

# Single-stage endovascular treatment in patients with severe extracranial large vessel stenosis and concomitant ipsilateral unruptured intracranial aneurysm

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## PURPOSE

We aimed to evaluate the safety and effectiveness of single-stage endovascular treatment in patients with severe extracranial large vessel stenosis and concomitant ipsilateral unruptured intracranial aneurysm.

## METHODS

Hospital database was screened for patients who underwent single-stage endovascular treatment between February 2008 and June 2013 and seven patients were identified. The procedures included unilateral carotid artery stenting (CAS) (n=4), bilateral CAS (n=2), and proximal left subclavian artery stenting (n=1) along with ipsilateral intracranial aneurysm treatment (n=7). The mean internal carotid artery stenosis was 81.6% (range, 70%–95%), and the subclavian artery stenosis was 90%. All aneurysms were unruptured. The mean aneurysm diameter was 7.7 mm (range, 5–13 mm). The aneurysms were ipsilateral to the internal carotid artery stenosis (internal carotid artery aneurysm) in five patients, and in the anterior communicating artery in one patient. The patient with subclavian artery stenosis had a fenestration aneurysm in the proximal basilar artery. Stenting of the extracranial large vessel stenosis was performed before aneurysm treatment in all patients. In two patients who underwent bilateral CAS, the contralateral carotid artery stenosis, which had no aneurysm distally, was treated initially.

## RESULTS

There were no procedure-related complications or technical failure. The mean clinical follow-up period was 18 months (range, 9–34 months). One patient who underwent unilateral CAS experienced contralateral transient ischemic attack during the clinical follow-up. There was no restenosis on six-month follow-up angiograms, and all aneurysms were adequately occluded.

## CONCLUSION

A single-stage procedure appears to be feasible for treatment of patients with severe extracranial large vessel stenosis and concomitant ipsilateral intracranial aneurysm.

The concomitance of severe extracranial large vessel stenosis and unruptured ipsilateral distal intracranial aneurysm is often detected incidentally and their management is not clear (1). Although there are many studies in the literature that report different treatment approaches, there is no definite consensus on the management of the concomitant lesions (2–14). Various treatment options have been suggested, such as initial treatment of the aneurysm before revascularization of the stenosis, treating both lesions in the same surgical session and correcting the stenosis without treating the aneurysm (1, 5, 6, 9–11, 14–16). Few studies have reported single-stage endovascular treatment of both lesions as an effective method (17–19). On the other hand, the treatment of each lesion by this technique may lead to procedure-related undesired events such as cerebral ischemia/stroke or aneurysm rupture.

In this study, we aimed to present the radiologic and clinical results of seven consecutive patients who underwent single-stage endovascular treatment of severe extracranial large vessel stenosis and concomitant unruptured ipsilateral intracranial aneurysm and discuss the safety and feasibility of this approach. In addition, distinct from the limited number of similar studies in the literature, we present our experience with bilateral carotid artery stenting (CAS) and proximal subclavian artery stenting during single-stage endovascular treatment.

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## Methods

### Patients

We retrospectively reviewed the data related to the patients who underwent single-stage endovascular treatment for extracranial severe large vessel stenosis and concomitant unruptured ipsilateral intracranial aneurysm from February 2008 to June 2013 at our center. In this period, 412 CAS procedures were performed in 370 patients; 73 patients underwent subclavian artery stenting; and 304 aneurysms were treated by an endovascular route in 288 patients. Seven intracranial aneurysms were treated by a single-stage endovascular method simultaneously with eight CAS procedures in six patients (bilateral stenting in two patients) and a left subclavian artery stenting in one patient. There were five male and two female patients. The mean age of the patients was 68.8 years (range, 53–84 years). Six patients with symptomatic internal carotid artery (ICA) stenosis were admitted with transient ischemic attack complaints such as hemiparesis and transient loss of consciousness, and one patient with left subclavian artery stenosis was admitted with upper limb claudication and vertebrobasilar insufficiency symptoms. The extent of stenosis was measured by angiography. Carotid artery stenosis was evaluated according to the North American Symptomatic Carotid Endarterectomy Trial criteria and the treatment indication was determined. The diameter of the normal

artery distal to the stenosis was considered as a reference in calculation of the left subclavian artery stenosis. Angiographic data was transmitted to a commercially available dedicated workstation (X-Leonardo with DynaCT; Siemens Medical Solutions) to measure the dimensions of the aneurysm. The mean carotid artery stenosis was 81.6% (range, 70%–95%), and the left subclavian artery stenosis was 90%. In all cases, the carotid artery stenosis was localized in the bulbous, and the left subclavian artery stenosis was localized in the proximal subclavian artery. All aneurysms were unruptured. The aneurysms were ipsilateral to the symptomatic carotid artery stenosis (ICA aneurysm) in five patients, and in the anterior communicating artery in one patient. The patient with left subclavian artery stenosis had a fenestration aneurysm in the proximal basilar artery. The mean aneurysm diameter was 7.7 mm (range, 5–13 mm). Characteristics of patients and lesions are summarized in the Table. Written informed consent was obtained from each patient before the procedure. The research was performed according to the World Medical Association Declaration of Helsinki.

### Endovascular procedure

All procedures were performed by a single neurointerventionalist under general anesthesia in a biplane, flat panel detector angiography unit (AXIOM Artis FD Biplane Angiosuite with DynaCT; Siemens Medical Solutions). The extracranial large vessel stenosis was stented before the aneurysm treatment in all patients. In two patients who underwent bilateral CAS, the contralat-

eral carotid artery stenosis that had no aneurysm distally was treated first.

Dual antiplatelet treatment with aspirin (Bayer) (100 mg/day) and clopidogrel (Plavix, Sanofi-Synthelabo Inc.) (75 mg/day) was given to each patient three days before the procedure. All patients were tested for clopidogrel resistance before the procedures. After introducing a 6F long vascular sheath (NeuronMax, Penumbra Inc.) into the right common femoral artery in all cases, intra-arterial heparin (Medac) (5000 IU) followed by hourly intravenous 1000 IU of heparin were administered to achieve an activated clotting time of 250–300 s. In CAS procedures, after positioning the 6F long vascular sheath in the common carotid artery (CCA), the stenosis was passed and a distal emboli protection device (Spider, EV3) was placed. Afterwards, predilatation with an undersized balloon (Viatrac 14 Plus, Abbott Vascular), stent deployment (Protégé, Covidien or Xact, Abbott Vascular) and postdilatation in patients with 30% residual stenosis were performed, respectively. Atropine (Sigma-Aldrich) (0.5–1.0 mg) was given to all patients intravenously before the predilatation. The emboli protection device was removed after CAS and the stented segment was passed with a 6F Fargo Max guiding catheter (Balt), which was advanced through the vascular sheath, and the aneurysm was accessed. Embolization was performed in three patients with Guglielmi detachable coils (GDC 18, Boston Scientific), and flow-diverter (FD) stent treatment was performed in three patients with Silk stents (Balt). In the patient with proximal left subclavian artery stenosis and

### Main points

- The management of patients with severe extracranial large vessel stenosis and concomitant ipsilateral intracranial aneurysm is unclear.
- Several treatment options such as correcting the stenosis without treating the aneurysm, embolization of the aneurysm before stenosis treatment, treating both lesions in single surgical session have been suggested in these cases.
- In this study, the concomitant ipsilateral intracranial aneurysms were successfully treated at a single stage endovascular procedure in four patients with unilateral carotid artery stenting (CAS), in two patients with bilateral CAS and in one patient with subclavian artery stenting.
- Stenting was performed first and then the aneurysm was treated in all patients.
- The single-stage endovascular treatment approach is an effective and safe method in the treatment of severe extracranial large vessel stenosis and concomitant ipsilateral intracranial aneurysm.

Table. Clinical and angiographic characteristics of seven patients

| Patient no. | Sex | Age (y) | Clinical presentation | Stenosis location      | Stenosis (%) | Aneurysm location           | Aneurysm size (mm) |
|-------------|-----|---------|-----------------------|------------------------|--------------|-----------------------------|--------------------|
| 1           | M   | 58      | TIA                   | Right ICA              | 80           | ACOM                        | 6                  |
| 2           | M   | 75      | TIA                   | Right ICA              | 95           | Right ICA-ACHA              | 13                 |
| 3           | M   | 73      | TIA                   | Right ICA              | 76           | Right ICA-PCOM              | 9.5                |
| 4           | F   | 64      | VBI                   | Left subclavian artery | 90           | Proximal basilar artery     | 7                  |
| 5           | M   | 53      | TIA                   | Left ICA               | 70           | Left ICA-paraclinoid        | 6                  |
|             |     |         |                       | Right ICA              | 95           |                             |                    |
| 6           | F   | 84      | TIA                   | Right ICA              | 70           | Right ICA-PCOM              | 5                  |
|             |     |         |                       | Left ICA               | 80           |                             |                    |
| 7           | M   | 75      | TIA                   | Right ICA              | 79           | Right ICA-ophthalmic artery | 8                  |

M, male; TIA, transient ischemic attack; ICA, internal carotid artery; ACOM, anterior communicating artery; ACHA, anterior choroidal artery; PCOM, posterior communicating artery; F, female; VBI, vertebrobasilar insufficiency.

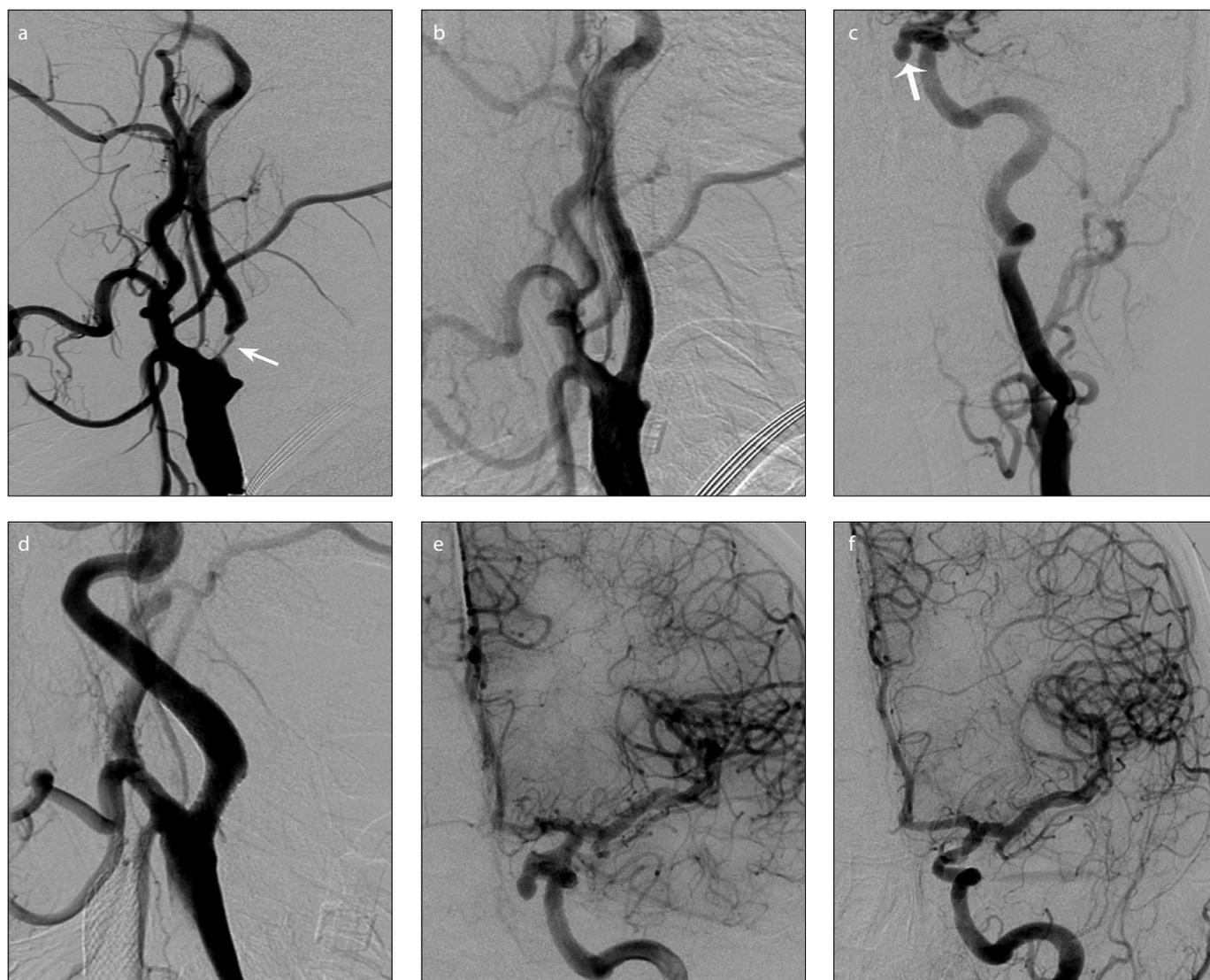
concomitant vertebrobasilar aneurysm, the 6F long vascular sheath (NeuronMax, Penumbra Inc.) was positioned proximal to the left subclavian artery, then a 0.035-inch hydrophilic guidewire (Glidewire, Terumo Medical Corp.) was passed through the stenosis and stenting was performed with a balloon-expandable stent (Genesis, Cordis Corporation). After achieving sufficient circulation in the left vertebral artery through subclavian artery stenting, the right vertebral artery was catheterized with a 6F guiding catheter (Envoy, Cordis Neurovascular). The aneurysm was then accessed by the microguidewire (Terumo 0.016-inch, double angled; Terumo Medical Corp.)

and microcatheter (Excelsior 18, Boston Scientific), which were advanced through the guiding catheter; the aneurysm and right vertebral artery were occluded with Guglielmi detachable coils (GDC 18, Boston Scientific).

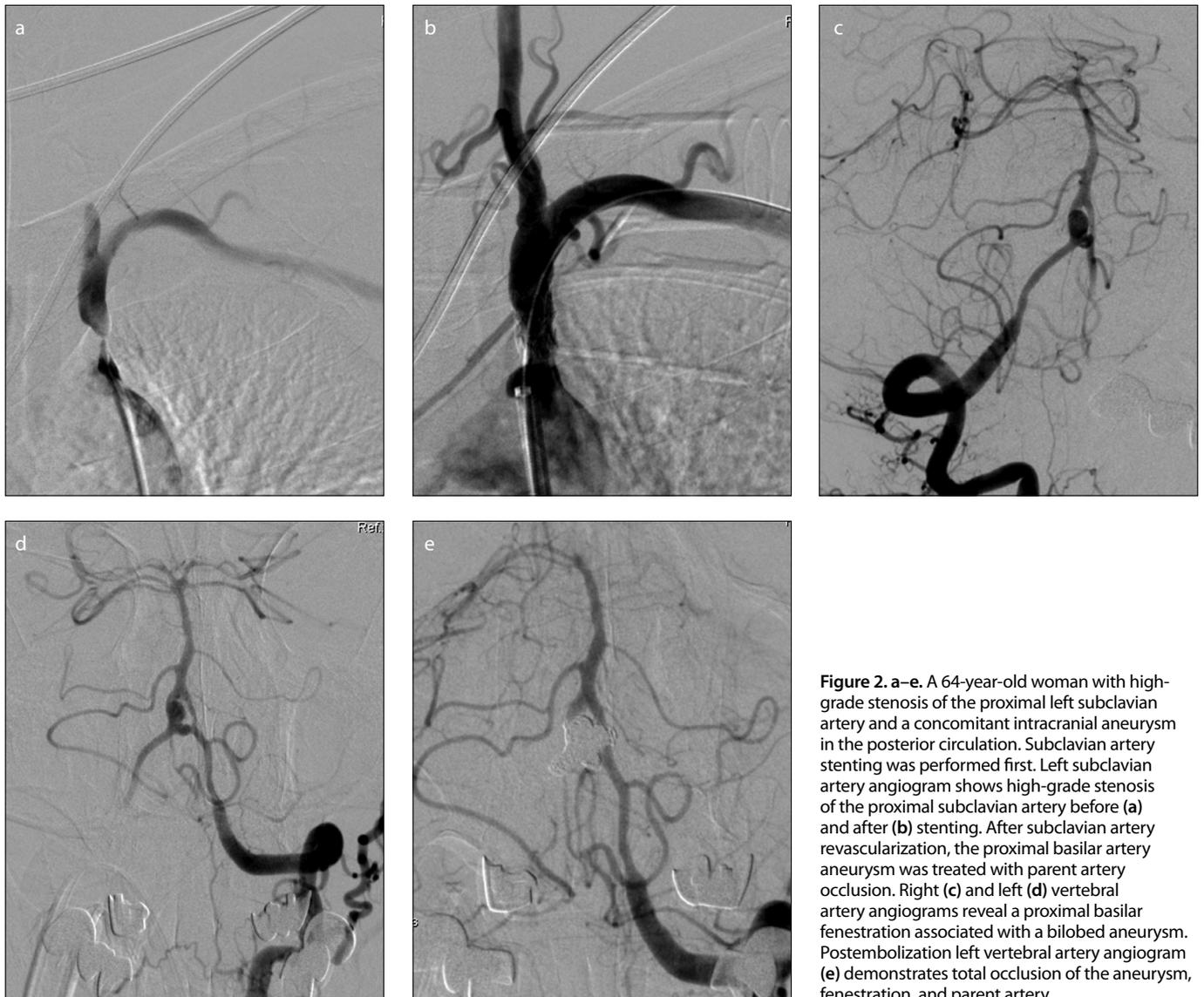
Technical success was considered in cases of less than 30% residual stenosis after stent placement, total (100%) and near total occlusion (90%–100%) of the aneurysm after the coil embolization, and reduced and delayed filling of the aneurysm sac with significant stagnation following the FD stenting.

All patients were admitted to the intensive care unit for 24 hours after the procedure. Blood pressure was closely moni-

tored during and after the procedure and systolic blood pressure was maintained at 110 to 120 mmHg. Bradycardia and hypotension despite atropine premedication during the procedure were treated with a second atropine dose (0.5–1.0 mg) and additional fluid administration (300–400 mL of 0.9% saline). Vasopressors or inotropes were not used because additional atropine and fluid administration were sufficient. All patients continued their regular antihypertensive medications through the morning of the procedure. Short-acting  $\beta$ -blockers were readily available throughout the procedure to intervene when systolic blood pressure increased. None of the patients



**Figure 1.** a–f. A 53-year-old man with bilateral severe carotid stenosis and a concomitant intracranial aneurysm. Contralateral carotid revascularization was performed first. Right common carotid artery (CCA) angiogram shows high-grade stenosis of the right internal carotid artery (ICA) bulb (arrow) before stenting (a). After stent placement (b), the right CCA angiogram confirms satisfactory revascularization. After right ICA repair, left carotid artery stenting and ipsilateral intracranial aneurysm treatment with flow-diverter stent were performed, respectively. Left CCA angiogram reveals severe stenosis of the left ICA bulb and an ipsilateral unruptured intracranial aneurysm (arrow) before treatment (c). Left CCA and ICA angiograms immediately after single-stage procedure (d, e) demonstrate successful treatment. Left CCA angiogram at six-month follow-up shows complete exclusion of the aneurysm from the circulation (f).



**Figure 2. a–e.** A 64-year-old woman with high-grade stenosis of the proximal left subclavian artery and a concomitant intracranial aneurysm in the posterior circulation. Subclavian artery stenting was performed first. Left subclavian artery angiogram shows high-grade stenosis of the proximal subclavian artery before (a) and after (b) stenting. After subclavian artery revascularization, the proximal basilar artery aneurysm was treated with parent artery occlusion. Right (c) and left (d) vertebral artery angiograms reveal a proximal basilar artery fenestration associated with a bilobed aneurysm. Postembolization left vertebral artery angiogram (e) demonstrates total occlusion of the aneurysm, fenestration, and parent artery.

required hypertension management. Low molecular weight heparin was administered to all patients for 48 hours after the procedure, and clopidogrel (75 mg/day) for three months and aspirin (100 mg/day) for lifetime were prescribed. Patients were called on day 10 and at the first month following discharge for clinical follow-up, and at the first and sixth months for angiographic follow-up.

## Results

Single-stage endovascular treatment was successfully performed in seven patients. No periprocedural or post-procedural complications were observed. The mean procedure time was 104.1 minutes (range, 70–136 minutes). The procedure time exceeded two hours (136 minutes) in one

patient who had left subclavian artery stenosis and concomitant vertebrobasilar aneurysm. The procedure time was less than two hours for others. The mean stenting time was 38.1 minutes (range, 25–64 minutes), and the mean aneurysm treatment time was 66 minutes (range, 45–111 minutes). Figs. 1–3 illustrate the single-stage endovascular treatment in three patients.

The mean clinical follow-up period was 18 months (range, 9–34 months). Motor weakness developed in the left arm of a patient 22 months after the procedure. Diffusion-weighted magnetic resonance imaging of this patient revealed small multifocal embolic infarcts in the contralateral cerebral hemisphere. All patients underwent angiographic follow-up at the first and sixth months. Restenosis was not observed in any of the patients whose extracranial large

vessel stenosis was stented. All aneurysms were adequately occluded. Six patients had total and one patient had near total occlusion.

## Discussion

This study confirmed that single-stage endovascular treatment of severe extracranial large vessel stenosis and concomitant unruptured ipsilateral intracranial aneurysm is feasible.

Detecting the coexistence of severe symptomatic extracranial large vessel stenosis and concomitant asymptomatic ipsilateral intracranial aneurysm leads to a quandary regarding the management (17). Much of the current data in the literature has been derived from case reports and case series suggesting that surgical carotid



**Figure 3. a–d.** A 75-year-old man with severe right internal carotid artery (ICA) stenosis and an ipsilateral intracranial aneurysm. Carotid stenosis was treated first. Right common carotid artery (CCA) angiogram (a), shows high-grade stenosis of the right ICA before stenting. After stenting (b), the right CCA angiogram reveals successful revascularization and an ipsilateral intracranial aneurysm (arrow). After carotid revascularization, the aneurysm was treated with a flow-diverter stent. Right ICA angiogram after flow-diverter stent deployment (c, d) demonstrates the reduced filling of the aneurysm sac with significant stagnation.

revascularization is safe for the treatment of patients with intracranial aneurysm. These studies argue that if the aneurysm is smaller than 5 mm, endarterectomy should be performed alone and the aneurysm should be followed whereas aneurysms greater than 10 mm should be treated. However, there is a lack of consensus for the treatment of aneurysms ranging from 5 mm to 10 mm (3–6, 9, 10, 16). Furthermore, a few studies reported that untreated aneurysms in patients who under-

went endarterectomy resulted in rupture (20–22). Moreover, theoretically, increased cerebral blood flow (CBF) following carotid revascularization, and long-term anticoagulant and antiplatelet use after the treatment may lead to rupture of the aneurysm (19). Therefore, securing the aneurysm distal to the stenosis should be taken into consideration in patients for whom carotid revascularization is planned (18).

It has been recently reported that both stenosis and aneurysm can be treated safely

by a single-stage endovascular approach in cases with severe carotid stenosis and a concomitant ipsilateral intracranial aneurysm (17–19). Initial CAS is suggested in single-stage endovascular treatment. Initial stenting facilitates subsequent reliable access to the intracranial aneurysm. Moreover, in this way, the risk of thromboembolic complications related to guiding catheter manipulation while passing through the stenosis decreases (17). Park et al. (17) reported that initial placement of the stent was useful for decreasing the risk of embolic complications in their 17 patients treated with a single-stage endovascular method. In another study, Badruddin et al. (18) performed CAS first, followed by treatment of the aneurysm in a single session successfully. Similarly, in our study the carotid stenosis was treated first, followed by the aneurysm treatment in all of our patients. None of the patients developed procedure-related complications. Therefore, we suggest that CAS should be performed first in single-stage endovascular treatment.

Perfusion-related undesired events are among the major problems in single-stage endovascular treatment. Decreased CBF due to severe carotid stenosis was reported to have a partially protective effect on the ipsilateral intracranial aneurysm distal to the stenosis. Correction of the carotid stenosis results in a sudden increase in CBF, which theoretically may lead to rupture of the aneurysm (1, 12, 23). Additionally, increased CBF after CAS may cause hyperperfusion syndrome in single-stage treatment. Close monitoring of blood pressure during and after the procedure may prevent the possible risks related to a sudden increase in CBF (24). Another possible issue that may negatively affect cerebral perfusion is hemodynamic depression. The prevalence of hemodynamic depression in carotid stenting is approximately 40%, and it presents with bradycardia and hypotension, secondary to carotid sinus reflex activation during balloon dilatation and stenting of the stenosis (25, 26). Additional hypotension due to hemodynamic depression in the patient who is under general anesthesia during single-stage treatment may decrease the perfusion pressure and lead to cerebral ischemia/stroke. Therefore, prevention of risks that could adversely affect cerebral hemodynamics during the procedure is important. Neither the previous studies nor our study experienced any perfusion-related undesired events. Atropine was rou-

tinely administered to all patients before dilatation in our study and the dilatation was performed with an undersized balloon. Periprocedural and post-procedural blood pressure was closely monitored and maintained within acceptable ranges, and volume expanders were infused when needed. Paying attention to these measures can prevent hemodynamic depression and risks related to increased perfusion in single-stage treatment.

Another important issue is the development of acute in-stent thrombosis. Low response or insufficient antiplatelet activity due to resistance may be responsible for this. Displacement of the guiding catheter due to the maneuvers of the microcatheter during treatment of the aneurysm and its inappropriate positioning in the stented segment may also cause in-stent thrombosis. Park et al. (17) suggested that these two factors were responsible for the thrombogenicity in one of their patients who developed in-stent thrombosis. We did not observe in-stent thrombosis in any of our patients. Clopidogrel resistance of all patients was tested before the procedure. Furthermore, no challenges were experienced in microcatheter and microguide-wire maneuvers during the procedure. We think that testing for clopidogrel resistance before the procedure and checking the position of the guiding catheter during the procedure can prevent the development of in-stent thrombosis.

In this case series, bilateral CAS and simultaneous aneurysm treatment was performed in two patients. To the best of our knowledge, bilateral CAS and concomitant aneurysm treatment in the same session has not been reported previously in the literature. Contralateral carotid stenosis without any distal aneurysm was treated first in these two patients. Severe contralateral carotid stenosis may lead to ischemic stroke by reducing the CBF along with general anesthesia during the procedure. This risk can be prevented by inclusion of contralateral carotid revascularization and performing this procedure first. In addition, the need for future treatment and associated costs as well as patient discomfort can be avoided by a single-stage procedure. On the other hand, hyperperfusion syndrome should be considered when contralateral CAS is included in a single stage procedure. As discussed before, hyperperfusion can be prevented by rigorous monitoring of blood pressure.

Endovascular treatment by angioplasty and stenting is an effective and safe treatment option for proximal subclavian artery stenosis (27–29). Moreover, as in carotid revascularization, a sudden increase in the intracranial blood flow following the subclavian stenting may create a risk of rupture for the concomitant posterior circulation aneurysm. In our literature review, we could find no cases of intracranial aneurysm rupture following subclavian stenting, but intracranial hemorrhage due to hyperperfusion was reported in two patients (30, 31). Therefore, it is necessary to secure the ipsilateral intracranial aneurysm in patients for whom subclavian artery stenting is planned. In this study, single-stage endovascular treatment was performed successfully in a patient with severe proximal left subclavian artery stenosis that caused vertebrobasilar insufficiency and a concomitant vertebrobasilar fenestration aneurysm. In this patient, first the subclavian artery stenosis was stented, followed by embolization of the aneurysm with parent artery occlusion. In this case, in addition to the stenosis treatment, the single-stage approach was effective in safe embolization of the aneurysm with parent artery occlusion by providing sufficient collateral circulation. Our experience may contribute to the literature as it demonstrates the effectiveness of single-stage endovascular treatment in the posterior circulation as well.

Two limitations of this study are its retrospective design and the small number of cases. Furthermore, lack of other treatment groups for comparison (staged endovascular treatment, surgical treatment, etc.) precluded us from obtaining more powerful results. The efficacy of single-stage endovascular treatment can be further clarified by randomized controlled studies with larger case series.

In conclusion, single-stage endovascular treatment approach is an effective and safe method in treatment of severe extracranial large vessel stenosis and concomitant unruptured ipsilateral intracranial aneurysm. Elimination of the need for additional treatment may be helpful for patient comfort and for decreasing possible complications that could arise due to staged procedures. In this approach, initial treatment of the stenosis can increase the technical success. Furthermore, single-stage endovascular treatment can also be performed safely for patients who have subclavian artery stenosis and severe bilateral carotid stenosis.

## Conflict of interest disclosure

The authors declared no conflicts of interest.

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