Carotid Artery Stenting in a Single Center: Are Six Years of Experience Enough to Achieve the Standard of Care?

C. Setacci,* E. Chisci, G. de Donato, F. Setacci, P. Sirignano and G. Galzerano

Department of Surgery, Vascular and Endovascular Surgery Unit, University of Siena, Viale Bracci, I-53100 Siena, Italy

Objectives. This study aims to determine safety, short and mid-term outcomes of Carotid Artery Stenting (CAS) and Endarterectomy (CEA) during the last 6 years in a single vascular surgery center.

Methods. We retrospectively reviewed 2624 consecutive carotid revascularizations performed between December 2000 and December 2006 in 2176 patients with severe carotid artery stenosis (symptomatic ≥70%, asymptomatic ≥80%), of which 1589 were CEA and 1035 CAS. Patients were followed up at 1, 3, 6 and 12 months after the procedure and then yearly.

Results. The percutaneous procedure was successful in 99.2% of the cases. No intra-procedural death occurred. The overall death and stroke rates at 30 days, 1 year and 3 years were 1.54%, 2.86%, 7.43% in the CAS group and 2.07%, 3.55%, 6.95% in the CEA group, respectively (p value not significant in any case).

Conclusions. At our vascular surgery centre the results of CEA and CAS are similar. CAS has become our standard of care in preventing strokes and is an effective alternative to CEA for low-risk patients as well.

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Keywords: Carotid artery; Carotid stenosis; Angioplasty; Stent; Endarterectomy; Stroke; Mortality rate; Review.

Introduction

In Western countries, stroke is the third leading cause of death and is the most common cause of permanent disability.1 A stenosis of the internal carotid artery may be responsible for 10% to 20% of all strokes or transient ischemic attacks (TIA). Carotid artery stenting (CAS) has emerged as a useful, potentially less-invasive alternative to carotid endarterectomy (CEA) but controversy presently surrounds this procedure.2 Part of the controversy arises from confusion regarding which physicians should treat carotid artery disease. Vascular surgeons, neurosurgeons, interventional cardiologists, neuroradiologists, radiologists, cardiac or general surgeons have openly embraced the treatment of carotid disease and in particular this new technology (CAS). At the same time, during the last decade there have been important innovations in the device, technical refinements and a better knowledge of patient selection. With the introduction of CAS, vascular surgeons have been challenged to change their point of view in managing severe carotid artery stenosis. The two most referenced trials in the current clinical decision-making process for carotid stenosis are the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the Asymptomatic Carotid Atherosclerosis Study (ACAS). Both concluded there was a clear benefit to CEA in patients with symptomatic and asymptomatic carotid occlusive disease.3,4 In current clinical practice, CAS has emerged as a viable alternative for patients who are deemed at high risk for surgery or poor candidates for CEA, which is considered the standard of care.5 Several trials have suggested equivalent results for CAS and CEA.6–9

The purpose of this report was to review our experience with CAS in comparing to CEA over the last 6 years.

Methods

Between December 2000 and December 2006, 1027 successful CAS procedures (out of 1035 attempted procedures: procedural success 99.2%) were performed in our center of Vascular and Endovascular Surgery at the University of Siena, in 937 patients (98 treated with staged bilateral procedures). This
represents 39.4% of all carotid lesions treated during the same period (CEA 1589 procedures in 1368 patients). Our indications for treatment were the presence of a symptomatic carotid-artery stenosis ≥70% or an asymptomatic stenosis of at least 80%. A large number of lesions were symptomatic (n = 1238, 47.2%).

The demographic data and neurological history of the two study groups (CAS vs CEA) are summarized in Table 1. Demographic variables, clinical data, intraoperative and follow-up data were collected by the operative team in a special database. Written informed consent for intervention was obtained from all patients. Carotid stenting was carried out using self-expandable stents in all cases. Cerebral protection devices were also used in all cases, involving distal filter devices (91.1%), occlusive distal balloon (0.9%) or proximal balloon protection (8%). The majority of procedures were elective (CAS n = 1002; CEA n = 1527) while the remaining were urgent interventions (CAS n = 33; CEA n = 62). The reasons for urgent treatment were the same for both groups: amaurosis fugax, crescendo TIA or acute minor stroke within 14-28 days from the onset of symptoms (modified Rankin scale score <3).

Data analysis included minor, major or fatal strokes and deaths (procedure-related and non-procedure-related), at discharge, at 30 days, at 1 and at 3 years and MI at 30 days. We also evaluated the overall death (procedure-related and non-procedure-related) and stroke rate at 30 days, 1 year and 3 years for CAS and CEA.

A transient ischemic attack (TIA) was defined as a focal, retinal or hemispheric event from which the patient made a complete recovery within 24 hours. A minor stroke was defined as a new neurological deficit that either resolved completely within 30 days or increased on the NIH (National Institutes of Health) Stroke Scale by ≤3. A major stroke was defined as a new neurological deficit that persisted >30 days and increased on the NIH Stroke Scale by ≥4. A fatal stroke was defined as death attributed to an ischemic stroke or intra-cerebral hemorrhagic stroke. MI was defined as new evidence of myocardial damage as indicated by elevation of either creatine kinase or CK-MB to more than 2 times the upper limit of normal and troponin T > 0.1 ng/mL, usually in the setting of chest pain or electrocardiogram changes. Table 2 shows baseline ultrasound lesion characteristics (Gray-Weale Classification10) between treatment arms.

### Table 1. Demographic data and neurological history of the patient groups. CAS, carotid artery stenting; CEA, endarterectomy; COPD, Chronic Obstructive Pulmonary Disease; ASA, Score of the American Society of Anesthesiologists

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>CAS No.</th>
<th>CEA No.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures</td>
<td>1035</td>
<td>1589</td>
<td>100.00</td>
</tr>
<tr>
<td>Mean age</td>
<td>74 S.D. 3</td>
<td>65 S.D. 6.4</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Over 80 years</td>
<td>141</td>
<td>13.65</td>
<td>24</td>
</tr>
<tr>
<td>Hypertension</td>
<td>736</td>
<td>71.11</td>
<td>1164</td>
</tr>
<tr>
<td>Smokers</td>
<td>605</td>
<td>58.5</td>
<td>838</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>321</td>
<td>30.98</td>
<td>524</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>458</td>
<td>44.22</td>
<td>706</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>285</td>
<td>27.52</td>
<td>410</td>
</tr>
<tr>
<td>Heart failure</td>
<td>231</td>
<td>22.37</td>
<td>381</td>
</tr>
<tr>
<td>COPD</td>
<td>321</td>
<td>30.98</td>
<td>459</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>221</td>
<td>21.32</td>
<td>331</td>
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<tr>
<td>Post-CEA restenosis</td>
<td>139</td>
<td>13.44</td>
<td>13</td>
</tr>
<tr>
<td>Post-attinic stenosis</td>
<td>35</td>
<td>3.04</td>
<td>3</td>
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<tr>
<td>Previous radical</td>
<td>49</td>
<td>4.72</td>
<td>7</td>
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<tr>
<td>surgery of the neck</td>
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<tr>
<td>Significant medical comorbid conditions</td>
<td>463</td>
<td>44.74</td>
<td>58</td>
</tr>
<tr>
<td>(ASA IV)</td>
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<td></td>
<td></td>
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<tr>
<td>Carotid post-stenting restenosis</td>
<td>18</td>
<td>1.74</td>
<td>5</td>
</tr>
<tr>
<td>Neurological history</td>
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</tr>
<tr>
<td>No. %</td>
<td>438</td>
<td>42.33</td>
<td>757</td>
</tr>
<tr>
<td>Symptomatic lesions</td>
<td>596</td>
<td>57.67</td>
<td>832</td>
</tr>
</tbody>
</table>

**CAS Procedure**

Carotid stenting was carried out using self-expanding stents exclusively. Cerebral protection devices were used in all cases. All patients were pretreated with acetylsalicylic acid at a mean dosage of 125 mg/d and with clopidogrel or ticlopidine at a mean dosage of 75 mg/d or 500 mg/d, respectively, for at least 4 to 5 days prior to admission. All the procedures were carried out percutaneously via puncture of the right and/or left femoral artery. Weight-adjusted (70 U/kg) heparin was administered and repeated as necessary to maintain an activated clotting time of 225 to 250 seconds throughout the procedure. Based on the experience with percutaneous coronary angioplasty and stenting, the common carotid artery (CCA) was selectively engaged directly by using an appropriate 8-F guiding catheter. When the use of a primary guide catheter was not possible due to the particular anatomy of the supra-aortic vessels, a stiff guidewire was placed into the external carotid artery to position a long sheath or a guiding catheter (coaxial technique) into the CCA. Atropine (0.5 to 1 mg) was given intravenously to most patients just before the post-stenting dilation phase to reduce bradycardia and hypotension potentially associated with carotid dilation. Atropine was not administered in patients with tachycardia and uncontrolled systemic hypertension. All patients underwent an angiographic
examination of the culprit carotid lesion in 2 projections and an angiographic examination of the intracranial circulation in anteroposterior and/or lateral projections. The same angiographic imaging was performed at the end of the procedure to determine whether there was any variation in the intracranial blood flow. Clopidogrel (75 mg/d) or ticlopidine (500 mg/d) was continued for at least 30 days after the interventional procedure (hemoglobin and white blood count were checked 7 to 10 days following the percutaneous intervention). Mono antiplatelet therapy (aspirin, clopidogrel, or ticlopidine) was continued indefinitely.11

CEA Procedure

Out of 1589 CEA procedures the majority (n = 1502, 94.5%) were performed using local anesthesia (cervical block plus local infiltration). The remaining 87 cases received general anesthesia due to reduced compliance to local anesthesia of the patients (n = 35) or to urgent cases (n = 62). 1424 (89.6%) CEAs were performed using a standard medial approach and 165 (10.4%) using a retrojugular12 approach to the carotid bifurcation. In 1253 (78.8%) CEAs a longitudinal arteriotomy was used and in 336 (21.2%) an eversion endarterectomy was employed. The use of temporary shunting and patch closure was selectively done. Dacron patch angioplasty was used in 82.1% cases, including in 87.5% of the female patients. Pre-procedure medical treatment was to stop anti-platelet therapy 5-6 days before the procedure and to continue low-molecular-weight heparin, 4000 IU SC a day until the day of procedure. Weight-adjusted (70 U/kg) heparin was administered during the procedure and repeated as necessary to maintain an activated clotting time of 225 to 250 seconds throughout the procedure. The day after the procedure, we started mono anti-platelet therapy (aspirin, clopidogrel or ticlopidine), which continued indefinitely.

Follow-Up

Echoduplex and neurological examinations of all patients were carried out at 1, 3, 6 and 12 months after the procedure and then yearly. Patients were instructed to inform the vascular surgeon when any new symptoms occurred after hospital discharge.

Statistical Analysis

All results were analyzed using SPSS statistical software (SPSS, Chicago, IL). All values were expressed as mean ± SD. The Fisher exact test was used to compare the rates between the two study groups (CEA vs. CAS) for categorical variables, and all probability values were two-tailed, with a value of p < 0.05 considered as statistically significant. The Pearson χ2 test was used to evaluate the relationship between the categorical variables and the two study groups. Logistic regression was used to compare the stroke and death rate between the two study groups at 30 days, 1 year and 3 years. To evaluate the fate of the CAS and CEA patients, Kaplan-Meier survival analyses were generated for overall survival and freedom from neurological events.

Results

CAS was successfully performed in 1027/1035 cases (99.2%). The eight failed attempts were due to complex vessel access and underwent immediate intraoperative conversion to CEA. In these 8 patients we did not have any neurological complications at 30 days. The mean intervention time was 24 ± 11 minutes (77 ± 26 minutes for CEA).

The neurological and cardiac complications are described in Table 3. No intra-procedural death occurred.

Thirty-Day Outcome

We reported 2 deaths in the CAS group (one procedure-related death -congestive heart failure- and one non-procedure-related death at postoperative day 25 -acute pulmonary edema in dilative cardiomyopathy), 3 fatal strokes (2 intracranial hemorrhages, 1 severe cerebral embolization at postoperative day 1), 3 major strokes (1 acute in-stent thrombosis) and 8 minor strokes. All patients who experienced a major complication were neurologically symptomatic before CAS. In asymptomatic patients there were a number of transient ischemic attacks (13/596; 2.18%), with
resolution of symptoms within 24 hours. We observed only 2 MIs.

In the subgroup of urgent CAS procedures, we observed a death/stroke rate of 6.06% at 30 days (no deaths, 2 minor strokes in patients already suffering from severe neurologic deficit before the procedure, and 1 TIA).

We observed 6 fatal strokes in the CEA group (5 intracranial hemorrhages, 1 massive ischemic lesion), 8 major strokes and 13 minor strokes. 65.7% of patients who had experienced a complication were neurologically symptomatic before CAS. Moreover we reported 4 procedure-related deaths (3 MIs at postoperative days 1, 3 and 7) and 2 non-procedure-related deaths at postoperative days 17 and 29 (road accident, re-activation of viral hepatitis). MI occurred in 7 patients.

In the subgroup of urgent CEA procedures, we observed a death/stroke rate of 6.45% at 30 days (1 death, 1 major stroke and 2 minor strokes).

The overall death and stroke rate at 30 days was 1.54% in the CAS group and 2.07% in the CEA group ($p = 0.37$).

Between the 30-day and 1 year periods (patients with complete follow-ups at 1 year were 735/937, 78.4%, for the CAS group and 1276/1368, 93.3%, for the CEA group), the incidence of new strokes was 0.95% and 1.00% respectively for CAS and CEA ($p > 1$).

At 1 year follow-up we observed 5 deaths (1 hemorrhagic stroke, 1 MI, 2 congestive heart failure, 1 acute lymphoma) in the CAS group and 8 deaths in the CEA group (3 hemorrhagic strokes, 3 MIs, 1 pneumonia, 1 gastric cancer), 3 major strokes (1 in the CAS group, 2 in the CEA group), 5 minor strokes (2 in the CAS group, 3 in the CEA group). The overall death and stroke rate at 1 year was 2.86% in the CAS group and 3.55% in the CEA group ($p = 0.45$).

The cumulative freedom from neurological events and cumulative survival analysis are shown in Figs. 1 and 2.

In-stent restenosis after CAS, at 1 year, occurred in 18 patients (2.45%) while restenosis after CEA occurred in 26 patients (2.04%) ($p = 0.63$).
lack of large randomized trials comparing endarterectomy to stenting and the fact that current trials have failed to establish a clear consensus.\textsuperscript{6,15–23} The recent EVA 3-S\textsuperscript{22} trial found CEA to be superior to CAS. However, many of these trials have been heavily criticised\textsuperscript{24–27} making interpretation of their findings difficult.

We are aware of 5 ongoing randomized trials.\textsuperscript{28–32} The results of these trials will provide a more robust level of evidence regarding the risks and benefits of CAS. The experiences of the CAS Registries combined with those of single centers are currently supplying more data about long term results.\textsuperscript{33–35} Our experience with CAS started six years ago. Initially we carefully selected patients and focused endovascular treatment on patients with \textit{anatomically complex situations} (hostile necks, deleterious neck surgery with tracheostomy, secondary interventions after endarterectomy, cervical radiotherapy, carotid stenosis after radiotherapy, large and short neck with high bifurcation, carotid bypass stenosis) or with \textit{poor clinical conditions where surgery offers worse results} (contralateral occlusions, deficient Circle of Willis, severe coronary diseases, neurological deficit, heart failure or pending coronary revascularization, 

![Fig. 1. Cumulative freedom from neurological events. CAS, carotid artery stenting; CEA, endarterectomy; TIA, Transient Ischemic Attack.](image1)

![Fig. 2. Cumulative survival analysis. CAS, carotid artery stenting; CEA, endarterectomy.](image2)
low life expectancy due to tumors, or old age [High-risk patients]. Year after year of experience with CAS optimized our learning curve and the results obtained supported our conviction of offering CAS as the first choice to patients with severe carotid stenosis as shown in Table 4.

At the moment CAS is relatively contraindicated in our center to the following categories of patients: patients with floating thrombus in the internal carotid or common carotid arteries,36 (some authors described a different approach to this open question37) or very young patients (≤ 50 years) if they are at standard risk for CEA (ASA ≤ 2, Score of the American Society of Anesthesiologists).

During these six years we observed a drastic drop in the number of CEA procedures and on the contrary a rapid growth in the number of CAS procedures as shown in Fig. 3. The very infrequent periprocedural strokes seen in this review were presumably related to small emboli released during the manipulation of the arch, previous to catheter access into the common carotid artery, before embolic filter protection was in place and at the post-dilatation of the stent. Despite the fact that the immediate periprocedural and inhospital results are encouraging, we are aware that embolic protection devices (in all their forms) allowed operators to protect the procedure.33,38,39

Long-term stroke prevention in our treated patients is the hallmark of successful carotid intervention. The 1 and 3 year rates of ipsilateral stroke for CAS in this review are 2.86 and 7.43%, respectively, similar to those of CEA (3.55% and 6.95%, \( p \) value not significant).

We believe that on the basis of the current evidence, CAS with cerebral protection, in the hands of experienced operators, can be considered equal if not superior to CEA in high-risk patients. On the basis of our results we demonstrate that if specific devices applied to specific lesions and/or anatomies are used (“tailored” CAS strategy),40 the endovascular procedure can be successful with a very low complications (Fig. 4). The “tailored” CAS strategy bases its rationale mostly on the complete knowledge of the patient’s clinical status, vascular anatomy, carotid plaque characteristics and complexity. We believe that the pathological conditions have to be matched to the technical features of the materials at the disposition of the operator. Another important factor is that the best medical treatment has also dramatically improved compared to 20–25 years ago (the NASCET “era”). There are now many more

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Table 4. Our management strategy for patients with carotid stenosis. MR, magnetic resonance; CT computed tomography; ICA, internal carotid artery; CCA, common carotid artery; CAS, carotid artery stenting; CEA, carotid endarterectomy; BMT, best medical treatment and ASA, Score of the American Society of Anesthesiologists

<table>
<thead>
<tr>
<th>CAROTID STENOSIS ≥70%</th>
<th>RECOMMENDATION OF CAS OR CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient choice (informed consent)</td>
</tr>
<tr>
<td></td>
<td>Echogenocity of the plaque</td>
</tr>
<tr>
<td></td>
<td>Neurological symptoms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STANDARD RISK PT</th>
<th>HIGH RISK PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA + BMT</td>
<td>CAS + BMT</td>
</tr>
<tr>
<td>Patients with floating thrombus in ICA or CCA</td>
<td></td>
</tr>
<tr>
<td>Patients very young (≤ 50 years) ASA ≤ 2</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CAS + BMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS + BMT</td>
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</tbody>
</table>

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medication to treat hypertension, dyslipidemia, coronary heart disease and diabetes. For example, there is convincing evidence that clopidogrel, a new generation of anti-platelet anti-aggregation drugs used widely for CAS in addition to aspirin, reduces the risk of myocardial infarction.41,42

We strongly believe as well that the treatment of severe carotid stenosis must be successfully managed by skilled operators in high-volume centers. These must be performed by centers of vascular surgery, because the vascular surgeon is the operator most familiar with the pathology, the anatomy, hemodynamics and the correlation between Echo-duplex findings and lesion characteristics. These, combined with correct patient and lesion analyses, should indicate the right intervention for each individual patient (“tailored” procedure). A “tailored” procedure is possible only when the operator is completely familiar with both procedures.

Conclusions

We present our experience of CAS compared to CEA. We have developed an approach to use CAS as a first option, and we indicate CEA only for younger patients and those with particular hypoechoic lesions at duplex imaging. In our center, with our experience, we can now offer both CEA and CAS to the patient with the same awareness and confidence. For now, the literature lacks evidence to support our conclusions, and additional trials and registers will be necessary. At this time in Italy there is a simple, clear and updated evidence-based consensus document drawn up by an Italian multidisciplinary task force (neurologists, neuroradiologists, radiologists, cardiologists, vascular surgeons) for CAS and the prevention and treatment of carotid artery disease (Carotid Artery Stenting. First Consensus Document of the ICCS-SPREAD Joint Committee).43

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Fig. 3. CAS and CEA procedure during the last 6 years. CAS, carotid artery stenting; CEA, endarterectomy.

Fig. 4. Stroke and Death rate at 30 days, from 2000 to 2006 for CAS and CEA. CAS, carotid artery stenting; CEA, endarterectomy.
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