Late Outcomes After Carotid Artery Stenting Versus Carotid Endarterectomy

Insights From a Propensity-Matched Analysis of the Reduction of Atherothrombosis for Continued Health (REACH) Registry

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Background—In patients with carotid artery disease, carotid endarterectomy (CEA) and carotid stenting (CAS) are treatment options. Controversy exists as to the relative efficacy of the 2 techniques in preventing late events.

Methods and Results—The Reduction of Atherothrombosis for Continued Health (REACH) Registry recruited >68,000 outpatients ≥45 years of age with established atherothrombotic disease or ≥3 risk factors for atherothrombosis. Patients with CAS or CEA were chosen and followed up prospectively for the occurrence of cardiovascular events. Propensity score matching was performed to assemble a cohort of patients in whom all baseline covariates would be well balanced. Primary outcome was defined as death or stroke at the 2-year follow-up. Secondary outcome was stroke or transient ischemic attack. Tertiary outcome was a composite of death, myocardial infarction, or stroke and the individual outcomes. Of the 68,236 patients with atherothrombosis, 3,412 patients (5%) had a history of carotid artery revascularization (70% asymptomatic carotid stenosis), 1,025 (30%) with CAS and 2,387 (70%) with CEA. Propensity score analyses matched 836 CAS patients with 836 CEA patients. At the end of 2 years of follow-up, in the propensity score–matched cohort, CAS was associated with a risk similar to CEA for the primary (hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.57 to 1.26), secondary (HR, 1.20; 95% CI, 0.73 to 1.96), and tertiary (HR, 0.72; 95% CI, 0.51 to 1.01) composite outcome, death (HR, 0.63; 95% CI, 0.40 to 1.00), and stroke (HR, 1.48; 95% CI, 0.79 to 2.80).

Conclusion—In a real-world cohort of patients with a history of carotid artery revascularization, CAS was comparable to CEA for late outcomes. (Circulation. 2010;122:1091-1100.)

Key Words: carotid arteries ▪ endarterectomy ▪ prognosis ▪ stents

Ischemic stroke is an important cause of major morbidity and mortality worldwide and is the third-leading cause of death in the United States. Atherosclerosis from supra-aortic vessels and especially from the common carotid bifurcation is a major cause of recurrent ischemic stroke, accounting for ~20% of all strokes. Of these, carotid occlusive disease amenable to revascularization accounts for 5% to 12% of new strokes.

Clinical Perspective on p 1100

Carotid artery stenting (CAS) has emerged as an alternative to carotid endarterectomy (CEA) for the treatment of carotid artery occlusive disease. Consequently, the American Heart Association and American Stroke Association guidelines consider CAS a reasonable strategy when performed by operators with established periprocedural morbidity and mortality rates of 4% to 6% (Class IIa). The European Society of Vascular Surgery recommends CAS in patients with a high risk for CEA done in high-volume centers with documented low perioperative stroke and death rates or in a randomized controlled trial. However, the safety and efficacy of CAS are controversial. In the recently concluded International Carotid Stenting...
Study (ICSS), comparing CEA with CAS in patients with recently symptomatic carotid stenosis who were eligible for either procedure, CEA was superior to CAS at 30 days after the procedure. The debate is exemplified by the Cochrane reviews on the topic. The 2005 Cochrane review concluded that CAS conferred a significant reduction in cranial nerve injury and was no different from CEA for the end points of 30-day death/any stroke, death/disabling stroke, death, stroke, or myocardial infarction (MI). The 2007 Cochrane review concluded that CAS conferred significant reductions in cranial nerve injury but that it was associated with a significant increase in the 30-day risk of death/stroke and any stroke. There was no difference in 30-day death and death/disabling stroke or the risk of late stroke. The 2009 Cochrane review found that CAS conferred significant reductions in not only cranial nerve injury but also MI and that it was associated with a significant increase in 30-day death/stroke, which was no longer significant in a random-effects model. Moreover, these studies evaluated mainly short-term outcomes, at which time the data are still not clear on any significant increase in perioperative morbidity and mortality with CAS. In addition, data on late outcomes from a real-world global population are unknown. The objective of our analysis was to evaluate the late outcomes in patients with CAS versus those with CEA in a large international cohort of patients with atherothrombosis enrolled in the Reduction of Atherothrombosis for Continued Health (REACH) Registry.

Methods

Study Participants

The design and methodology of the REACH Registry, an international prospective, observational registry, have been published elsewhere. Briefly, consecutive eligible patients ≥45 years of age with established coronary artery disease, cerebrovascular disease, or peripheral arterial disease or with at least 4 atherothrombotic risk factors (men ≥65 years of age or women ≥70 years of age, diabetes mellitus, diabetic nephropathy, systolic blood pressure of ≥150 mm Hg despite therapy for at least 3 months, hypercholesterolemia treated with medication, current smoking of at least 15 cigarettes per day, ankle-brachial index <0.9, asymptomatic carotid stenosis ≥70%, or carotid intima-media thickness ≥2 times of the adjacent sites) were enrolled in this international registry during a 7-month recruitment period between December 2003 and June 2004. Signed informed consent was obtained from all patients, and the protocol was approved by the institutional review board in each country according to local guidelines. For this study, patients with a history of either CEA or CAS were chosen. The study participants were from 6 geographical regions (North America, Latin America, Western Europe, Eastern Europe, Middle East, and Australasia).

Data Collection and Follow-Up

Data were collected centrally via use of standardized international case report forms completed at the study visit. Baseline demographic, medical history, risk factors, clinical examination, and baseline medications were recorded for each patient. Patients were followed up prospectively for up to 2 years for the occurrence of cardiovascular outcomes, hospitalization, or vascular interventions. The data were collected locally and then forwarded to a central clinical research organization that performed a quality check before incorporating the data for analyses. Family and general practitioners and specialists in cardiology, neurology, angiography, vascular disease, and endocrinology were involved in enrolling patients.

Outcomes Measures

The primary outcome of this analysis was a composite of death or nonfatal stroke at the end of 2 years of follow-up. The secondary outcome was stroke (fatal or nonfatal) or hospitalization for transient ischemic attack (TIA) at the end of follow-up. The tertiary outcome was a composite of death, MI, or stroke at the end of follow-up. We also explored the individual outcomes of death, MI, and stroke.

The determination of stroke or TIA required either hospital confirmation or neurologist confirmation of the event. Data were also analyzed on the basis of the presence or absence of symptoms of carotid disease. Thus, asymptomatic carotid artery disease was defined as patients with recent or past report of color-coded duplex ultrasound or angiography demonstrating ≥70% carotid stenosis with no history of TIA or stroke.

Carotid Revascularization Protocol

The need for carotid revascularization, the modality used (stenting versus surgery), and the technique used (embolic protection device or not) were left to the discretion of the physician. Procedural data and timing were not collected in the registry.

Statistical Analysis

Continuous variables were reported as mean±SD. Patient groups were compared by use of the Student t test for continuous variables and χ² test for categorical variables.

Univariate analyses were performed to determine differences between the CAS and CEA groups in baseline demographics, risk factors, and medications. The CAS and CEA groups were then compared for the risk of primary, secondary, and tertiary outcomes. Because of significant differences in key baseline characteristics between participants with CAS and those with CEA (Table 1 and Figure 1), we used propensity score matching to assemble a cohort in which all the measured baseline covariates would be well balanced. Propensity score is the conditional probability of having an exposure given a set of measured baseline covariates. Propensity scores for CAS versus CEA were estimated with a multivariable logistic regression model. In the model, CAS versus CEA was used as the dependent variable, and the 23 baseline characteristics displayed in Figure 1 were entered as covariates. Using a Greedy matching protocol, which is a 1:1 matching algorithm with no replacements, we matched the selected CAS patient with a CEA patient who had a similar propensity score. If more than 1 CEA patient met this criterion, we randomly selected a CEA patient. Once a match was established, the matched pair was eliminated from the algorithm and was not eligible for subsequent matching. We were able to match 836 CAS patients (82% of the CAS patients) with 836 CEA patients (35% of the CEA patients) who had similar propensity scores. We estimated absolute standardized differences for all 23 of the covariates before and after matching to assess prematch imbalance and postmatch balance. Absolute standardized differences directly quantify balance in the means (or proportions) of covariates across the groups and are expressed as percentages of pooled standardized differences. Bias reduction was assessed by comparing the absolute standardized differences of covariates before and after matching. An absolute standardized difference of 0% on a covariate indicates no between-group imbalance for that covariate, and values <10% indicate inconsequential imbalance. For example, the absolute standardized difference for the covariate ‘age’ between the CAS and CEA groups before matching was 42.8, suggesting significant difference between the groups for this covariate. After matching, the absolute standardized difference reduced to 5.3, suggesting an inconsequential difference between the 2 groups for the covariate.

In the propensity score–matched analysis, many CEA patients (65% of the total) remained unmatched and were thus excluded from the analysis (which may lead to slightly reduced efficiency). To factor this into the analyses, a regression adjustment with the propensity score (as a continuous variable) was also performed in which all the patients in the cohort were analyzed.
Table 1. Baseline Characteristics of Patients With CAS Versus CEA Before and After Propensity Score Matching

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Propensity Score Matching</th>
<th>After Propensity Score Matching</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAS (n=1025)</td>
<td>CEA (n=2387)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>70±9</td>
<td>69±9</td>
<td>0.260</td>
</tr>
<tr>
<td>Age (SD), y</td>
<td>68±10</td>
<td>72±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>709 (69.2)</td>
<td>1604 (67.2)</td>
<td>0.242</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>656 (64.0)</td>
<td>1849 (77.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>870 (84.9)</td>
<td>2026 (84.9)</td>
<td>0.999</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>434 (42.3)</td>
<td>892 (37.4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>820 (80.0)</td>
<td>1983 (79.3)</td>
<td>0.645</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>632 (61.7)</td>
<td>1658 (69.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Documented TIA, n (%)</td>
<td>168 (16.4)</td>
<td>758 (31.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Documented ischemic stroke, n (%)</td>
<td>164 (16.0)</td>
<td>705 (29.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stable angina, n (%)</td>
<td>350 (34.1)</td>
<td>678 (28.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unstable angina, n (%)</td>
<td>178 (17.4)</td>
<td>281 (11.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>457 (44.6)</td>
<td>707 (29.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary angioplasty/stenting, n (%)</td>
<td>788 (76.9)</td>
<td>547 (22.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>235 (22.9)</td>
<td>923 (38.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Known heart failure, n (%)</td>
<td>194 (18.9)</td>
<td>403 (16.9)</td>
<td>0.150</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>132 (12.9)</td>
<td>314 (13.2)</td>
<td>0.826</td>
</tr>
<tr>
<td>Baseline use of dual antiplatelets, n (%)</td>
<td>745 (72.7)</td>
<td>1673 (70.1)</td>
<td>0.126</td>
</tr>
<tr>
<td>Baseline use of any antiplatelets, n (%)</td>
<td>365 (35.6)</td>
<td>777 (32.6)</td>
<td>0.083</td>
</tr>
<tr>
<td>Baseline use of oral anticoagulants use, n (%)</td>
<td>863 (84.2)</td>
<td>2038 (85.4)</td>
<td>0.374</td>
</tr>
<tr>
<td>Baseline use of oral anticoagulants use, n (%)</td>
<td>247 (24.1)</td>
<td>412 (17.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline use of insulin use, n (%)</td>
<td>177 (17.3)</td>
<td>346 (14.5)</td>
<td>0.039</td>
</tr>
<tr>
<td>Baseline use of statin use, n (%)</td>
<td>806 (78.6)</td>
<td>1830 (76.7)</td>
<td>0.208</td>
</tr>
<tr>
<td>Baseline use of statin use, n (%)</td>
<td>339 (33.1)</td>
<td>880 (36.9)</td>
<td>0.034</td>
</tr>
<tr>
<td>Baseline use of ACE/ARB use, n (%)</td>
<td>598 (58.3)</td>
<td>1212 (50.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline use of ACE/ARB use, n (%)</td>
<td>667 (65.1)</td>
<td>1574 (65.9)</td>
<td>0.625</td>
</tr>
<tr>
<td>Baseline use of ACE/ARB use, n (%)</td>
<td>145 (14.1)</td>
<td>269 (11.3)</td>
<td>0.018</td>
</tr>
<tr>
<td>Aspirin use at follow-up, n (%)</td>
<td>539 (57.3)</td>
<td>1420 (70.8)</td>
<td>0.094</td>
</tr>
<tr>
<td>Use of other antiplatelets at follow-up, n (%)</td>
<td>285 (35.8)</td>
<td>723 (36.1)</td>
<td>0.895</td>
</tr>
<tr>
<td>Use of other antiplatelets at follow-up, n (%)</td>
<td>695 (86.7)</td>
<td>1740 (86.4)</td>
<td>0.854</td>
</tr>
<tr>
<td>Use of other antiplatelets at follow-up, n (%)</td>
<td>183 (23.0)</td>
<td>403 (20.2)</td>
<td>0.100</td>
</tr>
<tr>
<td>Use of oral anticoagulants at follow-up, n (%)</td>
<td>120 (15.1)</td>
<td>334 (16.7)</td>
<td>0.292</td>
</tr>
</tbody>
</table>

CAS indicates coronary artery bypass graft surgery; CCB, calcium channel blocker; ACE, angiotensin-converting enzyme inhibitor; and ARB, angiotensin receptor blocker.

To evaluate the risk of cardiovascular outcomes between the CAS and the CEA groups, we therefore performed the following survival analyses on the overall cohort: unadjusted analysis, propensity score–adjusted analysis stratified by geographic region, and propensity score–adjusted analysis with adjustment for relevant baseline risk factors (age, sex, smoking, diabetes mellitus, hypertension, hypercholesterolemia, prior MI, prior stroke, prior TIA, coronary stenting, coronary artery bypass graft surgery, atrial fibrillation) stratified by geographic region. Similarly, for the propensity score–matched cohort, we performed the following survival analyses: unadjusted analysis and analysis after adjustment for relevant baseline risk factors (age, sex, smoking, diabetes mellitus, hypertension, hypercholesterolemia, prior MI, prior stroke, prior TIA, coronary stenting, coronary artery bypass graft surgery, atrial fibrillation) stratified by geographic region.

Subgroup analyses were performed on the matched cohort based on age (<median age or >median age), sex (men versus women), and prior stroke or TIA. A test for interaction was assessed between each subgroup and the revascularization modality with Pinteraction <0.10 considered statistically significant.

All tests were 2 tailed, and except for the test for interaction, a value of P<0.05 was considered statistically significant. All analyses were performed with SAS software version 9.2 (SAS Institute, Cary, NC).

Data analysis and interpretation, as well as preparation, review, and approval of the manuscript, were done independently by academic authors who are not governed by the funding sponsors and under the control of an academic publications committee. The funding sponsors have the opportunity to review manuscript submissions but do not have authority to change any aspect of a manuscript. Dr Bhatt had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

From the registry of 68 236 patients with atherothrombosis, 3412 patients (5%) underwent carotid artery revascularization and formed the study group. Seventy percent of the patients treated had asymptomatic carotid artery disease. The main
results of all the registry patients have been published elsewhere. Among the 3412 patients, 92% had at least 12 months of follow-up and 83% of patients had at least 18 months of follow-up.

Baseline Characteristics: Unmatched Cohort
Among the 3412 patients who underwent carotid artery revascularization, 2387 (70%) underwent CEA and 1025 (30%) underwent CAS. The baseline characteristics are elaborated in Table 1. Patients who underwent carotid artery revascularization were elderly with elevated baseline risk factors (39% with diabetes mellitus, 85% with hypertension, 80% with hypercholesterolemia, 39% with prior coronary angioplasty or stenting, 34% with prior MI, 25% with prior stroke, 27% with prior TIA), and 85% of patients were taking antiplatelet therapy. Compared with the CEA group, patients who underwent CAS were more likely to be younger and diabetic; to have stable/unstable angina, prior MI, prior coronary angioplasty or stenting; and to be taking dual antiplatelet agents, oral anticoagulants, \( \beta \)-blockers, or insulin. However, they were less likely to be white, to be a past or current smoker, to have a history of coronary artery bypass graft surgery, to have symptomatic carotid artery disease (prior stroke or TIA), and to be taking calcium channel blockers, compared with the CEA group (Table 1).

Baseline Characteristics: Matched Cohort
Among the 3412 patients who underwent carotid artery revascularization, propensity score matching matched 836 CAS patients (82% of the CAS patients) with 836 CEA patients (35% of CEA patients) who had similar propensity scores (Table 1). After matching, 100% of the baseline variables matched had an absolute standardized difference \(<10\%\), suggesting adequate balance (Figure 1). A significantly greater number of CAS patients underwent coronary angioplasty or stenting, were taking dual antiplatelet agents, or were taking oral anticoagulants compared with the CEA group. Note that these variables were not included in the propensity score matching because they are inherently expected to be higher in the CAS group.

Primary Outcome

Overall Cohort
Among the 3412 patients, 269 patients (Kaplan–Meier estimate, 9.5%) reached the primary outcome of death or stroke.
at 24 months of follow-up. This included 64 patients (Kaplan–Meier estimate, 8.9%) in the CAS group and 205 patients (Kaplan–Meier estimate, 9.7%) in the CEA group (Figure 2A). There was a trend ($P<0.05$) toward decreased risk of primary outcome in the CAS group compared with the CEA group in the unadjusted analysis. However, in the adjusted models, the risk of primary outcome was similar between the 2 groups (Table 2).

**Matched Cohort**

There was no significant difference in the risk of primary outcome in the matched cohort for CAS compared with CEA (Figure 2B) in both the unadjusted (Kaplan–Meier estimates, 5.5% versus 5.1%; $P=0.67$) and adjusted models (Table 2).

**Secondary Outcome**

**Overall Cohort**

Among the 3412 patients, 161 patients (Kaplan–Meier estimate, 4.8%) reached the secondary outcome of stroke (fatal or nonfatal) or hospitalization for TIA at 24 months of follow-up. This included 43 patients (Kaplan–Meier estimate, 4.8%) in the CAS group and 118 patients (Kaplan–Meier estimate, 5.6%) in the CEA group (Figure 3A). There was no significant difference in the risk of secondary outcome between the CAS and CEA groups in the unadjusted and adjusted models (Table 2).

**Matched Cohort**

Similarly, there was no significant difference in the risk of secondary outcome in the matched cohort for CAS compared with CEA (Figure 3B) in both the unadjusted (Kaplan–Meier estimates, 5.5% versus 5.1%; $P=0.67$) and adjusted models (Table 2).

**Tertiary Outcomes**

**Overall Cohort**

Among the 3412 patients, 344 patients (Kaplan–Meier estimate, 11.9%) reached the tertiary outcome of death, MI, or stroke at 24 months of follow-up. This included 84 patients (Kaplan–Meier estimate, 11%) in the CAS group and 260 patients (Kaplan–Meier estimate, 12.1%) in the CEA group (Figure 4A). There was a trend ($P<0.05$) toward decreased risk of tertiary outcome in the CAS group compared with the CEA group in the unadjusted analysis. However, in the adjusted models, the risk was similar between the 2 groups (Table 2).

**Propensity Score-Matched Cohort**

Similarly, there was no significant difference in the risk of tertiary outcome in the matched cohort for CAS compared with CEA in the unadjusted analysis (Kaplan–Meier estimates, 11.8% versus 12.2%; $P=0.14$; Figure 4B). After adjustment for baseline variables and stratifying by region, there was a trend ($P=0.06$) toward decreased risk of tertiary outcome in the CAS versus CEA group (Table 2).

**Other Outcomes**

There was a decreased risk of all-cause mortality in the CAS group compared with the CEA group ($P=0.02$) in the unadjusted model for the overall cohort. Results trended ($P=0.05$) toward the same conclusion in the adjusted model for the matched cohort (Table 2), but this was not consistently seen in all models.

For the outcome of stroke, there was a trend toward increased risk in the CAS group compared with the CEA group ($P=0.05$) in the adjusted model for the overall cohort. However, in the matched cohort (both unadjusted and adjusted), there was no increased risk of stroke in the CAS group compared with the CEA group (Table 2).

CAS patients were at decreased risk for a MI compared with CEA patients in the adjusted and stratified model for the matched cohort ($P=0.02$). Some other models trended toward this same result (Table 2).

**Subgroup Analyses**

The risks of primary, secondary, and tertiary outcomes were comparable between CAS and CEA for various subgroups.
However, in the elderly (compared with the young), CAS was more efficacious than CEA at the prevention of primary (death/stroke) and tertiary (death/MI/stroke) outcomes. There was also a beneficial effect of CAS for the primary and tertiary outcomes in asymptomatic patients (without prior stroke/TIA) compared with symptomatic patients.

**Discussion**

Our results from a large international registry of patients with atherothrombosis indicate that CAS is comparable to CEA, even in propensity score–adjusted and propensity score–matched cohorts of patients, for late outcomes. In a subgroup analysis, CAS was better than CEA in the elderly (compared with the young) and in those with asymptomatic carotid artery disease.

**Long-Term Outcomes of Carotid Revascularization**

Few studies have evaluated the long-term outcomes between CEA and CAS. In the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, CAS with an embolic protection device resulted in a 12.2% 1-year major adverse events.
rate compared with 20.1% for CEA patients, and individual end points produced better results for CAS compared with CEA (death, 6.9% to 12.6%; stroke, 5.7% to 7.3%; MI, 2.5% to 7.9%). In this trial, at the end of 3 years of follow-up, there was no difference in the rate of death or stroke between the CAS and CEA (26.9% versus 24.6%; \( P = 0.71 \)) groups. The trial enrolled high-risk patients with medical comorbidities (heart failure, recent MI, unstable angina, severe pulmonary disease, recent cardiac surgery) and highlighted the importance of less invasive options in patients with high medical risk. However, the trial enrolled only 334 patients (169 patients randomized to CAS). A total of 70% of the patients enrolled in SAPPHIRE were asymptomatic. Our results are in many ways concordant with those of the SAPPHIRE trial. Our study enrolled patients with high medical comorbidities who largely had asymptomatic carotid artery disease (70%). In addition to showing no difference in late outcomes between the CAS and CEA groups, we noted a trend toward decreased risk of death/MI/stoke and decreased incidence of MI with CAS compared with CEA; these results are similar to the 1-year SAPPHIRE results. Although the lower incidence of MI in the CAS group cannot be directly attributed to carotid stenting, a significantly higher percentage of patients in the CAS group underwent coronary angioplasty/stenting. Moreover, CAS is less invasive than CEA. We also noted a beneficial effect of CAS compared with CEA in the elderly (>71 years of age) and in those with asymptomatic carotid artery disease. Of note, the mean age of the SAPPHIRE cohort was 72 years, and as stated above, the individual end points of death, MI, and stroke were better with CAS compared with CEA.

Similarly, in a retrospective investigation involving 3179 CAS procedures performed at 4 European carotid high-volume centers, the stroke rate at the end of 5 years was 8.1%, and the annual rate of neurological complications after CAS was comparable to that of conventional surgery as demonstrated by large randomized controlled trials involving both symptomatic patients (North American Carotid Surgery Trial [NASCET]) and European Carotid Surgery Trial [ECST]) and asymptomatic patients (Asymptomatic Carotid Atherosclerosis Study [ACAS] and Asymptomatic Carotid Surgery Trial [ACST]). Of note, the majority of stenting was done in asymptomatic patients (59%). In this analysis, the rate of
stroke or TIA at the end of 2 years was 5.4%,24 which is similar to the rate seen in our study.

The Endarterectomy Versus Angioplasty (EVA-3S)28 and Stent-Supported Percutaneous Angioplasty of the Carotid Artery Versus Endarterectomy (SPACE) 29 trials failed to reach the prespecified margin for noninferiority of CAS compared with CEA for 30-day events. However, longer-term follow-up of both of these trials showed that the rates of ipsilateral stroke were low and similar between the CAS and CEA groups at 2 and 4 years of follow-up.29,30 In addition, in the recently published Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) which enrolled 2502 patients with symptomatic or asymptomatic carotid artery disease, the risk of primary composite outcome (stroke, myocardial infarction, or death from any cause during the periprocedural period or any ipsilateral stroke within 4 years after randomization) was no different between the CAS and CEA groups at the end of 4-years of follow-up.31 There is thus a need for extended duration of follow-up in studies comparing CAS and CEA.

Finally, in the latest Cochrane review of all randomized trials comparing CEA versus CAS, there was no difference in the 24-month end point of death or stroke between the 2 groups (odds ratio, 1.26).12 However, the analysis for this end point had only 2 trials.

Our analysis from a large international cohort of patients gives valuable insight into the practice patterns around the world. First, in our cohort, most of the carotid artery revascularization was done in asymptomatic patients. This has been shown consistently in both European registries24 and American registries. Second, patients who underwent CAS had higher baseline medical comorbidities than patients undergoing CEA; thus, CAS may be considered a reasonable alternative in patients who are poor surgical candidates. Third, despite this higher baseline risk, CAS was comparable to CEA for late outcomes. Finally, similar to the SAPPHIRE trial results, we showed a lower incidence of death/MI/stroke (trend) and MI with CAS, and CAS was more beneficial in the elderly and those with asymptomatic carotid artery disease.

### Study Limitations

Our data were obtained from a large international registry of patients who underwent carotid artery revascularization in different geographic areas of the world with different practice patterns. We defined asymptomatic carotid disease as absence of stroke/TIA anytime in the past and did not use the 6-month cutoff used in contemporary studies. However, we did not have procedural data on these patients and thus were unable to compare outcomes of patients who underwent CAS with or without embolic protection devices. Periprocedural events also were not available for this analysis; hence, we were not able to compare the short-term results between the 2 groups. Events were reported by the REACH investigators, and there was no central adjudication of events. In this analysis, we considered “any” strokes, not just ipsilateral ischemic strokes. In addition, the determination of stroke or TIA did not mandate neurologist confirmation in all cases and could have led to underestimation of this
outcome in both groups. Finally, there were no data on restenosis in patients who underwent CAS or CEA.

Conclusions
In a real-world cohort of patients enrolled in this international registry, CAS was performed in patients with a higher risk of medical comorbidities. The late outcomes with CAS were comparable to those of surgery. Further long-term studies are required to define the role of CAS more precisely.

Acknowledgments
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Disclosures
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References


CLINICAL PERSPECTIVE

From the 68 236 patients with atherothrombosis enrolled in the Reduction of Atherothrombosis for Continued Health (REACH), we analyzed 3412 patients (5%) who had a history of carotid artery revascularization, 1025 (30%) with carotid artery stenting, and 2387 (70%) with carotid endarterectomy. At the end of 2 years of follow-up, in this real-world cohort of patients, carotid artery stenting was comparable to carotid endarterectomy for late outcomes. The results were consistent in a propensity score–matched model and in a regression model adjusted for propensity score. The Endarterectomy Versus Angioplasty (EVA-3S) and Stent-Supported Percutaneous Angioplasty of the Carotid Artery Versus Endarterectomy (SPACE) trials failed to show noninferiority of carotid artery stenting compared with carotid endarterectomy for 30-day events. However, longer-term follow-up of both of these trials showed that the rates of ipsilateral stroke were low and similar between the 2 groups at 2 and 4 years of follow-up. Similarly, in the recently published Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), the long term outcomes were similar. There is thus a need for extended duration of follow-up in studies comparing carotid artery stenting and carotid endarterectomy.
Late Outcomes After Carotid Artery Stenting Versus Carotid Endarterectomy. Insights From a Propensity-Matched Analysis of the Reduction of Atherothrombosis for Continued Health (REACH) Registry


for the REACH Registry Investigators

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