JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 75, NO. 6, 2020

PUBLISHED BY ELSEVIER

JACC REVIEW TOPIC OF THE WEEK

Carotid Artery Stenting in Asymptomatic Carotid Artery Stenosis

JACC Review Topic of the Week

Joshua A. Beckman, MD,[a] Gary M. Ansel, MD,[b] Sean P. Lyden, MD,[c] Tony S. Das, MD[d]

JACC JOURNAL CME/MOC/ECME

This article has been selected as the month's *JACC* CME/MOC/ECME activity, available online at http://www.acc.org/jacc-journals-cme by selecting the *JACC* Journals CME/MOC/ECME tab.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Carotid Artery Stenting in Asymptomatic Carotid Artery Stenosis: *JACC* Review Topic of the Week will be accredited by the European Board for Accreditation in Cardiology (EBAC) for 1 hour of External CME credits. Each participant should claim only those hours of credit that have actually been spent in the educational activity. The Accreditation Council for Continuing Medical Education (ACCME) and the European Board for Accreditation in Cardiology (EBAC) have recognized each other's accreditation systems as substantially equivalent. Apply for credit through the post-course evaluation. While offering the credits noted above, this program is not intended to provide extensive training or certification in the field.

Method of Participation and Receipt of CME/MOC/ECME Certificate

To obtain credit for *JACC* CME/MOC/ECME, you must:

1. Be an ACC member or *JACC* subscriber.
2. Carefully read the CME/MOC/ECME-designated article available online and in this issue of the *Journal*.
3. Answer the post-test questions. A passing score of at least 70% must be achieved to obtain credit.
4. Complete a brief evaluation.
5. Claim your CME/MOC/ECME credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME/MOC/ECME Objective for This Article: Upon completion of this activity, the learner should be able to: 1) identify the high risk factors of carotid revascularization; 2) discuss the adverse outcomes associated with carotid revascularization; 3) compare the outcomes of different carotid revascularization modalities in the CREST and ACT-1 clinical trials; and 4) identify the threshold of cases performed to establish best outcomes with endovascular carotid revascularization.

CME/MOC/ECME Editor Disclosure: *JACC* CME/MOC/ECME Editor Ragavendra R. Baliga, MD, FACC, has reported that he has no financial relationships or interests to disclose.

Author Disclosures: Dr. Beckman has been a consultant for Antidote Therapeutics, Amgen, AstraZeneca, Boehringer Ingelheim, Merck, Novo Nordisk, GlaxoSmithKline, and Sanofi; and has served on data and safety monitoring boards for Novartis and Bayer. Dr. Ansel has been a consultant for Medtronic, Boston Scientific, Phillips, CR Bard, Cook, Surmodics, Abbott Vascular, and W.L. Gore; and has received royalties from Cook Medical. Dr. Lyden has been a consultant for Endologix and PQ Bypass. Dr. Das has received honoraria from Abbott, Boston Scientific, LivMor, and National Cardiovascular Partners; has been a consultant for Abbott, Boston Scientific, Cardinal Health, and National Cardiovascular Partners; is a stockholder in Janacare and LivMor; and has received research funding from Boston Scientific and LivMor.

Medium of Participation: Print (article only); online (article and quiz).

CME/MOC/ECME Term of Approval

Issue Date: February 18, 2020
Expiration Date: February 17, 2021

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]Cardiovascular Division, Vanderbilt University Medical Center, Nashville, Tennessee; [b]Department of Cardiology, Riverside Methodist Hospital, Columbus, Ohio; [c]Department of Vascular Surgery, Heart and Vascular Institute, Cleveland Clinic Foundation, Cleveland, Ohio; and the [d]Heart and Vascular Division, Texas Health Dallas, Dallas, Texas. Dr. Beckman has been a consultant for Antidote Therapeutics, Amgen, AstraZeneca, Boehringer Ingelheim, Merck, Novo Nordisk, GlaxoSmithKline, and Sanofi; and has served on data and safety monitoring boards for Novartis and Bayer. Dr. Ansel has been a consultant for

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2019.11.054

Carotid Artery Stenting in Asymptomatic Carotid Artery Stenosis

JACC Review Topic of the Week

Joshua A. Beckman, MD,[a] Gary M. Ansel, MD,[b] Sean P. Lyden, MD,[c] Tony S. Das, MD[d]

ABSTRACT

The advance of therapies to reduce the stroke impact of asymptomatic carotid artery stenosis has proved difficult over the last decade. Disagreement concerning the underlying randomized control trials has limited entry into the care arena of endovascular therapies. Recently, advances in percutaneous therapies for carotid artery disease have been reported and provide a substantial database supporting the further incorporation of endovascular-based therapies in patients who need revascularization and meet selection criteria. With a second randomized control trial now published, it is time for a re-evaluation of endovascular therapy as a component of carotid artery care. This review describes the advances in the field in the last 5 years, clarifying the current position of these therapies in the care of the patient with asymptomatic carotid artery disease. (J Am Coll Cardiol 2020;75:648–56) © 2020 by the American College of Cardiology Foundation.

The advance of percutaneous, endovascular therapies for vascular disease has been unremitting over the last several decades. What began with coronary artery intervention incorporation into routine practice has progressed to include lower extremity artery disease, renal and visceral artery disease, and abdominal aortic aneurysm. In each of these vascular beds, devices have been created, demonstrated to be safe in humans, and tested against current standard of care followed by a rapid incorporation of their use in routine practice. The increase in these procedures has fostered an ongoing investment in the technology, with consequent improvements in procedural safety and patient outcomes.

Endovascular care in asymptomatic carotid artery stenosis has challenged that trend. Carotid artery intervention passed through the first several phases with early experience in humans to establish safety, the creation of registries to improve reporting and safety, the advance of technology, and then the definitive comparison with the established standard of care, carotid endarterectomy (CEA) (1). In 2001, the U.S. Centers for Medicare & Medicaid Services (CMS) approved coverage for a Category B U.S. Food and Drug Administration Investigational Device Exemption for carotid stenting clinical trials. In 2005, coverage was expanded to post-approval studies of carotid artery stenting (CAS) in symptomatic high-risk CEA patients with >70% stenosis, limited to a U.S. Food and Drug Administration–approved stent implanted using an embolic protection device. In 2006, CMS created a new category of post-approval extension studies. The definitive trial was started in 2006.

In the CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial), 2,502 patients were enrolled with symptomatic or asymptomatic carotid stenosis and randomly assigned to endovascular stenting or surgical revascularization (2). The primary endpoint, which included the composite of death, stroke, and myocardial infarction (MI), did not vary between groups. Similarly, there was no difference in the primary endpoint in the subgroup of 1,181 participants with asymptomatic disease (3). Indeed, there were 21 total events in each subgroup. This included 3 major strokes (persistent symptoms after 30 days) in the endovascular arm and 2 major strokes in the surgical arm.

Medtronic, Boston Scientific, Phillips, CR Bard, Cook, Surmodics, Abbott Vascular, and W.L. Gore; and has received royalties from Cook Medical. Dr. Lyden has been a consultant for Endologix and PQ Bypass. Dr. Das has received honoraria from Abbott, Boston Scientific, LivMor, and National Cardiovascular Partners; has been a consultant for Abbott, Boston Scientific, Cardinal Health, and National Cardiovascular Partners; is a stockholder in Janacare and LivMor; and has received research funding from Boston Scientific and LivMor.

Manuscript received November 8, 2019; accepted November 19, 2019.

ABBREVIATIONS AND ACRONYMS

CAS = carotid artery stenting

CEA = carotid endarterectomy

CMS = Centers for Medicare & Medicaid Services

MI = myocardial infarction

MRI = magnetic resonance imaging

RCT = randomized clinical trial

TCAR = transcarotid artery revascularization

VQI = Vascular Quality Initiative

Upon completion of this trial and the publication of the subgroups by symptomatic status, CMS commissioned a Medicare Evidence Development & Coverage Advisory Committee meeting in 2012 to determine "whether or not carotid artery stenting (CAS), CEA and best medical therapy improve outcomes in symptomatic and asymptomatic persons with carotid atherosclerosis" (4). To the participants, the meeting felt contentious, with a divergent set of opinions in opposition and support of the new technology.

The participants who supported the advance of carotid stenting relied on the National Institute of Neurological Disorders and Stroke-funded CREST trial and supportive registry data. The arguments in opposition to coverage for carotid stenting were disparate and included: approval of this technology would increase the number of patients with asymptomatic disease who undergo revascularization (5), nonfatal outcomes of the composite primary endpoint were placed in an artificial post hoc hierarchy (6,7), "real-world" data did not support the findings of the National Institutes of Health-sponsored clinical trial (8), and more data were needed. As a result of the mixed messages sent by the medical community, no further coverage for carotid stenting was promulgated. Over the last 7 years, a significant amount of new data have been reported, which provides an opportunity for re-evaluation of the current state of this technology. Here, we summarize the current state of CAS and provide recommendations for the next steps (**Central Illustration**).

HIGHLIGHTS

- Recent clinical trials have advanced the evidence supporting carotid artery stenting in asymptomatic internal carotid artery stenosis.
- With the current evidence base, carotid artery stenting should be reimbursed for use in appropriate patients.
- Standardization in training, data collection, and reporting should be developed and required.

ENDOVASCULAR THERAPY FOR THE ASYMPTOMATIC CAROTID ARTERY

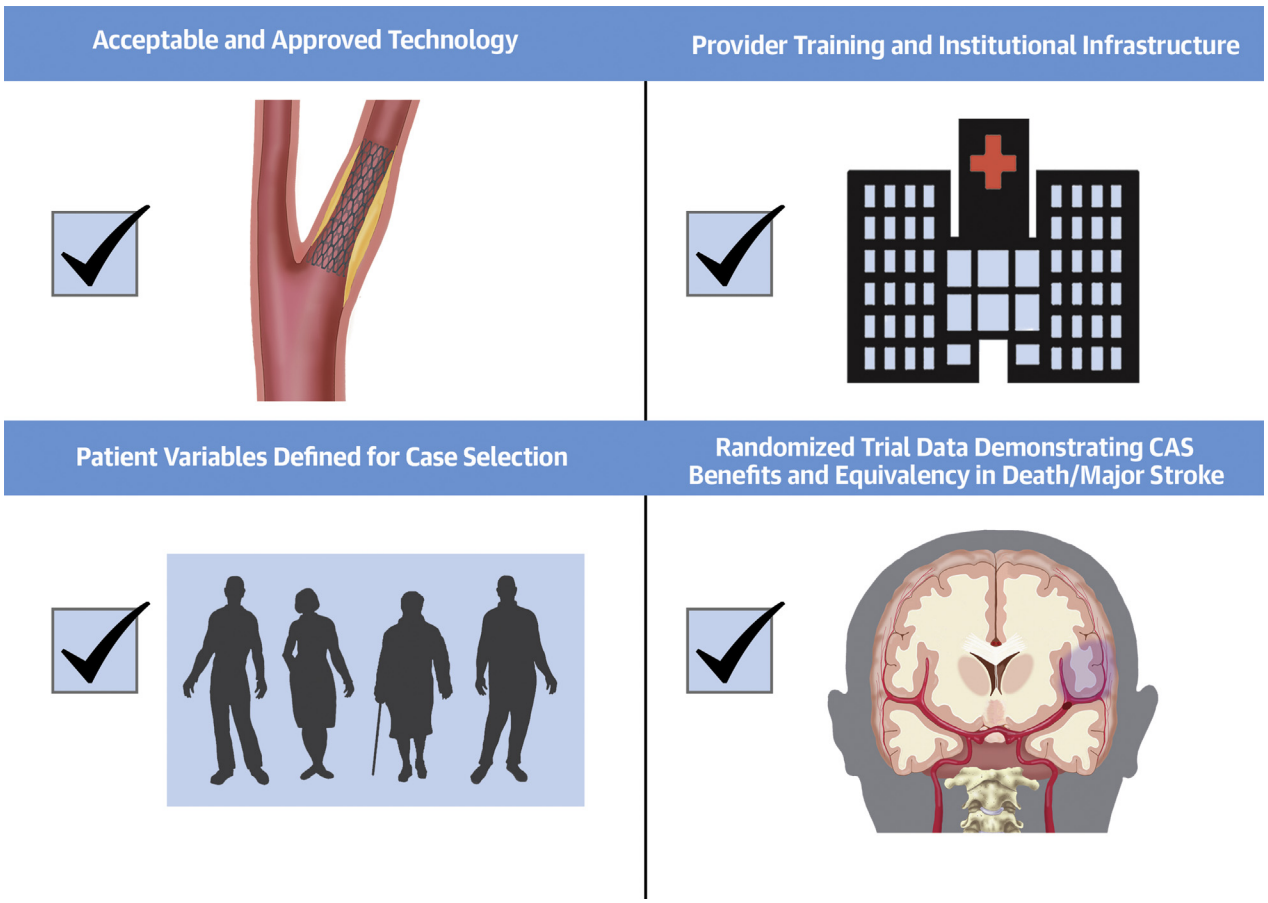
CAS in asymptomatic patients is likely the most-studied vascular procedure that has yet to gain coverage. The data available to understand the risks of intervention arise from disparate sources, ranging from registries, to data collected by the Society for Vascular Surgery Patient Safety Organization Vascular Quality Initiative (VQI) and randomized clinical trials (RCTs). Each source provides a window into event rates.

There are several issues to note before discussing the data. First, what is the key endpoint for a carotid revascularization trial? Early clinical trials used stroke and death. However, the Mayo Asymptomatic Carotid Endarterectomy trial demonstrated both a significant MI rate and a benefit to aspirin therapy in reducing MI (9). This trial reported in 1992, well after the first seminal surgical trial was underway, the Asymptomatic Carotid Artery Surgery trial (10), but studies thereafter, including the Asymptomatic Carotid Surgery Trial (11) and CREST included MI as a key endpoint. Opinions regarding the import of MI are mixed in the vascular community, and CREST-2 was planned without MI as a component of the primary endpoint (12). By contrast, the ACT 1 (Asymptomatic Carotid Trial) included MI (13).

The rates of adverse events for revascularization in asymptomatic patients are low for experienced providers. National data suggest a stochastic and unchanging ~1% mortality during the first decade of this century (14). In the VQI, the 30-day event rates after CEA include a death rate of ~0.7%, stroke rate of ~1.6%, and MI rate of ~1.2%. The composite endpoint occurred in 3.1% of patients (15). Data from the American College of Cardiology's National Cardiovascular Data Registry show death rates to be 0.8% in both CEA and CAS groups in non-Hispanic Whites. Stroke rates were nonstatistically higher in the CAS group at 3.9% versus 3.1%, whereas MI was the same at 0.8% (16). In risk-adjusted analyses by the VQI examining carotid revascularization from 2009 to 2016, stroke and death rates (as reported by the operators) varied significantly across the 17 regions, from 0.5% to 3% with CEA and 0.6% to 5% with CAS (17). The discrepancy in outcomes over the VQI regions suggests that variation in patient selection and technical expertise exert important effects. Controlling for competency and patient population would help to understand the value of both procedures with a stable background environment.

Two RCTs compared CEA to CAS in patients with asymptomatic internal carotid artery stenosis. The first is CREST (2), which included 1,181 patients with asymptomatic carotid artery disease who were randomized to CEA or CAS. Both groups were found to

CENTRAL ILLUSTRATION **The Checklist to Support Routine Use of Carotid Artery Stenting as a Therapeutic Modality in Appropriately Selected Patients**



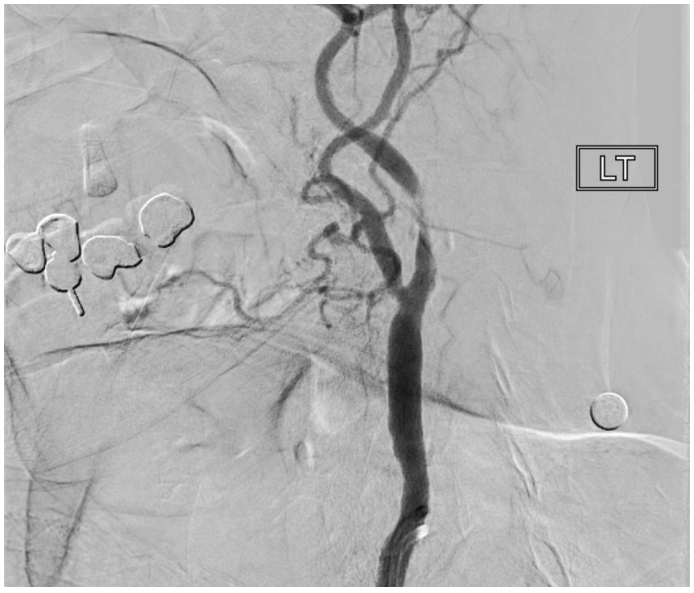
Beckman, J.A. et al. J Am Coll Cardiol. 2020;75(6):648–56.

This figure depicts the items necessary to support the incorporation of carotid artery stenting into vascular practice and provide substantiation for its acceptability for patient care by governmental agencies.

have 21 of the primary composite events, stroke/death/MI. There was an excess of minor MI in the CEA group and minor stroke in the CAS group, but no deaths were reported out to 30 days, and no difference was seen in major stroke between groups (3 for CAS vs. 2 for CEA) (3). Major stroke was defined as having symptoms present after 30 days. Moreover, in long-term follow-up, there was no difference in the primary composite outcome or the specific outcome of stroke (18). Recently, ACT-1 randomly assigned 1,453 patients to CAS or CEA in a 3:1 randomization scheme. Like CREST, there was no difference in stroke/death/MI rates between groups (3.3% for CAS and 2.6% for CEA; p = 0.60) (13) (**Figures 1 and 2**). Again, MI was in numerical excess for the CEA arm, and minor stroke for the CAS arm, but the differences were not statistically significant. Of note, major stroke rates were low and did not differ by revascularization modality (0.5% for CAS and 0.3% for CEA; p = 1.00). Two RCTs have now shown that, in expert hands, modality is not a significant determinant of cerebrovascular outcome.

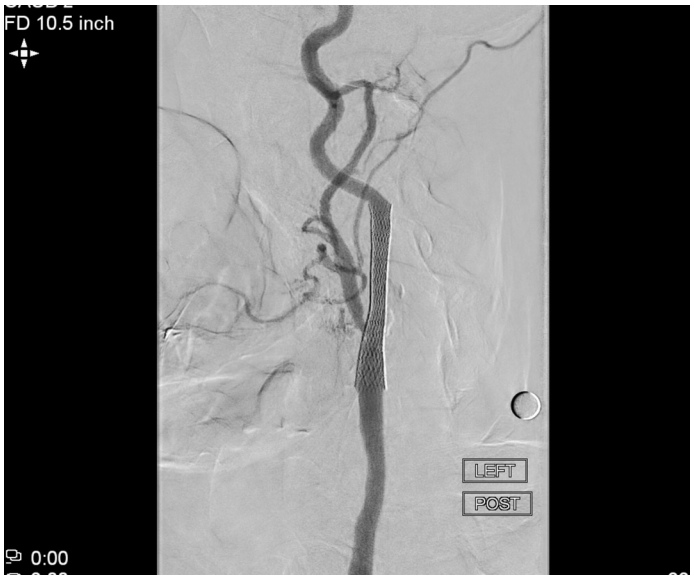
In the absence of variation by modality, there are patient-specific factors that associate with adverse outcomes. These would include Black race (19), the presence of a contralateral carotid artery occlusion (20), and adverse aorta anatomy, among others (21,22). At this time, with 2 RCTs and supportive registry data, CAS and CEA are proven equivalent modalities in expert hands when anatomic and

FIGURE 1 Contrast Angiogram of Internal Carotid Artery Stenosis in an Asymptomatic Patient



The image demonstrates the angiographic appearance of a severe stenosis in the internal carotid artery before endovascular revascularization.

FIGURE 2 Completion Contrast Angiogram After Placement of the Xact Stent



This stent was used in the ACT-1 (Asymptomatic Carotid Trial 1) clinical trial. This image shows the angiographic appearance after success insertion of an Xact stent (Abbott Vascular, Santa Clara, California) for the stenosis noted in Figure 1.

patient fitness factors are taken into account. Current societal recommendations for CAS in asymptomatic disease vary significantly and may be out of date (Table 1).

CURRENT RECOMMENDATIONS FOR REVASCULARIZATION IN ASYMPTOMATIC CAROTID STENOSIS

Multispecialty guidelines released in 2011 provide a Class IIa recommendation supporting revascularization of asymptomatic internal carotid artery stenosis of >70% if the risk of perioperative stroke, MI, and death is low (23). The benefit of revascularization was established by 2 large studies (11,24), but both studies began enrollment more than 25 years ago before the current standard of medical therapy for atherosclerosis. There is evidence that medical therapy may improve revascularization procedural outcomes (25). There is also evidence that effective antiatherosclerotic therapy reduces the development of carotid stenosis (26), and the need for revascularization is declining in the United States (27). Currently, all recommendations rely on remotely collected data and infer the importance of more recent medical therapies on revascularization. The question concerning the value of revascularization and medical therapy, per se, compared with medical therapy alone is currently under investigation in CREST-2 (28). CREST-2 will not provide additional direct comparative evidence concerning the value of CAS and CEA. The trial is actually 2 trials: a comparison of CEA with optimal medical therapy versus optimal medical therapy and a comparison of CAS with optimal medical therapy versus optimal medical therapy. With specific exclusion criteria for each revascularization modality, such as adverse neck anatomy for CEA and type 3 aorta for CAS, the populations in each section of the overall trial will vary importantly. We would note that the likelihood of demonstrating superiority of either modality will be difficult. The expected event rate is 3.6% for stroke and death at 4 years. The authors report an approximate 85% power to detect a difference if the event rate is 8.4% or 0.8% in the intensive medical therapy arm; in other words, a more than doubling or ~75% reduction in events.

It should be noted that this question, "Is revascularization beneficial?" remains apart from the modality employed for revascularization. For a while, these 2 questions were conflated (5,29) in discussions concerning novel revascularization technologies and sowed confusion more than clarity. For now, the value of revascularization is currently under study and will not be addressed further here.

TABLE 1 Current Societal Guidelines for the Use of CAS and CEA in Asymptomatic Carotid Artery Stenosis

Organization (Ref. #)	Year of Publication	CAS Recommendation	"High Risk for CEA" CAS Recommendation	CEA Recommendation	Multidisciplinary Team Recommendation
RACP (47)	2010	CAS should not be performed in the majority of patients	NA	CEA is gold standard	Determining suitability for procedures is often best done as a team approach
SVS (48)	2011	Insufficient data to recommend CAS	CAS should not be performed	I	No comment
AHA, ACCF (23)	2011	IIb	IIa	IIa	No comment
ESVS (49)	2017	IIb	IIb	IIa	I
ESC, ESVS (50)	2017	IIb	IIa	IIa	I

ACCF = American College of Cardiology Foundation; AHA = American Heart Association; CAS = carotid artery stenting; CEA = carotid endarterectomy; ESC = European Society of Cardiology; ESVS = European Society for Vascular Surgery; RACP = Royal Australasian College of Physicians; SVS = Society for Vascular Surgery.

ONGOING IMPROVEMENTS IN ENDOVASCULAR THERAPY SAFETY

Several factors can be appreciated in determining a particular revascularization modality's risk including aortic arch anatomy, prior revascularization, prior neck irradiation, proximal or distal vessel tortuosity, and subclavicular stenosis (21). These patient-related factors have been determined assuming current technology and expertise among providers.

Over the first decade of this century, there were rapid improvements in technology, experience, and expertise in the application of endovascular therapies to carotid stenosis which slowed after reimbursement was not provided. For example, novel methods for embolic protection have been developed to further reduce the risk of stroke during CAS. We would note the potential for better cerebral protection using different types of filters or even 2 kinds of protection at the same time. Both proximal balloon occlusion, as well as transcarotid artery revascularization (TCAR) proximal protection with reversed flow, have shown benefit.

Proximal cerebral protection was the subject of the ARMOUR (Proximal Protection With the MO.MA Device During Carotid Stenting) trial in the United States, which showed low rates of major adverse cardiovascular and cerebrovascular events of 2.3% and major stroke of 0.9% at 30 days (30). A meta-analysis by Stabile et al. (31) also indicated a significant 50% reduction in new ischemic lesions using proximal balloon occlusion. Evidence suggests that proximal balloon occlusion is superior and provides a safe platform for CAS. The National Cardiovascular Data Registry Carotid Artery Revascularization and Endarterectomy registry of 10,200 patients in the United States also showed that the risk of stroke was different with distal filters versus proximal balloons, although not significantly so (2.2% vs. 1.5%) (32). It should be noted that this technology continues to develop and independent distal filters have shown some promise (33).

Nonipsilateral events have been noted previously. In the ICSS (International Carotid Stenting Study) magnetic resonance imaging (MRI) subset, an increase in MRI lesions with stenting versus surgery is reported; however, 45% of CAS patients with new MRI lesions had nonipsilateral hits (34). The CAPTURE (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Unanticipated or Rare Events) registry looked at carotid stenting with distal filters and showed 18% of all strokes were nonipsilateral (35). These data make clear that the aortic arch is a significant contributor to new lesions seen on MRI. Moreover, the discovery of these new lesions has led to new questions: What is the impact of these lesions on neurological function, are they neurological events, and do they portend a different natural history after revascularization? Despite significant developments,

TABLE 2 Societal CAS Guidance Documents

Society	Year (Ref. #)
SVS	2008 (51), 2011 (52)
ESVS	2009 (53)
RACP, RACS, RANZCR	2010 (47), 2011 (54)
NICE	2011 (55)
ESC	2011 (56)
ASA, ACCF, AHA, AANN, AANS, ACR, ASNR, CNS, SAIP, SCAI, SIR, SNIS, SVM, SVS	2011 (23)
SCAI, SVM	2016 (57)

AANN = American Association of Neuroscience Nurses; AANS = American Association of Neurological Surgeons; ACR = American College of Radiology; ASNR = American Society of Neuroradiology; CNS = Congress of Neurological Surgeons; NICE = National Institute for Health and Care Excellence; RACP = Royal Australasian College of Physicians; RACS = Royal Australasian College of Surgeons; RANZCR = Royal Australian and New Zealand College of Radiologists; SAIP = Society of Atherosclerosis Imaging and Prevention; SCAI = Society for Cardiovascular Angiography and Interventions; SIR = Society of Interventional Radiology; SNIS = Society of NeuroInterventional Surgery; SVM = Society for Vascular Medicine; other abbreviations as in Table 1.

continued investigation is required to deepen understanding of the ramifications and further reduce the number of new post-procedure MRI lesions.

A recent review examined the 30-day strokes in a sample of CAS registries, cohort studies, and RCTs from the past 8 years, including CREST and ACT I. In this review, the patients who underwent the TCAR approach had proximal protection, no passage through the aortic arch, and the symptomatic and cumulative stroke rates were among the lowest reported (36). TCAR is more invasive than percutaneous approaches because it requires an incision. However, avoidance of the arch and the use of proximal protection may provide efficient particulate capture (37). In a systematic review and meta-analysis of TCAR compared with transfemoral approach for CAS that included 11,592 patients, the transcervical approach was associated with a lower risk for periprocedural stroke, but there were no differences in transient ischemic attack, MI, local hematoma, or death (38).

In addition to embolic protection, carotid stent design is improving as well. For example, carotid stent cell design affects outcomes significantly. Plaque prolapse occurs more frequently with open-cell stents rather than closed-cell stents (39). The SPACE (Stent-Protected Angioplasty versus Carotid Endarterectomy) randomized trial showed a significant difference, with the most-open-cell stent having the highest risk (40). A Belgian-Italian study showed the same thing, as well as more delayed events after stenting in general (41). Carotid stent development is occurring with greater attention to the local carotid environment including the preservation of the external carotid artery and better lesion containment. There are 3 such stents currently available: the Gore carotid stent (W.L. Gore & Associates, Newark, Delaware); the Terumo Roadsaver nitinol stent (Terumo, Tokyo, Japan), which is the subject of a prospective randomized trial; and in Europe, the CGuard by InspireMD (Tel Aviv, Israel). Evidence is starting to accumulate concerning these next-generation devices.

THE ROLE OF THE ADVANCED SKILL SET AND LIMITING PRACTITIONER REIMBURSEMENT

The risk of procedural complications, including stroke, provides an important backdrop to carotid disease, perhaps more so than other endovascular procedures. We would note that results for CAS continue to improve, even in patients at high risk for CEA. Acknowledging the importance of technological improvement, we believe the primary driver of improved outcomes is better case selection and operator experience. For example, in the CHOICE (Carotid Stenting for High Surgical-Risk Patients; Evaluating Outcomes Through the Collection of Clinical Evidence) multicenter prospective study, duration of experience was inversely associated with stroke risk (42). These results have been noted generally (43).

An analysis of the CAPTURE 2 study suggests an operator threshold of 72 cases to maintain a death and stroke rate of <3% in high surgical risk patients (43). A meta-analysis of data until 2010 supports the importance of operator experience and the fact that more experience is associated with lower-risk CAS (44). It should be noted that the same is true for CEA: Results from the NASCET (North American Symptomatic Carotid Endarterectomy Trial) and the ACAS (Asymptomatic Carotid Atherosclerosis Study) showed that the efficacy of CEA depends upon demonstrated institutional excellence (45), although more recent data do not show as strong a relationship in real-world practice (46).

Thus, as the science raises both the specter of new lesions on MRI after all procedures, device research continues to work to minimize emboli, operators improve in case selection, and standards are proffered for the provision of CAS, how should CMS regulate the provision of care? We would endorse several methods to ensure that an appropriately trained workforce provides this procedure. First, CAS reimbursement must be tied to experience and outcomes. We would note that many professional societies have put forward training and credentialing guidance (**Table 2**). This document will not place preference on any single standard; however, we agree with all stakeholders that minimum standards for training and ongoing experience are needed to ensure high-quality outcomes for the public.

Second, we would advocate for adjudicated outcomes and the creation of a carotid team to ensure standardized reporting of results. We would advance the idea of a Center of Excellence model to include routine case audits of cases. Minimum standards will be created with penalties for poor performance.

Third, the data created by these Centers of Excellence will be placed in a mandatory, monitored CAS registry, with documentation of operator, patient, and site required. We would recommend the inclusion of a pre- and post-stroke scale, history and physical examination parameters, and National Institutes of Health Stroke Scale results, among other pertinent data. We believe that linking participation in this type of registry should be tied to

reimbursement, similar to the reporting for coronary artery bypass grafting.

CONCLUSIONS

Asymptomatic internal carotid artery stenosis remains a significant contributor to stroke and is likely to remain important with the aging of the population and increasing prevalence of risk factors. We recognize that the treatment of asymptomatic carotid artery stenosis remains in development, resting on data collected well before and well below current medical therapy standards. As the question of revascularization remains under study, the advance of ever-safer tools to reduce the risk of revascularization must continue to facilitate a true current standard of care in the determination of benefit, neutrality, or harm in this disease process. We endorse the approval of CAS technology as just that: approval of a new tool in the care of patients with significant asymptomatic internal carotid artery stenosis.

ACKNOWLEDGMENTS The authors thank all the participants in the VIVA Vascular Leaders Forum on Carotid Artery Disease.

ADDRESS FOR CORRESPONDENCE: Dr. Joshua A. Beckman, Cardiovascular Division, Vanderbilt University Medical Center, 1215 21st Avenue South, MCE 5472, Nashville, Tennessee 37215. E-mail: Joshua.a.beckman@vumc.org. Twitter: @joshuabeckmanmd, @vivaphysicians.

REFERENCES

1. Robicsek F, Roush TS, Cook JW, Reames MK. From Hippocrates to Palmaz-Schatz, the history of carotid surgery. Eur J Vasc Endovasc Surg 2004;27:389–97.

2. Brott TG, Hobson RW 2nd., Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11–23.

3. 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;42:675–80.

4. Centers for Medicare & Medicaid Services. Management of Carotid Atherosclerosis. Bethesda, MD: Centers for Medicare & Medicaid Services, 2012.

5. Abbott AL, Adelman MA, Alexandrov AB, et al. Why the United States Center for Medicare and Medicaid Services (CMS) should not extend reimbursement indications for carotid artery angioplasty/stenting. Int Angiol 2012;31:85–9.

6. 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;123:2571–8.

7. Hill MD, Brooks W, Mackey A, et al. Stroke after carotid stenting and endarterectomy in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). Circulation 2012;126:3054–61.

8. Yeh RW, Kennedy K, Spertus JA, et al. Do postmarketing surveillance studies represent real-world populations? A comparison of patient characteristics and outcomes after carotid artery stenting. Circulation 2011;123:1384–90.

9. Mayo Asymptomatic Carotid Endarterectomy Study Group. Results of a randomized controlled trial of carotid endarterectomy for asymptomatic carotid stenosis. Mayo Clin Proc 1992;67:513–8.

10. The Asymptomatic Carotid Atherosclerosis Study Group. Study design for randomized prospective trial of carotid endarterectomy for asymptomatic atherosclerosis. Stroke 1989;20:844–9.

11. Halliday A, Mansfield A, Marro J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004;363:1491–502.

12. Lal BK, Meschia JF, Brott TG. Clinical need, design, and goals for the Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis trial. Semin Vasc Surg 2017;30:2–7.

13. Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. N Engl J Med 2016;374:1011–20.

14. Finks JF, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery. N Engl J Med 2011;364:2128–37.

15. Jim J, Dillavou ED, Upchurch GR Jr., et al. Gender-specific 30-day outcomes after carotid endarterectomy and carotid artery stenting in the Society for Vascular Surgery Vascular Registry. J Vasc Surg 2014;59:742–8.

16. Wayangankar SA, Kennedy KF, Aronow HD, et al. Racial/ethnic variation in carotid artery revascularization utilization and outcomes: analysis from the National Cardiovascular Data Registry. Stroke 2015;46:1525–32.

17. Shean KE, O'Donnell TFX, Deery SE, et al. Regional variation in patient outcomes in carotid artery disease treatment in the Vascular Quality Initiative. J Vasc Surg 2018;68:749–59.

18. Brott TG, Howard G, Roubin GS, et al. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. N Engl J Med 2016;374:1021–31.

19. Pothof AB, Soden PA, Deery SE, et al. The impact of race on outcomes after carotid endarterectomy in the United States. J Vasc Surg 2018;68:426–35.

20. Pothof AB, Soden PA, Fokkema M, et al. The impact of contralateral carotid artery stenosis on outcomes after carotid endarterectomy. J Vasc Surg 2017;66:1727–34.e2.

21. Fan Z, Liu X, Sun A, et al. Effect of longitudinal anatomical mismatch of stenting on the mechanical environment in human carotid artery with atherosclerotic plaques. Med Eng Phys 2017;48:114–9.

22. Naggara O, Touze E, Beyssen B, et al. Anatomical and technical factors associated with stroke or death during carotid angioplasty and stenting: results from the endarterectomy versus angioplasty in patients with symptomatic severe carotid stenosis (EVA-3S) trial and systematic review. Stroke 2011;42:380–8.

23. Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery. J Am Coll Cardiol 2011;57:e16–94.

24. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421–8.

25. Texakalidis P, Giannopoulos S, Kokkinidis DG, Jabbour P, Reavey-Cantwell J, Rangel-Castilla L. Outcome of carotid artery endarterectomy in statin users versus statin-naive patients: a

systematic review and meta-analysis. World Neurosurg 2018;116:444–50.e1.

26. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7–22.

27. Lichtman JH, Jones MR, Leifheit EC, et al. Carotid endarterectomy and carotid artery stenting in the US Medicare population, 1999-2014. JAMA 2017;318:1035–46.

28. Howard VJ, Meschia JF, Lal BK, et al. Carotid revascularization and medical management for asymptomatic carotid stenosis: protocol of the CREST-2 clinical trials. Int Stroke 2017;12:770–8.

29. Abbott AL, Adelman MA, Alexandrov AV, et al. Why calls for more routine carotid stenting are currently inappropriate: an international, multispecialty, expert review and position statement. Stroke 2013;44:1186–90.

30. Ansel GM, Hopkins LN, Jaff MR, et al. Safety and effectiveness of the INVATEC MO.MA proximal cerebral protection device during carotid artery stenting: results from the ARMOUR pivotal trial. Catheter Cardiovasc Interv 2010;76:1–8.

31. Stabile E, Sannino A, Schiattarella GG, et al. Cerebral embolic lesions detected with diffusion-weighted magnetic resonance imaging following carotid artery stenting: a meta-analysis of 8 studies comparing filter cerebral protection and proximal balloon occlusion. J Am Coll Cardiol Intv 2014;7:1177–83.

32. Giri J, Parikh SA, Kennedy KF, et al. Proximal versus distal embolic protection for carotid artery stenting: a national cardiovascular data registry analysis. J Am Coll Cardiol Intv 2015;8:609–15.

33. Scheinert D, Reimers B, Cremonesi A, et al. Independent modular filter for embolic protection in carotid stenting. Circ Cardiovasc Intervent 2017;10:e004244.

34. Bonati LH, Jongen LM, Haller S, et al. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). Lancet Neurol 2010;9:353–62.

35. Fairman R, Gray WA, Scicli AP, et al. The CAPTURE registry: analysis of strokes resulting from carotid artery stenting in the post approval setting: timing, location, severity, and type. Ann Surg 2007;246:551–6; discussion 556–8.

36. Kassavin DS, Clair DG. An update on the role of proximal occlusion devices in carotid artery stenting. J Vasc Surg 2017;65:271–5.

37. Plessers M, Van Herzeele I, Hemelsoet D, et al. Transcervical carotid stenting with dynamic flow reversal demonstrates embolization rates comparable to carotid endarterectomy. J Endovasc Ther 2016;23:249–54.

38. Texakalidis P, Giannopoulos S, Kokkinidis DG, et al. Direct transcervical access vs the transfemoral approach for carotid artery stenting: a systematic review and meta-analysis. J Endovasc Ther 2019;26:219–27.

39. Musialek P, Hopkins LN, Siddiqui AH. One swallow does not a summer make but many swallows do: accumulating clinical evidence for nearly-eliminated peri-procedural and 30-day complications with mesh-covered stents transforms the carotid revascularisation field. Postepy Kardiol Interwencyjnej 2017;13:95–106.

40. Siewiorek GM, Finol EA, Wholey MH. Clinical significance and technical assessment of stent cell geometry in carotid artery stenting. J Endovasc Ther 2009;16:178–88.

41. de Donato G, Setacci F, Sirignano P, Galzerano G, Cappelli A, Setacci C. Optical coherence tomography after carotid stenting: rate of stent malapposition, plaque prolapse and fibrous cap rupture according to stent design. Eur J Vasc Endovasc Surg 2013;45:579–87.

42. Shishehbor MH, Venkatachalam S, Gray WA, et al. Experience and outcomes with carotid artery stenting: an analysis of the CHOICE study (Carotid Stenting for High Surgical-Risk Patients; Evaluating Outcomes Through the Collection of Clinical Evidence). J Am Coll Cardiol Intv 2014;7:1307–17.

43. Gray WA, Rosenfield KA, Jaff MR, et al. Influence of site and operator characteristics on carotid artery stent outcomes: analysis of the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) clinical study. J Am Coll Cardiol Intv 2011;4:235–46.

44. Smout J, Macdonald S, Weir G, Stansby G. Carotid artery stenting: relationship between experience and complication rate. Int J Stroke 2010;5:477–82.

45. Wennberg DE, Lucas FL, Birkmeyer JD, Bredenberg CE, Fisher ES. Variation in carotid endarterectomy mortality in the Medicare population: trial hospitals, volume, and patient characteristics. JAMA 1998;279:1278–81.

46. Perri JL, Nolan BW, Goodney PP, et al. Factors affecting operative time and outcome of carotid endarterectomy in the Vascular Quality Initiative. J Vasc Surg 2017;66:1100–8.

47. Carotid Stenting Guidelines Committee, Bladin C, Chambers B, New G, Denton M, Lawrence-Brown M. Guidelines for patient selection and performance of carotid artery stenting. ANZ J Surg 2010;80:398–405.

48. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg 2011;54:e1–31.

49. Naylor AR, Ricco JB, de Borst GJ, et al. Editor's choice - management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018;55:3–81.

50. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Eur Heart J 2018;39:763–816.

51. Hobson RW 2nd., Mackey WC, Ascher E, et al. Management of atherosclerotic carotid artery disease: clinical practice guidelines of the Society for Vascular Surgery. J Vasc Surg 2008;48:480–6.

52. Ricotta JJ, Aburahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease: executive summary. J Vasc Surg 2011;54:832–6.

53. Liapis CD, Bell PR, Mikhailidis D, et al. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg 2009;37:1–19.

54. Carotid Stenting Guidelines Committee: an Inter-collegiate Committee of the RACP (ANZAN, CSANZ), RACS (ANZSVS) and RANZCR. Guidelines for patient selection and performance of carotid artery stenting. Intern Med J 2011;41:344–7.

55. National Institute of Health and Care Excellence. Carotid Artery Stent Placement for Asymptomatic Extracranial Carotid Stenosis. Interventional Procedures Guidance [IPG388. London, UK: NICE, 2011.

56. European Stroke Organisation, Tendera M, Aboyans V, Bartelink ML, et al. ESC guidelines on the diagnosis and treatment of peripheral artery diseases: document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). Eur Heart J 2011;32:2851–906.

57. 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.

KEY WORDS carotid artery, endarterectomy, stenosis, stent, stroke