Expansion of Stent and Lumen Diameters on Follow-up after Carotid Artery Stenting in Patients with Carotid Artery Stenosis

Kenta Fujimoto,1 Hiroyuki Hashimoto,1 Mitsuhisa Nishiguchi,1 Toshitaka Inui,1 Naoki Tani,1 Kaoru Horiuchi,1 Megumi Chatani,1 Ryuta Matsuoka,1 Takahide Yaegaki,1 Ichiro Nakagawa,2 and Hiroyuki Nakase2

Purpose: We examined postoperative stent and lumen expansions after carotid artery stenting (CAS) in patients with carotid artery stenosis. Furthermore, we investigated factors influencing the stent and lumen expansions in a follow-up period.

Subjects: 134 cases (128 patients) who underwent CAS and performed follow-up cerebral angiography 12 months after CAS were enrolled into this study. The stenosis rate based on the stent and lumen diameters on follow-up angiography as a percentage of that immediately after CAS was evaluated.

Results: Both the stent and lumen diameters were significantly dilated 12 months after CAS (p < 0.001). There were no significant stent-type-related differences in the stent expansion rate. In the symptomatic stenosis group, this expansion rate was significantly higher than in the asymptomatic stenosis group (p = 0.02). With respect to the presence or absence of a high signal intensity on time of flight (TOF) magnetic resonance (MR) images, the stent expansion rate was significantly higher in the high signal intensity group (p = 0.006). In patients with a plaque/sternocleidomastoid muscle signal intensity ratio of ≥1.50 on plaque images, it was significantly higher than in those with a value of <1.50 (p = 0.006). However, there were no significant differences in the lumen expansion rate among the groups.

Conclusion: Both the stent and vascular lumen were dilated 12 months after CAS. Plaque fragility influenced the stent expansion rate; however, there were no significant factor-related differences in the vascular lumen expansion rate.

Keywords ► carotid artery stenting, self-expansion, plaque

Introduction

Since carotid artery stenting (CAS) for stenosis of the carotid artery became covered by health insurance in April 2008, it has commonly been performed in Japan. Initially, this procedure was primarily performed for patients at high risk for carotid endarterectomy (CEA) based on the results of the SAPPHIRE study.1) However, in 2010, the CREST study2) showed that CAS was as effective as CEA, promoting its widespread application. On the other hand, the CREST3) and ICSS3) studies indicated that the incidence of perioperative stroke after CAS was higher than after CEA. Therefore, a reduction in the incidence is a key to an improvement in the results of CAS. Various studies have reported plaque assessment, medications, embolic protection devices, different cell-design stents, and procedures. Concerning procedures, studies using transcranial Doppler monitoring reported that distal embolism occurred most commonly on post-dilation after stenting.4,5) Several studies suggested that the incidence of embolic complications can be decreased by omitting or restricting post-dilation although an insufficient stent dilatation also can occur even using self-expanding stents.6,7) There was one report about postoperative stent expansion 3 months after CAS; however, the long-term degree of postoperative stent expansion after CAS has not been elucidated.8)

Our CAS strategy is targeting a residual stenosis rate of ≤30% using self-expanding stent considering both risk of embolic complications related to marked post-dilation and...
that of early complications related to insufficient dilation. In this study, we examined whether a stent itself expands or whether the vascular lumen is dilated in follow-up cerebral angiography based on the hypothesis that self-expansion may be serially achieved especially in patients with soft plaques. Furthermore, we investigated factors influencing postoperative self-expansion including the plaque fragility assessed by MRI and the stent design.

Subjects and Methods

Subjects
In our hospital, CAS for stenosis of the internal carotid artery has been performed for patients with ≥50% symptomatic stenosis or ≥75% asymptomatic stenosis (symptomatic: ≤50%, asymptomatic: ≤25% in accordance with the measurement method adopted in this study, as described below) according to the indication criteria adopted in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) after obtaining approval from the Ethics Review Board and informed consent between January 2006 and April 2008, when CAS had not been covered by health insurance. After CAS became covered by health insurance, it was indicated for patients with ≥50% symptomatic stenosis or ≥80% asymptomatic stenosis, as determined in the NASCET, at high risk for CEA, according to indication criteria in Japan. After the CREST study, CAS was selected as a first-choice procedure. CAS had been performed for 253 cases from January 2006, when CAS was introduced in our hospital, until December 2014. Of these, 134 cases (128 patients; 116 males, 18 females, age: 52–86 years, mean age: 72 years) in whom follow-up cerebral angiography could be conducted, excluding treatment for restenosis, were enrolled into this study.

Assessment of the degree of stenosis
To measure the degree of stenosis, the vascular diameter at the stenotic site was compared with the distal internal carotid artery diameter in accordance with the NASCET using lateral views on cerebral angiography. However, after dilation, the lumen at the stenotic site sometimes dilates to a diameter larger than the distal carotid artery diameter; therefore, the formula of stenotic site/distal diameter × 100 was adopted. When the lumen diameter at the stenotic site became larger than the distal carotid artery diameter, it was recorded as a value of ≥100. Furthermore, the stenosis rate on follow-up cerebral angiography after 1 year as a percentage of that immediately after CAS was compared. To evaluate the degree of stenosis on plain X-ray, the stent diameter (D2) at the stenotic site was calculated as a percentage of the distal normal internal carotid artery diameter (D1), (D2/D1 × 100) in accordance with cerebral angiography-based assessment. On plain X-ray after 1 year, it was also calculated, assuming the same position as observed on plain X-ray immediately after CAS. The stenosis rate after 1 year as a percentage of that immediately after CAS was investigated. To compare changes between two groups, Student’s t-test was used. A p value of 0.05 was regarded as significant.

Plaque assessment
Before CAS, carotid artery ultrasonography was performed for all patients. After January 2010, plaque assessment by the Black-blood method was conducted using MRI preoperatively, and the plaque/sternocleidomastoid muscle signal intensity ratio (SIR) was calculated. On T1-weighted magnetic resonance (MR) images (Black-blood method), the pixel values of the plaque were measured at six points. Similarly, those of the sternocleidomastoid muscle were measured at six points, and the ratio was calculated. In this study, the patients were divided into two groups: a group with an SIR of ≥1.5, at which plaque fragility may increase, and a group with an SIR of <1.5. Furthermore, some studies reported that plaques detected as a high signal intensity on time of flight (TOF) images were fragile and we also confirmed findings on TOF images, and retrospectively examined the presence or absence of a high signal intensity in the plaque area in previous patients. Furthermore, it was indicated that plaques in patients with symptomatic lesions were more fragile than in those with asymptomatic lesions; therefore, the results were examined with respect to the presence or absence of symptoms.

Techniques
In our hospital, CAS had been performed using a PRECISE stent (Cordis, Miami Lakes, FL, USA) under distal balloon protection with a Guardwire (Medtronic, Eden Prairie, MN, USA) between January 2006 and April 2008, when CAS had not been covered by health insurance. Pre-dilation was conducted, and when ≥70% dilation (<30% in accordance with NASCET measurement) was achieved after stenting, post-dilation was omitted. From April 2008 until June 2010, a PRECISE stent was used under distal filter protection with an Angioguard (Cordis). Pre-dilation was conducted, and when ≥70% dilation was achieved after stenting, post-dilation was omitted. From June 2010,
the device for distal filter protection was switched to a Filterwire EZ (Boston Scientific, Natick, MA, USA). After November 2010, distal balloon protection was selected when a collateral pathway was present and distal filter protection when it was absent. For tortuous lesions, a PRECISE stent was used, but a Carotid Wallstent (Boston Scientific) was used in patients in whom its insertion was considered possible. Pre-dilation was conducted using a balloon measuring 3.5 to 4.0 mm in diameter, and post-dilation using a balloon 0 to 0.5 mm smaller than the distal internal carotid artery diameter.

Follow-up
For medication, two of three antiplatelet drugs (clopidogrel at 75 mg, aspirin at 100 mg, and cilostazol at 200 mg) were administered for more than 1 week before CAS. The regimen was switched to monotherapy 3 months after CAS. Follow-up ultrasonography was performed once within 1 week after CAS, and, subsequently, every 3 months. When restenosis or stent plaques were suspected, cerebral angiography was conducted. When there was no problem, cerebral angiography was performed after 12 months. The stenosis rate on follow-up as a percentage of that immediately after CAS (stenosis rate on follow-up/stenosis rate immediately after CAS × 100 [%]) was compared between the stent and lumen diameters. Assuming that self-expansion may be more marked in patients with softer plaques or when adopting a stent with a stronger radial force, we examined stent expansion with respect to the plaque/sternocleidomastoid muscle SIR on MR images, obtained using the Black-blood method, presence or absence of a high signal intensity on TOF images, presence or absence of symptoms, and stent design.

Results
The subjects were 134 cases (128 patients), with a mean age of 72 years (range: 52–86 years). The male-to-female ratio was 116:18. Follow-up cerebral angiography was performed 6 to 24 months after CAS and 134 of 253 cases (53.0%) were adopted this criteria in this study. The average stenosis rate, measured using the above measurement method, on preoperative cerebral angiography was 22.9% ± 11.7% (range: 50 to 0%), whereas that on plain X-ray immediately after CAS was 77.0% ± 12.1%, but that on follow-up was 89.1% ± 15.1%, showing a significant increase (p < 0.001) (Fig. 1A). The mean stenosis rate on cerebral angiography immediately after CAS was
77.8% ± 15.6%, but that on follow-up was 82.5% ± 21.5%, showing a significant increase (p = 0.04) (Fig. 1B). We examined the stenosis rates immediately after CAS and on follow-up with respect to the plaque properties, stent design, and presence or absence of symptoms. Concerning the stent design, an open-cell stent was selected for 77 cases (Group O) and a closed-cell stent for 57 (Group C). The mean stent expansion rates were 118.4% ± 26.3% in Group O and 113.9% ± 11.8% in Group C. There was no significant difference in the expansion rate between the two groups (Fig. 2A). The mean lumen expansion rates on cerebral angiography were 110.3% ± 27.3% and 104.4% ± 26.4%, respectively, showing no significant difference (Fig. 2B).

Concerning symptoms, symptomatic stenosis was present in 70 cases and asymptomatic stenosis in 64 cases. The mean stent expansion rates in the former and latter were 120.9% ± 23.2% and 112.5% ± 19.2%, respectively (p = 0.02), showing a significant difference (Fig. 3A). However, the mean lumen expansion rates were 110.8% ± 30.1% and 105.3% ± 23.8%, respectively, showing no significant difference (Fig. 3B).

MR images of plaques were obtained in 90 cases. The plaque/sternocleidomastoid muscle SIR was ≥1.50, at which the incidences of plaque hemorrhage and lipid-rich necrotic core may increase, in 28 cases, and it was <1.50 in 62. In cases with an SIR of ≥1.50, the mean stent expansion rate was 125.4% ± 21.1%. In those with an SIR of <1.50, it was 112.5% ± 18.8%; the value was significantly higher in the former (p = 0.006) (Fig. 4A). The mean lumen expansion rates in the former and latter were 102.4% ± 27.4% and 110.6% ± 25.3%, respectively, showing no significant difference (Fig. 4B).

TOF images were obtained in 131 cases. A high signal intensity was detected in 39 cases ((+) group), but not in 92 ((-) group). The mean stent expansion rates in the (+) and (-) groups were 124.6% ± 22.2% and 113.3% ± 20.4%, respectively, showing a significant difference (p = 0.006) (Fig. 5A). However, the mean lumen expansion rates were 106.5% ± 28.4% and 108.4% ± 26.8%, respectively, showing no significant difference (Fig. 5B).

The high-signal-intensity appearance rate on diffusion-weighted MR images after CAS in the subjects was 15.3% (20/131). There were no neurological complications during CAS or immediately after CAS, but minor stroke was observed in three cases within 30 days after CAS, and hyperperfusion syndrome in one case. When adopting our measurement method, ≤50% (NASCET: ≥50%) restenosis
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Fig. 3 Stent (A) and lumen (B) expansion at 12 months after CAS according to symptom, average ± standard deviation (%). CAG: carotid angiography; CAS: carotid artery stenting; XP: X-ray photograph; NS: not significant

Fig. 4 Stent (A) and lumen (B) expansion at 12 months after CAS according to plaque/muscle SIR on MR plaque imaging, average ± standard deviation (%). CAG: carotid angiography; CAS: carotid artery stenting; MR: magnetic resonance; XP: X-ray photograph; NS: not significant; SIR: signal intensity ratio
was noted in six cases (4.5%). Of these, it was symptomatic in one case (0.8%), and additional treatment was performed for five cases (3.8%). The incidence of ≥50% restenosis was 2.4% (6/253), including cases in whom follow-up digital subtraction angiography (DSA) was not done. For all cases who underwent cerebral angiography within 6 months for some reason, additional cerebral angiography was performed during the study period. No patient received additional treatment within 6 months.

### Representative Case

#### Case 1

A 70-year-old man was referred from the Department of Ophthalmology with amaurosis fugax of the left eye. Carotid artery ultrasonography revealed a low-echoic plaque at the bifurcation of the left carotid artery. The peak systolic velocity (PSV) was 338.9 cm/s, confirming acceleration. MR images of the plaque were not evaluated, and there was no high signal intensity on TOF MRA. The stenosis rate on cerebral angiography was 11% (NASCET: 89%) in accordance with the measurement method adopted in this study (Fig. 6A). Under Angioguard protection, pre-dilation was conducted using an Amia (Cordis) measuring 4.0 × 30 mm, and a PRECISE stent measuring 9 × 40 mm was inserted. As dilation was considered sufficient, post-dilation was not performed. The stenosis rate immediately after CAS was 61% (Fig. 6B). Follow-up ultrasonography did not show any abnormalities, and cerebral angiography was conducted after 18 months. The stent had expanded from 59% to 130% (Figs. 6D and 6E), and the lumen had also expanded from 61% to 132% (Fig. 6C).

#### Case 2

A 63-year-old male presented with amaurosis fugax of the right eye was referred to our hospital for evaluation. Carotid artery ultrasonography revealed a low-echoic plaque at the bifurcation of the right carotid artery. MR images of the plaque showed a high signal intensity, with an SIR of 1.65 (Fig. 7A). On TOF MRA, a high signal intensity was detected (Fig. 7B). On cerebral angiography, the stenosis rate was 5% (NASCET: 95%)
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There were no changes in the stenosis rate or shape. The stent seemed to sink into the plaque (Fig. 8C). The lesion was asymptomatic, with a stenosis rate of 58% (NASCET: 42%), and additional treatment was considered unnecessary. Follow-up is being continued.

Discussion

Recently, CAS has commonly been performed, and several studies, including the CREST study, reported that its efficacy was similar to that of CEA.1,2) The most important issue of CAS to be overcome is the prevention of thromboembolic complications due to distal embolism. For this purpose, efforts to select high-risk patients and modify medications/procedures/devices to reduce the incidence of distal embolism have been made in the literature.

with the measurement method adopted in this study (Fig. 8A). Under Guardwire protection, pre-dilation was conducted using an Amia measuring 4.0 × 30 mm, leading to transient cardiac arrest. The chest was hit, and the heart beat promptly resumed. After the intravenous injection of atropine sulfate at 5 mg, a PRECISE stent measuring 9 × 40 mm was inserted. Post-dilation was not conducted, and the procedure was completed. There were no neurological symptoms, and there were no clinical problems. However, the stenosis rate immediately after CAS was 53% (Fig. 8B). During the follow-up, plain X-ray showed stent expansion, but ultrasonography revealed intra-stent thrombus formation; therefore, cerebral angiography was performed after 12 months. The stent had expanded from 59% to 130% (Figs. 8D and 8E), but lumen expansion was slight: from 53% (immediately after CAS) to 58%.

Fig. 6 CAG and plain cervical XP of Case 1. (A) Initial CAG, (B) CAG immediately after CAS, (C) CAG 18 months after CAS, (D) XP immediately after CAS, and (E) XP 18 months after CAS. CAG: carotid angiography; CAS: carotid artery stenting; XP: X-ray photograph
For the selection of high-risk patients, it is important to evaluate plaque properties based on preoperative diagnostic imaging findings. Some studies indicated the importance of plaque assessment using MRI, and, recently, it has been essential as preoperative assessment.\textsuperscript{10,11,15} Furthermore, others reported that TOF MRI is commonly used for preoperative plaque assessment because plaques detected as a high signal intensity on TOF images were fragile.\textsuperscript{12,13} Concerning procedures, several studies reported that post-dilation after stenting in the process of CAS was involved in distal embolism.\textsuperscript{4,5,16} Therefore, in our hospital, initially, CAS was performed using a PRECISE stent alone, and post-dilation was omitted when \(\leq 30\%\) (NASCET) residual stenosis was present. Since the introduction of a Carotid Wallstent, post-dilation has been conducted using a balloon smaller than the distal internal carotid artery diameter. As a result, residual stenosis has been observed in many patients immediately after CAS, and multimodalities including ultrasonography, CT angiography, cerebral angiography, and plain X-ray have been combined for follow-up evaluation.

The most accurate diagnostic modality to evaluate the stent and the lumen diameter is cerebral angiography; however, it is invasive, used contrast medium, and requiring admission; hence, it is difficult to do this procedure for all patients in practice. Instead of cerebral angiography, ultrasonography for the lumen diameter and plain X-ray for stent diameter were used. However, it is unclear whether the degree of subsequent lumen expansion is reflected by the stent expansion. Therefore, we examined changes immediately after CAS and on follow-up in 134 cases who could be followed up using cerebral angiography. Concerning the timing of follow-up, a study indicated that marked restenosis frequently occurred within 6 months after CAS, and that the incidence of restenosis decreased 12 months or more after CAS;\textsuperscript{17} based on these results, we decided to perform follow-up cerebral angiography at 12 months after CAS, considering that the incidence of restenosis should be less frequently.

Self-expanding stents are used for CAS; they may also expand after treatment. However, it is difficult to predict the degree of expansion. Previous studies reported that the periprocedural clinical results were favorable despite postdilatation procedure.\textsuperscript{5,7,18,19} However, few studies have examined the degree of stent expansion on follow-up.\textsuperscript{8} In this study, we investigated stent expansion and changes
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et al. indicated that stent expansion was more marked in patients in whom a closed-cell stent with a weak radial force was used. They selected the closed-cell stent for soft plaques, and there may have been a selection bias. In addition, the results suggest that plaque properties more markedly influence expansion compared with the stent design. Of our series, a PRECISE stent was selected for all patients in the initial phase, and, after 2011, a Carotid Wallstent was used regardless of plaque properties if possible; therefore, there might have been less stent-option-related selection bias.

Plaque properties
When a plaque is soft, a stent may expand more markedly. In this study, stent expansion was significantly more marked in a group with a plaque/sternocleidomastoid muscle SIR of \(\geq 1.5\) on assessment using the Black-blood method, in which plaques may have been soft, and in a group with a high signal intensity on TOF images. Furthermore, a study reported that plaques in symptomatic stenotic

Stent design
As an open-cell stent shows a stronger radial force compared with a closed-cell stent, its expansion may be more marked. However, in this study, there was no significant stent-type-related difference in the expansion rate. In contrast, Tanno

Fig. 8  CAG and plain cervical XP of Case 2. (A) Initial CAG, (B) CAG immediately after CAS, (C) CAG 12 months after CAS, (D) XP immediately after CAS, and (E) XP 12 months after CAS. CAG: carotid angiography; CAS: carotid artery stenting; XP: X-ray photograph

in the vascular lumen on cerebral angiography 1 year after CAS in patients who underwent CAS in our hospital, and in whom cerebral angiography findings could be evaluated. The stent stenosis rates immediately after CAS and on follow-up cerebral angiography were 77.0% \(\pm\) 12.1% and 89.1% \(\pm\) 15.1%, respectively, showing expansion (p < 0.001). Furthermore, the lumen stenosis rates on cerebral angiography immediately after CAS and on follow-up were 77.8% \(\pm\) 15.6% and 82.5% \(\pm\) 21.5%, respectively, showing a significant enlargement (p = 0.04). During the follow-up period, both the stent and lumen diameters on cerebral angiography had increased (Fig. 1). The stent design and plaque properties may be closely involved in expansion.
lesions were more fragile than in asymptomatic lesions.\textsuperscript{14)} In this study, stent expansion was more marked in the symptomatic stenosis group. However, there was no significant difference in lumen expansion.

As the reason why lumen expansion did not always accompany stent expansion, neointima formation in the lumen may have induced hyperplasia, thrombus attachment, or plaque protrusion into the stent.

Several studies using a self-expanding stent for the coronary artery and involving follow-up reported that stent expansion led to neointimal ingrowth, causing narrowing of the lumen.\textsuperscript{21–23)} Hong et al.\textsuperscript{23)} inserted a self-expanding nitinol stent into the coronary artery in an animal experiment using pigs, and examined its pathological sections. They confirmed an increase in the stent diameter 6 months after stenting, but the neointimal reaction of the vascular lumen reached a peak 4 to 8 weeks after stenting, and, after 6 months, the stent strut had reached the outer membrane in most pigs. In this study, in Case 2, the stent expanded, and sank into the plaque; the stent strut may have reached an area adjacent to the outer membrane.

Overall, lumen expansion during follow-up was confirmed, as shown in Fig. 1B. Thus, even when chronic-phase self-expansion is insufficient, self-expansion may be achieved through continuous follow-up rather than early additional treatment. However, there are some patients in whom expansion is not achieved. And of our series, the stent sank into the plaque in some patients, as demonstrated in Case 2. In our hospital, 30\% stenosis (NASCET) is targeted, and the procedure should be completed after obtaining an acceptable degree of expansion.

\section*{Limitations}

Of our series, 119 cases in whom follow-up cerebral angiography was not done (47\%) were excluded. Cerebral angiography has been performed if follow-up ultrasonography suggested abnormalities even in the presence of renal dysfunction; however, this may have affected the results. In our hospital, several angio-suits have been used, and there may be an error on measurement of absolute values, depending on the distance between the panel and lesion. Therefore, we have assessed the degree of stenosis, as a relative value, but not the absolute diameter at the most stenotic site; absolute-value assessment has not been conducted. Furthermore, stent options and techniques were modified between the early and late phases of the present study period, and this may have contributed to the results.

\section*{Conclusion}

After CAS, both the stent and lumen diameters were expanded. The stent expansion rates in patients with a high signal intensity on TOF images, in whom plaques were considered fragile, those with a high signal intensity on MRI (Black-blood method), and those with symptomatic stenosis were significantly higher, but there was no significant stent-type-related difference. The lumen diameter also expanded with an increase in the stent diameter. However, the lumen did not readily expand under conditions facilitating stent expansion. Although postoperative stent/lumen expansion may be achieved on follow-up, the degree of the expansion is unpredictable in practice. Therefore, ≥30\% (NASCET) acceptable expansion should be obtained during CAS.

\section*{Disclosure Statement}

The authors completed the self-reporting of conflict of interest (COI) to the Japan Neurosurgical Society. There is no conflict of interest to be disclosed regarding this study.

\section*{References}


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