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Original Article

# Safety and Risk Factors of Carotid Artery Stenting with Simple Distal Filter Protection: A Single-Center Retrospective Study

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**Objective:** Carotid artery stenting embolic protection devices offer various options, among which distal filter protection is the simplest and easiest to handle. However, compared to balloon protection systems, distal filter protection has more embolic complications. Therefore, we explored the risk factors of distal filter protection, intending to achieve a safer carotid artery stenting. This retrospective study was conducted to identify prognostic factors following carotid artery stenting with only distal filter protection from July 2010 to June 2021.

**Methods:** Information on patient background, procedures and devices, and complications was collected using medical records. The data pertaining to 187 patients were analyzed after excluding the data of patients in whom other protection devices (8 cases) were used. We used FilterWire EZ as the first choice for embolic protection device and SpiderFX when the patients had difficult-to-cross lesions.

**Results:** The patients' mean age was 71.9 ± 6.9 years, and 72 (38.5%) were symptomatic. Symptomatic (odds ratio: 2.02, p = 0.035) and difficult-to-cross lesions (odds ratio: 3.63, p = 0.0013) were factors independently associated with symptomatic complications.

**Conclusion:** This retrospective single-center study established independent prognostic factors for carotid artery stenting with distal filter protection. For patients with symptomatic lesions and severe stenosis or bends that are difficult to pass through, it is necessary to be careful when performing carotid artery stenting with distal filter protection.

**Keywords** carotid artery stenting, distal filter protection, severe stenosis, prognosis

## Introduction

Recently, protection devices for carotid artery stenting (CAS) are becoming more complex with several options available. No device is clearly the best, and randomized clinical trials have not shown a clear advantage of any of the available devices.[1,2] Two main types of embolic protection devices (EPD) are available: distal filter protection (DFP) and balloon protection system (BPS). Of these, DFP (41.4%) is the predominantly employed EPD in the recent Japanese Nationwide Retrospective Multi-Center Registries study, potentially owing to its ease of maneuverability.[3] However, it has been reported that embolic complications occur more frequently with DFP than with BPS,[4] and various techniques with BPS have been found useful, especially for patients with unstable plaques.[5–7] In theory, intricate protection systems are expected to yield fewer embolic complications. Nevertheless, the complexity of such systems introduces additional procedural steps, potentially leading to an increased risk of complications.[8] Therefore, it is important to understand the risks involved in simple CAS with DFP and to select target patients carefully to ensure adequate safety with a simple procedure.

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Furthermore, more complicated systems lead to higher costs. In Japan, the FilterWire EZ (Boston Scientific, Natick, Massachusetts, USA; hereafter referred to as FilterWire) was approved for national health insurance coverage for use in CAS in 2010,[9] and the SpiderFX (Medtronic, Minneapolis, MN, USA) was approved in 2012.

Since then, DFP has been consistently employed as the EPD in almost all CAS procedures conducted at our institution, including those involving unstable plaques. In the future, various types of DFP are expected to see increased utilization. The objective of this retrospective study was to pinpoint the risk factors influencing the outcomes and complications linked to DFP usage in CAS for patients with carotid artery stenosis, as well as to investigate secure indications for CAS with DFP.

## Materials and Methods

### Study design and patient population

This single-center retrospective cohort study explored the potential risk factors associated with the use of DFP during CAS. The medical records of patients with carotid artery stenosis who underwent CAS at our Medical Center between July 2010 and June 2021 were reviewed. All patients who underwent treatment at the facility during the study period were included in the study. After excluding eight cases in which CAS was performed with non-DFP devices, 187 patients were analyzed. Analyzed data included demographic, clinical, radiological, and treatment-related information, including sex, age, comorbidities (diabetes mellitus, hypertension, hyperlipidemia, and current smoker), symptomatic, stenosis diameter, plaque length, stenosis rate (the North American Symptomatic Carotid Endarterectomy Trial criteria [NASCET]), unstable plaque, and complication. We used preoperative cervical ultrasound examinations to analyze the plaque structure of all patients. An unstable plaque is considered dangerous; however, the choice of treatment method was based on the stenosis rate. We also analyzed procedural factors (i.e., protection device and stent type) and complications (i.e., new high-intensity signal on diffusion-weighted imaging [DWI], stroke event, puncture site hematoma or adverse event, hyperperfusion syndrome, and systemic complications). The protection device and type of stent were selected by the Vice Director. Among complications, stroke was defined as major stroke if it affected modified Rankin scale (mRS) and minor stroke if it did not, and new DWI high-intensity signals were classified as a complication, even if the patient was asymptomatic.

The study protocol was reviewed and approved by the Ethics Committee of Yokohama City University Medical Center, approval number B201100018. Because of the retrospective study design, the Ethics Committee of our Medical Center waived the requirement for written informed consent, offering participants an opt-out option, as per the Personal Information Protection Law and National Research Ethics Guidelines in Japan. The study procedures adhered to the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments.

### CAS procedure

All CAS procedures were performed under the supervision of instructors, and the devices were selected by the instructors. Antiplatelet therapy was initiated more than 7 days prior to the procedure, involving the use of two of the following agents: clopidogrel 75 mg, aspirin 100 mg, cilostazol 200 mg, prasugrel 5 mg, and ticlopidine 100 mg. CAS was performed with the patient under local anesthesia. An 8-Fr guiding catheter was inserted. The activated clotting time was maintained at approximately 280–300 s with intravenous heparin injection. The guidewire and EPD were advanced beyond the lesion, as necessary. FilterWire was the first choice for EPD. If the lesion was difficult to traverse and required preliminary expansion, SpiderFX was used. The Difficult cross to lesion was defined as cases with near total occlusion of the stenotic lesion, complicated ulcerative lesions, cases in which it was expected that FilterWire could not be guided sufficiently distally due to vascular flexion or in which FilterWire was difficult to guide. These were also determined by preoperative cerebral angiography or intraoperatively. The stent was retained after the pre-expansion of the lesion. Post-expansion was performed for each patient. The balloon diameter was set at 80% of the diameter of the internal carotid artery distal to the lesion. Subsequently, all inserted devices were extracted, and the puncture site was sealed through compression hemostasis or hemostatic devices. MRI encompassing DWI, was conducted within 24 h following CAS to assess the treated lesions. Furthermore, rigorous blood pressure control measures were implemented post CAS.

### Postoperative MRI

Patients underwent preprocedural MRI before CAS, followed by a postprocedural MRI within 24 hours after CAS. All imaging protocols incorporated DWI sequences to illustrate areas of acute brain ischemia.

### Procedural outcomes measures

Complications associated with CAS occurring up to 30 days postoperatively were evaluated; those related to CAS were categorized as symptomatic or asymptomatic ischemia, which was detected by a high signal intensity on DWI sequences of MRI, intracranial hemorrhage, hyperperfusion syndrome (HPS), and systemic complications (e.g., acute myocardial infarction, acute exacerbation of chronic kidney dysfunction).

After CAS procedure, optimal medical therapy to prevent stroke included smoking cessation, blood pressure control, and drugs (i.e., dual-antiplatelets-therapy [DAPT] and statins). All patients were administered DAPT for 90 days, with no criteria with regard to specific antiplatelet drugs to be used; after 90 days on DAPT, the medication was switched to single-antiplatelet-therapy (SAPT).

To check the treated lesion, the patients underwent ultrasound and MRI on day 30 and 90 after CAS. Thereafter, we set regular outpatient follow-ups at 6-month intervals.

### Statistical analysis

Results are presented as the mean, standard deviation, and frequency for normally distributed data. For comparisons between groups, Pearson's $\chi^2$ and Wilcoxon tests were performed. A log-rank regression model was used to determine significant differences in clinical variables and CAS procedural factors between the complication and no complication groups with multivariate analysis. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated. A p-value <0.05 was considered statistically significant, and statistical analysis was performed using JMP Pro 15 (SAS Institute Inc., Cary, NC, USA).

## Results

### Patient characteristics

From July 2010 to June 2021, 195 patients underwent CAS; eight were excluded due to the use of a different device in their CAS. Hence, 187 consecutive patients were enrolled in this study. The mean (±SD) participant age was 71.9 ± 6.9 years, and 163 (87.1%) were male. Seventy-two patients (38.5%) had symptomatic internal carotid stenosis. The mean diameter of ICA stenosis was 1.33 ± 0.76 mm, and the mean NASCET was 72.7 ± 14.9%. Prior to the procedure, all patients took >2 antiplatelet agents or anticoagulant combinations, and 127 (67.9%) took statins. Their comorbidities were as follows: hypertension in 154 (82.3%), hyperlipidemia in 135 (72.2%), diabetes in 58 (31.0%), and current smoking in 48 (25.7%) patients (**Table 1**).

**Table 1** Baseline clinical characteristics of patients

| Characteristics | Total number of patients (n = 187) |
|---|---|
| Age (years), mean ± SD | 71.9 ± 6.9 |
| Sex, male (%) | 163 (87.1) |
| Symptomatic | 72 (38.5) |
| Stenosis diameter (mm), mean ± SD | 1.33 ± 0.76 |
| Plaque length (mm), mean ± SD | 15.7 ± 6.7 |
| NASCET (%), mean ± SD | 72.7 ± 14.9 |
| Hypertension | 154 (82.3) |
| Hyperlipidemia | 135 (72.2) |
| Diabetes mellitus | 58 (31.0) |
| Current smoker | 48 (25.7) |
| Medication | |
| DAPT | 170 (91.0) |
| DAPT + anti-coagulation therapy | 17 (9.0) |
| Statin | 127 (67.9) |
| EPD | |
| Filter type | |
| SpiderFX | 10 (5.3) |
| FilterWire | 177 (94.7) |
| Proximal occlusion (Optimo) | 4 (2.1) |
| Stent | |
| Carotid WALLSTENT | 20 (10.7) |
| CASPER | 2 (1.1) |
| Precise | 122 (65.2) |
| Protégé | 43 (23.0) |

DAPT: dual antiplatelet therapy; EPD: embolic protection device; NASCET: North American Symptomatic Carotid Endarterectomy Trial; SD: standard deviation

### CAS procedures and complications

No patients were treated in the acute phase (i.e., within 14 days after ischemic stroke) and no staged CAS was performed. First, the right femoral artery was punctured; in 11 (5.9%) cases, the brachial artery was considered a more appropriate access route and was punctured instead.

In all cases, the EPD was DFP, and proximal balloon protection was used in four cases. The DFP devices used were FilterWire (177 cases, 94.7%) and SpiderFX (10 cases, 5.3%). A total of 10 cases were identified to have a difficult cross to lesion. In all cases, the lesions were successfully passed using SpiderFX (**Table 2**). In 9 of these cases, SpiderFX was used for EPD from the beginning of the procedure. In one case, FilterWire could not be guided sufficiently distally due to distal bending of the stenosis. Therefore, a change to SpiderFX was made intraoperatively and the lesion was allowed to pass. The CAS procedure was performed using an open-cell stent (165 cases,

**Table 2** Difficult to cross the lesion (use SpiderFX)

| Case No | How to use SpiderFX | Reason for using SpiderFX |
|---|---|---|
| 1 | Used from the beginning | Nearly total occlusion |
| 2 | Used from the beginning | Nearly total occlusion |
| 3 | Used from the beginning | Nearly total occlusion |
| 4 | Used from the beginning | Nearly total occlusion |
| 5 | Used from the beginning | Nearly total occlusion |
| 6 | Used from the beginning | Nearly total occlusion |
| 7 | Used from the beginning | Nearly total occlusion |
| 8 | Used from the beginning | Possibility of inability to guide FilterWire sufficiently distal |
| 9 | Used from the beginning | Complicated ulcerative lesions |
| 10 | Initially FilterWire, but changed to SpiderFX | Inability to guide FilterWire sufficiently distal |

**Table 3** Perioperative complications and adverse events within 30 days of CAS

| Event | Number (%) of patients (n = 187) | Asymptomatic lesion (n = 115) | Symptomatic lesion (n = 72) |
|---|---|---|---|
| New high-intensity lesion on DWI | 37 (19.8) | 23 (20.0) | 14 (19.4) |
| Major stroke* | 7 (3.7) | 1 (0.9) | 6 (8.3) |
| Hyperperfusion syndrome | 6 (3.2) | 2 (1.7) | 4 (5.6) |
| Minor stroke | 3 (1.6) | 1 (0.9) | 2 (2.8) |
| Slow/StopFlow | 3 (1.6) | 1 (0.9) | 2 (2.8) |
| TIA | 2 (1.1) | 1 (0.9) | 1 (1.4) |
| Puncture site hematoma or adverse event | 2 (1.1) | 1 (0.9) | 1 (1.4) |
| Death | 2 (1.1) | 1 (0.9) | 1 (1.4) |
| Acute myocardial infarction | 1 (0.5) | 1 (0.9) | 0 |
| Acute exacerbation of chronic kidney dysfunction | 1 (0.5) | 0 | 1 (1.4) |
| Total symptomatic complication | 15 (8.0) | 5 (4.4) | 10 (13.9) |

*Included cerebral infarction and hemorrhage due to hyperperfusion syndrome. CAS: carotid artery stenting; DWI: diffusion-weighted imaging; TIA: transit ischemic attack

88.2%: Precise, 65.2%; Protégé, 23.0%) and a closed-cell stent (22 cases, 11.8%: Carotid WALLSTENT, 10.7%; CASPER, 1.1%) (**Table 1**).

We achieved stenosis expansion for all CAS cases; major adverse events (exacerbated neurological symptoms) occurred in 15 (8.0%) cases. The overall stroke rate was 3.7%; all occurred within 3 days post CAS. One patient experienced myocardial infarction, and two died due to HPS. Cerebral infarction (CI) occurred in five patients (2.7%: two major CI, three minor CI), intracranial hemorrhage in five patients (in all patients due to HPS, 2.7%) and TIA or minor stroke in two patients (1.1%). DWI after CAS revealed a high-intensity area in 37 (19.8%) of 187 procedures.

Among the 115 asymptomatic patients, one patient experienced intracranial hemorrhage because of HPS, one experienced minor CI (0.9%) because of subacute in-stent thrombosis, one experienced TIA (0.9%) within 30 days after CAS, and DWI obtained 24 h after CAS revealed a high-intensity area in 23 procedures (20.0%). Among the 72 symptomatic patients, two patients encountered major CI (2.8%) because of thromboembolic complications; four patients experienced intracranial hemorrhages because of HPS; one experienced TIA (1.4%) within 30 days after CAS; and DWI obtained 24 h after CAS revealed a high-intensity area in 14 (19.4%) procedures (**Table 3**).

### Univariate and multivariate analysis of symptomatic complication risk factor for CAS with filter-type distal embolic protection

The results of the univariate and multivariate analyses of symptomatic complications after CAS are presented in **Table 4**. Overall, 15 patients had symptomatic complications after CAS. Symptomatic lesions (complication vs. no complication; 66.7% vs. 36.0%; $p = 0.019$), plaque length (complication vs. no complication; $18.1 \pm 9.1$ vs. $15.5 \pm 6.4$ mm; $p = 0.016$), and difficult-to-cross lesion (complication vs. no complication; 26.7% vs. 3.5%; $p < 0.001$) were associated with symptomatic complications. In the multivariate logistic analysis, symptomatic lesion (OR, 2.02; 95% CI, 1.08–4.11; $p = 0.035$) and difficult-to-cross lesion (OR, 3.63; 95% CI, 1.62–8.16; $p = 0.0013$) were independently associated with symptomatic complication of CAS with DFP.

**Table 4** Univariate and multivariate analysis of symptomatic complication risk factors for CAS with filter-type distal embolic protection

| | Symptomatic complications | | Univariate analysis | Multivariate analysis | |
|---|---|---|---|---|---|
| | Yes = 15 (%) | No = 172 (%) | p-Value | Odds ratio (95% CI) | p-Value |
| Age | 73.8 ± 2.6 | 71.0 ± 0.8 | 0.340 | 0.94 (0.85–1.02)* | 0.171 |
| Sex (male) | 13 (86.7) | 150 (87.2) | 0.951 | | |
| Comorbidity | | | | | |
| Hypertension | 15 (100) | 139 (80.8) | 0.062 | | |
| Hyperlipidemia | 13 (86.7) | 122 (70.9) | 0.192 | | |
| Diabetes mellitus | 3 (20.0) | 55 (32.0) | 0.336 | | |
| Current smoker | 3 (20.0) | 45 (26.2) | 0.600 | | |
| DAPT + anti-coagulation therapy | 1 (6.7) | 16 (9.3) | 0.733 | | |
| Statin | 11 (73.3) | 116 (67.4) | 0.639 | | |
| Lesion condition | | | | | |
| Symptomatic | 10 (66.7) | 62 (36.0) | **0.019** | 2.02 (1.08–4.11) | **0.035** |
| Left side lesion | 10 (66.7) | 88 (51.2) | 0.249 | | |
| Stenosis diameter, mean ± SD (mm) | 1.26 ± 0.20 | 1.33 ± 0.06 | 0.214 | | |
| Plaque length, mean ± SD (mm) | 18.1 ± 9.1 | 15.5 ± 6.4 | **0.016** | 0.94 (0.87–1.02)* | 0.102 |
| NASCET, mean ± SD (%) | 75.1 ± 15.3 | 72.5 ± 1.1 | 0.449 | | |
| Unstable plaque | 6 (40.0) | 79 (45.9) | 0.959 | | |
| Treatment | | | | | |
| Open cell stent | 8 (53.3) | 157 (91.3) | 0.40 | | |
| Stent size, mean ± SD (mm) | 8.4 ± 0.8 | 8.8 ± 1.1 | 0.236 | | |
| Stent length, mean ± SD (mm) | 35.2 ± 6.4 | 37.7 ± 5.1 | 0.070 | 1.06 (0.94–1.18)* | 0.320 |
| Post-stenting balloon size, median (range) | 3.5 (3.0-5.0) | 4.0 (2.0-5.0) | 0.065 | 2.18 (0.67–7.32)* | 0.197 |
| Difficult-to-cross the lesion (use SpiderFX) | 4 (26.7) | 6 (3.5) | **0.0001** | 3.63 (1.62–8.16) | **0.0013** |
| Catch debris in filter | 5 (33.3) | 71 (41.3) | 0.548 | | |
| Slow/StopFlow | 0 | 3 (1.7) | 0.606 | | |

*Unit odd ratio. p-values less than 0.05 are shown in boldface. CAS: carotid artery stenting; DAPT: dual antiplatelet therapy; NASCET: North American Symptomatic Carotid Endarterectomy Trial; SD: standard deviation.

After excluding the cases with difficult lesion crossing, the complication rate decreased to 6.2% (11/177). Three patients with asymptomatic lesions had worsening neurologic symptoms by one month, two of whom had HPS, and both cases required a microwire and microcatheter to cross the lesion.

### Illustrative case

An 80-year-old man had an asymptomatic right internal carotid artery stenosis (NASECT: 81.4%) (**Fig. 1A**). The microguidewire and microcatheter were passed through the lesion and replaced with a SpiderFX (**Fig. 1B**). We deployed SpiderFX distal to the lesion just before predilatation and maintained the embolic protection device until the end of the procedure. We performed predilatation with a 3 × 40-mm PTA balloon. After deployment of Protégé 8 × 4 mm, postdilatation of the lesion was performed with a 3.5 × 20 mm PTA balloon (**Fig. 1C**). Postoperative angiogram (**Fig. 1D** and **1E**) showed dilatation of the stenotic lesion and intracranial blood flow was unaffected. A few hours after surgery, the patient became unconscious, and CT showed intracranial hemorrhage (**Fig. 1F**).

## Discussion

We investigated the perioperative outcomes in patients undergoing CAS with DFP, which was FilterWire or SpiderFX. We used FilterWire as the first choice for EPD and SpiderFX when the patients had lesions that were difficult to cross. Our major finding was that CAS with DFP did not increase the rate of major adverse events at 30 days, although it was an independent predictor for complications in difficulty for FilterWire use.

We chose FilterWire as our first choice. The SpiderFX was used in cases where cerebral angiography showed that the stenosis was a difficult cross to lesion. FilterWire and SpiderFX are filter-type distal embolic protection devices. The FilterWire is a 0.014-inch filtered guidewire that is inserted into the vessel and temporarily implanted distal to the target lesion. On the other hand, the SpiderFX is a protection device that is a separate system from the wire. Compatible wires are 0.014–0.018 inch. The filter is guided after the guidewire has passed through the lesion first. Even in cases with lesion bends or severe stenosis, the

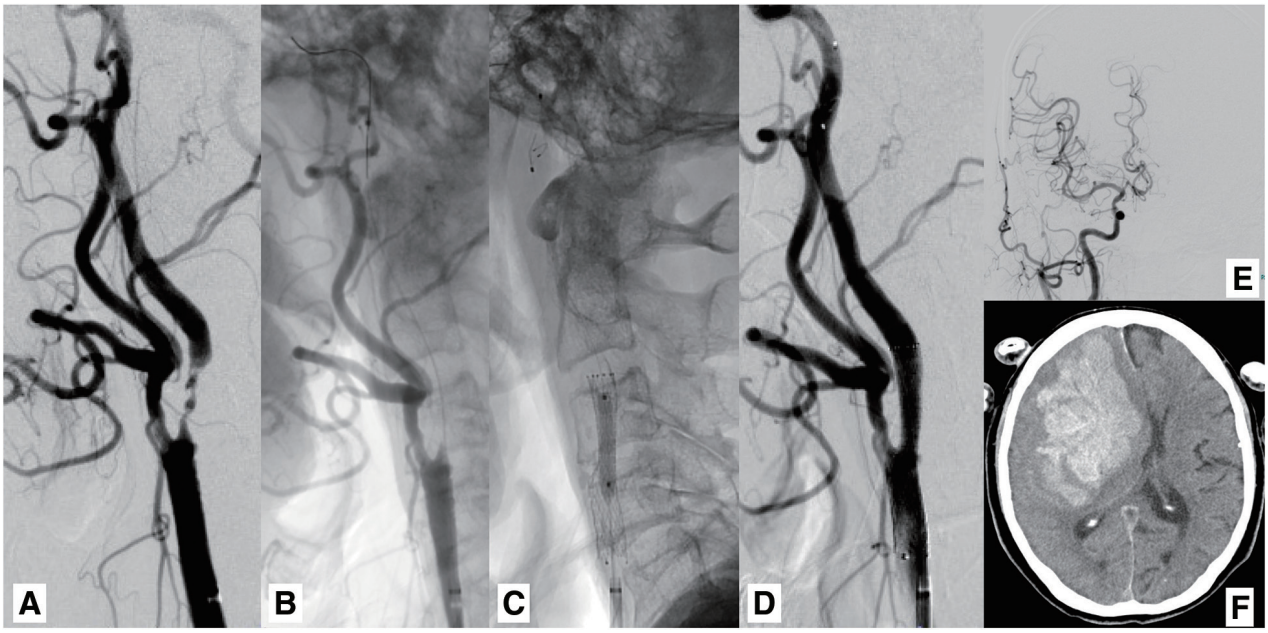


**Fig. 1** Illustrative case using a SpiderFX protection device and resulting in postoperative HPS. Preoperative angiogram (**A**) shows asymptomatic severe stenosis of right internal carotid artery. The microguidewire and microcatheter were passed through the lesion and replaced with a SpiderFX (**B**). We deployed SpiderFX distal to the lesion just before predilatation and maintained the embolic protection device until the end of the procedure. After deployment of Protégé 8 × 40 mm, postdilatation of the lesion was performed (**C**). Postoperative angiogram (**D, E**) showed dilatation of the stenotic lesion and intracranial blood flow was normalized. A few hours after CAS, the patient became unconscious and CT imaging showed cerebral hemorrhage (**F**). CAS: carotid artery stenting; HPS: hyperperfusion syndrome

features of the SpiderFX allow delicate wire manipulation and help to pass the lesion. Furthermore it is also very useful in cases of pseudo-obstruction. In these cases, balloon dilatation may be required for passage of the EPD. This is not an option with the FilterWire.

In this study, the treatment results were limited to two types of filter devices to prevent distal embolism. Distal emboli cause ischemic complications including MRID-WI-positive lesions in carotid artery stenting. The DWI positive rate and ischemic complications in this study were comparable compared with previous reports. A variety of EPDs are available, and no superiority in terms of anti-ischemic efficacy has been demonstrated.[10–12] Theoretically, Protection system using balloon device should be superior in preventing distal embolism than using filter device. But some reports comparing distal filter protection and distal balloon protection found that distal filter protection had a lower DWI positive rate.[13] A protection system using flow reversal or flow stasis, with occlusion of the ECA and CCA, has been proposed.[14–16] Furthermore, Goto et al. reported a method to further enhance the ischemic prevention effect by combining this method with a filter device.[6] They emphasized that the method is a safe technique and applicable to all patients undergoing CAS.[6] However, it is questionable whether strict protection is necessary in all cases, and in our study, many cases could be treated without complication with simple filter protection. Hence, CAS might be conducted with an acceptable level of safety using simple filter protection, provided that cases presenting evident risks, such as unstable plaques and challenging lesion crossings, are consciously avoided, and meticulous case selection is exercised.

A trial comparing carotid endarterectomy and stenting showed no significant difference in the risk of the composite primary outcome of stroke, myocardial infarction, or death between the carotid endarterectomy and CAS groups.[17] However, CAS was associated with a higher risk of stroke in the perioperative period. Careful patient selection (i.e., not performing CAS on high-risk patients) minimizes this risk. Even when experts perform CAS, embolism remains the most serious complication.[14,15] On the other hand, cerebral HPS is also a serious complication after CAS.[18,19] HPS develops within a few days after carotid revascularization due to an excessive increase in cerebral blood flow above the metabolic demands of the brain tissue. It occasionally results in intracranial hemorrhage (ICH) with significant neurological sequelae.[20–22] However, the rates of HPS (1.1%) and ICH (0.7%) were lower after CAS in the

Japanese Society for Treatment at Neck in Cerebrovascular Disease (JASTNEC) Study.[23] Iwata et al.[24] reported HPS and ICH rates of 14.1% and 4.7%, respectively, among 64 patients who underwent CAS. Hayakawa et al.[25] reported HPS and ICH rates of 10.5% and 5.3%, respectively, among 419 patients who underwent CAS in a multi-center study. In their study, multivariate analysis showed that age and use of SpiderFX were significantly associated with HPS-causing ICH, and they suggested that in elderly patients with difficult-to-cross lesions, interventions such as staged CAS may be considered to prevent HPS.[25] In our study, six patients developed HPS. SpiderFX was used in two of these cases. (i.e., hyperperfusion occurred in patients with severe stenosis or highly tortuous lesions that were difficult to cross). This included both symptomatic and asymptomatic carotid stenosis, with no significant differences. Thus, the risk of complications and HPS was higher in cases requiring the use of SpiderFX.

The second-generation FilterWire Embolic Protection System has an efficient debris capture potential due to a 110-μm pore filter that permits continuous antegrade blood flow while maintaining efficient debris capture.[16] The pore size of FilterWire is smaller than that of SpiderFX (200 μm). Nii et al.[26] compared FilterWire and SpiderFX; they reported that new emboli were found in 29.1% of the FilterWire group and 40.4% of the SpiderFX group, but this difference was not statistically significant. The SpiderFX can follow the micro guidewire after it has passed through the lesion. Therefore, when a stenotic lesion is too severe for FilterWire or an anterior dilatation balloon to traverse, the micro guidewire can be passed through the lesion to allow the anterior dilatation balloon to pass through and then be followed by the anterior dilatation balloon or SpiderFX. Although the degree of stenosis alone was not significantly associated with complications, CAS in highly stenotic lesions requires particular attention with regard to the development of HPS. Furthermore, in this study, all deaths were due to HPS. Therefore, CAS should be considered more carefully in patients with severe stenosis in whom lesion crossing is difficult. Staged CAS and measures to avoid over-dilatation of the occluded vessel are also necessary.

Various complex protection methods reportedly avoid distal migration of plaque fragments, such as a new protection system using flow reversal or stagnation by occluding the ECA and CCA and universal protection methods using a combination of CCA balloon, ECA balloon, and ICA filter.[5–7,27] However, the costs for these devices are higher; complex protection costs approximately three times more than the CAS method used by us.[8] Hence, a pertinent query arises regarding the universal applicability of employing complex protection measures in all instances, particularly when considering cost-effectiveness. Herein, we chose a simple and inexpensive method that resulted in a major stroke rate of 3.7% and a minor stroke rate of 1.6%. The BEACH study investigated the outcomes of CAS with distal EPD using Carotid Wallstent and FilterWire EX/EZ in patients at high surgical risk for Carotid endarterectomy (CEA); among 747 patients, the complications were death (1.5%), stroke (4.4%), and myocardial infarction (1.0%).[28] The CABERNET trial also evaluated outcomes with NexStent and FilterWire EX/EZ in patients at high operative risk undergoing CAS; among 454 patients, complications were stroke (5%), death (4.3%), and myocardial infarction (4.1%).[29] Since the rate of stroke occurrence in our study was not significantly different from those reported in previous studies (stroke; 4.4%–5.0%[28,29]) and the rates of other complications were also slightly lower in our study, we believe our treatment was relatively safe.

Our study has several limitations. First, the design was that of a single-center retrospective study rather than that of a case-controlled study. Second, we used closed-cell stents in 22 patients (11.8%) and open-cell stents in 165 patients (88.2%) but did not omit posterior dilatation by using open-cell stents. Due to the strong stent type bias, we were not able to examine the differences in complications between stent types. Third, this analysis could be improved by a longer radiological and clinical follow-up period to further evaluate the clinical significance. Finally, there is a strong device selection bias in using SpiderFX for cases where lesion crossing is difficult and microcatheters and micro guidewires are needed to traverse the lesion. Further study is needed to determine whether staged CAS or CEA should be used. In past cases, cerebral blood flow assessment by single-photon emission computed tomography was not always done preoperatively and the study included cases with inadequate risk assessment for hyperperfusion.

## Conclusion

We believed that CAS could be performed safely with a simple DFP, although we must take great care for patient selection. According to our results, while some cases require complex protection, there are also cases in which CAS can be performed safely with simple protection. Thus, we need to make a clear distinction between the two. Particularly in patients with nearly total occlusion lesions

or in whom it is difficult to deploy an EPD distal to the lesion, treatment selection might require careful attention owing to the risk of HPS.

## Ethics Statement

### Study approval statement

This study protocol was reviewed and approved by the Ethics Committee of Yokohama City University Medical Center, approval number B201100018.

### Consent to participate statement

Due to the retrospective study design, the Ethics Committee of Yokohama City University Medical Center waived the requirement for written informed consent, offering participants an opt-out option, as per Personal Information Protection Law and National Research Ethics Guidelines in Japan.

## Disclosure Statement

None of the authors have any financial interests relevant to this study.

## References


1) Wodarg F, Turner EL, Dobson J, et al. Influence of stent design and use of protection devices on outcome of carotid artery stenting: a pooled analysis of individual patient data. *J Neurointerv Surg* 2018; 10: 1149–1154.
2) Clavel P, Hebert S, Saleme S, et al. Cumulative incidence of restenosis in the endovascular treatment of extracranial carotid artery stenosis: a meta-analysis. *J Neurointerv Surg* 2019; 11: 916–923.
3) Tokuda R, Yoshimura S, Uchida K, et al. Real-world experience of carotid artery stenting in Japan: analysis of 8458 cases from the JR-NET3 Nationwide retrospective multi-center registries. *Neurol Med Chir (Tokyo)* 2019; 59: 117–125. 20190315.
4) Henry M, Henry I, Klonaris C, et al. Benefits of cerebral protection during carotid stenting with the PercuSurge GuardWire system: midterm results. *J Endovasc Ther* 2002; 9: 1–13.
5) Nakazaki M, Nonaka T, Takahashi A, et al. Double balloon protection during carotid artery stenting for vulnerable carotid stenosis reduces the incidence of new brain lesions. *Acta Neurochir (Wien)* 2016; 158: 1377–1386. 20160502.
6) Goto S, Ohshima T, Kato K, et al. Efficacy of carotid artery stenting by the universal protection method. *J Stroke Cerebrovasc Dis* 2018; 27: 2187–2191. 20180418.
7) Bijuklic K, Wandler A, Hazizi F, et al. The PROFI study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid artery stenting): a prospective randomized trial. *J Am Coll Cardiol* 2012; 59: 1383–1389. 20120125.
8) Ishida A, Asakuno K, Shiramizu H, et al. Very low rate of new brain lesions after vulnerable carotid artery stenting cases using only FilterWire EZ as distal embolic protection. *World Neurosurg* 2020; 141: e145–e150.
9) Takayama K, Taoka T, Nakagawa H, et al. Initial experience of carotid artery stenting using the Carotid Wallstent and FilterWire EZ in Japan. *Jpn J Radiol* 2011; 29: 51–58.
10) Giri J, Parikh SA, Kennedy KF, et al. Proximal versus distal embolic protection for carotid artery stenting: A national cardiovascular data registry analysis. *JACC Cardiovasc Interv* 2015; 8: 609–615.
11) Omran J, Mahmud E, White CJ, et al. Proximal balloon occlusion versus distal filter protection in carotid artery stenting: A meta-analysis and review of the literature. *Catheter Cardiovasc Interv* 2017; 89: 923–931.
12) Texakalidis P, Letsos A, Kokkinidis DG, et al. Proximal embolic protection versus distal filter protection versus combined protection in carotid artery stenting: A systematic review and meta-analysis. *Cardiovasc Revasc Med* 2018; 19(5 Pt A): 545–552.
13) Iko M, Tsutsumi M, Aikawa H, et al. Distal protection filter device efficacy with carotid artery stenting: Comparison between a distal protection filter and a distal protection balloon. *Jpn J Radiol* 2013; 31: 45–49.
14) Touzé E, Trinquart L, Chatellier G, et al. Systematic review of the perioperative risks of stroke or death after carotid angioplasty and stenting. *Stroke* 2009; 40: e683–e693. 20091105.
15) Schnaudigel S, Gröschel K, Pilgram SM, et al. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke* 2008; 39: 1911–1919. 20080403.
16) Khalid N, Javed H, Rogers T, et al. Adverse events and modes of failure related to the FilterWire EZ Embolic Protection System: lessons learned from an analytic review of the FDA MAUDE database. *Catheter Cardiovasc Interv* 2019; 94: 157–164.
17) Brott TG, Howard G, Roubin GS, et al. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med* 2016; 374: 1021–1031.
18) Morrish W, Grahovac S, Douen A, et al. Intracranial hemorrhage after stenting and angioplasty of extracranial carotid stenosis. *AJNR Am J Neuroradiol* 2000; 21: 1911–1916.
19) McCabe DJ, Brown MM, Clifton A. Fatal cerebral reperfusion hemorrhage after carotid stenting. *Stroke* 1999; 30: 2483–2486.

20) Bernstein M, Fleming JF, Deck JH. Deck jh: Cerebral hyperperfusion after carotid endarterectomy: A cause of cerebral hemorrhage. *Neurosurgery* 1984; 15: 50–56.
21) Solomon RA, Loftus CM, Quest DO, et al. Incidence and etiology of intracerebral hemorrhage following carotid endarterectomy. *J Neurosurg* 1986; 64: 29–34.
22) Sundt T Jr., Sharbrough F, Piepgras D, et al. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy, with results of surgery and hemodynamics of cerebral ischemia. *Surv Anesthesiol* 1982; 26: 200–201.
23) Ogasawara K, Sakai N, Kuroiwa T, et al. Intracranial hemorrhage associated with cerebral hyperperfusion syndrome following carotid endarterectomy and carotid artery stenting: retrospective review of 4494 patients. *J Neurosurg* 2007; 107: 1130–1136.
24) Iwata T, Mori T, Tajiri H, et al. Predictors of hyperperfusion syndrome before and immediately after carotid artery stenting in single-photon emission computed tomography and transcranial color-coded real-time sonography studies. *Neurosurgery* 2011; 68: 649–655; discussion, 656.
25) Hayakawa M, Sugiu K, Yoshimura S, et al. Effectiveness of staged angioplasty for avoidance of cerebral hyperperfusion syndrome after carotid revascularization. *J Neurosurg* 2019; 132: 51–61.
26) Nii K, Tsutsumi M, Maeda H, et al. Comparison of flow impairment during carotid artery stenting using two types of eccentric filter embolic protection devices. *Neurol Med Chir (Tokyo)* 2016; 56: 759–765.
27) Kim MS, Rho MH, Hong HP, et al. Comparison of embolic protection with proximal and distal protection devices: periprocedural complications, clinical outcomes, and cerebral embolic lesions on diffusion-weighted magnetic resonance imaging. *World Neurosurg* 2020; 135: e731–e737.
28) White CJ, Iyer SS, Hopkins LN, et al. Carotid stenting with distal protection in high surgical risk patients: the BEACH trial 30 day results. *Catheter Cardiovasc Interv* 2006; 67: 503–512.
29) Hopkins LN, Myla S, Grube E, et al. Carotid artery revascularization in high surgical risk patients with the NexStent and the Filterwire EX/EZ: 1-year results in the Cabernet trial. *Catheter Cardiovasc Interv* 2008; 71: 950–960.