June 2, 2022

VIA ELECTRONIC MAIL TO NCDREQUEST@CMS.HHS.GOV

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RE: Formal Request for Reconsideration of NCD 20.7

Dear Ms. Syrek Jensen and Dr. Chin:

On behalf of the Multispecialty Carotid Alliance (MSCA), we formally request a reconsideration of National Coverage Determination (NCD) 20.7: Percutaneous Transluminal Angioplasty (PTA) that provides coverage for carotid artery stenting (CAS), with the most recent version effective January 1, 2013. The associated National Coverage Analysis is CAG-00085R7: Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting, last updated in December 2009.

MSCA is a group of medical experts from the relevant specialties associated with CAS, including leaders from neurology, neuroradiology, neurosurgery, interventional radiology, vascular surgery, vascular medicine, and interventional cardiology. The Alliance includes experts who have been performing CAS and other revascularization procedures since they were developed nearly 30 years ago and who have played a leadership role in developing the current extensive evidence base that exists for CAS and carotid endarterectomy (CEA).

Medicare began covering CAS nationally in March 2005, when the Centers for Medicare & Medicaid Services (CMS) implemented coverage with specific criteria for patient selection, facility requirements, and operator qualifications. In the 12 years since the 2009 reconsideration of national coverage, extensive new clinical evidence has been generated demonstrating that CAS improves health outcomes in broader patient populations than currently covered. Based on evidence published since 2009, NCD 20.7 should be updated to provide coverage for the full range of patients for whom scientific evidence now supports the clinical benefits of this procedure.

When CMS first agreed to cover CAS, the NCD imposed a list of minimum standards that were largely based on professional society recommendations for competency to perform a novel procedure which had yet to be widely disseminated to the broader patient and physician populations. To be eligible for coverage, facilities were required to meet certain standards delineated by CMS, modeled in part on professional society statements regarding operator competency and facility requirements. These requirements included equipment and staffing resources, physiologic monitoring, emergency management equipment, operator privileging processes, and data collection, along with registration requirements either through a Food and Drug Administration (FDA) approved site for a clinical trial or through an affidavit of compliance with the CMS minimum standards. The reasoning for these minimum standards was understandable for the initial coverage decision in 2005. At the time, few hospitals or clinicians had

extensive experience with CAS, and the evidence supporting the procedure was limited to well-controlled clinical trials that had similar requirements for enrolling sites. Further, specialty societies, the general medical community, and institutions were not yet prepared to enforce clinical standards as they would for more established medical procedures.

Today, CAS has become a mature and widely performed procedure with much improved safety and health outcomes and robust evidence supporting indications extending to broader patient groups.[1] Furthermore, procedural volumes across the country have increased, outcomes have been excellent, and medical societies have provided guidance to the medical community in the same manner as for other well established procedures. Thus, the rationale for the restrictive coverage requirements in the initial NCD, intended to enhance safety of a new procedure with relatively limited clinical experience in carefully controlled trials, no longer is relevant. Since the initial coverage determination, CAS has undergone extensive and robust clinical evaluation and scientific scrutiny, summarized in detail in **Appendix 2**. Furthermore, the favorable outcomes from CAS have now been shown to be generalizable to a broad spectrum of patients, including when performed by a wide variety of operators from different specialties.[2]

We fully support CMS's goal to ensure that Medicare beneficiaries receive excellent quality medical care with robust evidence of improved patient outcomes. Once a service has accumulated extensive evidence demonstrating excellent outcomes to the level now achieved for CAS, the enforcement of quality standards can be effectively ensured through the oversight through standards established by the medical community and specialty societies, as is the case for other mature medical procedures. The collective view of the broad range of experts represented by MSCA is that CMS-mandated operator and facility requirements specifically for CAS are no longer necessary to ensure optimal outcomes for Medicare beneficiaries. Robust facility credentialing and quality assurance procedures now exist and have been widely implemented to ensure consistent patient benefit from this mature procedure.

In this formal request for reconsideration, we request that CMS revise NCD 20.7, as described below, to reflect the results from expanded research trials and the extensive clinical evidence base now available. The evidence supporting each of these changes is summarized in this letter and explained in detail in the attached evidence review (Appendix 2).

1. Expand patient selection criteria to reflect the established data from research:
    a. Revise the patient selection criteria for PTA and CAS with embolic protection to cover the following:
        i. Patients who have asymptomatic carotid artery stenosis ≥ 70% and
        ii. Patients who have symptomatic carotid artery stenosis ≥ 50%;
    b. Eliminate the requirement that patients be at high risk for CEA;
2. Eliminate the minimum standards for facility requirements; and

[1] Appendix 2: CREST-2 Interventional Management Committee, *Percutaneous Carotid Stenting 2021: Evidence for Coverage Reconsideration*.

[2] Lal BK, Roubin GS, Rosenfield K, Heck D, Jones M, Jankowitz B, Jovin T, Chaturvedi S, Dabus G, White CJ, Gray W, Matsumura J, Katzen BT, Hopkins LN, Mayorga-Carlin M, Sorkin JD, Howard G, Meschia JF, Brott TG. Quality Assurance for Carotid Stenting in the CREST-2 Registry. J Am Coll Cardiol. 2019 Dec 24;74(25):3071-3079.

3. Leave coverage for any CAS procedures not described by the NCD to the discretion of the local Medicare Administrative Contractors (MACs).

Based on the enumerated revisions, our **recommended language** is presented in **Appendix 1** attached to this formal request for reconsideration.

NEW SCIENTIFIC EVIDENCE TO SUPPORT RECONSIDERATION

Background

Since the last CAS NCD reconsideration in 2009, significant advances in the field have occurred. Most notably, four large, multicenter randomized controlled trials (RCTs) enrolled a total of 6,772 patients and have demonstrated equivalence with CEA in procedural outcomes, long-term stroke prevention, and durability. These studies are summarized below in Table 1. Refinement of patient selection criteria for CAS has further minimized procedural complications; the development of novel technologies including embolic protection devices and dual-layered stents may lead to further improvement in outcomes for CAS. These facts, further detailed in **Appendix 2**, have led MSCA to request that current NCD policies for CAS be reconsidered and coverage be expanded.

As a result of this clinical and scientific scrutiny, it is now clear that, for patients identified as candidates for carotid revascularization to prevent future stroke who are equally good candidates for CEA or CAS based on the patient selection criteria, clinical equipoise exists for these procedures. Accordingly, for such patients, an informed decision regarding revascularization strategy is appropriate, taking into account the local physician-surgeon expertise, institutional experience, and the patient's preference.

Revising Patient Selection Criteria to Reflect Current Evidence

The current NCD limits coverage to symptomatic patients with carotid artery stenosis of at least 70%. If enrolled in an Investigational Device Exemption (IDE) clinical trial or post-approval study, symptomatic patients with 50%-70% stenosis, or asymptomatic patients with at least 80% stenosis are covered. Patients must also be considered to be at high surgical risk for CEA. These restrictions are now obsolete and do not reflect the current state of clinical evidence.

First, it no longer is necessary to restrict CAS to patients who are documented to be at high surgical risk for CEA. A large body of evidence now demonstrates candidates for carotid revascularization who are not at high risk for CEA and are equally good candidates for CEA or CAS to prevent future stroke. Silver et al. reported on the outcomes from the CREST Trial stratified by symptomatic status (≥50% symptomatic and ≥70% asymptomatic); there were no significant differences between CAS and CEA for the primary endpoint of death, stroke, or myocardial infarction (MI) in either subgroup (5.2% versus 4.5%; hazard ratio, 1.18; 95% CI, 0.82 to 1.68; P=0.38).[3] In total, 1,321 symptomatic and 1,181 asymptomatic patients were included in the analysis. There was no difference in the periprocedural primary endpoint of death, stroke, or MI in symptomatic patients (6.7% for CAS and 5.4% for CEA, HR: 1.26; 95% CI, 0.81 to 1.96; P=0.30) or asymptomatic patients (3.5% for CAS and 3.6% for CEA, HR, 1.02; 95% CI, 0.55 to 1.86; P=0.96).

[3] Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, Goldstein LB, Meschia JF, Ferguson RD, Moore WS, Howard G, Brott TG and Investigators C. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke*. 2011;42:675-80.

Similarly, we ask CMS to update the patient selection criteria in the NCD to reflect the evidence now available. Previously, when deciding to restrict coverage for CAS to limited patient group, CMS cited a lack of RCTs comparing CEA to CAS to best medical therapy (BMT) for asymptomatic patients.[4] In 2009, CMS reconsidered the carotid coverage decision again following publication of SAPPHIRE Worldwide[5] (n=2,001), CAPTURE 2[6] (n=4,175) and the XACT[7] (n=2,145) registries that included more than 8,000 high surgical risk patients. The outcomes of these registries demonstrated an American Heart Association (AHA) 30-day death and stroke rate threshold of ≤ 6% in symptomatic and ≤ 3% in asymptomatic high-surgical risk patients across varying levels of physician experience. CMS declined to expand coverage at that time, citing the need for additional peer-reviewed evidence.

Multiple new RCTs and high quality observational studies demonstrating similar favorable outcomes in standard surgical risk patients have since been published, reaffirming the data from high surgical risk patients. These new studies provide robust evidence from additional large prospective randomized trials in asymptomatic patients comparing CAS to CEA,[8] including the ACT 1 (Asymptomatic Carotid Trial), the CREST long term outcomes report, the ACT 1/CREST Meta-analysis of Asymptomatic Patients,[9] the SPACE-2 Trial,[10] and the recent publication of the five-year outcomes of the Asymptomatic Carotid Surgery Trial-2 (ACST-2).[11] Additional non-randomized data also are supportive, including prospective CMS-sponsored registries[12] and administrative Data Base Analysis,[13] as

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[4] PTA of the Carotid Artery Concurrent with Stenting, Coverage Analysis Decision Memo, CAG-0085R7, §§ VII-VIII, Dec. 9, 2009, *available at*: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=230&ver=29&NcaName=Carotid+Artery+Stenting.

[5] Massop D, Dave R, Metzger C, Bachinsky W, Solis M, Shah R, Schultz G, Schreiber T, Ashchi M, Hibbard R and Investigators SW. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHIRE Worldwide Registry first 2,001 patients. *Catheter Cardiovasc Interv.* 2009;73:129-36.

[6] Gray WA, Chaturvedi S, Verta P, Investigators and the Executive C. Thirty-day outcomes for carotid artery stenting in 6320 patients from 2 prospective, multicenter, high-surgical-risk registries. *Circ Cardiovasc Interv.* 2009;2:159-66.

[7] *Id.*

[8] Rosenfield K, Matsumura JS, Chaturvedi S, Riles T, Ansel GM, Metzger DC, Wechsler L, Jaff MR, Gray W and Investigators AI. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis. *N Engl J Med.* 2016;374:1011-20.

[9] Matsamura JS et al KR, Bret Hanlon, Jenifer Voeks, George Howard, Gary Roubin, Thomas Brott on behalf of the ACT I and CREST Investigators Treatment of Carotid Stenosis in Asymptomatic, Non-Octogenarian, Standard Risk Patients with Stenting versus Endarterectomy: A Pooled Analysis of the CREST and ACT I Trials *Journal of Vascular Surgery.* 2021.

[10] Reiff T, Eckstein HH, Mansmann U, Jansen O, Fraedrich G, Mudra H, Bockler D, Bohm M, Bruckmann H, Debus ES, Fiehler J, Lang W, Mathias K, Ringelstein EB, Schmidli J, Stingele R, Zahn R, Zeller T, Hetzel A, Bodechtel U, Binder A, Glahn J, Hacke W and Ringleb PA. Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical treatment: One-year interim results of SPACE-2. *Int J Stroke.* 2019:1747493019833017.

[11] Halliday A, Bulbulia R, Bonati LH, Chester J, Cradduck-Bamford A, Peto R, Pan H and Group A-C. Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet.* 2021:1065-73.

[12] Lal BK, Roubin GS, Rosenfield K, Heck D, Jones M, Jankowitz B, Jovin T, Chaturvedi S, Dabus G, White CJ, Gray W, Matsumura J, Katzen BT, Hopkins LN, Mayorga-Carlin M, Sorkin JD, Howard G, Meschia JF and Brott TG. Quality Assurance for Carotid Stenting in the CREST-2 Registry. *J Am Coll Cardiol.* 2019;74:3071-3079.

[13] Cole TS, Mezher AW, Catapano JS, Godzik J, Baranoski JF, Nakaji P, Albuquerque FC, Lawton MT, Little AS and Ducruet AF. Nationwide Trends in Carotid Endarterectomy and Carotid Artery Stenting in the Post-CREST Era. *Stroke.* 2020;51:579-587.

well as consensus reviews on the state of the art of carotid stenting.[14] Several of the recent RCT outcomes are summarized below in Table 1. Results from all four RCTs report equivalent patient outcomes for CAS and CEA. In addition, new evidence from the Oxford Vascular study has emerged indicating a significantly higher stroke risk than previously thought to be the case in asymptomatic patients with >70% treated with contemporary medical therapy without revascularization.[15]

Table 1. Randomized Trials of CAS vs CEA in Asymptomatic Patients Since Last Reconsideration

Study/Year	Patients (n)	EPD Use	30-Day S/D/MI	Comment
CREST, 2010	CAS = 594 CEA = 587	YES	CAS = 3.5% CEA = 3.6%	ASR, >60% stenosis, Primary endpoint[#] CAS = 5.6%, CEA 4.9% (p = NS). S/D at 4 yrs CAS = 4.5%, CEA = 2.7% (p = 0.07). No difference between groups at 10 yrs.
ACT-1, 2016	CAS = 1,089 CEA = 364	YES	CAS = 3.3% CEA = 2.6%	ASR, Stenosis >70%, Primary endpoint was CAS = 3.8%, CEA = 3.4%* (p = NS).
SPACE-2, 2019	CAS = 197 CEA = 203 MED = 113	Optional (36%)	CAS = 2.5% CEA = 2.5% MED = 0%	ASR, Stenosis >70%, Primary endpoint CEA = 2.5%, CAS = 3.0%, MED = 0.9%; (p = NS).* In all CAS patients with major secondary outcome events, no EPD was used.
ACST-2, 2021	CAS = 1,811 CEA = 1,814	YES (85%)	CAS = 3.9% CEA = 3.2%	ASR, Stenosis >60%, Non-procedural stroke during follow-up CAS = 5.2%, CEA = 4.5%.

* = death, stroke, or myocardial infarction within 30 days after the procedure or death or ipsilateral stroke between 31 days and 1 year. [#] = the composite of any stroke, myocardial infarction, or death during the periprocedural period or ipsilateral stroke within 4 years after randomization. EPD = embolic protection device, S = stroke, D = death, MI = myocardial infarction, HSR = high surgical risk, ASR = average surgical risk, CAS = carotid artery stent, CEA = carotid endarterectomy, MED = medical therapy, NS = not significant.

Collectively, the evidence base supports full coverage, rather than coverage limited to high surgical risk symptomatic patients and Category B IDE clinical trials and post-approval studies, both for patients with symptomatic carotid artery stenosis of at least 50% and patients with asymptomatic carotid artery stenosis of at least 70%.

[14] Beckman JA, Ansel GM, Lyden SP and Das TS. Carotid Artery Stenting in Asymptomatic Carotid Artery Stenosis: JACC Review Topic of the Week. *J Am Coll Cardiol.* 2020;75:648-656.
[15] Howard DPJ, Gaziano L, Rothwell PM and Oxford Vascular S. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol.* 2021;20:193-202.

Remove Facility and Operator Requirements and Leave Them to the Local Facilities in Which CAS is Performed in Accordance with Guidelines

The current NCD imposes detailed requirements for facilities and operators to obtain coverage for CAS procedures. We strongly agree that, as is the case with other invasive procedures, operator experience and training as well as facility preparedness are key to assuring optimal patient outcomes in CAS. However, with the extensive additional clinical experience and scientific evidence now supporting CAS, we believe that the facility and operator requirements are more appropriately handled through long-standing hospital credentialing processes and guidelines typically driven by recommendations produced by medical society and expert consensus guidelines.

For CAS specifically, there are several sources available to provide local facilities with the necessary guidance to ensure that the facilities and operators are adequately prepared for performing the CAS procedure.[16] Most recently, the Society for Cardiovascular Angiography and Interventions (SCAI) and the Society of Vascular Medicine (SVM) have published an updated multidisciplinary expert consensus statement on physician training and credentialing guidance to facilitate the safe and effective incorporation of CAS into clinical practice.[17] This update includes recommendations that operators and facilities collect data on volume, outcome and other quality metrics, such as conference attendance and continuing medical education (CME) credits. Examples of relevant outcome measures include procedural success, in-hospital complications (death, stroke, MI, vascular injury, blood transfusion, and contrast nephropathy), and death and stroke at 30 days. Institutional participation in a quality assurance registry is encouraged to ensure consistent reporting and to enable ongoing benchmarking of CAS outcomes. In addition, published national standards for risk-adjusted stroke outcomes can be used to assess hospital CAS outcomes.[18]

As the CAS procedure has matured, the risks associated with the procedure have diminished. It is appropriate at this juncture, consistent with other well-established procedures, to shift the responsibility for monitoring and enforcing facility and operator requirements from CMS to the facilities in which the procedures are performed. The diminishing risk of CAS over time, as shown in Figure 1 below, with an overall downward trend in periprocedural death and stroke rates over time, is a reflection of the maturity of CAS.

[16] Hopkins LN, Roubin GS, Chakhtoura EY et al. The Carotid Revascularization Endarterectomy versus Stenting Trial: Credentialing of Interventionalists and Final Results of Lead-in Phase. Journal of Stroke and Cerebrovascular Diseases 2010;19:153-162; Lal BK, Meschia JF, Roubin GS et al. Factors influencing credentialing of interventionists in the CREST-2 trial. J Vasc Surg 2020;71:854-861; Nallamothu BK, Gurm HS, Ting HH et al. Operator experience and carotid stenting outcomes in Medicare beneficiaries. JAMA 2011;306:1338-43; Rosenfield KM, Committee SSSW. Clinical competence statement on carotid stenting: training and credentialing for carotid stenting--multispecialty consensus recommendations. J Vasc Surg 2005;41:160-8.

[17] Aronow HD, Collins TJ, Gray WA et al. SCAI/SVM expert consensus statement on carotid stenting: Training and credentialing for carotid stenting. Catheter Cardiovasc Interv 2016;87:188-99.

[18] Matsumura JS, Gray W, Chaturvedi S et al. CAPTURE 2 risk-adjusted stroke outcome benchmarks for carotid artery stenting with distal embolic protection. J Vasc Surg 2010;52:576-83, 583 e1-583 e2.

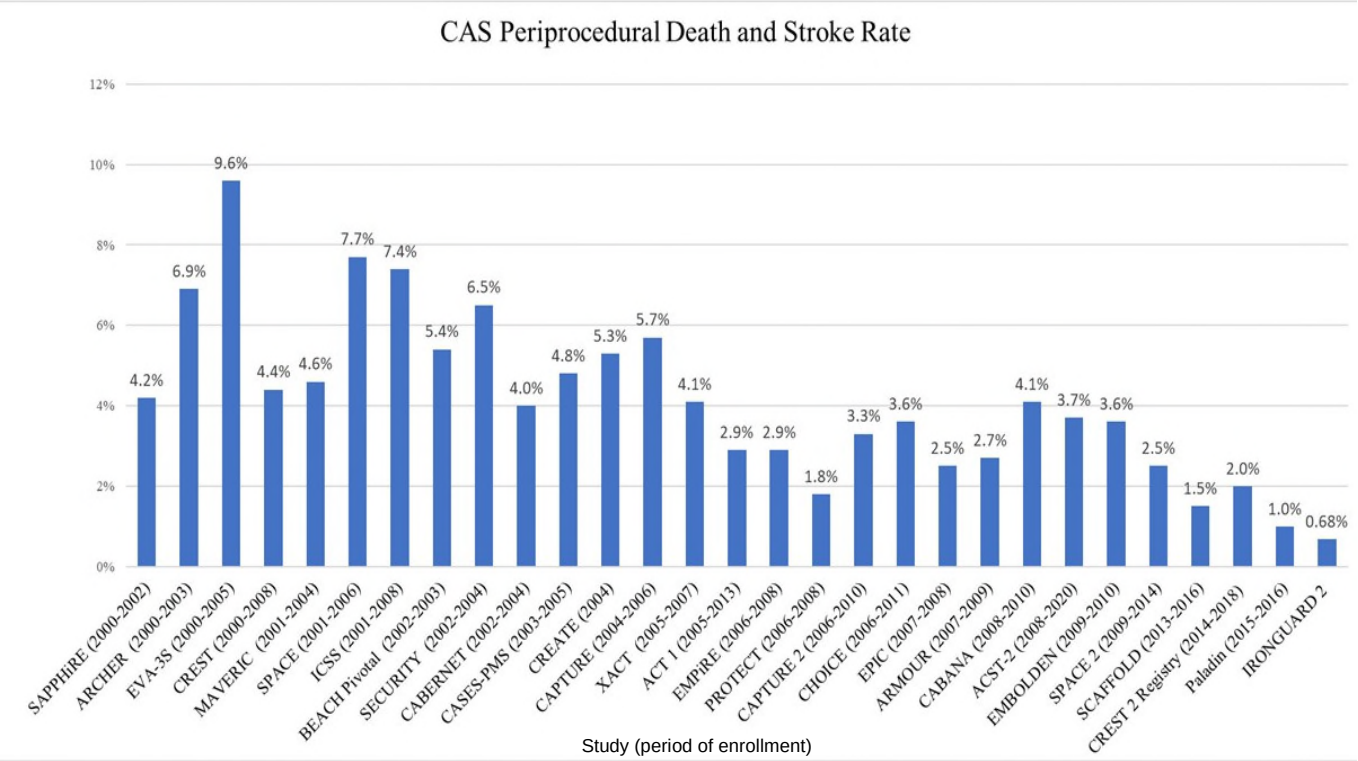

Figure 1: A downward trend in periprocedural death and stroke rates is observed when CAS studies are compared in sequential order by period of enrollment

Privileging and Credentialing Performed by Facilities

Privileging for all invasive and surgical procedures at individual health care facilities is overseen by medical executive and credentialing committees. As noted above, over the last 20 years, established standards have been accepted and integrated into these healthcare facilities credentialing processes.[19] These standards have been demonstrated to result in high-quality outcomes in studies of CAS in Medicare beneficiaries, even with varying specialties and hospitals.[20] As with other invasive procedures, approval of privileges and annual renewal should continue under the purview of the credentialing and recredentialing process of each individual facility. The well-established facility credentialing processes allow for optimal ongoing peer review, quality assurance, and identification of procedural issues and deviations from standard of care. Further, as technology and experience changes, existing local processes

[19] *See*, Hopkins LN, Roubin GS, Chakhtoura EY et al. The Carotid Revascularization Endarterectomy versus Stenting Trial: Credentialing of Interventionalists and Final Results of Lead-in Phase. Journal of Stroke and Cerebrovascular Diseases 2010;19:153-162; Lal BK, Meschia JF, Roubin GS et al. Factors influencing credentialing of interventionists in the CREST-2 trial. J Vasc Surg 2020;71:854-861; Nallamothu BK, Gurm HS, Ting HH et al. Operator experience and carotid stenting outcomes in Medicare beneficiaries. JAMA 2011;306:1338-43; Rosenfield KM, Committee SSSW. Clinical competence statement on carotid stenting: training and credentialing for carotid stenting--multispecialty consensus recommendations. J Vasc Surg 2005;41:160-8.

[20] Lal BK, Meschia JF, Roubin GS et al. Factors influencing credentialing of interventionists in the CREST-2 trial. J Vasc Surg 2020;71:854-861; Beckman JA, Ansel GM, Lyden SP and Das TS. Carotid Artery Stenting in Asymptomatic Carotid Artery Stenosis: JACC Review Topic of the Week. *J Am Coll Cardiol.* 2020;75:648-656.

will allow for evolving societal or specialty guidance, including real-time modification of recommendations to keep current with knowledge in the field and the accepted standard of care.

Facility Equipment Requirements Should be Removed

As with the operator credentialing requirements, it is important that facilities have all of the necessary equipment to perform the CAS procedure safely and effectively. However, it should not fall to CMS, through the coverage criteria, to monitor and enforce each of the facility and equipment requirements. Instead, local facilities and specialty societies should ensure that providers follow best practices. This change would appropriately bring Medicare coverage of the CAS procedure into parity with coverage of other procedures based on the years of experience with the CAS procedure.

Handle Data Collection at the Local Level

There is no longer a need for CMS to require data collection as one of the facility criteria for CAS. As noted throughout this letter, extensive evidence has been published since the 2009 NCD, and additional studies will continue as the field continues to evolve. In addition, there is the longstanding recognition that quality assurance through performance oversight utilizing the peer review process is an essential element of the delivery of high-quality healthcare and to ensure patient safety. Similar to other medical procedures, the quality assurance process for CAS is best implemented at the local level, where it can be performed efficiently and with the ability to institute corrective actions in a timely fashion. As a result, CMS's mandatory data collection requirements for CAS no longer are required to promote either evidence development nor to assure quality oversight in this field.

BENEFIT CATEGORY DETERMINATION

For an item or service to be covered by the Medicare program, it must fall within one of the statutorily defined benefit categories outlined in the Social Security Act. PTA of the carotid artery concurrent with stenting, at a minimum, falls under the benefit categories set forth in section §1861(b) (inpatient hospital services), a Part A benefit under §1812(a)(1) and §1861(s)(1) (physician services), a Part B benefit. This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

SUMMARY OF REQUEST FOR RECONSIDERATION OF PTA NCD

Based on the above, we formally request that CMS reconsider NCD 20.7 and National Coverage Analysis CAG-00085R7 and expand Medicare beneficiary access to PTA and CAS. Research over the last decade-and-a-half has demonstrated the benefits of CAS within broader patient populations than those currently covered by Medicare. Further, with respect to CAS, hospitals have improved and expanded their credentialing and privileging processes. Medical specialty societies now provide guidelines and recommendations for best practices to ensure facilities are appropriately resourced and proper policies and procedures are in place to ensure safety and effectiveness of CAS. We strongly encourage CMS to expand coverage to patients using selection criteria consistent with the most recent evidence and to enable facility and provider requirements to be led by the medical community, similar to the processes employed for other surgical and endovascular procedures.

We look forward to working with you to expand Medicare beneficiary access to this important, potentially lifesaving procedure.

Respectfully Submitted,

The Multispecialty Carotid Alliance

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Attachments:

Appendix 1: Proposed Coverage Language

Appendix 2: The Multispecialty Carotid Alliance (MSCA), *Percutaneous Carotid Stenting 2021: Evidence for Coverage Reconsideration*

Appendix 1: Proposed Coverage Language

Replace Section 4 of NCD 20.7: Percutaneous Transluminal Angioplasty (PTA) with the following:

Effective [Month] [Date], 2022, Medicare covers PTA and stenting with embolic protection of the carotid artery for the following:

- Patients who have asymptomatic carotid artery stenosis ≥ 70% and
- Patients who have symptomatic carotid artery stenosis ≥ 50%.

Coverage for all other CAS procedures not described above will be determined by local Medicare Administrative Contractors (MACs).

Percutaneous Carotid Stenting 2021: Evidence for Coverage Reconsideration

Prepared for Centers for Medicare & Medicaid Services in Consideration of Coverage for Standard Risk Carotid Endarterectomy Patients

Prepared and endorsed by:

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1. Executive Summary

Carotid artery stenting (CAS) was developed in the 1990's as an endovascular alternative to carotid endarterectomy (CEA) to manage carotid artery stenosis. Over the last three decades, clinical evidence on the safety and efficacy of this procedure has continued to accumulate. The last reconsideration of the Centers for Medicare & Medicaid Services (CMS) National Coverage Decision (NCD) for CAS was undertaken in 2009. Outside of clinical trials, CMS currently covers CAS only for beneficiaries who are at high risk for CEA and who also have symptomatic carotid artery stenosis ≥ 70%. Asymptomatic patients are not covered. (Within the confines of pre- or post-approval clinical studies, CMS also covers carotid stenting in patients at high risk for CEA with lesser degrees of symptomatic carotid artery stenosis (50% to 70%) and patients at high risk for CEA with asymptomatic carotid artery stenosis >80%).

This decision was based on early randomized trials that show beneficial results with CAS, despite being performed with first generation technology. This technology was applied in combination with a naïve understanding of appropriate patient selection and best technical practice. There have been significant advances in the knowledge of patient selection, technique and technology since 2009 that warrant review and a subsequent update to CMS coverage.

Additional consideration from the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) was undertaken in 2012.[1] At that time, an argument was made that there was insufficient information on asymptomatic patients to warrant coverage of this group. Since 2012, a large amount of new data have been reported, including data from additional prospective randomized trials on asymptomatic patients comparing CAS to CEA[2] and CAS to medical management[3], as well as a large meta-analysis[4], prospective registries[5] and an administrative data base analysis[6], consensus reviews[7], and the recent publication of the five year outcomes of the Asymptomatic Carotid Surgery Trial-2 (ACST-2)[8].

There have been substantial advances in the field of CAS including: new randomized trial data, recent Professional Societal statements for competency, new techniques, new devices, and perhaps most importantly, operator understanding of how to better select candidates for CAS to avoid periprocedural complications. Given these advances, current CMS the coverage decision is outdated. When the current evidence is considered, it strongly supports an indication for CAS

performed by qualified operators[9] in appropriately selected patients (both high surgical risk and average surgical risk) for symptomatic patients with ≥ 50% and ≤ 99% carotid stenosis and asymptomatic patients with ≥ 70% and ≤ 99% stenosis.

2. Introduction

CAS was introduced to the clinical community as an alternative to CEA in 1994.[10] Few medical procedures have been subjected to such rigorous and extensive scientific scrutiny. Preparations for the landmark National Institute of Neurological diseases (NINDS) CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial) began in 1997.[11] The four-year outcomes from CREST were published in 2010[12] and following the publication, the NINDS declared: "The overall safety and efficacy of the two procedures (e.g. CAS and CEA) was largely the same, with equal benefit for both men and for women, and for patients who had previously had a stroke and for those who had not." [13]

The last CMS National Coverage Decision reconsideration for CAS was undertaken in 2009. Special interest groups presented arguments to inhibit CMS coverage[14] and for two decades, they have been successful in restricting access to this valuable and well validated procedure for Medicare beneficiaries.

Substantial additional evidence confirming the safety and efficacy of carotid stenting has accumulated since the last CMS coverage decision, including two large prospective randomized trials in the United States that validated the safety and efficacy of CAS when compared to CEA (Table 1).[2, 12] Additional evidence includes short and long-term outcomes, quality of life analyses and sub-population analyses. Notably, this additional evidence has demonstrated that carotid stenting outcomes have continued to improve over the last 20 years, driven in part by better patient selection and advances in techniques and technology.[7, 15]

The purpose of this document is to summarize the accumulated evidence supporting the safety and efficacy of CAS, including in standard risk patients, and demonstrate why it is a reasonable and necessary treatment for all appropriately selected Medicare beneficiaries. The vast body of evidence supports percutaneous CAS as a less invasive alternative to CEA in appropriate patients with overall less morbidity complicating the procedure. In the interests of best patient care for

Medicare recipients, access to percutaneous carotid stenting through CMS coverage should be reconsidered.

3. Background and History

Assessment of Medicare coverage decisions are based on the same general question for almost all requests: "Is the evidence sufficient to conclude that the application of the technology under study will improve net health outcomes for Medicare patients?" The assessment recognizes that the effect of an intervention depends substantially on how it is delivered (technique, equipment, and experience), to whom it is applied (patient selection), and the alternatives to which it is being compared (surgery and medical therapy).

CAS has undergone an extensive history of robust clinical evaluation and scientific scrutiny (Table 1). Initial clinical research started through the collaboration of individuals in cardiology, neurology, neurosurgery and neuroradiology.[10] At that time, there were no devices specifically designed for carotid intervention, and procedures were performed with technology approved for cardiac and peripheral vascular interventions. As the study of CAS progressed, other medical centers began to adopt this percutaneous approach. The experience identified the need for dedicated stent devices and for embolic protection devices (EPD). Investigational device exemption (IDE) studies were started in the late 1990's with the first generation of stents and EPDs designed for CAS.

Table 1: Clinical Studies Leading to FDA CAS Device Approval, 510(k) Clearance, Extension of Indication, and Asymptomatic Studies

Study (enrollment)	Enrollment Period	N (CAS)	30-day Stroke or Death
Early European Trials			
CAVATAS	1992-1997	251	10%
EVA-3S	2000-2005	265	9.1%
SPACE	2001-2006	599	7.7%
ICSS	2001-2008	853	7.0%
Early US IDE Trials			
SAPPHIRE	2000-2002	565	4.2%
ARCHER	2000-2003	581	6.9%
MAVERIC	2001-2004	449	4.6%
BEACH Pivotal	2002-2003	480	5.4%
SECURITY	2002-2004	305	6.5%
CABERNET	2002-2004	488	3.9%
CREATE	2004	419	5.3%
CREST	2000-2008	1262	4.4%
Later US IDE Trials (studying new embolic protection devices)			
EMPIRE	2006-2008	245	2.9%
PROTECT	2006-2008	320	1.8%
EPIC	2007-2008	237	2.5%
ARMOUR	2007-2009	228	3.6%
EMBOLDEN	2009-2010	250	2.7%
Asymptomatic Trials			
ACT I	2005-2013	1089	2.9%
CREST/ACT-1 Analysis	2000-2008 2005-2013	2,544	2.7%
SPACE-2	2009-2014	197	2.5%
ACST-2	2008-2020 (still enrolling)	1,811	3.7%

Medicare coverage for CAS began in 2001 for procedures conducted within Category B Food and Drug Administration (FDA) investigational device exemption (IDE) studies. CMS expanded coverage to include post-approval studies in 2004.

CMS expanded coverage again in 2005 to include patients outside of clinical studies who are at high risk for CEA with symptomatic carotid artery stenosis ≥ 70%. The 2005 CMS decision was as follows:

CMS has determined that the evidence is adequate to conclude that CAS with embolic protection is reasonable and necessary for the following:

1. Patients who are at high risk for CEA and who also have symptomatic carotid artery stenosis ≥ 70%. Coverage is limited to procedures performed using FDA approved carotid artery stenting systems and embolic protection devices;
2. Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the National Coverage Determination on CAS post approval studies (Medicare NCD Manual 20.7);
3. Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥ 80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials.

Two randomized prospective trials were available for review at that time and informed the basis for the CMS Coverage decision in 2005; The SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) Trial[16] and the CAVATAS (Carotid and Vertebral Artery Transluminal Angioplasty Study) Trial.[17] The SAPPHIRE Trial was a prospective multicenter randomized study comparing CAS and CEA in 334 patients deemed to be at high surgical risk for CEA. Symptomatic and asymptomatic patients were included. The trial was performed under an FDA IDE in support of pre-market approval (PMA) of the Precise Stent and Angioguard EPD (Cordis Inc.). The SAPPHIRE trial outcomes favored CAS over CEA. The primary endpoint of death, stroke, or MI at 30 days plus ipsilateral stroke or death from neurological cause between day 31 and 1 year occurred in 12.2% in the CAS group and 20.1% in the CEA group (P = 0.004 for non-inferiority). The cumulative incidence of the primary endpoint at one year was 16.8% for CAS as compared with 16.5% for CEA (P = 0.95). The CAVATAS Trial[17], an early European randomized trial, was performed without designated use of stents (only 26% of the endovascular arm was treated with a stent) and without EPD. The stroke and death (S/D) rate at 30 days was equivalent for CAS and CEA but high (10%) for both revascularization methods.

In 2007, multiple societies put in a request to CMS to expand coverage to "patients who are at high risk for CEA due to defined anatomic factors and have either symptomatic carotid stenosis of 50% -69% (or greater) or asymptomatic carotid artery stenosis > 80%." The requestors explained there was clinical rationale to support this request and that these patients did not have an acceptable surgical option. No change was made to coverage. CMS stated a lack of randomized controlled trials (RCTs) comparing CEA to CAS to best medial therapy (BMT) for asymptomatic patients.

In 2009, CMS reconsidered the carotid coverage decision again following publication of SAPPHIRE Worldwide[18] (n=2,001), CAPTURE 2[19] (n=4,175) and the XACT[19] (n=2,145) registries, which included more than 8,000 high-risk patients. Despite the outcomes of these registries demonstrating AHA 30-day death and stroke rate threshold of ≤ 6% in symptomatic and ≤ 3% in asymptomatic patients across varying levels of physician experience, coverage was still not expanded.

An additional consideration from the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) was undertaken in 2012. The primary focus of this MEDCAC meeting was on "whether or not CAS, CEA and best medical therapy (BMT) improve outcomes in symptomatic and asymptomatic persons with carotid atherosclerosis."

This CMS coverage request was made by Abbott Vascular, Inc. after FDA approval of the Acculink carotid stent and EPD device. Abbott Inc. had collaborated with the CREST Trial investigators in the sponsored national multicenter prospective randomized trial. The CREST trial randomized 2,502 patients to CAS or CEA. There was no significant difference between groups in the primary endpoint, defined as periprocedural stroke, MI or death or any ipsilateral stroke within four years (7.2% for the CAS group vs. 6.8% for the CAE group, p=0.51).[12]

CMS also considered the results of three early European trials that had recently been published; SPACE[20], EVA-3S[21] and ICCS[22]. These trials focused on symptomatic patients. SPACE demonstrated no difference in 30-day stroke and death (S/D) outcomes between CAS and CEA. ICCS and EVA3S both demonstrated an excess of non-disabling strokes at 30 days in the CAS cohort. In all three trials, S/D outcomes for CAS were higher than seen in CREST and would be

considered unacceptable by 2021 standards.[12] All three trials have been justly criticized[23] for the inexperience and lack of credentialing of CAS operators, as well as the technology and procedural techniques used at that time.

Those opposing approval cited a variety of arguments, including the strength of data with respect to asymptomatic patients, the inclusion of MI as a component in the composite endpoint, "real-world" data not supporting the findings of the National Institutes of Health–sponsored clinical trial, and more data being needed. Coverage was continued only for symptomatic patients under the age of 80 years at high risk for CEA and patients recruited in FDA trials and certain other sanctioned registries. Despite the findings of the US CREST Trial that recruited both symptomatic and asymptomatic patients, CMS again denied broader coverage for CAS.

Although CREST included both symptomatic and asymptomatic patients, in the 2012 CMS MEDCAC discussions an argument was made that there was insufficient information regarding asymptomatic patients to warrant coverage of this group.

Since 2012, a large amount of new data have been reported, including robust evidence from additional prospective randomized trials in asymptomatic patients comparing CAS to CEA[2]. These include ACT 1 (Asymptomatic Carotid Trial), CREST long term outcomes report, the ACT 1/CREST Meta-analysis of Asymptomatic Patients[4], SPACE-2[24], prospective CMS sponsored registries[5] and administrative Data Base Analysis[6], consensus reviews of the state of carotid stenting[7], and the recent publication of the five year outcomes of the Asymptomatic Carotid Surgery Trial-2 (ACST-2)[8]. In addition, new knowledge has also emerged suggesting a higher stroke risk than previously thought in asymptomatic patients with >70% treated with contemporary medical therapy without revascularization.[25]

4. Advances in Carotid Stenting

Future coverage decisions must take into account developments that have been made with CAS since the original pivotal prospective randomized trials. There have been significant advances in patient selection, technique, and technology, which has led to an improvement in outcomes. A steady decline in the rate of periprocedural death and stroke rates has been observed over time (Figure 1).

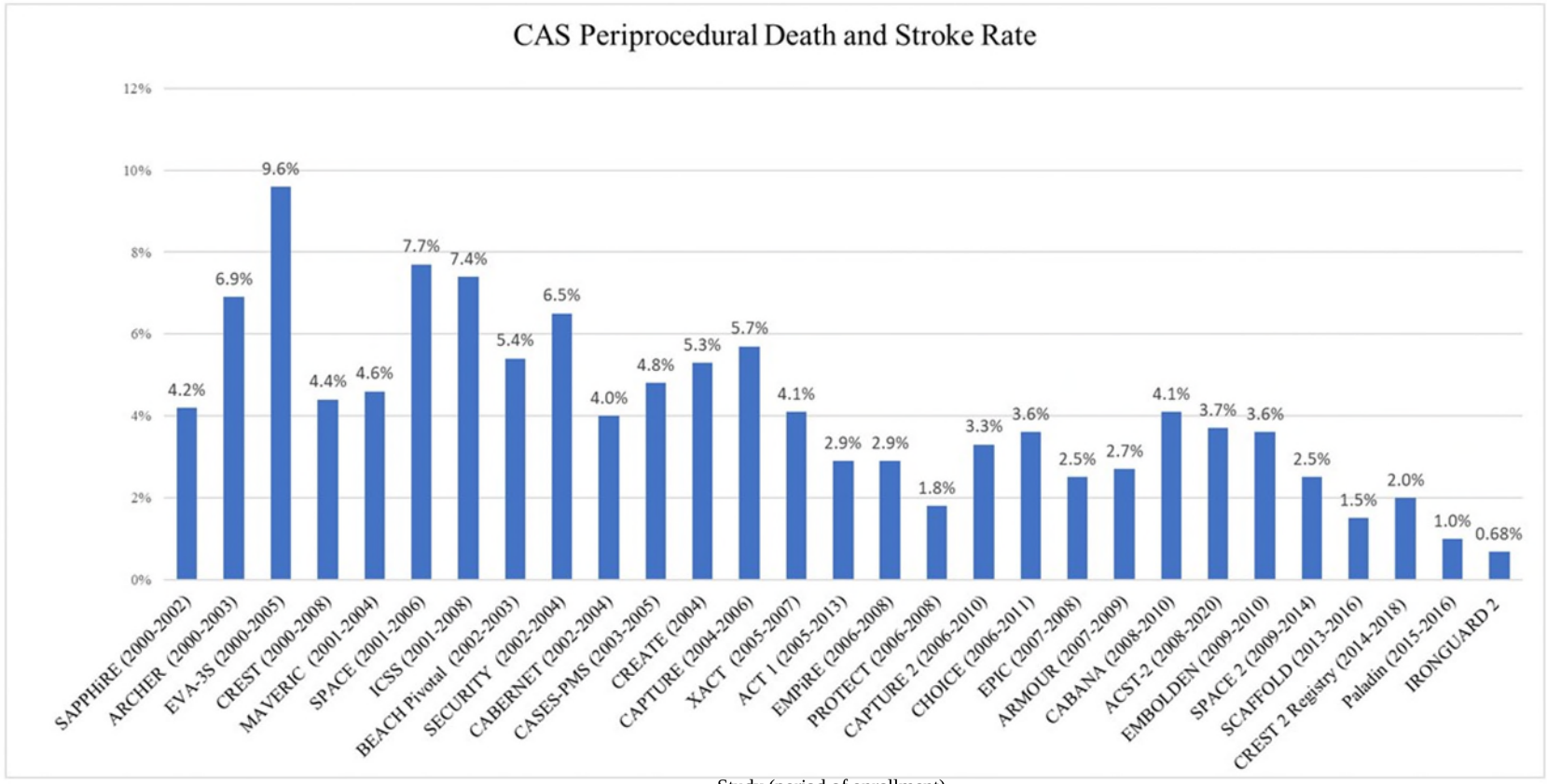

Figure 1: A downward trend in periprocedural death and stroke rates is observed when CAS studies are compared in sequential order by period of enrollment

Advances in Patient Selection:

The knowledge base concerning selection of appropriate patients for CAS could only come from increasing multicenter experience, accumulation of clinical and anatomical data and subsequent analysis of outcomes. The vast majority of this information has only emerged in the last decade.[25-40] Appropriate attention was not paid to specific anatomical indications for CAS in the early trials comparing CAS to CEA. CEA had benefited from 40 years of clinical experience at that time. Surgeons had documented factors that defined high risk for CEA while CAS had only been underway for approximately four years. The only specified anatomical exclusion was angiographic evidence of mobile thrombus.

Knowledge and outcome data accumulated over the last two decades have documented a compilation of anatomic and clinical characteristics that have been associated with increased risk or high-risk CAS (Table 2).[3, 5-7, 22, 23, 25-41] All of these factors are taken into special consideration when evaluating patients over 75 years of age. Advanced age, a surrogate for many of the high-risk anatomical factors, is also a predictor of increased risk for CAS.[37, 42] Most importantly, biological age may not be a defining factor but rather is associated with an increased prevalence of adverse vascular anatomy or underlying cerebral parenchymal disease.[27] Importantly, lesion severity, which is associated with increased stroke risk for medically managed patients, [32, 41] is not a risk factor for CAS. It should be noted that the large majority of patients presenting with severe symptomatic or asymptomatic carotid stenosis do not demonstrate the adverse vascular anatomy listed in Table 2. Scoring systems have been developed and validated to assist operators in assessing relative risk for CAS.[39]

It should also be noted that in all of the comparative prospective randomized trials conducted, the term "standard risk" refers to CEA standard risk. Thus, patients at high risk for CEA were excluded while those at high risk for CAS were not, in large part because the features that confer high risk for CAS were not well understood. This misguided approach dating back to the SAPPHIRE Trial, CREST, ACT1 and European Trials must be considered in assessing these early trials. The importance of vascular anatomy and appropriate patient selection for CAS was not considered and not placed in any protocol of the earlier randomized trials. The CREST-2 Trial[29] (currently enrolling) is the first to acknowledge the importance of excluding high risk CAS patients in a

population of asymptomatic patients who have therapeutic alternatives including CEA and optimal medical management.

For any medical intervention, there are absolute and relative contraindications. These do not necessarily detract from the safety and efficacy of the procedure when applied to appropriate recipients of the therapy. It needs to be emphasized that the majority of patients with high grade carotid stenosis do not present with adverse vascular anatomy. In the conclusion of a systemic review and meta-analysis comparing CAS to CEA, Liu et al. [43] summarized the situation perfectly; "These procedures may be considered complementary rather than competing modes of therapy, each of which can be optimized with careful patient selection."

Table 2: Anatomical and Clinical Characteristics Associated with High-Risk CAS

Anatomical Factors	Clinical Factors
▪ vasculopathy ▪ atherosclerotic (friable) aortic arch ▪ complex aortic arch/great vessel anatomy ▪ type 2-3 aortic arch ▪ atherosclerosis or stenosis of the origin of the innominate or CCA ▪ excessive tortuosity of the CCA ▪ 90-degree origin of ICA from the CCA ▪ excessive tortuosity of the ICA ▪ long, complex and non-contiguous stenosis ▪ stenosis in severely angulated segments ▪ heavy and concentric calcification of the stenosis ▪ mobile thrombus at the lesion	▪ advanced age if associated with adverse anatomy ▪ inability to tolerate dual high dose antiplatelet therapy in the periprocedural period ▪ hemorrhage risk after a large recent stroke ▪ diffuse intracranial cerebral vascular or parenchymal disease with or without cognitive impairment

Advances in Technique and Technology:

Technology, operator experience and technique have evolved and improved substantially in the last 20 years.[7] The initial CAS trials were performed with first generation open cell stent devices, totally or partially without EPD, without currently accepted optimal anti-platelet and anti-thrombin therapy, with excessive use of contrast injections, with an over-emphasis on balloon angioplasty and without other refinements in technique.

An analysis reported by Gray et al.[15] reviewed data collected in sequential studies [ARCHer (200-2003), CAPTURE (2004-2006), CAPTURE 2 (2006-2010) and CHOICE (2006-2021)] using the same CAS system (Acculink stent system and Accunet EPD) to eliminate any device specific differences. The authors reported similar demographics, but octogenarians were enrolled at a higher rate in the post-market studies. In symptomatic subsets, the rate of periprocedural stroke and death decreased from 11.6% in the earliest study (ARCHeR) to 5.1% in the most recent study (CHOICE). The same relative decrease was seen in the asymptomatic patients with the periprocedural stroke and death dropping from 5.4% to 2.8%, respectively (Figure 2). Because the same devices were used through these studies and patient demographics were similar across them, other factors, such as technique and operator experience, are responsible for this improvement in outcomes.

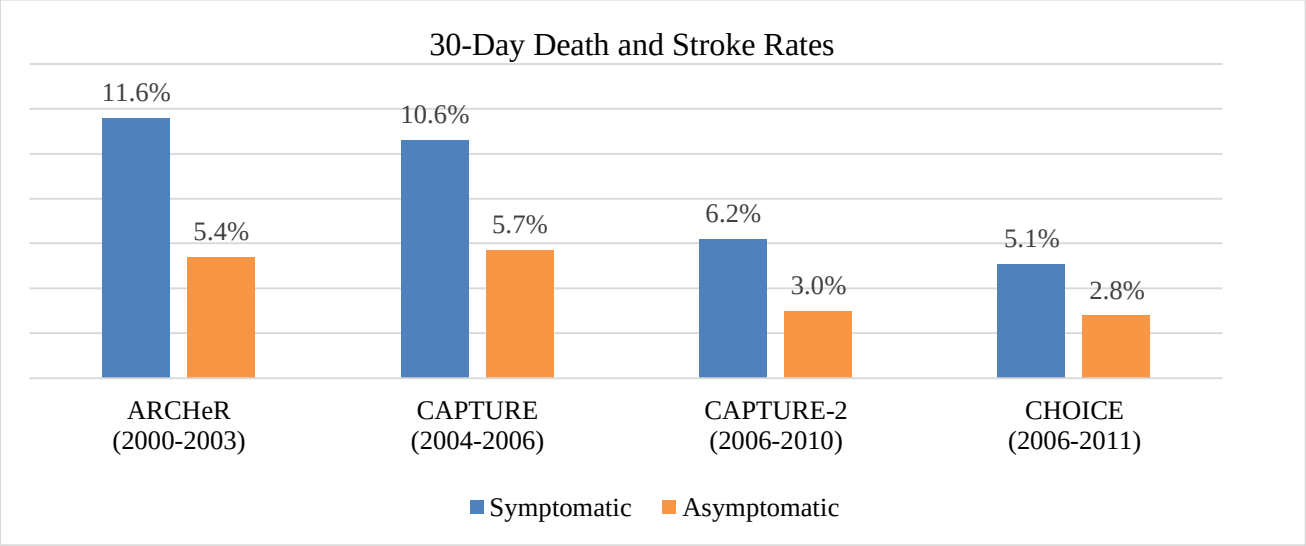

Figure 2: 30-Day Death and Stroke Rates in High Surgical Risk Patients Across Sequential Studies

Embolic Protection Devices:

The necessity of EPD during CAS is indisputable and two meta-analyses demonstrated that EPD use during CAS results in a reduction in both stroke and death.[44, 45] There are currently two types of EPD, proximal protection with flow-reversal and distal filters designed to capture downstream emboli. The low incidence of peri-procedural strokes during CAS requires a large body of data to demonstrate differences in efficacy across EPDs. Sensitive markers of embolization such as the appearance of lesions on diffusion weighted magnetic resonance imaging (DW-MRI) or Doppler trans-carotid detection of micro-embolic signals (MES) have been used as surrogate endpoints, but

do not correlate with clinical events. Thus, superiority of any EPD has not been demonstrated. Several large meta-analyses have demonstrated no differences in 30-day mortality or stroke rates when comparing distal and proximal EPDs.[46,47]

Embolic risk during a CAS procedure is highest during the stent deployment and post-dilation phases of the procedure.[48, 49] The majority of these embolic particles are smaller than 100 µ and may reach the cerebral circulation despite the use of distal filters due to vessel wall mal-apposition or through the filter pores. This microembolization may contribute to the higher risk of procedural minor stroke seen with CAS.[50] To address this need, a PTA balloon with an integrated embolic filter with 40 µ pores was developed. This double filtration strategy demonstrated a 30-day death/stroke/MI rate of 1%.[50]

Covered Carotid Stents:

Post-procedure cerebral embolism may be due to plaque material protruding through the open cells of first-generation nitinol stents.[51, 52] Mesh-covered and dual-layered stents were developed to address this issue. The SCAFFOLD trial evaluated a novel mesh-covered sent in 312 patients. The proportion of patients with death, stroke or an MI at one year was 4.5% and was significantly lower than the prespecified performance goal of 16.9% ($p < .00001$). The proportion with ipsilateral stroke from 31 to 365 days was 1.2%.[53] IRONGUARD 2 was a physician-initiated registry that prospectively enrolled 733 patients treated with the CGuard Stent System. The stroke or death rate was 0.68% at 30 days and 1.90% at 1 year.[54, 55]

A patient-level meta-analysis on clinical studies evaluating dual-layered stents including 556 patients reported a periprocedural stroke or death rate of 1.43%. The only predictor of death or stroke was symptomatic status.[56] And, in a randomized trial comparing four groups treated with either a traditional stent or dual-layered stent and with distal or proximal protection, the combination of proximal protection with a dual-layered stent had the lowest MES count.[57] Recent randomized trial data demonstrated that the MicroNet-covered stent significantly reduced periprocedural and abolished postprocedural cerebral embolism in relation to a conventional carotid stent.[58]

These advances in CAS technology serve to further enhance the safety and efficacy of percutaneous treatment of carotid stenosis.

5. Level 1 Clinical Evidence

International Carotid Stenting Study (ICSS):

ICSS randomized (1:1) symptomatic patients to CAS (n=855) or CEA (n=858).[59] The primary endpoint was fatal or disabling stroke in any territory after randomization to the end of follow-up. Patients were followed for a median of 4.2 years (IQR 3.0–5.2, maximum 10.0). The number of fatal or disabling strokes (CAS = 52 vs CEA = 49) and cumulative five-year risk did not differ significantly between the CAS and CEA groups (6.4% *vs* 6.5%; HR, 1.06; 95% CI, 0.72–1.57; P = 0.77). These results were achieved despite the fact that inexperienced operators were allowed to enroll patients by requiring only 10 CAS procedures to qualify. Tutoring of operators was also allowed during enrollment. Two supervised (vs. "experienced") stent operators at different centers were suspended after enrolling 11 CAS patients of which five (45%) experienced disabling stroke or death. These patients were included in the final analyses, accounting for 20.8% (5/24) of all fatal or disabling strokes in the CAS arm.[59]

Carotid Revascularization Endarterectomy versus Stenting Trial (CREST):

CREST studied the safety and efficacy of CAS and CEA in symptomatic and asymptomatic subjects with average surgical risk, and it set the standard for operator qualification.[12, 60, 61] The primary endpoint, a composite of periprocedural stroke, myocardial infarction and death at 30 days and ipsilateral stroke during four years of follow up was not significantly different between CAS and CEA (7.2% and 6.8%, respectively; HR with stenting, 1.11; 95% CI: 0.81 to 1.51; P=0.51).[12] The secondary endpoint of procedural stroke and death and ipsilateral stroke was not significantly different during the four years follow-up. The federal sponsoring agency (NINDS) concluded that CAS was as efficacious and as safe as CEA. The primary long-term endpoint was postprocedural ipsilateral stroke through 10 years, which occurred in 6.9% of CAS patients and in 5.6% in the CEA group. These rates were not significantly different (HR 0.99; 95% CI, 0.64 to 1.52).[60]

Silver et al. reported on the outcomes stratified by symptomatic status; there were no significant differences between CAS vs CEA for the primary endpoint in either subgroup.[62] In total, 1321 symptomatic and 1181 asymptomatic patients were included in the analysis. For symptomatic patients, the periprocedural stroke, MI and death rates were 6.7% for CAS and 5.4% for CEA (HR:

1.26; 95% CI, 0.81 to 1.96; *P*=0.30). For asymptomatic patients, the stroke, MI and death rates were 3.5% for CAS and 3.6% for CEA (HR: 1.02; 95% CI, 0.55 to 1.86; *P*=0.96).

Both the CEA and CAS cohorts had similar disease specific quality of life (QOL) metrics and showed equivalent and excellent stroke prevention. Both MI and stroke events predicted increased and equivalent mortality during follow-up.[63, 64] The prospectively recorded physical and mental QOL data showed no difference in the large number of metrics analyzed though CAS was nominally or significantly superior in most metrics in the first 30 days.[64] But in the current era, the stroke events that occurred in CREST require closer examination. Strokes in the CAS cohort were numerically more likely to be multi-territory raising the question of an aortic arch source and were more likely to occur in the most elderly. They were also associated with long or ulcerated lesions.[64] This knowledge concerning patient selection and the later development of refined techniques and technology over the last 20 years has reduced the incidence of periprocedural stroke.[5-7]

Evidence on Surgical Complications and Quality of Life:

Careful analysis of CREST results show mental and physical quality of life metrics nominally favored CAS. This is seemingly related to surgical complications associated with CEA. Cohen et al[64] measured HRQOL at baseline, and after two weeks, one month, and one year among 2,502 patients randomly assigned to either CAS or CEA in CREST. The HRQOL was assessed using the Medical Outcomes Study Short-Form 36 (SF-36) and six disease-specific scales designed to study HRQOL in patients undergoing carotid revascularization. At both two weeks and one month, CAS patients had better outcomes for multiple components of the SF-36, with significant ($p<0.01$) differences for physical function, pain, and the physical component summary scale. On the disease-specific scales, CAS patients reported less difficulty with driving, eating/swallowing, neck pain, and headaches but more difficulty with walking and leg pain (all $p < 0.05$). Patients who had periprocedural stroke reported worse HRQOL scores at one year for seven of eight domains of the SF-36 when compared with patients who had no periprocedural events. Given the reduction in periprocedural strokes seen in current outcome data sets, a greater delta in the HRQOL advantage for CAS might be expected.

But given the totality of the periprocedural events for CAS and CEA (stroke, myocardial infarction and surgical operative and wound complications) in CREST, CAS was found to provide better

quality of life for five of the eight subscales measured. These were physical function at two weeks and one month; physical role limitations at two weeks and one month; vitality at two weeks; bodily pain index at two weeks; social function at two weeks and one month and physical functioning at two weeks and one month. [65]

The detailed and rigorous analysis of CREST patients and the surgical complications observed is supported by a large amount of data from the CAVATAS, ICCS and EVA3S trials. In CAVATAS[17] CNI was 0% for CAS and 8.7% for CEA and access site and operative site hematomas 1.2% for CAS and 6.7% for CEA, respectively. CNI in ICCS[20, 22] was 0.1% for CAS and 5.3% for CEA; CNI in EVA-3S[21] was 0.1% for CAS and 7.7% for CEA. In determining the merits of CMS coverage for CAS in Medicare recipients, these patient-centric quality of life metrics should be an essential consideration. Quality of life is important to patients and plays a prominent role in the shared decision-making process.

Long-term Outcomes:

It is important to note that in all of the prospective randomized trials comparing CAS to CEA, five-l0 year outcomes have demonstrated stability of the stent site in terms of lesion restenosis and excellent and equivalent results with stroke prevention.[2, 12,60] Stroke prevention and late stroke events have been comprehensively studied for CAS and CEA.[2, 60, 66] In the CREST and ACT-1 studies, the incidence of ipsilateral stroke was 0.4% per annum.

An individual patient-pooled analysis of four early RCTs enrolling 4,775 symptomatic patients (EVA-3S, SPACE, ICSS, CREST) showed very low and similar stroke recurrence rates following CAS and following CEA out to 10 years.[66] After the periprocedural period, the annual rates of ipsilateral stroke per person year were similar (0.60% for CEA and 0.64% for CAS).

Analysis of United States Administrative Database:

Cole et al[6] recently published an analysis of the Nationwide Readmissions Database to identify patients undergoing CEA and CAS for asymptomatic and symptomatic carotid stenosis from 2010 to 2015. Patients were matched based on demographics, comorbidities, and severity of illness. Before matching, more CAS patients than CEA patients experienced periprocedural stroke (1.9%

versus 1.2%), similar to the findings of CREST and other major randomized controlled studies. After matching, however, a greater periprocedural stroke risk was observed among those with CEA than among those with CAS (2.6% versus 1.9%; odds ratio [OR], 1.41 [CI, 1.25–1.59]; *P*<0.001). To further investigate this, procedure-specific outcomes for the matched cohort were separately compared on the basis of symptomatic status. The difference in periprocedural stroke risk appears to be driven largely by higher periprocedural stroke rates among symptomatic CEA patients compared with symptomatic CAS patients (8.1% versus 5.6%; OR, 1.47 [CI, 1.29–1.68]; *P*<0.001), with no significant difference in periprocedural stroke observed in asymptomatic patients (0.3% versus 0.2%; *P*=0.113). This is despite no difference in elective status and a higher number of chronic comorbid conditions in the symptomatic CAS group compared with the symptomatic CEA group (8.0 versus 7.7; *P*<0.001). No significant differences in perioperative myocardial infarction (*P*=0.062) or any cardiac complication risk (*P*=0.304) were found in the overall cohort. Among asymptomatic patients, periprocedural myocardial infarction was lower in the CAS group (0.8% versus 1.2%; OR, 1.58 [CI, 1.27–1.97]; *P*<0.001), with no difference seen among symptomatic patients (2.6% versus 2.3%; *P*=0.24); this was also found for any cardiac complication. Without separating by symptomatic status, CEA patients were less likely than CAS patients to experience in-hospital mortality (0.8% versus 1.4%; OR, 0.57 [CI, 0.48–0.88]; *P*<0.001). Among asymptomatic patients, there was no in-hospital mortality difference. However, significantly greater mortality was seen among symptomatic CAS patients (4.0% versus 2.0%; OR, 0.47 [CI, 0.39–0.58]; *P*<0.001). Regarding this increased mortality risk among symptomatic CAS patients, it is important to note that, even after matching, the symptomatic CAS subgroup was observed to have a higher percentage of patients with admission mortality risk defined as extreme (12.5% versus 10.3%; *P*<0.001) and a higher percentage of patients with admission severity of illness defined as extreme loss of function (11.9% versus 9.61%; *P*<0.001), compared with the symptomatic CEA subgroup. This observation undoubtedly reflects the current CMS policy of coverage for CAS only in patients deemed to be at high risk for CEA including medical co-morbidities and advanced age - patients aged 70 to 80 years.

6. Evidence in Asymptomatic Patients

CAS in asymptomatic patients may be the most studied vascular procedure that has yet to gain CMS coverage.[7] Approximately 75% of carotid revascularization procedures are performed in asymptomatic patients to prevent a future stroke. We have learned that CAS technique and patient

selection are important for good outcomes, as reflected in the improvement in clinical study outcomes over time (Figure 3). As with CEA, operator experience is essential, and an association exists between higher experience level and lower-risk CAS.[67]

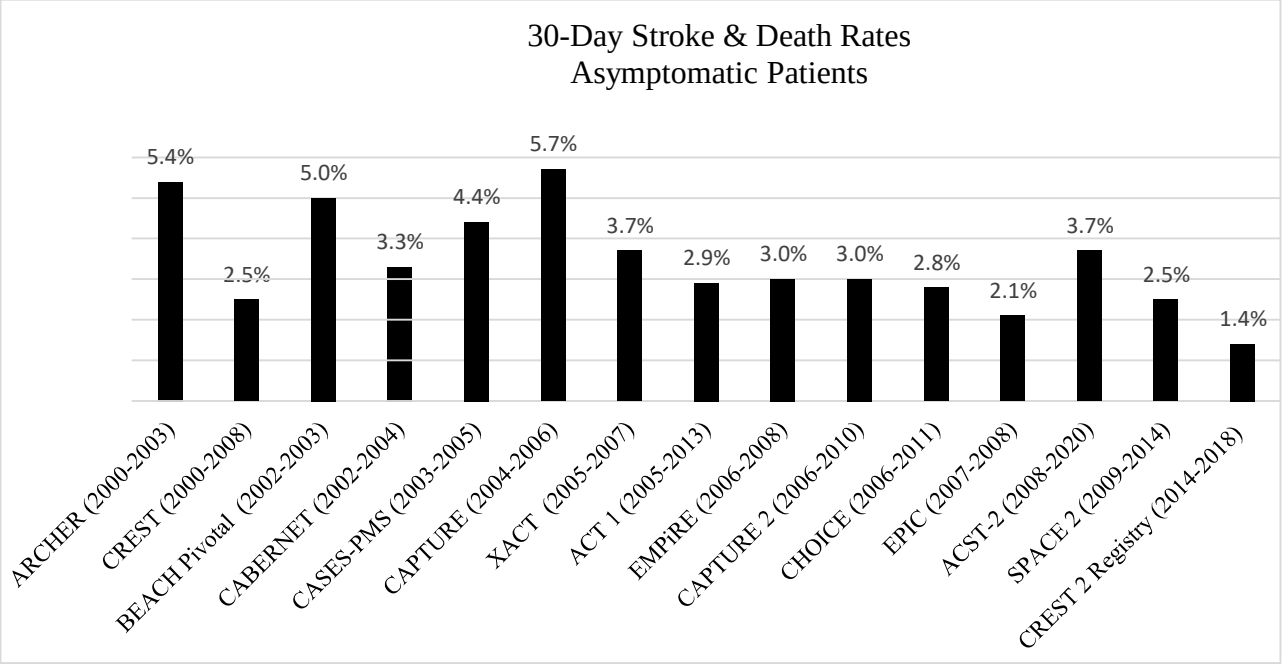

Figure 3: The rate of periprocedural stroke and death in asymptomatic patients has dropped over time due to operator experience, patient selection and technology advancements

There are four modern RCTs, (CREST[68], Asymptomatic Carotid Trial (ACT-1)[2], Stent Protected Angioplasty versus Carotid Endarterctomy-2 (SPACE-2)[24] and Asymptomatic Carotid Surgery Trial-2 (ACST-2)[8]) comparing CAS to CEA in ASR asymptomatic patients with carotid artery stenosis. All have shown comparable outcomes for periprocedural complications (stroke, death, and MI) as well as rates of ipsilateral stroke during follow-up comparing CAS to CEA (Table 3).

Table 3. Randomized Trials of CAS vs CEA in Asymptomatic Patients

Study/Year	Patients (n)	EPD Use	30-Day S/D/MI	Comment
Brooks et al, 2004[69]	CAS = 43 CEA = 42	NO	CAS = 0 CEA = 0	ASR, Stenosis >80%, Similar hospital costs.
SAPPHIRE, 2004[70]	CAS = 117 CEA = 119	YES	CAS = 5.4% CEA = 10.2%	HSR, >80% stenosis, Primary endpoint CAS = 9.9%, CEA 21.5% (p = 0.02)*
CREST, 2010[68]	CAS = 594 CEA = 587	YES	CAS = 3.5% CEA = 3.6%	ASR, >60% stenosis, Primary endpoint[#] CAS = 5.6%, CEA 4.9% (p = NS). S/D at 4 yrs CAS = 4.5%, CEA = 2.7% (p = 0.07). No difference between groups at 10 yrs.
ACT-1, 2016[2]	CAS = 1,089 CEA = 364	YES	CAS = 3.3% CEA = 2.6%	ASR, Stenosis >70%, Primary end point was CAS = 3.8%, CEA = 3.4%* (p = NS)
SPACE-2, 2019[24]	CAS = 197 CEA = 203 MED = 113	Optional (36%)	CAS = 2.5% CEA = 2.5% MED = 0%	ASR, Stenosis >70%, Primary endpoint CEA = 2.5%, CAS = 3.0%, MED = 0.9%; (p = NS)* In all CAS patients with major secondary outcome events, no EPD was used.
ACST-2, 2021[8]	CAS = 1,811 CEA = 1,814	YES (85%)	CAS = 3.9% CEA = 3.2%	ASR, Stenosis >60%, Non-procedural stroke during follow-up CAS = 5.2%, CEA = 4.5%.

* = death, stroke, or myocardial infarction within 30 days after the procedure or death or ipsilateral stroke between 31 days and 1 year. # = the composite of any stroke, myocardial infarction, or death during the periprocedural period or ipsilateral stroke within 4 years after randomization. EPD = embolic protection device, S = stroke, D = death, MI = myocardial infarction, HSR = high surgical risk, ASR = average surgical risk, CAS = carotid artery stent, CEA = carotid endarterectomy, MED = medical therapy, NS = not significant.

Asymptomatic Carotid Trial (ACT-1):

The ACT-1 Trial results were published in 2016.[2] This trial randomized 1,453 asymptomatic patients to CAS or CEA between 2005 and 2013. Similar to CREST, CAS was noninferior to CEA with regard to the primary composite endpoint of death, stroke or MI within 30 days of the procedure, 3.8% and 3.4%, respectively (P=0.01 for noninferiority). The rate of stroke or death

within 30 days was 2.9% in the CAS group and 1.7% in the CEA group (P=0.33). From 30 days to 5 years after the procedure, the rate of freedom from ipsilateral stroke was 97.8% in the stenting group and 97.3% in the CEA group (P=0.51), and the overall survival rates were 87.1% and 89.4%, respectively (P=0.21). The cumulative 5-year rate of stroke-free survival was 93.1% in the stenting group and 94.7% in the endarterectomy group (P=0.44).

CREST/ ACT-1 Combined Asymptomatic Analysis:

Matsumura et al[4] analyzed patient-level data from 2,544 asymptomatic subjects with ≥ 70% carotid stenosis who were randomized to CAS or CEA in addition to standard medical therapy for cardiovascular risk factors. CREST enrolled 1,091 (548 CAS, 543 CEA) and ACT-1 enrolled 1,453 (1089 CAS, 364 CEA) asymptomatic patients less than 80 years old (upper age eligibility in ACT I). Independent neurologic assessment and routine cardiac enzyme screening were performed, and patients were followed for four years. The pre-specified, primary composite endpoint, defined as stroke, MI, or death during the periprocedural period or any ipsilateral stroke within four years after randomization, was 5.1% with CEA and 5.3% with CAS (HR:1.02, 95% CI, 0.7-1.5, P=0.91). Stroke trended to be higher after CAS and MI was more frequent after CEA. Nonprocedural ipsilateral stroke over four years was 2.2% after CEA and 2.3% after CAS.
The analysis confirmed CAS as noninferior to CEA when evaluating the composite endpoint at one year. At one year, the event rate (+/- SE) for the composite endpoint was 3.87 +/- 0.48% in CAS compared to 3.87 +/- 0.65% in CEA. The upper limit of the one-sided 95% confidence interval for the difference was 1.33% (P < .001 for noninferiority), which is below the prespecified margin. Secondary outcomes of interest included freedom from any stroke, cumulative over four years, and was 95.1% with CEA and 93.2% with CAS, P=0.10. Survival over four years was 90.2% for CEA and 91% for CAS, P=0.923.

Space-2 Trial:

The SPACE-2 trial[24] was a prospective multicenter randomized trial examining revascularization compared to BMT in asymptomatic patients with ≥ 70% stenosis. Patients were enrolled 2009 through 2014. SPACE-2 was planned as a three-armed, randomized controlled trial (BMT alone vs. CEA plus BMT vs. CAS plus BMT). The trial was stopped after enrolling 513 patients due to slow recruitment. The trial did provide insight into short- and long-term outcomes comparing CAS and

CEA. At 30-days, stroke and death was 2.5% in the CAS cohort and 2.5% in the CEA group (p=0.962). At one-year, periprocedural stroke and death and ipsilateral stroke did not differ significantly between groups; 2.5% for CAS, 3.0% for CEA, and 0.9% for BMT (P=0.53). The consistency in outcomes among the CREST, ACT-1 and SPACE-2 trials for asymptomatic patients is remarkable.

Asymptomatic Carotid Surgery Trial (ACST-2):

The second Asymptomatic Carotid Surgery Trial (ACST-2) was an international multicenter randomized trial of CAS versus CEA among asymptomatic patients with severe stenosis thought to require intervention.[8] Patients were enrolled if they had severe unilateral or bilateral carotid artery stenosis (>60% stenosis by ultrasound) and both doctor and patient agreed that a carotid procedure should be undertaken, but they were substantially uncertain which one to choose. Patients were randomly allocated to CAS or CEA and followed up at one month and then annually, for a mean of five years. Between 2008 and 2020, 3,625 patients in 130 centers were randomly allocated, 1,811 to CAS and 1,814 to CEA. Importantly, CAS operators needed to qualify to participate in this trial. Potential investigators submitted a record of their CAS or CEA experience and procedural outcomes. To be included in the trial the risks of any stroke or death had to be 6% or lower for symptomatic patients and 3% or lower for asymptomatic patients. Peri-procedurally, the overall risk of death or disabling stroke was similar: CAS 1.0% (17/1653) versus CEA 0.9% (15/1788). Of 1,788 with CEA as the first intervention, 96 (5.4%) had cranial nerve palsy described on the one-month form while CAS did not cause cranial nerve palsy. Kaplan-Meier estimates of five-year non-procedural stroke were 2.5% in each group for fatal or disabling stroke, and 5·3% with CAS versus 4·5% with CEA for any stroke (rate ratio [RR] 1.16, 95% CI 0.86–1.57; p=0.33).

7. On-going Research

CREST 2 Trial:

Stroke occurrence with current BMT in asymptomatic patients is controversial, especially in high grade (>70%) stenosis. Relative stroke prevention from BMT is the subject of investigation in the CREST-2 Trial, the first trial to compare medial therapy to CAS.[71] Based on available clinical trial evidence and standard best practice, the CREST-2 Trial included parallel arms of CAS and CEA as revascularization methods to compared to BMT. While there is considerable overlap, CAS and CEA are considered to be complimentary procedures each best serving certain patient subsets. Patients considered high risk for CEA may be low risk for CAS and conversely patients at high risk for CAS may be low "standard" risk for CEA. Accordingly, CREST-2 is comparing medical therapy alone against both medical therapy and either CAS or CEA in a two-arm trial. The CAS and CEA arms will be different populations and not comparable in terms of outcome. Current BMT is the experimental arm(s).

CREST-2 Registry:

The CREST-2 Registry (C2R) is a collaborative effort by the National Institutes of Health (NIH), CMS the Society for Vascular Surgery (SVS), the American College of Cardiology (ACC), industry partners, and the CREST-2 leadership.[5] The results of this prospective analysis of the current outcomes from CAS in the United states were published in 2020 and represent outcomes from CAS recorded from 2014 through 2018. The C2R had 187 selected interventionists from 98 selected sites across 37 states, and included 85 (45.5%) interventional cardiologists, 44 (23.5%) vascular surgeons, 25 (13.4%) interventional radiologists/neuro-radiologists, 23 (12.3%) neurosurgeons and 10 (5.3%) interventional neurologists. Of the 2,330 cases performed for primary atherosclerosis, follow-up data was not available for 111 cases (4.8%). The remaining 2,219 CAS procedures were done in 2,141 patients (78 had bilateral disease). All subsequent results pertain to the first procedure for each patient (n=2,141) in this group. Among the asymptomatic patients in C2R, 264 (22.4%) were potentially eligible for CREST-2 but could not be enrolled in the trial due to patient refusal; these patients underwent CAS under the Registry, and their data were included in C2R. A total of 1,180 CAS procedures were performed on patients with asymptomatic stenoses (55.1%) and 961

(44.9%) on symptomatic stenoses. The mean age of patients undergoing CAS was 67.8 ± 7.8 years (mean ± SD) and a majority were male.

Among all patients with primary atherosclerosis, the periprocedural rate of S/D was 2.0%. Among the symptomatic patients, the rate of S/D was 2.8%, and there were four deaths, 23 strokes, two MIs, and four major access site complications. Among the asymptomatic patients, the rate of S/D was 1.4%, and there were four deaths, 12 strokes, two MIs, and nine major access site complications. A portion (n=264, 22.4%) of potentially CREST-2 eligible patients (normal-risk asymptomatic) were enrolled into the Registry and underwent CAS by the selected interventionists. The rate of S/D among these patients was 0.8% compared to 1.5% for the remaining trial-ineligible patients enrolled in C2R. These results provide important knowledge about the safety of CAS when applied to patients by experienced operators using appropriate patient selection and contemporary techniques.

The results of the C2R Registry reflect the outcomes from a large number of operators from multiple disciplines practicing in a broad variety of medical centers, both academic and community based. The operators were selected largely on the basis of experience and familiarity with best CAS practice. Outcomes in the community at large might be expected to be different from the CREST 2 Registry. That said, most current comparisons show CAS with a competitive if not superior safety profile compared to CEA.

CMS Coverage and Implications for CREST-2 Trial:

CREST-2 is designed to answer a critically important question in furthering the science of carotid disease management and stroke prevention in asymptomatic patients. The CREST 2 investigators and NINDS recognized that CAS and CEA are complimentary procedures with relative indications and contraindications for each method of revascularization. And importantly, the CREST-2 investigators and the NINDS scientists recognized the available evidence supported the inclusion of CAS in the trial as a safe and effective procedure for the management of asymptomatic standard CEA risk patients.

Accordingly, CREST-2 has a parallel arm design, CAS and medical management vs. medical management alone and CEA and medical management vs. medical management alone. The trial is sponsored by the NINDS and is being undertaken with support of associated Health and Human Services (HHS) organizations, the FDA and CMS. In order to facilitate the experience and credentialling of CAS operators to participate in CREST-2, CMS has supported coverage of procedures performed by qualified operators under the auspices of the CREST-2 Registry. This endeavor initially succeeded in the credentialling of over 180 operators and has undoubtedly supported successful recruitment into the CAS arm of the CREST-2 Registry.

Over the last 18 months, CAS enrollment lagged significantly behind that of enrollment into the CEA arm of the trial. Two issues deserve consideration. First, CEA is fully covered by CMS, and this has not inhibited recruitment into the CEA arm of CREST-2. Second is the current clinical environment and referral patterns that continue to inhibit the availability of patients for recruitment into the CAS arm of the trial. Because CMS does not provide broad coverage for CAS, patients are being primarily referred to surgeons (predominantly vascular surgeons) who can perform CEA. The patients are thus being offered CEA or, increasingly, carotid stenting done using neck surgery. This latter procedure, transcarotid artery revascularization (TCAR) is being covered through a CMS-approved post marketing registry (ROASTER 2 Registry NCT02536378) for the devices marketed for this approach to “CAS”. It needs to be noted that all evidence to date for TCAR comes from single-arm studies or registries. TCAR has not been evaluated in any prospective randomized study.

CAS CMS coverage for standard CEA risk patients will correct this imbalance in enrollment and will ensure the successful completion of recruitment of patients into the CAS arm of CREST-2. The trial will expand our knowledge on how best to manage asymptomatic patients, but results are still two to three years in the future. Regardless, there already exists sufficient evidence to support the use of CAS in asymptomatic patients. CAS will still have an important role in our clinical armamentarium for asymptomatic patients that may fail best medical therapy, as well as for symptomatic patients. There exists no scientific or clinical justification for CAS to have a different CMS coverage profile than CEA.

8. Current Clinical Practice of Carotid Stenting

Currently, CAS is widely practiced as a revascularization method in Medicare patients with acute stroke (with or without intracranial thrombus removal), in patients with a symptomatic, attributable stenosis (> 50%) and in asymptomatic patients with high grade carotid stenosis (>70%).

The last multi-societal guidelines were published 10 years ago in 2011.[72] Evidence available at that time again came from SAPPHIRE, CREST and the European Trial results. The guidelines recommend a class 1 indication as follows.

> Symptomatic Patients: "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 more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6%. *(Level of Evidence: B)"*
>
> Asymptomatic Patients: Evidence available at that time again came from consideration of CREST results. Based on the evidence at that time they recommended a Class 2b indication. "Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established. *(Level of Evidence: B)."*

Carotid Artery Stenting Trends in the United States:

The most comprehensive and current analysis of CAS utilization was published in 2020.[6] The data show that nationwide, a total of 378,354 CEA and 57,273 CAS patients were available for analysis between 2010 and 2015. The combined volume of both procedures declined significantly during this time period (P=0.001). Although the relative percentage of patients undergoing elective CEA procedures has not significantly changed (P=0.15), there was a national decline in elective CAS procedures by approximately 5% during the six-year period (P=0.034). The percentage of symptomatic patients undergoing CEA or CAS has been increasing (P<0.001 and P=0.002, respectively). The number of asymptomatic patients undergoing CAS has been decreasing more

rapidly. This has occurred at the same time that additional prospective randomized trial evidence has shown that outcomes from CAS and CEA in asymptomatic patients are comparable and have continued to improve.[3, 5, 8]

9. Indications and Limitations to Coverage

Symptomatic Patients:

Carotid revascularization should be considered in patients with a >50% stenosis and ipsilateral ischemic symptoms attributable to the carotid lesion. The evidence for revascularization of symptomatic lesions is considered established.[72] The procedural risk of stroke and death must be less than 6%. In any individual case, the risk and benefits of CEA, CAS and best medical management alone should be considered. The lowest risk option should be recommended, and when two available options are deemed equivalent, the patient should have a choice.

Asymptomatic Patients:

Carotid revascularization should be considered in asymptomatic patients with a ≥70% stenosis. The procedural risk must be ≤3%. In any individual case, the risks and benefits of CEA, CAS and best medical management alone should be considered. The lowest risk option should be recommended, and when two available options are equivalent, the patient should have a choice.

In a recently reported community-based cohort study, and a systematic literature review and meta-analysis[25], the risk of stroke in asymptomatic patients with high grade stenosis may be considerably higher than previously thought. The authors note “Contrary to assumptions in current guidelines, the stroke risk in cohort studies was highly dependent on the degree of asymptomatic stenosis, being less than 5% after five years on contemporary medical therapy for moderate stenosis, but approximately 15% for patients with severe stenosis.”

The multi-societal guidelines recommend CAS in asymptomatic as a class 2b indication.[72] The evidence for prophylactic revascularization of asymptomatic lesions is more controversial than for symptomatic lesions. Since earlier randomized studies supporting revascularization, medical therapies directed at risk modification have expanded. The question of the efficacy and safety of optimal medical therapy compared to revascularization is the subject of the ongoing CREST-2. The

results of this trial will not be available until 2024 - 2025. While CREST-2 is of critical importance in furthering the science of carotid disease management, it should be noted that medical therapy is widely acknowledged as the "experimental" arm of the trial. This view is supported by the evidence from recent randomized trials comparing CAS and CEA.[73] These demonstrate that the annual risk of ipsilateral stroke for CAS (and CEA) after the periprocedural period is extremely low and approximately 0.4-6% per annum. These observations are balanced against recent analyses that question the annual stroke risk of patients receiving current "best" medical therapy that range between 5% and 15%.[25] These timely analyses are important because, for the first time, investigators comprehensively analyzed data examining the difference between stroke outcomes in moderate (50% -70%) stenoses against severe (70% - 99%) stenoses. They concluded that the stroke risk in cohort studies was highly dependent on the degree of the asymptomatic stenosis, being less than 5% after five years on contemporary medical therapy for moderate stenosis but approximately 15% for patients with severe stenosis.

Table 4: Current CMS Coverage, Indications and Coverage Gaps

	Current CMS Coverage		**Current Gap in CMS Coverage**
Symptomatic	• high risk for CEA and who also have symptomatic carotid artery stenosis ≥ 70% • high risk for CEA, 50% -70% stenosis and enrolled in IDE clinical trials or post-approval studies	• >50% stenosis and ipsilateral ischemic symptoms • procedural risk of stroke and death must be less than 6% • procedural risk of death or stroke based on anatomical and clinical considerations ≤ CEA	• standard CEA risk 50%-70% stenosis outside of IDE clinical trial • procedural risk of stroke and death must be less than 6% • procedural risk of death or stroke based on anatomical and clinical considerations ≤ CEA
Asymptomatic	• high risk for CEA, ≥ 80% stenosis, and enrolled in an IDE clinical trial	• ≥70% stenosis • procedural risk of stroke and death must be ≤ 3% • procedural risk of death or stroke based on anatomical and clinical considerations ≤ CEA or BMT	• standard CEA risk ≥70% stenosis (outside of a clinical trial) • procedural risk of stroke and death must be ≤ 3% • procedural risk of death or stroke based on anatomical and clinical considerations ≤ CEA or BMT

Additional Coverage Considerations:

Carotid revascularization is practiced by a wide variety of specialists in most community medical centers. CEA is practiced in the United States by vascular surgeons, neuro-surgeons and general surgeons. CAS is performed by interventional cardiologists, vascular surgeons, interventional radiologists, neuro-surgeons, neuro-radiologists and interventional neurologists. These physicians from disparate disciplines are generally members of five hospital departments. Complicating the situation (using TAVR as a comparison) are the referral patterns to each of these practitioners from family physicians, internists, clinical cardiologists, general surgeons and neurologists depending on the clinical environment and local referral patterns. CAS and CEA are complimentary procedures and should be covered equally in the current scientific and clinical environment. As described in this document, CAS technique and patient selection have matured to the point where there are no meaningful differences in complications compared to CEA in appropriately selected patients in the care of trained operators.

Privileging and Credentialing

Hospitals should establish credentialing standards for CAS (and CEA) operators. Aronow and associates have published a comprehensive expert consensus statement on physician training and credentialing guidance to facilitate the safe and effective incorporation of CAS into clinical practice.[9] They argue that all CAS programs should maintain a clearly delineated process for initial credentialing and re-credentialing of operators for CAS privileges. Maintenance of CAS privileges should be based on CAS volume, outcomes and other quality parameters such as conference attendance and CME credits. Outcomes should include procedural success, in-hospital complications (death, stroke, myocardial infarction, vascular injury, blood transfusion, contrast nephropathy), and death and stroke at 30 days. Radiation exposure, anticoagulation status, and EPD dwell times should be monitored and recorded for each patient. It is strongly recommended that institutions participate in at least one national registry, such as the National Cardiovascular Database Registry (NCDR) Peripheral Vascular Interventions (NCDR- PVI) or SVS Vascular Quality Initiative (SVS-VQI) database, to ensure consistent reporting and for bench marking.

The coverage criteria, though, should leave privileging and credentialing to hospitals based on current guidelines in the same way as other procedures. This process relies on the noted hospital processes, specialty societies, and institutions.

Data Collection Requirements

Quality assurance is paramount for the delivery of healthcare services. The peer review process is the appropriate mechanism for conducting oversight to ensure quality for patients. Facilities in which CAS procedures are performed currently have these peer review and quality assurance mechanisms in place. Quality assurance processes should be managed at the local level for CAS as it is for other procedures. CAS is a mature procedure, and there is no longer a need for CMS to require data collection as a facility criteria for coverage of CAS. Quality assurance processes for CAS are already implemented, and they should be left to the local level rather than managed by CMS. This will allow for more efficient and effective oversight of the services provided to ensure quality for patients.

Evaluation of Facilities

Currently, to obtain coverage for CAS procedures, a facility must either be approved by FDA to enroll patients in one of the enumerated clinical trials or must submit an affidavit to CMS attesting to meeting the outlined facility standards. This requirement is obsolete, as CAS is now approved by the FDA for the outlined risk and symptom categories of patients above. Further, the cited clinical trials have long since been completed.

Facilities Equipment Requirements

The coverage policy currently contains several requirements regarding necessary equipment for facilities to perform the CAS procedure. While it is important for facilities to maintain the equipment and capabilities to perform the CAS procedure safely and effectively, these requirements should not be monitored and enforced by CMS through the coverage criteria. Local facilities and medical specialty societies should ensure that facilities and operators are following the best practices with respect to maintaining the necessary equipment and capabilities. Moving these guidelines from the Medicare coverage policy to the local facilities and specialty societies would

appropriately bring the Medicare coverage of the CAS procedure into parity with coverage of other procedures based on the years of experience facilities and operators have with the CAS procedure.

10. Conclusion

As summarized above, there have been substantial advances in the field of CAS including: new randomized trial data, recent Professional Society statements for competency, new techniques, new devices, and perhaps most importantly, improved operators' understanding of how to better select candidates for CAS to avoid periprocedural complications. Given these advances, the current CMS coverage decision is outdated. The current evidence strongly supports Medicare coverage for CAS performed by qualified operators[9] in appropriately selected patients (both high surgical risk and average surgical risk) for symptomatic patients with ≥ 50% and ≤ 99% carotid stenosis and asymptomatic patients with ≥ 70% and ≤ 99% stenosis. Further, given the maturity of the CAS procedure and the medical specialty societies' guidelines and recommendations for best practices, facility and operator requirements should be managed at the local facility level as it is for other procedures, rather than strictly managed by the Medicare coverage policy.

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