The safety of carotid artery stenting in the elderly

Jun MORIOKA1) Kei HARADA2) Syogo OSHIKATA1) Kosuke KAKUMOTO1) Shigenari KIN1)
1)Department of Neurosurgery, Fukuoka Shin-Mizumaki Hospital
2)Department of Neurosurgery, Fukuoka Wajiro Hospital

● Abstract ●

Objective: The impact of advanced age on the safety and efficacy of carotid artery stenting (CAS) is controversial. The aim of this study was to retrospectively evaluate the safety of CAS in the elderly.

Methods: In total, 111 patients (119 procedures) from October 2008 to November 2011 were included; of these, 28 patients (31 procedures) aged <70 years, 49 patients (52 procedures) were septuagenarians, and 34 patients (36 procedures) were octogenarians. The primary outcome event for the analysis was any stroke within 30 days after CAS. The secondary outcome event was new diffusion-weighted imaging (DWI) lesions on the day following stenting.

Results: The incidence of stroke was 3.4% (4 of 119 procedures; two in the <70 years of age, one in the septuagenarians, and one in the octogenarians). The incidence of new DWI lesions immediately after CAS was 17% and was highest in the group aged ≥80 years.

Conclusion: Advanced age alone does not exclude adequate CAS, but care must be taken regarding plaque vulnerability at the target site and atherosclerotic change of the access route.

● Key words ●
carotid artery stenting, carotid artery stenosis, age

Introduction

The impact of advanced age on the safety and efficacy of carotid artery stenting (CAS) is controversial. Octogenarians are generally considered to be at high risk for carotid endarterectomy (CEA), and have been excluded from most randomized trials. According to the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, CAS was found to be noninferior to CEA in patients with coexisting conditions that might otherwise preclude CEA, including age over 80 years. In contrast, in several randomized trials, subgroup analyses by age have revealed that the postoperative risk of stroke, myocardial infarction, and death following CAS increases with age.

We devised a treatment protocol for carotid artery stenosis that uses CAS in preference to CEA in the elderly (Fig. 1). The present study sought to retrospectively evaluate the safety of CAS in the elderly.

Materials and Methods

Patients at five participating centers who underwent CAS because of diagnoses of either carotid atherosclerotic disease or stenosis between October 2008 and November 2011 were enrolled. Patients could be enrolled twice if they had recurrent or bilateral disease. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) method was used to assess stenosis: all asymptomatic patients were required to have a carotid artery stenosis of ≥80%, whereas symptomatic patients required a stenosis of ≥50%. Ultrasound, MRI, and/or CTA were used for plaque assessment and imaging of access route. We excluded any...
patients requiring emergency CAS to treat acute ischemic stroke, as well as any patient with plaques considered too fragile based on black blood (BB) T1-weighted MRI or ultrasound. The signal intensity ratio (SIR) was defined as the ratio of signal intensity evaluated by BB-MRI in carotid plaques to that of sternocleidomastoid muscle. SIR ≥ 2.0 was defined as “too fragile.”

All patients received both aspirin (100 mg/day) and clopidogrel (75 mg/day) or cilostazol (200 mg/day) for at least 7 days prior to the procedure. After the procedure, all antiplatelet drugs were continued for 2 months; only one is continued thereafter, at the clinician’s discretion.

All procedures were conducted by the same two interventionists. CAS was performed using either the Carotid Wallstent (Boston Scientific, Natick, Massachusetts, USA) or the Precise stent (Cordis, Miami Lakes, Florida, USA). The protection systems comprised 1) a simple distal filter using Angioguard XP (Cordis, Miami, FL, USA) or FilterWire EZ (Boston Scientific, Mountain View, CA, USA), 2) a simple distal balloon using Carotid PS GuardWire temporary occlusion system (Medtronic, CardioVascular, Mineapolis, MN, USA), or 3) a distal filter with flow reversal using a guiding catheter with a temporary balloon occlusion using OPTIMO (8F or 9F; Tokai Medical Products, Aichi, Japan) or CELLO (Fuji System Corp., Tokyo, Japan) positioned at the common carotid artery. Furthermore, the GuardWire was placed, if necessary, at the external carotid artery. The protection systems were chosen according to the interventionists’ preference and commercial availability. There was no established rule to select the protection methods, however, we preferred distal filter with flow reversal. Especially, since December 2010, we had usually used flow reversal using not only a guiding catheter with a balloon positioned at the common carotid artery, but also the carotid GuardWire positioned at the external carotid artery in order to prevent distal embolism related to blood flow from the external carotid artery to the internal carotid artery for a patient with fragile plaque.

In case of technical difficulties with primary stenting, the lesion was predilated. Angiograms of the target carotid lesion and intracranial arteries were performed at the beginning and end of the procedure, and evaluated for severity and morphology of the target carotid stenosis and for occlusions of intracranial branches.

MRI was performed 1 day after stenting, and at any time in the event of neurological deterioration. Ischemic lesions were evaluated by diffusion-weighted imaging (DWI) scans (b=1,000). The MRI sequence parameters for DWI were as follows: echo time (TE)=minimum, repetition time (TR)=7,000 ms, field of view=240 mm, matrix 128x128, and 6-mm slice thickness. In case of new DWI lesions that had not been detected at baseline, they were assumed to be new ischemic lesions after stenting.
Data analysis

The primary outcome event for the analysis was any stroke within 30 days after CAS. Stroke was defined as an acute symptomatic focal neurological deficit resulting from intracranial hemorrhage or cerebral ischemia, including transient ischemic attack (TIA). The secondary outcome event was new DWI lesions on the day following stenting.

The data were analyzed with a logistic regression model to obtain overall estimates of risk ratios and 95% confidence intervals of the outcome events. The interaction between the effect of CAS on the outcome events and each of the following variables were examined in the logistic regression analysis: age, sex, protection method, history of ischemic stroke ipsilateral to the study artery before CAS (symptomatic or asymptomatic), and stent type. All statistical analyses were performed with use of StatView, version 5.0 (SAS Institute Inc., NC, USA).

Patients were divided in three groups by age in years: <70, 70–79, and ≥80. The incidence of new DWI lesions was estimated in each group, and compared among them using the Kruskal-Wallis test and Mann-Whitney U-test.

Results

In total, 111 patients underwent 119 CAS procedures; 1 procedure was repeated because of recurrence, and 7 patients required bilateral therapy. There were 98 men and 13 women aged 57–89 years (mean, 74.3). Of the 119 procedures, 31 (26%) were in <70 years, 52 (44%) were in septuagenarians, and 36 (30%) in octogenarians. Of the 119 lesions, 75 (63%) were symptomatic. Two patients underwent transbrachial CAS because standard transfemoral approach was impossible.

The Carotid Wallstent was used in 33 lesions, and the Precise stent in 86 lesions. The protection systems used were as follows: 33 cases used a simple distal filter, 16 cases used a simple distal balloon, and 70 cases used a distal filter combined with flow reversal using a guiding catheter with balloon positioned at the common carotid artery. Furthermore, we positioned a carotid PS GuardWire temporary occlusion system at the external carotid artery in 18 of the latter 70 cases.

In the postoperative period (up to 30 days), the incidence of stroke was 3.4% (4 of 119 procedures; 2 in the sexagenarians, 1 in septuagenarians, and 1 in octogenarians). The incidence of stroke events limited to patients aged ≥75 years was 3.1% (2 of 63 procedures). There was no age-related increase in postoperative stroke (Table 1). Other variables also did not significantly correlate with the incidence of stroke.

The incidence of new DWI lesions on the day following CAS was 17.9% (20 of 112 procedures, no MRI data on the other 7). Only the protection method used was a significant factor on appearance of new DWI lesions (Table 2); the use of distal filter protection with proximal protection (flow reversal) decreased the appearance of new DWI lesions. In the logistic regression analysis, no significant correlation was found between the incidence of new DWI lesions and the following variables: age, sex, history of ischemic
stroke before CAS (symptomatic or asymptomatic), and stent type.

The incidence of new DWI lesions on the day following the procedure, according to age group, was highest among those aged ≥80 years (Fig. 2). There was a significant difference between those aged <80 and those aged ≥80 years of age (Mann-Whitney U test, p=0.0269). No significant difference was found among the 3 age groups composed of age <70, ≥70 and <80, and ≥80 (Kruskal-Wallis test, p=0.077).

### Representative case presentation

A 78-year-old man presented with transient left hemiparesis. The patient had had hypertension, hyperlipidemia, and diabetes mellitus. He was diagnosed with symptomatic right carotid artery stenosis (Fig. 3, upper left), and underwent CAS (Fig. 3, upper right). During the procedure, he presented with impaired consciousness. The DWI one day after the procedure showed high intensity areas in bilateral posterior lobes and the left thalamus (Fig. 3, lower left). These lesions suggested embolism from a proximal source (e.g., the aortic arch or the innominate artery), rather than the target stenosis of the carotid artery. The unconsciousness was not completely recovered. He died of severe pneumonia two months after the CAS.

### Discussion

Advanced age is a recognized risk factor for poor outcomes in CEA, and some studies have shown increasing patient age to be a risk factor for stroke in CAS performed in the elderly. Prior analysis of the Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) demonstrated that the risk for the primary end point (i.e., any stroke during the periprocedural period and ipsilateral stroke during the subsequent 4-year period) in the CAS group increased 1.77 times per 10-year increment in age, although there was no evidence of increased risk in the CEA group. At our institution, we continued to adopt CAS in the
elderly. The present study found no age-related increase in postoperative stroke, whereas the incidence of new DWI lesions significantly increased in patients aged ≥80 years compared with those aged <80 years. The reasons for this need to be considered.

Plaque vulnerability at the target site might potentially increase the risk of stroke among elderly patients undergoing CAS. van Lammeren, et al.⁷ revealed that elderly patients had higher incidence of unstable plaques with low smooth muscle cell content, higher amount of large lipid cores, and more calcified plaques than younger patients. As a rule, we excluded patients from CAS with plaques considered too fragile based on BB T1-weighted MRI or ultrasound. This may explain the lower incidence of new DWI lesions in our study (17%), than that reported by Schnaudigel, et al.⁸ (37%), which were based on the

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Fig. 3
Right carotid angiograms just before stenting (upper left) and after stenting with flow reversal without balloon occlusion of the external carotid artery (upper right). Diffusion-weighted imaging one day after stenting showed high intensity areas bilaterally in the posterior lobes and left thalamus (lower left). The plain CT image showed calcification of the ascending aorta (lower right, arrow).
systematic analysis of all peer-reviewed studies published between January 1990 and June 2007.

The newly developed protection devices may decrease the incidence of DWI lesions in the immediate postoperative period. We previously reported that combining distal filter protection and a guide catheter with temporary balloon occlusion significantly decreased visible debris captured by the distal filter and the occurrence of postprocedural cerebral infarctions detected by DWI\(^9\). Micari, et al.\(^{10}\) showed that CAS performed using a proximal endovascular occlusion device (Mo. Ma device; Invatec, Roncadelle, Italy) was safe and feasible in octogenarians. Although we did not use the same device, the flow reversal system used in 18 cases was similar; using a guiding catheter with a temporary balloon occlusion positioned at the common carotid artery, combined with the carotid GuardWire positioned at the external carotid artery. Thus, it is possible that using a distal filter protection with proximal occlusion (flow reversal) decreased the appearance of new DWI lesions. However, in contrast to the distal filter protection alone, this modality requires complete interruption of antegrade carotid artery flow during balloon angioplasty and stent deployment. Because cerebral intolerance is not an infrequent occurrence with this approach, clinicians must be aware of management strategies for transient cerebral intolerance\(^{11}\).

Atherosclerotic change at the access route might be another contributing factor to the increased risk of stroke among elderly patients undergoing CAS\(^{12-15}\). The elderly have an increased incidence of unfavorable arch elongation, arch calcification, common carotid artery or innominate artery origin stenosis, and common carotid artery tortuosity. Preliminary manipulation of a guide catheter through these routes might contribute to cerebral lesions as shown in the representative case presentation (Fig. 3).

To decrease the risk of stroke for elderly patients undergoing CAS, it is important to understand two major factors, namely plaque vulnerability at the target site and atherosclerosis of the access route. As mentioned above, improving protection against distal embolism can decrease the risk from plaque vulnerability at the target site. To overcome the drawbacks of femoral access for CAS and to decrease embolic load, some have proposed cervical access\(^{16-20}\). This offers hope of a solution to atherosclerotic change of the access route. Noninvasive medical treatment should also be considered for elderly patients with too fragile plaques at the target site and/or atherosclerosis of the access route that cannot be overcome even with transcervical or transbrachial approach. Especially to asymptomatic carotid artery stenosis, the risk of ischemic stroke might have decreased in recent years owing to improvements in medical treatment\(^{21}\).

Subgroup analysis by age in CREST has revealed that the risk of stroke within periprocedural period in patients aged $\geq 75$ was 6.9% for CAS, and 3.1% for CEA\(^5\). The incidence of stroke events within periprocedural period in our study was 3.1% (2 of 63 procedures) for patients aged $\geq 75$ years, which was lower than that for CAS and equal to that for CEA in the CREST study, although the results of the two studies might not be comparable to each other simply as the sample size was different. The stroke events after CAS were lower in our study than in the CREST study because (a) we excluded any patient with too fragile plaques and (b) the protection methods differed in the two studies—70 cases (59%) in our study used a distal filter combined with flow reversal using a guiding catheter with balloon, whereas only distal filter was used in the CREST study. It is possible that using a distal filter protection with proximal occlusion decreased ipsilateral stroke events. Furthermore, CAS under our protocol was noninferior to CEA in the CREST. Thus, advanced age alone should not preclude the use of CAS.

Conclusion

The incidence of new DWI lesions after CAS was the highest in the group aged $\geq 80$ years; however, there was no age-related increase in the incidence of postoperative stroke. Advanced age alone should not preclude the use of CAS, though attention must be paid to plaque vulnerability at the target site and atherosclerosis of the access route.

The authors declare that they have no conflicts of interest.
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