Policy Statement

Carotid angioplasty with associated stenting and embolic protection may be considered medically necessary in patients with all of the following:

- 50% to 99% stenosis (North American Symptomatic Carotid Endarterectomy Trial [NASCET] measurement)
- Symptoms of focal cerebral ischemia (transient ischemic attack or monocular blindness) in the previous 120 days, symptom duration less than 24 hours, or nondisabling stroke
- Anatomic contraindication for carotid endarterectomy (e.g., prior radiotherapy or neck surgery, lesions surgically inaccessible, spinal immobility, or tracheostomy)

Carotid angioplasty with associated stenting and embolic protection is considered investigational for all other indications, including but not limited to, patients with carotid stenosis who are suitable candidates for carotid endarterectomy (CEA) and patients with carotid artery dissection.

Carotid angioplasty without associated stenting and embolic protection is considered investigational for all indications, including but not limited to, patients with carotid stenosis who are suitable candidates for carotid endarterectomy (CEA) and patients with carotid artery dissection.

Policy Guidelines

The intent of the second investigational policy statement is that carotid angioplasty with embolic protection but without stenting is investigational. There may be unique situations where the original intent of surgery was to perform carotid angioplasty with stenting and embolic protection, but anatomic or other considerations prohibited placement of the stent.

Coding

The following CPT codes are used to report open and percutaneous transcatheter placement of stent(s) in the cervical carotid artery and include angioplasty when performed, and all associated radiologic supervision and interpretation:

- **37215**: Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; with distal embolic protection
- **37216**: Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; without distal embolic protection

The following CPT code is also available:

- **37217**: Transcatheter placement of an intravascular stent(s), intrathoracic common carotid artery or innominate artery by retrograde treatment, via open ipsilateral cervical carotid artery exposure, including angioplasty, when performed, and radiological supervision and interpretation

*Note: This code indicates the procedure is performed by transcervical or retrograde approach, but is considered carotid stenting.*
Description

Carotid artery angioplasty with stenting is a treatment for carotid stenosis that is intended to prevent a future stroke. It is an alternative to medical therapy and a less-invasive alternative to carotid endarterectomy (CEA).

Related Policies

- Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)
- Endovascular Therapies for Extracranial Vertebral Artery Disease

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

A number of CAS and EPDs have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) or the 510(k) process. Table 1 lists the original PMA's with product code NIM and Table 2 lists 510(k) approvals with product code NTE.

Table 1. FDA Premarket Approvals for Carotid Artery Stents and Embolic Protection Devices

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>PMA</th>
<th>PMA Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cordis Corp.</td>
<td>Cordis Precise Nitinol Stent System</td>
<td>P030047</td>
<td>Sept 2006</td>
</tr>
<tr>
<td>Abbott Vascular</td>
<td>Acculink Carotid Stent System and Rx Acculink Carotid Stent System</td>
<td>P040012</td>
<td>Aug 2004</td>
</tr>
<tr>
<td>Abbott Vascular</td>
<td>XACT Carotid Stent System</td>
<td>P040038</td>
<td>Sep 2005</td>
</tr>
<tr>
<td>Boston Scientific Corp.</td>
<td>Endotex Nexstent Carotid Stent and Delivery System and Endotex Carotid Stent and Monorail Delivery System</td>
<td>P050025</td>
<td>Oct 2006</td>
</tr>
<tr>
<td>Medtronic Vascular</td>
<td>iProtege GPS and Protege Rx Carotid Stent Systems</td>
<td>P060001</td>
<td>Jan 2007</td>
</tr>
<tr>
<td>Silk Road Medical, Inc.</td>
<td>Enroute Transcarotid Stent System</td>
<td>P140026</td>
<td>May 2015</td>
</tr>
<tr>
<td>W. L Gore &amp; Associates, Inc.</td>
<td>Gore Carotid Stent</td>
<td>P180010</td>
<td>Nov 2018</td>
</tr>
<tr>
<td>PMA: Premarket approval</td>
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</table>

Table 2. FDA 510(k) Carotid Artery Stents and Embolic Protection Devices

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Carotid Stents</th>
<th>510(k) Number</th>
<th>PMA/510(k) Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guidant, now Abbott Vascular</td>
<td>Accunet and RX Accunet Embolic protection system</td>
<td>K042218</td>
<td>Aug 2004</td>
</tr>
<tr>
<td>Guidant, now Abbott Vascular</td>
<td>Rx Accunet 2 Embolic Protection System</td>
<td>K042908</td>
<td>Nov 2004</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Stents and Devices</td>
<td>510(k) Number</td>
<td>PMA/510(k) Date</td>
</tr>
<tr>
<td>--------------</td>
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<tr>
<td>Guidant, now Abbott Vascular</td>
<td>Rx AccuNet Embolic Protection System</td>
<td>K052165</td>
<td>Aug 2005</td>
</tr>
<tr>
<td>Abbott Vascular</td>
<td>Emboshield™ embolic protection system</td>
<td>K052454</td>
<td>Sep 2005</td>
</tr>
<tr>
<td>Cordis Corp.</td>
<td>AngioGuard™ XP and RX emboli capture guidewire systems</td>
<td>K062531</td>
<td>Sep 2006</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td>FilterWire EZ™ embolic protection system</td>
<td>K063313</td>
<td>Dec 2006</td>
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<tr>
<td>EV3 Inc</td>
<td>Spidex</td>
<td>K052659</td>
<td>Feb 2007</td>
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<tr>
<td>EV3 Inc</td>
<td>Spidexx</td>
<td>K063204</td>
<td>Nov 2007</td>
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<tr>
<td>GORE</td>
<td>GORE® Flow Reversal System</td>
<td>K083300</td>
<td>Feb 2009</td>
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<tr>
<td>GORE</td>
<td>GORE® Embolic Filter</td>
<td>K103500</td>
<td>May 2011</td>
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<tr>
<td>Medtronic/Invatec</td>
<td>Mo.Ma® Ultra Proximal Cerebral Protection Device</td>
<td>K092177</td>
<td>Oct 2009</td>
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<tr>
<td>Silk Road Medical</td>
<td>ENROUTE™ Transcarotid Stent System and ENROUTE Transcarotid Neuroprotection System</td>
<td>K143072</td>
<td>Feb 2015</td>
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<tr>
<td>Gardia Medical</td>
<td>Wirion</td>
<td>K143570</td>
<td>Jun 2015</td>
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<tr>
<td>Abbott Vascular</td>
<td>Rx AccuNet Embolic Protection System</td>
<td>K153086</td>
<td>Nov 2015</td>
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<tr>
<td>Silk Road Medical, Inc.</td>
<td>Enroute Transcarotid Neuroprotection System</td>
<td>K153485</td>
<td>Mar 2016</td>
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<tr>
<td>Gardia Medical Ltd.</td>
<td>Wirion</td>
<td>K180023</td>
<td>Mar 2018</td>
</tr>
<tr>
<td>Contego Medical, LLC</td>
<td>Paladin Carotid Post-Dilation Balloon System With Integrated Embolic Protection (Paladin System)</td>
<td>K181128</td>
<td>Sep 2018</td>
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<tr>
<td>Contego Medical, LLC</td>
<td>Vanguard LE Peripheral Balloon Angioplasty System With Integrated Embolic Protection</td>
<td>K181529</td>
<td>Dec 2018</td>
</tr>
<tr>
<td>Abbott Vascular</td>
<td>Emboshield Nav6 Embolic Protection System, Barewire Filter Delivery Wires</td>
<td>K191173</td>
<td>Jul 2019</td>
</tr>
</tbody>
</table>

FDA: Food and Drug Administration; PMA: premarket approval.

Each FDA-approved carotid stent is indicated for combined use with an EPD to reduce risk of stroke in patients considered at increased risk for periprocedural complications from CEA who are symptomatic with greater than 50% stenosis, or asymptomatic with greater than 80% stenosis with degree of stenosis assessed by ultrasound or angiogram, with computed tomography angiography also used. Patients are considered at increased risk for complications during CEA if affected by any item from a list of anatomic features and comorbid conditions included in each stent system’s Information for Prescribers.

The RX AccuLink™ Carotid Stent System is also approved for use in conventional risk patients (not considered at increased risk for complications during CEA) with symptoms and 70% or more stenosis by ultrasound or 50% or more stenosis by angiogram, and asymptomatic patients with 70% or more stenosis by ultrasound or 60% or more stenosis by angiogram.

The FDA-approved stents and EPDs differ in the deployment methods used once they reach the target lesion, with the rapid exchange devices designed for more rapid stent and filter expansion. The FDA has mandated postmarketing studies for EPDs, including longer follow-up for patients already reported to the FDA and additional registry studies, primarily to compare outcomes as a function of clinician training and facility experience. Each manufacturer’s system is available in various configurations (e.g., straight or tapered) and sizes (diameters and lengths) to match the vessel lumen that will receive the stent.

In 2015, the ENROUTE™ Transcarotid Neuroprotection System was cleared for marketing by the FDA through the 510(k) process. ENROUTE™ is a flow reversal device designed to be placed via direct carotid access.

FDA product codes: NIM (stents) and NTE (EPDs).
Rationale

Background
Combined with optimal medical management, carotid angioplasty with or without stenting has been evaluated as an alternative to carotid endarterectomy (CEA). Carotid artery stenting (CAS) involves the introduction of coaxial systems of catheters, microcatheters, balloons, and other devices. The procedure is most often performed through the femoral artery but a transcervical approach can also be used to avoid traversing the aortic arch. The procedure typically takes 20 to 40 minutes. Interventionalists almost uniformly use an embolic protection device (EPD) to reduce the risk of stroke caused by thromboembolic material dislodged during CAS. EPDs can be deployed proximally (with flow reversal) or distally (using a filter). Carotid angioplasty is rarely performed without stent placement.

The proposed advantages of CAS over CEA include:
- General anesthesia is not used (although CEA can be performed under local or regional anesthesia)
- Cranial nerve palsies are infrequent sequelae (although almost all following CEA resolve over time)
- Simultaneous procedures may be performed on the coronary and carotid arteries.

Literature Review
Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function - including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens, and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Clinical Context and Therapy Purpose
The purpose of carotid artery stenting is to provide a treatment option for carotid artery stenosis that is an alternative to medical therapy and a less-invasive alternative to carotid endarterectomy.

The question addressed in this evidence review is: Does the use of carotid artery stenting improve the net health outcome in patients with carotid stenosis?

The following PICO was used to select literature to inform this review.

Patients
The relevant population of interest is individuals with carotid artery stenosis.

Interventions
The therapy being considered is carotid artery stenting.
Comparators
The comparator of interest is carotid endarterectomy.

Outcomes
The general outcomes of interest are overall survival, morbid events, treatment-related mortality, and treatment-related morbidity.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs and systematic reviews;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Risk-Benefit Ratio of Invasive Carotid Procedures
Endovascular carotid artery stenting (CAS) and surgical endarterectomy (CEA) for carotid artery disease trades procedure-related harms of stroke and death for the benefit of reduced stroke risk over subsequent years; the balance determines whether either intervention will result in a net clinical benefit. That balance has been scrutinized for CEA but not for CAS; accordingly, results from trials of CEA must be extrapolated to assess outcomes for CAS.

Review of Evidence
A series of landmark clinical trials from the late 1980s through the 1990s compared the benefits and harms of CEA with best medical therapies then available in symptomatic and asymptomatic individuals with carotid artery stenosis.1,2,3,4,5,6,7 Those trial results defined the magnitude of risk reduction for stroke and the periprocedural stroke and death rates for 30 days, that must be offset to achieve a net clinical benefit (benefit outweighing harm), less than 3% for asymptomatic (>60% stenosis), and less than 6% for symptomatic patients (50%-69% or 70%-99% stenosis). Furthermore, because periprocedural harms are immediate, but benefit accrues over time, a net clinical benefit is obtained only for those patients surviving long enough to counterbalance the immediate harms. The necessary life expectancy defined by the trial duration needed to demonstrate benefit is summarized in Table 3.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Stenosis, %</th>
<th>Acceptable Periprocedural Death/Stroke Rate, %</th>
<th>Anticipated Life Expectancy, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>60-99</td>
<td>&lt;3</td>
<td>5</td>
</tr>
<tr>
<td>Yes</td>
<td>50-69</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>70-99</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

CEA: carotid endarterectomy.

As an example of the fine line between benefit and harm, Arazi et al (2008)8 performed a decision analysis of benefit for patients with asymptomatic stenosis using a base case derived from the Asymptomatic Carotid Surgery Trial (periprocedural death/stroke rate, 1.8%).9 Over a five-year time horizon, CEA provided four days of stroke-free survival and a net harm when periprocedural death or disabling stroke rates exceeded 2.1%.

Since the landmark trials, there has been considerable improvement in medical care resulting in a substantial decline in stroke rates among patients with asymptomatic carotid disease.9,10 Current medical therapies such as aggressive lipid-lowering medications, were inconsistently used in the landmark trials. Also, surgeons in contemporary clinical trials have achieved CEA periprocedural death and stroke rates lower than those in the pivotal trials used to establish the benchmarks. For example, in the Carotid Revascularization Endarterectomy vs
Stenting Trial (CREST), the death or stroke rate for symptomatic patients was 3.2% and for asymptomatic patients was 1.4%. 

Accordingly, the benchmarks established decades ago may no longer be appropriate. A recent consensus document by De Rango et al (2013) has suggested benchmarks of 2.0% for asymptomatic and 4.0% for symptomatic individuals. 

Excluded from landmark CEA trials were patients with significant comorbidities judged likely to cause death within five years that might also increase periprocedural and anesthetic risk for complications. Therefore, CAS has appeal as a treatment option for patients with potentially higher periprocedural risk due to medical (e.g., severe cardiac dysfunction, requirement for combined coronary and carotid revascularization, severe renal or pulmonary dysfunction, and other characteristics associated with increased surgical risk), or anatomic reasons (e.g., surgically inaccessible stenosis, prior radiation, prior neck surgery, spinal immobility, prior laryngeal nerve palsy, contralateral occlusion, prior ipsilateral CEA, restenosis after CEA).

Although the general anesthetic risk is considered a potential reason to use CAS, CEA can be safely performed under local or regional anesthesia, as confirmed in the 95-center General Anesthesia versus Local Anesthesia trial. The General Anesthesia versus Local Anesthesia trial investigators randomized 3526 patients undergoing CEA to general or local anesthesia and found no difference in 30-day death, stroke, or myocardial infarction (MI) rates based on anesthetic approach (relative risk [RR], 0.94; 95% confidence interval [CI], 0.70 to 1.3).

Randomized Controlled Trials of Carotid Artery Stenting versus Carotid Endarterectomy

SAPPHIRE Trial
The first major RCT comparing CAS with CEA was the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial reported by Yadav et al (2004). The relevant conclusions are summarized below:

- For patients with symptomatic stenosis at increased risk for periprocedural complications from CEA (n=96), the sample size was small, resulting in wide CIs for estimated effects; differences between arms in 30-day and 1-year outcomes were not statistically significant.
- For patients with asymptomatic stenosis at increased risk for periprocedural complications from CEA (n=238), differences in 30-day outcomes also had wide CIs and were not statistically significant.
- Early study closed early due to slow recruitment as nonrandomized stent registries were established, resulting in fewer study patients than planned, which compromised the evaluation of noninferiority.
- Variance in differential complication rates for the 2 treatments across sites might have influenced results, because 5 of 34 sites contributed 64% of randomized patients, and data were unavailable for comparison.
- Direct comparative evidence was lacking for optimal medical management alone as an alternative to adding CAS with an embolic protection device (EPD) or CEA for patients with increased risk of surgical complications.

Long-term follow-up of SAPPHIRE was reported at three years. For asymptomatic and symptomatic patients combined, ipsilateral strokes from day 31 to day 1080 were observed in 4.4% of patients undergoing CAS and in 3.6% with CEA (estimated from digitized figure). Cumulative 3-year repeat target vessel revascularization (a proxy for restenosis) was more common after CEA but the difference was not statistically significant (7.1% vs 3.0%; p=0.26).

SPACE Trial
Ringleb et al (2006) published results from the Stent-supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial. This trial randomized 1200 patients within 180 days of neurologic symptoms, transient ischemic attack, or moderate (nondisabling) stroke, and with 50% or more stenosis of the ipsilateral carotid artery, to CAS (n=605) with or without EPD (73%
of procedures performed without), or to CEA (n=595). The analysis (n=1183) failed to conclude that CAS was noninferior to CEA by a margin of 2.5% for the primary outcome of ipsilateral ischemic stroke or death by 30 days after randomization. Periprocedural (30-day) event rates were 6.8% for the CAS group and 6.3% for the CEA group. The absolute between-group difference favored CEA and was 0.5% (90% CI, -1.9% to 2.9%) by intention-to-treat analysis and 1.3% (90% CI, -1.1% to 3.8%) in per-protocol analysis.

Editorialists pointed to some methodologic issues raised with the SPACE trial, including the high rate of rejection for potential participating collaborators (>25%, based on their prior outcomes records, but review criteria were not reported), and the lack of a requirement to use an EPD with CAS (although 30-day event rates were 7.3% with vs 6.7% without EPD).

Long-term follow-up of the SPACE trial was reported at two years. Approximate annual ipsilateral stroke rates from day 31 through longest follow-up for CAS and CEA were 0.4% in each group. Following the periprocedural period (ie, 31 days to longest follow-up), stroke risk reduction in symptomatic patients not selected based on medical or anatomic comorbidities was similar for CAS and CEA. Recurrent stenosis greater than 70% was more frequent at 2 years with CAS (10.7%) than with CEA (4.6% p=0.001).

EVA-3S Trial
The Endarterectomy Versus Stenting in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial was a noninferiority comparison of CAS (with EPD in 92%) to CEA in symptomatic patients at average risk for complications from CEA with 60% or more stenosis of the ipsilateral carotid artery. The trial was terminated prematurely (n=527 enrolled; original target, n=872), based on interim analysis of 30-day outcomes. The incidence of any stroke or death through 30 days was 3.9% (95% CI, 2.0% to 7.2%) after CEA and 9.6% (95% CI, 6.4% to 14%) after CAS (RR=2.5; 95% CI, 1.2 to 5.1; p=0.01).

Over a mean 2.1 years of follow-up, restenosis (>50%) was more frequent following CAS (12.5%) than CEA (5.0%). Long-term follow-up from EVA-3S was reported at four years. Approximate annual ipsilateral stroke rates from day 31 through longest follow-up for CAS and CEA, respectively, were 1.1% and 0.9%. These results supported a conclusion that following the periprocedural period (ie, 31 days to longest follow-up), stroke risk reduction in symptomatic patients not selected based on medical or anatomic comorbidities was similar for CAS and CEA. Editorialists criticized EVA-3S for recommending but not requiring antiplatelet premedication (three days of aspirin plus ticlopidine or clopidogrel) and for not requiring interventionalists to be adequately experienced with the specific stent, and EPDs used to treat trial subjects. Participating interventionalists were required to have completed 12 or more CAS procedures with 25 or more CEAs for vascular surgeons. EVA-3S also permitted the use of five different stents and seven different EPD types but required only two prior procedures with a new device before an investigator could use that device on a patient randomized to CAS.

Mas et al (2014) published long-term follow-up (median, 7.2 years) from the EVA-3S trial. Complete follow-up until death or the final telephone interview was obtained in 493 (94%) of the 527 patients. At the 5-year follow-up, the main composite endpoint (ipsilateral stroke after randomization or procedural stroke or death) occurred in 29 (11%) of 265 subjects in the CAS group and 16 (6.1%) of 262 subjects in the CEA group (5-year absolute risk reduction, 4.7%). The hazard ratio (HR) for CAS vs CEA was 1.85 (95% CI, 1.0 to 3.40; p=0.04). At the 10-year follow-up, the HR for the main composite endpoint for CAS vs CEA was 1.70 (95% CI, 0.95 to 3.06; p=0.07).

International Carotid Stenting Study
The International Carotid Stenting Study (ICSS) enrolled 1713 symptomatic patients at 50 academic medical centers across Europe, Australia, New Zealand, and Canada between May 2001 and October 2008. EPDs were recommended but not required (used in 72% of procedures), and a number of different stents and EPD types were used. Based on plausible event rates, a target study sample size of 1500 was estimated to be able to define a between-
group difference less than 3.3% in disabling stroke or death and a 3.0% difference in 30-day stroke, death, or MI. Only interim 30- and 120-day results were included in the initial report. From a per-protocol analysis, the 7.1% periprocedural death or stroke death rates accompanying CAS both exceeded the rate established to provide a net clinical benefit and was more than twice that following CEA (3.4%). In a subgroup analysis of 231 ICSS participants, new ischemic brain lesions were approximately 3-fold more frequent following CAS, and protective devices did not appear to mitigate their occurrence. Interim results were consistent with the accompanying editorialist’s conclusion that “routine stenting in symptomatic patients must now be difficult to justify.”

Bonati et al (2015) published longer term follow-up results from ICSS. The cumulative 5-year risk of fatal or disabling stroke did not differ significantly between the CAS (6.4%) and the CEA groups (6.5% HR=1.06; 95% CI, 0.72 to 1.57; p=0.77). However, the 5-year cumulative risk of any stroke was higher in the CAS group (15.2%) than in the CEA group (9.45% HR=1.71; 95% CI, 1.28 to 2.3; p<0.001). The authors noted that the difference between CEA and CAS groups in stroke risk after the procedural period was mainly attributable to strokes occurring in the contralateral carotid or vertebrobasilar territory in the CAS group. Functional outcomes, measured by modified Rankin Scale scores, did not differ significantly between groups.

Altinbas et al (2014) reported that periprocedural rates of hemodynamic instability in the ICSS differed between CEA and CAS groups. Hemodynamic depression occurred more commonly in CAS patients (13.8% vs 7.2%; RR=1.9; 95% CI, 1.4 to 2.6; p<0.000), while hypertension requiring treatment occurred less commonly in CAS patients (RR=0.2; 95% CI, 0.1 to 0.4; p<0.000). Hemodynamic instability was not associated with the ICSS study’s primary composite outcome. Featherstone et al (2016) published a health technology assessment on ICSS funded by the National Institute for Health Research. The assessment reviewed the data presented above, concluding that “the functional outcome after stenting is similar to endarterectomy, but stenting is associated with a small increase in the risk of nondisabling stroke. The choice between stenting and endarterectomy should take into account the procedural risks related to individual patient characteristics.”

CREST

CREST (Carotid Revascularization Endarterectomy Versus Stenting Trial) was conducted between December 2000 and July 2008, and enrolled 2522 patients at 117 centers across the U.S. and Canada. Of 427 interventionalists who applied to participate in CREST, only 224 (52%) were approved. Inclusion was initially restricted to recently symptomatic patients. Due to slow enrollment, the protocol was amended to include asymptomatic patients. A March 2004 protocol amendment excluded further enrollment of patients 80 years and older due to poor outcomes. Of the 1271 patients randomized to CAS, 65 underwent CEA and 54 neither procedure; of the 1251 patients randomized to CEA, 13 underwent CAS and 44 neither procedure. Twenty patients were excluded from one site due to reported data fabrication. A sample size of 2500 was targeted to detect a 46% reduction in the HR for the primary endpoint of any stroke, MI, or death during the periprocedural period or ipsilateral stroke within 4 years after randomization.

In the entire sample (symptomatic and asymptomatic patients), investigators reported no difference between CAS and CEA for the primary outcome. Stroke was more frequent following CAS; MI more frequent after CEA. The periprocedural MI rate after CEA (2.3%) was considerably higher in CREST than any comparable trial (e.g., in EVA-3S, 0.8%; SPACE, 0%; ICSS, 0.6%). This might be attributable to a somewhat higher prevalence of coronary artery disease among participants and routine cardiac enzyme assays, but the relative difference was large. Periprocedural CAS death or stroke rates were the lowest reported in any trial. Although participating interventionalists performing CAS were highly selected, periprocedural death or stroke rates following CAS exceeded those for CEA: in symptomatic patients, 5.6% vs 2.4% respectively (the lowest rate for CAS reported in any trial); in asymptomatic patients, 2.6% vs 1.4% respectively. The RR for periprocedural death or stroke in the symptomatic group was
1.89 (95% CI, 1.11 to 3.21) and in the asymptomatic group, it was 1.85 (95% CI, 0.79 to 4.34). The trial had limited power to detect a difference between procedures in the asymptomatic group. In CREST, 2-year restenosis (>70%) or reocclusion rates were similar following CEA (6.3%) and CAS (6.0%) - 2-year restenosis alone was 5.8% with either procedure.33.

Brott et al (2016) reported on long-term follow-up from CREST. There were no significant differences in the primary composite outcome (any periprocedural stroke, MI, death, or postprocedural ipsilateral stroke) between the CEA (9.9%) and CAS (11.8% HR=1.10) groups when measured out to 10 years.34. The second primary endpoint (postprocedural ipsilateral stroke rates) also did not differ significantly between CEA (5.6%) and CAS (6.9% HR=0.99).

Interventionalists in CREST were the most carefully selected in any trial, and the lack of similar selection criteria has been a critique of the other trials.35. Analyses of CAS in Medicare patients between 2005 and 2007 found that few CAS operators had the experience of CREST investigators.36. Among the 11846 procedures with documented operator experience, 68% were performed by operators having performed fewer than 12 procedures.

In a follow-up analysis of CREST data, Gonzales et al (2014) reported no differences in efficacy and safety outcomes for subjects based on receiving treatment in high-, medium-, or low-volume centers.37.

**Asymptomatic Carotid Trial**
The Asymptomatic Carotid Trial I was a noninferiority trial reported by Rosenfield et al (2016) who compared CAS with CEA in asymptomatic individuals, not at high-risk for surgical complications.38. Enrollment began in 2005, with a target of 1658 participants; but, because of slow enrollment, the trial was halted in 2013 at 1453 participants. The primary composite endpoint (death, stroke, or MI within 30 days or ipsilateral stroke within 1 year) was met by 3.8% of CAS and 3.4% of CEA patients, while the cumulative 5-year rate of stroke-free survival was 93.1% with CAS and 94.7% with CEA (p=0.44). This trial did not answer how best to treat asymptomatic patients, because it did not include a medical therapy arm. Patients treated with current best medical therapy might have had an ipsilateral stroke rate of only 0.5% to 1% per year.39.

**Additional RCTs**
Several other smaller trials have compared CEA with CAS. Li et al (2014) published a trial that randomized 130 subjects at high-risk of stroke due to angiographically confirmed carotid stenosis (≥50%) to CEA (n=65) or CAS (n=65).40. The authors reported a 3-month postoperative risk of mortality of 1.5% with CAS compared with 9.2% with CEA. However, “existence of complete follow-up data” was an inclusion criterion, and insufficient details were provided about enrollment and randomization procedures to permit conclusions about the trial.

Kulha et al (2015) published results of an RCT that allocated 150 subjects with at least 70% internal carotid artery stenosis to CEA (n=73) or CAS (n=77).41. New infarctions on magnetic resonance imaging were found more frequently after CAS (49% vs 25%; p=0.002).

Reiff et al (2019) published one-year interim results of the Stent-supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy 2 (SPACE-2) RCT.42. The SPACE-2 RCT was originally planned to compare best medical treatment (BMT) to CEA plus BMT or CAS plus BMT in 3550 patients with high grade asymptomatic extracranial carotid artery stenosis. But, because patient recruitment was slow, the RCT was amended in 2013 to become two parallel randomized studies (BMT alone versus CEA plus BMT, and BMT alone versus CAS plus BMT). After recruitment continued to be slow, SPACE-2 was ultimately stopped early in 2016 after only 513 patients were randomized. Although the interim analysis did not find significant differences between CEA and CAS in one-year rates of stroke or all-cause mortality, SPACE-2 authors noted that it is insufficiently powered to detect such differences.
Section Summary: Randomized Controlled Trials of Carotid Artery Stenting versus Carotid Endarterectomy

RCTs comparing CEA with CAS enrolled a mix of symptomatic and asymptomatic patients and employed different selection criteria for participating centers. Periprocedural stroke and death rates following CAS exceeded those after CEA. Following the early perioperative period (≥31 days), the rates of ipsilateral stroke and/or transient ischemic attack appear to be similar for the 2 procedures. While some trials found higher restenosis rates after CAS (SAPPHIRE, SPACE, EVA-3S), restenosis in CREST occurred at similar frequency following either procedure. The rates of early complications in SPACE, EVA-3S, and ICSS exceeded 6.0%. In CREST, periprocedural death or stroke rates with CAS were less than 6% in symptomatic and 3% in asymptomatic patients. Interventionists in CREST were the most carefully selected in any trial, and the criteria used to credential in other trials has been a focus of criticisms, along with the inconsistent use of EPDs.43, No RCTs have compared CAS with medical therapy. Therefore, it is not possible to determine whether CAS is superior to medical therapy. Since the pivotal CEA vs medical therapy trials, there has been a marked improvement in medical therapy and declining stroke rates in asymptomatic patients with carotid stenosis. In 1993, the Asymptomatic Carotid Surgery Trial reported that the annual ipsilateral stroke rate was approximately 2.0% with medical therapy. A meta-analysis of studies completing enrollment between 2000 and 2010 found a pooled estimate for annual ipsilateral stroke incidence of 1.13%. This decrease in stroke risk has been used to argue that medical therapy in asymptomatic patients is preferable to surgical intervention.27,44,45,

Review of Evidence

Systematic Reviews

Several Blue Cross Blue Shield Association Technology Evaluation Center (TEC) Assessment and meta-analyses have been published, all reporting similar findings.46,47,48,49,50,51, In average-risk symptomatic patients, the body of evidence has demonstrated worse periprocedural outcomes with CAS than with CEA. While data have shown secular improvement in periprocedural outcomes following CAS, there is evidence of net harm compared with CEA.32,52, A 2010 individual patient data meta-analysis of SPACE, EVA-3S, and ICSS indicated some uncertainty in comparative periprocedural death or stroke rates for younger symptomatic patients.53, Still, that subgroup result must be considered carefully given the larger body of evidence, lack of stratified randomization, as well as the evidence on restenosis. Meta-analyses have generally found that restenosis is more common following CAS than CEA. In a meta-analysis of 13 trials, among those reporting restenosis rates, Bangalore et al (2011) reported pooled relative odds for restenosis following CAS compared with CEA of 2.8 (95% CI, 2.0 to 4.0; P=0%).45 Of note was the individual patient data meta-analysis (n=3433) of SPACE, EVA-3S, and ICSS.53 In these symptomatic patients, the 30-day death or stroke risk (per-protocol analyses) with CAS was 7.7% vs 4.4% following CEA (RR=1.74; 95% CI, 1.32 to 2.30).

The Carotid Stenting Trialists’ Collaboration (2016) published an individual patient data meta-analysis (total N=4754 patients) of SPACE, EVA-3S, and ICSS data, plus data from symptomatic patients in CREST to evaluate the association between age and risk of stroke or death with CEA and CAS.54 The periprocedural period was defined as 120 days, which is considerably longer than the conventional 30-day periprocedural definition. For symptomatic patients assigned to CEA, there was no increase in the periprocedural or postprocedural risk of death or stroke for patients older than 65 compared with those younger than 60. In contrast, for patients assigned to CAS, the risk of periprocedural events increased with age, from a 2.1% risk for patients less than 60 years, to 11% for patients over 70 years. These analyses found increased periprocedural stroke risk for CAS vs CEA in patients approximately 65 years and older, but not among those younger patients (an age threshold was not defined). Age was not significantly associated with postprocedural stroke risk. The results would suggest that the risk-benefit profile for CAS in symptomatic patients enrolled in these trials could be modified by age, but there was considerable imprecision in the age-specific CAS vs CEA comparisons for periprocedural risk. For example, among patients ages 60 to 64 years, the HR comparing CAS with CEA for the periprocedural risk of stroke or death was 1.07 (95% CI, 0.56 to 2.01). In 2019, on behalf of the
Carotid Stenting Trialists' Collaboration, Brott et al (2019) published another individual patient data meta-analysis of the same symptomatic patient group (total n=4775 patients) from SPACE, EVA-3S, ICSS, and CREST to evaluate long-term outcomes (mean follow-up of 4 years). Periprocedural and postprocedural risks continued to favor CEA.

Paraskevas et al (2014) conducted a systematic review of studies comparing cognitive outcomes after CEA with those after CAS. Thirteen studies were included, with heterogeneity in the types of cognitive outcome measures reported. In qualitative analysis, reviewers found that most studies did not report a significant difference between CEA and CAS regarding cognitive outcomes and that heterogeneity across outcomes reported precluded more definitive conclusions.

Galyfós et al (2014) reported on results of a meta-analysis that included 9 trials (total n = 5959 patients) with a focus on the risk of periprocedural symptomatic or asymptomatic myocardial ischemia or MI. Four trials did not report their definitions for myocardial ischemia, and other studies varied in their definitions. In the pooled analysis, compared with CEA, CAS was associated with decreased risk of cardiac damage (pooled RR=0.37; 95% CI, 0.22 to 0.61; p<0.000). However, reviewers provided incomplete information on the selection of studies for inclusion, which limits conclusions that can be drawn.

Vincent et al (2015) conducted a meta-analysis of 8 RCTs (total n=7091 patients). Studies selected compared CAS with CEA, enrolled more than 50 patients, and reported periprocedural or long-term outcomes. Included were the CREST, ICSS, SPACE, EVA-3S, and SAPPHIRE trials (described above), along with the Carotid and Vertebral Artery Transluminal Angioplasty Study, an RCT comparing surgical management with endovascular treatment in 504 patients with symptomatic carotid stenosis. CAS was associated with an increased risk of any periprocedural stroke (RR=1.49; 95% CI, 1.11 to 2.01), a similar risk of a disabling or major stroke, and a decreased risk of periprocedural MI (RR=0.47; 95% CI, 0.29 to 0.78) compared with CEA. However, in long-term follow-up (range, 2-10 years), stenting was associated with an increased risk of stroke (RR=1.36; 95% CI, 1.16 to 1.61) and an increased risk of the composite endpoint of ipsilateral stroke, periprocedural stroke, or periprocedural death (RR=1.45; 95% CI, 1.20 to 1.75) compared with CEA. This analysis supported a conclusion that CEA remains the treatment of choice for most patients due to the increase in adverse events with CAS.

Section Summary: Systematic Reviews

The systematic reviews have corroborated the results of individual RCTs that early adverse events are higher with CAS than with CEA, that long-term stroke rates following the perioperative period are similar, and that restenosis rates are higher with CAS. These data would indicate that, for the average-risk patient with carotid stenosis, CAS is associated with net harm compared with CEA.

Periprocedural Death or Stroke Rates Following Carotid Artery Stenting

Systematic Reviews

Questions of periprocedural death or stroke rates were assessed in a TEC Assessment (2010). Given that CAS (like CEA) trades the procedure-related risks of stroke and death for a reduced risk of stroke over subsequent years, and limits for periprocedural stroke and death rates that can be assumed to achieve a net clinical benefit outlined in current guidelines are less than 3% for asymptomatic and less than 6% for symptomatic patients, the Assessment sought evidence to address two questions: (1) Is the periprocedural rate of death or stroke with CAS less than 3% for asymptomatic and less than 6% for symptomatic patients? (2) For those subgroups defined by (a) medical comorbidities or (b) unfavorable anatomy, are periprocedural rates of death or stroke with CAS less than 3% for asymptomatic and less than 6% for symptomatic patients?

To the first question, the Assessment identified 18 multicenter prospective registries collectively enrolling 20194 patients. Eleven of those registries enrolled patients in accordance with the U.S. Food and Drug Administration labeling and with 30-day outcomes available for analysis by...
symptomatic status (13783 asymptomatic, 3353 symptomatic). In 9 of those registries, 30-day death or stroke rates were either reported or obtained from investigators and in the remaining 2, death or stroke rates were estimated from 30-day death/stroke/MI and MI rates. An independent assessment of neurologic outcomes was required in all but one registry. For asymptomatic patients, the pooled periprocedural death or stroke rate was 3.9% (95% CI, 3.3% to 4.4%; I²=57%); for symptomatic patients, it was 7.4% (95% CI, 6.0% to 9.0%; I²=59%).

A subsequent systematic review, without consideration to the Food and Drug Administration labeling, reported results consistent with the TEC Assessment (pooled periprocedural death/stroke rates in asymptomatic patients of 3.3% [95% CI, 2.6% to 4.1%] [23 studies; n=8504 patients] and in symptomatic patients of 7.6% [95% CI, 6.3% to 9.1%] [42 studies; n=4910 patients]).

To the second question, the Assessment found that combined data from 2 registries reported periprocedural death or stroke rates for patients with unfavorable anatomy, but included only 371 asymptomatic (30-day death or stroke rate, 2.7%; 95% CI, 1.5% to 4.9%) and 60 symptomatic patients (30-day death or stroke rate, 1.7% 95% CI, 0.3% to 8.9%). No other registry reported results by symptomatic status for those subgroups.

Since of the 2010 TEC Assessment, additional evidence has been published on rates of periprocedural stroke and death following CAS, particularly for subgroups defined by medical comorbidities. Spangler et al (2014) evaluated patients treated with isolated primary CEA (n=11336) or primary CAS (n=544) at 29 centers between 2003 and 2013 to assess periprocedural mortality and stroke risks for those considered at medially high-risk. A Cox proportional hazards model was used to generate predicted five-year mortality, and patients in the highest risk score quartile were considered high-risk. For asymptomatic patients, there were no significant differences between CEA and CAS for major periprocedural outcomes (major or minor stroke, MI, death) for either high- or low-risk patients. Periprocedural death or stroke rates with CAS were 1.1% for low-risk patients and 1.6% for high-risk patients. For symptomatic patients, periprocedural death or stroke rates were higher with CAS than with CEA for both low- and high-risk groups. For low-risk symptomatic patients, periprocedural death or stroke rates were 6.0% for CAS and 2.2% for CEA (p<0.01). For high-risk symptomatic patients, periprocedural death or stroke rates were 9.3% for CAS and 2.5% for CEA (p<0.01).

Retrospective Analyses
Salzler et al (2017) conducted a large retrospective analysis of the increased use of CAS since the Centers for Medicare & Medicaid guidelines recommended CAS for high-risk patients needing carotid revascularization. Data from the Nationwide Inpatient Sample were searched for patients undergoing carotid revascularization. From 2005 (when the guidelines were published) to 2011, 20079 CEAs and 3447 CASs were performed on high-risk patients. During the study period, CAS utilization increased significantly among all high-risk patients. A subgroup analysis of symptomatic high-risk patients did not show an increase in CAS use, indicating that the increase in CAS was primarily in asymptomatic high-risk patients. The odds of in-hospital mortality (odds ratio, 2.6; 95% CI, 1.2 to 5.6) and postoperative in-hospital stroke (odds ratio, 1.5; 95% CI, 1.1 to 3.7) were independently and significantly higher in patients undergoing CAS compared with CEA in the overall sample of high-risk patients.

Carotid Artery Stenting for Carotid Dissection
Carotid dissection is uncommon (incidence≈2 per 100000/year) and generally occurs in younger individuals. With a frequently favorable prognosis, conservative therapy with anticoagulants to restore blood flow is typically employed while surgical intervention is reserved for patients whose symptoms fail to respond to conservative care. Some have described CAS as a potential treatment in those instances; however, there are no clinical trials comparing alternative strategies and interventions. Current guidelines (detailed below) rate CAS for this indication as a class IIb (level of evidence: C) recommendation.
Summary of Evidence
For individuals who have carotid artery stenosis who receive carotid artery stenting (CAS), the evidence includes randomized controlled trials and systematic reviews of these trials. Relevant outcomes are overall survival, morbid events, and treatment-related mortality and morbidity. A substantial body of randomized controlled trial evidence has compared outcomes of CAS with CEA for symptomatic and asymptomatic patients with carotid stenosis. The evidence does not support the use of CAS in carotid artery disease for the average-risk patient because early adverse events are higher with CAS and long-term outcomes are similar between the two procedures. Data from randomized controlled trials and large database studies have established that the risk of death or stroke with CAS exceeds the threshold considered acceptable to indicate overall benefit from the procedure. Therefore, for patients with carotid stenosis who are suitable candidates for CEA, CAS does not improve health outcomes. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

Supplemental Information
Clinical Input From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 4 physician specialty societies (6 reviewers) and 4 academic medical centers in 2009. (Also, an unsolicited response from a specialty society was received.) Input strongly supported the use of carotid artery stenting (CAS) in recently symptomatic patients where surgical carotid endarterectomy cannot be performed due to anatomic reasons, although acknowledging the limited evidence about this subgroup. The lack of alternative treatments for recently symptomatic patients and the established increased risk of stroke were factors supporting this opinion.

Practice Guidelines and Position Statements
American Stroke Association
The American Stroke Association (2011), with 13 other medical societies, issued guidelines on the management of extracranial carotid and vertebral artery diseases, which are summarized in Table 4.

Table 4. Guidelines for Managing Patients With Extracranial Carotid and Vertebral Artery Disease

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS is indicated as an alternative to CEA for symptomatic patients at average or low-risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by &gt;70% as documented by noninvasive imaging or &gt;50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is &lt;6% (360)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>When revascularization is indicated for patients with TIA or stroke and there are no contraindications to early revascularization, intervention within 2 wk of the index event is reasonable rather than delaying surgery</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound)</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>
but its effectiveness compared with medical therapy alone in this situation is not well established

In symptomatic or asymptomatic patients at high-risk of complications for carotid revascularization by either CEA or CAS because of comorbidities, the effectiveness of revascularization versus medical therapy alone is not well established

Carotid angioplasty and stenting might be considered when ischemic neurologic symptoms have not responded to antithrombotic therapy after acute carotid dissection

Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is not recommended when atherosclerosis narrows the lumen by <50%

Carotid revascularization is not recommended for patients with chronic total occlusion of the targeted carotid artery

Carotid revascularization is not recommended for patients with severe disability caused by cerebral infarction that precludes preservation of useful function

Society for Vascular Surgery
The Society for Vascular Surgery (2011) updated its guidelines on the management of the extracranial carotid disease. Recommendations from the guidelines are summarized in Table 5.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GOE</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>In most patients with carotid stenosis who are candidates for intervention, CEA is preferred to CAS for reduction of all-cause and periprocedural death</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>CAS is preferred over CEA in symptomatic patients with &gt;50% stenosis and tracheal stoma, situations where local tissues are scarred and fibrotic from prior ipsilateral surgery or external beam radiotherapy, prior cranial nerve injury, and lesions that extend proximal to the clavicle or distal to the C2 vertebral body</td>
<td>II</td>
<td>B</td>
</tr>
<tr>
<td>CAS is preferred over CEA in symptomatic patients with &gt;50% stenosis and severe uncorrectable coronary artery disease, congestive heart failure, or chronic obstructive pulmonary disease</td>
<td>II</td>
<td>C</td>
</tr>
<tr>
<td>There are insufficient data to recommend CAS as primary therapy for neurologically asymptomatic patients with 70%-99% diameter stenosis. In properly selected asymptomatic patients, CAS is equivalent to CEA in the hands of experienced interventionalists with a combined stroke and death rate &lt;3%</td>
<td>II</td>
<td>B</td>
</tr>
</tbody>
</table>

CAS: carotid artery angioplasty with stenting; CEA: carotid endarterectomy; GOE: grade of evidence; LOE: level of evidence.

a Grade I: benefit clearly outweighs risk; grade II: benefits and risks are more closely matched and are more dependent on specific clinical scenarios.

b Level B (moderate quality); level C (low quality).

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
The Center for Medicaid & Medicare Services (CMS; 2001) issued national coverage policy that restricted coverage for carotid angioplasty and stenting to patients participating in a clinical trial with category B investigational device exemption (IDE) designation from the U.S. Food and Drug Administration (FDA). Percutaneous transluminal angioplasty of the vertebral and cerebral arteries remained noncovered.

When the FDA approved the first (Guidant) devices, Medicare coverage under the IDE was no longer available for that manufacturer’s devices and was not applicable to the FDA-required
postapproval studies. Thus, in 2004, Medicare broadened its national coverage policy and “determined that the evidence is adequate to conclude that percutaneous transluminal angioplasty with carotid stent placement is reasonable and necessary when performed consistent with the FDA approval of the carotid stent device and in an FDA required post-approval study.” For unapproved stents and embolic protection devices, the prior policy remained in effect and restricted coverage to patients participating in an FDA-approved category B IDE trial of stent placement in the cervical carotid artery.

While the Medicare decision differed from the conclusions of this evidence review, Medicare made a public policy decision “that making available new, effective therapies aimed at addressing treatment and prevention of cerebrovascular disease was important to Medicare beneficiaries.” Medicare also noted that it recognized the value in supporting postapproval studies as “the collected data may provide an opportunity for practitioners to determine which patients are most appropriate for carotid artery stenting and to reinforce IDE trial data on health outcomes and adverse events.”

CMS provides a continually updated listing of facilities eligible for Medicare reimbursement that meet CMS’s minimum facility standards for performing CAS for high-risk patients.

In 2005, CMS determined that CAS with embolic protection devices was reasonable and necessary for patients at high-risk for carotid endarterectomy (CEA) who also have symptomatic carotid artery stenosis 70% or more. CMS limited coverage for these patients to procedures performed using the FDA-approved devices. CMS also limited coverage for patients at high-risk for CEA with symptomatic carotid artery stenosis between 50% and 70% and for patients at high-risk for CEA with asymptomatic stenosis 80% or more, to the FDA-approved category B IDE clinical trials for unapproved devices, or to the FDA-required postapproval studies for approved devices. CMS defined patients at high-risk for CEA as having significant comorbidities and/or anatomic risk factors (ie, recurrent stenosis and/or previous radical neck dissection) who would be poor candidates for CEA in the opinion of a surgeon.

In 2007, a decision memo reaffirmed CMS’s previous decision following a request to expand coverage while clarifying that “CAS is only covered when used with an embolic protection device and is, therefore, not covered if deployment of the distal embolic protection device is not technically possible.” In 2008, in a sixth reconsideration, and in 2009, in a seventh reconsideration, CMS reaffirmed its prior coverage decisions.

In 2012, CMS convened a Medicare Evidence Development & Coverage Advisory Committee panel to consider management of carotid atherosclerosis. Medicare Evidence Development & Coverage Advisory Committee panel members voted on specific questions using a scale of 1 (low confidence) to 5 (high confidence). For symptomatic patients not considered at high-risk, the mean scores to the question of whether CAS is the favored treatment strategy in this population was 1.85 and for CEA 3.6. For asymptomatic patients not considered high-risk, the evidence was judged to have not reached a level of certainty to determine a favored treatment.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 6. There are no ongoing or direct comparisons of CAS with CEA in patients at increased risk for CEA complications. Particularly problematic is the lack of adequate data, from either randomized or nonrandomized studies, to separately compare outcomes of the alternatives (CAS vs CEA vs current optimal medical management) in symptomatic and asymptomatic increased-risk subgroups.
Table 6. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
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<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02538276</td>
<td>Carotid Endarterectomy and Carotid Artery Stenting in Brazil</td>
<td>500</td>
<td>Jul 2019</td>
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<td>NCT00883402</td>
<td>Asymptomatic Carotid Surgery Trial-2 (ACST-2): an International Randomised</td>
<td>3600</td>
<td>Dec 2019</td>
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<tr>
<td></td>
<td>Trial to Compare Carotid Endarterectomy With Carotid Artery Stenting to</td>
<td></td>
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<tr>
<td></td>
<td>Prevent Stroke</td>
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<tr>
<td>ISRCTN78592017</td>
<td>Stent-protected angioplasty in asymptomatic carotid artery stenosis vs</td>
<td>5000</td>
<td>Jul 2020</td>
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<tr>
<td></td>
<td>endarterectomy: two two-arm clinical trials (SPACE-2)</td>
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<tr>
<td>NCT02089217</td>
<td>Carotid revascularization and medical management for asymptomatic carotid</td>
<td>2480</td>
<td>Dec 2020</td>
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<tr>
<td></td>
<td>stenosis trial (CREST-2)</td>
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<tr>
<td>ISRCTN97744893</td>
<td>European Carotid Surgery Trial 2 (ECST-2): a randomized controlled trial</td>
<td>2000</td>
<td>Mar 2022</td>
</tr>
</tbody>
</table>

ISRCTN: International Standard Randomized Controlled Trial Number; NCT: national clinical trial.

References


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ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on
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report of the American College of Cardiology Foundation/American Heart Association
Task Force on Practice Guidelines, and the American Stroke Association, American
Association of Neuroscience Nurses, American Association of Neurological Surgeons,
American College of Radiology, American Society of Neuroradiology, Congress of
Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for
Cardiovascular Angiography and Interventions, Society of Interventional Radiology,
Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for
ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on
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stenting for carotid artery stenosis. Cochrane Database Syst Rev. Sep 12 2012; (9):
CD000515. PMID 22972047
2020).

Documentation for Clinical Review

Please provide the following documentation:
- History and physical and/or consultation notes including:
  - Stenosis measurement
  - Documentation of focal cerebral ischemia including duration or nondisabling stroke
  - Reason carotid endarterectomy is contraindicated

Post Service (in addition to the above, please include the following):
- Operative report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according
to product design; therefore, contract language should be reviewed before applying the terms
of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or
provider reimbursement.

MN/IE
The following services may be considered medically necessary in certain instances and
investigational in others. Services may be considered medically necessary when policy criteria
are met. Services may be considered investigational when the policy criteria are not met or
when the code describes application of a product in the position statement that is investigational.

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<th>Description</th>
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<td>0075T</td>
<td>Transcatheter placement of extracranial vertebral artery stent(s), including radiologic supervision and interpretation, open or percutaneous; initial vessel</td>
</tr>
<tr>
<td>CPT®</td>
<td>0076T</td>
<td>Transcatheter placement of extracranial vertebral artery stent(s), including radiologic supervision and interpretation, open or percutaneous; each additional vessel (List separately in addition to code for primary procedure)</td>
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<tr>
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<td>None</td>
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<td>37215</td>
<td>Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; with distal embolic protection</td>
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<tr>
<td>37216</td>
<td>Transcatheter placement of intravascular stent(s), cervical carotid artery, open or percutaneous, including angioplasty, when performed, and radiological supervision and interpretation; without distal embolic protection</td>
</tr>
<tr>
<td>37217</td>
<td>Transcatheter placement of intravascular stent(s), intrathoracic common carotid artery or innominate artery by retrograde treatment, open ipsilateral cervical carotid artery exposure, including angioplasty, when performed, and radiological supervision and interpretation</td>
</tr>
</tbody>
</table>

**Policy History**

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/18/2009</td>
<td>New policy Portions of this policy have been derived from the previously existing BSC Medical Policy Extracranial Carotid Angioplasty and Stenting and Cerebral Angioplasty and Stenting for Atherosclerosis, Stroke and Vasospasm</td>
</tr>
<tr>
<td>04/01/2011</td>
<td>Policy title change from Extracranial Carotid Angioplasty and Stenting with position change</td>
</tr>
<tr>
<td>01/01/2015</td>
<td>Coding Update</td>
</tr>
<tr>
<td>06/30/2015</td>
<td>Policy title change from Carotid (Extracranial) Angioplasty and Stenting Policy revision with position change</td>
</tr>
<tr>
<td>08/01/2016</td>
<td>Policy title change from Extracranial Carotid Angioplasty/Stenting Policy revision without position change</td>
</tr>
<tr>
<td>07/01/2017</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>09/01/2018</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>07/01/2019</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>07/01/2020</td>
<td>Annual review. No change to policy statement. Literature review updated.</td>
</tr>
</tbody>
</table>

**Definitions of Decision Determinations**

**Medically Necessary:** Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis;
(c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member’s illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements (as applicable to your plan)**

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member’s health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member’s eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.