

PERIPHERAL

# Carotid Artery Stenting

## Investigation of Plaque Protrusion Incidence and Prognosis



Masashi Kotsugi, MD,<sup>a</sup> Katsutoshi Takayama, MD,<sup>b</sup> Kaoru Myouchin, MD,<sup>b</sup> Takeshi Wada, MD,<sup>c</sup>  
Ichiro Nakagawa, MD,<sup>d</sup> Hiroyuki Nakagawa, MD,<sup>c</sup> Toshiaki Taoka, MD,<sup>c</sup> Shinichiro Kurokawa, MD,<sup>a</sup>  
Hiroyuki Nakase, MD,<sup>d</sup> Kimihiko Kichikawa, MD<sup>c</sup>

### ABSTRACT

**OBJECTIVES** This study sought to clarify the incidence and prognosis of PP in carotid artery stenting (CAS).

**BACKGROUND** Projections thought to be plaque may be observed inside the stent on angiography or intravascular ultrasound (IVUS) during CAS. Known as plaque protrusion (PP), the incidence and prognosis of this complication are unclear.

**METHODS** A total of 354 consecutive carotid atherosclerotic stenoses in 328 patients (285 men, 43 women; age range 51 to 97 years [mean age 73.6 years]; 158 symptomatic cases; stenosis rate, 50% to 99% [mean 81.0%]) who underwent CAS under IVUS between October 2007 and March 2016 were retrospectively analyzed. PP was defined as plaque seen inside the stent lumen on both digital subtraction angiography and IVUS. The incidence and prognosis (rate of stroke within 30 post-operative days) of PP and the rate of ischemic lesions on the treated side on diffusion-weighted imaging performed within 48 post-operative hours within the PP group were investigated.

**RESULTS** PP was observed in 9 cases (2.6%). Ischemic stroke occurred in 6 of 9 PP cases (66.7%; 1 major, 5 minor). Ischemic lesions were observed on diffusion-weighted imaging in 8 of 9 cases (88.9%). PP was strongly associated with perioperative ischemic stroke. A significant increase in PP susceptibility was observed with open-cell stent use and unstable plaque.

**CONCLUSIONS** The incidence of PP in CAS was 2.6%, with a high risk of ischemic complications if PP was observed. The present findings indicate the necessity of appropriate device selection to avoid PP.  
(J Am Coll Cardiol Intv 2017;10:824-31) © 2017 by the American College of Cardiology Foundation.

Carotid artery stenting (CAS) is effective for patients at high risk and for those at conventional risk for carotid endarterectomy (CEA), and it is becoming an alternative to CEA (1). Recent randomized controlled trials of CAS and CEA for asymptomatic carotid artery stenosis among patients at conventional risk for surgical complications (2) also

concluded that CAS and CEA are equally effective. On the other hand, the rate of periprocedural stroke is higher with CAS than with CEA (1,3). Factors involved in periprocedural ischemic complications in CAS include protection devices, stent design, technical expertise, patient age, and plaque characteristics (4-10). Furthermore, periprocedural stroke is closely

From the <sup>a</sup>Departments of Neurosurgery, Ishinkai Yao General Hospital, Yao, Japan; <sup>b</sup>Department of Radiology and Interventional Neuroradiology, Ishinkai Yao General Hospital, Yao, Japan; <sup>c</sup>Department of Radiology, Nara Medical University, Nara, Japan; and the <sup>d</sup>Department of Neurosurgery, Nara Medical University, Nara, Japan. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

associated with distal embolization of embolic material from plaque during CAS (11); thus, reducing the amount of embolic material such as plaque is important.

SEE PAGE 832

The projection of plaque into the stent lumen during coronary artery stenting is referred to as plaque protrusion (PP) and plaque prolapse, and it occurs at a rate of 11% to 22.5% (12,13). PP is not associated with periprocedural ischemic events (14), but it has similarly been recognized during CAS (15,16), although its incidence and prognosis have remained unclear. The present study therefore aimed to clarify the incidence and prognosis of PP during CAS.

## METHODS

A total of 354 consecutive carotid atherosclerotic stenoses in 328 patients (285 men, 43 women; age range 51 to 97 years [mean age 73.6 years]; 158 symptomatic cases; stenosis rate (NASCET [North American Symptomatic Carotid Endarterectomy Trial] method), 50% to 99% [mean 81.0%]) who underwent CAS under intravascular ultrasound (IVUS) at our hospital or an affiliated institution between October 2007 and March 2016 were retrospectively analyzed. The study was approved by each hospital's research ethics committee.

**CAS PROCEDURE.** At least 1 week before CAS, 100 mg aspirin and 1 other antiplatelet agent (clopidogrel 75 mg/day, cilostazol 200 mg/day, or ticlopidine 100 to 200 mg/day) were administered and continued for at least 30 days after CAS. Unfractionated heparin was administered during the procedure to maintain an activated clotting time over 300 s in cases using Angioguard (Cordis Endovascular, Miami, Florida) and over 275 s in cases when other embolic protection devices (EPDs) were used. CAS was performed by standard techniques using an EPD and conservative post-dilatation using a percutaneous transluminal angioplasty balloon (balloon diameter  $\leq$ 80% of the normal lumen diameter of the distal internal carotid artery) in all cases. IVUS was performed before the procedure and immediately following post-dilatation. Technical success was defined that the minimum lesion diameter after post-dilatation on IVUS was at least over 2 mm or residual stenosis was  $<$ 30% on digital subtraction angiography (DSA).

**INTRAVASCULAR ULTRASOUND.** A Volcano Visions PV 0.014 inch (between October 2007 and June 2014) or a Volcano Visions PV 0.014 inch (between July 2014 and March 2016) IVUS (Volcano Corporation, Rancho Cordova, California) catheter and the Volcano s5 Imaging System were used. ChromaFlo IVUS (Volcano Corporation), which can be used with this system, colorizes the flow and displays the results immediately. The addition of colorized flow assists the IVUS operator to more readily recognize the true lumen and verify the presence of blood flow.

## MAGNETIC RESONANCE IMAGING TECHNIQUE.

**MR plaque imaging.** Magnetic resonance (MR) imaging for plaque characterization was performed on 1.5- or 3-T scanners. A 2-dimensional T1-weighted fast spin echo sequence was performed using a black blood, double inversion, recovery preparation pulse, and a fat-saturation pulse. The signal intensities were evaluated for the carotid plaque at the most severely stenotic level. Main plaque components were classified as unstable plaque (intraplaque hemorrhage and lipid-rich or necrotic core) and stable plaque (fibrous tissue and dense calcification) based on the signal pattern of the plaque images.

**Diffusion-weighted imaging.** A high-signal area of  $\leq$ 10 mm on the ipsilateral side on diffusion-weighted imaging (DWI) was defined as an ischemic lesion, with  $\geq$ 10 lesions defined as multiple lesions.

**Definition of PP.** PP was defined as observation of plaque inside the stent lumen after post-dilatation on both DSA and IVUS.

**Endpoint.** The primary endpoint of the study was the incidence and prognosis of PP. Prognosis was defined as rate of stroke within 30 post-operative days. Stroke was defined as an ischemic neurologic deficit that persisted for more than 24 h. It was classified as major or minor using the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) (major: NIHSS score  $>$ 5 or mRS score  $>$ 2; minor: NIHSS score  $\leq$ 4 and mRS score  $\leq$ 2). A transient ischemic attack (TIA) was defined as temporary neurological symptoms lasting  $<$ 24 h; TIAs were not included in stroke. The secondary endpoint of the study was the rate of new ipsilateral ischemic lesions on DWI within 48 h after the procedure within PP group.

**STATISTICAL ANALYSIS.** Data are expressed as mean  $\pm$  SD for continuous variables and as frequencies for categorical variables. Continuous variables were compared by the 2-sample *t* test or the

## ABBREVIATIONS AND ACRONYMS

- CAS** = carotid artery stenting
- CEA** = carotid endarterectomy
- DSA** = digital subtraction angiography
- DWI** = diffusion-weighted imaging
- EPD** = embolic protection device
- IVUS** = intravascular ultrasound
- MR** = magnetic resonance
- NIHSS** = National Institutes of Health Stroke Scale
- mRS** = modified Rankin Scale
- PP** = plaque protrusion
- TIA** = transient ischemic attack

	PP (+) Group (n = 9)	PP (-) Group (n = 345)	p Value	Standardized Difference
Age, yrs	74.1 ± 6.6	73.6 ± 7.6	0.84	0.070
Male	8 (88.9)	301 (87.2)	0.88	0.050
Female	1 (11.1)	44 (12.8)	0.88	0.050
Stenosis, %	79.8 ± 9.4	81.1 ± 11.6	0.73	0.123
Hypertension	8 (88.9)	280 (81.2)	0.56	0.218
Diabetes mellitus	6 (66.7)	141 (40.9)	0.12	0.536
Hyperlipidemia	3 (33.3)	179 (51.9)	0.27	0.382
Smoker	1 (11.1)	111 (32.2)	0.18	0.529
Hemodialysis patients	0 (0.0)	5 (1.5)	0.72	0.171
Symptomatic lesion	2 (22.2)	156 (45.2)	0.17	0.501
Pre-operative statin treatment	6 (66.7)	204 (59.1)	0.65	0.156
Antiplatelet agent				
Aspirin 100 mg + clopidogrel 75 mg	4 (44.4)	214 (62.0)	0.27	0.358
Aspirin 100 mg + cilostazol 200 mg	4 (44.4)	117 (33.9)	0.53	0.217
Aspirin 100 mg + ticlopidine 100-200 mg	1 (11.1)	10 (2.9)	0.16	0.326
Clopidogrel 75 mg only	0 (0.0)	1 (0.3)	0.87	0.076
Lesion length				
Short (≤20 mm)	7 (77.8)	205 (59.4)	0.26	0.403
Long (>20 mm)	2 (22.2)	140 (40.6)		
Stent				
Precise	9 (100.0)	204 (59.1)	0.013*	1.176
Carotid wall stent	0 (0.0)	116 (33.6)	0.034*	1.007
Protege	0 (0.0)	25 (7.2)	0.4	0.395
Embolic protection device				
Angioguard	5 (55.6)	123 (35.7)	0.22	0.408
Filter Wire EZ	2 (22.2)	143 (41.4)	0.25	0.422
Moma Ultra	2 (22.2)	70 (20.3)	0.87	0.047
Spider	0 (0.0)	7 (2.0)	0.67	0.204
PercuSurge	0 (0.0)	2 (0.6)	0.82	0.108

Values are mean ± SD or n (%). Precise (Cordis, Johnson & Johnson, Miami, Florida); Carotid wall stent (Boston Scientific, Natick, Massachusetts); Protege (ev3, Plymouth, Minnesota); embolic protection device, Angioguard (Cordis Endovascular, Miami, Florida); Filter Wire EZ (Boston Scientific); Moma Ultra (ev3 Covidien, Irvine, California); Spider (ev3 Covidien); PercuSurge (Medtronic, Minneapolis, Minnesota). \*p < 0.05.  
PP = plaque protrusion.

Wilcoxon rank sum test, and categorical variables were compared by the chi-square test or Fisher exact test. Multiple logistic regression analysis was performed to identify independent predictors of PP. Significance was defined as a 2-sided p value <0.05. JMP version 9 (SAS Institute, Cary, North Carolina) was used for all statistical analyses.

## RESULTS

**Table 1** shows the patient's baseline clinical characteristics.

**CAS PROCEDURE DETAILS.** CAS was successfully performed for all 354 cases. The following EPDs were used: Angioguard (Cordis Endovascular),

Technical success	354/354 (100)
30-day major adverse event rate	13 (3.7)
Stroke	11 (3.1)
Ipsilateral stroke	10 (2.8)
Major stroke	1 (0.3)
Minor stroke	9 (2.5)
Transient ischemic attack	9 (2.5)
Myocardial infarction	2 (0.6)
Death	0 (0.0)

Values are n (%).

n = 128; FilterWire EZ (Boston Scientific, Natick, Massachusetts), n = 145; MoMa Ultra (ev3 Covidien, Irvine, California), n = 72; Spider (ev3 Covidien), n = 7; and PercuSurge (Medtronic, Minneapolis, Minnesota), n = 2. The following stents were used: Precise (Cordis, Johnson & Johnson, Miami, Florida), n = 213; Carotid Wallstent (Boston Scientific), n = 116; and Protege (ev3, Plymouth, Minnesota), n = 25 (**Table 1**).

**ANTIPLATELET AGENT.** Basically, 100 mg aspirin and 1 other antiplatelet agent (clopidogrel 75 mg/day, n = 218; cilostazol 200 mg/day, n = 121; or ticlopidine 100 to 200 mg/day, n = 11) were administered. In only 1 case, 1 antiplatelet agent (clopidogrel 75 mg/day) was administered. In 3 cases, information about antiplatelet agent use was not available.

**STATIN THERAPY.** Statins were administered before CAS in 210 lesions: pitavastatin 1 to 4 mg/day, n = 47; rosuvastatin 2.5 to 5.0 mg/day, n = 106; pravastatin 5 to 20 mg/day, n = 30; atorvastatin 5 to 10 mg/day, n = 26; and fluvastatin 30 mg/day, n = 1. In 1 case, information about statin use was not available.

## OUTCOMES OF THE PROCEDURE AT 30 DAYS.

Ipsilateral ischemic stroke occurred within 30 post-operative days in 10 cases (2.8%), of which 1 (0.3%) was a major stroke. A TIA occurred in 9 cases (2.6%). There were no deaths (**Table 2**). In most cases, stroke symptoms were observed immediately post-dilatation. In 2 cases, a TIA occurred on day 5 and day 7 after CAS. All cases were hospitalized for at least 1 week after the procedure.

## NEW ISCHEMIC LESIONS ON DWI AND MR PLAQUE IMAGING.

DWI was performed for 344 cases within 48 h after the procedure. DWI could not be performed in 4 cases due to a pacemaker. Further DWI was not performed in 3 cases for unspecified reasons. Ipsilateral ischemic lesions on DWI were observed in 124 cases (35.7%).

**TABLE 3 IVUS and DSA Findings for PP**

	PP (+) on DSA	PP (-) on DSA
PP (+) on IVUS	9	18
PP (-) on IVUS	0	325

Values are n.  
 DSA = digital subtraction angiography; IVUS = intravascular ultrasound;  
 PP = plaque protrusion.

In all but 19 cases, lesions were evaluated by MR plaque imaging within 1 month before CAS. On pre-operative MR plaque imaging, 141 cases (42.1%) were classified as unstable plaque, and 194 cases (57.9%) were classified as stable plaque. In cases classified as unstable plaque, ipsilateral ischemic lesions on DWI were observed in 52 cases (37.1%), and in cases classified as stable plaque, ipsilateral ischemic lesions on DWI were observed in 65 cases (33.5%). In 1 case, MR imaging after CAS could not be performed because of implantation of a temporary pacemaker. There was no significant difference in the rate of ischemic lesions between the unstable plaque group and the stable plaque group ( $p = 0.49$ ).

Ipsilateral ischemic lesions were observed on DWI in 238 cases (39.1%) in which CAS was performed using open-cell stents, whereas ipsilateral ischemic lesions were observed on DWI in 116 cases (26.7%) in which CAS was performed using closed-cell stents; the difference was significant ( $p = 0.016$ ).

**PP INCIDENCE ON IVUS.** Pre-CAS IVUS was performed in 354 cases, and post-CAS IVUS was performed in 352 cases. In 2 cases, IVUS after stent placement could not be performed because the IVUS probe caught the stent strut and broke. There were 27 cases (7.6%) in which PP could be confirmed with IVUS. On the other hand, there were only 9 cases (2.6%) in which PP could be confirmed with DSA. There were no cases of PP that could be confirmed by DSA but could not be confirmed by IVUS (Table 3).

**INCIDENCE AND PROGNOSIS OF PP.** PP that was confirmed by DSA and IVUS was observed in 9 cases (2.6%). Ischemic stroke occurred in 6 of 9 cases of PP (66.7%; Table 4), 1 of which (11.1%) was a major stroke. Stent-in-stent placement was performed for 4 of 9

cases of PP. There was a significant difference in the rate of ischemic stroke between the PP (+) group and the PP (-) group (Table 4). In all 6 cases in which ischemic stroke occurred (Figure 1), symptoms were observed within 24 h after the procedure. Ischemic symptoms occurred more than 24 h after the procedure in 2 cases, but in both cases, no PP was recognized during the procedure. In 1 case, the onset of symptoms occurred on day 5, and in another case, the onset of symptoms occurred on day 7. In both cases, PP was suspected on carotid ultrasound examination, so emergency angiography was performed. Because PP was observed with IVUS and DSA, stent-in-stent placement was performed using EPD, and PP disappeared. In both cases, the symptoms disappeared within 24 h from the onset of symptoms. TIA and ischemic symptoms were not observed between day 7 and day 30 after the procedure.

**NEW IPSILATERAL ISCHEMIC LESIONS ON DWI IN PP CASES.** In 9 cases of PP, ipsilateral ischemic lesions were observed on DWI in 8 cases (88.9%), 7 of which (77.8%) were multiple lesions.

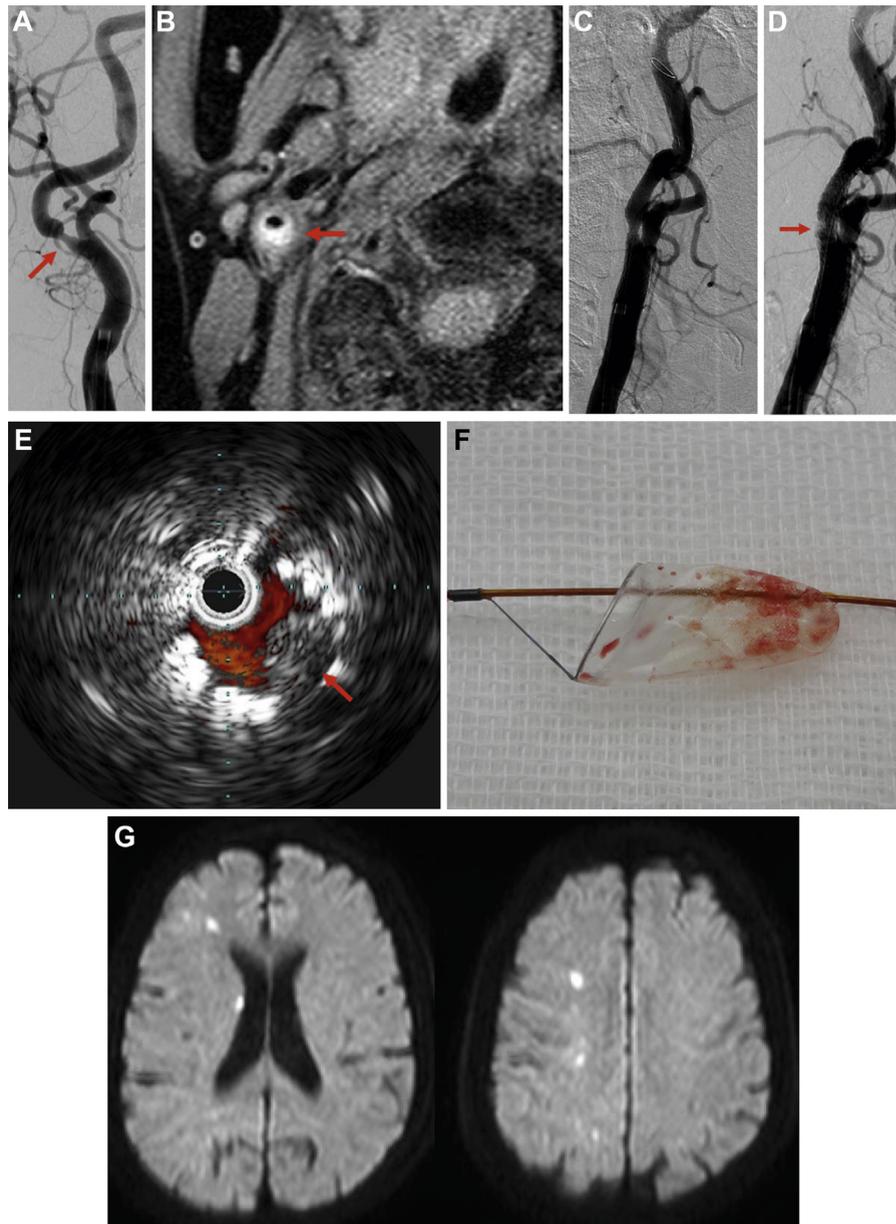
**RISK FACTORS FOR PP.** An open-cell stent was used for initial stenting in all cases in the PP (+) group. A significant increase in PP susceptibility was observed with open-cell stent use (Table 5). Pre-operative symptomatic lesions were present in 2 cases, and 8 of 9 cases had unstable plaque on MR plaque imaging. A significant increase in PP susceptibility was also observed in cases with unstable plaque (Table 6).

Comorbidities of the study group included hypertension in 288 (81.4%), diabetes mellitus in 147 (41.5%), hyperlipidemia in 182 (51.4%), smoking in 112 (31.6%), and hemodialysis in 5 (1.4%). There were no significant differences in parameters other than stent design between the PP (+) group and the PP (-) group: age ( $74.1 \pm 6.6$  years vs.  $73.6 \pm 7.6$  years); sex (male 8, female 1 vs. male 301, female 44); type of lesion (symptomatic: 2 vs. 156, asymptomatic: 7 vs. 189); length of lesion (short,  $\leq 20$  mm: 7 vs. 205; long,  $> 20$  mm: 2 vs. 140); hypertension (8 vs. 280); diabetes mellitus (6 vs. 141); hyperlipidemia (3 vs. 179); smoking (1 vs. 111); hemodialysis (0 vs. 5); severity of stenosis ( $79.8 \pm 9.4\%$  vs.  $81.1 \pm 11.6\%$ ); antiplatelet agent (aspirin + clopidogrel: 4 vs. 214; aspirin + cilostazol: 4 vs. 117; aspirin + ticlopidine: 1 vs. 10); pre-operative statin treatment (6 [pitavastatin: 1, rosuvastatin: 2, pravastatin: 2, atorvastatin: 1] vs. 204 [pitavastatin: 46, rosuvastatin: 104, pravastatin: 28, atorvastatin: 25, fluvastatin: 1]); EPD (Angioguard: 5 vs. 123; FilterWire EZ: 2 vs. 143; MoMa Ultra: 2 vs. 70; Spider: 0 vs. 7; PercuSurge: 0 vs. 1).

**TABLE 4 Ischemic Stroke Rate in the 2 Groups**

	PP (+) Group (n = 9)	PP (-) Group (n = 345)
Stroke (+)	6	4
Stroke (-)	3	341

Values are n.  $p < 0.0001$ .  
 PP = plaque protrusion.

**FIGURE 1** Plaque Protrusion Case During Carotid Artery Stenting Using the FilterWire EZ and Precise Stent

(A) Right common carotid artery angiograms (lateral view) show high-grade stenosis of the right internal carotid artery (arrow). (B) Magnetic resonance plaque imaging shows unstable plaque at the right internal carotid artery stenosis (arrow). (C) Post-dilatation with a balloon (4-mm diameter) following stent placement. (D) Right CCA angiogram immediately following post-dilatation shows plaque protrusion inside the stent lumen (arrow). (E) Intravascular ultrasound shows plaque inside the stent lumen after post-dilatation (arrow). (F) Retrieved filter, which contains a large amount of debris. (G) Diffusion-weighted imaging on the next day reveals multiple bright lesions on the ipsilateral side.

## DISCUSSION

Cases of PP in CAS have been reported; only 2 papers on intraoperative PP have been published, reporting a

rate of 7.8% to 10% (15,16). In the present study, the PP rate was 2.6%, which was much lower than in the previous study, because PP was confirmed on both IVUS and DSA. In the present study, the PP rate on

**TABLE 5 PP Incidence by Stent Design**

	PP (+) Group (n = 9)	PP (-) Group (n = 345)
Open-cell stent	9	229
Closed-cell stent	0	116

Values are n. p < 0.034.  
 PP = plaque protrusion.

IVUS alone also was 7.6%. This result was similar to that of a previous study. Shinozaki et al. (16) also reported that the PP rate was 7.8% with IVUS and 2.6% with DSA. This result demonstrated that PP can be detected more frequently by IVUS than by DSA.

Although PP was strongly associated with perioperative ischemic stroke in the present study, 2 previous studies showed no correlation with ischemic complications. This result may be due to the small sample size (n = 30 and n = 77, respectively) and to fewer cases of large-volume convex PP that could be confirmed by DSA compared with the current study. This study confirmed that the risk factor of PP was associated with unstable plaque. Based on this finding, distal embolism may have occurred because of soft plaque.

Conversely, many studies have indicated a correlation between post-operative PP and symptomatic complications. In an investigation of 32 consecutive cases (17), PP was found in 8 cases (25%), of which 1 (12.5%) developed a minor stroke. Ozaki et al. (18) reported a rate of delayed PP of 4.95% (5 of 101), of which 1 case (approximately 1%) developed ischemic complications. With regard to the timing of onset of PP, various timings of onset of post-operative PP have been reported, such as within a week or within 1 to 4 weeks (17,18). Ischemic complications can arise with post-operative PP even if the PP does not occur immediately after stenting. In the present study, PP occurred later in 2 cases in which PP was not confirmed during the CAS procedure. Ischemic stroke did not occur because emergency additional treatment was performed, though ischemic stroke may have occurred had there been no additional treatment. Huibers et al. (19) reported that in 761 CAS cases ischemic strokes occurred in 76.4% within 24 h after the procedure, and in 12.7% between day 1 and day 7 after the procedure.

**TABLE 6 PP Incidence by Plaque Morphology**

	PP (+) Group (n = 9)	PP (-) Group (n = 326)
Stable plaque	1	193
Unstable plaque	8	133

Values are n. p < 0.004.  
 PP = plaque protrusion.

Although the rate of PP was not evaluated in this study (19), the result suggests that PP may be associated with delayed ischemic complications.

The advantage of CAS under IVUS is that it is possible to select the optimal stent size, because accurate vessel diameter can be measured. It is also possible to evaluate lumen diameter and stent malposition just after stent placement. A previous study suggested that larger stent diameters induced embolization of unstable plaque elements (20). Thus, PP may be reduced by choosing optimal stent diameters using IVUS. Furthermore, the lumen after stent placement can be evaluated immediately using ChromaFlo-IVUS, and PP can be confirmed more easily. Among the limitations of IVUS in the setting of carotid artery assessment, it is difficult to accurately evaluate lumens and PP because of artifacts if there is advanced calcification. Furthermore, there is the risk of distal embolism and vascular injury due to operation of the IVUS, and there is a possibility that the IVUS catheter cannot pass through the lesion because of advanced calcification. However, none of these occurred in the current study.

In the present study, there was a significant association between PP and ischemic stroke, unlike in previous studies. This result may indicate that ischemic stroke was not associated with small-volume PP but with large-volume PP. Shinozaki et al. (16) suggested that their PP cases did not become symptomatic because additional stenting for PP successfully resolved any PP that occurred intraoperatively. In the present study, no additional treatment was given to the 5 early cases of PP. In 4 cases, stroke was observed. In the 4 recent PP cases, and in the 2 delayed PP cases, stent-in-stent placement was performed until PP disappeared. However, except for 4 cases, stroke was observed, and 1 case was a major stroke. Thus, to prevent perioperative ischemic stroke, it is more important to not induce PP.

Our recent strategy is as follows: if PP occurs, we perform IVUS and then check large-volume PP to determine if it is convex. In a case of convex PP, we perform stent-in-stent placement using closed-cell stents until the PP disappears. In a case of non-convex PP, we observe for 5 to 10 min, and, then, if the PP is not changed, careful clinical follow-up is considered within 30 days after CAS. If the PP enlarges, stent-in-stent placement is performed until PP disappears.

A significantly lower rate of ipsilateral ischemic lesions on DWI after CAS has been already reported with closed-cell stent use than with open-cell stent use in CAS (31% vs. 51%), with a DWI-positive rate similar to the present result. However, in the PP

group, ipsilateral ischemic lesions were observed in 8 cases (88.9%), 7 of which (77.8%) were multiple lesions. This DWI-positive rate was very high compared with a DWI-positive rate of 35.7% in all of the present cases or in previous studies. New ischemic lesions, even without corresponding focal deficits, might also lead to long-term clinical consequences, including cognitive decline and dementia (21). Thus, reducing ischemic lesions as much as possible is essential in CAS, and even if a patient with PP is asymptomatic, PP should be avoided.

The present findings showed that PP was related to ischemic stroke, although an EPD was used in all cases. The present results suggest that the protective effect of an EPD against stroke may be limited in cases of PP and may indicate it is not the EPD but rather avoiding PP that is necessary to prevent periprocedural ischemic stroke. The risk factors for unstable plaque and open-cell stents were present in the current study; placement of open stents with a high radial force may have led to disintegration of soft, unstable plaque, causing PP. Investigation of the rate of ischemic complications by stent-free cell size also demonstrated a lower rate of post-operative ischemic complications as stent-free cell area became smaller (5). CAS should be performed using a stent with as small a free cell area as possible to prevent PP.

Micromesh stents with a small free cell area, such as Roadsaver (Terumo, Tokyo, Japan) (closed-cell design; cell size, 375 to 500  $\mu\text{m}$ ) or C-guard (inspireMD, Boston, Massachusetts) (open cell, 150 to 180  $\mu\text{m}$ ) stents, have recently been developed. The PARADIGM study using the Roadsaver (Terumo) reported 1 case of a minor stroke event from among 106 cases (0.9%) (22). In their investigation of 100 CAS cases using C-guard stents (inspireMD), Musialek *et al.* (23) also reported only 1 case of a minor stroke event (1.0%). As an explanation, Schofer *et al.* (24) stated that the structural characteristics of the C-guard (inspireMD) stent reduce the incidence of PP and ischemic complications that can be confirmed on post-operative MR imaging. These reports suggest that use of a micromesh stent reduces ischemic complications by reducing PP occurrence. Thus, stent selection is important for preventing PP and avoiding ischemic complications, and expectations for micromesh stents are high. On the basis of this

study, we now select a closed-cell stent first when the plaque is evaluated as unstable before the procedure. It appears that the incidence of PP is decreased by reducing the free cell area of the stent.

**STUDY LIMITATIONS.** The design was retrospective, and all PP occurred in the setting of 1 open stent cell type. The length of follow-up was limited to 30 days, and IVUS was not routinely performed in clinical practice after CAS. Furthermore, PP occurred in only a few cases, and only 1 stroke was a major stroke. Therefore, further investigation with a larger number of cases is required to evaluate the incidence of PP and associated risk factors.

## CONCLUSIONS

The incidence of PP in CAS in the present study was 2.6%, and PP was strongly correlated with perioperative ischemic complications. Preventive device selection and technique are necessary to avoid PP.

**ACKNOWLEDGEMENT** The authors would like to acknowledge Takashi Inoue, MPH (Institute for Clinical Translational Science, Nara Medical University), for his help with data analysis.

**ADDRESS FOR CORRESPONDENCE:** Dr. Masashi Kotsugi, Departments of Neurosurgery, Ishikai Yao General Hospital, 1-41 Numa Yao, Osaka 581-0036, Japan. E-mail: [igustok@naramed-u.ac.jp](mailto:igustok@naramed-u.ac.jp).

## PERSPECTIVES

**WHAT IS KNOWN?** The incidence and prognosis of PP during CAS have been unclear.

**WHAT IS NEW?** The present study showed that the incidence of PP was 2.6%, and PP was strongly associated with ischemic stroke. The risk factors for PP were unstable plaque and open-cell stent use.

**WHAT IS NEXT?** Selecting a stent with a small free cell area is necessary to avoid PP, and a micromesh stent is expected to contribute greatly to the prevention of PP.

## REFERENCES

1. Brott TG, Hobson RW 2nd, Howard G, *et al.* Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;363:11–23.
2. Rosenfield K, Matsumura JS, Chaturvedi S, *et al.* Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med* 2016;374:1011–20.
3. Ederle J, Dobson J, Featherstone RL, *et al.* Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an

interim analysis of a randomised controlled trial. *Lancet* 2010;375:985-97.

4. Hobson RW 2nd, Howard VJ, Roubin GS, et al. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. *J Vasc Surg* 2004;40:1106-11.
5. Bosiers M, de Donato G, Deloose K, et al. Does free cell area influence the outcome in carotid artery stenting? *Eur J Vasc Endovasc Surg* 2007;33:135-41; discussion 142-3.
6. Jansen O, Fiehler J, Hartmann M, Bruckmann H. Protection or nonprotection in carotid stent angioplasty: the influence of interventional techniques on outcome data from the SPACE Trial. *Stroke* 2009;40:841-6.
7. Lal BK, Brott TG. The Carotid Revascularization Endarterectomy vs. Stenting Trial completes randomization: lessons learned and anticipated results. *J Vasc Surg* 2009;50:1224-31.
8. Hopkins LN, Roubin GS, Chakhtoura EY, et al. The Carotid Revascularization Endarterectomy versus Stenting Trial: credentialing of interventionalists and final results of lead-in phase. *J Stroke Cerebrovasc Dis* 2010;19:153-62.
9. Sakamoto M, Taoka T, Nakagawa H, et al. Magnetic resonance plaque imaging to predict the occurrence of the slow-flow phenomenon in carotid artery stenting procedures. *Neuroradiology* 2010;52:275-83.
10. Yoshimura S, Yamada K, Kawasaki M, et al. High-intensity signal on time-of-flight magnetic resonance angiography indicates carotid plaques at high risk for cerebral embolism during stenting. *Stroke* 2011;42:3132-7.
11. Wehman JC, Holmes DR Jr., Ecker RD, et al. Intravascular ultrasound identification of intraluminal embolic plaque material during carotid angioplasty with stenting. *Catheter Cardiovasc Interv* 2006;68:853-7.
12. Hong MK, Park SW, Lee CW, et al. Long-term outcomes of minor plaque prolapsed within stents documented with intravascular ultrasound. *Catheter Cardiovasc Interv* 2000;51:22-6.
13. Agrawal M, Hakeem A, Ahmed Z, Uretsky BF. Utility of frequency domain optical coherence tomographic evaluation of angiographically optimized stented lesions. *J Invasive Cardiol* 2016;28:94-7.
14. Qiu F, Mintz GS, Witzenbichler B, et al. Prevalence and clinical impact of tissue protrusion after stent implantation: an ADAPT-DES Intravascular Ultrasound Substudy. *J Am Coll Cardiol* 2016;9:1499-507.
15. Chiocchi M, Morosetti D, Chiaravalloti A, Loreni G, Gandini R, Simonetti G. Intravascular ultrasound assisted carotid artery stenting: randomized controlled trial. Preliminary results on 60 patients. *J Cardiovasc Med (Hagerstown)* 2013 Jan 3 [E-pub ahead of print].
16. Shinozaki N, Ogata N, Ikari Y. Plaque protrusion detected by intravascular ultrasound during carotid artery stenting. *J Stroke Cerebrovasc Dis* 2014;23:2622-5.
17. Hashimura N, Mutoh T, Matsuda K, Matsumoto K. Evaluation and management of plaque protrusion or thrombus following carotid artery stenting. *Neurol Med Chir (Tokyo)* 2015;55:149-54.
18. Ozaki S, Tagawa M, Matsumoto S, et al. [Pathogenesis of in-stent thrombosis after carotid artery stenting]. *No Shinkei Geka* 2014;42:1009-17.
19. Huibers A, Calvet D, Kennedy F, et al. Mechanism of procedural stroke following carotid endarterectomy or carotid artery stenting within the International Carotid Stenting Study (ICSS) randomised trial. *Eur J Vasc Endovasc Surg* 2015;50:281-8.
20. Casserly IP, Abou-Chebl A, Fathi RB, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: predictors and clinical outcome. *J Am Coll Cardiol* 2005;46:1466-72.
21. Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol* 2009;8:1006-18.
22. Bosiers M, Deloose K, Torsello G, et al. The CLEAR-ROAD study: evaluation of a new dual layer micromesh stent system for the carotid artery. *EuroIntervention* 2016;12:e671-6.
23. Musialek P, Mazurek A, Trystula M, et al. Novel PARADIGM in carotid revascularisation: Prospective evaluation of All-corer perCutaneous cArotid revascularisation in symptomatic and Increased-risk asymptomatic carotid artery stenosis using CGuard MicroNet-covered embolic prevention stent system. *EuroIntervention* 2016;12:e658-70.
24. Schofer J, Musialek P, Bijuklic K, et al. A prospective, multicenter study of a novel mesh-covered carotid stent: the CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet). *J Am Coll Cardiol Intv* 2015;8:1229-34.

---

**KEY WORDS** carotid artery stenting, intravascular ultrasound, IVUS, plaque prolapse, plaque protrusion