenoses (8 ostia of the vertebral artery [VA], 2 intradural VAs, 1 CCA, and 1 subclavian artery), and a subclavian artery lesion associated with the ostium of the VA.

The ipsilateral lesion group ($n = 17$) included patients with adjacent tandem lesions ($n = 6$) and remote tandem lesions ($n = 11$) (Fig 1). Adjacent tandem lesions were located in the cavernous ICA ($n = 3$), M1 ($n = 1$), carotid bulb and adjacent CCA ($n = 1$), and in the vertebrobasilar junction and adjacent basilar artery (BA) ($n = 1$). Remote tandem lesions were located in the carotid bulb and cavernous ICA ($n = 4$), the carotid bulb and petrous ICA ($n = 3$), intradural and cervical VAs ($n = 2$), carotid bulb and proximal CCA ($n = 1$), and BA and VA ostium ($n = 1$). The triple lesion group ($n = 5$) had lesions located in the carotid bulb plus intradural VA and VA ostium (remote tandem lesion) ($n = 2$), carotid bulb plus contralateral adjacent CCA ($n = 1$) (Fig 2), carotid bulb plus CCA plus ostium of the VA ($n = 1$), and in the bilateral carotid bulbs and CCA ($n = 1$).

A complete history was taken of each study patient, and a neurologic examination was performed by independent neurologists who were not involved in the interventional procedure. The occurrence of adverse events (AEs) was evaluated at 30 days after stent placement and again at 6 months and yearly thereafter. If patients was not followed in an outpatient clinic, an experienced nurse telephoned them ($n = 13$) to evaluate the occurrence of any clinically relevant event and mRS transformed from functional outcome including dependency, living situation, mobility, dressing, and toilet functions.[12]

The mean clinical follow-up period was 11 months (range, 1~25 months; median, 10.5 months). Follow-up imaging studies were obtained from 28 patients (24 Doppler sonograms and 4 catheter cerebral angiograms) between 6 and 44 months after treatment.

Table 3: Adverse events after multiple concomitant stenting in the fifty patients at thirty days after revascularization procedure

	Adverse Events				
Lesion Groups	Minor Stroke	Major Stroke	Death	Total	No. of Patients
Separate lesion group					
Bilateral carotid lesions	1			1	15
ICA lesion plus other supra-aortic lesions*					12
Subclavian artery plus VA ostium					1
Triple lesion					5
Ipsilateral lesion group					
Adjacent tandem	1	1		2	6
Remote tandem	1		1	2	11
Total	3	1	1	5	50

Note:—ICA indicates internal carotid artery.
* Other supra-aortic lesions include vertebral artery (VA) ostium ($n = 8$), intradural VA ($n = 2$), common carotid artery ($n = 1$) and subclavian artery ($n = 1$).

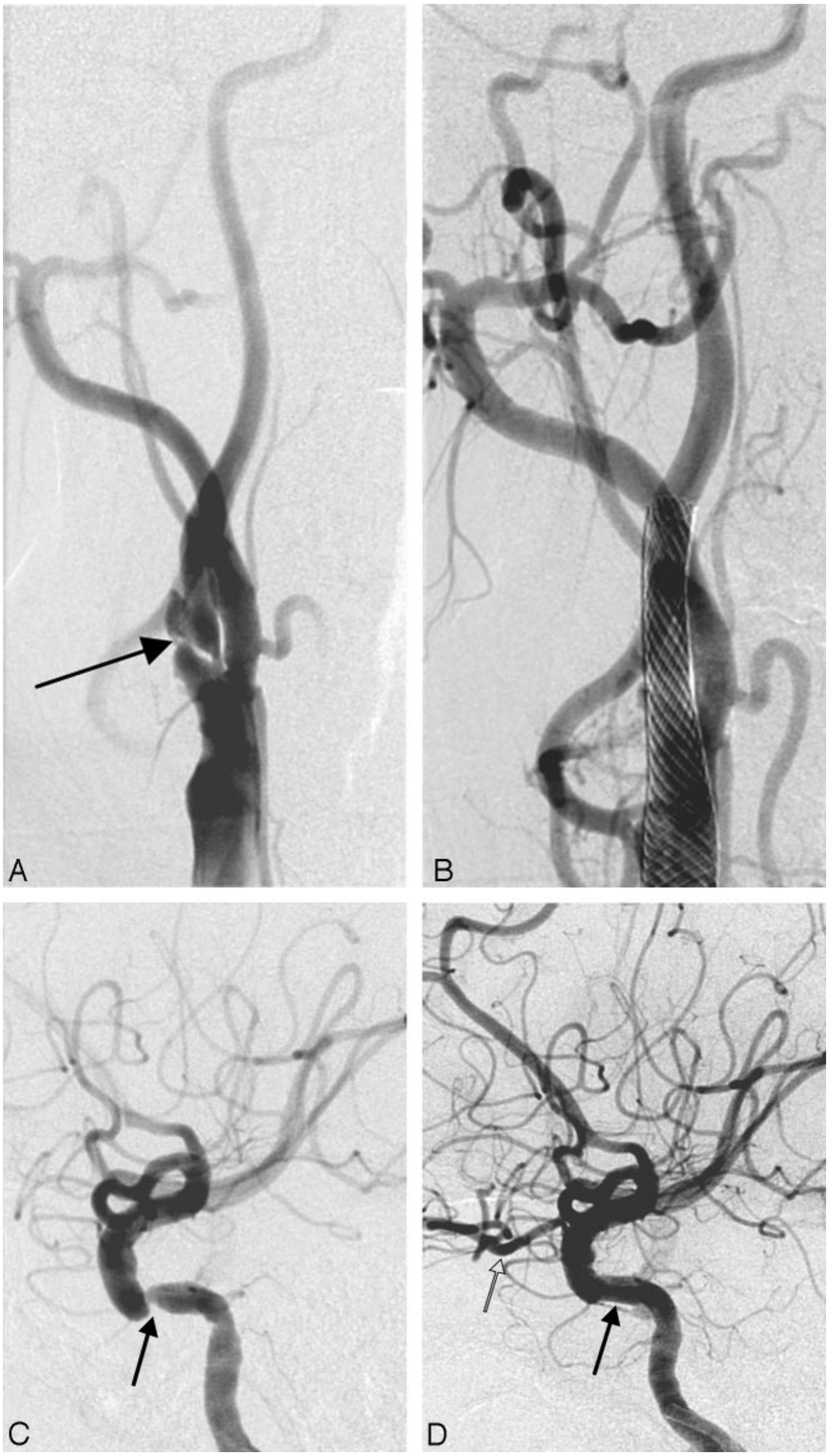

Fig 1. A 66-year-old man with hypertension and a history of smoking presented with chest pain and vertigo and was found to have multiple stenoses (ipsilateral remote tandem lesions) before coronary artery bypass surgery. *A–B*, The severe stenosis in the right carotid bulb with undermining ulceration (*arrow*), was revascularized first (*anteroposterior view*). *C–D*, Concomitant severe (more than 70%) stenosis (*arrow in C*) of the right cavernous segment was also revascularized during the same session. Note antegrade filling of the ophthalmic artery (*open arrow in D*). The patient underwent coronary artery bypass surgery and had no neurologic symptoms during the 6-month follow-up period.

Angio-Interventional Procedures

The patients in our study were premedicated daily with 100 mg of aspirin and either 75 mg of clopidogrel or 250 mg of ticlopidine for at least 4 days before the procedure. In the case of an emergency procedure, 300 mg of clopidogrel was given. All procedures were done with the patients under local anesthesia with sedatives. After a 6F to 8F sheath was introduced into the femoral artery, the baseline activated clotting time (ACT) was obtained. A bolus injection of 70 to 100 IU/kg of heparin was followed by 1000 IU/hr as necessary to achieve an ACT of more than 250 s.

We performed revascularization with angioplasty or stent placement, or both. A carefully measured undersized balloon was used for angioplasty. A small (1.5–5 mm) balloon was used in the intracranial arteries and in the VA. A large (4–6 mm) balloon was used for the carotid bulb. A self-expandable stent (6–10 mm diameter) was used in the proximal ICA, including the bulb, CCA, and subclavian stenosis. A 2.25- to 5-mm sized balloon-expandable stent was deployed in the distal ICA, middle cerebral artery (MCA), and vertebrobasilar artery. In a patient who presented with dizziness and a brief loss of consciousness as a result of severe stenosis in the BA, VA ostium, and carotid bulb, angioplasty was only performed for the basilar artery stenosis near the origin of both the anteroinferior cerebellar arteries, which resulted in less than 30% residual stenosis. Then, the VA ostial and carotid stenoses were subsequently stented.

An experienced radiographer, who was unaware of the study goal, analyzed the angiographic results using a quantitative vascular analysis (Pie Medical Imaging, Maastricht, the Netherlands) on the basis of the WASID methods.[13] The percentage of the diameter of the stenosis, minimal diameter of the lumen, and reference diameter before and after stent placement were all measured. The lesion of the carotid bulb was also measured with the North American Symptomatic Carotid Endarterectomy (NASCET) method[14] or with a Doppler sonogram of at least more than 230 cm/s peak systolic velocity.[15]

Definitions

We defined procedural success as a final luminal narrowing of less than 30% of the normal luminal diameter. We defined a tandem lesion as 2 isolated stenoses in 1 or more arteries in the same arterial territory, which could not be covered by a stent or treated by a stent placement procedure. Adjacent or remote tandem lesions were classified according to the distance between the 2 stenotic lesions. We defined an adjacent tandem lesion as 2 stenotic lesions in the same arterial segment. For example, 2 separate stenotic lesions in the ipsilateral M1 were regarded as an adjacent tandem lesion. We defined a remote tandem lesion as 2 stenotic lesions in different arterial segments of the same artery. Therefore, the presence of ostial stenosis of the VA associated with ipsilat-

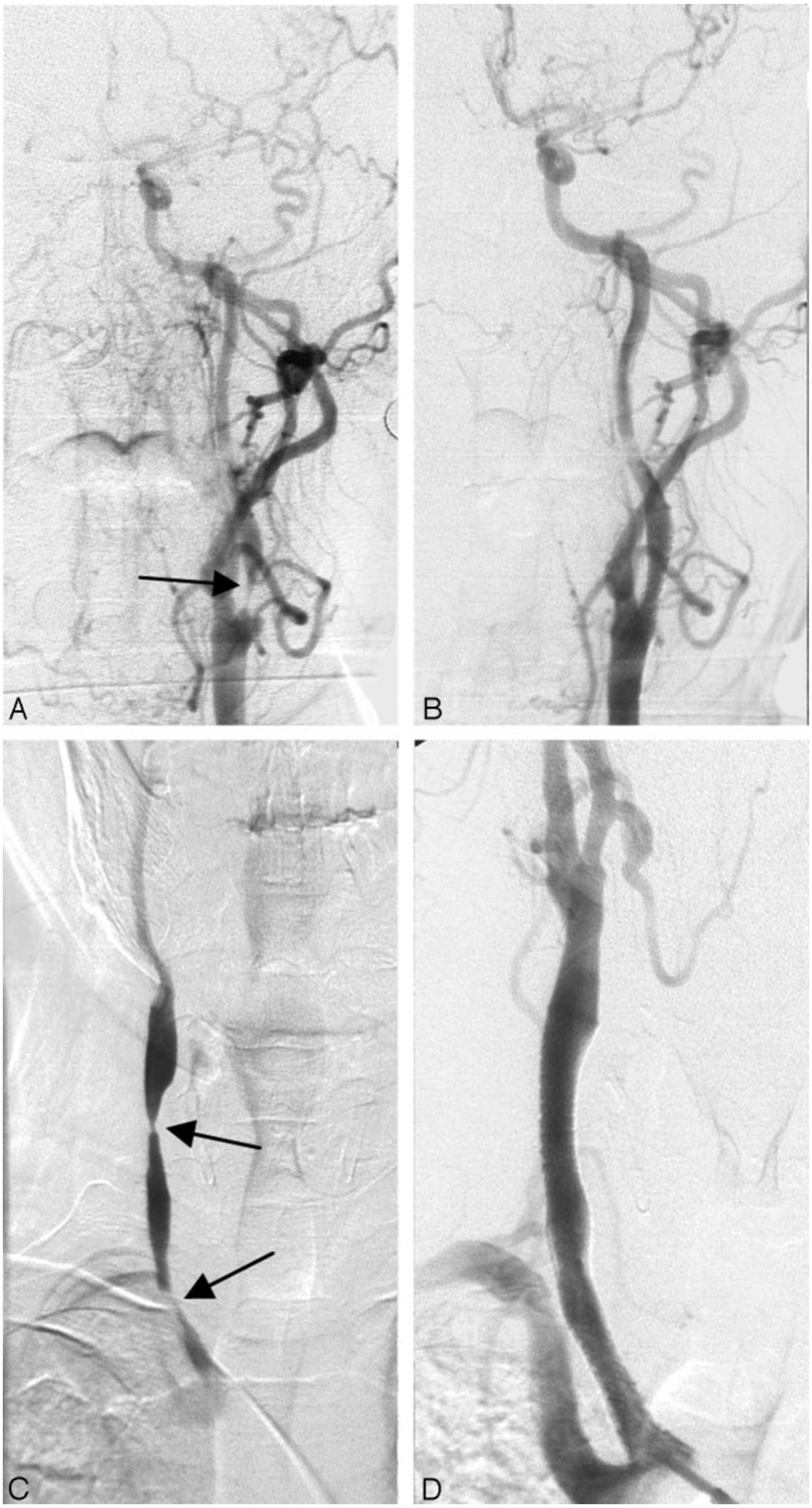

Fig 2. A 50-year-old man presented with vertigo, ataxia, and right arm weakness. An angiogram of the left CCA revealed a symptomatic severe stenosis of the left carotid bulb (*arrow*) (*A*) and patency after stent placement (*B*). There were multiple severe stenoses (*arrows*) of the right CCA (*adjacent tandem lesions*) (*C*). Good patency was obtained after concomitant stent placement (*D*). He underwent additional angioplasty at the right CCA at 18 months because of asymptomatic severe restenosis (not shown) and remains asymptomatic during a 32-month follow-up period.

eral intradural vertebral arterial stenosis would be classified as an ipsilateral remote tandem lesion. We defined a separate lesion as each stenotic lesion in the other's vascular territory. The presence of M1 stenosis as well as intradural VA stenosis would be classified as a separate lesion.

We defined patients who were stable as those who had the symptom pattern of resolved, improving, or stationary symptoms and patients who were unstable as those who had the symptom pattern of progressive or fluctuating neurologic symptoms with a change of more than 4 on the NIHSS corresponding to the symptomatic stenosis.

AEs were defined as a minor stroke, major stroke, or death. A minor stroke was defined as a new, nondisabling neurologic deficit or as an increase in 3 on the NIHSS, but one that resolved completely within 30 days of its occurrence. A major stroke was defined as a new neurologic deficit that persisted longer than 30 days and increased by 4 on the NIHSS.

Statistical Analysis

We performed a Fischer exact test to determine whether the incidence of an early complication within 2 days after stent placement was significantly different in the separate versus ipsilateral lesion groups and unstable versus stable patient groups.

Results

The mean degree of stenosis in our study was 75.8 ± 9.2%, and the mean length of the lesions was 12.0 ± 7.3 mm. Postprocedural residual stenosis was 9.8 ± 6.9%. Angiographic success (ie, less than 30% residual stenosis) was achieved in all patients. Forty-five patients did not have any further symptoms or recurrence of symptoms after the procedure as seen on the 30-day follow-up.

There were 5 periprocedural complications within 30 days after the procedure (Table 3, 4). Four complications (4/5) occurred 2 days after the procedure (Fig. 3) and the others (1/5), more than 10 days after the procedure. Three of the 5 patients who experienced AEs recovered completely. The Fischer exact test revealed that the early complication rate within 2 days after the stent placement procedure in the ipsilateral group (4/17) was significantly greater than the complication rate in the separate group (0/28) ($P = .016$). A major stroke and a death (major events) occured in 2 (4%) patients. Both of them had presented with progressively deteriorating symptoms. The risk of major events was higher in the unstable patient group (2/7) than in the stable patient group (0/38) ($P = .029$).

We performed a subgroup analysis of the ipsilateral lesion group with intracranial and extracranial lesions (remote tan-

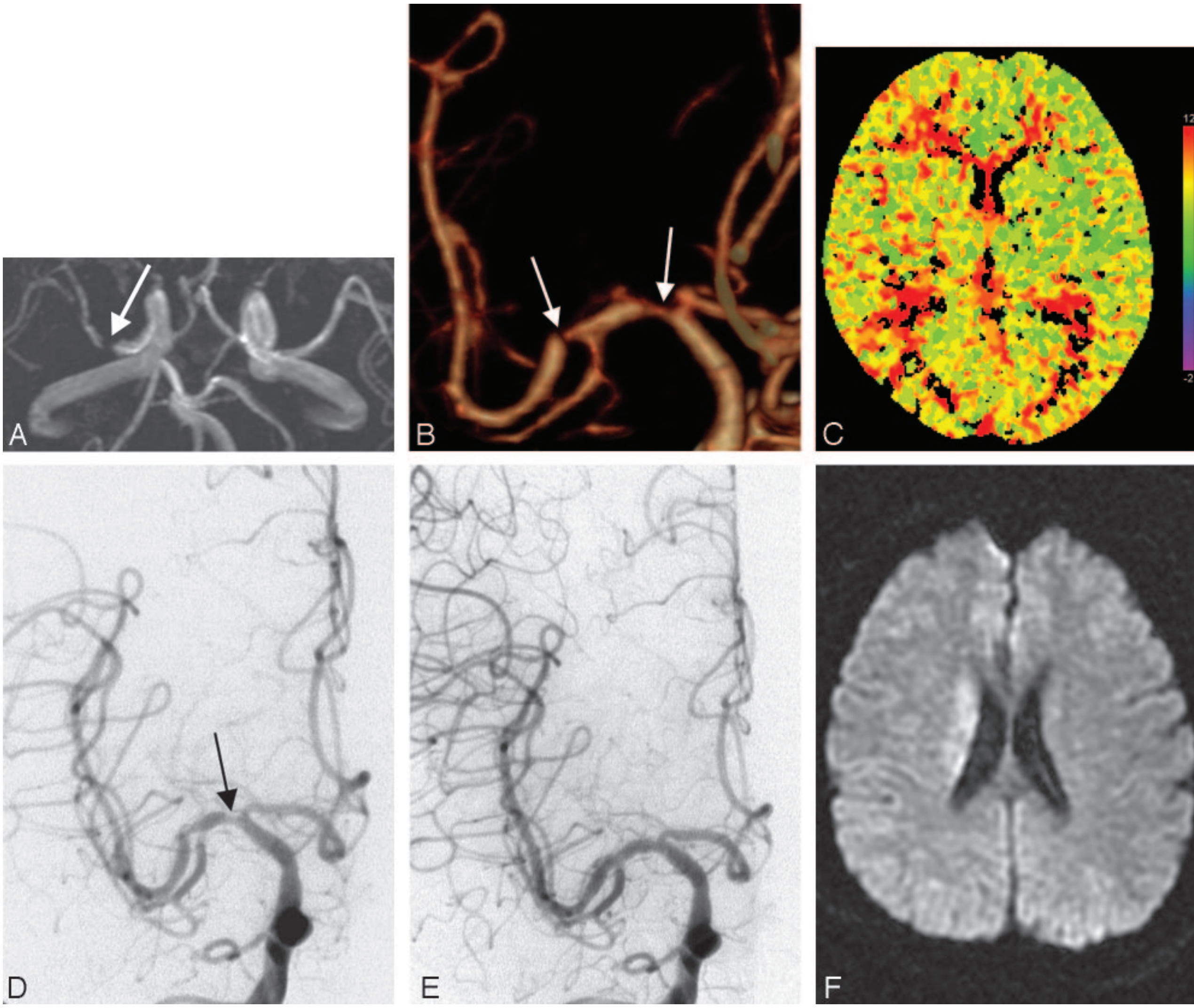

Fig 3. A 45-year-old male presented after multiple TIAs. Adjacent tandem lesions of the right MCA, are revealed by the arrows in *A* and *B*. *A*, The initial MRA showed a severe stenosis of right M1 (*arrow in A*) and failed to demonstrate an adjacent distal tandem lesion because of the decreased signal intensities distal to the first stenotic lesion. *B*, The oblique CT angiogram shows both severe tandem lesions (*arrows*) with more than 70% stenosis. *C*, There was an increased time-to-peak delay on CT perfusion image in the right MCA territory. *D*, The M1 lesion did not seem to be severe (*arrow*) on the anteroposterior view of cerebral angiogram due to the marked eccentricity of the M1 lesions. *E*, Final angiogram after concomitant stenting revealed good patency of the right M1 and improved angiographic flow into the right MCA territory. *F*, Diffusion-weighted MR imaging performed 2 days later, revealed acute ischemic change in the right caudate nucleus. The newly developed mild extremity weakness (minor stroke) eventually disappeared completely. There was no evidence of restenosis on TCD at 7 months and no symptomatic recurrence during the 17-month follow-up.

dem, $n = 11$) and the bilateral carotid bulb lesion group ($n = 15$). Although there were 2 (1 death, 1 minor stroke) events in the ipsilateral group and 1 (minor stroke) event in the bilateral carotid bulb lesion group, the event rate had no statistical significance according to the Fisher exact test ($P = .556$).

A death not related to the stent placement was noted in a 68-year-old symptomatic male patient with bilateral carotid bulb stenoses at 3 months. He had hypertension, previous stroke, a history of smoking, renal failure, and Parkinson syndrome and had no additional event at 3 months. The death was related to a cardiopulmonary complication as a result of the renal failure.

There were 4 (8%) restenoses of 48 lesions in 3 of 28 patients during a mean of 12 months (range, 6–44 months). The restenotic lesions included 3 carotid bulbs and a CCA. Two patients, including a patient with symptomatic restenosis (cognitive dysfunction), were treated with angioplasty. Two other patients, who were asymptomatic, were not retreated.

Discussion

Our study revealed that multiple concomitant revascularizations were feasible in supra-aortic arteries, including intracranial vessels. To the best of our knowledge, these are the first data of multiple concomitant revascularizations in cranial vessels. There were 2 lesion groups in our study that required multiple concomitant revascularizations, ie, multifocal stenoses in different vascular territories (separate lesion group) and tandem lesions (remote or adjacent) in the ipsilateral vascular territories (ipsilateral lesion group). Each lesion group may require different strategies of revascularization. If the multiple lesions are in the same vascular territories, it would be mandatory to open the proximal stenosis to proceed to the distal lesion because the concomitant stent placement might im-

Table 4: Summary of periprocedural events

Age/Sex	Presenting Symptom	Initial NIHSS	Type of Lesion	Adverse Event	Time Interval after Procedure	Imaging Finding	Possible Cause of Event	F/U Period (months)	Final Status (mRS)
60/M	Progressively deteriorating	13	Ipsilateral remote tandems (BA + vertebral ostium)	Death	4 hours	ICH + SAH on CT	Hyperperfusion, bleeding tendency or basilar arterial injury	–	6
45/M	TIA	0	Ipsilateral adjacent tandems (M1 segment)	Minor stroke	1 day	Ischemia of basal ganglia on MR Imaging	Partial stent thrombosis	17	0
67/M	TIA	1	Bilateral ICA bulb lesions	Minor stroke	11 days	Small ICH on CT	Delayed hyperperfusion	15	0
69/M	Fluctuating after repeated strokes	10	Ipsilateral adjacent tandems (Intradural VA + VBJ)	Major stroke	1 day	Pontine ischemic change	Perforator ischemia	13	5
68/M	TIA	2	Ipsilateral remote tandems (cavernous ICA + carotid bulb)	Minor stroke	2 days	Cortical HSI	Thromboembolic events	6	0

Note:—ICA indicates internal carotid artery; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; TIA, transient ischemic attack; HSI, high signal intensity; BP, blood pressure; mRS, modified Rankin Scale; VBJ, vertebrobasilar junction; VA, vertebral artery; BA, basilar artery.

prove the distal runoff and thereby potentially reduce thromboembolic complications after stent placement.

In cases of multifocal stenoses in different vascular territories, it is optional to perform revascularization in a stepwise fashion or during the same session. We suggest that revascularization of multiple significant stenoses during the same session is both feasible and cost-effective as well as reducing the procedural burden to the patient unless further risk is anticipated.[16] We assume that when only a target vessel is opened, improved flow into the target vascular territory as well as into the collaterals to the other compromised vascular territory may aggravate the hyperperfusion syndrome or may accelerate further occlusion of the other stenosis.[17] However, further study, such as a randomized controlled trial, may be required to verify the effect of multiple concomitant revascularizations and to compare the results of a stepwise approach as opposed to simultaneous treatment.

There were 5 (10%) complications in the 105 stent placement procedures of our 50 patients. The outcomes of single angioplasty and/or stent placement procedures revealed that the periprocedural stroke and death rate was 4.8% in 84 procedures (62 angioplasty + 22 stent placements)[18] and 5.8% in 120 procedures (104 angioplasty +16 stent placements).[19] Although the SSYLVIA trial (Stent placement of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries) included anterior intracranial and extracranial VAs, the complication rate of single-lesion stent placement for treatment of vertebral or intracranial artery stenosis in that study revealed 6.6% strokes in the first 30 days after the procedure.[20] Although the event rate in our study seems to be higher than that in other studies, the results of our study are comparable considering that our study included patients who only underwent multiple concomitant stent placement procedures and also included patients with unstable symptoms who were generally not treated for 4 to 6 weeks after the acute event.[18-20]

Three of our 5 patients who developed complications recovered completely. Both a death and a major stroke developed in the patients with an ipsilateral tandem lesion and a progressively deteriorating clinical status (unstable symptom pattern). To reach the intracranial target lesion (ie, basilar artery), a precedent procedure in proximal lesion (VA ostium) might have caused an additional risk, especially in a patient with unstable symptoms (more than 4 on the NIHSS). Therefore, our study showed that the periprocedural event rate in the ipsilateral lesion group was significantly higher than in the separate lesion group. In addition, major events including major stroke and death were more common in the unstable than in the stable patient group. Therefore, we suggest that multiple concomitant revascularizations be more carefully done in the ipsilateral lesion group, especially in patients with unstable symptoms.

In our study, the most important factor in deciding the order for multiple stent insertions was the exact correlation of the presenting symptoms with the stenosis. All patients with severe bilateral carotid bulb stenoses first underwent revascularization in the artery corresponding to the ischemic hemisphere. In the cases of patients with both adjacent and remote tandem lesions, exact symptomatic lesion localization was an important factor that we carefully analyzed.

Conclusion

In our study, concomitant multiple revascularization of the supra-aortic arteries during a single procedure was feasible. The high procedural success rate and an acceptable periprocedural complication rate usually indicated a favorable short-term outcome. The clinical symptom patterns, lesion localization, and hemodynamic evaluation in potential patients are important factors for deciding how to undertake multiple revascularizations. Early complications tended to be more common in the ipsilateral lesion group. Therefore, multiple concomitant revascularizations should be done more carefully in patients with ipsilateral lesions, especially in patients with unstable symptoms.

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