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Original Article

Mid-/Long-Term Outcome of Neuroendovascular Treatment for Chronic Carotid Artery Total Occlusion

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Objective: The natural course of chronic carotid artery total occlusion (CTO) is poor. Previous reports suggested that carotid artery stenting (CAS) improves the clinical outcome of CTO. However, its long-term efficacy has not been established. This study assessed the mid- and long-term clinical outcome of CAS for CTO.

Methods: We evaluated the clinical outcome of 15 patients who underwent CAS for CTO between September 2010 and October 2019.

Results: The technical success rate of recanalization was 93.3% (14 of 15 patients). Eight patients were treated using self-expanding stents, and six were treated using self-expanding coronary stents. Symptomatic procedure-related complications developed in two patients (13.3%). During the follow-up period (mean 34.9 months), symptomatic ipsilateral stroke was not noted. One patient (7.1%) developed asymptomatic re-occlusion, but stent patency was preserved in 13 patients (92.9%).

Conclusion: CAS for CTO may be safe and feasible based on the mid- and long-term outcome.

Keywords ▶ chronic carotid artery total occlusion, carotid artery stenting, ischemic stroke, long and mid-term outcome

Introduction

Several previous studies reported that chronic carotid artery total occlusion (CTO) causes ipsilateral stroke in 6%–20% of cases regardless of the best medical treatment, suggesting the usefulness of revascularization in some patients.[1,2] As surgical treatments, extracranial–intracranial bypass (EC-IC bypass) and carotid endarterectomy (CEA) are performed. The Japanese EC-IC bypass trial[3] revealed that the preventive effects of EC-IC bypass on ipsilateral stroke were more marked than those of medical treatment. However, the COSS trial[4] denied the usefulness of EC-IC bypass. Furthermore, another study reported the success rate of CEA for CTO to be 34%.[5]

Revascularization for chronic total occlusion of the coronary or iliac arteries using a stent leads to a high recanalization rate with a low incidence of complications, resulting in a favorable vascular patency rate and ischemic symptom prevention during long-term follow-up.[6,7] Recent studies, including one conducted by Terada et al.,[1] reported revascularization by percutaneous carotid artery stenting (CAS) for CTO, and suggested favorable treatment results from the viewpoint of stroke prevention.[1,2,8–10]. However, its long-term outcome remains to be clarified.

In this study, we report the mid-/long-term postoperative outcome of treatment in 15 patients in whom CAS for CTO was performed at our institution.

Materials and Methods

CAS was performed at our institution on 15 patients of 27 patients diagnosed with CTO between September 2010 and October 2019 (**Table 1**). Their ages ranged from 37 to 83 years, with a mean of 66.6 years. They consisted of 12 males and 3 females. Left lesions were present in six patients, internal carotid artery-localized

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Table 1 Baseline characteristics of 15 cases of chronic carotid artery total occlusion

Characteristics	Value(%)
Mean age (years) [range]	66.6 [37–83]
Male: sex	12 (80.0)
Left lesion	6 (40.0)
CCA occlusion	3 (20.0)
Medical history	
Hypertension	12 (80.0)
Dyslipidemia	9 (60.0)
Diabetes	6 (40.0)
History of smoking	9 (60.0)

CCA: common carotid artery

occlusion in 12, and common carotid artery occlusion in three patients. Patients with medical treatment-resistant cerebral infarction or transient ischemic attacks in whom neither CT nor MRI revealed extensive cerebral infarction involving the vascular territory were included. Single-photon emission CT was performed on 8 of the 15 patients. In these, cerebral blood flow on the affected side was reduced, but the acetazolamide tolerance test was not conducted; in this study, the cerebral circulatory reserve was not considered when determining the indication of surgery. Concerning medical history, 12 patients had a history of hypertension, 9 had a history of dyslipidemia, 6 had a history of diabetes mellitus, and 9 had a history of smoking. Patients in whom at least cavernous segment of the internal carotid artery was retrogradely visualized through a collateral pathway on cerebral angiography were included.

Dual-antiplatelet therapy (DAPT) with aspirin at 100 mg/day and clopidogrel at 75 mg/day was started at least 1 week before surgery. After the introduction of a Verify Now system (Accumetrics, San Diego, CA, USA), it was confirmed that each patient was not a hyporesponder to DAPT before surgery. On all patients, surgery was performed under general anesthesia. During surgery, intracerebral oxygen saturation monitoring was conducted using an INVOS non-invasive mixed blood oxygen saturation monitoring system (Covidien Japan, Tokyo, Japan), and heparin was administered in order for the activated coagulation time to be ≥300 seconds. A 9Fr Optimo balloon guiding catheter (Tokai Medical Products, Aichi, Japan) was guided into the common carotid artery proximal to the site of internal or common carotid artery occlusion through the femoral artery. Initially, a Tempo4 (Cordis, Miami Lakes, FL, USA) and 0.035-inch Radifocus guidewire (Terumo Corporation, Tokyo, Japan) imparted torque were carefully passed through the site of occlusion. During the operation, whether the guidewire (GW) had passed through the vascular lumen was confirmed using an ultrasonic probe for carotid ultrasonography. When the Optimo was advanced to the internal carotid artery following the GW and Tempo4, the balloon was dilated for proximal protection. When the GW reached the carotid canal, cone-beam CT (CBCT) was performed to confirm whether the GW was correctly placed in the carotid canal based on the positional relationship between the bone and GW. Subsequently, percutaneous transluminal angioplasty (PTA) of the internal carotid artery proximal to the carotid canal was performed using a balloon catheter, Gateway (Boston Scientific, Natick, MA, USA). In the area distal to the carotid canal, a microcatheter (MC) and microguidewire (MGW) were allowed to penetrate the site of occlusion. As an MGW, a 0.014-inch CHIKAI (Asahi Intecc, Tokyo, Japan) was used in many patients, but it was combined with devices for peripheral blood vessels differing in rigidity or shape, such as an Astato, Treasure (Asahi Intecc), and Runthrough (Terumo Corporation), in some patients. When an MC was considered to have penetrated the site of occlusion, aspiration was manually performed through the MC, and it was confirmed that the true lumen was secured by blood reflux. Subsequently, angiography through the MC was conducted to confirm an area distal to the site of occlusion. Subsequently, PTA using a Gateway was performed through the area distal to the site of occlusion. When vascular stenosis or dissection remained after PTA, stents were inserted overlapping with each other such that a proximal normal blood vessel was connected with a distal normal blood vessel. A bare metal stent for the coronary artery region, MULTI-LINK VISION (Abbott, Tokyo, Japan), was used for the intracranial internal carotid artery, and a Protégé (Medtronic, Santa Rossa, CA, USA), Precise (Cordis), and Carotid Wallstent (Boston Scientific) were used for the cervical carotid artery. A Carotid Wallstent was selected for relatively straight blood vessels, a Precise was selected for flexed lesions, and a Protégé was selected for patients with differences in the vascular diameter. Due to the off-label use of a MULTI-LINK VISION, informed consent was received before treatment, and its use was approved by the unapproved drug evaluation committee of our institution before insertion. Monitoring using an INVOS monitoring system was continued for 11 hours after surgery, and the systolic blood pressure was maintained at approximately 100–120 mmHg. The patency of

the carotid artery was confirmed using CTA or ultrasonography 6 months after surgery. It was evaluated using cerebral angiography 1 year after surgery. Thereafter, ultrasonography or CTA was performed at 6-month to 1-year intervals. As antiplatelet therapy, DAPT was continued for 1 year after surgery. Subsequently, the in-stent state was confirmed using ultrasonography, CTA or cerebral angiography. When stenosis was absent, DAPT was switched to monotherapy with a single antiplatelet drug.

Results

In 14 (93.3%) of the 15 patients, the procedure was technically successful. In nine patients in whom the cervical internal carotid artery was responsible for occlusion, a carotid artery stent alone was used. In five with lesions of the intracranial internal carotid artery, a coronary artery stent was combined with a carotid artery stent, leading to recanalization (**Table 2**). Additional stenting was required due to a long extent of occlusion in two patients (Cases 12 and 14) with common carotid artery occlusion and due to malposition of the proximal end of a stent to the common carotid artery in one patient (Case 9); therefore, ≥5 stents were used. In one patient (Case 6) in whom recanalization was not achieved, a GW reached a distal normal blood vessel beyond the site of occlusion, but carotid-cavernous fistula was detected and the procedure was finished during the course. After surgery, there was no new neurological disorder. In 2 (13.3%) of the 15 patients, perioperative complications were observed. In 1 (Case 14), occlusion of the central retinal artery due to procedure-associated distal thromboembolism was noted, and a visual field defect remained. In this patient, aortic arch branching variation was bovine-type and it was difficult to advance an Optimo from the femoral artery to the common carotid artery; an Axcelguide (Medikit, Tokyo, Japan) was used as a guiding catheter from the brachial artery, and proximal protection was impossible. In the other patient (Case 4), acute re-occlusion of the internal carotid artery and mild cerebral infarction were observed the day after surgery. Additional PTA and CAS led to the absence of neurological disorder. In the 15 patients, follow-up periods ranged from 5 to 71 months, with a mean of 34.9 months. During the follow-up period, there was no symptomatic ipsilateral stroke. In 1 (Case 4) of 14 patients in whom recanalization was achieved, asymptomatic re-occlusion was noted 41.8 months after surgery, but there was no re-occlusion during this period in any of the other 13 patients (92.9%).

Case Presentation

Case 15: An 83-year-old man. He had a history of hypertension, dyslipidemia, and diabetes mellitus. Furthermore, he had smoked. Mild motor paralysis of the right upper and lower limbs and dysarthria developed, and he was admitted under a diagnosis of diffuse left cerebral infarction and left cervical internal carotid artery occlusion. Cerebral angiography revealed occlusion of the left cervical internal carotid artery. The collateral pathway via the ophthalmic artery from the ipsilateral external carotid artery to cavernous segment of internal carotid artery was retrogradely and slowly enhanced (**Fig. 1A** and **1B**). Endovascular treatment was performed 27 days after onset. After guiding an MC to the site of occlusion, PTA was performed, and angiography demonstrated that stenosis of the intracranial internal carotid artery remained. Four MULTI-LINK VISIONs 3 × 15 mm, 3 × 23 mm, 3 × 28 mm, and 3.5 × 15 mm, and a Precise 6 × 30 mm were placed overlapping with each other (**Fig. 1C** and **1D**). After surgery, there were no new symptoms and the patient was discharged. CTA 4 months after surgery confirmed the favorable patency of the left internal carotid artery (**Fig. 1E**).

Discussion

As revascularization for CTO, no procedure has been established, excluding the indication of EC-IC bypass demonstrated in the JET study.[3] However, stenting (CTO-CAS) has been reported with advances in endovascular treatment and evidence has accumulated.[1,2,8–10] According to previous studies, the recanalization rate after endovascular treatment ranges from 65 to 93.3%. As the reason why recanalization was not achieved, the true lumen was unable to be secured using a GW. As a factor involved in the success rate of the procedure, Chen et al.[11] compared patients in whom the collateral pathway to the clinoidal segment was enhanced on retrograde angiography with those in whom the collateral pathway to the ophthalmic or communicating segment was enhanced, and reported that the success rate of the procedure was higher in the former. Furthermore, the incidence of perioperative complications ranges from 0 to 6.7%, and vascular dissection, perforation during the procedure and distal embolism have been reported. For CTO-CAS, when passing a GW through the site of occlusion, it is difficult to evaluate whether the GW is present in the true lumen, and GW insertion into a false lumen may cause perforation or dissection. Lin et al.[2] reported that distal embolism was

Table 2 Summary of 15 cases

Case No.	Age (years)/ Sex	Initial results			Follow-up (mo.)	Follow-up results	
		Stent type	Recanalized	Complication		Reocclusion	Ipsilateral major stroke
1	37/M	Precise ×3	Yes	None	71	-	-
2	79/M	Precise ×1	Yes	None	12	-	-
3	67/M	Precise ×3, Multilink ×3	Yes	None	55	-	-
4	61/M	Precise ×3, Multilink ×3	Yes	Reocclusion and minor stroke	51	+	-
5	75/M	Precise ×3	Yes	None	25	-	-
6	45/F	–	No	CCF	N/A	N/A	N/A
7	68/F	Protégé ×2	Yes	None	54	-	-
8	74/M	Precise ×1	Yes	None	5	-	-
9	75/M	Precise ×3, Protégé ×2, Multilink ×5	Yes	None	41	-	-
10	74/M	Precise ×2, Protégé ×1	Yes	None	46	-	-
11	72/M	Precise ×2, CarotidWallstent ×1	Yes	None	24	-	-
12	61/M	Precise ×5, Multilink ×4	Yes	None	20	-	-
13	56/F	Precise ×4	Yes	None	23	-	-
14	72/M	Precise ×5, Protégé ×1	Yes	Central retinal artery occlusion	21	-	-
15	83/M	Precise ×1, Multilink ×4	Yes	None	6	-	-

CCF: carotid cavernous fistula; N/A: not applicable

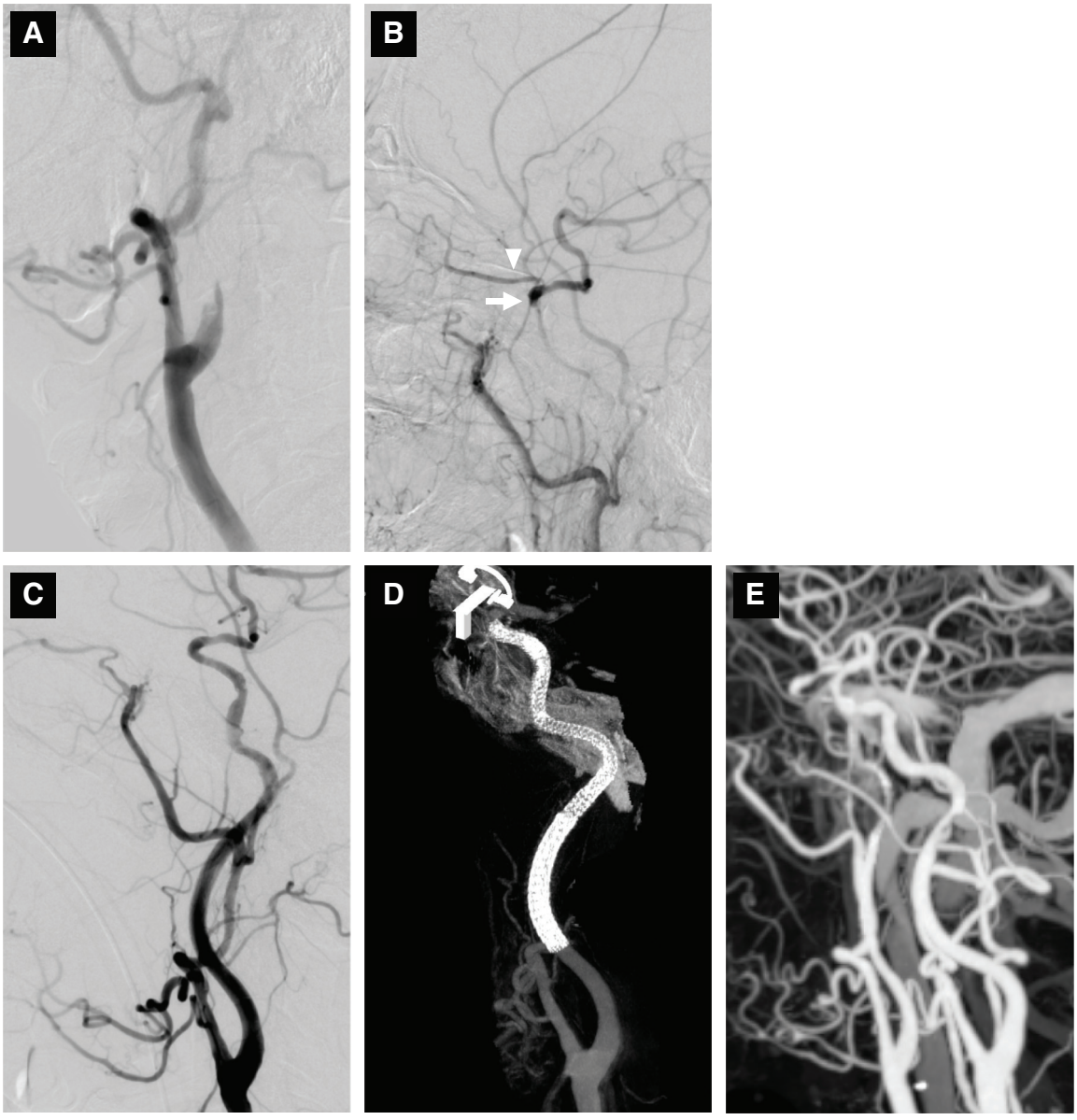

Fig. 1 Case 15. Angiographic findings. (**A**) Lateral left carotid angiogram showed complete occlusion of the cervical ICA. (**B**) Lateral left cerebral angiogram showed opacification of the proximal part of the cavernous segment of the ICA (arrow) via collateral channels from the external carotid artery to the ophthalmic artery (arrowhead). (**C**) Lateral left carotid angiogram showed complete recanalization after CAS. (**D**) Cone-beam CT showed stent placement and complete reconstitution of the ICA. (**E**) 3D-CT angiography showed the patency of the left ICA 6 months after CAS. CAS: carotid artery stenting; ICA: internal carotid artery

observed in 4% of patients treated by CTO-CAS. However, in these patients, proximal protection was not conducted. Terada et al.[12] found that a flow reversal system was useful for preventing distal embolism and that there was no distal embolism under flow reversal.

In this study, the recanalization rate after CTO-CAS was 93.3% and the incidence of perioperative symptomatic complications was 6.7%. This was because patients in whom at least the collateral pathway to cavernous segment of the internal carotid artery was enhanced were selected. Furthermore, we devised technical strategies in order for a GW to accurately reach the distal area of the true lumen. Initially, PTA at the site of cervical internal carotid artery occlusion was performed and a guiding catheter was guided to a distal area to improve supportability. Simultaneously, a balloon was dilated to prevent distal embolism. Subsequently, whether the GW passed through the true vascular lumen at the site of occlusion was confirmed using carotid ultrasonography or CBCT. A previous study reported that carotid ultrasonography was useful for evaluating the

Table 3 Summary of reported articles and current study

Authors	Number of cases	Mean follow-up period (mo.)	Ipsilateral major stroke	Reocclusion
Terada T, et al.[1]	15	26.1	0.0%	0.0%
Kao HL, et al.[14]	30	16.1	3.4%	13.6%
Ikeda N, et al.[10]	10	17.2	0.0%	0.0%
Current study	15	34.9	0.0%	7.1%

GW position.[13] However, we performed CBCT in addition to this procedure, facilitating accurate assessment of the distal GW position, which cannot be evaluated using ultrasonography. When it was difficult to guide a device to an area distal to the site of occlusion, MGWs varying in rigidity or shape, such as those for peripheral blood vessels, were used to manage hard thrombi. On the other hand, the bovine-type aortic arch was observed in one patient with central retinal artery occlusion after surgery, and it was difficult to guide an Optimo into the common carotid artery from the femoral artery. In this study, proximal protection was impossible only in this patient. Balloon guiding catheters may be important for CTO-CAS.

Few studies have reported long-term follow-up after CTO-CAS, and previous studies are presented in **Table 3.**[1,10,14] In these studies, including this study with a mean follow-up of 34.9 months, the incidence of symptomatic ipsilateral cerebral infarction ranged from 0 to 3%. These studies also suggested that CTO-CAS is useful for preventing recurrent cerebral infarction.

In this study, the incidence of recurrent cerebral infarction during mid-/long-term follow-up after CTO-CAS was low. As a reason for this, when a vascular lesion suggestive of dissection or stenosis was detected, a stent was overlapped from an area distal to the lesion site to the proximal normal vascular wall and placed without a gap. This method is termed "full-metal jacket" in revascularization for chronic total occlusion of the coronary artery.[15] The possibility that atherosclerotic plaque remains is lower than the intermittent protection of a dissected or stenotic site alone with a stent. Favorable long-term vascular patency may be achieved and ischemic complications can be prevented. As the limitation of this method, in Japan, it is currently difficult to obtain bare metal stents due to the decrease in their demand in the coronary artery region, although they were used for intracranial lesions in this study. For future CTO treatment, alternative stents available for intracranial blood vessels should be developed. On the other hand, the safety of the off-label use of drug-eluting stents, which are primarily used in the coronary artery region, for intracranial arteries must be considered.

Furthermore, most patients had a history of hypertension or dyslipidemia, which are risk factors for arteriosclerosis. However, strict medical management was continued after surgery; postoperative medical treatment in addition to the surgical procedure may have led to the favorable outcome. On the other hand, according to a previous study, the incidence of re-occlusion during follow-up ranges from 0 to 13.6%. Stenting for complete occlusion of the iliac artery led to long-term vascular patency in comparison with that of the coronary artery, and the incidence of re-occlusion decreased when the diameter of the target blood vessel was ≥3 mm.[1] CTO-CAS involving a large target blood vessel diameter may facilitate favorable long-term vascular patency. In this study, re-occlusion was noted 41.8 months after surgery in one patient (7.1%). When performing stenting for complete occlusion of the iliac artery, diabetes mellitus is a risk factor for re-occlusion.[7] A previous study reported diabetes mellitus as a risk factor for neurological complications related to CAS.[16] In the above patient with re-occlusion, medical treatment was discontinued and diabetes control was poor. For CTO-CAS, the continuation of medical treatment may be important to achieve long-term in-stent patency and prevent ischemic complications.

This study presented the results of long-term follow-up in comparison with previous studies, suggesting the mid-/long-term efficacy of CTO-CAS. No study has reported the safety or patency rate during a longer follow-up period. In the future, the long-term course must be followed-up in a larger number of patients.

Conclusion

We reported 15 patients who underwent CAS for CTO. A favorable recanalization rate was achieved and there was no symptomatic ipsilateral stroke, with a mean follow-up of 34.9 months. Marked preventive effects on recurrent stroke were achieved. Further long-term follow-up is necessary, but

CAS for CTO may be an effective and safe treatment method for the prevention of ipsilateral stroke from a mid- and long-term perspective.

Disclosure Statement

The authors declare no conflict of interest.

References

1) Terada T, Okada H, Nanto M, et al: Endovascular recanalization of the completely occluded internal carotid artery using a flow reversal system at the subacute to chronic stage. *J Neurosurg* 2010; 112: 563–571.
2) Lin MS, Lin LC, Li HY, et al: Procedural safety and potential vascular complication of endovascular recanalization for chronic cervical internal carotid artery occlusion. *Circ Cardiovasc Interv* 2008; 1: 119–125.
3) Kataoka H, Miyamoto S, Ogasawara K, et al: Results of prospective cohort study on symptomatic cerebrovascular occlusive disease showing mild hemodynamic compromise [Japanese Extracranial-Intracranial Bypass Trial (JET)-2 Study]. *Neurol Med Chir (Tokyo)* 2015; 55: 460–468.
4) Powers WJ, Clarke WR, Grubb RL, et al: Extracranial-intracranial bypass surgery for stroke prevention in hemodynamic cerebral ischemia: the Carotid Occlusion Surgery Study randomized trial. *JAMA* 2011; 306: 1983–1992.
5) Paty PS, Adeniyi JA, Mehta M, et al: Surgical treatment of internal carotid artery occlusion. *J Vasc Surg* 2003; 37: 785–788.
6) Mehran R, Claessen BE, Godino C, et al: Long-term outcome of percutaneous coronary intervention for chronic total occlusions. *JACC Cardiovasc Interv* 2011; 4: 952–961.
7) Leville CD, Kashyap VS, Clair DG, et al: Endovascular management of iliac artery occlusions: extending treatment to TransAtlantic Inter-Society Consensus class C and D patients. *J Vasc Surg* 2006; 43: 32–39.
8) Ohta T, Nakahara I, Matsumoto S, et al: Revascularization for chronic total occlusion of internal carotid arteries: review of the literature and future perspective. *JNET J Neuroendovasc Ther* 2014; 8: 3–13. (in Japanese)
9) Shojima M, Nemoto S, Morita A, et al: Protected endovascular revascularization of subacute and chronic total occlusion of the internal carotid artery. *AJNR Am J Neuroradiol* 2010; 31: 481–486.
10) Ikeda N, Abiko M, Sakakura T, et al: Endovascular treatment of chronic total occlusion of the internal carotid artery. *Surg Cereb Stroke (Jpn)* 2014; 42: 109–115. (in Japanese)
11) Chen YH, Leong WS, Lin MS, et al: Predictors for successful endovascular intervention in chronic carotid artery total occlusion. *JACC Cardiovasc Interv* 2016; 9: 1825–1832.
12) Terada T, Yamaga H, Tsumoto T, et al: Use of an embolic protection system during endovascular recanalization of a totally occluded cervical internal carotid artery at the chronic stage. Case report. *J Neurosurg* 2005; 102: 558–564.
13) Rostambeigi N, Khatri R, Hassan AE, et al: Duplex ultrasound assisted endovascular revascularization of chronic internal carotid artery occlusion: technical note. *J Vasc Interv Neurol* 2013; 6: 42–46.
14) Kao HL, Lin MS, Wang CS, et al: Feasibility of endovascular recanalization for symptomatic cervical internal carotid artery occlusion. *J Am Coll Cardiol* 2007; 49: 765–771.
15) Yamamoto K, Sakakura K, Adachi Y, et al: Comparison of mid-term clinical outcomes between "complete full-metal jacket strategy" versus "incomplete full-metal jacket strategy" for diffuse right coronary artery stenosis with drug-eluting stents. *J Cardiol* 2017; 69: 823–829.
16) Kim NY, Choi JW, Whang K, et al: Neurologic complications in patients with carotid artery stenting. *J Cerebrovasc Endovasc Neurosurg* 2019; 21: 86–93.