Incidence of embolism associated with carotid artery stenting: open-cell versus closed-cell stents

Clinical article

Keun Young Park, M.D.,1,3 Dong Ik Kim, M.D., Ph.D.,1 Byung Moon Kim, M.D., Ph.D.,1 Hyo Suk Nam, M.D., Ph.D.,2 Young Dae Kim, M.D., Ph.D.,2 Ji Hoe Heo, M.D., Ph.D.,2 and Dong Joon Kim, M.D., Ph.D.1

Departments of 1Radiology and 2Neurology, Yonsei University College of Medicine, Seoul; and 3Department of Neurosurgery, National Health Insurance Corporation Ilsan Hospital, Goyang-si, Gyeonggi-do, Republic of Korea

Object. Carotid artery stenting (CAS) can be an alternative option for carotid endarterectomy in the prevention of ischemic stroke caused by carotid artery stenosis. The purpose of this study was to evaluate the influence of stent design on the incidence of procedural and postprocedural embolism associated with CAS treatment.

Methods. Ninety-six symptomatic and asymptomatic patients, consisting of 79 males and 17 females, with moderate to severe carotid artery stenosis and a mean age of 69.0 years were treated with CAS. The stent type (48 closed-cell and 48 open-cell stents) was randomly allocated before the procedure. Imaging, procedural, and clinical outcomes were assessed and compared. The symptomatic subgroup (76 patients) was also analyzed to determine the influence of stent design on outcome.

Results. New lesions on postprocedural diffusion-weighted imaging (DWI) were significantly more frequent in the open-cell than in the closed-cell stent group (24 vs 12, respectively; p = 0.020). The 30-day clinical outcome was not different between the 2 stent groups. In the symptomatic patient group, stent design (p = 0.017, OR 4.173) and recent smoking history (p = 0.036, OR 4.755) were strong risk factors for new lesions on postprocedural DWI.

Conclusions. Stent design may have an influence on the risk of new embolism, and selecting the appropriate stent may improve outcome.

(http://thejns.org/doi/abs/10.3171/2013.5.JNS1331)

Key Words • carotid stenosis • stenting • embolism • vascular disorders

Carotid endarterectomy is an effective treatment method for the prevention of stroke in patients with symptomatic carotid artery stenosis.2,10 However, along with the development of neurointervention techniques and devices, CAS has emerged as an alternative option. Recently, the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) investigators reported similar outcomes and safety for both CAS and CEA.4 Despite its decreased invasiveness, however, CAS has mostly failed to show superiority over CEA in preventing stroke recurrence.

Coronary and peripheral artery stents are essentially designed to improve perfusion to the distal bed. On the other hand, the most common pathomechanism of stroke in carotid atherosclerosis is distal embolism and thrombotic occlusion with distal emboli.8 In terms of the atheroma, CEA and CAS both allow correction of the luminal narrowing and turbulent flow from the atherosclerotic stenosis that may predispose to thrombus formation. However, the atheroma is removed via CEA but only displaced via CAS, and thus may remain a potential source of embolism until neointima formation is complete. Recent interest has focused on the effectiveness of EPDs in preventing intraprocedural embolism.14,21 However, these devices do not offer prevention in the post-CAS period. Currently, controversy exists regarding the influence of stent design on the prevention of recurrent stroke, with only a few reports available.3,5,7,18,19,24

The purpose of the current study was to evaluate the influence of stent design on the incidence of procedural and postprocedural embolism associated with CAS treatment.

Methods

In the period from January 2007 to June 2009 at our institute, 135 patients were treated with CAS for symptom-
Carotid artery stenting and stent design

atic (stenosis \( \geq 50\% \), per the NASCET) or asymptomatic (stenosis \( \geq 70\% \), per the NASCET) atherosclerotic carotid artery stenosis. Patients treated for simultaneous bilateral carotid artery lesions or intracranial lesions, those requiring an unavailable stent size, and those for whom the surgeon preferred a specific stent were excluded from our analysis. Finally, 96 cases in which there was no preference for a specific type of stent were included. Stent type was randomly allocated to a closed-cell (Wallstent, Boston Scientific Corp.; 48 cases) or an open-cell (Precise, Cordis Corp.; 48 cases) stent by using a random number generator (http://www.random.org, odd number = open-cell stent, even number = closed-cell stent) immediately before the procedure. Clinical, procedural, and imaging outcomes were assessed and compared. Besides being grouped according to stent type, the patients were also divided into 2 groups according to their initial symptoms (asymptomatic 20 patients, symptomatic 76 patients), and analysis was performed to determine the influence of stent design in both groups. All data were prospectively collected and reviewed. Informed consent to participate in this study was obtained from the patient or legal representatives.

Imaging and Procedural Assessment

Characteristics of the carotid artery lesion were evaluated on DSA. The degree of stenosis was measured using the NASCET criteria. Stenosis of 50%–69% was considered moderate; and stenosis \( \geq 70\% \), as severe. The morphology of the target lesion was described as either smooth or irregular according to its shape on 2D DSA. The presence of any ulceration or calcification at the lesion site was also evaluated using DSA. The technical success rates and the immediate postprocedural distal branch embolism, residual ulcer, and in-stent filling defects were assessed. Immediate postprocedural distal branch embolism was defined as any occlusion or missing distal intracranial arteries on immediate postprocedural DSA.

The retrieved filters were checked for the presence of any captured debris. Immediate postprocedural DWI (3-T) was performed within 24 hours after the CAS procedure in 91 patients (94.8%). Imaging was not performed in the other 5 patients because of patient refusal (2 patients), presence of pacemaker (2 patients), or hyperperfusion syndrome (1 patient). Diffusion-weighted images were evaluated for the presence of any new lesions in the ipsilateral hemisphere, compared with the latest images before the CAS procedure. One neuroradiologist (D.J.K.) and one neurosurgeon (K.Y.P.), blinded to patient identity and stent type, analyzed the images and agreed on the results.

Clinical Assessment

Stroke risk factors were evaluated and recorded via history taking, physical examination, and laboratory investigation at the initial admission. Each patient was classified into 1 of 3 categories according to his or her main symptom: 1) none, 2) TIA or amaurosis fugax, or 3) cerebral infarction. Symptom duration was defined as the interval from symptom onset to successful intervention. The clinical end point was defined as any TIA, stroke, or death within 30 days of stent treatment. Stroke included any minor or major stroke. “Death” was defined as any death related to neurovascular causes. A board-certified neurologist evaluated clinical outcomes immediately after the stent procedure, daily during hospitalization, and at the 30-day follow-up visit.

Neurointerventional Procedure

Dual antiplatelet agents (aspirin 100 mg and clopidogrel 75 mg) were prescribed to all patients for 5 or more days before the procedure. If emergent intervention was needed, a loading dose of dual antiplatelets (aspirin 300 mg and clopidogrel 300 mg) was prescribed before the procedure. Two experts (D.J.K. and D.I.K.) performed all procedures after inducing local anesthesia. After gaining femoral access, we introduced a 6-Fr Envoy guiding catheter (Cordis Corp.) or Shuttle guiding sheath (Cook Medical Inc.) into the common carotid artery. A bolus of 3000 IU of heparin was intravenously infused to achieve an activated clotting time of longer than 250 seconds. In general, an EPD was initially introduced into the distal internal carotid artery (Filterwire EZ, Boston Scientific, 86 cases; Angioguard RX, Cordis Corp., 5 cases). We performed preballooning followed by stent placement. After an intravenous injection of 0.5–1.0 mg atropine, postballooning for optimal dilation of the lesion was performed as well, as was careful vital sign monitoring. Finally, the EPD was retrieved. At the end of the procedure, 2 neurointerventionists (operator and first assistant) visually assessed the EPD to evaluate the captured emboli within.

Statistical Analysis

Univariate analysis was done for comparisons between the 2 stent groups by using the chi-square test, Fisher exact test, and standard t-test. Multivariate analysis was done for evaluation of the embolic risk factors in the symptomatic group by using binary logistic regression. For multivariate analysis, patient age and duration of symptoms were stratified into 2 groups (\(< 70 \text{ vs } \geq 70\text{ years and } < 2 \text{ vs } \geq 2\text{ weeks, respectively}\) ). Multivariate analysis could not be performed for the asymptomatic group because of the small number of cases. Significance was defined as \( p < 0.05 \). These statistical analyses were performed using IBM SPSS Statistics 20.0 for Windows (IBM Corp.).

Results

Baseline characteristics of the patients are summarized and compared in Table 1. No statistically significant difference in baseline characteristics, MRI interval, lesion morphology, or technique was observed between the open- and closed-cell stent groups.

Overall, the patients included 79 males and 17 females, with a mean age of 69.0 years (range 52–87 years). Initial symptoms were TIA or amaurosis fugax (34 patients [35.4%]), cerebral infarction (42 patients [43.8%]), or absent (asymptomatic, 20 patients [20.8%]). Among the 76 symptomatic patients, the mean duration of symptoms was 1.5 ± 2.09 months. Thirty-one (40.8%) of these patients were treated in the early phase (< 2 weeks from symptom onset).

In terms of lesion morphology, 81 cases (84.4%) demonstrated severe stenosis. Sixty-one cases (63.5%) showed...
an irregular lesion. Calcification and ulceration of the target lesion was detected in 41 cases (42.7%) and 26 cases (27.1%), respectively.

In terms of technique, a single-stage procedure (diagnostic angiogram and interventional procedure at the same time) was performed in 55 cases (57.3%), while in 41 patients the interventional procedure was performed a day or more after the initial diagnostic angiography (mean 2.1 days, range 1–5 days). Embolic protection devices were used in 91 cases overall (94.8%; closed-cell stent group = 48 cases [100.0%]; open-cell stent group = 43 cases [89.6%]). Preballooning was performed in 84 cases (87.5%), including 43 cases (89.6%) in the closed-cell stent group and 41 cases (85.4%) in the open-cell stent group. Postballooning was performed in all cases. There were no instances of technical failure in delivering the stent.

**Imaging and Procedural Outcome**

On the postprocedural DSA, 35 cases (36.4%) had a residual ulcer or gap between the stent strut and inner margin of the lesion. This finding was more frequently observed with the closed-cell stent group (p < 0.001; Table 2). There were no significant differences in immediate postprocedural distal branch embolism and in-stent filling defect rates between the stent groups.

**TABLE 1: Baseline characteristics in the closed-cell and open-cell stent groups**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall</th>
<th>Closed-Cell Stent Group</th>
<th>Open-Cell Stent Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>96</td>
<td>48</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>sex (M:F)</td>
<td>79 (82.3%): 17 (17.7%)</td>
<td>36 (75.0%): 12 (25.0%)</td>
<td>43 (89.6%): 5 (10.4%)</td>
<td>0.107</td>
</tr>
<tr>
<td>mean age in yrs</td>
<td>69.0 ± 7.56 (52–87)</td>
<td>68.8 ± 7.66</td>
<td>69.1 ± 7.54</td>
<td>0.841</td>
</tr>
<tr>
<td>no. w/ age &lt;70 yrs: &gt;70 yrs</td>
<td>53 (55.2%): 43 (44.8%)</td>
<td>27 (56.3%): 21 (43.8%)</td>
<td>26 (54.2%): 22 (45.8%)</td>
<td>1.000</td>
</tr>
<tr>
<td>preop symptom</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>20 (20.8%)</td>
<td>8 (16.7%)</td>
<td>12 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>TIA or amaurosis fugax</td>
<td>34 (35.4%)</td>
<td>15 (31.3%)</td>
<td>19 (39.6%)</td>
<td></td>
</tr>
<tr>
<td>infarction</td>
<td>42 (43.8%)</td>
<td>25 (52.1%)</td>
<td>17 (35.4%)</td>
<td></td>
</tr>
<tr>
<td>mean duration in mos</td>
<td>1.5 ± 2.09</td>
<td>1.4 ± 2.38†</td>
<td>1.7 ± 1.76‡</td>
<td>0.571</td>
</tr>
<tr>
<td>duration &lt;2 wks: ≥2 wks</td>
<td>31 (40.8%): 45 (59.2%)</td>
<td>18 (45.0%): 22 (55.0%)</td>
<td>13 (36.1%): 23 (63.9%)</td>
<td>0.488</td>
</tr>
<tr>
<td>stroke risk factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>82 (85.4%)</td>
<td>44 (91.7%)</td>
<td>38 (79.2%)</td>
<td>0.146</td>
</tr>
<tr>
<td>diabetes</td>
<td>26 (27.1%)</td>
<td>15 (31.3%)</td>
<td>11 (22.9%)</td>
<td>0.491</td>
</tr>
<tr>
<td>dyslipidemia</td>
<td>32 (33.3%)</td>
<td>13 (27.1%)</td>
<td>19 (39.6%)</td>
<td>0.279</td>
</tr>
<tr>
<td>old CVA history</td>
<td>22 (22.9%)</td>
<td>11 (22.9%)</td>
<td>11 (22.9%)</td>
<td>1.000</td>
</tr>
<tr>
<td>recent smoking history</td>
<td>44 (45.8%)</td>
<td>23 (47.9%)</td>
<td>21 (43.8%)</td>
<td>0.838</td>
</tr>
<tr>
<td>mean interval from preop to postop MRI in days (range)§</td>
<td>25.3 ± 26.59 (1–79)</td>
<td>21.07 ± 17.23</td>
<td>29.18 ± 32.75</td>
<td>0.156</td>
</tr>
<tr>
<td>lesion morphology</td>
<td></td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>moderate</td>
<td>15 (15.6%)</td>
<td>8 (16.7%)</td>
<td>7 (14.6%)</td>
<td></td>
</tr>
<tr>
<td>severe</td>
<td>81 (84.4%)</td>
<td>40 (83.3%)</td>
<td>41 (85.4%)</td>
<td></td>
</tr>
<tr>
<td>smooth:irregular</td>
<td>35 (36.4%): 61 (63.5%)</td>
<td>20 (41.7%): 28 (58.3%)</td>
<td>15 (31.2%): 33 (68.8%)</td>
<td>0.397</td>
</tr>
<tr>
<td>calcification at lesion site</td>
<td>41 (42.7%)</td>
<td>21 (43.8%)</td>
<td>20 (41.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>ulceration at lesion site</td>
<td>26 (27.1%)</td>
<td>13 (27.1%)</td>
<td>13 (27.1%)</td>
<td>1.000</td>
</tr>
<tr>
<td>single-stage CAS</td>
<td>55 (57.3%)</td>
<td>28 (58.3%)</td>
<td>27 (56.2%)</td>
<td>1.000</td>
</tr>
<tr>
<td>EPD type</td>
<td></td>
<td>0.109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>5 (5.2%)</td>
<td>0</td>
<td>5 (10.4%)</td>
<td></td>
</tr>
<tr>
<td>Filterwire EZ</td>
<td>86 (89.6%)</td>
<td>45 (93.8%)</td>
<td>41 (85.4%)</td>
<td></td>
</tr>
<tr>
<td>Angioguard RX</td>
<td>5 (5.2%)</td>
<td>3 (6.2%)</td>
<td>2 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>preballooning</td>
<td>84 (87.5%)</td>
<td>43 (89.6%)</td>
<td>41 (85.4%)</td>
<td>0.759</td>
</tr>
<tr>
<td>postballooning</td>
<td>96 (100.0%)</td>
<td>48 (100.0%)</td>
<td>48 (100.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* CVA = cerebrovascular accident; NS = not statistical.
† Value or percentage based on 40 patients.
‡ Value or percentage based on 36 patients.
§ Overall value based on 91 patients: 44 patients with a closed-cell stent and 47 with an open-cell stent.
New lesions were detected on postprocedural DWI studies in 36 patients (39.6%). The incidence of new DWI signals was higher in the open-cell stent group (24 [51.1%] vs 12 [27.3%], \(p = 0.020\); Table 2).

**Clinical Outcome**

Clinical follow-up at 30 days was possible in 93 patients (96.9%). The overall 30-day TIA, stroke, and death rates were 2.2% (2 of 93 patients), 1.1% (1 of 93 patients), and 1.1% (1 of 93 patients), respectively. Although 30-day stroke and death were not significantly different between the 2 stent groups (\(p = 0.495\)), all postprocedural embolic events (TIA and stroke) occurred in the closed-cell group (6.4% vs 0%). One patient (1.1%) in the study died as a result of intracranial hemorrhage from hyperperfusion syndrome, which occurred immediately after stent treatment.

**Symptomatic and Asymptomatic Stenosis**

Among 76 symptomatic patients, 40 (52.6%) and 36 (47.4%) patients were treated using the closed-cell and open-cell stents, respectively. According to univariate and multivariate analysis, new lesions on DWI were noted more frequently in the open-cell stent group (55.6% vs 29.7%, \(p = 0.026\)). Stent design was a strong risk factor for new lesions on DWI (\(p = 0.049\), OR 3.71, 95% CI 1.28–11.05; Table 3). Recent smoking history was also correlated with new lesions on DWI (\(p = 0.036\), OR 0.47, 95% CI 0.22–0.96). In the asymptomatic group (closed-cell stent, 8 patients [40.0%]; open-cell stent, 12 patients [60.0%]), no significant difference in the occurrence of new lesions on DWI was observed between the stent groups (14.3% in closed-cell vs 36.4% in open-cell stent group, \(p = 0.596\)).

**Discussion**

The results of our study show that stent design may influence the incidence of embolism in CAS. Our comparison of an open-cell stent, with its larger free cell area, and a closed-cell stent, with its smaller free cell area, showed that patients with the open-cell design were more susceptible to new lesions, as demonstrated on DWI.

**Stent Design and Outcome**

The design of the carotid artery stent cells can be largely divided into open- and closed-cell types. Bridge connections between the apices of individual cells appear in the closed-cell type. Generally, the absence of bridge connections—as is found in the open-cell type—allows free movement between individual stent cells, thus increasing the flexibility and conformability of the stent.22 Accordingly, closed-cell stents are characterized by less conformability and a higher probability of suboptimal stent apposition.22 On the other hand, these closed-cell stents are often characterized by a smaller free cell area and greater coverage of plaque compared with the open-cell stents.20 An in vitro study has shown that open-cell stents may be more prone to penetration of atherosclerotic particles because of a larger free cell area and open apices of the cells.13 There is controversy surrounding the issue of whether these stent characteristics actually have clinical significance. In the studies by Hart et al.5 and Bosiers et al., a lower postprocedural event rate for the closed-cell stent group, especially in the symptomatic population, was shown. However, these studies included a wide variety of stents, although they tended to be of the closed-cell type.

Our patient population was evenly distributed between the stent types. The variety of stents was limited to the Wallstent and the Precise stents. Although our study did not reveal a clinical difference between the stent designs, we did note a significant difference in the incidence of embolism associated with CAS. The occurrence of new lesions on DWI was strongly associated with the open-cell stents. Despite the clinically silent nature of many new embolisms, these lesions may not be completely innocuous and may be important surrogate indices revealing the different effects of the stent design on the therapeutic and preventive mechanisms of embolism.
The greater frequency of residual ulcer or gap in patients with the closed-cell stent may raise concerns regarding delayed embolic events. Other studies have shown that residual ulceration disappears or improves without any significant risk of embolism; however, these studies did not compare outcomes according to the stent design. In our study, all 30-day clinical events occurred in the closed-cell stent group. It may be hypothesized that although the new lesion rate was lower in the closed-cell stent group, the stagnant flow in the residual ulcer or gap may have caused clinically significant embolism and stroke. Our study could not reveal a statistical correlation between residual ulcer or gap and the incidence of new lesions or 30-day event rates because of the small number of cases. Whether the characteristics of compromised conformability and smaller cell size of the closed-cell stents cause more frequent, clinically significant periprocedural stroke and long-term restenosis should be determined in larger studies with longer follow-ups.

**Therapeutic Implications**

Our results suggest that the choice of stent may influence the incidence of new embolism, and thus selection of the stent design should be incorporated into the CAS treatment planning. The higher incidence of new lesions on DWI associated with open-cell stents suggests that a larger free cell area (Wallstent 1.08 mm², Precise 5.89 mm²) may be more vulnerable to a new microembolism. Hence, closed-cell types, with their smaller free cell areas, may be preferred in symptomatic patients with vulnerable plaques. On the other hand, when residual ulceration or gap is expected, open-cell type stents may be preferable. Open-cell type stents in conjunction with a proximal balloon type of EPD may also be preferred in cases in which conformability may be compromised because of the severe tortuosity of the carotid artery.

There are some limitations to our study. First, the intervals between preprocedural and postprocedural MRI were long. Although postprocedural MRI was performed within 24 hours of CAS, silent recurrent strokes may have occurred before the procedure but after the initial MRI study. Only new lesions in the acute phase on DWI were regarded as significant in this study, and there was no difference in the MRI interval between the 2 groups of patients. Nonetheless, the incidence of CAS-related embolism may have been overestimated. Second, because of the small number of cases, captured debris in the EPD and new lesions on DWI were not quantitatively analyzed. Quantification of the new emboli should be performed in larger prospective studies. Third, only 2 types of stents were used to represent each type of stent design; thus, it may be difficult to generalize our results to all open- or closed-cell type stents. On the other hand, other factors, such as the stent profile, deliverability, shortening, and radial force—which may also be confounding factors—could be limited by including only a single type of stent representative of either the open- or closed-cell design.

**Conclusions**

Stent design may affect the periprocedural embolism in CAS. The selection of the stent design should be incorporated into the planning process when treating carotid atherosclerotic lesions.

**Disclosure**

This work was supported by Grant No. A085136 from the Korea Healthcare technology R&D Project, Ministry for Health, Welfare & Family Affairs, Republic of Korea.

Author contributions to this study and manuscript preparation include the following. Conception and design: DJ Kim. Acquisition of data: Park, Nam, YD Kim, Heo. Analysis and interpretation of data: Park. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: DJ Kim. Statistical analysis: Park. Administrative/technical/material support: DI Kim, BM Kim. Study supervision: DJ Kim.

**References**

Carotid artery stenting and stent design

MO.MA proximal cerebral protection device during carotid artery stenting: results from the ARMOUR pivotal trial. *Catheter Cardiovasc Interv* **76:**1–8, 2010


Manuscript submitted January 6, 2013.

Accepted May 14, 2013.

Please include this information when citing this paper: published online June 21, 2013; DOI: 10.3171/2013.5.JNS1331.

Address correspondence to: Dong Joon Kim, M.D., Ph.D., Department of Radiology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea.

email: djkimmd@yuhs.ac.