Fate of the external carotid artery following carotid interventions

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OBJECTIVE: The external carotid artery (ECA) is an important collateral pathway for cerebral blood flow. Carotid artery stenting (CAS) typically crosses the ECA, while carotid endarterectomy (CEA) includes deliberate ECA plaque removal. The purpose of the present study was to compare the long-term patency of the ECA following CAS and CEA as determined by carotid duplex ultrasound.

METHODS: Duplex ultrasounds and hospital records were reviewed for consecutive patients undergoing CAS between February 2002 and April 2008, and were compared with those undergoing CEA in the same time period. Preoperative and postoperative ECA peak systolic velocities were normalized to the common carotid artery (CCA) as ECA/CCA ratios. A significant (80% or greater) ECA stenosis was defined as an ECA/CCA ratio of 4.0. A change of ratio by more than 1 was defined as significant. Data were analyzed using Student's *t* test and χ^2 analysis.

RESULTS: A total of 86 CAS procedures in 83 patients were performed (81 men, mean age 69.9 years). Among them, 38.4% of patients had previous CEA, 9.6% of whom had contralateral internal carotid

artery occlusion. Sixty-seven CAS and 65 CEA patients with complete duplex data in the same time period were included in the analyses. There was no difference in the incidence of severe ECA stenosis on preoperative ultrasound evaluations. During a mean follow-up of 34 months (range four to 78 months), three postprocedure ECA occlusions were found in the CAS group. The likelihood of severe stenosis or occlusion following CAS was 28.3%, compared with 11% following CEA ($P<0.025$). However, 62% of CEA patients and 57% of CAS patients had no significant change in ECA status. Reduction in the patient's degree of ECA stenosis was observed in 9.4% of CAS versus 26.6% of CEA patients. Overall, immediate postoperative ratios of both groups were slightly improved, but there was a trend of more disease progression in the CAS group during follow-up.

CONCLUSION: CAS is associated with a higher incidence of post-procedure ECA stenosis. Despite the absence of neurological symptoms, a trend toward late disease progression of ECA following CAS warrants long-term evaluation.

Key Words: Carotid endarterectomy; Carotid stenosis; Carotid stent; External carotid artery

There is little question about the role and contribution of the internal carotid artery (ICA) to the brain. Less known is the exact contribution of the external carotid artery (ECA). However, the ECA is a well-recognized collateral pathway to the intracranial circulation through different tributaries of the head, neck and meninges (1,2). Much discussion and attention has been given to the natural history and pathology of ECA disease. Also of interest has been the role of the ECA following ICA stenosis and occlusion (3,4).

During carotid endarterectomy (CEA), surgeons not only preserve the ECA, but different techniques are often used to preserve and even improve inflow to this vessel (5,6). In recent years, carotid artery stenting (CAS) has been adopted for high-risk patients with severe ICA stenosis. Unlike CEA, CAS attempts to treat the plaque by excluding the lesion, rather than removing it. Because carotid disease is most commonly found at the bifurcation, this often necessitates placing a stent across the ECA. Long-term patency of the ECA is seldom a concern or even examined during CAS. We examined the fate of the ECA by comparing the long-term rates of stenosis and patency following both CEA and CAS. We also evaluated the clinical significance of the results.

METHODS

Patients

From February 2002 to April 2008, 86 CAS procedures were performed in 83 patients in a single Stanford University-affiliated institution (California, USA). A total of 67 patients

with ECA information on follow-up ultrasound evaluations were included in the present study. During the same time period, 65 CEA patients with comparable preoperative carotid ultrasound information were also evaluated. No patients from this group were lost to follow-up during the study period. All data were collected in a retrospective manner and the project was approved by the Stanford University Institutional Review Board.

In addition to detailed duplex information for the carotid arteries for each patient, various clinical information was also documented. These factors included the presence of hypertension, hyperlipidemia, smoking status, diabetes mellitus, obesity defined by a body mass index of greater than 30 kg/m², coronary artery disease (CAD), chronic obstructive pulmonary disease, documented peripheral vascular disease, atrial fibrillation, history of ipsilateral CEA, presence of contralateral carotid artery stenosis and preoperative neurological symptoms.

Surgical and interventional techniques

Patients were identified based on carotid ultrasound results; carotid angiography was not routinely performed. CEA with patch angioplasty was performed under general anesthesia in a fashion similar to that described elsewhere (7,8), which is briefly discussed here. Following dissection and identification, systemic anticoagulation was administered. An arteriotomy was made and a shunt was inserted exclusively. An endarterectomy was performed in a standard fashion with visualization of both the proximal and distal ends of the carotid

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TABLE 1
Patient medical comorbidities

Characteristic	CAS (n=67)	CEA (n=65)	P
Current smoker	54 (80)	36 (55)	0.002
Diabetes mellitus	36 (54)	25 (38)	0.08
Hypertension	63 (94)	59 (90)	0.48
Hyperlipidemia	64 (96)	56 (86)	0.06
Obesity	17 (25)	15 (23)	0.76
CAD	57 (85)	29 (45)	<0.001
COPD	19 (28)	13 (20)	0.26
PVD	30 (45)	24 (37)	0.36
Atrial fibrillation	10 (15)	6 (9)	0.32

Data presented as n (%). CAD Coronary artery disease; CAS Carotid artery stenting; CEA Carotid endarterectomy; COPD Chronic obstructive pulmonary disease; PVD Peripheral vascular disease

plaque; endarterectomizing the ECA was also attempted using an eversion technique. Following removal of the offending plaque, a patch with a running nonbraided suture was placed before re-establishing the in-line flow. The type of patch and shunt were left to the discretion of the individual surgeon. Patients were admitted to the intensive care unit for close observation before they were discharged home the following day on lifelong acetylsalicylic acid.

All CAS procedures were performed in an Endovascular Suite (GE Medical Systems, USA) with routine use of an embolic protection device (EPD). An anesthesiologist was present to monitor the blood pressure as recorded by an arterial line. Oxymetry and continuous electrocardiography were similarly monitored. The technical details of CAS have been described in previous studies (9,10). Briefly, a carotid angiogram was performed to confirm severe ICA stenosis. Then, under fluoroscopic guidance, a stiff wire was securely placed and maintained in the ECA over which a 6 Fr, 90 cm carotid guiding sheath was advanced. Once this was secured in the distal common carotid artery (CCA), a selective digital carotid angiogram was then performed via the sideport of the guiding sheath. An appropriate embolic EPD and stent device were selected based on length and morphology of the lesion, as well as the diameter of the CCA and ICA. EPDs used included FilterWire EZ system (Boston Scientific Corporation, USA), RX ACCUNET (Abbott Laboratories, USA), Angioguard (Cordis Corporation, USA) or Emboshield (Abbott Laboratories) and were chosen at the discretion of the intervening surgeon. Following activation of the EPD, a coaxial angioplasty balloon was used to predilate the carotid lesion if necessary. Next, an appropriate self-expanding United States Food and Drug Administration-approved mono-rail carotid stent was deployed across the internal carotid stenosis. Stents used included ACCULINK (Guidant Inc, USA), Precise (Cordis Corporation) and Xact (Abbott Laboratories). Poststenting angioplasty was performed for greater than 20% residual stenosis. A completion carotid angiogram was performed before capture of the EPD to document the satisfactory result of the intervention and to exclude thromboembolism proximal to the EPD. After the EPD was captured, two-view cerebral angiograms were obtained. Finally, the groin puncture sites were routinely closed with a closure device. Following CAS procedures, the patients were transferred to the intensive care unit for close hemodynamic monitoring. Most patients were discharged home the following day on lifelong acetylsalicylic acid and six weeks of daily clopidogrel.

Duplex scanning

All duplex ultrasound scans were performed by two experienced sonographers. All scans were performed using an iU22 ultrasound system (Philips Healthcare, USA) with an L9-3 MHz linear array transducer or an HDI 5000 ultrasound system (Philips Healthcare) with an L7-4 MHz linear array transducer. All waveforms were obtained with an angle of 60° or less. Standard longitudinal colour-coded flow and B-mode images were routinely obtained and stored in a digital database.

A duplex scan was performed on all patients during the pre-operative period, within 60 days before the procedure. Additional duplex scans were performed on all study participants in the postoperative period within one month and again within six months. Data were collected prospectively, and recorded retrospectively.

CCA velocity was routinely evaluated at three locations. The most distal measurement proximal to the bifurcation was used in calculations, unless an anatomical abnormality or an associated stenosis existed. In such instances, the transducer was moved proximally along the vessel to normal CCA. The degree of ICA stenosis was estimated according to the velocity criteria developed and validated in the clinical vascular laboratory under standard protocol. The ECA was measured within 1 cm of the bifurcation, unless a significant stenosis was present, at which point the measurement was taken at the site of the stenosis, but no greater than 3 cm from the bifurcation.

Grading of the ECA stenosis was performed in a fashion similar to that in the guidelines set forth by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (11) for evaluating ICA stenosis. ECA stenosis was evaluated as a measure of peak systolic velocity (PSV) and normalized to the CCA (maximal PSV of ECA divided by the PSV of CCA). These were compared as a ratio. A significant stenosis in the ECA was defined as a ratio of ECA/CCA of greater than 4.0. This value was correlated with an approximately 80% stenosis of the ECA. For the present study, a change in ratio of greater than 1.0 was considered to be significant.

Statistical analyses

Data analyses were performed by using Stata version 10.0 (StataCorp, USA). Statistical analyses were performed using the pooled Student's *t* test and uncorrected Pearson χ^2 test when comparing ECA velocities between the CAS and CEA groups. $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 67 CAS patients (97% men) and 65 CEA patients (100% men) with complete data were analyzed. The average age of the patient population was 69.4 years; there was no age difference between the two study groups. Among multiple risk factors evaluated between the two groups, there was no difference in hypertension, hyperlipidemia, diabetes mellitus, chronic obstructive pulmonary disease, obesity and atrial fibrillation. However, there was a significantly higher number of smokers in the CAS group compared with the CEA group (80% versus 55%, $P = 0.002$). Similarly, a significantly higher number of patients in the CAS group ($n = 57$, 85%) had a history of CAD compared with the CEA group ($n = 29$, 45%, $P < 0.001$) (Table 1).

TABLE 2
Patient demographics and preoperative characteristics

Characteristic	CAS (n=67)	CEA (n=65)	P
Mean age (range), years	69.9 (52–91)	68.9 (52–85)	NS
Male sex	65 (97)	65 (100)	NS
Right-sided disease	34 (51)	32 (49)	NS
Contralateral ICA $\geq$ 80% stenosis	6 (9)	2 (3)	NS
Contralateral ICA occlusion	4 (6)	5 (7.7)	NS
Ipsilateral CEA	21 (31.1)	3 (4.6)	<0.001
Severe ECA stenosis	5 (7.5)	8 (12.3)	NS
Preoperative neurological symptoms	33 (49.2)	29 (44.6)	NS

Data presented as n (%) unless otherwise indicated. CAS Carotid artery stenting; CEA Carotid endarterectomy; ECA External carotid artery; ICA Internal carotid artery; NS Not significant

TABLE 3
Multivariate logistic regression analysis for progression to severe stenosis

	OR	95% CI	P
Preoperative ECA velocity	1.01	1.00–1.02	0.019
Diabetes mellitus	0.23	0.04–1.40	0.111
Previous neurological symptoms	21.26	2.65–169.89	0.004

$R^2=23.14\%$. ECA External carotid artery

A total of 62 patients (47%) had preoperative neurological symptoms and there was no difference between the two groups with respect to the presence of symptoms (49.2% in the CAS group versus 44.6% in the CEA group, $P=0.71$). There was also no difference in the contralateral carotid stenosis or occlusion. Four patients in the CAS group and five patients in the CEA group had contralateral ICA occlusion, and severe contralateral stenosis (80% to 99%) was seen in 9% of CAS and 3% of CEA patients ($P=0.76$). Nonetheless, there were significantly more patients who had previous ipsilateral CEA in the CAS group compared with the CEA group (31.1% versus 4.6%, $P<0.001$) (Table 2).

Risk factors for progression to severe stenosis were also analyzed using multivariate logistic regression analysis. It was demonstrated that an elevated preoperative ECA velocity, the presence of diabetes mellitus and a history of neurological symptoms were predictors for having a postoperative elevated ECA velocity (Table 3). While diabetes mellitus is a weak predictor with an OR of 0.23, an elevated preoperative ECA velocity and previous neurological symptoms were strong predictors with ORs of 1.01 and 21.26, respectively.

Preoperative ultrasound evaluations demonstrated no significant difference in the PSV of the ECA in the two groups. The PSV in the CAS group was 182.5 cm/s and in the CEA group was 186.5 cm/s ($P=0.85$). Similarly, there was no difference in ECA/CCA ratios between the groups (2.64 versus 2.65) or in the patients with severe ECA stenoses (ECA/CCA greater than 4) (Table 2). Five patients in the CAS group had severe ECA stenosis, compared with eight patients in the CEA group (Table 2).

During a mean follow-up period of 34 months (range four to 78 months), three patients had postprocedure ipsilateral ICA occlusions (4.3%) in the CAS group versus one patient (1.5%) in the CEA group. The percentage of patients who progressed to severe stenosis or complete occlusion following CAS was 28.3%, while only 11% of CEA patients progressed to severe stenosis or occlusion ($P<0.025$) (Table 4).

TABLE 4
Follow-up evaluations (mean 34 months, range four to 78 months)

	CAS (n=67)	CEA (n=65)	P
Ipsilateral ICA occlusion	3 (4.3)	1 (1.5)	NS
Severe ECA stenosis or occlusion	19 (28.3)	7 (11)	0.025
Unchanged ECA status	38 (57)	40 (62)	NS
Improved ECA status	6 (9.4)	17 (26.6)	NS

Data presented as n (%). CAS Carotid artery stenting; CEA Carotid endarterectomy; ECA External carotid artery; ICA Internal carotid artery; NS Not significant

TABLE 5
External carotid artery peak systolic velocity (PSV), cm/s

PSV	CAS (n=67)	CEA (n=65)	P
Preoperative	182.5	186.5	0.85
Postoperative	179.6	176.9	0.88

CAS Carotid artery stenting; CEA Carotid endarterectomy

Nonetheless, the majority of CAS patients (57%) had no change in the status of their ECA following the procedure, and there was an overall 9.4% reduction in the degree of ECA stenosis following CAS. Similarly, 62% of CEA patients had no change in the degree of their ECA stenosis following surgery and there was an overall 26.6% reduction in the degree of ECA stenosis following CEA (Table 4). The PSV of the ECA following surgery was not significantly different between the two groups. The mean PSV was 179.6 cm/s in the CAS group and 176.9 cm/s in the CEA group ($P=0.88$) (Table 5). Among patients with severe stenosis or complete occlusions of ECA following carotid interventions, no associated neurological symptoms were identified.

DISCUSSION

With the increased popularity of CAS, multiple clinical trials have critically examined the outcomes of CAS, particularly the procedure-related neurological and cardiopulmonary complications. Mid- to long-term follow-ups were primarily focused on patency rates of ICA and restenosis rates of carotid stents. Only a few studies (12–16) have evaluated ECA status following carotid interventions. The present study added valuable information to our limited knowledge of ECA status following carotid interventions.

Most studies examining ECA status investigated increases in ECA velocity that reflected moderate stenoses. Because there was no standard criterion for defining ECA stenosis, researchers have adapted velocity criteria for moderate ICA stenosis. Willfort-Ehringer et al (13) discovered a 17.5% early ipsilateral ECA stenosis rate (70% or greater) immediately following stenting. At six months, this number increased significantly to 35.7%. However, this rate appeared to remain relatively stable at two years (38.3%). This same group had a 4.6% occlusion rate during the same follow-up period. Conversely, de Borst et al (14) found a higher rate of significant stenosis, although they defined significant stenosis as an ECA PSV of greater than 125 cm/s, which correlated to 50% or greater stenosis as per the authors' definition of stenosis. During their follow-up period of 60 months, they found 49.1% ECA stenosis at three months, which increased to 56.4% at 12 months. By 60 months, the degree of stenosis had levelled to approximately 74%. They had a 1.8% occlusion rate during the same period.

Unlike other studies, we specifically examined patients with 80% or greater ECA stenosis following carotid interventions because we believe that severe ECA stenosis is most likely associated with clinical sequelae. We identified a significant higher incidence of severe ECA stenosis/occlusion in the patients who underwent CAS compared with those who received CEA during follow-up despite similar ECA status during preoperative ultrasound evaluation. Although no associated neurological symptoms were identified, progression of ECA stenosis is a concern and warrants long-term evaluation. Accordingly, we would recommend continued surveillance with annual follow-up ultrasounds to evaluate for further progression of disease in the ECA following ICA stenting. It is conceivable that, over a longer follow-up period, an increase in the degree of ECA stenosis will be demonstrated. Because there is a higher incidence of restenosis of carotid stents in the CAS group, it would certainly be valuable to evaluate whether this correlates with the development of neurological symptoms in this group. It may also be important to maintain a prolonged follow-up of patients at the highest risk for developing ECA stenosis – patients with previous symptoms and patients who had an elevated preoperative ECA velocity.

A study by Woo et al (15) also compared rates of ipsilateral ECA stenosis following both CAS and CEA. They concluded that the PSVs of “ECA in the CAS group were significantly higher than in the CEA group”. All patients in their study remained free from any neurological symptoms. Similarly, we did not identify any associated neurological symptoms in patients with severe ECA stenoses. However, we showed a similar mean ECA PSV between the CEA and CAS groups. Nonetheless, a significantly higher number of patients developed severe ECA stenoses in the CAS group compared with the CEA group (28.3% versus 11%) during follow-up.

The clinical significance of our findings is still undetermined. The impact of ECA stenosis and occlusion remains poorly defined. It has been documented that high-grade ECA stenosis may predispose patients to subsequent cerebral hypoperfusion (17). However, this usually occurs when the ICA is occluded, thus making the ECA the dominant collateral to the cerebrum

ipsilaterally. In our study and other studies like it, the converse is true: there exists a newly revascularized ipsilateral ICA. It may very well be that those symptoms, which would normally be present in a patient with an occluded ipsilateral ICA, remain occult when it remains patent. Again, it would be important to document whether any neurological sequelae develop in a patient with severe ECA stenosis who develops recurrent ICA stenosis over the long term, particularly in the CAS group.

Admittedly, the present study had several limitations. The study is a retrospective review of carotid interventions. All patients who underwent CAS procedures during the study period were evaluated and those with follow-up ECA ultrasound information were included. Only a limited number of patients who received CEA for their occlusive disease were included. Although we selected a similar number of CEA patients with comparable preoperative ECA statuses, there was still a large number of CEA patients during the same time period who were not included in the study. Additionally, due to our selection criteria for CAS, it was not surprising that there was a significantly higher number of patients with CAD and post-CEA restenosis in the CAS group. Although unlikely, it is possible that carotid stenosis with previous CEA may have contributed to ECA disease progression in the CAS group. In addition, although also unlikely, temporary wire placement in the ECA during CAS might have induced ECA stenosis. Although a wire was advanced atraumatically into the ECA and was kept there for only a short time during guiding sheath placement, it is impossible to exclude whether it caused any changes in the degree of stenosis following ECA wire placement. We suspect such changes are minute and do not affect the overall result. Finally, there was a significantly higher number of active smokers in the CAS group than in the CEA group. Smoking may have contributed to a more rapid ECA disease progression in the CAS group. Prospective evaluations of patients with comparable preoperative ultrasound information, demographics and medical comorbidities are required to illuminate the incidence of ECA stenosis following carotid interventions and the importance of ECA in the cerebral circulation.

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