

Regence

Extracranial Carotid Angioplasty and Stenting

Effective: January 1, 2025

Next Review: September 2025

Last Review: December 2024

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Extracranial carotid angioplasty/stenting (CAS) is the insertion of a stent (wire-mesh tube) into a narrowed carotid artery. CAS is a treatment for carotid stenosis that is intended to prevent future stroke.

MEDICAL POLICY CRITERIA

Note: This policy does not address percutaneous angioplasty and stenting of veins, which is addressed in a separate policy (see Cross References section).

- I. Extracranial carotid angioplasty and stenting may be considered **medically necessary** for the treatment of carotid artery dissection.
- II. Extracranial carotid angioplasty with associated stenting and embolic protection may be considered **medically necessary** when all of the following criteria (A. – B.) are met:
 - A. Documented stenosis including either of the following:
 1. At least 80% stenosis; or
 2. At least 50% stenosis along with symptoms with duration less than 24 hours of focal ischemia (transient ischemic attack or monocular blindness) in previous 120 days, or nondisabling stroke; and

- B. One or more of the following anatomic contraindications for carotid endarterectomy are present:
1. Tissue changes from prior extensive ipsilateral neck radiation
 2. Prior ipsilateral radical neck resection
 3. Anatomical malformation that prevents collateral circulation to the brain during open carotid endarterectomy
 4. Lesions surgically inaccessible (such as high internal carotid lesion that cannot be accessed from the neck)
 5. Spinal immobility preventing open carotid endarterectomy
 6. Tracheostomy

III. Extracranial carotid angioplasty is considered **investigational** for all indications that do not meet Criteria I or II.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Current symptomology
- Documentation of percent of stenosis
- Documentation of focal ischemia, including duration and date of occurrence, or nondisabling stroke, for symptomatic patients
- Contraindications for carotid endarterectomy, including one or more listed in policy

CROSS REFERENCES

1. [Percutaneous Angioplasty and Stenting of Veins](#), Surgery, Policy No. 109

BACKGROUND

The extracranial carotid angioplasty and stenting (CAS) procedure is proposed as an alternative to medical therapy and a less invasive alternative to carotid endarterectomy (CEA). CAS involves the insertion of a stent (wire-mesh tube) into a narrowed carotid artery. A catheter (a long hollow tube) is inserted into a groin or neck artery and guided through the arteries to the narrowing in the carotid artery. A balloon at the end of the catheter is inflated to push open the narrowed area, and a metal stent is inserted to keep this area from narrowing again. The procedure is performed with the patient fully awake and without sedation. At present, most practitioners also use a distally placed embolic protection device (EPD) that is designed to reduce the risk of stroke caused by thromboembolic material dislodged during CAS. Carotid angioplasty is rarely performed without stent placement.

REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) has approved several carotid artery stents and EDPs from various manufacturers. The FDA has mandated postmarketing studies for these devices. Each FDA-approved carotid stent system is indicated for combined use with a EPD.

EVIDENCE SUMMARY

This evidence review is focused on carotid angioplasty with stenting (CAS) compared with carotid endarterectomy (CEA) for treatment of carotid stenosis, and not on carotid stenting as a treatment for carotid artery dissection. Evidence from well-designed, well-conducted randomized controlled trials (RCTs) is necessary to establish the safety and efficacy of CAS as compared with CEA for stenosis treatment.

SYSTEMATIC REVIEWS

Loufopoulos (2024) published as systematic review (SR) with meta-analysis evaluating new ischemic cerebral lesions using postprocedural magnetic resonance imaging in carotid artery stenting versus carotid endarterectomy (CEA).^[1] A total of 25 studies reporting on 1827 CEA and 1500 CAS interventions were included. The incidence of new cerebral ischemic lesions was significantly lower after CEA compared to CAS, regardless of the time of MRI assessment (first 24 hours; OR: 0.33, 95% CI: 0.17-0.64, $p < 0.001$), (the first 72 hours, OR: 0.25, 95% CI 0.18-0.36, $p < 0.001$), (generally within a week after the operation; OR: 0.24, 95% CI: 0.17-0.34, $P < 0.001$). Also, the rate of stroke (OR: 0.38, 95% CI: 0.23-0.63, $P < 0.001$) and the presence of contralateral new cerebral ischemic lesions (OR: 0.16, 95% CI 0.08-0.32, $p < 0.001$) were less frequent after CEA. Subgroup analysis based on the study design and the use of embolic protection device during CAS showed consistently lower rates of new lesions after CEA.

Gasior (2023) published a SR with network meta-analysis evaluating the management of asymptomatic carotid artery stenosis (ACAS), including carotid endarterectomy (CEA), carotid artery stenting (CAS), and best medical treatment (BMT).^[2] The study assessed peri-operative (within 30 days) and long term (30 days - five years) stroke and mortality risk between ACAS interventions. Seventeen reports (14 310 patients) with $> 50\%$ ACAS were included. CEA reduced the odds of a peri-operative stroke event occurring vs. CAS (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.1 - 2.2 [0 - 20 fewer/1 000]). CEA and CAS reduced the long-term odds of minor strokes (OR 0.35, 95% CI 0.21 - 0.59 [20 fewer/1 000]) and ipsilateral strokes (OR 0.27, 95% CI 0.19 - 0.39 [30 fewer/1 000]) vs. all BMT. CEA reduced the odds of major strokes and combined stroke and mortality vs. traditional BMT; however, no difference was found between CEA and modern BMT. CAS reduced the odds of peri-operative MI (OR 0.49, 95% CI 0.26 - 0.91) and CNI (OR 0.07, 95% CI 0.01 - 0.42) vs. CEA. The authors conclude that BMT carries the potential to reduce the requirement for surgical intervention in patients with ACAS.

A 2020 Cochrane review found CAS associated with an increased risk of periprocedural death or stroke compared with CAE, based on 10 RCTs that included 5,396 patients (odds ratio [OR] 1.70, 95% confidence interval [CI] 1.31 to 2.19). Risk of periprocedural death or stroke remained higher with CAS in subgroup analysis of patients younger than age 70 years (OR 1.11, 95% CI 0.74 to 1.64) and in those patients aged 70 years and older (OR 2.23, 95% CI 1.61 to 3.08), although this estimate was not statistically significant. The effect was similar in asymptomatic patients based on seven trials of 3,378 individuals (OR 1.72, 95% CI 1.00 to 2.97). The review also found CAS associated with a significantly increased risk of at least moderate ($\geq 50\%$) restenosis (four RCTs, $n=2,115$, OR 2.00, 95% CI 1.12 to 3.60) and a

nonsignificant risk of severe ($\geq 70\%$) restenosis (nine RCTs, $n=5,744$, OR 1.26, 95% CI 0.79 to 2.00) in a pooled group of symptomatic and asymptomatic patients.

A systematic review and meta-analysis of RCTs by Li (2016) assessed the long-term efficacy and safety of CAS compared to CEA.^[3] Eight trials, including the large RCTs ACT I, CREST, ICCS, EVA-3S, CAVATAS, and BACASS, with a total of 7,005 patients were included in the analysis. All studies had at least four years of follow-up. Seven of the trials contributed data on stroke risk, which was significantly higher with stenting event rate (9.3% vs 6.8%, OR 1.45, 95% CI 1.22 to 1.73, $p<0.0001$). Stenting was also associated with an increased risk for the composite endpoint of death, ipsilateral stroke, or periprocedural stroke compared with CEA in eight trials (OR 1.25, 95% CI 1.05 to 1.48, $p=0.01$).

Vincent (2015) conducted a similar meta-analysis of eight RCTs (total $n=7,091$ patients).^[4] Studies were selected that compared CAS to CEA, enrolled more than 50 patients, and reported periprocedural or long-term outcomes, and included CREST, ICSS, SPACE, EVA-3S, CAVATAS, and SAPHIRE. CAS was associated with an increased rate of any type of periprocedural stroke (relative risk [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 myocardial infarction (RR 0.47, 95% CI 0.29 to 0.78). However, in follow-up ranging from 2 to 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 a composite end point of ipsilateral stroke, periprocedural stroke, or periprocedural death (RR 1.45, 95% CI 1.20 to 1.75). This analysis supports the conclusion that CEA remains the treatment of choice for most patients, due to the increase in adverse events with CAS.

Three systematic reviews and meta-analyses compared CEA and CAS outcomes in patients with asymptomatic stenosis. The review by Kakkos (2017) included nine RCTs with a total of 3,709 patients (CEA $n=1,479$, CAS $n=2,230$).^[5] In this analysis, CAS was associated with a higher rate of stroke or death at 30 days (2.9% vs. 1.9% with CEA, OR 1.57, 95% CI 1.01 to 2.44). Myocardial infarction (MI) at 30 days did not differ significantly between groups, but cranial nerve injury at 30 days was lower in the CAS group (OR 0.13, 95% CI 0.07 to 0.26). The composite outcome of stroke or death at 30 days plus ipsilateral stroke at one year was higher for CAS than CEA (OR 1.51, 95% CI 1.02 to 2.24). A similar review by Moresoli (2017) included 11 reports of five RCTs with 3,019 asymptomatic patients.^[6] They found a trend toward higher incidences of periprocedural stroke with CAS, which was not statistically significant (RR 1.95, 95% CI 0.98 to 3.89). A review by Galyfos (2019) included 10 randomized trials (total $n=8,771$) and concluded that CEA was associated with a lower risk of early stroke in asymptomatic patients compared with CAS, but other outcomes were not significantly different.^[7]

Paraskavas (2014) conducted a systematic review of studies comparing cognitive outcomes after CEA with those after CAS.^[8] Thirteen studies were included, with heterogeneity in the types of cognitive outcome measures reported. In a qualitative analysis, the authors report that the majority of studies did not report a significant difference between CEA and CAS in terms of cognitive outcomes, but that the heterogeneity in outcomes reported precluded more definitive conclusions.

Galyfos (2014) reported results of a systematic review that included nine trials ($n=5,959$) with a focus on risk of periprocedural symptomatic or asymptomatic myocardial ischemia or infarction.^[9] Four studies did not report their definition used for myocardial ischemia, and other studies varied in their definitions. In pooled analysis, compared with CEA, CAS was associated

with decreased risk for cardiac damage (pooled RR 0.37, 95% CI 0.22 to 0.61, p=0.0001). However, the study provides incomplete information about selection of studies for inclusion, which limits conclusions that can be drawn.

A 2012 updated Cochrane Review systematically reviewed all RCTs comparing carotid angioplasty and stenting with carotid endarterectomy or medical care.^[10] The Cochrane Review found strong evidence that endovascular treatment in patients with symptomatic carotid stenosis is associated with a higher risk of death or stroke than CEA up to 30 days after the procedure. The evidence was also rated strong for an association between patient age and excess risk with endovascular treatment. There was insufficient evidence to determine whether the comparative risks of endovascular treatment versus CEA depended on the patient's sex, vascular anatomy, or characteristics of atherosclerotic plaque. Little is known on the long-term durability of endovascular treatment beyond four years, especially with respect to restenosis and recurrent stroke rates. The combined results of two large^[11, 12] and three small trials showed no significant increase in severe restenosis after primary stenting compared with endarterectomy, but there was a wide confidence interval surrounding the effect measure and evidence of substantial heterogeneity ($I^2 = 58\%$). The available evidence does not rule out the possibility of a small increase in restenosis rates among patients receiving stent treatment compared with endarterectomy, and it is not known if restenosis increases the risk of recurrent stroke. The existing evidence does not allow any firm conclusions on the comparative safety and efficacy of endovascular treatment versus endarterectomy in patients with asymptomatic carotid stenosis.

A 2012 Agency for Healthcare Research and Quality (AHRQ) report evaluated the evidence from 60 eligible studies of treatment strategies for patients with asymptomatic carotid artery stenosis.^[13, 14] The report noted that the definitions of "asymptomatic" patients were heterogeneous across the evaluated studies (i.e., patients without symptoms, patients with symptoms present for at least six months before their enrollment in the study but recently [within six months] asymptomatic, or patients with symptoms in a vascular territory other than ipsilateral carotid [e.g., vertebrobasilar territory]). The report focused on evidence for the following treatments:

- Medical therapy alone
- CEA and medical therapy compared with medical therapy alone
- CAS and medical therapy compared with medical therapy alone
- CAS and medical therapy compared with CEA and medical therapy.

For evidence on CAS and medical therapy compared with CEA and medical therapy, the review concluded that "one recent large trial (CREST) reported higher rates of postprocedural ipsilateral stroke (including any periprocedural stroke) and its composite primary endpoint in the CAS[group], as compared with CEA, but this did not reach statistical significance in patients with asymptomatic carotid stenosis. The CREST and the SAPHIRE trials randomized patients with symptomatic and asymptomatic carotid stenosis stratified according to symptom status. Therefore, the treatment assignment was randomized among the subgroup of patients with asymptomatic carotid stenosis. However, neither trial was powered to detect a significant difference in the primary composite endpoint among subgroups of patients with asymptomatic carotid stenosis. The failure to find a significant difference does not rule out the possibility that real difference exists between the intervention modalities tested." The authors also stated that "future trials should focus not only on whether CAS is equivalent or superior to

CEA, but also on whether an invasive interventional procedure is likely to translate into any significant benefit to the patient treated with current best medical therapy.”

The 2007 and 2009 BlueCross BlueShield Association Technology Evaluation Center (TEC) assessments did not identify reliable evidence in support of CAS.^[15, 16] Five major randomized trials of CAS vs. CEA were reviewed in the TEC Assessments (SPACE, EVA-3S, SAPPHIRE, ICSS, and CREST) and all had significant limitations, including early termination (SPACE and EVA-3S), small numbers of symptomatic vs. asymptomatic patients (SAPPHIRE), significant loss to follow-up (CREST),^[17] and lack of power to reliably detect differences between treatment arms overall as well as in the subanalyses (CREST)^[17].

Khan (2014) published a systematic review with meta-analysis of risk factors associated with stroke and/or death in patients undergoing CAS.^[18] The following were reported to be independent risk factors for 30-day stroke and death following CAS:

- Symptomatic carotid stenosis compared with asymptomatic stenosis
- Age >80 years for 30-day stroke/death
- Age >70 years for 4-year stroke/death
- Lesion characteristics (e.g., ulceration, irregularity, calcification, length)
- Final residual stenosis >30%

No significantly increased risk of 30-day post-CAS stroke and/or death was found for gender, cardiac disease, or cardiovascular risk factors including hypertension, hyperlipidemia chronic obstructive pulmonary disease, peripheral artery disease, cigarette smoking. Mixed and unclear associations with risk were found for chronic renal failure, diabetes mellitus, high C-reactive protein levels, timing of procedure relative to the index ischemic event. Pre- and postprocedural use of statin medications was reported to be associated with lower periprocedural stroke and/or death.

Many other meta-analyses of the studies that compare carotid angioplasty/stenting (CAS) with endarterectomy (CEA) have been published.^[19-33] These analyses reported inconsistent findings, most of which favor CEA over CAS for symptomatic carotid stenosis. The reliability of the conclusions from these meta-analyses is limited by pooling results from unreliable, heterogeneous primary studies (different patient samples, endovascular procedures, duration of follow-up and/or completion status of the trials). A review of 17 systematic reviews comparing these procedures found that none fulfilled all items of the AMSTAR-2, an appraisal tool for systematic reviews, and graded the overall confidence in the results of 16 of the reviews as critically low.^[34]

RANDOMIZED CONTROLLED TRIALS

The Asymptomatic Carotid Trial (ACT I)

The Asymptomatic Carotid Trial (ACT) I was a noninferiority trial of CAS versus CEA in asymptomatic individuals who were not at high risk for surgical complications.^[35] Enrollment began in 2005 with a target of 1,658 participants, but because of slow enrollment, the trial was halted in 2013 with 1,453 participants. The primary composite endpoint of death, stroke, MI within 30 days, or ipsilateral stroke within one year was obtained in 3.8% of CAS and 3.4% of CEA patients, while the cumulative five-year rate of stroke-free survival was 93.1% with CAS and 94.7% with CEA ($p=0.44$). This study does not answer the question of how best to treat asymptomatic patients, since it does not include a medical therapy arm. Patients who are

treated with current best medical therapy may have an ipsilateral stroke rate of only 0.5% to 1% per year.^[36]

The Asymptomatic Carotid Surgery Trial 2 (ACST-2)

The second asymptomatic carotid surgery trial (ACST-2) was a multicenter RCT comparing CAS and CEA in 3,625 asymptomatic patients with severe carotid stenosis.^[37] There was no significant difference between groups in the composite of death, MI, or stroke with CAS or CEA (3.9% vs. 3.2%, $p=0.26$) within 30 days of the procedure. Five-year non-procedure related stroke was also similar between groups (5.3% with CAS vs. 4.5% with CEA, RR=1.6, 95% CI 0.86 to 1.57, $p=0.33$). The authors considered the long-term outcomes of these procedures to be similar with uncommon serious complication

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)

Meschia (2022) published a post hoc analysis of 826 asymptomatic patients enrolled in CREST with no stroke symptoms at baseline and with at least one completed follow-up Questionnaire for Verifying Stroke-free Status (QVSS).^[38] The hazards ratio (HR) for adjudicated stroke with CAS compared to CEA in this analysis was nonsignificant at 1.02 (95% CI, 0.57 to 1.85). However, significant treatment differences for CAS versus CEA were detected for the outcome of stroke symptoms (HR, 1.54; 95% CI, 1.15 to 2.08) and the composite outcome of adjudicated stroke or stroke symptoms (HR, 1.38; 95% CI, 1.04 to 1.83). The authors concluded that inclusion of stroke symptoms to broaden the outcome of stroke prevention trials should be considered to permit sufficiently powered analyses in low-risk populations.

Brott (2016) reported long-term follow-up for CREST.^[39] 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. The second primary endpoint of post procedural ipsilateral stroke rate was also not significantly different between CEA (5.6%) and CAS (6.9%, HR 0.99).

Several publications have analyzed data from the CREST trial to compare specific outcomes of CAS vs. CEA or investigate the safety of these procedures in different subgroups.^[40-42] However, any findings based on the CREST data are unreliable due to the biases introduced by the loss to follow-up and inadequate statistical power. In a follow up analysis of the CREST trial data, Gonzalez (2014) reported no differences in outcomes for subjects treated in high-, medium-, or low-volume centers.^[43]

The International Carotid Stenting Study (ICSS)

Featherstone (2016) published a health technology assessment (HTA) on ICSS funded by the U.K.'s National Institute for Health Research Health Technology Assessment program.^[44] The HTA reviewed the all of the data from the study, concluding that “the functional outcome after stenting is similar to endarterectomy, but stenting is associated with a small increase in the risk of non-disabling stroke. The choice between stenting and endarterectomy should take into account the procedural risks related to individual patient characteristics.”

Altinbas (2014) reported that periprocedural rates of hemodynamic instability in ICSS differed between CEA and CAS groups.^[45] Hemodynamic depression occurred more commonly in CAS patients (13.8% vs 7.2%, RR 1.9, 95% CI 1.4 to 2.6, $p<0.0001$), while hypertension requiring treatment occurred less commonly in CAS patients (RR 0.2, 95% CI 0.1 to 0.4, $p<0.0001$).

Hemodynamic instability was not associated with the ICSS study's primary composite outcome.

Other Randomized Controlled Trials

Reiff (2022) published 5-year outcomes from Stent-supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy 2 (SPACE-2) RCT.^[46] Median follow-up was 59.9 months (interquartile range, 46.6 to 60). The cumulative incidence of any stroke (ischemic or hemorrhagic) or death from any cause within 30 days, or any ipsilateral ischemic stroke within five years of follow up was 2.5% (95% CI, 1.0 to 5.8), 4.4% (95% CI, 2.2 to 8.6), and 3.1% (95% CI, 1.0 to 9.4) with CEA plus Best Medical Treatment (BMT), CAS plus BMT, and BMT alone, respectively. No significant difference in risk for the primary efficacy endpoint was found for CEA plus BMT versus BMT alone (HR, 0.93; 95% CI, 0.22 to 3.91; $p=.93$) or for CAS plus BMT versus BMT alone (HR, 1.55; 95% CI, 0.41 to 5.85; $p=.52$). Since superiority of CEA or CAS to BMT was not demonstrated, noninferiority testing was not conducted. In both the CEA and CAS groups, five strokes and no deaths occurred in the 30-day periprocedural period. During 5-year follow-up, three ipsilateral strokes occurred in both the CAS plus BMT and BMT alone groups compared to none in the CEA plus BMT group.

Reiff (2019) published one-year interim results of the Stent-supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy 2 (SPACE-2) RCT.^[47] The SPACE-2 RCT was originally planned to compare best medical treatment (BMT) to CEA plus BMT or CAS plus BMT in 3,550 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.

Additional smaller trials not included in the systematic reviews above have compared CEA with CAS. A study by Li (2014) randomized 130 subjects at high risk of stroke due to angiographically confirmed carotid stenosis ($\geq 50\%$) to CEA ($n=65$) or CAS ($n=65$).^[48] The authors reported a three-month post-operative risk of mortality of 1.5% with CAS, compared with 9.2% with CEA. However, "existence of complete follow-up data" is an inclusion criterion, and insufficient details are provided about enrollment and randomization procedures to allow conclusions to be drawn about the study. Kuliha (2015) published results of an RCT which randomized 150 subjects with at least 70% carotid stenosis to CEA ($n=73$) or CAS ($n=77$). New infarctions on MRI were found more frequently after CAS (49% vs 25%, $p=0.002$).^[49] A randomized trial comparing CAS to CEA in 136 asymptomatic patients with $>70\%$ carotid stenosis was published by Mannheim and Karmeli (2016). After a mean follow-up time of 26 months, they found no difference in short- or long-term outcomes.^[50]

NON-RANDOMIZED STUDIES

Columbo (2018) published an analysis of long-term outcomes for registry patients who underwent CEA ($n=29,235$) or CAS ($n=4,415$) between 2003 and 2013.^[51] Mortality among these patients from the Vascular Quality Initiative registry was tracked through the patients' Medicare claims files. After adjustment for age, sex and comorbidities, CEA was associated

with lower five-year mortality compared with CAS (HR 0.75, 95% CI 0.69 to 0.82). Similar results were seen in a propensity-matched analysis (n=4,261 matched pairs).

Hussain (2017) reported on a multi-center, population-based Canadian study comparing long-term outcomes for CAS and CEA for 15,525 patients treated between 2002 and 2014.^[52] The incidence of the primary composite outcome, which included 30-day death, stroke, or MI, and any stroke during follow-up, was higher with CAS than CEA (adjusted hazard ratio [HR] 1.57, 95% CI 1.43 to 1.73, p<0.001). This was primarily due to the higher rates of 30-day death, 30-day stroke, and stroke during follow-up seen in patients with stenting. However, CAS was associated with a lower incidence of 30-day MI (adjusted HR 0.70, 95% CI 0.57 to 0.86).

Salzler (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.^[53] Data from the Nationwide Inpatient Sample were searched for patients undergoing carotid revascularization. From 2005 (when the guidelines were published) to 2011, 20,079 CEAs and 3,447 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 (OR 2.6, 95% CI 1.2 to 5.6) and postoperative in-hospital stroke (OR 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.

Additional evidence has been published related to rates of periprocedural stroke/death following CAS, particularly related to subgroups defined by medical comorbidities. Spangler (2014) evaluated patients treated with isolated primary CEA (n=11,336) or primary CAS (n=544) at 29 centers between 2003 and 2013 to assess periprocedural mortality and stroke risks for patients considered medically high risk.^[54] 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, myocardial infarction, death) for either high- or low-risk patients. Periprocedural death/stroke rates with CAS were 1.1% for low-risk patients and 1.6% for high-risk patients. For symptomatic patients, periprocedural death/stroke rates were higher with CAS than CEA for both low- and high-risk groups. For low-risk symptomatic patients, periprocedural death/stroke rates were 6.0% for CAS, compared with 2.2% for CEA (p<0.01). For high-risk symptomatic patients, periprocedural death/stroke rates were 9.3% for CAS, compared with 2.5% for CEA (p<0.01).

A number of other nonrandomized studies, case series, and registries on carotid angioplasty and stenting (CAS) have been published.^[54-72] While these studies contribute to the body of knowledge by providing direction for future research, evidence from these studies does not permit conclusions due to methodological limitations such as nonrandom allocation of treatment and lack of appropriate comparison groups. In addition, registry data may be unreliable due to incomplete reporting. Finally, the technology under investigation may change over time, further limiting the ability to carry out reliable comparisons based on the registry data.

PRACTICE GUIDELINE SUMMARY

AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION (AHA/ASA)

The American Heart Association and the American Stroke Association (2021) issued guidance for the prevention of stroke in patients with stroke and transient ischemic attack (TIA).^[73] They recommended that for patients with severe extracranial carotid artery stenosis ipsilateral to a nondisabling stroke or TIA, the choice between CEA and CAS in patients who are candidates for intervention should be patient specific. Specific recommendations for CAS or CEA include the following:

- In patients with a TIA or nondisabling ischemic stroke within the past 6 months and ipsilateral severe (70%-99%) carotid artery stenosis, CEA is recommended to reduce the risk of future stroke, provided that perioperative morbidity and mortality risk is estimated to be <6%. (Class of recommendation [COR]: 1, Level of evidence [LOE]: A)
- In patients with recent TIA or ischemic stroke and ipsilateral moderate (50%-69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging, CEA is recommended to reduce the risk of future stroke, depending on patient-specific factors such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6%. (COR: 1, LOE: B-R)
- In patients ≥ 70 years of age with stroke or TIA in whom carotid revascularization is being considered, it is reasonable to select CEA over CAS to reduce the periprocedural stroke rate. (COR: 2a, LOE: B-R)
- In patients in whom revascularization is planned within 1 week of the index stroke, it is reasonable to choose CEA over CAS to reduce the periprocedural stroke rate. (COR: 2a, LOE: B-R)
- In patients with symptomatic severe stenosis ($\geq 70\%$) in whom anatomic or medical conditions are present that increase the risk for surgery (such as radiation-induced stenosis or restenosis after CEA) it is reasonable to choose CAS to reduce the periprocedural complication rate. (COR: 2a, LOE: C-LD)
- In symptomatic patients at average or low risk of complications associated with endovascular intervention, when the ICA stenosis is $\geq 70\%$ by noninvasive imaging or $> 50\%$ by catheter-based imaging and the anticipated rate of periprocedural stroke or death is <6%, CAS may be considered as an alternative to CEA for stroke prevention, particularly in patients with significant cardiovascular comorbidities predisposing to cardiovascular complications with endarterectomy. (COR: 2b, LOE: A)

ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS

The 2011 Guideline on the Management of Patients with Extracranial Carotid and Vertebral Artery Disease^[74] specifies the circumstances in which CAS may be indicated as an alternative to CEA, as well as the circumstances when it may be reasonable to choose CAS over CEA. However, the recommendations are based on B level of evidence, the lower level of evidence defined in the guideline as derived from a single randomized trial or non-randomized studies. Further, the specific randomized trials referenced for these determinations are the CREST and SAPHIRE trials. The findings from these trials are considered unreliable due to significant study limitations as explained above.

SOCIETY FOR VASCULAR SURGERY

The Society for Vascular Surgery published updated guidelines for management of extracranial cerebrovascular disease in 2022.^[75] They recommended CEA over CAS in low- and standard-risk patients with more than 50% symptomatic artery stenosis (strong evidence of high quality). The guidelines note that while present data are inadequate to make a

recommendation on the role of transcarotid arterial revascularization (TCAR) in low surgical risk patients with symptomatic carotid stenosis, TCAR is superior or preferable to TF-CAS or CEA for patients with high anatomic and/or physiologic surgical risk.

SUMMARY

There is enough research to show that carotid artery stenting (CAS) can improve health outcomes for patients with carotid artery dissection. Therefore, CAS is considered medically necessary for this indication.

There is enough research to show that carotid artery stenting (CAS) improves health outcomes compared with carotid endarterectomy (CEA) for certain higher-risk patients with carotid artery stenosis that should not have CEA, and in these patients, CAS may provide better health outcomes. Therefore, CAS is considered medically necessary for patients who meet policy criteria.

There is not enough research to show that carotid artery stenting (CAS) improves health outcomes compared with carotid endarterectomy (CEA) except in a select group of patients identified in the policy criteria. Therefore, for patients that do not meet these criteria, CAS is considered investigational.

REFERENCES

1. Loufopoulos G, Manaki V, Tasoudis P, et al. New Ischemic Cerebral Lesions in Postprocedural Magnetic Resonance Imaging in Carotid Artery Stenting Versus Carotid Endarterectomy: A Systematic Review and Meta-Analysis. *Ann Vasc Surg.* 2024;106:297-311. PMID: 38825067
2. Gasior SA, O'Donnell JPM, Davey M, et al. Optimal Management of Asymptomatic Carotid Artery Stenosis: A Systematic Review and Network Meta-Analysis. *Eur J Vasc Endovasc Surg.* 2023;65(5):690-99. PMID: 36682406
3. Li Y, Yang JJ, Zhu SH, et al. Long-term efficacy and safety of carotid artery stenting versus endarterectomy: A meta-analysis of randomized controlled trials. *PloS one.* 2017;12(7):e0180804. PMID: 28708869
4. Vincent S, Eberg M, Eisenberg MJ, et al. Meta-Analysis of Randomized Controlled Trials Comparing the Long-Term Outcomes of Carotid Artery Stenting Versus Endarterectomy. *Circulation Cardiovascular quality and outcomes.* 2015;8(6 Suppl 3):S99-108. PMID: 26515216
5. Kakkos SK, Kakisis I, Tsolakis IA, et al. Endarterectomy achieves lower stroke and death rates compared with stenting in patients with asymptomatic carotid stenosis. *J Vasc Surg.* 2017;66(2):607-17. PMID: 28735954
6. Moresoli P, Habib B, Reynier P, et al. Carotid Stenting Versus Endarterectomy for Asymptomatic Carotid Artery Stenosis: A Systematic Review and Meta-Analysis. *Stroke.* 2017;48(8):2150-57. PMID: 28679848
7. Galyfos G, Sachsamanis G, Anastasiadou C, et al. Carotid Endarterectomy versus Carotid Stenting or Best Medical Treatment in Asymptomatic Patients with Significant Carotid Stenosis: A meta-analysis. *Cardiovascular revascularization medicine : including molecular interventions.* 2019;20(5):413-23. PMID: 30057288

8. Paraskevas KI, Lazaridis C, Andrews CM, et al. Comparison of cognitive function after carotid artery stenting versus carotid endarterectomy. *Eur J Vasc Endovasc Surg.* 2014;47(3):221-31. PMID: 24393665
9. Galyfos G, Sigala F, Karanikola E, et al. Cardiac damage after carotid intervention: a meta-analysis after a decade of randomized trials. *Journal of anesthesia.* 2014;28(6):866-72. PMID: 24828849
10. Bonati LH, Lyrer P, Ederle J, et al. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *The Cochrane database of systematic reviews.* 2012;9:CD000515. PMID: 22972047
11. Arquizan C, Trinquart L, Touboul PJ, et al. Restenosis is more frequent after carotid stenting than after endarterectomy: the EVA-3S study. *Stroke.* 2011;42(4):1015-20. PMID: 21311065
12. Eckstein HH, Ringleb P, Allenberg JR, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. *Lancet Neurol.* 2008;7(10):893-902. PMID: 18774746
13. Raman G, Moorthy D, Hadar N, et al. Management strategies for asymptomatic carotid stenosis: a systematic review and meta-analysis. *Annals of internal medicine.* 2013;158(9):676-85. PMID: 23648949
14. Raman G, Kitsios GD, Moorthy D, et al. *Management of Asymptomatic Carotid Stenosis.* Rockville MD, 2012, pp.
15. TEC Assessment 2007. "Angioplasty and Stenting of the Cervical Carotid Artery with Embolic Protection of the Cerebral Circulation." BlueCross BlueShield Association Technology Evaluation Center, Vol. 22, Tab 1.
16. TEC Assessment 2009. "Angioplasty and Stenting of the Cervical Carotid Artery with Embolic Protection of the Cerebral Circulation." BlueCross BlueShield Association Technology Evaluation Center, Vol. 24, Tab 12.
17. Brott TG, Hobson RW, 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *The New England journal of medicine.* 2010;363(1):11-23. PMID: 20505173
18. Khan M, Qureshi AI. Factors Associated with Increased Rates of Post-procedural Stroke or Death following Carotid Artery Stent Placement: A Systematic Review. *Journal of vascular and interventional neurology.* 2014;7(1):11-20. PMID: 24920983
19. Luebke T, Aleksic M, Brunkwall J. Meta-analysis of randomized trials comparing carotid endarterectomy and endovascular treatment. *Eur J Vasc Endovasc Surg.* 2007;34(4):470-9. PMID: 17683960
20. Ringleb PA, Chatellier G, Hacke W, et al. Safety of endovascular treatment of carotid artery stenosis compared with surgical treatment: a meta-analysis. *J Vasc Surg.* 2008;47(2):350-5. PMID: 18241759
21. Brahmanandam S, Ding EL, Conte MS, et al. Clinical results of carotid artery stenting compared with carotid endarterectomy. *J Vasc Surg.* 2008;47(2):343-9. PMID: 18241758
22. Arya S, Pipinos, II, Garg N, et al. Carotid Endarterectomy is Superior to Carotid Angioplasty and Stenting for Perioperative and Long-Term Results. *Vasc Endovascular Surg.* 2011. PMID: 21646236
23. Yavin D, Roberts DJ, Tso M, et al. Carotid endarterectomy versus stenting: a meta-analysis of randomized trials. *Can J Neurol Sci.* 2011;38(2):230-5. PMID: 21320825

24. Bonati LH, Fraedrich G. Age modifies the relative risk of stenting versus endarterectomy for symptomatic carotid stenosis--a pooled analysis of EVA-3S, SPACE and ICSS. *Eur J Vasc Endovasc Surg.* 2011;41(2):153-8. PMID: 21269847
25. Economopoulos KP, Sergentanis TN, Tsivgoulis G, et al. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. *Stroke.* 2011;42(3):687-92. PMID: 21233476
26. Fokkema M, Vrijenhoek JE, Den Ruijter HM, et al. Stenting Versus Endarterectomy for Restenosis Following Prior Ipsilateral Carotid Endarterectomy: An Individual Patient Data Meta-analysis. *Annals of surgery.* 2014. PMID: 24979605
27. Luebke T, Brunkwall J. Carotid artery stenting versus carotid endarterectomy: updated meta-analysis, metaregression and trial sequential analysis of short-term and intermediate-to long-term outcomes of randomized trials. *The Journal of cardiovascular surgery.* 2016;57(4):519-39. PMID: 26883249
28. Howard G, Roubin GS, Jansen O, et al. Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. *Lancet.* 2016;387(10025):1305-11. PMID: 26880122
29. Sardar P, Chatterjee S, Aronow HD, et al. Carotid Artery Stenting Versus Endarterectomy for Stroke Prevention: A Meta-Analysis of Clinical Trials. *J Am Coll Cardiol.* 2017;69(18):2266-75. PMID: 28473130
30. Rantner B, Kollerits B, Roubin GS, et al. Early Endarterectomy Carries a Lower Procedural Risk Than Early Stenting in Patients With Symptomatic Stenosis of the Internal Carotid Artery: Results From 4 Randomized Controlled Trials. *Stroke.* 2017;48(6):1580-87. PMID: 28455318
31. Texakalidis P, Giannopoulos S, Kokkinidis DG, et al. Carotid Artery Endarterectomy versus Carotid Artery Stenting for Patients with Contralateral Carotid Occlusion: A Systematic Review and Meta-Analysis. *World neurosurgery.* 2018. PMID: 30189300
32. Texakalidis P, Chaitidis N, Giannopoulos S, et al. Carotid Revascularization in Older Adults: A Systematic Review and Meta-Analysis. *World neurosurgery.* 2019;126:656-63 e1. PMID: 30797928
33. Brott TG, Calvet D, Howard G, et al. Long-term outcomes of stenting and endarterectomy for symptomatic carotid stenosis: a preplanned pooled analysis of individual patient data. *Lancet Neurol.* 2019;18(4):348-56. PMID: 30738706
34. Mendoza JFW, Latorraca COC, Oliveira RA, et al. Methodological quality and redundancy of systematic reviews that compare endarterectomy versus stenting for carotid stenosis. *BMJ evidence-based medicine.* 2019. PMID: 31266765
35. Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis. *The New England journal of medicine.* 2016;374(11):1011-20. PMID: 26886419
36. Spence JD, Naylor AR. Endarterectomy, Stenting, or Neither for Asymptomatic Carotid-Artery Stenosis. *The New England journal of medicine.* 2016;374(11):1087-8. PMID: 26890473
37. Halliday A, Bulbulia R, Bonati LH, et al. Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet.* 2021;398(10305):1065-73. PMID: 34469763
38. Meschia JF, Brott TG, Voeks J, et al. Stroke Symptoms as a Surrogate in Stroke Primary Prevention Trials: The CREST Experience. *Neurology.* 2022;99(21):e2378-e84. PMID: 36028326

39. Brott TG, Howard G, Roubin GS, et al. Long-Term Results of Stenting versus Endarterectomy for Carotid-Artery Stenosis. *The New England journal of medicine*. 2016;374(11):1021-31. PMID: 26890472
40. Blackshear JL, Cutlip DE, Roubin GS, et al. Myocardial Infarction After Carotid Stenting and Endarterectomy: Results From the Carotid Revascularization Endarterectomy Versus Stenting Trial. *Circulation*. 2011;123(22):2571-78. PMID: 21606394
41. Howard VJ, Lutsep HL, Mackey A, et al. Influence of sex on outcomes of stenting versus endarterectomy: a subgroup analysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *Lancet Neurol*. 2011;10(6):530-37. PMID: 21550314
42. Silver FL, Mackey A, Clark WM, et al. Safety of Stenting and Endarterectomy by Symptomatic Status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke*. 2011;42(3):675-80. PMID: 21307169
43. Gonzales NR, Demaerschalk BM, Voeks JH, et al. Complication rates and center enrollment volume in the carotid revascularization endarterectomy versus stenting trial. *Stroke*. 2014;45(11):3320-4. PMID: 25256180
44. Featherstone RL, Dobson J, Ederle J, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): a randomised controlled trial with cost-effectiveness analysis. *Health technology assessment (Winchester, England)*. 2016;20(20):1-94. PMID: 26979174
45. Altinbas A, Algra A, Brown MM, et al. Effects of carotid endarterectomy or stenting on hemodynamic complications in the International Carotid Stenting Study: a randomized comparison. *International journal of stroke : official journal of the International Stroke Society*. 2014;9(3):284-90. PMID: 23834300
46. Reiff T, Eckstein HH, Mansmann U, et al. Carotid endarterectomy or stenting or best medical treatment alone for moderate-to-severe asymptomatic carotid artery stenosis: 5-year results of a multicentre, randomised controlled trial. *Lancet Neurol*. 2022;21(10):877-88. PMID: 36115360
47. Reiff T, Eckstein HH, Mansmann U, et al. Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical treatment: One-year interim results of SPACE-2. *International journal of stroke : official journal of the International Stroke Society*. 2019;15(6):1747493019833017. PMID: 30873912
48. Li FM, Zhong JX, Jiang X, et al. Therapeutic effect of carotid artery stenting versus endarterectomy for patients with high-risk carotid stenosis. *International journal of clinical and experimental medicine*. 2014;7(9):2895-900. PMID: 25356155
49. Kuliha M, Roubec M, Prochazka V, et al. Randomized clinical trial comparing neurological outcomes after carotid endarterectomy or stenting. *The British journal of surgery*. 2015;102(3):194-201. PMID: 25511816
50. Mannheim D, Karmeli R. A prospective randomized trial comparing endarterectomy to stenting in severe asymptomatic carotid stenosis. *The Journal of cardiovascular surgery*. 2016. PMID: 27332677
51. Columbo JA, Martinez-Cambor P, MacKenzie TA, et al. A comparative analysis of long-term mortality after carotid endarterectomy and carotid stenting. *J Vasc Surg*. 2018. PMID: 29914828
52. Hussain MA, Mamdani M, Tu JV, et al. Long-term Outcomes of Carotid Endarterectomy Versus Stenting in a Multicenter Population-based Canadian Study. *Annals of surgery*. 2017. PMID: 28498234
53. Salzler GG, Farber A, Rybin DV, et al. The association of Carotid Revascularization Endarterectomy versus Stent Trial (CREST) and Centers for Medicare and Medicaid

- Services Carotid Guideline Publication on utilization and outcomes of carotid stenting among "high-risk" patients. *J Vasc Surg.* 2017;66(1):104-11 e1. PMID: 28502543
54. Spangler EL, Goodney PP, Schanzer A, et al. Outcomes of carotid endarterectomy versus stenting in comparable medical risk patients. *J Vasc Surg.* 2014. PMID: 24953899
 55. White CJ, Iyer SS, Hopkins LN, et al. Carotid stenting with distal protection in high surgical risk patients: the BEACH trial 30 day results. *Catheter Cardiovasc Interv.* 2006;67(4):503-12. PMID: 16548004
 56. Safian RD, Bresnahan JF, Jaff MR, et al. Protected carotid stenting in high-risk patients with severe carotid artery stenosis. *J Am Coll Cardiol.* 2006;47(12):2384-9. PMID: 16781363
 57. Gray WA, Hopkins LN, Yadav S, et al. Protected carotid stenting in high-surgical-risk patients: the ARChER results. *J Vasc Surg.* 2006;44(2):258-68. PMID: 16890850
 58. Gray WA, Yadav JS, Verta P, et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. *Catheter Cardiovasc Interv.* 2007;69(3):341-8. PMID: 17171654
 59. Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS) phase I clinical trial: 1-year results. *J Vasc Surg.* 2005;42(2):213-9. PMID: 16102616
 60. Katzen BT, Criado FJ, Ramee SR, et al. Carotid artery stenting with emboli protection surveillance study: thirty-day results of the CASES-PMS study. *Catheter Cardiovasc Interv.* 2007;70(2):316-23. PMID: 17630678
 61. Spes CH, Schwende A, Beier F, et al. Short- and long-term outcome after carotid artery stenting with neuroprotection: single-center experience within a prospective registry. *Clin Res Cardiol.* 2007;96(11):812-21. PMID: 17694382
 62. Iyer SS, White CJ, Hopkins LN, et al. Carotid artery revascularization in high-surgical-risk patients using the Carotid WALLSTENT and FilterWire EX/EZ: 1-year outcomes in the BEACH Pivotal Group. *J Am Coll Cardiol.* 2008;51(4):427-34. PMID: 18222352
 63. Wang FW, Esterbrooks D, Kuo YF, et al. Outcomes after carotid artery stenting and endarterectomy in the medicare population. *Stroke.* 2011;42(7):2019-25. PMID: 21617150
 64. Veselka J, Zimolova P, Spacek M, et al. Comparison of Carotid Artery Stenting in Patients With Single Versus Bilateral Carotid Artery Disease and Factors Affecting Midterm Outcome. *Ann Vasc Surg.* 2011. PMID: 21530157
 65. Longmore RB, Yeh RW, Kennedy KF, et al. Clinical referral patterns for carotid artery stenting versus carotid endarterectomy: results from the Carotid Artery Revascularization and Endarterectomy Registry. *Circ Cardiovasc Interv.* 2011;4(1):88-94. PMID: 21224465
 66. Tallarita T, Oderich GS, Lanzino G, et al. Outcomes of carotid artery stenting versus historical surgical controls for radiation-induced carotid stenosis. *J Vasc Surg.* 2011;53(3):629-36 e1-5. PMID: 21216558
 67. Schirmer CM, Atalay B, Malek AM. Endovascular recanalization of symptomatic flow-limiting cervical carotid dissection in an isolated hemisphere. *Neurosurgical focus.* 2011;30(6):E16. PMID: 21631217
 68. Ohta H, Natarajan SK, Hauck EF, et al. Endovascular stent therapy for extracranial and intracranial carotid artery dissection: single-center experience. *Journal of neurosurgery.* 2011;115(1):91-100. PMID: 21417710
 69. Koraen-Smith L, Troeng T, Bjorck M, et al. Urgent carotid surgery and stenting may be safe after systemic thrombolysis for stroke. *Stroke.* 2014;45:776-80. PMID: 24525950

Codes	Number	Description
		artery, open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same artery, with intravascular ultrasound (initial noncoronary vessel) during diagnostic evaluation and/or therapeutic intervention, including radiological supervision and interpretation
HCPCS	C7563	Transluminal balloon angioplasty (except lower extremity artery(ies) for occlusive disease, intracranial, coronary, pulmonary, or dialysis circuit), open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same artery, initial artery and all additional arteries

Date of Origin: May 2010