Prospective Analysis of Cerebral Infarction After Carotid Endarterectomy and Carotid Artery Stent Placement by Using Diffusion-Weighted Imaging

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BACKGROUND AND PURPOSE: Small emboli arising from a friable plaque during carotid endarterectomy (CEA) and carotid artery stent placement (CAS) constitute a potentially important cause of periprocedural ischemic complications. To evaluate the frequency and significance of cerebral ischemic lesions of embolic origin after CEA and CAS, we examined patients with moderate to severe carotid stenosis by using diffusion-weighted (DW) imaging.

METHODS: Twenty-four patients undergoing 26 CEAs and 20 patients undergoing 22 CAS were prospectively studied with pre- and post-treatment DW imaging of the brain within 7 days (mean, 2.3 days) before and within 7 days (mean, 3.2 days) after treatment. DW images were analyzed by two neuroradiologists blinded to the clinical results after CEA and CAS. Any new hyperintense lesion on DW image was interpreted as a post-treatment ischemic lesion. We compared post-treatment ischemic lesions with change in neurologic status, presence of plaque ulcerations, and severity of stenosis and compared the frequency of overall post-treatment complications between the two procedures.

RESULTS: In 25 (96%) of 26 CEAs, post-operative brain DW images were unchanged. In one patient (4%), a new single asymptomatic hyperintensity was observed in the striatocapsule on the surgical side. In 14 (64%) of 22 CAS procedures, post-operative brain DW images were unchanged. In eight CAS cases (36%), new hyperintensities were seen on DW images. Among them, two were symptomatic with a major neurologic deficit lasting more than 7 days. Post-treatment brain or retinal major stroke rates were 4% (n = 1) for CEA and 14% (n = 3) for CAS. Overall symptomatic complication rates were 19.2% and 13.6%, respectively.

CONCLUSION: Rate of ischemic brain lesions was significantly lower after CEA than after CAS, although most of these brain lesions were silent. Also, CEA is a safer procedure carrying a lower risk of post-operative cerebral ischemia. CAS, however, may be a comparable procedure considering the total complication rate and can be a more reliable procedure with advances in neuroprotective means.

Although carotid endarterectomy (CEA) and carotid artery stent placement (CAS) are performed to re-

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rotid artery stenosis (7–13). CAS is currently being investigated as an alternative treatment to CEA, and many recent studies suggest that CAS is also effective in the treatment of carotid artery stenosis (3, 4, 11, 14–21).

Diffusion-weighted (DW) imaging is highly sensitive and specific in the diagnosis of ischemic stroke (22–24). Ischemic stroke may occur as a complication of any vascular intervention from the heart to the head. DW imaging is being used in many interventional and surgical procedures as a marker of ischemic complications (1, 2, 5, 22, 25–29).

In the present prospective study, our principal objective was to evaluate the frequency and significance of ischemic brain lesions of embolic origin after CEA and CAS by using DW imaging and to compare imaging findings with post-treatment neurologic status, angiographic morphology of the atheromatous plaque, and severity of stenosis.

Methods

Patient Selection and Data Collection

Forty-eight consecutive procedures were performed in a total of 44 patients (42 men and two women) with moderate or severe (>40%) carotid artery stenosis. Twenty-six CEA and 22 CAS procedures were performed from July 1998 through February 2001 (two patients underwent bilateral CEA and two patients underwent bilateral CAS). CEA was performed by two experienced vascular surgeons: one (B.B.L.) had extensive experience for more than 2 decades in the United States with an American-trained and American board-certified background to be specialized in carotid surgery before establishment of Korea-first Carotid Clinic for stroke prevention; the other was an associate (D.-I.K.) who was trained in Korea by the first vascular surgeon. CAS was performed by one experienced (more than 30 cases) interventional neuroradiologist (H.S.B.).

The patients were not randomized to two treatment groups. The appropriate treatment technique was selected based on consensus among the multidisciplinary team members of the Carotid Clinic, which included interventional neuroradiologists (H.G.R., H.S.B., J.W.R., D.G.N., W.J.M.), a vascular surgeon (B.B.L., D.-I.K.), cardiologist, and neurologist. Priority was given to CAS for the patients who were considered to be at high surgical risk (i.e., high carotid bifurcation, unstable cardiopulmonary disease, bilateral severe carotid disease) following the full disclosure of the investigational nature of the CAS procedure to the patient as a clinical option to replace CEA. However, CAS was not implemented as a treatment option in patients with a severely tortuous aorta or floating thrombus, patients with a severely tortuous aorta or floating thrombus, or patients with a severely tortuous aorta or floating thrombus.

Protocol for CAS

Ticlopidine (250 mg twice/day) and aspirin (150 mg/day) were administered orally at least 48 hours before CAS. Vascular access was gained by placement of a 9F sheath in the common femoral artery. A 6F sheath was placed in the femoral vein for a temporary cardiac pacemaker. Heparin (usually 80 IU/kg) was administered intravenously to achieve an activated clotting time of 2–3 times greater than normal. With use of a hydrophilic guidewire (0.038- or 0.035-inch Terumo) with an exchange length (260 or 300 cm), the 5F neuroangiographic catheter was advanced into the ipsilateral external carotid artery. The 5F catheter was withdrawn, and the 7F, 90-cm guiding sheath (Shuttle Flexor; Cook, Inc., Bloomington, IN) was then advanced in the CCA over the exchange wire. For very tortuous vessels, a 0.038-inch extra-support Amplatz wire (Boston Scientific/Medi-Tech, Newton, MA) was used with considerable success. After positioning the tip of the 7F guiding catheter 3–4 cm below the carotid bifurcation, a baseline carotid angiogram was obtained, and the interventional neuroradiologist estimated the length and severity of the lesion and the length and size of the stent required. The critical measurement was the diameter of the CCA just proximal to the bifurcation, which was used to size the Easy Wallstent (Boston Scientific/Schneider, Minneapolis, MN) to be deployed. In most cases, the stenotic lesion was crossed with a 0.038- or 0.035-inch Terumo wire without great difficulty. In one difficult case, a microcatheter and 0.014-inch wire were used. The stenotic lesion was predilated with a 4-mm diameter angioplasty balloon (Ultra-thin Diamond, Boston Scientific/Medi-Tech, Newton, MA) except in three cases with moderate stenosis and two cases with severe stenosis. After this, or as a primary procedure, a self-expanding Easy Wallstent was positioned across the lesion and deployed. Once the stent was deployed, the lesion was dilated with an appropriately sized balloon (usually 5- or 6-mm diameter, Ultra-thin Diamond) to permit full expansion of the stent within the ICA and CCA. Up to two balloon inflations—no more than 10 seconds each—were permitted. After angioplasty...
and stent deployment, a completion angiographic examination was performed.

**MR Imaging Examination**

Pretreatment MR imaging was performed as close to treatment as possible within 7 days (mean, 2.3 days [CEA, 2.4 days; CAS, 2.2 days]; range 0–7 days), with the post-treatment imaging performed a mean of 3.1 days (CEA, 3.3 days; CAS, 2.9 days) after the procedure (range 1–7 days). There was no specific difference in time to MR imaging between the two groups. All preoperative MR imaging in the CEA group was performed after transfemoral carotid arteriography for exclusion of angiography-related infarction. Imaging was performed with a 1.5-T apparatus (Signa Horizon or Signa CV/I; GE Medical Systems, Milwaukee, WI) equipped with a head coil. The pre- and post-treatment MR imaging routinely included the following: axial spin-echo T1-weighted, fast spin-echo T2-weighted, fluid-attenuated inversion-recovery (FLAIR), DW, perfusion-weighted, and post-contrast spin-echo T1-weighted imaging. The DW images were acquired with an echo-planar sequence. An isotropic sequence was used (6500/97/1 TR/TE/TEX, field of view 280 mm, matrix 128 × 128), with b values of 0 and 1000 ms/mm². The DW images were then evaluated by two neuroradiologists (H.G.R., H.S.B.) blinded to the clinical status of the patients. Any presence of new hyperintensity in the brain was interpreted as a sign of new ischemic lesions after CEA or CAS.

**Statistical Analysis**

The new hyperintensities on DW images and overall complications of the patients in the CEA and CAS groups were compared by using the Fisher exact test. Significance was defined as \( P < .05 \).

**Results**

Recanalization of ICA stenosis by CEA or CAS was technically successful in all 48 procedures. There was no death associated with the procedures. The mean age of the patients at the time of the procedures was 63.4 ± 8.5 years (range, 37–80 years). Of the 48 carotid artery stenoses cases, 37 (77%) were symptomatic lesions (eight with transient ischemic attacks or amaurosis fugax and 29 with cerebral or retinal infarcts) and 11 (23%) were asymptomatic. The contralateral ICA was occluded in nine (19%) of 48 procedures and severely stenotic in six (12%). Table 1 shows the baseline demographics and clinical characteristics of the two treatment groups. Table 2 shows neurologic and other non-neurologic complications after treatment.

**CEA Series**

In 25 (96%) of 26 CEA procedures, post-operative brain DW images were unchanged. A new, small, asymptomatic hyperintense signal was observed in only one patient (4%), in the striatocapsule of the surgical side (Fig 1). This patient had ipsilateral moderate stenosis (46%) of the right ICA with plaque ulceration and contralateral severe stenosis (70%) at the same time. There were five cases with nonischemic complications (19%). Four lower cranial nerve injuries, two temporary and another two permanent, occurred in three patients. Also, two hyperperfusion syndromes developed. Of four cranial nerve paralyses, hypoglossal nerve injury was noted in one patient, vagus nerve injury in one patient, and both glossopharyngeal and hypoglossal nerve injuries in one patient. All three patients were assessed to have a high carotid bifurcation above C2 level preoperatively and subsequently required mandibular subluxation or dislocation to have adequate exposure to carry out the procedure properly. Of the two cases with hyperperfusion syndrome, one had only severe transient headache with no neurologic deficit and the other had significant neurologic deficit and seizure lasting more than 7 days with cerebral edema and hemorrhage (Fig 2).

**CAS Series**

In 14 (64%) of 22 CAS procedures, post-treatment brain DW images were unchanged. New, small hyperintense signals were observed in eight cases (36%). However, only two of them were symptomatic with...
neurologic deficit lasting more than 7 days after CAS. All new lesions measured several mm in diameter, but were smaller than 1 cm. There was no evidence of major artery occlusion or territorial infarction. In one case, intraarterial thrombolysis of the central sulcal branch of the right MCA was performed with urokinase after CAS because the patient claimed left upper extremity weakness immediately after stent placement. DW images and findings at neurologic examination after CAS and thrombolysis were normal. There were two cases with visual field defect due to retinal infarction: one with symptomatic hyperintensities in the ipsilateral brain on DW images (Fig 3), the other with no new hyperintensity. So, the total number of cases with post-treatment neurologic or retinal deficit was three (14%). Non-neurologic complications were not observed in this series. There was no obvious trend in the frequency of ischemic lesions on DW images with regard to whether or not plaque ulceration and severe contralateral stenosis or occlusion were present. In the subgroup who underwent CAS without predilatation (n = 5), new hyperintense signals were observed in two cases (40%).

Comparison of Complications of CEA and CAS

Rates of post-treatment brain lesions on DW images were 4% and 36% in the CEA and CAS series, respectively. Frequency of ischemic brain lesions of embolic origin after CEA was significantly lower than that of CAS (P = .005). Post-treatment brain or retinal stroke rates were 4% (n = 1) and 14% (n = 3), and the overall symptomatic ischemic and nonischemic complication rates were 19% (n = 5) and 14% (n = 3), respectively. Although strokes were more common after CAS than after CEA, overall complications were less common in CAS. However, these differences were not significant statistically (P = .21 and P = .27, respectively).

Because of the small sample of this prospective study and the rarity of observed cerebral events, no evident statistical relationship could be established between angiographic variables (such as plaque ulceration and contralateral stenosis or occlusion) and the occurrence of embolic brain lesions on DW images (Table 3).

Discussion

The treatment of ICA stenosis has significantly evolved during the last 40 years. The NASCET and Asymptomatic Carotid Atherosclerosis Study (ACAS), for example, have proved the absolute or relative benefit of CEA in reducing the stroke risks for symptomatic (7, 10, 13) and asymptomatic patients with significant carotid artery stenosis (8). Subsequently, the traditional surgical treatment with CEA became the standard of care in treating cervical carotid artery stenosis. However, it was found to have certain limitations. In the initial results from NASCET, 5.8% of the patients had perioperative major stroke or death (7). In the ACAS, the perioperative stroke rate was 2.3% (8). Recently, further results from NASCET showed 6.5% perioperative stroke and death, 2.0% permanently disabling stroke and death, 9.3% wound complication, and 8.6% cranial nerve paralysis (10).
The European Carotid Surgery Trial, similar in size to that of NASCET, reported final results with comparable perioperative rates of stroke and death (13). Among the 1745 patients who received CEA, there were 122 nonfatal major strokes or death (7.0%); the death rate at 30 days was 1.0%, the disabling stroke rate 2.5%, and the non-disabling stroke rate 3.5% (13). Neck dissection and retraction necessary to reach the carotid artery may injure cranial nerves during CEA. Cranial and cervical nerve palsies have been reported in up to 27% of patients (7, 10, 17, 30–33), even in recent studies. There were four cranial nerve injuries in three patients (11.5%) in our CEA series although two were temporary and all developed among the patients with a high carotid bifurcation. Independent predictors of adverse outcome after CEA include contralateral occlusion, previous ipsilateral CEA, and combined coronary and carotid artery disease, although ongoing debates exist (10, 34–38).

CAS has recently emerged as a rational alternative to CEA, especially to the high surgical risk group, although CAS has not been completely out of investigational status. CAS, compared with CEA, is now well accepted for its advantages and benefit because CAS can avoid surgical incision, requires only local anesthetic in the groin, and may be more cost-effective because of a shorter hospital stay and the reduced use of expensive intensive care unit (20, 39, 40). Furthermore, CAS may have advantages over CEA in specific clinical subgroups such as patients with substantial coexistent morbidities (e.g., severe cardiopulmonary disease), contralateral carotid occlusion, post-endarterectomy restenosis, radiation-induced stenosis, and surgically inaccessible (high, low, or tandem) lesions. CAS is not limited to the cervical portion of the carotid artery (4, 16, 40).

Since 1996, there have been many individual CAS series (4, 6, 9, 14, 15, 24, 39–45). Comparative analysis of these studies is difficult because of the heterogeneity in the sample populations, lesion characteristics, endovascular techniques, and outcome data.

**Fig 2.** Case of a 68-year-old man with severe stenosis (91%) of the right ICA, who claimed severe unilateral headache after the third post-CEA day.

A–D, Pre-CEA angiogram (A), post-CEA T2-weighted MR image (B), post-CEA DW image (C), and post-CEA gradient-echo MR image (D). Post-CEA MR images show severe vasogenic edema with focal hemorrhage (arrow) in the right cerebral hemisphere.
However, the overall reported rate of technical success is greater than 93%, procedure-related mortality rates (including cardiac deaths) are 0–4.5%, and stroke rates are 0–13%. The reported stroke and death rates after CAS were heterogeneous, and complication rates in many reports were higher than the postulated limit of 6% for symptomatic stenoses and 3% for asymptomatic stenoses (7, 8, 19, 24).

In 1996, Diethrich et al (39) reported two deaths (1.8%), seven strokes (6.3%), and five transient neurologic events (4.5%) after CAS. The authors concluded that the frequency of periprocedural neurologic complications was excessive. Diethrich, in an accompanying editorial, suggested that CAS be re-

![Image of a 58-year-old man with symptomatic moderate stenosis (69%) of the right ICA.](image)

**TABLE 3: Rate of new hyperintensity on DW image according to the angiographic variables**

<table>
<thead>
<tr>
<th>Angiographic Variables</th>
<th>CEA (n = 26)</th>
<th>CAS (n = 22)</th>
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<tr>
<td>Ipsilateral ICA stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0 of 19)</td>
<td>29 (4 of 14)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (1 of 7)</td>
<td>50 (4 of 8)</td>
</tr>
<tr>
<td>Contralateral ICA stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion or severe</td>
<td>33 (1 of 3)</td>
<td>33 (4 of 12)</td>
</tr>
<tr>
<td>Normal to moderate</td>
<td>0 (0 of 23)</td>
<td>40 (4 of 10)</td>
</tr>
<tr>
<td>Ipsilateral ICA plaque ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>5 (1 of 21)</td>
<td>33 (6 of 18)</td>
</tr>
<tr>
<td>Absent</td>
<td>0 (0 of 5)</td>
<td>50 (2 of 4)</td>
</tr>
</tbody>
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Note.—Data are percentage (number) of procedures in which a new hyperintensity was noted for that angiographic variable.
stricted to cases of carotid restenosis after prior CEA, instances in which the internal carotid stenosis was anatomically higher than readily treated by CEA, and patients with radiation-induced stenosis (46). However, in a larger prospective study of 271 CAS procedures in 231 patients reported by Mathur et al (45) in 1998, there was one death, two major strokes (0.7%), and 17 (6.2%) minor strokes. Roubin et al (43) updated their previous report with inclusion of 604 procedures in 528 patients. The overall 30-day stroke and death rate was 7.4%.

Recently, results of an initial randomized multicenter clinical trial of Carotid and Vertebral Artery Transluminal Angioplasty Study were reported (20). Carotid angioplasty with or without stent placement had similar major risks and effectiveness at preventing stroke during 3 years compared with CEA. These results suggested that CAS might be comparable to CEA.

The efficacies of CEA and CAS in preventing stroke depend on the ability of the vascular surgeon and interventional neuroradiologist to achieve complication-free results. Ongoing refinements and advances in the techniques and devices are aimed at reducing the occurrence of neurologic complications. Most neurologic complications occurring during or immediately after CEA and CAS are said to result from cerebral embolism. Principally, three mechanisms have been implicated in stroke complicating CEA. The first is cerebral embolization during dissection of the carotid arteries and from the endarterectomy surface (47–49); the second, stroke as a result of hypoperfusion during clamping of the carotid arteries (49); and the third, stroke due to cerebral hemorrhage following clamp release and hyperperfusion (49, 50). Intraoperative hypoperfusion should rarely be a problem because brain perfusion can be maintained by collateral channels or selective shunt surgery. In contrast, small emboli arising from a friable plaque during arterial dissection and cross clamping may constitute an unavoidable risk of perioperative ischemic complications. There was one post-operative hemorrhage following clamp release and hyperperfusion (49, 50). Intraoperative hypoperfusion should rarely be a problem because brain perfusion can be maintained by collateral channels or selective shunt surgery. In contrast, small emboli arising from a friable plaque during arterial dissection and cross clamping may constitute an unavoidable risk of perioperative ischemic complications. There was one post-operative hemorrhage following clamp release and hyperperfusion (49, 50).

During CAS, while the risk of hypoperfusion is likely to be less, the frequency of embolization has been demonstrated to be much greater. For CAS of a tight carotid stenosis, a guidewire, balloon catheter, and stent introducer must be passed across the narrowing point and the plaque dilated or have a stent placed. This process is associated with a high frequency of cerebral embolization demonstrated on transcranial Doppler sonograms of the MCA (51). Long or multiple stenoses were suggested as independent predictors of stroke during CAS (45).

In these consecutive 48 procedures of 44 patients undergoing elective CEA or CAS, all new acute lesions were small and most could not be seen with conventional brain MR imaging. Older studies that used CT demonstrated new asymptomatic cerebral infarcts in 0–6% after CEA (52–54). The significance of those studies was obviously limited by the low sensitivity of CT scanning for acute ischemic changes. In studies that used conventional MR imaging techniques, such as T1- and T2-weighted, FLAIR, and proton density-weighted sequences, the rate of postoperative silent infarction was higher than that in CT-based reports and ranged from 9–24% (55, 56). Recently, several DW imaging studies about embolic infarction after CEA have been reported (1, 2, 5, 57), and the rate of ischemic lesion on DW images ranged from 0–4.2%.

Our study has some limitations, including a relatively small sample and rarity of stroke in the two groups, relatively inconsistent time window for DW imaging even within one week, and different patient characteristics between the two groups. Angiographic variables such as plaque ulceration, degree of ipsilateral carotid artery stenosis, and contralateral carotid artery stenosis or occlusion could not be compared statistically with the occurrence of embolic brain lesions on DW images. Although DW imaging would provide a more specific and sensitive evaluation of acute ischemic lesion in comparison with prior CT and MR imaging studies, it may not demonstrate all ischemic lesions. We might have missed transiently or permanently reversible, short-lived ischemic lesions in some cases (58, 59). In the CAS series of 22 procedures, 54% (n = 12) had a contralateral ICA occlusion or severe stenosis; however, only 11.5% (n = 3) occurred in the CEA series of 26 procedures. Because of this relatively unfavorable patient selection, this small study from a single center may not be representative of the general results of CEA and CAS.

Conclusion

In this small series, the frequency of ischemic brain lesions of embolic origin following CEA was significantly lower than that of CAS, and therefore, CEA in general seems to be a safer procedure with a lower risk of post-operative cerebral or retinal ischemia, as long as meticulous surgical technique, reliable intraoperative monitoring, and neuroprotective measures are consistently applied. However, most hyperintensities on DW images were silent, and the overall symptomatic complications were higher in the CEA series than in the CAS series. CAS may be able to become a comparable procedure to CEA in view of its relatively low total complication rate and can be a more reliable procedure with continued advances in neuroprotective devices in the near future.

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