Predictors of Neurological Events Associated With Carotid Artery Stenting in High-Surgical-Risk Patients
Insights From the Cordis Carotid Stent Collaborative

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Background—Comorbid and anatomic characteristics that portend higher procedural risk are well defined for carotid endarterectomy but less so for carotid artery stenting.

Methods and Results—We pooled carotid stent data from 4 Cordis-sponsored trials (n=2104) with similar patient cohorts and end point determination to identify predictors of neurological death or stroke within 30 days of the procedure. Median age was 74 years (24% >80 years), 36% were women, and 24.2% were symptomatic in the previous 6 months. There were 88 (4.2%) neurological deaths or strokes at 30 days. Among symptomatic patients, the risk of adverse neurological outcome declined with increasing time between the incident neurological event and carotid stent procedure. In a logistic regression model that included preprocedural and procedural variables, significant multivariable predictors of 30-day neurological death or stroke were older age (continuous), black race, angiographically visible thrombus in symptomatic patients, procedural use of glycoprotein IIb/IIIa inhibitors, procedural transient ischemic attack, final residual stenosis >30%, and periprocedural use of protamine or vasopressors.

Conclusions—In this pooled analysis, a number of preprocedural and procedural factors predicted higher risk of stroke and neurological death within 30 days of a carotid stent procedure. Identification of such predictors may help to guide patient selection and further refine procedural technique. (Circ Cardiovasc Interv. 2010;3:577-584.)

Key Words: carotid arteries ■ stents ■ stroke ■ follow-up studies

A number of comorbid and anatomic patient characteristics that increase the risk of carotid endarterectomy (CEA) have been identified. These characteristics have consistently been used as inclusion criteria for ongoing1 (Stenting and Angioplasty With Protection in Patients at High-Risk for Endarterectomy [SAPPHIRE] Worldwide) and completed2–8 high-surgical-risk carotid artery stent (CAS) trials. Because of the relatively small number of deaths and strokes that have occurred in any one of these studies, identification of factors that predict adverse neurological outcomes postprocedure has been difficult with single-study data. We pooled data from 4 Cordis-sponsored studies of high-surgical-risk patients undergoing CAS in an attempt to identify predictors of 30-day adverse neurological outcome.

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Methods

Patients

Patients who were referred from cardiology, vascular surgery, neurosurgery, neurology, or interventional radiology practices and who were randomized to and underwent CAS in the SAPPHIRE trial2 or entered into the SAPPHIRE CAS registry because they were not eligible for CEA in the opinion of a surgeon (406 patients at 29 sites enrolled between August 1, 2000, and March 25, 2002), enrolled in the Carotid Artery Stenting With Emboli Protection Surveillance (CASES)-Post Marketing Study (1057 patients at 73 sites enrolled between September 24, 2004, and October 7, 2005),7 enrolled in the Carotid Stenting With Protection for the Treatment of Obstructive Carotid Artery Disease (CNC) registry (435 patients at 7 sites enrolled between August 12, 2003, and February 28, 2005), or participated in the Feasibility Study Evaluating Acute Neuropsychological Changes Following Carotid Stenting With Distal Protection (ADVANCE) study (39 patients at 4 sites enrolled between September 10, 2004, and February 7, 2005) were included. Inclusion and exclusion criteria were similar across studies. Patients were eligible for enrollment if aged >18 years; were with symptomatic (stroke, transient ischemic attack [TIA], or amaurosis fugax in the 180 days preceding the CAS procedure) or asymptomatic carotid artery stenosis on invasive angiography of ≥50% and ≥80% by North American Symptomatic Carotid Endarterectomy Trial9 methodology, respectively; and had at least 1 coexisting condition that increased the risk of performing CEA. High-surgical-risk criteria included significant cardiac disease, severe pulmonary disease, contralateral carotid occlusion, contralateral laryngeal nerve palsy, recurrent stenosis after CEA, previous radical neck surgery or radiation therapy to the neck, and age >80 years.

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Carotid Stent Procedure

Patients were treated with 81 to 325 mg of aspirin for ≥72 hours and either ticlopidine 250 mg bid or clopidogrel 75 mg daily for ≥24 to 48 hours before the procedure. Heparin boluses were administered during the procedure to maintain an activated clotting time of approximately 300 seconds. Procedures were performed through either a guide catheter or sheath, usually from a femoral access site. An Angioguard XP embolic protection device (EPD) was used in all studies. Information on predilation before EPD placement was not collected. Pre- and postdilation angioplasty were not mandatory. Studies used either a 5.5-F or 6.5-F Precise over-the-wire nitinol stent. Patients were treated with 81 to 325 mg of aspirin indefinitely and ticlopidine 250 mg bid or clopidogrel 75 mg daily for at least 2 weeks postprocedure. Angiographic descriptors were provided by sites in the majority of patients, with angiographic core laboratory analysis available only for SAPPHIRE.

Clinical Outcomes

An independent neurologist performed a complete neurological examination preprocedure, in-hospital postprocedure, and at 30 days. Neurological death was defined as any death because of a major stroke, a complication of neurosurgery, or in which a neurological cause could not be excluded. Stroke was defined as any nonconvulsive, focal neurological deficit of abrupt onset, persisting for ≥24 hours and corresponding to a vascular territory. Strokes were classified as major or minor using the National Institutes of Health Stroke Scale (NIHSS), Rankin index, and Barthel index (major, NIHSS ≥15, Rankin ≥2, Barthel ≤60; minor, NIHSS ≤4, Rankin <2, Barthel ≥90). The term *procedural TIA* was used to indicate any nonconvulsive, focal neurological deficit of abrupt onset corresponding to a vascular territory where the symptoms began during the CAS procedure and completely resolved by the conclusion of the procedure. Myocardial infarction (MI) included both Q-wave and non-Q-wave events. A Clinical Events Committee, independent of the sponsor, adjudicated all major adverse events for all studies. Data were monitored independent of the sponsor and collected and analyzed by an independent data management group (Harvard Clinical Research Institute, Boston, Mass).

Statistical Analysis

A composite of death, MI, or stroke at 30 days served as a primary end point in each of the pooled studies. The primary outcome in the present study was a composite of 30-day neurological death or stroke. Continuous variables appear as medians with interquartile ranges (IQRs) and categorical variables as frequencies and percentages. Unadjusted comparisons were made with Mann-Whitney and chi² tests. Simple logistic regression was used to identify unique predictors of 30-day neurological death or stroke. Variables measured in any of the pooled studies were eligible for inclusion in univariable models. Quadratic and third-order polynomial regression models relating age to the risk for 30-day neurological death or stroke were constructed. In the latter, its second derivative was set to zero.

### Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>CNC (n=435)</th>
<th>CASES (n=1057)</th>
<th>SAPPHIRE Randomized (n=167)</th>
<th>SAPPHIRE Registry (n=406)</th>
<th>ADVANCE (n=39)</th>
<th>Total (n=2104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (277/435)</td>
<td>63.7</td>
<td>62.3 (658/1057)</td>
<td>66.5 (111/167)</td>
<td>64.3 (261/406)</td>
<td>66.7 (26/39)</td>
<td>63.4 (1333/2104)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (395/435)</td>
<td>90.8</td>
<td>94.2 (996/1057)</td>
<td>96.4 (160/166)</td>
<td>94.1 (382/406)</td>
<td>94.7 (36/38)</td>
<td>93.7 (1969/2102)</td>
</tr>
<tr>
<td>Black (264/435)</td>
<td>6.0</td>
<td>4.0 (42/1057)</td>
<td>3.0 (5/166)</td>
<td>2.7 (11/406)</td>
<td>0 (0/38)</td>
<td>4.0 (84/2102)</td>
</tr>
<tr>
<td>Asian (0/435)</td>
<td>0</td>
<td>0.4 (4/1057)</td>
<td>0 (0/166)</td>
<td>0.2 (1/406)</td>
<td>2.6 (1/38)</td>
<td>0.3 (6/2102)</td>
</tr>
<tr>
<td>Other (14/435)</td>
<td>3.2</td>
<td>1.4 (15/1057)</td>
<td>0.6 (1/166)</td>
<td>3.0 (12/406)</td>
<td>2.6 (1/38)</td>
<td>2.0 (43/2102)</td>
</tr>
<tr>
<td>Renal insufficiency (Cr ≥ 2.5 mg/dL)</td>
<td>6.2 (27/435)</td>
<td>6.6 (70/1054)</td>
<td>6.0 (10/166)</td>
<td>7.4 (30/405)</td>
<td>10.3 (4/39)</td>
<td>6.7 (141/2099)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31.5 (157/435)</td>
<td>35.0 (370/1056)</td>
<td>25.3 (42/166)</td>
<td>30.8 (125/406)</td>
<td>23.7 (9/38)</td>
<td>33.5 (703/2101)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.7 (399/435)</td>
<td>89.7 (945/1054)</td>
<td>85.5 (141/165)</td>
<td>84.4 (342/405)</td>
<td>89.7 (35/39)</td>
<td>88.8 (1862/2098)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>89.1 (386/433)</td>
<td>...</td>
<td>78.5 (128/163)</td>
<td>73.9 (289/391)</td>
<td>84.6 (33/39)</td>
<td>81.5 (836/1026)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>80.2 (329/410)</td>
<td>70.3 (714/1015)</td>
<td>...</td>
<td>...</td>
<td>79.5 (31/39)</td>
<td>73.4 (1074/1464)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>...</td>
<td>...</td>
<td>85.8 (133/155)</td>
<td>68.9 (259/376)</td>
<td>...</td>
<td>73.8 (392/531)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>39.2 (168/429)</td>
<td>34.0 (346/1018)</td>
<td>29.7 (46/155)</td>
<td>33.4 (122/365)</td>
<td>28.2 (11/39)</td>
<td>34.5 (693/2006)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>33.4 (143/428)</td>
<td>38.4 (391/1019)</td>
<td>34.8 (56/161)</td>
<td>21.2 (83/392)</td>
<td>23.1 (9/39)</td>
<td>33.4 (682/2039)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>39.5 (172/428)</td>
<td>...</td>
<td>43.4 (72/166)</td>
<td>31.5 (128/406)</td>
<td>30.8 (12/39)</td>
<td>36.7 (384/1046)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>21.3 (90/422)</td>
<td>...</td>
<td>17.2 (27/157)</td>
<td>18.0 (67/373)</td>
<td>18.4 (7/38)</td>
<td>19.3 (191/990)</td>
</tr>
<tr>
<td>COPD</td>
<td>18.1 (78/430)</td>
<td>...</td>
<td>17.0 (28/165)</td>
<td>17.9 (72/403)</td>
<td>11.1 (4/36)</td>
<td>17.6 (182/1034)</td>
</tr>
<tr>
<td>Renal insufficiency (Cr &gt; 2.5 mg/dL)</td>
<td>...</td>
<td>...</td>
<td>6.2 (24/1054)</td>
<td>7.4 (30/405)</td>
<td>10.3 (4/39)</td>
<td>6.7 (141/2099)</td>
</tr>
<tr>
<td>Previous percutaneous carotid intervention</td>
<td>3.0 (13/434)</td>
<td>3.6 (38/1057)</td>
<td>1.2 (2/164)</td>
<td>2.5 (10/405)</td>
<td>2.6 (1/39)</td>
<td>3.0 (64/2099)</td>
</tr>
<tr>
<td>Prior carotid endarterectomy</td>
<td>29.4 (128/435)</td>
<td>30.1 (318/1057)</td>
<td>28.3 (47/166)</td>
<td>45.2 (183/405)</td>
<td>25.6 (10/39)</td>
<td>32.6 (686/2102)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>15.8 (67/424)</td>
<td>24.2 (255/1055)</td>
<td>29.9 (50/167)</td>
<td>30.6 (124/405)</td>
<td>23.7 (9/38)</td>
<td>24.2 (505/2089)</td>
</tr>
</tbody>
</table>

Data are presented as % (no./n), except for age, which is presented as median (IQR). CABG indicates coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; Cr, creatinine; PCI, percutaneous coronary intervention.
null
Breslow-Day test for homogeneity of ORs was significant for only 2 variables: prior MI ($P=0.032$) and GP IIb/IIIa inhibitor ($P=0.035$). To adjust for any residual confounding, a sensitivity analysis was performed using modeling techniques identical to those described previously, where study cohort was entered as a dummy variable.

**Results**

**Patients**
Clinical and procedural characteristics appear in Tables 1 and 2, respectively. There were 2104 patients who underwent CAS in the pooled cohort. Median age was 74 years (IQR, 67 to 80 years) and 24.1% were aged $\geq$80 years. Women comprised 36% and symptomatic patients 24.2% of the cohort. Characteristics were well balanced across studies.

**Unadjusted Outcomes**
Unadjusted outcomes stratified by trial and in the overall cohort appear in Table 3. There were 28 deaths (9 neurological), 25 MIs, and 87 strokes. Of all strokes, 39% were major and 81% ipsilateral to the CAS. The composite end point of 30-day neurological death or stroke occurred in 88 (4.2%) patients. The risk of neurological death or stroke at 30 days declined over time (Figure 1), with the majority of these events noted on the day of (52%) or the day following (18%) the CAS procedure; 91% of events were evident on or before day 14.

**Age**
In unadjusted analyses, increasing age was associated with a significantly greater likelihood of neurological death or stroke during 30-day follow-up (Figure 2). An inflection point in risk of 30-day neurological death or stroke was identified at age 66 ($P=0.0001$). Both quadratic and third-order polynomial models fit the data well ($R^2=0.81$ and 0.92, respectively; model fit $P=0.0002$ and $P<0.0001$, respectively).

**Symptomatic Status**
Unadjusted outcomes stratified by symptomatic status appear in Table 4. Thirty-day neurological death or stroke occurred in 3.8% of asymptomatic and 5.3% of symptomatic patients ($P=0.13$). Neurological death or ipsilateral stroke occurred in 3.2% of asymptomatic and 4.8% of symptomatic patients during that period. The incidence of major ipsilateral stroke was significantly higher among symptomatic than among asymptomatic patients. In the symptomatic cohort, data on

<table>
<thead>
<tr>
<th>Variable</th>
<th>CNC (n=435)</th>
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<th>SAPPHIRE Registry (n=406)</th>
<th>ADVANCE (n=39)</th>
<th>Total (n=2104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological death or any stroke</td>
<td>2.3 (10)</td>
<td>4.4 (47)</td>
<td>3.6 (6)</td>
<td>4.9 (20)</td>
<td>12.8 (5)</td>
<td>4.2 (88)</td>
</tr>
<tr>
<td>Death, any stroke, or MI</td>
<td>3.4 (15)</td>
<td>5.6 (59)</td>
<td>4.8 (8)</td>
<td>6.9 (28)</td>
<td>17.9 (7)</td>
<td>5.6 (117)</td>
</tr>
<tr>
<td>Death</td>
<td>0.7 (3)</td>
<td>1.1 (12)</td>
<td>1.2 (2)</td>
<td>2.2 (9)</td>
<td>5.1 (2)</td>
<td>1.3 (28)</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>0.7 (3)</td>
<td>0.4 (4)</td>
<td>0.6 (1)</td>
<td>1.0 (4)</td>
<td>2.6 (1)</td>
<td>0.6 (13)</td>
</tr>
<tr>
<td>Noncardiac death</td>
<td>0 (0)</td>
<td>0.4 (4)</td>
<td>0 (0)</td>
<td>0.5 (2)</td>
<td>0 (0)</td>
<td>0.3 (6)</td>
</tr>
<tr>
<td>Neurological death</td>
<td>0 (0)</td>
<td>0.4 (4)</td>
<td>0.6 (1)</td>
<td>0.7 (3)</td>
<td>2.6 (1)</td>
<td>0.4 (9)</td>
</tr>
<tr>
<td>MI</td>
<td>0.9 (4)</td>
<td>0.8 (8)</td>
<td>2.4 (4)</td>
<td>1.7 (7)</td>
<td>5.1 (2)</td>
<td>1.2 (25)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.3 (10)</td>
<td>4.4 (46)</td>
<td>3.6 (6)</td>
<td>4.9 (20)</td>
<td>12.8 (5)</td>
<td>4.1 (87)</td>
</tr>
<tr>
<td>Major ipsilateral stroke</td>
<td>0.5 (2)</td>
<td>1.5 (16)</td>
<td>0.6 (1)</td>
<td>2.5 (10)</td>
<td>2.6 (1)</td>
<td>1.4 (30)</td>
</tr>
<tr>
<td>Major nonipsilateral stroke</td>
<td>0 (0)</td>
<td>0.2 (2)</td>
<td>0.6 (1)</td>
<td>0.5 (2)</td>
<td>0 (0)</td>
<td>0.2 (5)</td>
</tr>
<tr>
<td>Minor ipsilateral stroke</td>
<td>1.8 (8)</td>
<td>2.0 (21)</td>
<td>2.4 (4)</td>
<td>1.7 (7)</td>
<td>7.7 (3)</td>
<td>2.0 (43)</td>
</tr>
<tr>
<td>Minor nonipsilateral stroke</td>
<td>0 (0)</td>
<td>0.8 (8)</td>
<td>0.6 (1)</td>
<td>0.5 (2)</td>
<td>2.6 (1)</td>
<td>0.6 (12)</td>
</tr>
</tbody>
</table>

Table 3. Major Adverse Events at 30 Days

Data are presented as % (no.).
time from antecedent stroke or TIA until the index CAS procedure were available on 236 of 505 patients. In this subgroup, the 30-day risk of neurological death or stroke declined with increasing time since the antecedent stroke or TIA (Figure 3).

Volume and Outcome
When centers were grouped according to the total number of CAS patients enrolled (median 2, 5, 10, 19, and 33 for groups 1 to 5, respectively), no consistent relationship was observed between number of patients enrolled per site and 30-day rate of neurological death or stroke. The numbers and rates of endpoint events observed in groups 1 to 5 were 4/49 (8.2%), 4/130 (3.1%), 15/288 (5.2%), 26/512 (5.1%), 39/1125 (3.5%), respectively.

Multivariable Predictors
Separate models were constructed with all available variables (overall), and only those measured before the procedure were performed (preprocedure). In the overall model (Figure 4), a number of variables independently predicted a higher likelihood of neurological death or stroke during the 30 days following a CAS. These variables were older age (continuous), black race, angiographically visible thrombus in a symptomatic patient, procedural use of GP IIb/IIIa inhibitors, procedural TIA, final residual stenosis ≥30%, and use of protamine or vasopressors during or following the procedure. When age was entered as a categorical rather than continuous variable with age <70 years as the reference group, the OR (95% CI) for neurological death or stroke within 30 days following a CAS was 1.56 (0.70 to 3.49; P=0.28), 3.31 (1.66 to 6.59; P<0.001), 2.93 (1.46 to 5.88; P=0.003), 2.86 (1.22 to 6.67; P=0.015), and 6.94 (2.25 to 21.38; P<0.001) for patients aged 70 to 74, 75 to 79, 80 to 84, 85 to 89, and ≥90 years, respectively. In the model restricted to preprocedure variables, only increasing age (OR, 1.05; 95% CI, 1.03 to 1.08; P<0.001) and symptomatic patients who had a stroke within the prior 180 days (OR, 2.56; 95% CI, 1.13 to 5.79; P=0.024) independently predicted neurological death or stroke at 30 days.

Sensitivity Analysis
When study cohort was entered as a dummy variable into a model of 30-day neurological death or stroke, its effect was not significant (P=0.17), identical predictor variables were selected for inclusion, and OR (95% CI) estimates varied only slightly when compared with the study’s main results: age, 1.05 (1.03 to 1.08); black race, 2.62 (1.10 to 6.19); symptomatic with thrombus, 8.06 (1.67 to 38.92); GP IIb/IIIa used during index procedure, 6.03 (3.11 to 11.70); procedural TIA, 3.29 (1.24 to 8.72); final residual stenosis ≥30%, 0.44 (0.20 to 0.97); protamine, 2.16 (1.09 to 4.28); and intravenous vasopressors, 1.85 (1.16 to 2.96).

Discussion
Because the number of events accrued in any individual high-surgical-risk CAS study has been relatively small, it has been difficult to identify factors that independently predict the risk of adverse neurological outcomes postprocedure.1,6,10,11 In one of the largest series to date, we pooled data from CAS randomized and registry studies and observed that the composite risk of periprocedural neurological events was well within the range deemed acceptable by American Heart
Association guidelines on carotid revascularization. We also identified a number of factors that independently predict the 30-day risk of neurological death or stroke following carotid artery stenting, including increasing age; black race; symptomatic patients with angiographically evident thrombus; procedural TIA; greater degree of postprocedure residual stenosis; and perioperative use of GP IIb/IIIa inhibitors, vasopressors, and protamine. Symptomatic status and stenosis severity are commonly used to estimate stroke risk among medically treated patients with carotid stenosis. These risk estimates are incorporated into decisions on the appropriateness of carotid artery revascularization. Using an analogous approach, symptomatic status and age might be routinely used to predict neurological event risk associated with CAS, thereby facilitating decisions regarding the appropriateness of this particular revascularization modality. Observations from the Carotid Revascularization Endarterectomy versus Stenting Trial would support this concept. In this trial, older patients were at higher risk of stroke and death when undergoing CAS than endarterectomy.

Preprocedural Predictors of Neurological Events

Age
Our observation that increasing age is associated with poorer outcome following CAS is consistent with other studies. Some studies have arbitrarily separated patients into those aged >80 and those <80 and found that octogenarians are at higher risk of events following CAS than nonoctogenarians. Consequently, many clinicians have concluded that CAS should not be performed in those aged >80. However, stratification of patients above and below an arbitrary age cut point may yield misleading results because it will skew the apparent average risk in the higher age category toward the oldest patients in that category. We observed that the risk of neurological death or stroke at 30 days increased with age but found no particular inflection point at age 80.

Symptomatic Status
The risk of 30-day neurological events following CAS is generally greater among symptomatic than asymptomatic patients, and most CAS trials have excluded patients with target lesion thrombus seen on angiography. We observed that symptomatic patients with angiographically evident thrombus were at even greater risk of neurological death or stroke following CAS than symptomatic patients without thrombus, suggesting that patients with both features represent a particularly high-risk subgroup in which CAS should be avoided. That the risk of adverse neurological outcome following CAS in symptomatic patients declined with increasing time between the incident neurological event and the procedure itself is also consistent with this observation and may suggest that such patients have thrombotic lesions that organize or dissolve over time. Deferral of CEA for up to 4 weeks after a neurological event may optimally balance procedural risk with that of recurrent events. Postponement of CAS for a period of time might yield similar benefits under these circumstances.

Race
Black race was a significant predictor in the overall model but not when in a model that included only preprocedural variables. Although blacks appear to have higher perioperative risk following CEA, further study will be needed to assess whether outcome is affected by race among patients undergoing CAS.

Volume and Outcome
There are conflicting data regarding the relationship between center procedural volume and CAS outcome, with some studies identifying fewer complications in higher volume centers and others failing to do so. In our pooled analysis, we observed no consistent relationship between center volume and 30-day neurological outcome. However, the total (study and nonstudy) CAS volume of any given center was not known. Consequently, we cannot rule out that such a relationship exists.

Procedural Predictors of Neurological Events

Pharmacological Agents
A number of pharmacological agents predicted worse 30-day neurological outcome following CAS. Some, such as GP...
IIb/IIa inhibitors,22,23 have been associated with poorer outcome in prior CAS studies, whereas others, such as protamine and vasopressors, have not. Nevertheless, it is not possible to discern whether the greater risk associated with these was due to the circumstances under which they were administered or whether it was associated with exposure to the agents themselves.

**Procedural TIA**

Little is known regarding CAS-associated TIA. We observed that transient neurological deficits occurring during the CAS procedure but resolving completely by its conclusion were a harbinger of neurological death or stroke at 30 days. To our knowledge such transient events have not been related to adverse outcome following CAS in other studies.

**Residual Stenosis**

Although residual stenosis in part defines procedural success and has been related to the propensity for restenosis following CAS,24 greater residual stenosis has not been associated with a higher risk of neurological death or stroke in this setting. In fact, Gray and colleagues6 identified residual stenosis of >10% as a univariable predictor of worse outcome following CAS. We observed a greater risk of neurological death or stroke following CAS when the final residual diameter stenosis was ≥30%. It is not clear whether the higher associated risk was due to greater residual stenosis or was simply a reflection of higher-risk patients in whom lesser residual stenosis was not attainable. The degree of residual stenosis did not differ between patients with and without vessel calcification.

**Strengths and Limitations**

A number of strengths of this analysis are worth highlighting. Patient characteristics were similar across pooled studies, and end points were consistently defined. Data from each of the pooled trials were independently managed and analyzed; neurological evaluations were performed by independent neurologists; and all major events were adjudicated by an independent, blinded committee. Despite these strengths, a number of limitations warrant mention as well. We studied only high-surgical-risk patients in whom a single type of CAS and EPD were used. As a consequence, event rates may not be generalizable to non-high-surgical-risk patients who undergo CAS. Further analysis using national registry data would be necessary to discern whether identified predictors are common across other CAS and EPD platforms.25 Not all CAS studies captured the same information; consequently, some significant univariable predictors were not considered in our multivariable models. Inclusion bias can influence the results of pooled analyses, but we do not believe that this influenced our study because aggregate event rates and predictors of adverse events were not known for each of the included studies at the time this analysis was initiated. Finally, there were relatively few neurological deaths. Larger studies will be required to identify predictors of this end point.

**Conclusion**

We identified a number of important predictors of neurological death and stroke within 30 days of a CAS procedure. Such factors may help to guide patient selection and further refine procedural technique.

**Disclosures**

Dr Mishkel has received honoraria from Abbott Vascular for teaching carotid stent courses. Dr Wang is employed by Cordis Corporation. The other authors have no potential conflicts of interest to disclose.

**References**


**CLINICAL PERSPECTIVE**

The factors that portend higher periprocedural risk of neurological events with carotid endarterectomy have been identified; however, less is known about those factors that predict neurological outcome in the setting of carotid stenting. We pooled randomized trial and registry data from 4 Cordis-sponsored carotid stent studies to identify predictors of neurological death or stroke within 30 days of the procedure. The only significant preprocedural predictors were older age and symptomatic status. Among symptomatic patients, the risk declined with increasing time from the antecedent neurological event. When both preprocedural and procedural predictors were considered, including age; black race; angiographically visible thrombus in a symptomatic patient; procedural transient ischemic attack; final residual stenosis >30%; and periprocedural use of protamine, vasopressors, or glycoprotein IIb/IIIa inhibitors all independently predicted worse outcome. These findings may help to guide patient selection and further refine procedural technique. Further studies are needed to confirm these predictors and identify others.
Predictors of Neurological Events Associated With Carotid Artery Stenting in High-Surgical-Risk Patients: Insights From the Cordis Carotid Stent Collaborative
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