



**ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on
Carotid Stenting: A Report of the American College of Cardiology Foundation
Task Force on Clinical Expert Consensus Documents
(ACCF/SCAI/SVMB/SIR/ASITN Clinical Expert Consensus Document
Committee on Carotid Stenting)**

American Society of Interventional & Therapeutic Neuroradiology, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, Eric R. Bates, Joseph D. Babb, Donald E. Casey, Jr, Christopher U. Cates, Gary R. Duckwiler, Ted E. Feldman, William A. Gray, Kenneth Ouriel, Eric D. Peterson, Kenneth Rosenfield, John H. Rundback, Robert D. Safian, Michael A. Sloan, Christopher J. White, Robert A. Harrington, Jonathan Abrams, Jeffrey L. Anderson, Eric R. Bates, Mark J. Eisenberg, Cindy L. Grines, Mark A. Hlatky, Robert C. Lichtenberg, Jonathan R. Lindner, Gerald M. Pohost, Richard S. Schofield, Samuel J. Shubrooks, JR, James H. Stein, Cynthia M. Tracy, Robert A. Vogel and Deborah J. Wesley

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ACCF/SCAI/SVMB/SIR/ASITN CLINICAL EXPERT CONSENSUS DOCUMENT

ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting

A Report of the American College of Cardiology Foundation Task Force
on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN
Clinical Expert Consensus Document Committee on Carotid Stenting)

*Developed in Collaboration With the American Society of Interventional & Therapeutic
Neuroradiology, Society for Cardiovascular Angiography and Interventions, Society for Vascular
Medicine and Biology, and Society of Interventional Radiology*

Writing Committee Members

Eric R. Bates, MD, FACC, *Chair*

Joseph D. Babb, MD, FACC, FSCAI
Donald E. Casey, JR, MD, MPH, MBA,
FACC

Christopher U. Cates, MD, FACC, FSCAI*

Gary R. Duckwiler, MD, FASITN†

Ted E. Feldman, MD, FACC, FSCAI*

William A. Gray, MD, FACC, FSCAI*

Kenneth Ouriel, MD, FACC

Eric D. Peterson, MD, MPH, FACC

Kenneth Rosenfield, MD, FACC, FSCAI*‡

John H. Rundback, MD, FSIR§

Robert D. Safian, MD, FACC, FSCAI,
FSVMB

Michael A. Sloan, MD, MS, FACC

Christopher J. White, MD, FACC, FSVMB,
FSCAI‡

*Society for Cardiovascular Angiography and Interventions Representative; †American Society of Interventional & Therapeutic Neuroradiology Representative; ‡Society for Vascular Medicine and Biology Representative; §Society of Interventional Radiology Representative

Task Force Members

Robert A. Harrington, MD, FACC, *Chair*

Jonathan Abrams, MD, FACC¶

Jeffrey L. Anderson, MD, FACC

Eric R. Bates, MD, FACC

Mark J. Eisenberg, MD, MPH, FACC

Cindy L. Grines, MD, FACC

Mark A. Hlatky, MD, FACC

Robert C. Lichtenberg, MD, FACC

Jonathan R. Lindner, MD, FACC

Gerald M. Pohost, MD, FACC

Richard S. Schofield, MD, FACC

Samuel J. Shubrooks, JR, MD, FACC

James H. Stein, MD, FACC

Cynthia M. Tracy, MD, FACC

Robert A. Vogel, MD, FACC||

Deborah J. Wesley, RN, BSN

¶Former Task Force Member during writing effort; ||Immediate Past Chair

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Preamble

This document has been developed by the American College of Cardiology Foundation (ACCF) Task Force on Clinical Expert Consensus Documents (CECD), and was cosponsored by the Society for Cardiovascular Angiography and Interventions (SCAI), the Society for Vascular Medicine and Biology (SVMB), the Society of Interventional Radiology (SIR), and the American Society of Interventional & Therapeutic Neuroradiology (ASITN). It is intended to provide a perspective on the current state of carotid artery stenting (CAS). The CECDs are intended to inform practitioners, payers, and other interested parties of the opinion of the ACCF and cosponsors concerning evolving areas of clinical practice and/or technologies that are widely available or new to the practice community. Topics chosen for coverage by expert consensus documents are so designed because the evidence base, the experience with technology, and/or the clinical practice are not considered sufficiently well developed to be evaluated by the formal American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines process. Often the topic is the subject of ongoing investigation. Thus, the reader should view the CECD as the best attempt of the ACCF and the cosponsors to inform and guide clinical practice in areas where rigorous evidence may not be available or the evidence to date is not widely accepted. When feasible, CECDs include indications or contraindications. Some topics covered by CECDs will be addressed subsequently by the ACC/AHA Practice Guidelines Committee.

The Task Force on CECDs makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest to inform the writing effort. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. The relationships with industry information for writing committee members and peer reviewers are published in the appendices of the document.

*Robert A. Harrington, MD, FACC
Chair, ACCF Task Force on Clinical Expert
Consensus Documents*

Executive Summary (recommendations are highlighted in green text for easy identification)

Introduction

Stroke is the third leading cause of death (164,000 deaths/year) in the U.S., behind heart disease and cancer. There are approximately 1 million stroke-related events each year, including 500,000 new strokes, 200,000 recurrent strokes, and 240,000 transient ischemic attacks (TIAs). Carotid occlusive disease amenable to revascularization accounts for 5% to 12% of new strokes.

Evaluation

Patients with temporary retinal or hemispheric neurological deficits should be screened for extracranial carotid artery disease. In asymptomatic patients, there are no guidelines to support routine screening for carotid artery stenosis, except for some patients scheduled for coronary artery bypass graft surgery (CABG). **Prior to CABG, carotid duplex screening is recommended in asymptomatic patients with age greater than 65 years, left main coronary stenosis, peripheral arterial disease, history of smoking, history of TIA or stroke, or carotid bruit.** In other patients with asymptomatic carotid bruits, diagnostic tests for carotid disease should only be performed in those patients who are also considered good candidates for carotid revascularization.

Imaging

Noninvasive imaging is useful to assess carotid stenosis severity and guide treatment. **Carotid duplex is the most widely available and least expensive noninvasive imaging procedure.** When carotid duplex results are unclear, diagnostic accuracy may increase to greater than 90% when it is used in conjunction with computed tomographic angiography and/or magnetic resonance angiography. **Vascular laboratories must have strict quality assurance programs to**

establish optimal internal diagnostic criteria, employ credentialed vascular technologists, and obtain vascular laboratory accreditation. Recognition of normal and variant anatomy of the aortic arch and the cervicocerebral circulation is required for successful performance of carotid angiography and endovascular intervention. Selective angiography of both carotid arteries was recommended prior to CAS.

Medical Therapy

Cardiovascular risk factor modification to target levels with medical therapy is recommended to limit progression of atherosclerosis and decrease clinical events, irrespective of carotid artery revascularization. Antiplatelet therapy is recommended for symptomatic patients. Either aspirin (81 to 325 mg), extended-release dipyridamole plus aspirin, or clopidogrel can be used. Medical therapy alone is preferred for patients in whom the risk of revascularization outweighs its benefits, including patients who are at low risk for stroke with medical therapy (symptomatic stenosis less than 50%, asymptomatic stenosis less than 60%), and those with a high risk of procedure-related stroke or death due to clinical or technical factors.

Carotid Endarterectomy (CEA)

Current AHA guidelines recommend CEA in symptomatic patients with stenosis 50% to 99%, if the risk of perioperative stroke or death is less than 6%. For asymptomatic patients, AHA guidelines recommend CEA for stenosis 60% to 99%, if the risk of perioperative stroke or death is less than 3%. The 2005 guidelines from the American Academy of Neurology recommend that eligible patients should be 40 to 75 years old and have a life expectancy of at least 5 years.

Carotid Stenting

Carotid artery stenting is a reasonable alternative to CEA, particularly in patients at high risk for CEA. Although there are no randomized studies comparing CAS with and without embolic protection devices (EPDs), **the use of EPDs appears to be important in reducing the risk of stroke during CAS. Careful neurological assessment is required before and after CAS.** The Centers for Medicare & Medicaid Services (CMS) reimbursement is limited to qualified institutions and physicians when using Food and Drug Administration (FDA)-approved stents and EPDs for high-risk patients with symptomatic stenosis greater than 70%, and for high-risk patients (symptomatic stenosis greater than 50%, asymptomatic stenosis greater than 80%) enrolled in a Category B Investigational Device Exemption (IDE) trial or post-approval study. **At the present time, there is insufficient evidence to support CAS in high-risk patients with asymptomatic stenosis less than 80% or in any patient without high-risk features.** The results of ongoing randomized trials will define the future role of CAS in low-risk patients. Further study is needed in asymptom-

atic high-risk patients to determine the relative merits of CAS compared with best medical therapy.

Training and Credentialing

Operators should previously have achieved a high level of proficiency in catheter-based intervention, complete dedicated training in CAS, and be credentialed at their hospital. Detailed clinical documents on training and credentialing for CAS have been published by 2 multispecialty consensus groups. The elements for competency include requirements for cognitive, technical, and clinical skills, including cervicocerebral angiography and CAS. Hospitals are required to maintain independent oversight of CAS outcomes by a hospital-based oversight committee. The CMS has created facility credentialing requirements for CAS reimbursement. Individual operators and institutions are required by CMS to track their outcomes and to make their data available for submission to a national database.

Introduction

The Writing Committee consisted of acknowledged experts in the field of carotid artery disease. In addition to members of ACCF, the Writing Committee included representatives from the SCAI, SVMB, SIR, ASITN, and Society for Vascular Surgery (SVS). Representation by an outside organization does not necessarily imply endorsement. The document was reviewed by 4 official representatives from by the ACCF and SCAI and 12 organizational reviewers from the SVMB, SIR, ASITN, and SVS, as well as 6 content reviewers. This document was approved for publication by the governing bodies of ACCF in September 2006. In addition, the governing boards of the SCAI, SVMB, SIR, and ASITN reviewed and formally endorsed this document. This document will be considered current until the Task Force on CECDs revises or withdraws it from publication or a guideline relevant to the topic is published.

Background

Stroke is the third leading cause of death (164,000 deaths/year) in the U.S., behind heart disease and cancer (1). There are approximately 1 million stroke-related events each year, including 500,000 new strokes, 200,000 recurrent strokes, and 240,000 TIAs (1,2). On average, someone has a stroke every 45 s and someone dies of stroke every 3 min. Stroke is the leading cause of serious long-term disability, causing functional limitations in more than 1.1 million Americans. The risk of stroke increases with each decade of life, and the growth in the elderly population will be a source of increasing disability due to stroke. African Americans, Hispanics, and diabetics are at increased risk for stroke mostly due to their strong association with hypertension (3).

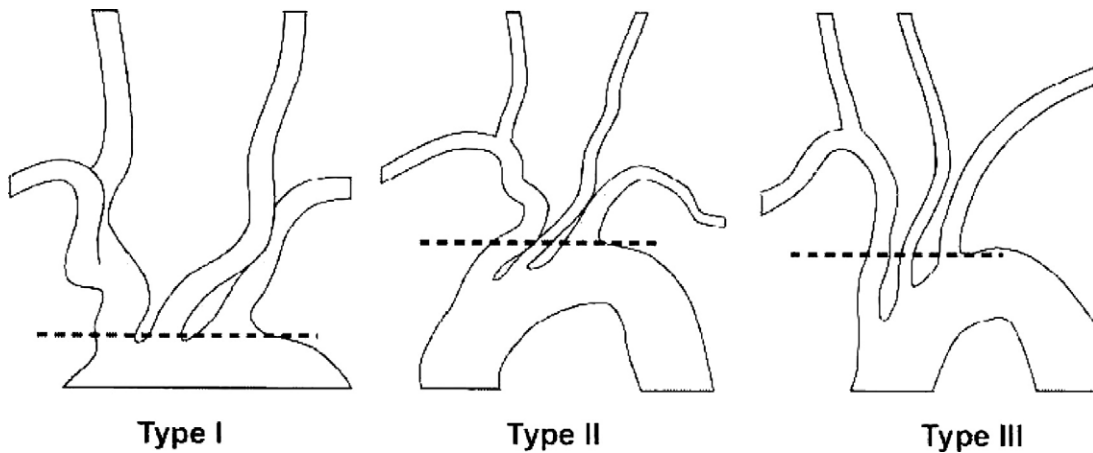


Figure 1. Aortic Arch Types

Reprinted with permission from Casserly IP, Yadav JS. Carotid intervention. In: IP Casserly, R Sachar, JS Yadav, editors. Manual of peripheral vascular intervention. Philadelphia, PA: Lippincott Williams & Wilkins, 2005:83–109 (13).

In 2006, the direct and indirect cost of stroke is estimated at \$57.9 billion (1).

Atherosclerosis accounts for up to one-third of all strokes. Approximately 50% of strokes occur in the distribution of the carotid arteries, and while extracranial carotid disease is more frequent in Caucasians, intracranial disease is more frequent in African Americans, Hispanics, and Asians (4–7). Carotid occlusive disease amenable to revascularization accounts for 5% to 12% of new strokes (8–11). The pattern of progression of carotid stenosis is unpredictable, and disease may progress swiftly or slowly, or remain stable for many years. Nearly 80% of strokes due to embolization in the carotid distribution may occur without warning, emphasizing the need for careful patient follow-up (8–10).

Current annual carotid revascularization volumes include 117,000 CEA (1) and 7,000 to 10,000 CAS procedures. The first devices for CAS in high-risk patients were approved by the FDA in August 2004, and limited reimbursement for CAS was approved by the CMS in March 2005. Carotid artery stenting is less invasive than CEA, and the number of CAS procedures may increase rapidly, depending on the outcomes of ongoing registries and randomized clinical trials, and on CMS reimbursement. The purpose of this document is to summarize what is currently known about CAS and to lay the foundation for the development of interdisciplinary guidelines.

Carotid Artery Disease

Neurovascular Anatomy and Physiology

Recognition of normal and variant anatomy of the aortic arch and the cervicocerebral circulation is required for successful performance of carotid angiography and endovascular intervention (12). It is important to recognize the type of aortic arch and the configuration of the great

vessels, since these anatomic features influence procedure complexity. There are 3 types of aortic arch that are based on the relationship of the innominate artery to the aortic arch (Fig. 1) (13). The Type I aortic arch is characterized by origin of all 3 great vessels in the same horizontal plane as the outer curvature of the aortic arch. In the Type II aortic arch, the innominate artery originates between the horizontal planes of the outer and inner curvatures of the aortic arch. In the Type III aortic arch, the innominate artery originates below the horizontal plane of the inner curvature of the aortic arch. The more inferior the origin of the target artery (i.e., Type II or III aortic arch), the greater the difficulty in gaining access to the carotid artery.

In addition to the type of aortic arch, the configuration of the great vessels is important. In the usual configuration, the innominate artery, the left common carotid artery (CCA), and the left subclavian artery have separate origins from the aortic arch (Fig. 2). The most common anomalies of the great vessels are a common origin of the innominate artery and the left CCA, and the origin of the left CCA as a separate branch of the innominate artery (so-called “bovine configuration”) (Table 1) (14). The distal CCA usually bifurcates into the internal carotid artery (ICA) and the external carotid artery (ECA) at the level of the thyroid cartilage, but an anomalous bifurcation may occur anywhere within 5 cm above or below this level, and there are many variations in the position of the ICA relative to the ECA. The dilated origin of the ICA is the carotid bulb, which usually extends 2 cm from the origin, at which point the diameter of the ICA becomes more uniform. There is considerable variation in ICA length and tortuosity, with up to 35% of individuals having some form of undulation, coiling, or kinking of the ICA, particularly the elderly. The intracranial ICA begins at the skull base when it enters the petrous bone (15).

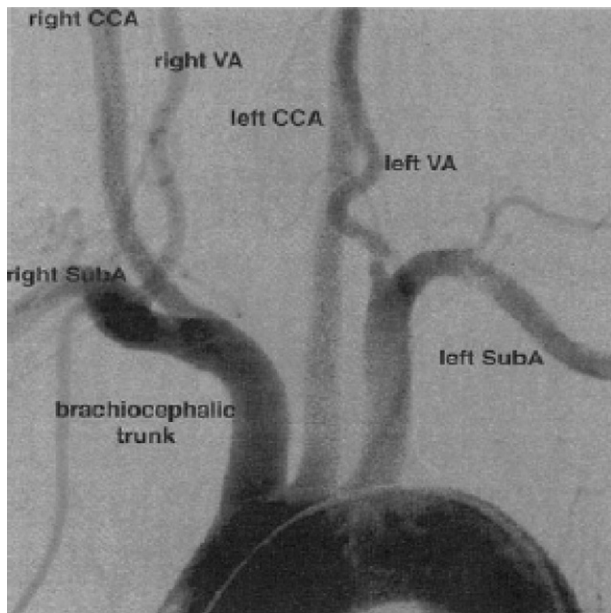


Figure 2. Great Vessel Anatomy

CCA = common carotid artery; SubA = subclavian artery; VA = vertebral artery. Reprinted with permission from Cho L, Mukherjee D. Basic cerebral anatomy for the carotid interventionalist: the intracranial and extracranial vessels. *Catheter Cardiovasc Interv* 2006;68:104-11. Copyright © 2006 John Wiley & Sons (15a).

After passing through the petrous bone in the carotid canal, the ICA transitions into the cavernous segment and eventually enters the subarachnoid space of the brain near the level of the ophthalmic artery. As the ICA turns

Table 1. Anatomical Variants and Anomalies in Cerebral Angiography

Aortic arch

- Innominate and left common carotid artery share common trunk (20%)
- Left common carotid artery originates from innominate artery (bovine arch; 7%)
- Left common carotid artery and left subclavian artery form common trunk (1%)
- Left vertebral artery originates from arch (0.5%)
- Aberrant right subclavian artery originates from left side of the arch and passes posterior to esophagus (<0.5%)

Internal carotid artery

- Location of carotid bifurcation may be T2 to C1
- Absence of internal carotid artery
- Anomalous origin of the internal carotid artery (directly from the arch)
- Hypoplasia of the internal carotid artery
- Duplication of the internal carotid artery
- Anomalous branches of the internal carotid artery (ascending pharyngeal, occipital)
- Aberrant petrous internal carotid artery (course through middle ear)
- Persistent stapedia artery
- Isolated internal carotid artery (fetal origin of the PCA and absent A1 segment)
- Early bifurcation of the middle cerebral artery

Reprinted with permission from Schneider P. Advanced cerebrovascular arteriography: applications in carotid stenting. In: P Schneider, W Bohannon, M Silva, editors. *Carotid Interventions*. New York, NY: Marcel Dekker, 2004:69-91 (14).
PCA = posterior communicating artery.

posteriorly and superiorly, it gives rise to the posterior communicating artery, which communicates with the posterior cerebral artery from the vertebrobasilar circulation (Fig. 3). The ICA then bifurcates into the anterior cerebral artery and the middle cerebral artery. The anterior cerebral arteries communicate through the anterior communicating artery. The communicating arteries and their parent segments form the circle of Willis. There are several important cranial collateral pathways, including those from the ECA to the ICA (via the internal maxillary branch of the ECA to the ophthalmic branch of the ICA), ECA to the vertebral artery (via the occipital branch of the ECA), vertebrobasilar system to the ICA (via the posterior communicating artery), and ICA to the ICA (via interhemispheric circulation through the anterior communicating artery). The configuration of the circle of Willis is highly variable, with a complete circle of Willis being present in fewer than 50% of individuals.

Selective angiography of both carotid arteries is recommended prior to CAS to evaluate carotid stenosis severity and morphology, carotid tortuosity and calcification, and intracranial circulation for stenoses, collateral circulation, aneurysm formation, and arteriovenous malformation that might impact treatment recommendations.

Recognition of normal vascular physiology is necessary for understanding possible cardiovascular responses to ca-

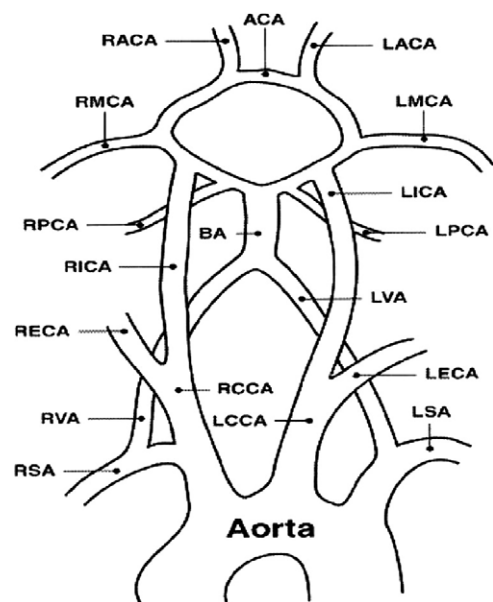


Figure 3. Extracranial and Intracranial Circulation

Reprinted with permission from White CJ, Ramee SR, Bendick PJ, Safian RD. *Peripheral Vascular Intervention: The Manual of Interventional Cardiology*. 3rd edition. Royal Oak, MI: Physicians' Press, 2001:831-901 (15b). ACA = anterior communicating artery; BA = basilar artery; LACA = left anterior cerebral artery; LCCA = left common carotid artery; LECA = left external carotid artery; LICA = left internal carotid artery; LMCA = left middle cerebral artery; LPCA = left posterior cerebral artery; LSA = left subclavian artery; LVA = left vertebral artery; RACA = right anterior cerebral artery; RCCA = right common carotid artery; RECA = right external carotid artery; RICA = right internal carotid artery; RMCA = right middle cerebral artery; RPCA = right posterior cerebral artery; RSA = right subclavian artery; RVA = right vertebral artery.

rotid intervention. Compression or stretching of the carotid sinus can cause a vasovagal (hypotension and bradycardia) or vasodepressor (hypotension without bradycardia) response and systemic hypotension. These responses are mediated via stimulation of the carotid sinus nerve (a branch of the glossopharyngeal nerve) in the carotid baroreceptor, and vagus nerve activation leading to inhibition of sympathetic tone. The sensitivity of the carotid baroreceptors is variable and may be affected by medications (e.g., vasodilators and beta-blockers might increase sensitivity), the presence of calcified plaque in the carotid bulb (increased sensitivity), or prior CEA (decreased sensitivity).

Pathology and Pathophysiology

Although atherosclerosis is the most common disease of the carotid circulation, it is important to be aware of other conditions that may be associated with cerebral ischemia and infarction. These conditions include diseases of the aorta (dissection, aneurysm, aortitis), arteritis, fibromuscular dysplasia, dissection, dolichoectasia, primary vascular tumors, trauma, and complications of head and neck cancer.

Atherosclerosis is a systemic disease, and the pathophysiology of carotid atherosclerosis is similar to that in other vascular beds. However, atherosclerosis in the carotid artery is usually unifocal, and 90% of lesions are located within 2 cm of the ICA origin (15). The degree of carotid stenosis is associated with stroke risk. Carotid atherosclerosis can produce retinal and cerebral symptoms by 1 of 2 major mechanisms, including progressive carotid stenosis leading to in-situ occlusion and hypoperfusion (less common), or intracranial arterial occlusion resulting from embolization (more common). Patients with and without carotid stenosis may develop symptomatic cerebral hypoperfusion from systemic causes. Patients presenting with carotid distribution cerebral ischemia should be thoroughly evaluated for treatable causes, including sources of emboli from the carotid arteries, heart, and aortic arch.

Natural History and Risk Stratification

Patients with asymptomatic carotid bruits are more common than patients with symptomatic carotid stenosis. A carotid bruit is identified in 4% to 5% of patients age 45 to 80 years, and should be heard in the majority of patients with carotid stenosis greater than or equal to 75% (15). Carotid stenoses greater than or equal to 50% have been identified in 7% of men and 5% of women older than 65 years (16). However, a bruit may be absent if there is slow flow through a severe stenosis, so cervical bruits are neither specific nor sensitive for identifying severe carotid stenosis. The risk of progression of carotid stenosis is 9.3% per year; risk factors for progression include ipsilateral or contralateral ICA stenosis greater than 50%, ipsilateral ECA stenosis greater than 50%, and systolic blood pressure greater than 160 mm Hg (17).

The annual stroke risk in patients with carotid stenosis is most dependent on symptom status and stenosis severity, but is also influenced by the presence of silent cerebral infarction, contralat-

eral disease, extent of collaterals, the presence of atherosclerotic risk factors, plaque morphology, and other clinical features. The stroke risk is much higher in symptomatic patients than in asymptomatic patients, and the risk is highest immediately after the initial ischemic event. In the NASCET (North American Symptomatic Carotid Endarterectomy Trial) (18,19), the risk of stroke in the first year was 11% for carotid stenosis 70% to 79% and 35% for carotid stenosis greater than or equal to 90%. Patients with carotid stenosis 70% to 99% had a 2-year ipsilateral stroke risk of 26%. Interestingly, patients with near-occlusion have a lower stroke risk, ranging from 8% at 5 years (20) to 11% at 1 year (21). The annual ipsilateral stroke rate drops to about 3% within 2 to 3 years.

In asymptomatic patients, the annual stroke risk is much lower than in symptomatic patients, and is less than 1% for carotid stenoses less than 60% and 1% to 2.4% for carotid stenoses greater than 60% (22,23). In the ACST (Asymptomatic Carotid Surgery Trial), there was no relationship between the risk of stroke and increasing stenosis severity from 60% to 99% (23). Patients referred for CABG have a particularly high incidence of asymptomatic carotid stenosis with a prevalence of 17% to 22% for carotid stenosis greater than 50% and 6% to 12% for carotid stenosis greater than 80%. The risk of perioperative stroke after CABG is 2% for carotid stenosis less than 50%, 10% for carotid stenosis 50% to 80%, and as high as 19% for carotid stenosis greater than 80% (24).

Other factors that influence the risk of stroke include the clinical manifestations of TIA, prior silent stroke, contralateral disease, intracranial disease, intracranial collaterals, and plaque morphology. In the NASCET study, the 3-year risk of ipsilateral stroke was 10% after retinal TIAs and 20.3% after hemispheric TIAs (25). The presence of concomitant intracranial disease raised the 3-year risk of stroke from 25% to 46% in patients with carotid stenosis 85% to 99% (26). The prevalence of silent cerebral infarction in patients with asymptomatic carotid stenosis is estimated to be 15% to 20% (22), and appears to be associated with a higher risk of subsequent stroke. In patients with ICA occlusion, the annual stroke risk is influenced by the number of intracranial collateral pathways (27). In NASCET patients with carotid stenosis 70% to 99%, the presence of contralateral carotid occlusion increased stroke risk by more than 2-fold (28), whereas the presence of collaterals decreased the stroke risk by more than 2-fold (29). Stroke risk in symptomatic patients may also be influenced by plaque morphology, including the presence of hypoechoic or echolucent plaque (30,31) and plaque ulceration (32,33) irrespective of the degree of stenosis.

Patient Evaluation

Clinical Evaluation

Clinical syndromes associated with extracranial carotid occlusive disease are summarized in Table 2. Transient ischemic attacks are medical emergencies, characterized by

Table 2. Clinical Syndromes Associated With Extracranial Carotid Occlusive Disease

- A. Retinal syndromes
 - 1. TIA
 - a. Amaurosis fugax or transient monocular blindness
 - b. Amaurosis fugax variants
 - 2. Retinal infarction
 - a. Central retinal artery occlusion
 - b. Branch retinal artery occlusion
 - 3. Anterior ischemic optic neuropathy
- B. Hemispheric syndromes
 - 1. TIA
 - a. Transient hemisphere attack
 - b. Limb-shaking TIA
 - 2. Infarction (stroke)
 - a. Watershed infarction
 - b. Thromboembolic stroke
- C. Global cerebral syndromes
 - 1. Bilateral or alternating TIAs
 - 2. Bilateral simultaneous TIA, suggesting vertebrobasilar insufficiency
 - 3. Bilateral cerebral infarction

TIA = transient ischemic attack.

temporary focal retinal and/or hemispheric neurological deficits that resolve within 24 h. In one study (34), 11% of patients developed a stroke within 90 days after TIA, one-half occurring within the first 2 days. Patients with both retinal and hemispheric symptoms usually have severe extracranial carotid disease. Rarely, patients with bilateral high-grade ICA stenosis or occlusion may have transient bilateral hemispheric symptoms, which may be mistaken for vertebrobasilar insufficiency.

A careful history is required to determine whether symptoms are attributable to carotid stenosis. Transient monocular blindness is classically described as a shade coming down over one eye. Hemispheric symptoms include unilateral motor weakness, sensory loss, speech or language disturbances, or visual field disturbances. Vertebrobasilar symptoms include brainstem symptoms (dysarthria, diplopia, dysphagia); cerebellar symptoms (limb or gait ataxia); and simultaneous motor, sensory, and visual loss, which may be unilateral or bilateral. It is important to distinguish between hemispheric and vertebrobasilar symptoms, since patients may have vertebrobasilar insufficiency and asymptomatic carotid stenosis. Accurate localization of symptoms will greatly assist with clinical management and timing of revascularization, if appropriate.

A complete neurological assessment includes the cardiovascular examination (auscultation of the neck for carotid bruits and transmitted murmurs), fundoscopic examination (to detect retinal embolization), and a focused neurologic examination (to correlate neurological symptoms with an ischemic territory). For example, aphasia usually localizes to the left hemisphere, irrespective of the patient's handedness, and hemispatial neglect in the setting of left motor, sensory, or visual signs indicates a right hemisphere lesion. The

National Institutes of Health Stroke Scale (NIHSS) (35) is used to quantify the neurological deficit and predict outcome after ischemic stroke (36). Clinical findings must be correlated with brain and vascular imaging to determine whether or not a carotid stenosis is symptomatic.

Imaging is critical to assess the anatomy and structural pathology of the brain (e.g., mass, old or new stroke, hemorrhage, atrophy, or other confounding disease state) and the carotid artery (e.g., anatomic configuration, stenosis, plaque morphology, associated lesions, vasculitis, or dissection), and guide treatment. In asymptomatic patients, there are no guidelines to support routine screening for carotid artery stenosis, except for some patients scheduled for CABG. Prior to CABG, carotid duplex screening is recommended in asymptomatic patients with age greater than 65 years, left main coronary stenosis, peripheral arterial disease, history of smoking, history of TIA or stroke, or carotid bruit (24). In other patients with asymptomatic carotid bruits, diagnostic tests for carotid disease should only be performed in those patients who are also considered good candidates for carotid revascularization.

Noninvasive Testing

Carotid duplex, magnetic resonance angiography (MRA), and computed tomographic angiography (CTA) are often recommended for the initial evaluation of most patients with carotid artery disease, allowing assessment of lesion characteristics (i.e., ulceration, composition) and stenosis severity. The NASCET (18,19) and the ECST (European Carotid Surgery Trial) (37,38) studies showed benefit for CEA in patients with symptomatic carotid stenosis greater than 50%, and the ACAS (Asymptomatic Carotid Atherosclerotic Study) (22) and ACST (23) trials showed benefit for CEA in asymptomatic patients with carotid stenosis greater than 60%. Although the NASCET, ECST, and ACAS studies utilized angiographic criteria for stenosis severity, noninvasive studies are usually performed in place of angiography, to assess stenosis severity and guide decisions about revascularization. Small differences in stenosis severity may impact decisions about revascularization by as much as 20% (39).

Carotid Duplex

Carotid duplex utilizes spectral Doppler, color-flow, and B-mode (gray-scale) to evaluate the cervical carotid arteries from their supraclavicular origin to their retromandibular entrance into the skull base. The mainstay of carotid duplex evaluation is the determination of flow velocity using spectral Doppler analysis. Color-encoded and power Doppler imaging assist in assessment of stenosis severity in individuals with carotid tortuosity, where angle-corrected velocities can be unattainable (40), and may allow detection of residual flow in patients with subtotal occlusions or vascular calcification (41). B-mode imaging is used to identify sites for more focused Doppler evaluation, to directly evaluate cross-sectional narrowing, and to provide

information regarding plaque morphology predictive of stroke risk, including surface irregularity (42), ulceration (33), and echolucency (30,43,44). B-mode may also be useful in measuring intima-media thickness, a possible marker of systemic atherosclerotic burden and cardiovascular risk used predominantly in trials assessing primary risk intervention strategies (45,46).

Diagnostic criteria for carotid duplex rely on peak systolic and end-diastolic velocities in the ICA and CCA, spectral patterns, and ICA/CCA velocity ratios. Unlike the linear measurements of diameter stenosis obtained with angiography, spectral velocities illustrate the effects of cross-sectional luminal narrowing. There are numerous diagnostic criteria for grading stenosis severity. Meta-analyses (39,47) and a multidisciplinary consensus conference (48) suggest that peak systolic velocity is the single most accurate duplex parameter for determination of stenosis severity. Compared with angiography, carotid duplex has a sensitivity of 77% to 98% and a specificity of 53% to 82% to identify or exclude an ICA stenosis greater than or equal to 70% (39). Women have higher flow velocities than men (49), which may affect decisions about revascularization.

In patients with a severe carotid stenosis or occlusion, compensatory increases in contralateral blood flow may result in spuriously high velocities in the contralateral ICA. In this situation, the ICA/CCA velocity ratio (ratio of peak systolic flow velocities in the proximal ICA and the distal CCA) is a better determinant of stenosis severity (50–52). Compensatory increased flow is also favored when color-flow or power Doppler show no evidence of a flow-limiting stenosis.

The accuracy of diagnostic criteria may vary between laboratories (53–55), optimal diagnostic criteria may change over time (56), and there is significant intraobserver variability (39,53,57). Vascular laboratories must have strict quality assurance programs to establish optimal internal diagnostic criteria, employ credentialed vascular technologists, and obtain vascular laboratory accreditation (Intersocietal Commission for the Accreditation of Vascular Laboratories; American College of Radiology). It is likely that reimbursement for these studies will be limited to accredited laboratories in the future.

It may be difficult to differentiate slow-velocity “trickle flow” (58) from complete occlusion, so power Doppler imaging or intravenous ultrasound contrast agents may be useful (59–61). Cardiac arrhythmias, arterial kinking, extensive calcification, high bifurcation, or unusual diseases (such as fibromuscular dysplasia or dissection) may make image interpretation more difficult. Lesions in the intracranial ICA and aortic arch cannot be imaged, although these occur infrequently (2% to 5% of cases) and rarely affect surgical decisions (58,62). Overall, despite these limitations, there is very high concordance between high quality carotid duplex and angiography; in some studies, the findings on subsequent angiography altered the revascularization decision in only 1% to 6% of cases (62–64). When carotid

duplex results are unclear, diagnostic accuracy may increase to greater than 90% when it is used in conjunction with CTA and/or MRA (65).

Transcranial Doppler (TCD)

TCD, with or without color-coding, measures intracranial blood flow patterns, and indirectly assesses the effects of stenoses proximal or distal to the sites of insonation. It is particularly useful for assessment of intracranial stenosis (66). TCD alone is rarely useful for recognition of cervical carotid stenosis, but when used as an adjunct to carotid duplex, sensitivity is nearly 90% (67).

The clinical role for TCD in determining the appropriateness of carotid revascularization remains to be determined. However, several studies suggest that impaired cerebrovascular reserve by TCD, manifested by impaired cerebral blood flow augmentation in response to breath-holding or CO₂ inhalation, may predict a 3-fold higher risk of subsequent neurological events in asymptomatic patients with extracranial carotid stenosis. In such patients, successful revascularization results in normalization of vasomotor reserve (68). Another study showed that absence of embolic signals in patients with asymptomatic carotid stenosis predicts a stroke rate of 1% per year (69).

MRA

Perhaps more than any other imaging modality, MRA has benefited from dramatic technology advancements that have improved image quality. MRA allows imaging of intrathoracic and intracranial lesions not accessible by carotid duplex, although image quality is degraded by breathing artifact and venous contamination (70). Newer reconstruction algorithms (70,71), as well as the universal availability of MRA contrast agents, have increased imaging speed and enhanced MRA imaging consistency. When compared with conventional angiography, first-pass contrast enhanced three-dimensional MRA maximum intensity projections correlate with digital subtraction angiography stenosis in 90% of cases, and correlation is best for severe stenoses (72). Interpretability is enhanced by evaluating axial, sagittal, and coronal projections (73) and with 3-T magnets.

Advantages of MRA include avoidance of nephrotoxic contrast and ionizing radiation. Limitations include the inability to perform MRA due to claustrophobia, pacemakers, implantable defibrillators, and obesity; misdiagnosis of subtotal stenoses as total occlusions; or overestimation of carotid stenoses secondary to movement artifact. These errors may be lessened by short acquisition sequences, contrast enhancement (74), and by combining MRA and duplex data (75). The combination of these 2 tests provides better concordance with digital subtraction angiography than either test alone (combined 96% sensitivity and 80% specificity), but is not cost-effective for routine use (76).

MRA techniques may allow plaque characterization, including fibrous cap thickness and disruption, and intraplaque lipid content and hemorrhage (77,78). MRA has

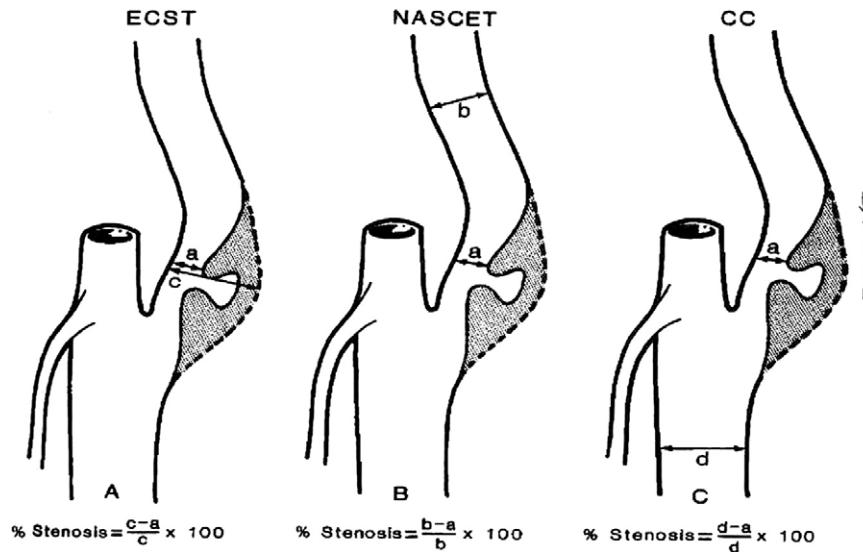


Figure 4. Angiographic Methods for Determining Carotid Stenosis Severity

Reprinted with permission from Osborn AG. *Diagnostic Cerebral Angiography*. 2nd edition. Philadelphia, PA: Williams & Wilkins, 1999 (12). CC = common carotid; ECST = European Carotid Surgery Trial; NASCET = North American Symptomatic Carotid Endarterectomy Trial.

been used experimentally to predict flow profiles and wall stress dynamics affecting image quality and plaque stability (79). MRA evaluation of carotid arteries after stent placement has been performed, although artifacts due to magnetic susceptibility or Faraday shielding may lead to misdiagnosis (80).

CTA

CTA allows orthogonal carotid imaging and simultaneous intracranial evaluation, but requires ionizing radiation and potentially nephrotoxic iodinated contrast. Like MRA, CTA is useful when carotid duplex is ambiguous, permitting visualization of aortic arch or high bifurcation pathology, reliable differentiation of total and subtotal occlusion, assessment of ostial and tandem stenoses, and evaluation of carotid disease in patients with arrhythmias, valvular heart disease, or cardiomyopathy. Since CTA relies on the recognition of contrast filling of the stenotic vessel lumen, it is less prone to overestimate stenosis severity due to turbulence and arterial tortuosity. Although CTA is extremely sensitive to the presence of calcification, it is less reliable than carotid duplex or MRA for assessing plaque vulnerability (81). When compared with carotid duplex, CTA is more specific for high-grade lesions, and in 1 study altered surgical planning in 11% of cases (82). When compared with enhanced MRA, 1 study showed that CTA was less reliable (70). With CTA, the sensitivity and specificity for detecting carotid stenosis greater than 70% was 85% to 95% and 93% to 98%, respectively (83,84). CTA sensitivity and accuracy can be increased by examining axial source images (83) and volume rendered projections

(85), and by use of faster high resolution multislice scanners (86).

Choice of Noninvasive Diagnostic Test

Carotid duplex is the most widely available and least expensive noninvasive imaging procedure. Whereas the advantages and limitations of each imaging procedure are previously described, we recommend that physicians learn about the tests available in their own institutions, and choose the best imaging modality.

Carotid Angiography

Catheter-based arch and cerebral artery angiography is the reference standard for the evaluation of carotid artery disease. Single-plane angiography may underestimate the tortuosity of the great vessels, so orthogonal views, biplane angiography, or rotational acquisition is preferred. The purpose of angiography is to define the aortic arch type, the configuration of the great vessels, the presence of tortuosity and atherosclerotic disease in the arch and great vessels, and the condition of the intracranial circulation, particularly with respect to intracranial stenosis, aneurysm, arteriovenous malformations, and patterns of collateral blood flow. Such information will influence choice of catheters and the interventional strategy.

There are 3 methods for assessment of carotid stenosis severity, and each relies on different reference segments, resulting in different estimates of stenosis severity (87,88) (Fig. 4). By convention, the NASCET method has been adopted, utilizing the diameter of the proximal ICA above the carotid bulb as the reference diameter. Although decisions about the need for CEA are often made based on noninvasive imaging without carotid arteriography, all pa-

Table 3. Risk Factor Modification Treatment Goals

Risk Factor	Goal	Intervention
Blood pressure	BP <140/90 mm Hg BP <130/80 mm Hg with chronic kidney disease or diabetes	Weight control, increased physical activity, alcohol moderation, sodium reduction, medications
Smoking	Smoking cessation Avoid environmental tobacco smoke	Smoking cessation programs, nicotine replacement, bupropion, varenicline
Lipid management	LDL-C <100 mg/dl (optional goal <70 mg/dl if high CAD risk) Non-HDL-C ≤130 mg/dl	Diet low in saturated fat, weight control, increased physical activity, statins, niacin, fibrates
Diabetes mellitus	HbA1c <7%	Diet, weight control, oral hypoglycemic agents, insulin
Physical activity	30 minutes, 7 days/week Minimum 5 days/week	Walking, biking, swimming, gardening, household work
Weight management	BMI 18.5–24.9 kg/m ² Waist circumference: ≤40 inches men; ≤35 inches women	Physical activity, caloric intake, behavioral programs, rimonabant

Modified with permission from Smith S, Allen J. AHA/ACC secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2005 update. *Circulation* 2006;113:2363–72 (92).
 BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

tients being considered for CAS must undergo angiography. In these patients, the NASCET definition for stenosis severity must be used, irrespective of estimates of stenosis severity by noninvasive methods.

Although angiography is superb for assessment of stenosis severity and calcification, it is less reliable for evaluating plaque morphology. In one study (33), catheter-based angiography had a sensitivity of 46%, specificity of 74%, and positive predictive value of 72% for detecting histologically confirmed plaque ulceration.

As an invasive procedure, cervicocerebral angiography shares the same potential complications with other angiographic techniques, including access site injury, blood transfusion, contrast nephropathy, anaphylactoid reactions, and atheroembolism. In patients with symptomatic cerebral atherosclerosis undergoing diagnostic cerebral angiography, the risk of stroke is 0.5% to 5.7%, and the risk of TIA is 0.6% to 6.8% (89). In asymptomatic patients in the ACAS trial, stroke occurred in 1.2% of patients after angiography (22). More recent studies reported neurological complication rates in less than 1% of patients, suggesting that the risk may be lower than previously reported (90,91). Possible explanations for these differences are improvements in equipment, technique, and operator experience; monitoring of catheter-tip pressure during angiography; and use of procedural heparin and antiplatelet agents.

Medical Therapy

Risk Factor Modification

Identification of risk factors for stroke is important for stroke prevention, since modification of many of these risk factors can reduce the risk of stroke. Ethnicity, age, and family history are important determinants of stroke risk, but these cannot be modified. Although not specifically evaluated in patients with severe carotid artery

stenosis, cardiovascular risk factor modification and medical therapy are recommended to limit progression of atherosclerosis and decrease clinical events, irrespective of carotid artery revascularization. Treatment goals are listed in Table 3 (92,93).

Hypertension Therapy

Hypertension is the pre-eminent risk factor for ischemic and hemorrhagic stroke, by virtue of its direct atherogenic effects on the systemic and cerebral circulations, and by its strong association with myocardial infarction (MI) and atrial fibrillation, both of which increase the risk of cerebral embolization (94). There is a linear relationship between increasing blood pressure and increased risk of stroke, even within the normal blood pressure range. The stroke risk increases 3-fold when systolic blood pressure is greater than 160 mm Hg. The impact of systolic and diastolic blood pressure on the risk of stroke is similar, and isolated systolic hypertension is an especially important risk factor in the elderly (95). Control of blood pressure is the cornerstone of therapy to modify atherogenic risk factors, and the benefits of antihypertensive therapy extend to all patient subgroups, especially diabetics. Even small reductions in systolic (10 mm Hg) and diastolic (3 to 6 mm Hg) blood pressure result in a 30% to 42% decline in the risk of stroke (96,97). Selection of drugs should be based on Joint National Committee (JNC)-7 guidelines (98), and will be influenced by the presence of comorbid medical conditions (e.g., diabetes, left ventricular dysfunction, renal failure) and ethnicity. At least two-thirds of patients will require multiple medications to achieve blood pressure control.

Smoking Cessation

Smoking nearly doubles the risk of ischemic and hemorrhagic stroke (particularly subarachnoid hemorrhage), and the risk is directly proportional to the number of cigarettes smoked (99,100). The risk is even higher in female smokers who use oral contraceptives. Passive exposure to cigarette

smoke nearly doubles the risk of stroke in spouses of smokers compared with their nonsmoking neighbors (101). The risk of stroke decreases to that of nonsmokers within 5 years after smoking cessation (102). Enrollment in a formal smoking cessation program, which includes nicotine replacement, bupropion, social support, and skills training, has proven to be the most effective approach for smoking cessation.

Dyslipidemia Therapy

Although the epidemiological relationship between dyslipidemia and coronary artery disease is incontrovertible, its relationship with stroke is less well established. In fact, there is an inconsistent relationship between blood lipids and stroke. This is partly a result of combining ischemic and nonischemic stroke in the clinical reports. However, there is a strong relationship between total cholesterol, low-density lipoprotein cholesterol, and the extent of extracranial carotid artery atherosclerosis and wall thickness (103). A summary of over 70,000 patients at high risk for or with established coronary artery disease described a 21% relative risk reduction and a 0.9% absolute risk reduction for stroke within 5 years of treatment (104). These observations suggest a potential beneficial effect of lipid-lowering treatment on plaque stabilization, endothelial function, and inflammation in patients with cerebrovascular disease.

Diabetes

Although diabetes is strongly associated with hypertension and hyperlipidemia, it is a potent independent risk factor for stroke, increasing the risk 2-fold compared with nondiabetics (105). The combination of diabetes and hypertension increases the risk of stroke 6-fold higher than in normal patients, and 2-fold higher than normotensive diabetics. Although tight glycemic control is unequivocally useful for prevention of microvascular complications (nephropathy, neuropathy, retinopathy) (106), the benefit for stroke reduction is less certain.

Obesity

Abdominal obesity contributes more than body mass index to the presence of insulin resistance, hypertension, dyslipidemia, and the risk for stroke (107,108). There are no reports demonstrating reduction in stroke risk with weight loss, although diet and exercise are prudent because of their beneficial impact on hypertension, hyperlipidemia, and insulin resistance.

Other Risk Factors

Elevated fibrinogen, C-reactive protein, and blood homocysteine levels are each independently associated with increased risk of cardiovascular disease and stroke, although dietary supplementation with vitamin B or folic acid does not alter this risk (109–111). There is an increased risk of stroke in women using oral contraceptives, although most of the risk appears to be concentrated in smokers and women

older than 35 years of age; women under the age of 35 appear to have a low risk if other risk factors are absent (112). A stroke risk profile can assess the risk of stroke based on age, systolic blood pressure, antihypertensive therapy, diabetes, cigarette smoking, and history of coronary artery disease, congestive heart failure, left ventricular hypertrophy, or atrial fibrillation, although other factors (ethnicity, severity of carotid stenosis, history of TIA or stroke) are not included in this profile (113).

Pharmacological Therapy

All patients with carotid artery disease should be placed on medical therapy, including antiplatelet therapy and other medications to treat modifiable atherogenic risk factors. For asymptomatic patients with one or more risk factors for atherosclerosis, antiplatelet therapy is indicated for primary prevention of cardiovascular events. For symptomatic patients (recent TIA or minor CVA), the recommendations for antiplatelet therapy are based on large stroke prevention studies (114–126) that included patients with different stroke etiologies (Table 4).

Aspirin

Primary prevention trials show that aspirin decreases the risk of first MI in men, but has little impact on the risk of ischemic stroke. In contrast, in one large primary prevention trial in women, aspirin lowered the risk of stroke without affecting the risk of MI or death (127). Aspirin is approved for secondary prevention in persons with a history of TIA or stroke. The relative risk reduction is 16% for fatal stroke and 28% for nonfatal stroke (128). Aspirin for 3 weeks after acute stroke prevents 9 subsequent strokes per 1,000 treated; 29 months of treatment prevents 36 events per 1,000 treated. Based on randomized trials, aspirin is superior to CEA for symptomatic patients with carotid stenosis less than 50% (18,19,37,38) and for asymptomatic patients with carotid stenosis less than 60% (22,23). Early studies suggested benefit with low-dose aspirin (114–116). The risk of MI, stroke, and death within 1 to 3 months of CEA was lower for patients taking low-dose aspirin (81 mg or 325 mg daily) than for high-dose aspirin (650 mg or 1,300 mg daily) (117). There are no data to support the use of aspirin in doses greater than 325 mg daily, even in patients with recurrent TIAs despite low-dose aspirin.

Dipyridamole

Dipyridamole is not recommended for primary prevention of cardiovascular disease or stroke. The role of dipyridamole for secondary prevention of stroke is supported by 2 trials. Extended-release dipyridamole alone and extended-release dipyridamole plus aspirin were superior to placebo, but extended-release dipyridamole alone was no different than aspirin alone in the second ESP II (European Stroke Prevention Study) (118). In the ESPRIT (European/Australian Stroke Prevention in Reversible Ischemia Trial), extended-release dipyridamole plus aspirin was superior to

Table 4. Major Antithrombotic Therapy Trials for Secondary Stroke Prevention After TIA/Stroke

Trial	N	Drugs	Dose (mg)	Follow-Up (months)	Outcome	Hazard Ratio
SALT (114)	1,360	ASA Placebo	75	32	MI, stroke, death	0.82 ($p = 0.02$)
UK TIA (115)	2,435	ASA ASA Placebo	1,200 300	48	MI, stroke, death	0.85 ($p = 0.01$) for combined ASA vs. placebo
Dutch TIA (116)	3,131	ASA ASA	30 283	30	MI, stroke, vascular death	0.97 ($p = ns$)
ACE (117)	2,849	ASA ASA	81 or 325 650 or 1,300	3	MI, stroke, death	0.74 ($p = 0.03$)
ESPS II (118)	6,602	ERDP ASA ASA/ERDP Placebo	400 50 50/400	24	Stroke, death	0.85 ($p = 0.015$) 0.87 ($p = 0.016$) 0.76 ($p = 0.001$)
ESPRIT (119)	2,739	ASA ASA/ERDP	30–325 30–325/400	42	Major bleeding, MI, stroke, vascular death	0.80 ($p = 0.05$)
CATS (120)	1,072	Ticlopidine Placebo	500	24	MI, stroke, vascular death	0.77 ($p = 0.02$)
TASS (121)	3,069	Ticlopidine ASA	500 1,300	36	MI, stroke, death	0.88 ($p = 0.05$)
CAPRIE (122)	19,185	Clopidogrel ASA	75 325	22	MI, stroke, vascular death	0.93 ($p = 0.04$)
MATCH (123)	7,599	Clopidogrel ASA/clopidogrel	75 75/75	18	MI, stroke, rehospitalization, and vascular death	0.94 ($p = ns$)
CHARISMA (124)	15,603	ASA/clopidogrel ASA	75–162/75 75–162	28	MI, stroke, vascular death	0.93 ($p = ns$)
WARSS (125)	2,206	Warfarin ASA	INR 1.4–2.8 325	24	Stroke, death	1.13 ($p = ns$)
WASID (126)	569	Warfarin ASA	INR 2–3 1,300	21	Stroke, vascular death	1.04 ($p = ns$)

ACE = ASA and carotid endarterectomy; ASA = aspirin; CAPRIE = Clopidogrel Versus Aspirin in Patients at Risk of Ischemic Events; CATS = Canadian-American Ticlopidine Study; CHARISMA = Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance; ERDP = extended release dipyridamole; ESPS = European Stroke Prevention Study; ESPRIT = European/Australian Stroke Prevention in Reversible Ischemia Trial; INR = international normalized ratio; MATCH = Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance; MI = myocardial infarction; SALT = Swedish Aspirin Low-Dose Trial; TASS = Ticlopidine Aspirin Stroke Study; TIA = transient ischemic attack; UK = United Kingdom; WARSS = Warfarin Aspirin Recurrent Stroke Study; WASID = Warfarin Aspirin Symptomatic Intracranial Disease.

aspirin alone for the secondary prevention of MI, stroke, or vascular death (119). Extended-release dipyridamole plus aspirin is being tested against clopidogrel in the PROFESS (Prevention Regimen for Effectively Avoiding Second Strokes) trial.

Thienopyridines

Ticlopidine and clopidogrel have not been evaluated in large studies for primary prevention of major cardiovascular outcomes. Ticlopidine was useful for secondary prevention after stroke in the CATS (Canadian-American Ticlopidine Study) trial, and resulted in a 23% reduction in cardiovascular events compared with placebo (120). The TASS (Ticlopidine Aspirin Stroke Study) studied patients after TIA or major stroke (121); ticlopidine caused significantly fewer cerebrovascular events and less bleeding, but neutropenia complicated therapy in 0.9% of patients.

Clopidogrel has largely replaced ticlopidine because of a superior safety profile and once daily dosing. For preventing stroke in secondary prevention trials, clopidogrel was similar to aspirin in the CAPRIE (Clopidogrel Versus Aspirin in Patients at Risk of Ischemic Events) trial (122). The

combination of clopidogrel plus aspirin was similar to aspirin alone in the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) trial (124). In the MATCH (Atherothrombosis with Clopidogrel in High-Risk Patients With Recent Transient Ischemic Attack or Ischemic Stroke) trial, the combination of aspirin plus clopidogrel increased the risk of systemic and intracerebral hemorrhage, but did not decrease the risk of stroke compared with clopidogrel alone (123). In summary, aspirin and clopidogrel appear to have similar efficacy for secondary prevention of stroke, but the combination may increase the risk of serious bleeding, and is not superior to either drug alone.

Antiplatelet Treatment Failures

Recurrent events can occur despite therapy with antiplatelet agents. One treatment option is the addition of warfarin therapy. Another treatment option, given the issue of aspirin or clopidogrel nonresponders, is dual antiplatelet therapy with aspirin plus clopidogrel. In some cases, triple drug therapy with aspirin and clopidogrel, plus either aspirin/dipyridamole, cilostazol, or warfarin may be war-

ranted. None of these options are based upon clinical trial evidence, and there may be a higher risk of bleeding.

Warfarin

Unless contraindicated, warfarin is recommended for primary and secondary prevention of stroke in patients with atrial fibrillation. However, in patients with noncardioembolic stroke enrolled in the WARSS (Warfarin Aspirin Recurrent Stroke Study) trial, there were no differences between warfarin and aspirin in stroke, death, or major bleeding (125). Moreover, the WASID (Warfarin Aspirin Symptomatic Intracranial Disease) trial failed to show an advantage for warfarin compared with aspirin (126). Therefore, based upon extrapolation from these trials, antiplatelet therapy is favored over warfarin in patients with carotid artery disease who are not at risk for cardioembolic stroke (129).

Lipid-Lowering Therapy

Gemfibrozil reduced stroke rates by 24% in the VA-HIT (Veterans Affairs High Density Lipoprotein Cholesterol Intervention Trial) study (130). Niacin reduced stroke by 22% compared with placebo in the Coronary Drug Project (131). Pravastatin, simvastatin, and atorvastatin are approved by the FDA for stroke prevention in patients with coronary artery disease (132–134) although the benefits may be mediated by anti-inflammatory, plaque stabilization, and neuroprotective effects, rather than cholesterol reduction per se. Statins may be effective for secondary prevention in patients undergoing CEA (135). The SPARCL (Stroke Prevention with Aggressive Reduction of Cholesterol Levels) trial studied atorvastatin 20 mg for secondary prevention of stroke in 4,731 patients without coronary artery disease and documented a 16% relative risk reduction for recurrent stroke (136,136a). The National Cholesterol Education Program (NCEP) guideline recommends statins in patients with prior TIA or stroke or carotid stenosis greater than 50% stenosis (137). The American Stroke Association (ASA) also recommends statins for patients with ischemic TIA or stroke (138).

Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs)

In patients with hypertension, the reduction in stroke risk is directly related to the reduction in blood pressure, regardless of which antihypertensive agents are prescribed. However, recent trials of ACE inhibitors and ARBs suggest that these agents may have benefits for stroke reduction that extend beyond their antihypertensive effects. The HOPE (Heart Outcomes and Prevention Evaluation) trial studied 9,297 patients with high cardiovascular risk, including 1,013 patients with previous TIA or stroke (139). Patients were randomized to ramipril 10 mg daily or placebo, and ramipril was associated with a 32% reduction in stroke over 5 years. Although ramipril was associated with a significant

antihypertensive effect (2 to 3 mm Hg decline in systolic and diastolic blood pressure) and less carotid intima-media thickening (140), these benefits were felt to be insufficient to explain the dramatic decline in stroke. The PROGRESS (Perindopril Protection Against Recurrent Stroke Study) trial also supported the benefits of blood pressure lowering with ACE inhibitors (141). In the LIFE (Losartan Intervention for Endpoint) trial (142), losartan and atenolol achieved similar degrees of blood pressure reduction, but losartan was associated with a 13% reduction in cardiovascular events and a 25% reduction in stroke. Besides blood pressure reduction, other potential benefits of ACE inhibitors and ARBs include inhibition of angiotensin II-mediated vasoconstriction and vascular smooth cell proliferation, improved endothelial function, and enhanced fibrinolysis.

CEA

Historical Perspective

Before 1950, the etiologies of stroke were poorly defined and there was no definitive treatment. After the association between carotid bifurcation disease and stroke was recognized (143), the first successful CEA was performed in 1953, but was not reported until 1975 (144). The first published report of carotid revascularization was in 1954 (145). By the early 1980s, CEA was the most frequently performed vascular surgical procedure. However, the failure of the external carotid–internal carotid bypass operation to prevent stroke (146) and the absence of clinical trial data provoked challenges about the safety and efficacy of CEA (147). Subsequently, in the late 1980s and early 1990s, 6 randomized clinical trials established the efficacy of CEA plus aspirin compared with aspirin alone in preventing stroke in patients with atherosclerotic carotid bifurcation stenosis (18,19,22,23,37,38,148,149). CEA is now the standard revascularization therapy against which CAS must be compared.

Technique

CEA operative technique was developed prior to the understanding that embolization was the most common pathophysiologic mechanism underlying TIA and stroke in the carotid distribution. Initially, TIA and stroke were attributed to diminished blood flow across a severe carotid stenosis, so it was fortuitous that CEA addressed the etiologic plaque, irrespective of stenosis severity or embolic potential. From a technical standpoint, controversial issues include the type of anesthesia (general vs. local) (150), the type of endarterectomy (eversion vs. standard open endarterectomy) (151), the need for and type of intraoperative cerebral monitoring, and the need for carotid shunting and patch repair.

Most perioperative strokes are due to embolization rather than hypoperfusion, and the risk of stroke is similar, with or

Table 5. Randomized Trials of CEA Versus Medical Therapy for Carotid Artery Stenosis

Trial	N	Stenosis	Follow-Up	End Point	Medical (%)	CEA (%)	p	RRR (%)	ARR (%)	NNT
Symptomatic										
ECST (38)	3,018	≥80%	3 yrs	Major stroke or death	26.5	14.9	<0.001	44	11.6	8.6
NASCET (18)	659	≥70%	2 yrs	Ipsilateral stroke	26	9	<0.001	65	17	5.9
VA 309 (148)	189	>50%	1 yr	Ipsilateral stroke or TIA or surgical death	19.4	7.7	0.011	60	11.7	8.5
NASCET (19)	858	50%–69%	5 yrs	Ipsilateral stroke	22.2	15.7	0.045	29	6.5	15.4
NASCET (19)	1,368	≤50%	5 yrs	Ipsilateral stroke	18.7	14.9	0.16	20	3.8	26.3
Asymptomatic										
ACAS (22)	1,662	>60%	5 yrs	Ipsilateral stroke, surgical death	11	5.1	0.004	54	5.9	16.9
ACST (23)	3,120	≥60%	5 yrs	Any stroke	11.8	6.4	0.0001	46	5.4	18.5
VA (149)	444	≥50%	4 yrs	Ipsilateral stroke	9.4	4.7	<0.06	50	4.7	21.3

ACAS = Asymptomatic Carotid Atherosclerotic Study; ACST = Asymptomatic Carotid Surgery Trial; ARR = absolute risk reduction; CEA = carotid endarterectomy; ECST = European Carotid Surgery Trial; NASCET = North American Symptomatic Carotid Endarterectomy Trial; NNT = needed to treat; RRR = relative risk reduction; TIA = transient ischemic attack; VA = Veterans Affairs.

without a shunt (152). Although a small subset of patients may have such poor collateral flow that even a 30- to 60-min period of carotid occlusion results in cerebral infarction, the vast majority of patients anticoagulated with heparin can safely tolerate a prolonged period of occlusion without shunting. Many surgeons utilize intraoperative cerebral monitoring (carotid stump pressures, intraoperative electroencephalography, TCD) and the adequacy of angiographic collaterals to identify patients in need of shunting (153–155).

After CEA, the carotid artery may be closed with or without a patch. Although patch repair seems to be associated with less early thrombosis and late restenosis (156,157), there is a 1% risk of patch “blow-out” or infection. The choice between prosthetic patch or vein patch appears to be less critical (158,159).

Observational Studies

For nonrandomized observational studies, the 30-day risk of perioperative stroke or death after CEA was approximately 7% for patients with symptomatic stenosis and 3% to 5% for patients with asymptomatic stenosis (160,161). Stroke rates were higher in women, octogenarians, after repeat CEA, and in patients undergoing formal neurological evaluation. In contrast, rates were lower for high-volume operators and high-volume centers (162,163). Follow-up ipsilateral stroke risk was 1% per year and restenosis rates ranged from 5% to 10%.

Randomized Clinical Trials

Three randomized trials compared CEA plus aspirin to aspirin alone in symptomatic patients: NASCET (18,19), ECST (37,38), and Veterans Affairs CSP 309 (148) (Table 5). The VA trial was stopped prematurely when the results of the other 2 studies were announced. Entry criteria for these trials included carotid artery stenosis and ipsilateral TIA, nondisabling stroke, or retinal infarction within 4 to 6 months. Pooled analysis of 6,092 patients

with 35,000 patient-years follow-up using uniform definitions of stenosis severity and outcome revealed a 1.1% mortality and a 7.1% incidence of stroke or death at 30 days after CEA (87). After 5 years, CEA was associated with 48% relative risk reduction in ipsilateral stroke in patients with stenosis 70% to 99%, 28% relative risk reduction in ipsilateral stroke in patients with stenosis 50% to 69%, and no benefit in patients with stenosis less than 50% (Table 6). Interestingly, subgroup analysis did not demonstrate a benefit of CEA in women with stenosis 50% to 69%, in patients with near-occlusion of the carotid artery, or in patients with retinal events.

Three randomized trials compared CEA plus aspirin with aspirin alone in asymptomatic patients: the Veterans Affairs Cooperative Study (149), ACAS (22), and ACST (23). These trials randomized 5,223 patients with 17,037 patient-years follow-up, averaging 3.3 years per patient (164). At 30 days, the risk of stroke or death after CEA was 2.9%. In comparison with aspirin alone, CEA was associated with a 31% relative risk reduction in stroke or perioperative death during the study period, but the absolute risk reduction was only 1% per year. Whereas in the pooled analysis, virtually all of the risk reduction in asymptomatic patients was in

Table 6. Risk Reduction of Any Stroke or Operative Death at 5 Years After CEA in Symptomatic Patients From 3 Randomized Clinical Trials

Stenosis (%)	ARR (%; 95% CI)	p	RRR (95% CI)
Near-occlusion	–0.1 (–10.3 to 10.2)	0.6	0.98 (0.61 to 1.59)
70–99	15.6 (9.8 to 20.7)	0.00001	0.52 (0.40 to 0.64)
50–69	7.8 (3.1 to 12.5)	0.002	0.72 (0.58 to 0.86)
30–49	2.6 (–1.7 to 6.9)	0.7	0.90 (0.75 to 1.04)
<30	–2.6 (–6.2 to 0.9)	0.03	1.17 (0.90 to 1.43)

Modified with permission from Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet* 2003;361:107–16 (87).

ARR = absolute risk reduction; CEA = carotid endarterectomy; CI = confidence interval; RRR = relative risk reduction.

men (51% relative risk reduction) rather than in women (4% relative risk reduction), and in younger patients rather than older patients, ACST demonstrated benefit for CEA in asymptomatic women with stenosis greater than 60%. Unlike CEA in symptomatic patients, outcome after CEA in asymptomatic patients was not associated with stenosis severity.

Despite the excellent design and results of the randomized trials, several concerns have been raised about CEA. First, the surgeons and the patients were carefully selected in the randomized trials, raising concern that the results might not be applicable to community practice (165). In fact, operative mortality is higher in Medicare audits (166,167) and in high-risk patients who would have been excluded from the randomized trials (168,169). Second, the standard medical therapy for the randomized CEA trials was aspirin, and many physicians believe that “best medical therapy” with statins, ACE inhibitors, and excellent risk factor control may be superior to aspirin alone (170). Although many patients in the ACST study received appropriate medical therapy, the end points of medical treatment were not specified, and the nature of the medical treatment varied with the time of patient enrollment and randomization. Finally, standard practice after CEA does not include routine evaluation by a neurologist. In a large meta-analysis of nearly 16,000 symptomatic patients with CEA, the 30-day risk of stroke and death was 7.7% if a neurologist evaluated the patient, and 2.3% if a vascular surgeon performed the evaluation (171). These data support the need for independent neurological evaluation following CEA or CAS.

Indications

Recommendations for CEA are based primarily on the symptomatic status of the patient and stenosis severity. Current AHA guidelines (93,172) recommend CEA in symptomatic patients with stenosis 50% to 99%, if the risk of perioperative stroke or death is less than 6%. For asymptomatic patients, AHA guidelines recommend CEA for stenosis 60% to 99%, if the risk of perioperative stroke or death is less than 3%. Although clinical trial data support CEA in asymptomatic patients with carotid stenosis 60% to 79% (22,23), the AHA guidelines indicate that some physicians delay revascularization until there is greater than 80% stenosis in asymptomatic patients (172). These general recommendations may be influenced by other important clinical factors (anticipated life expectancy, age, gender, and the presence of other comorbid medical conditions) and by the documented outcomes of the surgeon performing the CEA, which together may increase (or decrease) the risk of CEA and attenuate (or improve) its benefits for preventing stroke. These clinical factors and surgical outcomes must be considered when making recommendations to a specific patient. Furthermore, the 2005 guidelines from the American Academy of Neurology recommend that eligible pa-

tients should be 40 to 75 years old and have a life expectancy of at least 5 years (173).

In symptomatic patients, the greatest benefits of CEA are in elderly men with hemispheric, not ocular, symptoms (18,19). Considering the 30-day risk of stroke or death of 6%, the number of patients needed to treat (NNT) to prevent 1 stroke over a 2-year period is 6 for symptomatic stenosis greater than or equal to 70%, 20 for symptomatic stenosis 50% to 69%, and 17 for asymptomatic stenosis greater than 60% (18,22). In a combined 5-year analysis of the NASCET and ECST patients with symptomatic stenosis greater than or equal to 50% (174), the NNT is 9 for men and 36 for women; 5 for age greater than or equal to 75 years and 18 for less than 65 years; and 5 if randomized within 2 weeks of the last TIA and 125 if randomized greater than 12 weeks after the last TIA.

Contraindications

The 1998 AHA expert consensus panel recommended aspirin and risk factor modification instead of CEA when the predicted perioperative risk of stroke or death was greater than 3% for asymptomatic patients, greater than 6% for symptomatic patients, and greater than 10% for repeat CEA (172). Comorbid medical conditions and anatomic features that are associated with increased complications after CEA are listed in Table 7.

Complications

Potential complications after CEA are shown in Table 8, and include cardiovascular complications (vasovagal and vasodepressor reaction, myocardial infarction), neurological complications (stroke, hyperperfusion syndrome, intracranial hemorrhage, seizures, cranial nerve injury), wound problems (infection, hematoma), injury to the carotid artery (dissection, thrombosis, restenosis), and death. Risk factors for stroke or death after CEA are shown in Table 9. Except for cranial nerve injuries (most of which resolve within 30 days), the complications observed after CEA may also be observed after CAS.

CAS

Historical Perspective

The first balloon angioplasty for carotid stenosis was performed in 1979; reports in the early 1980s (175–178) included a balloon occlusion system to reduce embolic complications (177). Although the first balloon-expandable stent was deployed in the carotid artery in 1989, these stents were prone to extrinsic compression, and major adverse events occurred in more than 10% of patients at 30 days (179,180). Subsequently, issues about stent deformation were resolved by use of the self-expanding Wallstent (181) and later by self-expanding nitinol stents.

However, risk of embolic stroke was the major concern that limited early enthusiasm for endovascular treatment. Initial strategies focused on neurological rescue with intra-

Table 7. High-Risk Criteria for CEA

Anatomical Criteria	Medical Comorbidities
Lesion at C-2 or higher	Age ≥ 80 yrs
Lesion below clavicle	Class III/IV congestive heart failure
Prior radical neck surgery or radiation	Class III/IV angina pectoris
Contralateral carotid occlusion	Left main/≥2 vessel coronary disease
Prior ipsilateral CEA	Urgent (<30 days) heart surgery
Contralateral laryngeal nerve palsy	LV ejection fraction ≤30%
Tracheostoma	Recent (<30 days) myocardial infarction
	Severe chronic lung disease
	Severe renal disease

CEA = carotid endarterectomy; LV = left ventricular.

arterial fibrinolytic agents and/or catheter-directed techniques to dissolve, dislodge, or remove embolic debris, but angiography was unable to identify a lesion amenable to neurological rescue in some patients, and rescue efforts were unsuccessful in others. Accordingly, treatment strategies shifted from neurological rescue to neurological protection, utilizing specialized EPDs to capture and remove embolic debris that were generated during the course of the interventional procedure. With the evolution and maturation of CAS equipment and technique, CAS is now a reasonable alternative to CEA, particularly in patients at high risk for CEA. Many nonrandomized and randomized CAS clinical trials have been performed (Table 10).

Technique

From a clinical standpoint, the main goal of carotid revascularization is to prevent stroke, and since most strokes are due to thromboembolism, most experts feel that it is more important to reduce the risk of embolization than to completely eliminate the carotid stenosis. Fortunately, both

Table 8. Potential Complications of Carotid Endarterectomy

Cardiovascular
Hypertension (20%)
Hypotension (5%)
Myocardial infarction (1%)
Wound
Infection (1%)
Hematoma (5%)
Neurological
Hyperperfusion syndrome
Intracerebral hemorrhage
Cranial nerve injury (7%)
Seizures
Stroke (2%–6%)
Carotid artery
Carotid artery thrombosis
Carotid artery dissection
Restenosis (5%–10%)
Death (1%)

Table 9. Risk for Periprocedural Stroke or Death After Carotid Endarterectomy

Characteristic	OR (95% CI)	p
Symptomatic vs. asymptomatic	1.62 (1.45–1.81)	<0.0001
Hemispheric vs. ocular TIA	2.31 (1.72–3.13)	<0.001
Urgent vs. non-urgent	4.9 (3.4–7.1)	<0.001
Reoperation vs. primary	1.95 (1.21–3.16)	<0.018

Modified with permission from Bond R, Rerkasem K, Rothwell PM. Systematic review of the risks of carotid endarterectomy in relation to the clinical indication for and timing of surgery. *Stroke* 2003;34:2290–301 (160).

CI = confidence interval; OR = odds ratio; TIA = transient ischemic attack.

plaque passivation and lumen enlargement can be readily accomplished by CAS and by CEA. From a technical standpoint, the main goals of CAS are to enlarge the lumen by successful placement of the EPD and stent, without complications. Imaging of the carotid artery and intracranial circulation before and after CAS and successful management of the vascular access site are also technical goals.

Carotid Access

Selection of equipment for CAS is most dependent on the anatomy of the aortic arch and of the CCA proximal to the target lesion. While most operators prefer a retrograde femoral artery approach to access the CCA, a right brachial or radial approach may facilitate access to an anomalous left carotid artery originating from the proximal innominate artery. Access to the CCA involves using either a guiding catheter or an interventional sheath. The choice of technique is largely dependent on operator preference, although there are several anatomic factors that might favor one technique over another. When treating patients with simple arch and carotid anatomy, a 6-F interventional sheath or an 8-F guiding catheter will permit the operator to acquire excellent images, and advance and retrieve the interventional equipment, since both have similar internal diameters (0.087 to 0.090 inches). When using an interventional sheath or multipurpose guiding catheter, the tip is usually positioned in the distal CCA, a few centimeters below the carotid bifurcation. When using a more aggressive guiding catheter shape, the tip of the guide is usually positioned in the proximal (intrathoracic) segment of the CCA, although this generally provides less support for the procedure. Careful attention to the placement of the tip of guiding catheter or interventional sheath will help prevent spasm, thrombosis, or dissection. Strict management of catheter flushing and elimination of air will help avoid emboli.

Carotid Artery Angioplasty and Stenting

An activated clotting time (ACT) of 250 to 300 s should be confirmed after access has been achieved with the guiding catheter or interventional sheath. The next phase of the intervention requires placement of the EPD, angioplasty and stenting of the target lesion, and retrieval of the EPD (Fig. 5). Since proximal EPDs are not yet available in the U.S., the discussion below pertains to the use of distal

Table 10. Acronyms for CAS Registries and Clinical Trials

ACT	Asymptomatic Carotid Stenosis Stenting vs. Endarterectomy Trial
ARCHer	Acculink for Revascularization of Carotids in High-Risk Patients
BEACH	Boston Scientific EPI: A Carotid Stenting Trial for High Risk Surgical Patients
CABANA	Carotid Stenting Boston Scientific Surveillance Program
CABERNET	Carotid Artery Revascularization using Boston Scientific EPI Filterwire EX/EZ and the EndoTex NexStent
CAPTURE	Carotid Acculink/Accunet Post Approval Trial to Uncover Rare Events
CaRESS	Carotid Revascularization using Endarterectomy or Stenting Systems
CASES-PMS	Carotid Stenting with Emboli Protection Surveillance-Post-Marketing Study
CREATE	Carotid Revascularization with ev3 Arterial Technology Evaluation
CREST	Carotid Revascularization: Endarterectomy versus Stent Trial
ELOCAS	European Long-term Carotid Artery Stenting Registry
EMPIRE	EMPIRE Embolic Protection with Reversed Flow
EVA-S3	Endarterectomy Versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis
ICSS	International Carotid Stenting Study (CAVATAS II)
MAVERIC	Evaluation of the Medtronic AVE Self-expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis
MO.MA	Multicenter Registry to Assess the Safety and Efficacy of the MO.MA Cerebral Protection Device During Carotid Stenting
PASCAL	Performance and Safety of the Medtronic AVE Self Expandable Stent in the Treatment of Carotid Artery Lesions
PRINCE	Prospective Investigation of Nitinol Carotid Stent with Embolic Filter
ProCAS	Prospective Registry of Carotid Angioplasty and Stenting
ProCAR	Protégé Stent in the Treatment of Carotid Artery Stenosis with Adjunctive Use of a Filter Embolic Protection Device
RULE-Carotid	Rubicon Filter-Carotid
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy
SECURITY	Registry Study to Evaluate the NeuroShield Bare Wire Cerebral Protection System and X-Act Stent in Patients at High Risk for Carotid Endarterectomy
SHELTER	Stenting of High-risk Patients with Embolic Removal
SPACE	Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy
VIVA	Vivexx Carotid Revascularization Trial
XACT	Emboshield and Xact Post Approval Carotid Stent Trial

EPDs. Although issues about the EPD will be discussed later, it is important to emphasize here that it is most desirable to deploy the EPD first, before any intervention is performed on the target lesion. Although it is less desirable to dilate the lesion before the distal circulation is protected, this may be necessary using a 2 mm balloon to facilitate passage of the distal EPD.

In the context of CAS, balloon angioplasty is an adjunctive technique that serves to dilate the carotid stenosis before and after stenting. Several general caveats are worth emphasizing. First, the target lesion should be subjected to as little mechanical injury as possible, to minimize the risk of embolization. Second, after placement of the EPD, undersized angioplasty balloons (3 to 4 mm in diameter and 15 to 40 mm in length; a balloon:ICA ratio of 0.5 to 0.6) are selected to allow passage of the stent delivery system. Failure to predilate the lesion may impair the operator's ability to remove the stent delivery catheter. Third, undersized angioplasty balloons (4.5 to 6 mm in diameter and 15 to 30 mm in length; a balloon:ICA ratio of 0.6 to 0.8) are selected to expand the stent.

The goal of CAS is to passivate the lesion and decrease the risk of stroke; a moderate residual stenosis (30% to 40%) is acceptable. Carotid stent operators generally do not pursue a perfect angiographic result for several reasons.

First, multiple and aggressive balloon inflations appear to increase the risk of complications. Accordingly, 2 balloon inflations are reasonable, 1 before and 1 after stent deployment. Second, the most common reason for moderate residual stenosis after stenting is heavy calcification of the target lesion, which generally does not respond to repeated balloon inflations. Third, self-expanding stents have a tendency to continue to expand the lumen after the procedure, and it is possible that a moderate residual stenosis immediately after intervention may remodel into a mild residual stenosis a few months later. Finally, hemodynamic perturbations such as vasovagal or vasodepressor reactions may limit the number of balloon inflations. In any case, late endothelialization of the stent will likely decrease the risk of stroke, even if a moderate residual stenosis persists.

The choice of stents is straightforward. Balloon-expandable stents are generally used for intrathoracic lesions at the origin of the CCA. However, over 90% of stenoses involve the cervical portion of the distal CCA or proximal ICA. For these stenoses, self-expanding stents are preferable to balloon-expandable stents because of superior conformability and resistance to stent deformation during neck movement or compression. Nitinol self-expanding stents are preferred by most operators over stainless steel stents because of better conformability, lack

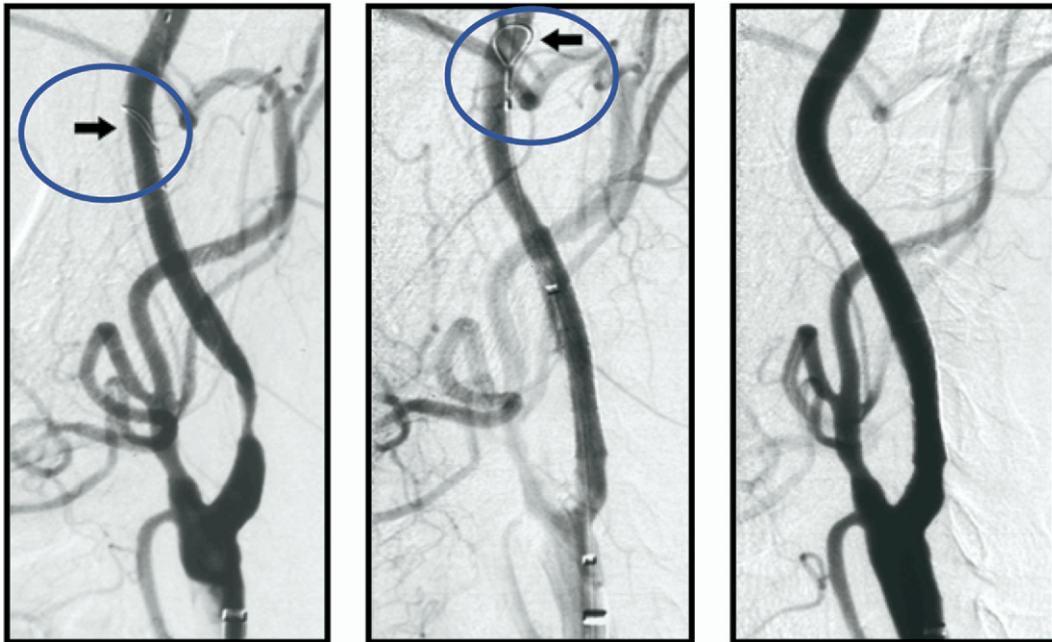


Figure 5. Carotid Embolic Protection Device and Stent Deployment

of stent shortening, and predictable deployment (Table 11), although early and late results appear to be similar, regardless of stent design. All self-expanding carotid stents have delivery systems that are compatible with 0.014-inch guidewires, which is the most common platform for distal EPDs. Most companies manufacture stents with rapid exchange delivery systems. Many nitinol stents are available in tapered designs to conform to the tapered transition from the larger CCA (8 to 10 mm in diameter) to the smaller ICA (5 to 7 mm in diameter), although there are no data to suggest better outcomes compared with nontapered designs. Stent lengths (most commonly 30 to 40 mm) are usually chosen to achieve complete lesion coverage (normal-to-normal from the distal CCA to the proximal ICA).

Embolic Protection

Although the primary purpose of carotid artery revascularization is stroke prevention, CEA and CAS each have inherent risks of procedure-related stroke. Hence, excessive risk of procedure-related stroke may negate the benefits of revascularization, particularly in asymptomatic patients. Whereas the efficacy of EPDs has been established in saphenous vein graft intervention, there are no randomized studies comparing CAS with and without EPD. Nevertheless, the availability of EPDs appears to be important in reducing the risk of stroke during CAS, and physicians performing these procedures must be familiar and skilled with these devices. It seems unlikely that major CAS trials will be performed without EPDs.

Types of EPDs

There are 2 broad types of EPDs: proximal EPDs and distal EPDs (Table 12). Proximal EPDs have the theoretical advantage of providing embolic protection during all phases of the intervention, except during placement of the guiding catheter or interventional sheath. Proximal protection relies on both transient occlusion of the CCA proximal to the target lesion with 1 balloon and the ECA with a second balloon, resulting in stagnant or reversed flow in the ICA. Embolic protection is established even before the lesion is crossed with a guidewire, to reduce the risk of distal embolization. After stent deployment and adjunctive angioplasty, aspiration of blood from the carotid bifurcation removes any debris, followed by removal of the proximal EPD. Proximal EPDs are theoretically appealing, and preliminary observations from Europe support further investigation.

In contrast to proximal EPDs, distal EPDs mandate that the target lesion be crossed first with the guidewire, followed by deployment of the EPD distal to the target lesion. In all cases, the system consists of a protection device and an integrated guidewire, so that angioplasty and stenting are performed along the wire that is integrated into the distal EPD. During distal protection, embolization may occur during placement of the guiding catheter or interventional sheath (as is true with proximal protection devices), and during guidewire passage through the lesion, before the EPD is deployed.

Distal EPDs rely on 2 different approaches to embolic protection. The first relies on transient balloon-mediated

Table 11. Carotid Stents

Stent Type	Company	Name	Tapered Stent Prox/ Dist Diameter (mm) Length (mm)	Straight Stent Diameter (mm) Length (mm)
Stainless steel	Boston Scientific	Wallstent	Not available	6 (×22), 8 (×21, 29, 36), 10 (×24, 31, 37)
Open-cell nitinol	Guidant	Acculink*	10/7, 8/6 30, 40	5, 6, 7, 8, 9, 10 20, 30, 40
	Medtronic	Exponent	20, 30, 40	6, 7, 8, 9, 10 20, 30, 40
	Bard	Vivexx	12/8, 10/7, 8/6 30, 40	5, 6, 7, 8, 9, 10, 12 20, 30, 40
	ev3	Protege	10/7, 8/6 30, 40	6, 7, 8, 9, 10 20, 30, 40, 60
	Cordis	Precise*	Not available	5, 6, 7, 8, 9, 10 20, 30, 40
	Closed-cell nitinol	Endotex	NexStent	Not available
Abbott Vascular		Xact*	10/8, 9/7, 8/6 30, 40	7, 8, 9, 10 20, 30
Medinol		Nirtinol	10/7, 8/6 30, 44	5, 6, 7, 8 21, 30, 44

*Food and Drug Administration approved as of November 2006.

occlusion of the distal cervical portion of the ICA. Complete interruption of antegrade blood flow prevents embolic debris from reaching the intracranial circulation. After completion of the intervention, embolic debris is removed by manual aspiration, followed by balloon deflation and removal of the protection system. The other approach to distal protection relies on deployment of a filter device in the distal ICA (Table 13, Fig. 6). After the intervention is completed, the filter is captured and removed from the patient, along with embolic debris in the filter.

Advantages and Limitations of EPDs

All EPDs share the common goal of preventing embolic debris from reaching the intracranial circulation, leading to stroke. Large scale studies of proximal EPDs, and comparative studies of various distal EPDs, have not been performed. Available data suggest that all distal EPDs have advantages and limitations, and that the ideal device has not yet emerged. Although all distal EPDs appear to be able to capture and remove embolic debris, proper use of these devices does not ensure that distal embolization will not occur. Possible modes of failure of EPDs include inability to deliver or deploy the device to the intended location, inadvertent device-induced vessel injury or embolization, cerebral ischemia due to device-induced carotid occlusion (either from the occlusion balloon or from filter occlusion), incomplete capture or retrieval of embolic debris, or embolization into proximal branches (such as the ophthalmic artery) that might supply collaterals to the intracranial circulation (Table 14).

Early CAS Experience

In the U.S., the results of 604 CAS procedures without EPD were first published in 2001 (181). Subsequently, over 40 single-center observational studies were published. Many were limited by small numbers of patients, short-term follow-up, and inconsistent use of EPDs and independent neurological assessment. To address some of these limitations, 1 study reported the results of CAS after pooling data from 26 observational studies between 1990 and 2002, which included nearly 3,500 CAS procedures (182). This analysis revealed that stroke or death at 30 days was observed in 5.5% of patients who were treated without EPD and 1.8% of patients with EPD. Furthermore, CAS without EPD was associated with more major (1.1% vs. 0.3%) and minor (3.7% vs. 0.5%) strokes. The benefits of improved equipment and technique, increased operator experience, and better patient selection in the later EPD trials may explain these findings.

To enhance the consistency of data collection, several large nonrandomized multicenter voluntary registries were created. As voluntary registries, the technique of CAS and independent oversight were not standardized. Nevertheless, these large registries included more than 17,000 patients and provided important observations about CAS.

The Global Carotid Artery Stent Registry (183) was a survey of 12,392 CAS procedures in 11,243 patients from 53 sites from 1997 to 2002. Technical success rate was observed in 98.9% of procedures. Event rates at 30 days included TIA in 3.1%, minor stroke in 2.1%, major stroke in 1.2%, death in 0.6%, and stroke or death in 4.7%. The risk

Table 12. Comparison of Proximal and Distal Embolic Protection

Advantages	Disadvantages
Proximal Embolic Protection With Balloon Occlusion	
Transient reversal of flow in distal ICA	More cumbersome to use than other devices; large profile, large sheath size
Operator can select a guidewire of choice	Imaging during device advancement via stagnant contrast
Avoids embolization during initial passage of guidewire and throughout procedure	Arterial occlusion may be poorly tolerated
Distal Embolic Protection With Balloon Occlusion	
Easy to use	No antegrade flow
Compatible with all stents	2%–5% are intolerant
Aspirate large and small particles	Balloon-induced injury
Reliably trap debris	Not as steerable as PTCA guidewires
	Difficult to image during the procedure
	Loss of apposition during procedure
Distal Embolic Protection With Filter Devices	
Preserve antegrade flow	May not capture all debris
Contrast imaging is possible throughout the procedure	Difficult to evaluate retrieval of debris during the procedure
Some devices allow operator to select an independent guidewire to cross target lesion	Filters may clog
	Delivery/retrieval catheters may cause embolization
	Filter entrapment in the stent
	Some EPDs are not as steerable as PTCA guidewires

EPD = embolic protection device; ICA = internal carotid artery; PTCA = percutaneous transluminal coronary angioplasty.

of stroke or death was 2.8% with EPD, 6.2% without EPD, 4.9% in symptomatic patients, and 2.9% in asymptomatic patients. At 1, 2, and 3 years of follow-up, restenosis rates by carotid duplex were 2.7%, 2.6%, and 2.4%, and new ipsilateral neurological events were observed in 1.2%, 1.3%, and 1.7%, respectively.

The Pro-CAS (Prospective Registry of Carotid Angioplasty and Stenting) included 3,853 CAS procedures from 38 sites over a 4-year period (184). Technical success was observed in 98%, and in-hospital events included TIA in 6.0%, stroke in 2.5%, and stroke or death in 2.8%. The risk of stroke or death was 2.1% with EPD, 2.2% without EPD, 3.1% in symptomatic patients, and 2.4% in asymptomatic patients.

The ELOCAS (European Long-term Carotid Artery Stenting Registry) (185) included 2,172 CAS patients from

4 centers. Technical success was observed in 99.7%, and the 30-day rate of stroke or death was 1.2%. During 1, 3, and 5 years of follow-up, restenosis was observed in 1%, 2%, and 3.4% of patients, and stroke or death occurred in 4.1%, 10.1%, and 15.1%, respectively.

Contemporary Prospective Multicenter Registries

In contrast to earlier voluntary registries, contemporary prospective multicenter registries were designed to assess the safety and efficacy of CAS with EPD in high-risk patients (Table 15). In most cases, the primary safety end point was the combined incidence of MI, stroke, or death at 30 days after CAS, and the primary efficacy end point was the incidence of ipsilateral stroke or death between 30 days and 1 year after CAS. These registries had predefined

Table 13. Comparison of Selected Distal Embolic Protection Filters

Characteristic	Spider	Filterwire	AngioGuard*†	Accunet*	Emboshield*	Interceptor‡	GFS	Rubicon‡
Manufacturer	ev3	BSC	CJJ	GDT	ABT	MDT	Gore	BSC
Material	N	N, PU	N, PU	N, PU	N, PU	N	N,PTFE,FEP	N,PU
Guidewire (inch)	0.018	0.014	0.014	0.014	0.018	0.014	0.014	0.014
RX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Independent wire	Yes	No	No	No	Yes†	No	No	No
Sheath (FR)	6	6	7	6	7	6	6	6
Vessel size (mm)	3–6	3.5–5.5	4–8	4.5–7.5	3–6	4.5–6.5	2.5–5.5	3–6
Profile (FR)	3.2	3.2	3.2–3.9	3.5–3.7	3.9	2.7	3.2	2.1–2.7
Pore size (μ)	167–209	110	100	150	140	100	100	100

*Food and Drug Administration approved as of November 2006. †Embotrac guidewire is an independent wire that must be used with the Emboshield filter to prevent filter migration and embolization. ‡Rubicon and Interceptor are deployed by remote activation, rather than by retraction of a distal constraining sheath.
 †ABT = Abbott Medical Corporation; BSC = Boston Scientific Corporation; CJJ = Cordis/Johnson & Johnson Inc.; FEP = fluorinated ethylene propylene; FR = French; GDT = Guidant Corporation; GFS = Gore Filter System; MDT = Medtronic Corporation; N = nitinol; PTFE = polytetrafluoroethylene; PU = polyurethane; RX = rapid exchange.

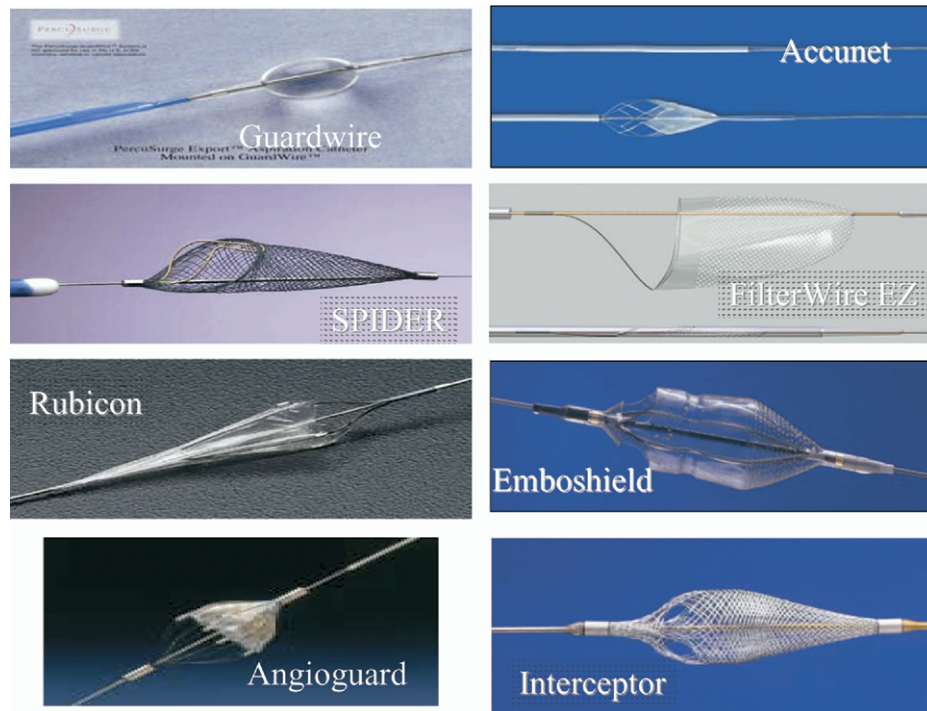


Figure 6. Examples of Filter-Type Embolic Protection Devices

inclusion and exclusion criteria, independent neurological assessment before and after CAS, and oversight committees to ensure patient safety and adherence to protocol requirements. In many cases, these registries were conducted as IDE trials to acquire FDA marketing approval in the U.S. or CE marking approval in Europe. In other cases, registries were performed after device approval, as part of FDA requirements for post-marketing approval (PMA), to evaluate safety and efficacy end points in larger numbers of patients. For the most part, inclusion and exclusion criteria were similar among the various registries, and included clinical and anatomical features that would be considered high risk for CEA (Table 6). Since these registries did not employ a control group, sponsors of the studies utilized a historically weighted estimate of stroke or death of 14.5% at 30 days after CEA.

At the time of this writing, the results have been published for 3 multicenter prospective CAS registries in high-risk patients (186–188).

The BEACH (Boston Scientific EPI: A Carotid Stent for High Risk Surgical Patients) study (186) enrolled 747 symptomatic and asymptomatic high-risk patients (189 roll-in patients, 480 patients in the pivotal trial, 78 patients in a bilateral stent registry). Technical success was achieved in 98.2% of patients. The incidence of MI, stroke, and death at 30 days was 5.8% for all patients, and at 1 year was 9.1% for pivotal patients, 8.7% in the roll-in group, and 7.1% in the bilateral stent group.

The CREATE (Carotid Revascularization with ev3 Arterial Technology Evolution) study (187) was a prospective nonrandomized multicenter registry of 419 patients with severe carotid stenosis and 1 or more high-risk features for CEA. Technical success was achieved in 97.4% and major adverse events at 30 days were observed in 6.2%, including MI in 1%, non-fatal stroke in 3.3%, and death in 1.9%. Independent predictors of stroke or death at 30 days included duration of filter deployment, symptomatic carotid

Table 14. Potential Modes of Failure of Embolic Protection Devices

Inability to deliver or deploy the device
Large device profile
Lack of steerability
Excessive vessel tortuosity
Device-induced complications
Injury to the internal carotid artery from the guidewire or protection device
Embolization due to passage of the device through the lesion
Cerebral ischemia
Patient intolerance due to balloon occlusion
Filters may become packed with debris causing flow limitations
Incomplete capture or retrieval of debris
Pores in filter may allow passage of small particulate debris
Burden of debris may overwhelm the protection device
Incomplete apposition of device to carotid wall may allow embolization
Embolization into proximal branches
External carotid (ophthalmic artery)

Table 15. Carotid Artery Stent Registries

Registry	N	Stent	EPD	Comments*
ARCHeR	581	Acculink	Accunet	30 days MI/stroke/D 8.3%* 1 yr stroke/D 9.6%
BEACH	480	Wallstent	FilterWire	30 days MI/stroke/D 5.8%* 1 yr MI/stroke/D 9.1%
CABERNET	454	NexStent	FilterWire	30 days MI/stroke/D 3.8% 1 yr MI/stroke/D 4.5%
CAPTURE	2,500	RX Acculink	Accunet	30 days MI/stroke/D 5.7%
CaRESS	143	Wallstent	Guardwire Plus	30 days stroke/D 2.1%
CREATE Pivotal	419	Protege	SPIDER OTW	30 days MI/stroke/D 6.2%*
CREATE SpideRx	125	Acculink	SpideRx	30 days MI/stroke/D 5.6%
CREST	749	RX Acculink	RX Accunet	30 days stroke/D 4.4%
MAVeRIC I	99	Exponent	GuardWire	30 days MI/stroke/D 5.1%
MAVeRIC II	399	Exponent	GuardWire	30 days MI/stroke/D 5.3%
MO.MA	157	Any	MO.MA	30 days stroke/D 5.7%
PRIAMUS	416	Any	MO.MA	30 days stroke/D 4.6%
SECURITY	398	Xact Carotid Stent	Embosfield	30 days MI/stroke/D 8.5%

*Indicates data published in peer review journals. Otherwise, data have been presented in international meetings, but not subjected to careful peer review.

ARCHeR = Acculink for Revascularization of Carotids in High-Risk Patients; BEACH = Boston Scientific EPI: A Carotid Stenting Trial for High Risk Surgical Patients; CABERNET = Carotid Artery Revascularization using Boston Scientific EPI Filterwire EX/EZ and the EndoTex NexStent; CAPTURE = Carotid Acculink/Accunet Post Approval Trial to Uncover Rare Events; CaRESS = Carotid Revascularization using Endarterectomy or Stenting Systems; CREATE = Carotid Revascularization with ev3 Arterial Technology Evaluation; CREST = Carotid Revascularization Endarterectomy versus Stent Trial; d = days; D = death; EPD = embolic protection device; MAVeRIC = Endarterectomy Versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis; MI = myocardial infarction; MO.MA = Multicenter Registry to Assess the Safety and Efficacy of the MO.MA Cerebral Protection Device During Carotid Stenting; SECURITY = Registry Study to Evaluate the NeuroShield Bare Wire Cerebral Protection System and X-Act Stent in Patients at High Risk for Carotid Endarterectomy.

stenosis, and baseline renal insufficiency. The SpideRx trial was a prospective registry of 125 high-risk patients who underwent CAS using the rapid-exchange version of the Spider Distal Embolic Protection System and the Acculink carotid stent. Technical success was achieved in 97.5% of patients, and major adverse cardiac and cerebrovascular events at 30 days after CAS were observed in 5.6%.

The ARCHeR (Acculink for Revascularization of Carotids in High-Risk Patients) trial (188) enrolled 581 patients in North America, Europe, and Argentina, including 158 patients treated without EPD (ARCHeR-1), 278 patients with EPD (ARCHeR-2), and 145 patients using a rapid-exchange EPD (ARCHeR-3). Inclusion criteria included symptomatic stenosis greater than 50% or asymptomatic stenosis greater than 80% and at least 1 high-risk feature. The primary end point was a composite of MI, stroke, or death at 30 days, plus ipsilateral stroke between 31 days and 1 year. The 30-day event rate was 8.3%, and the composite 1-year event rate was 9.6%.

At the time of this writing, the results of other high-risk registries have not been subjected to peer review, but have been presented at several international meetings. Data for these registries should be considered preliminary, and the future published data may differ slightly from the content of this document. The SECURITY (Registry Study to Evaluate the Neuroshield Bare Wire Cerebral Protection System and X-Act Stent in Patients at High Risk for Carotid Endarterectomy) registered 398 patients with symptomatic stenosis greater than or equal to 50%, asymptomatic stenosis greater than or equal to 80%, and at least 1 high-risk feature. The 30-day rate of MI, stroke, or death was 8.5% (see <http://www.fda.gov/cdrh/mda/docs/p040038.html>).

The MAVeRIC (Evaluation of the Medtronic AVE Self-expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis) trial enrolled 99 high-risk patients in phase I (MAVeRIC-I) and 399 patients in phase II (MAVeRIC-II) (189). The incidence of MI, stroke, or death at 30 days was 5.1% in MAVeRIC-I and 5.3% in MAVeRIC-II.

The CABERNET (Carotid Artery Revascularization using Boston Scientific EPI Filterwire EX/EZ and the EndoTex NexStent) trial enrolled 454 high-risk patients, including patients with symptomatic stenosis greater than 50% or asymptomatic stenosis greater than 60% (189a). The incidence of MI, stroke, or death was 3.8% at 30 days and 4.5% at 1 year.

There are 4 large post-marketing surveillance registries that are in various stages of completion at the time of this writing. Inclusion and exclusion criteria and study end points are similar to other high-risk registries. Enrollment in the CASES (Cordis/Johnson & Johnson; Angioguard filter and Precise stent) registry has been completed, but results are not yet available. Enrollment in the XACT (Abbott Vascular; Embosfield filter and Xact stent) registry and the CABANA (Boston Scientific; Filterwire EZ and carotid Wallstent) registry are ongoing at this time. The CAPTURE (Carotid Rx Acculink/Rx Accunet Post Approval Trial to Uncover Unanticipated or Rare Events) registry enrolled 2,500 high-risk patients (189b). Patients were treated by 315 physicians with a broad range of CAS experience, including interventional cardiologists, interventional radiologists, interventional neuroradiologists, vascular surgeons, and neurosurgeons. Within 30 days after CAS, the incidence of MI, stroke, or death was

5.7% and of major stroke or death was 2.5%. The risk of stroke was not related to operator experience, but was higher in octogenarians.

Early Randomized Clinical Trials

Early randomized clinical trials of carotid angioplasty or CAS compared with CEA were limited by poor technology, inexperience, and lack of EPDs, and patient outcomes were very unpredictable (Table 16). The first trial enrolled symptomatic low-risk patients with carotid stenosis greater than 70% (190). After 5 of 7 CAS patients suffered a stroke, the study was terminated. The Wallstent trial was a multicenter study in patients with symptomatic stenosis greater than 60% (191). The study was stopped prematurely; the 30-day incidence of stroke or death was 12.1% after CAS and 4.5% after CEA. Another study in 104 patients with symptomatic stenosis greater than 70% and 85 patients with asymptomatic stenosis greater than 80% reported no in-hospital stroke or death after CEA or CAS (192,193). The CAVATAS (Carotid and Vertebral Artery Transluminal Angioplasty Study) was an international multicenter randomized trial in 504 patients (168), and only 22% of the angioplasty group received stents. Although stroke or death rates at 30 days occurred in 10% of patients in both groups, angioplasty was associated with less cranial neuropathy, major hematoma, MI, and pulmonary embolism, and more restenosis at 1 year (14% vs. 4%; p less than 0.001). Stroke or death at 3 years was similar (14.2%).

Contemporary Randomized Clinical Trials in High-Risk Patients

The SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) study (169,194) is the only randomized clinical trial in high-risk patients that compared contemporary CAS with EPD against CEA. A total of 334 patients were randomized, but the trial was stopped prematurely because of slow enrollment, since most of the patients initially considered for the trial were excluded because they were too high risk for CEA. Inclusion criteria included symptomatic stenosis greater than 50% or asymptomatic stenosis greater than 80%, plus at least 1 high-risk criterion. Technical success was achieved in 95.6% of CAS patients. The 30-day incidence of MI, stroke, or death was 4.8% after CAS and 9.8% after CEA ($p = 0.09$). The primary end point (composite of MI, stroke, or death within 30 days plus neurological death or ipsilateral stroke between 31 days and 1 year) occurred in 12.2% of CAS patients and 20.1% of CEA patients ($p = 0.004$ for noninferiority and $p = 0.053$ for superiority). When MI was removed, the primary end point occurred in 5.5% with CAS and 8.4% with CEA ($p = 0.36$). In patients with symptomatic stenosis, the primary end point after CAS and CEA was similar (16.8% vs. 16.5%). In asymptomatic patients, there were fewer primary end points after CAS (9.9% vs. 21.5%). At 1 year, CEA was associated with more cranial nerve palsy (4.9% vs. 0%; $p = 0.004$) and target vessel revascularization (4.3% vs. 0.6%; $p = 0.04$). The 3-year incidence of stroke (7.1% vs. 6.7%; $p =$

Table 16. Randomized CAS Versus CEA Trials

Trial	N	Patient Subset	EPD Stent	Primary End Point	Comment
Wallstent (184)	219	Low risk Symptomatic	None Wallstent	1 yr stroke/D	CAS 10.4%, CEA 4.4%; stopped prematurely
SAPPHIRE (160)	334	High risk Symptomatic, Asymptomatic	AngioGuard Precise	30 days MI/stroke/D plus 1 yr ipsilateral stroke/D	CAS 12.2%, CEA 20.1%; stopped prematurely for slow enrollment
CREST	2,500	Low risk Symptomatic, Asymptomatic	AccUNET Acculink	30 days MI/stroke/D and 4 yr ipsilateral stroke	Active enrollment
SPACE (196a)	1,183	Low risk Symptomatic	Various Various	30 days ipsilateral stroke/D	CAS 6.8%, CEA 6.3%; stopped prematurely
EVA-3S (198a)	527	Low risk Symptomatic	Various Various	30 days stroke/D and 4 yr ipsilateral stroke	CAS 9.6%, CEA 3.9%; stopped prematurely
ICSS (CAVATAS II)	1,500	Low risk Symptomatic	Various Various	30 days MI/stroke/D and 3 yr disabling stroke/D	Active enrollment
ACT-1	1,540	Low risk Asymptomatic	EmboShield Xact	30 days MI/stroke/D plus 1 yr ipsilateral stroke	Active enrollment
ACST-2	5,000	Any risk Asymptomatic	Various Various	30 days MI/stroke/D 1 yr stroke/D	Active enrollment

ACT = Asymptomatic Carotid Stenosis Stenting vs Endarterectomy Trial; ACST = Asymptomatic Carotid Surgery Trial; CAS = carotid artery stenting; CAVATAS = Carotid and Vertebral Artery Transluminal Angioplasty Study; CEA = carotid endarterectomy; CREST = Carotid Revascularization Endarterectomy vs. Stent Trial; D = death; EPD = embolic protection device; EVA = Endarterectomy Versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis; ICSS = International Carotid Stenting Study; MI = myocardial infarction; SAPPHIRE = Stenting and Angioplasty with Protection in Patients at High Risk; SPACE = Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy.

NS) and target vessel revascularization (3.0% vs. 7.1%; $p =$ NS) was similar for CAS and CEA.

A meta-analysis of 5 early and contemporary randomized clinical trials compared endovascular care and CEA, and reported no difference in stroke or death at 30 days (8.1% vs. 6.3%) (195); MI, stroke, or death at 30 days (8.1% vs. 7.8%); or stroke or death at 1 year (13.5% vs. 13.3%). The analysis was limited by the inconsistent use of stents and EPDs, failure to stratify patients by symptomatic status or surgical risk, and premature termination of 3 studies. Importantly, there was no control group that received medical therapy alone.

Randomized Clinical Trials in Progress

There are at least 6 randomized clinical trials under consideration or in progress, comparing CEA and CAS with EPD in low-risk patients (Table 16). Three studies are enrolling only symptomatic patients (SPACE [196], EVA-3S [197,198], and ICSS [199]), 2 studies are enrolling only asymptomatic patients (ACT-1 [see <http://www.ClinicalTrials.gov>] and ACST-2 [see <http://controlled-trials.com>]), and 1 study is enrolling both asymptomatic and symptomatic patients (CREST [Carotid Revascularization Endarterectomy vs. Stent Trial]) (200,201). All studies require serial follow-up by a neurologist or approved surrogate.

The CREST (200) is sponsored by the National Institute of Neurological Disorders and Stroke (NINDS) and is randomizing 1,400 symptomatic patients (carotid stenosis greater than 50% by angiography or greater than 70% by carotid duplex) and 1,100 asymptomatic patients (carotid stenosis greater than 60% by angiography or greater than 70% by carotid duplex). The primary end point is MI, stroke, or death at 30 days and ipsilateral stroke at 1 to 4 years.

The SPACE (Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy) (196,196a) enrolled 1,183 patients with symptomatic stenosis greater than 50%. There were 35 participating centers in Germany, Austria, and Switzerland. The primary outcome of ipsilateral stroke or death at 30 days occurred in 6.8% after CAS and 6.3% after CEA.

The EVA-3S (Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis) trial (197,198,198a) is a French trial that enrolled 527 patients with symptomatic stenosis greater than 70%. The primary end points of stroke or death at 30 days occurred in 9.6% after CAS and 3.9% after CEA.

The International Carotid Stenting Study (ICSS or CAVATAS-II) (199) is enrolling 1,500 patients with symptomatic stenosis greater than 70%. The primary end point is stroke or death at 30 days. Secondary outcomes include MI, stroke, or death within 30 days; cranial nerve palsy; hematoma; and restenosis greater than 70% by carotid duplex. Economic measures and quality of life will also be evaluated during 5 years of follow-up.

The ACT I (Asymptomatic Carotid Stenosis Stenting vs. Endarterectomy Trial) is enrolling 1,540 patients with asymptomatic stenosis greater than 70% and randomizing them on a 3:1 basis to CAS or CEA. The primary end point is MI, stroke, or death at 30 days plus ipsilateral stroke between 31 and 365 days. Secondary end points include target lesion revascularization, device and procedural success, ipsilateral stroke at 5 years, and economic and quality of life indicators (see <http://www.ClinicalTrials.gov>).

The ACST-2 (Second Asymptomatic Carotid Surgery Trial) will randomize 5,000 asymptomatic patients to CAS or CEA. The primary end points will be MI, stroke, or death within 30 days and stroke or death at 5 years (see <http://www.controlled-trials.com>).

The TACIT (Transatlantic Asymptomatic Carotid Intervention Trial) will study 2,400 asymptomatic patients, comparing CAS with EPDs plus optimal medical therapy to optimal medical therapy alone (see http://www.evtoday.com/PDFArticles/0806/EVT0806_17.pdf).

Other CAS Trial Designs

There are 2 other nonrandomized CAS studies that cannot be classified with other high-risk registries or randomized trials. The lead-in phase of the CREST (Carotid Revascularization: Endarterectomy versus Stent Trial) (201) included high- and low-risk patients with symptomatic and asymptomatic carotid stenosis. The 30-day risk of stroke or death was 5.7% in 229 symptomatic patients and 3.7% in 516 asymptomatic patients. Event rates rose with increasing age, and were 1.7% in patients less than 60 years, 1.3% in patients age 60 to 69 years, 5.3% in patients age 70 to 79 years, and 12.1% in octogenarians.

The CaRESS (Carotid Revascularization using Endarterectomy or Stenting Systems) study (202,203) was a nonrandomized prospective multicenter equivalent-cohort study (143 patients treated with CAS, 254 patients treated with CEA). Patients were treated according to physician discretion, and although this design introduced potential bias, outcomes were adjudicated by an independent neurologist. There was no difference in the incidence of stroke or death at 30 days (3.6% CEA vs. 2.1% CAS) or at one year (13.6% CEA vs. 10.0% CAS). A registry is recruiting 3,000 patients.

Nonatherosclerotic Disease

Carotid artery dissection causes 10% to 25% of strokes in younger people and 2% of all ischemic stroke (204). About 50% of patients with carotid dissection do not have identifiable predisposing factors to dissection, such as traumatic injury to the head and neck. Antithrombotic therapy is usually sufficient, but CAS may be useful in patients with recurrent ischemia and persistent significant stenosis (205). External beam radiation for head and neck cancer can cause carotid artery stenosis. Lesions are often long, involve the CCA, and are surgical challenges. Only anecdotal reports on CAS exist for radiation-induced carotid artery stenosis

Table 17. CMS Reimbursement Criteria for CAS*

- Patients at high risk for CEA and symptomatic stenosis $\geq 70\%$. Coverage is limited to CAS with FDA-approved stents and EPDs.
- Patients at high risk for CEA and symptomatic stenosis 50% to 69%, and who are enrolled in Category B IDE clinical trials (regulation 42 CFR 405.201), or CAS post-approval studies (Medicare NCD Manual 20.7), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1).
- Patients at high risk for CEA and asymptomatic stenosis $\geq 80\%$ who are enrolled in Category B IDE clinical trials (regulation 42 CFR 405.201), or CAS post-approval studies (Medicare NCD Manual 20.7), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1).

*Effective March 2005.

CAS = carotid artery stenting; CEA = carotid endarterectomy; CFR = Code of Federal Regulations; CMS = Centers for Medicare & Medicaid Services; EPD = embolic protection device; FDA = Food and Drug Administration; IDE = Investigational Device Exemption; NCD = National Coverage Determinations.

(206). Similarly, CAS has been reported in a few patients with fibromuscular dysplasia (207) and in Takayasu’s arteritis (208).

Indications

CAS is less invasive than CEA, and the SAPPHERE study suggests potential safety advantages when applied to high-risk patients (Table 6) with symptomatic stenosis greater than 50% and asymptomatic stenosis greater than 80% (209). In contrast, CMS reimbursement is limited to qualified institutions and physicians when using FDA-approved stents and EPDs for high-risk patients with symptomatic stenosis greater than 70% (Table 17), and for high-risk patients (symptomatic stenosis greater than 50%, asymptomatic stenosis greater than 80%) enrolled in a Category B IDE trial or post-approval study. At the present time, there is insufficient evidence to support CAS in high-risk patients with asymptomatic stenosis less than 80% or in any patient without high-risk features. The results of ongoing randomized trials will define the future role of CAS in low-risk patients. Further study is needed in asymptomatic high-risk patients to determine the relative merits of CAS compared with best medical therapy.

Table 18. Contraindications to Carotid Artery Stenting

Neurological
Major functional impairment
Significant cognitive impairment
Major stroke within 4 weeks
Anatomical
Inability to achieve safe vascular access
Severe tortuosity of aortic arch
Severe tortuosity of CCA or ICA
Intracranial aneurysm or AVM requiring treatment
Heavy lesion calcification
Visible thrombus in lesion
Total occlusion
Long subtotal occlusion (string sign)
Clinical
Life expectancy <5 yrs
Contraindication to aspirin or thienopyridines
Renal dysfunction precluding safe contrast medium administration

AVM = arterioventricular valve malfunction; CCA = common carotid artery; ICA = internal carotid artery.

Contraindications

Potential contraindications to CAS can be classified as neurological, anatomical, and clinical contraindications (Table 18).

Complications of CAS

Complications of CAS may be classified as cardiovascular complications, carotid artery injury, neurological complications, general complications related to invasive procedures, and death (usually due to cardiovascular or neurological complications) (Table 19).

Clinical Decision Making

Medical Therapy Versus Revascularization

The main goal of therapy is to minimize the risk of stroke or death due to extracranial carotid artery disease. The choice between medical therapy and revascularization should be based upon the assessment of the risk of stroke

Table 19. Potential Complications of Carotid Artery Stenting

Cardiovascular
Vasovagal reaction (5%–10%)
Vasodepressor reaction (5%–10%)
Myocardial infarction (1%)
Carotid artery
Dissection (<1%)
Thrombosis (<1%)
Perforation (<1%)
ECA stenosis or occlusion (5%–10%)
Transient vasospasm (10%–15%)
Restenosis (3%–5%)
Neurological
TIA (1%–2%)
Stroke (2%–3%)
Intracranial hemorrhage (<1%)
Hyperperfusion syndrome (<1%)
Seizures (<1%)
General
Access site injury (5%)
Blood transfusion (2%–3%)
Contrast nephropathy (2%)
Contrast reactions (1%)
Death (1%)

ECA = external carotid artery; TIA = transient ischemic attack.

over time and the risk of stroke due to revascularization itself. In medically treated patients, the risk of stroke is most dependent on symptomatic status and stenosis severity, whereas in the patient considering revascularization, the risk of procedure-related major complications (MI, stroke, or death) is most dependent on the presence or absence of high risk features (Table 6). Best medical therapy should be given to all patients, regardless of the intent to revascularize, and includes both atherosclerotic risk factor modification and antiplatelet therapy (92,93,172).

Medical therapy alone is preferred for patients in whom the risk of revascularization outweighs its benefits, including patients who are at low risk for stroke with medical therapy (symptomatic stenosis less than 50%, asymptomatic stenosis less than 60%), and those with a high risk of procedure-related stroke or death due to patient-related factors or to excessive operator complications. Current guidelines (93,172) suggest that it is reasonable to consider revascularization for patients with asymptomatic stenosis greater than 60% or symptomatic stenosis greater than 50%, provided the risk of revascularization is less than 3% and less than 6%, respectively. The nuances of this decision-making process are discussed in the following text.

Revascularization in Symptomatic Patients

The AHA and the ASA recently published guideline recommendations for revascularization in patients with symptomatic carotid stenosis (Table 20) (93). These guidelines seem to establish higher thresholds for stenosis severity for CEA in symptomatic patients who are expected to have a greater risk of complications (e.g., advanced age, presence of significant comorbidities) and/or less benefit (e.g., women, retinal TIAs) after CEA.

Revascularization in Asymptomatic Patients at Low Risk for CEA

Patients with asymptomatic carotid stenosis represent 80% to 90% of patients undergoing carotid revascularization by CEA or CAS, so management of this patient subset is extremely important. There are 2 controversial issues relating to the management of these patients, 1 dealing with the

strength of evidence for revascularization in general, and the other with the stenosis threshold for revascularization. Proponents of revascularization argue that this issue has been resolved by ACAS (22) and ACST (23), both of which demonstrated superiority of CEA and aspirin compared with aspirin alone in patients at low risk for surgical complications. In contrast, proponents of a more conservative approach suggest that ACAS is outdated, since aggressive risk factor modification and “best medical therapy” were not routine. Furthermore, although ACST was better in their approach to medical therapy, the percent of patients on statin therapy was only 17% in those randomized in 1993 to 1996 and 58% in those randomized in 2000 to 2003. Although 70% to 90% of ACST patients were taking antiplatelet, antihypertensive, and lipid-lowering treatment at the time of last follow-up, there is no available information about the attainment of current treatment goals. Clearly, further studies of revascularization therapy are warranted and should include a treatment arm of “best medical therapy” alone.

The other controversial issue is the appropriate threshold for recommending CEA. Both the ACAS and ACST studies concluded that CEA was superior to aspirin in patients with asymptomatic stenosis greater than 60%, but the ACST studies did not demonstrate any difference in the risk of stroke for increasing stenosis severity between 60% to 99% (this issue was not evaluated by the ACAS trial). Since the absolute reduction in stroke is about 1% per year for CEA compared with aspirin, it is reasonable to wonder whether the threshold for carotid revascularization of asymptomatic patients should be increased to 80%. The 1998 revised AHA guidelines (172) raised this issue and modified the earlier guidelines by recommending CEA for asymptomatic stenosis greater than 60% for patients with surgical risk less than 3%, and for asymptomatic stenosis greater than 75% for patients with surgical risk 3% to 5%. It is also notable that the AHA guidelines did not clearly indicate whether stenosis severity should be judged by angiographic or noninvasive techniques, even though most of the randomized CEA trials relied on contrast angiogra-

Table 20. AHA/ASA Recommendations for Revascularization in Symptomatic Patients

1. For patients with recent TIA or ischemic stroke within the last 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, CEA is recommended by a surgeon with a perioperative morbidity and mortality rate of <6%. Class I, Level A.
2. For patients with recent TIA or ischemic stroke and ipsilateral moderate (50% to 69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, gender, comorbidities, and severity of initial symptoms. Class I, Level A.
3. When degree of stenosis is <50%, there is no indication for CEA. Class III, Level A.
4. When CEA is indicated, surgery within 2 weeks rather than delayed surgery is suggested. Class IIa, Level B.
5. Among patients with symptomatic severe stenosis (>70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or when other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, CAS is not inferior to CEA and may be considered. Class IIb, Level B.
6. CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4%–6%, similar to that observed in trials of CEA and CAS. Class IIa, Level B.

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CAS = carotid artery stenting; CEA = carotid endarterectomy; TIA = transient ischemic attack.

phy and most surgeons rely on carotid duplex without angiography.

Randomized clinical trial data supporting revascularization only exist for CEA. If current trials of CEA versus CAS show equivalence or superiority of CAS, then CAS may become the technique of choice for patients at low risk for CEA.

Revascularization in Asymptomatic Patients at High Risk for CEA

Management is controversial for asymptomatic patients with severe carotid stenosis who are at high risk for CEA because they were excluded from the randomized trials of CEA and medical therapy. There are insufficient data in these high-risk patients to define the natural history of medically or surgically treated disease with respect to 5-year stroke-free survival, although the risks of CEA are clearly higher than in low-risk patients. It is important to recognize that the benefits of revascularization are negated if the risk of revascularization is high, and the fact that CEA is associated with more risk does not mandate that patients undergo CAS. There is a real need for additional studies of high-risk asymptomatic patients who are treated with best medical therapy, since this could be the best treatment option. In the meantime, to gather additional data, it is reasonable to enroll these high-risk patients in nonrandomized registries.

Age

With increasing age, there is an increased risk of systolic hypertension, atrial fibrillation, generalized atherosclerosis, and cerebrovascular disease, all of which contribute to the higher risk of stroke in the elderly (210). In a given patient, it may be difficult to assess the relative risk of each factor, and multiple treatments may be needed. In determining the best course of treatment for stroke prevention, it is clear that medical therapy with aspirin, beta-blockers, statins, and ACE inhibitors is safe and well tolerated, and these agents are associated with a reduction in cardiovascular morbidity and mortality, even in the elderly. In contrast, the elderly are at higher risk for complications after CEA, and many of the randomized CEA trials excluded elderly patients for this reason. Although the SAPHIRE study reported fewer adverse events in high-risk patients at 30 days and 1 year after CAS compared with CEA, the CREST study suspended enrollment of octogenarians in the lead-in phase of the study because of higher risk of stroke and death after CAS (201). In the CREATE trial (187), the strongest independent predictor of stroke at 30 days was the duration of filter deployment; age was not an independent predictor of outcome. The authors postulated that factors such as Type III aortic arch and tortuosity of the brachiocephalic circulation, both of which are common in the elderly, may predispose patients to long and complex CAS procedures, increasing the risk of complications. Accordingly, the best treatment for the elderly patient with asymptomatic carotid

stenosis is not known. It is certainly reasonable to treat with medical therapy and risk factor modification. Medical therapy alone is especially reasonable for elderly patients with a life expectancy less than 5 years. For symptomatic patients with life expectancy greater than 5 years, revascularization is reasonable, particularly in men. The choice of revascularization technique is less certain, although available data suggest that CAS may be safer and less invasive than CEA. Further study is needed to assess the relative merits of medical therapy and CAS, but in the meantime, continued enrollment in one of the high-risk CAS registries is reasonable (211).

Women

Women greater than 65 years of age, African-American women, and female diabetics have a greater risk of atherosclerosis and stroke compared with their younger, Caucasian, and nondiabetic counterparts, and aspirin is reasonable in these high-risk subgroups for primary prevention of stroke. Data from the NASCET study (18,19) suggest that symptomatic women with carotid stenosis 70% to 99% have better stroke-free survival after CEA than with aspirin alone, but the symptomatic women with 50% to 69% stenosis did not benefit from CEA. In asymptomatic women in the ACAS trial (22), there was no benefit of CEA compared with aspirin, but the ACST study (23) suggested modest benefit for CEA in women. The discordance in benefits of CEA for women compared with men appears to be due to a higher risk of complications after CEA in women (174). In contrast, there are no reported gender differences in stroke or death at 30 days or 1 year after CAS in the high-risk registries. Further study is needed in high- and low-risk women with asymptomatic and symptomatic carotid stenosis. In the meantime, women should be enrolled without bias in the ongoing CAS registries and randomized trials, as long as they meet appropriate inclusion and exclusion criteria.

Need for CABG in Patients With Carotid Stenosis

In patients who require CABG, the risk of perioperative stroke is 4-fold higher in those with a past history of TIA or stroke and 10-fold higher in asymptomatic patients with carotid stenosis greater than 75% (212). Patients being considered for cardiac surgery should undergo a preoperative carotid duplex exam if any of the following are present: carotid bruit, age greater than 65 years, peripheral arterial disease, history of TIA or stroke, smoking, or left main coronary artery disease (24). Patients with a significant carotid stenosis are candidates for carotid revascularization. The timing and sequence of revascularization are influenced by the symptom status of the patient, the severity of disease, and the urgency of revascularization.

CABG alone is reasonable for patients with asymptomatic carotid stenosis and critical left main disease, refractory acute coronary syndromes, or other indications for urgent CABG. In contrast, patients with recent (less than 2 weeks) TIA and

carotid stenosis greater than 50% should be considered for urgent CEA, if CABG can be safely deferred for several days. The most recent guidelines (24) suggest that CEA is recommended before or concomitant to CABG in patients with symptomatic carotid stenosis greater than 50% or asymptomatic carotid stenosis greater than 80%. The risks of simultaneous CEA and CABG are not clearly higher than the risks of separate surgery and include death in 4.7%, stroke in 3.0%, and MI in 2.2% (173). If the procedures are to be staged, complication rates are lower when carotid revascularization precedes CABG. For patients who can defer CABG for 4 to 5 weeks, enrollment in one of the high-risk CAS registries is a potential option. Since CAS patients are treated with clopidogrel for one month, it is best to defer CABG for 5 weeks.

Preoperative Assessment Prior to Noncardiac Surgery

A careful neurological examination is recommended in patients with an asymptomatic carotid bruit who are anticipating noncardiac surgery. The risk of stroke is low in the absence of symptoms or neurological findings, so carotid revascularization is not necessary before noncardiac surgery. In contrast, carotid revascularization is recommended before elective surgery for symptomatic carotid stenosis greater than 50%.

Atrial Fibrillation

Cardiogenic cerebral embolism is responsible for 20% of ischemic strokes and the majority of these are associated with paroxysmal or persistent atrial fibrillation. Approximately one-third of patients with atrial fibrillation and stroke will have another cause of stroke, including carotid stenosis, so carotid duplex should be performed on all patients. For these patients, treatment is focused on chronic anticoagulation with warfarin and carotid revascularization. The indications and technique for carotid revascularization are similar to those for other patients with carotid stenosis, although some high-risk CAS registries excluded patients with atrial fibrillation.

Carotid Artery Dissection

Carotid dissection may lead to neurological injury by embolization, arterial occlusion, or pseudoaneurysm formation. With conservative management, as many as 80% of arterial dissections will heal completely. Therapy includes anticoagulation and antiplatelet therapy. In patients with recurrent ischemia and angiographic evidence of persistent dissection, CAS may be a reasonable treatment option, and is probably safer than surgery.

Intracranial Disease

Many patients with asymptomatic intracranial disease are identified during the evaluation for carotid artery disease. The presence of asymptomatic intracranial stenosis usually does not influence decision-making about extracranial carotid revascularization. For patients with symptomatic intracranial disease, a formal neurological evaluation is rec-

ommended, since these patients have a 19% risk for stroke within 2 years (213). Most CAS trials exclude patients with symptomatic intracranial disease.

Management of the Carotid Stent Patient

Preprocedural Management

CAS requires careful patient selection, procedure planning, and full disclosure of all treatment options and their associated benefits and risks. The patient should be treated with aspirin and clopidogrel for at least 24 h before the procedure, and preferably for 4 days (Table 21). Careful neurological assessment is required before and after CAS.

Intraprocedural Management

Intraprocedural management consists of mild sedation and analgesia, anticoagulation, hemodynamic monitoring and support, the technical elements of procedure performance, and neurological monitoring throughout the procedure.

Antithrombotic Medications

Once arterial access has been achieved, sufficient unfractionated heparin is given to maintain the activated clotting time between 250 to 300 s. There are no published data on low-molecular-weight heparin. The use of bivalirudin was permitted in some CAS trials, but data in large numbers of patients are not available (214). Potential advantages with bivalirudin include lower bleeding risk, rapid offset that permits early sheath removal, and no need for ACT monitoring. The benefits of glycoprotein IIb/IIIa inhibitors have not been established (215,216), so these agents are not recommended during CAS.

Hemodynamic Monitoring and Support

Continuous electrocardiographic monitoring, intra-arterial monitoring, and femoral venous access are recommended, particularly in high-risk patients. Vasovagal or vasodepressor reactions are common during the procedure, and although most reactions are transient, sustained hypotension lasting 12 to 48 h is not rare. Atropine (0.5 to 1.0 mg intravenous) may be used prior to CAS, particularly in patients with resting heart rates less than 80 beats/min. Vasopressors such as neosynephrine (10 to 100 mg/min intravenous) and dopamine (5 to 15 mcg/kg/min intravenous) should be readily available in the event hypotension does not respond readily to atropine and fluid administration. Sustained bradycardia is quite unusual, but a temporary transvenous pacemaker should be readily available. Hypertension should be treated if the systolic blood pressure is greater than 180 mm Hg, to decrease the risk of hyperperfusion syndrome and intracranial hemorrhage.

Neurological Evaluation and Rescue

The neurological status of the patient must be monitored throughout the procedure, emphasizing the level of alert-

Table 21. Sample Stent Protocol

Premedications
ASA: 81–325 mg/day × 4 days
Clopidogrel: 300–600 mg po loading, then 75 mg/day × 4 days
Preprocedure
History and physical
Neurological examination and NIH stroke scale to document preinterventional deficits
Basic laboratory tests including renal function, coagulation profile, and blood counts
Noninvasive assessment of carotid stenosis (carotid duplex, CTA, or MRA)
CT/MRI of the brain in patients with prior neurological symptoms
Arch and carotid angiography
Informed written consent
Appropriate hydration
Procedure
Mild sedation
Head restrained in a specially designed head cradle
Squeezing toy in contralateral hand
Careful monitoring of hemodynamics and cardiac rhythm
Vascular access
Intravenous heparin to maintain ACT 250–300 s
Placement of carotid sheath or guide catheter
Placement of EPD
EPD deployment
Optional intravenous atropine
Balloon inflation
Stent deployment
Repeat balloon inflation if necessary
Stent only one side if bilateral disease
Postprocedure angiography of ipsilateral carotid artery and intracranial circulation
Postprocedure
Remove sheath when ACT <150 s, vascular closure device at operator discretion
Hemodynamic monitoring
Aim for early ambulation
ASA 81–325 mg qd indefinitely
Clopidogrel 75 mg qd for at least 30 days
Neurological examination and NIH stroke scale to document postinterventional deficits
Carotid ultrasound within 30 days, 6 months, and annually

ACT = activated clotting time; ASA = aspirin; CT = computed tomography; CTA = computed tomographic angiography; EPD = embolic protection device; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; NIH = National Institutes of Health; po = by mouth; qd = daily.

ness, speech and communication, and limited motor function. These functions are readily assessed by the physician or nurse, simply by asking the patient to respond to simple questions and to squeeze a plastic toy in the contralateral hand. Heavy pre-procedural sedation should be avoided, but low-dose benzodiazepines (Versed 0.5 to 1 mg intravenous) are frequently useful to alleviate anxiety without interfering with the neurological assessment.

If patients develop manifestations of focal neurological injury during the procedure, it is generally best to complete the intervention, retrieve the EPD, and reassess the patient

clinically and angiographically. It is important to have a thorough understanding of the extracranial and intracranial arterial circulation, and to assess the suitability of the patient for neurological rescue. In some cases, removal of the protection device (or deflation of the occlusion balloon) will result in resolution of the neurological deficit. In other patients, neurological impairment may persist, and angiographic evidence for vasospasm, vascular occlusion, or discrete arterial embolization should be sought and corrected if necessary and feasible, particularly when major branches of the middle cerebral artery are involved. For patients with acute stroke and thromboembolic occlusion of a major intracranial artery while still on the table, immediate revascularization (without antecedent computed tomography [CT] or magnetic resonance imaging [MRI]) is reasonable. For physicians without experience in mechanical techniques for intracranial revascularization, consultation with a physician skilled in acute stroke intervention is crucial. Fibrinolytic therapy is not recommended for patients with neurological impairment who do not have discrete thromboembolic occlusion. Patients with profound alterations in consciousness may have hyperperfusion syndrome or intracranial hemorrhage and should be treated in an intensive care unit with neurological or neurosurgical evaluation, careful fluid and blood pressure management, and mannitol or hyperventilation for treatment of increased intracranial pressure.

Postprocedural Management

Postprocedure assessments of access site and neurological status should be routinely performed on a telemetry monitor unit. All patients should undergo a formal neurological evaluation (including assessment of National Institutes of Health [NIH] stroke scale) within 24 h of CAS, or sooner if neurological symptoms are apparent. Patients can be categorized into 3 broad groups, which dictate their management. Patients who are neurologically and hemodynamically stable (90% of patients) can usually be discharged the following day. Outpatient medications should be restarted as tolerated, aspirin should be continued for life, and clopidogrel should be given for at least 4 weeks. Carotid duplex surveillance is performed at 1 month, 6 months, and annually to assess for restenosis. Patients (5% to 10%) who are neurologically intact but with hemodynamic fluctuation (hypotension, hypertension, and/or bradycardia) require further inpatient observation and management. Fluid administration, vasoactive agents, and early ambulation are usually effective in restoring normal blood pressure. Patients with new neurological deficits (less than 5% of patients) require appropriate imaging, treatment, and intensive care unit observation.

Most neurological events are apparent during or shortly after CAS, but may be delayed for several days. Hyperperfusion syndrome and intracranial hemorrhage seem to have a bimodal distribution, and may occur within days or several weeks after revascularization by

CEA or CAS. Poorly controlled hypertension and the presence of an isolated hemisphere with high-grade bilateral stenoses may increase the risk of these complications. Patients who develop acute stroke after leaving the interventional suite should undergo immediate CT or MRI of the brain to exclude intracranial hemorrhage, and the need for angiographic evaluation and immediate revascularization should be assessed.

Interventional Suite Training, Credentialing, and Regulatory Issues

Individual operators and institutions are required by CMS to track their outcomes as a part of ongoing quality assurance. In addition, hospitals are required to maintain independent oversight of CAS outcomes by a hospital-based oversight committee. Finally, CMS facility certification requires that hospitals must make their CAS outcomes data available for review. The mandate to meet these CMS requirements has served as an impetus for the development of discrete recommendations for physician training and credentialing.

Physician Training and Credentialing

Cognitive and Technical Training

Stroke is a recognized risk of CAS and CEA. Therefore, operators must have appropriate cognitive and technical training, proficiency, and experience with CAS to maximize patient safety. Physicians interested in CAS represent a variety of subspecialties with different backgrounds, experience, and expertise. Physicians who have completed their residency and fellowship training without formal CAS instruction will need to acquire the requisite cognitive and technical skills from outside resources. They should previously have achieved a high level of proficiency in catheter-based intervention, be credentialed to perform peripheral or neurological interventions at their hospital, and complete dedicated training in CAS. In the future, CAS training will predominantly be accomplished during dedicated residency and fellowship training programs.

Professional specialty societies have recommended comprehensive training programs structured to acquire cognitive and technical skills. Detailed clinical competence statements on training and credentialing for CAS have been published by 2 multispecialty consensus groups (Tables 22 and 23): the SCAI/SVMB/SVS (Society for Cardiovascular Angiography & Interventions, Society for Vascular Medicine and Biology, and the Society for Vascular Surgery) (217), and the AAN/AANS/ASITN/ASNR/CNS/SIR (American Academy of Neurology, American Association of Neurological Surgeons, American Society of Interventional and Therapeutic Neuroradiology, American Society of Neuroradiology, Congress of Neurological Surgeons, and the Society of Interventional Radiology), collectively known as

the NeuroVascular Coalition (89). The elements for competency include requirements for cognitive, technical, and clinical skills, including cervicocerebral angiography and CAS.

These 2 documents differ in some significant ways, and their parent organizations do not feel that they are interchangeable. CMS has made it clear, however, that using criteria endorsed by the professional organization that are specific to the operator's background is appropriate. There is general agreement that proficiency in CAS requires competency in the diagnosis, management, and postprocedure care of CAS patients, and that CAS involves unique cognitive, interventional, and clinical management skills compared with those in other vascular beds. The cognitive skills include knowledge of extracranial and intracranial cerebrovascular anatomy and pathology, the clinical manifestations of stroke syndromes, the natural history of carotid disease, and the knowledge of other intracranial diseases. The technical skills include expertise in coaxial catheter manipulation, the performance and interpretation of cervicocerebral angiography, and appropriate utilization of guiding catheters, guidewires, EPDs, angioplasty balloons, and self-expanding stents in the carotid circulation. The clinical management skills include the diagnosis, management, and risk factor modification of patients with carotid and systemic atherosclerosis, as well as the use of conscious sedation and intraprocedural management of the vascular, neurologic, and hemodynamic consequences of CAS.

A tiered curriculum has been developed by the SCAI that includes an evaluation of cognitive and technical expertise before SCAI certification. This approach is to address the need for training for experienced interventional cardiologists. The first tier includes intensive case-based didactic education in a board review format. The second tier consists of an online review and self-assessment modules that require successful completion prior to advancement to the third tier. The third tier reinforces case-based learning at regional simulation centers, including exposure to live cases, taped cases, and metric-based simulation cases. Trainees are expected to perform simulated cases using proctored feedback, until the expected level of proficiency is achieved. The SCAI-tiered approach demonstrates the potential for a professional society to certify new CAS operators, and may serve as a model for future training and certification for other procedures in cardiovascular medicine.

Procedure Volume

There is a learning curve associated with achieving competency in CAS, and the importance of operator experience cannot be overstated. The incidence of stroke after CAS decreases with increasing operator experience, so operator training is important for patient safety (See Part B, Technical, in Tables 22 and 23).

The first CAS training document from the ASITN/ASNR/SIR (218) and the subsequent AAN/AANS/

Table 22. SCAI/SVMB/SVS Requirements for Performance of Carotid Stenting

A. COGNITIVE: Cognitive elements including the fund of knowledge regarding cerebrovascular disease, its natural history, pathophysiology, diagnostic methods, and treatment alternatives.

I) Pathophysiology of carotid artery disease and stroke

- a) Causes of stroke
 - i. Embolization (cardiac, carotid, aortic, other)
 - ii. Vasculitis
 - iii. Arteriovenous malformation
 - iv. Intracranial bleeding (subdural, epidural)
 - v. Space-occupying lesion
- b) Causes of carotid artery narrowing
 - i. Atherosclerosis
 - ii. Fibromuscular dysplasia
 - iii. Spontaneous dissection
 - iv. Other
- c) Atherogenesis (pathogenesis and risk factors)

II) Clinical manifestations of stroke

- a) Knowledge of stroke syndromes (classic and atypical)
- b) Distinction between anterior and posterior circulation events

III) Natural history of carotid artery disease

IV) Associated pathology (e.g., coronary and peripheral artery disease)

V) Diagnosis of stroke and carotid artery disease

- a) History and physical examination
 - i. Neurologic
 - ii. Non-neurologic (cardiac, other)
- b) Noninvasive imaging and appropriate use thereof
 - i. Duplex ultrasound
 - ii. MRA
 - iii. CTA

VI) Angiographic anatomy (arch, extracranial, intracranial, basic collateral circulation, common anatomic variants, and non-atherosclerotic pathologic processes)

VII) Knowledge of alternative treatment options for carotid stenosis and their results (immediate success, risks, and long-term outcome)

- a) Pharmacotherapy (e.g., antiplatelet agents, anticoagulation, lipid-lowering agents)
- b) Carotid endarterectomy
 - i. Results from major trials (NASCET, ACAS, ECST, ACST)
 - ii. Results in patients with increased surgical risk
- c) Stent revascularization
 - i. Results with and without distal embolic protection

VIII) Case selection

- a) Indications and contraindications for revascularization to prevent stroke
- b) High risk criteria for carotid endarterectomy
- c) High risk criteria for percutaneous intervention

IX) Role of postprocedure follow-up and surveillance

B. TECHNICAL: Technical requirements for performance of carotid stenting*

Minimum numbers of procedures to achieve competence

I) Diagnostic cervicocerebral angiograms –30 (\geq half as primary operator)†

II) Carotid stent procedures –25 (\geq half as primary operation)†

Technical elements for competence in both diagnostic angiography and interventional techniques

I) High level of expertise with antiplatelet therapy and procedural anticoagulation

II) Angiographic skills

- a) Vascular access skills
- b) Selection of guidewires and angiographic catheters
- c) Appropriate manipulation of guidewires and catheters
- d) Use of “closed system” manifold
- e) Knowledge of normal angiographic anatomy and common variants
- f) Knowledge of circle of Willis and typical/atypical collateral pathways
- g) Proper assessment of aortic arch configuration, as it affects carotid intervention
- h) Familiarity with use of angulated views and appropriate movement of the X-ray gantry

Table 22. Continued

- III) Interventional skills
 - a) Guide catheter/sheath placement
 - b) Deployment and retrieval of embolic protection devices
 - c) Pre- and postdilatation
 - d) Stent positioning and deployment
 - IV) Recognition and management of intraprocedural complications
 - a) Cerebrovascular events
 - i. Stroke or cerebrovascular ischemia
 - ii. Embolization
 - iii. Hemorrhage
 - iv. Thrombosis
 - v. Dissection
 - vi. Seizure and loss of consciousness
 - b) Cardiovascular events
 - i. Arrhythmias
 - ii. Hypotension
 - iii. Hypertension
 - iv. Myocardial ischemia/infarction
 - c) Vascular access events
 - i. Bleeding
 - ii. Ischemia
 - iii. Thrombosis
 - V) Management of vascular access
 - a) Proper sheath removal and attainment of hemostasis
 - b) Closure device utilization
- C. CLINICAL:** Clinical requirements for performance of carotid stenting*
- Clinical elements, including the ability to manage inpatients and outpatient care
- I) Determine the patient's risk/benefit for the procedure
 - II) Outpatient responsibilities
 - a. Adjust medications preprocedure
 - b. Counsel patient and family
 - III) Inpatient responsibilities
 - a. Admit patients (privileges required) and write orders
 - b. Obtain informed consent for procedures
 - c. Provide pre- and postprocedure hospital care
 - i. Neurological evaluation pre- and postprocedure
 - ii. Postprocedure pharmacotherapy
 - iii. Monitoring of hemodynamic and cardiac rhythm status
 - IV) Coordinate post-stent surveillance and clinical outpatient follow-up

Reprinted with permission from Rosenfield K, Babb JD, Cates CU, et al. Clinical competence statement on carotid stenting: training and credentialing for carotid stenting—multispecialty consensus recommendations: a report of the SCAI/SVMB/SVS Writing Committee to develop a clinical competence statement on carotid interventions. *J Am Coll Cardiol* 2005;45:165–74 (217).

*In addition to baseline cognitive skills encompassed in reference 220. †Angiograms and stenting procedures may be performed in the same sitting (e.g., in the same patients), provided that one performs 15 angiograms as primary operator before performing the first stent as primary operator.

ACAS = Asymptomatic Carotid Surgery Trial; ACST = Asymptomatic Carotid Surgery Trial; CTA = computed tomographic angiography; ECST = European Carotid Surgery Trial; MRA = magnetic resonance arteriography; NASCET = North American Symptomatic Carotid Endarterectomy Trial.

ASITN/ASNR/CNS/SIR document (89) included preparatory requirements for both the performance of cerebral angiography and stenting before performing CAS independently. The documents define 100 supervised cerebral angiograms and either 25 noncarotid stent procedures, 4 supervised carotid stent procedures, and 16 h of continuing medical education (CME); or 10 supervised CAS procedures with acceptable results as the minimum requirements. The 16 h of CME include a didactic program of formal instruction in the cognitive and clinical elements described in Table 23, combined

with hands-on technical instruction on the procedure and devices utilized during CAS.

The SCAI/SVMB/SVS document (217) specifies that new operators in these specialties perform a minimum of 30 supervised diagnostic cervicocerebral angiograms (at least 15 as a primary operator) and a minimum of 25 supervised carotid interventions (at least 13 as primary operator) prior to performing CAS independently. Fewer studies required by the cardiology and vascular surgery organizations reflect their belief that previous experience with coronary (minimum of 300 diagnostic coronary

Table 23. AAN/AANS/ASITN/ASNR/CNS/SIR Requirements for Performance of Carotid Stenting

A. COGNITIVE: Cognitive elements including:

- I. A fund of knowledge regarding stroke syndromes and TIA etiologies, evaluation of traumatic and/or atherosclerotic neurovascular lesions, and inflammatory conditions of the central nervous system.
- II. Formal training that imparts an adequate depth of cognitive knowledge of the brain and its associated pathophysiological vascular processes, including management of complications of endovascular procedures.
- III. Diagnostic and therapeutic acumen, including the ability to recognize and manage procedural complications.
- IV. Ability to recognize clinical intra- or postprocedural neurological symptoms, as well as pertinent angiographic findings and the proper cognitive and technical skills to offer the most appropriate therapy. This might also entail optimal hemodynamic management necessitating sufficient neurointensive skills.

B. TECHNICAL: Technical requirements for performance of carotid stenting, including adequate procedural skill achieved by repetitive training in an approved clinical setting by a qualified instructor. This includes the ability to correctly interpret a cervicocerebral angiogram, which serves as the prerequisite and foundation for the technical performance of cervicocerebral angiography.

Minimum numbers of procedures to achieve competence: 100 diagnostic cervicocerebral angiograms.

C. CLINICAL: Clinical elements include the ability to manage inpatient and outpatient care.

- I. In addition to procedural technical experience requirements, a minimum of 6 months of formal cognitive neuroscience training in an ACGME-approved training program in radiology, neuroradiology, neurosurgery, neurology, and/or vascular neurology is required.
- II. Formal training and competency in the National Institutes of Health Stroke Scale.
- III. Maintenance of proficiency by lifelong CME and continuing performance of cases with adequate success and outcomes with minimal complications.

Modified with permission from Connors JJ III, Sacks D, Furlan AJ, et al. Training, competency, and credentialing standards for diagnostic cervicocerebral angiography, carotid stenting, and cerebrovascular intervention: a joint statement from the American Academy of Neurology, American Association of Neurological Surgeons, American Society of Interventional and Therapeutic Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, AANS/CNS Cerebrovascular Section, and Society of Interventional Radiology. *Radiology* 2005;234:26–34 (89).
CME = continuing medical education; TIA = transient ischemic attack.

angiograms and 250 coronary interventions) (219) and peripheral interventional procedures (minimum of 100 diagnostic peripheral angiograms and 50 peripheral interventions) (220) are transferable to neurovascular intervention.

Documentation of experience in CAS should include the trainee's role in the procedure and patient outcomes. "Supervised" experience means that the trainee is scrubbed alongside an experienced operator. "Primary operator" means that the trainee is handling the catheter, guidewire, EPD, balloon, and stent, under the direct supervision of the mentoring physician. Furthermore, only 1 trainee can be considered the primary operator on any 1 CAS procedure.

Simulator-Based Training

Simulator training may decrease surgical errors (221), and CAS simulators may be useful for training and assessment of technical and clinical skills, relying on a benchmark performance of skilled operators (222). While simulator training may provide considerable experience, it is not intended as a substitute for live experience.

Proctoring

Once a physician has completed the requisite training for CAS, hospitals may require a minimum number of proctored cases, prior to independent performance of CAS and final credentialing. The precise number of proctored cases may vary among institutions, but 2 to 5 CAS procedures is reasonable.

Credentialing

Credentialing in CAS is necessary to guarantee high performance standards and patient safety, and it is a

requirement for CMS reimbursement. It is essential that hospitals establish credentialing requirements that include professional society recommendations for competency in cervicocerebral angiography and CAS. In addition, the credentialing process must ensure cognitive and technical proficiency prior to allowing independent performance of CAS. Finally, hospitals must establish standards for data collection, quality assurance, and maintenance of hospital privileges. The expectation is that CAS operators will maintain a lifelong commitment to medical education and high performance standards, but the precise requirements for maintenance of CAS proficiency have not been developed.

Device-Specific Training

The FDA has approved industry training programs specific for CAS and EPDs. There are FDA-mandated industry device certification requirements for each of the approved products. These programs should augment, not supplant, professional society training and volume recommendations.

Facility Requirements

Interventional Suite

In accordance with CMS requirement (Table 24), the facility must provide optimal radiological, monitoring, and patient support equipment, including high resolution fluoroscopy and digital processing; continuous information about the patient's oxygenation, electrocardiogram, heart rate, heart rhythm, and blood pressure; and resuscitative equipment and temporary pacing. All equipment must be available and in good operating order. Adjunctive medications including sedatives, hemodynamic

Table 24. CMS Credentialing Requirements for CAS Reimbursement*

CMS has determined that CAS with EPD is reasonable and necessary only if performed in facilities that have been determined to be competent in performing the evaluation, procedure, and follow-up necessary to ensure optimal patient outcomes. Standards to determine competency will include specific physician training standards, facility support requirements, and data collection to evaluate outcomes during a required reevaluation.

CMS has created a list of minimum standards modeled in part on professional society statements on competency. All facilities must at least meet CMS's standards to receive coverage for CAS for high-risk patients.

•Facilities must have necessary imaging equipment, device inventory, staffing, and infrastructure to support a dedicated CAS program. Specifically, high-quality X-ray imaging equipment is a critical component of any carotid interventional suite, such as high resolution digital imaging systems with the capability of subtraction, magnification, road mapping, and orthogonal angulation.

•Advanced physiologic monitoring must be available in the interventional suite. This includes real time and archived physiologic, hemodynamic, and cardiac rhythm monitoring equipment, as well as support staff who are capable of interpreting the findings and responding appropriately.

•Emergency management equipment and systems must be readily available in the interventional suite such as resuscitation equipment, a defibrillator, vasoactive and antiarrhythmic drugs, endotracheal intubation capability, and anesthesia support.

•Each institution should have a clearly delineated program for granting CAS privileges and for monitoring the quality of the individual interventionalists and the program as a whole. The oversight committee for this program should be empowered to identify the minimum case volume for an operator to maintain privileges, as well as the (risk-adjusted) threshold for complications that the institution will allow before suspending privileges or instituting measures for remediation. Committees are encouraged to apply published standards from national specialty societies recognized by the American Board of Medical Specialties to determine appropriate physician qualifications. Examples of standards and clinical competence guidelines include those published in the December 2004 edition of the *American Journal of Neuroradiology*, and those published in the August 18, 2004, *Journal of the American College of Cardiology*.

•To continue to receive Medicare payment for CAS under this decision, the facility or a contractor to the facility must collect data on all CAS procedures done at that particular facility. This data must be analyzed routinely to ensure patient safety, and will also be used in the process of re-credentialing the facility. This data must be made available to CMS upon request. The interval for data analysis will be determined by the facility but should not be less frequent than every 6 months.

Since there currently is no recognized entity that evaluates CAS facilities, CMS has established a mechanism for evaluating facilities. Facilities must provide written documentation to CMS that the facility meets one of the following:

- 1.The facility was an FDA-approved site that enrolled patients in prior carotid artery stenting IDE trials, such as SAPHIRE, and ARChER;
- 2.The facility is an FDA-approved site that is participating and enrolling patients in ongoing carotid artery stenting IDE trials, such as CREST;
- 3.The facility is an FDA-approved site for one or more FDA post approval studies; or
- 4.The facility has provided a written affidavit to CMS attesting that the facility has met the minimum facility standards.

*Effective March 2005.

ARChER = Acculink for Revascularization of Carotids in High-Risk Patients; CAS = carotid artery stenting; CEA = carotid endarterectomy; CMS = Centers for Medicare & Medicaid Services; CREST = Carotid Revascularization: Endarterectomy versus Stent Trial; EPD = embolic protection device; FDA = Food and Drug Administration; IDE = investigational device exemption; SAPHIRE = Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy.

agents, anticoagulants, and antiplatelet agents must be readily available.

Interventional Equipment

The necessary sheaths, catheters, guidewires, balloons, stents, and EPDs must be present, and a variety of each of these devices must be available. Catheter snares and thrombectomy devices must be available for management of complications.

Personnel

The nursing, technical, and support staff must be experienced and knowledgeable about the CAS procedure and equipment, and be able to respond quickly to emergencies and unusual situations. Cardiothoracic surgery, vascular surgery, neurosurgery, neurology, respiratory care, and anesthesia are essential services that may be called upon to respond to emergencies.

Quality Assessment Monitoring

Concurrent patient and quality data collection, including independent neurological assessment, are mandatory to effectively assess procedural success and complication rates for each operator. Patient characteristics, procedural data, process-of-care, and in-hospital outcomes must be recorded, analyzed, and reported in a standardized fashion and compared with national benchmarks. Multidisciplinary conferences must be held routinely to review

CAS procedures, objectively evaluate outcomes, and identify cooperative opportunities for improvement. Individual and institutional outcomes must be reported to one or more national data registries and reviewed on a regular basis by appropriate quality assurance monitoring committees.

National Data Registries

The ACC and the SVS have established separate CAS data collection registries. The ACC National Cardiovascular Data Registry (ACC-NCDR[®]) Carotid Artery Revascularization and Endarterectomy Registry[™] complements the CathPCI Registry[™] and the ICD Registry[™]. The NCDR[®] offers a secure, confidential, Health Insurance Portability and Accountability Act (HIPAA)-compliant quality improvement data registry that will also satisfy the needs of payers, regulators, and hospital administrators. Data entry is accomplished via on-line data collection. The NCDR[®] Carotid Artery Revascularization and Endarterectomy Registry[™] has a built-in oversight mechanism and an on-site auditing strategy to assure complete and accurate data collection. It will be imperative for the NCDR to periodically refine quality and patient safety performance measurements, consistent and interoperable data standards for information systems, and credible national benchmarks for processes of care and patient outcomes according to the most currently

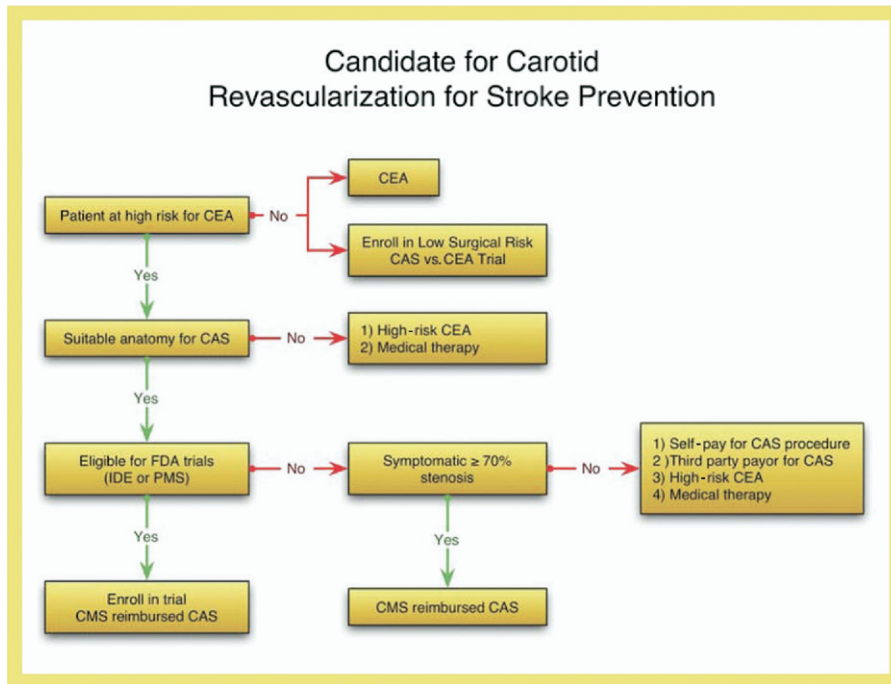


Figure 7. Reimbursement Algorithm

CAS = carotid artery stenting; CEA = carotid endarterectomy; CMS = Centers for Medicare & Medicaid Services; FDA = Food and Drug Administration; IDE = investigational device exemption; PMS = postmarketing surveillance.

available evidence. The NCDR now provides standardized quarterly and annual benchmark reports for participating physicians and their hospitals.

In contrast, the SVS has established The Vascular Registry, which allows on-line entry of CEA and CAS outcomes data from participating institutions. The New England Research Institutes (NERI) Advanced Data Entry and Protocol Tracking (ADEPT) data management system is HIPAA-compliant and satisfies CMS requirements for data collection. The Vascular Registry allows real-time access to institutional data and automated reports to assess outcomes.

In addition to ACC and SVS registries, the Agency for Healthcare Research and Quality (AHRQ), the National Committee for Quality Assurance (NCQA), and the SCAI are considering a national multispecialty registry to assess CAS outcomes, with the hope of influencing reimbursement policy.

Reimbursement

CMS reimbursement for CAS mandates institutional adherence to their CAS requirements (Table 24). When this condition is met, CMS reimbursement is available for patients with symptomatic carotid stenosis greater than 70% who are at high risk for CEA. For CAS in high-risk patients with symptomatic carotid stenosis 50% to 69% or patients with asymptomatic carotid stenosis greater than 80%, CMS reimbursement will be available only if the patient is enrolled in an FDA-approved postapproval registry or clinical trial. Reimbursement of other patients is by third party payer or self-pay (Fig. 7).

Future Directions

Training and Proficiency

Several professional societies have published guidelines for CAS training. However, ongoing postmarket approval registries may further refine the standards for training, since these registries are encouraged to include operators with varying degrees of experience. As more physicians acquire CAS expertise, discordant recommendations from different professional societies may converge into consensus-based standards. Eventually, CAS training will be incorporated into appropriate ACGME training programs.

Quality Assessment and Improvement

Quality assessment in CAS is in its formative stages. Currently, structural characteristics, such as a specialty designation, training experience, and volume, are the only tools available. As the field evolves and there is more widespread availability of national registry data, process of care and outcomes metrics will likely replace these less sensitive structural features.

A model registry would have universal provider participation, cross all interventional and surgical specialties, capture independently adjudicated neurological outcomes for CAS and CEA, and consistently assess the short- and long-term risk of restenosis and other late events. Minimal components of such a registry would include patient

risk factors to both define surgical risk and risk-adjust outcomes, indications for intervention, anatomic factors that are associated with technical difficulty, procedural process of care, and post-procedure complications. The assessment would record outcomes over an extended period of time to track temporal trends, detect unexpected safety concerns, and permit the delineation of those factors independently associated with adverse cardiovascular and neurological events according to specialty, prior simulated and hands-on catheter-based training, and procedure volumes. To facilitate these goals, all third party payers should strongly consider “Pay for Participation,” since quality data collection and reporting will require additional hospital resources.

New Devices

Refinements in CAS technology are evolving steadily. New delivery sheaths, guiding catheters, and access catheters; improvements in design of distal and proximal EPDs; new stent materials and coatings; and the potential for absorbable or degradable stents to facilitate late imaging and reduce restenosis are all expected.

New Trials

New trials are enrolling low-risk patients to evaluate the safety and efficacy of CEA and CAS. Further studies are needed to evaluate the efficacy of “best medical therapy” in high- and low-risk patients compared with revascularization therapy.

New Indications

Depending on the results of ongoing and future trials, CAS may become the treatment of choice for many patients who are now treated by CEA and for patients who require revascularization but are at high risk for CEA. Evaluation of percutaneous methods for chronic total occlusions and intracranial disease are in the early stages of development. Catheter-based interventions are rapidly emerging for the management of acute stroke, but timely access for these patients remains a major limitation and will require ongoing efforts in public education regarding stroke awareness.

Staff

American College of Cardiology Foundation

John C. Lewin, MD, Chief Executive Officer
Thomas E. Arend, Jr, Esq., Chief Operating Officer
Lisa Bradfield, Associate Director, Clinical Policy and Documents
María Velásquez, Specialist, Clinical Policy and Documents
Erin A. Barrett, Specialist, Clinical Policy and Documents
Peg Christiansen, Librarian

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APPENDIX 1. ACCF/SCAI/SVMB/SIR/ASITN WRITING COMMITTEE TO DEVELOP A CLINICAL EXPERT CONSENSUS DOCUMENT ON CAROTID STENTING—AUTHOR RELATIONSHIPS WITH INDUSTRY

Name	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. Eric R. Bates (Chair)	None	None	None	None	None	None	None
Dr. Joseph D. Babb	None	• Guidant • Cordis	None	None	None	None	None
Dr. Donald E. Casey, Jr.	None	None	None	None	None	None	None
Dr. Christopher U. Cates	• Cordis	None	• Boston Scientific • Medicines Co.	None	None	None	None
Dr. Gary R. Duckwiler	None	None	• Johnson & Johnson • Stroke Management Group	None	None	None	None
Dr. Ted E. Feldman	• Boston Scientific • Cardiac Dimensions • Cordis • Guidant • Myocor • XStent	• Boston Scientific • Abbott • Atritech • Guidant • Cardiac Dimensions • Cordis • Evalve • ev3	None	None	None	None	None
Dr. William A. Gray	• Cordis • Endo • Boston Scientific • MedSN • Abbott • Guidant	None	None	None	None	None	None
Dr. Kenneth Ouriel	• Terumo Medical Corp.	None	None	None	None	None	None
Dr. Eric D. Peterson	None	• Bristol-Myers Squibb • Sanofi • Schering-Plough	None	None	None	None	None
Dr. Kenneth Rosenfield	• Abbott • Boston Scientific • Cordis • Guidant • Medtronic	• Abbott • Boston Scientific • Cordis • Guidant • Medtronic	None	None	None	None	None
Dr. John Rundback	None	• Medtronic • Boston Scientific	None	None	None	None	None
Dr. Robert D. Safian	None	• Medtronic • Boston Scientific • Cordis • ev3	None	None	None	None	None
Dr. Michael A. Sloan	• Terumo Medical Corp.	• NINDS • Abbott • Boston Scientific • Guidant • Cordis	None	• Boehringer-Ingelheim • Bristol-Myers Squibb/ Sanofi	None	None	None
Dr. Christopher J. White	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry that were reported orally at the initial writing committee meeting and updated in conjunction with all meetings and conference calls of the writing committee during the document development process. It does not necessarily reflect relationships with industry at the time of publication.

APPENDIX 2. PEER REVIEWER RELATIONSHIPS WITH INDUSTRY—ACCF/SCAI/SVMB/SIR/ASITN WRITING COMMITTEE TO DEVELOP A CLINICAL EXPERT CONSENSUS DOCUMENT ON CAROTID STENTING

Name	Representation	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. Robert M. Bersin	• Official Reviewer—SCAI	• Cordis Corp. • Guidant Corp.	• Cordis Corp. • Boston Scientific • ev3 • Guidant • Sanofi-Aventis • Medicines Co.	• Cordis Corp. • Boston Scientific	• Boston Scientific • ev3 • Sanofi-Aventis • Medicines Co.	None	• Cordis	• Cordis—Spouse's Employer, Proctor/ Trainer
Dr. Michael J. Cowley	• Official Reviewer—SCAI	None	None	None	None	None	None	None
Dr. David R. Holmes, Jr.	• Official Reviewer—ACCF Board of Trustees	None	None	None	None	None	None	None
Dr. Stuart A. Winston	• Official Reviewer—ACCF Board of Trustees	None	• Guidant • Medtronic • Biotronic	None	None	None	None	None
Dr. Seemant Chaturvedi	• Content Reviewer	• Boehringer Ingelheim • Bristol-Myers Squibb/Sanofi	• Boehringer Ingelheim • Pfizer	None	• Boehringer Ingelheim • Bristol-Myers Squibb/Sanofi	None	None	None
Dr. Leslie Sung Hee Cho	• Content Reviewer—ACCF PVD Committee	None	None	None	None	None	None	None
Dr. Michael R. Jaff	• Content Reviewer	None	None	None	None	None	None	None
Dr. Elizabeth Ratchford	• Content Reviewer	• Vasogen, Inc.	None	None	None	None	Merck	None
Dr. Keith Calligaro	• Organizational Reviewer—SVS	None	None	None	None	None	None	None
Dr. Colin P. Derdeyn	• Organizational Reviewer—ASITN	None	None	None	None	None	None	None
Dr. Anthony Furlan	• Organizational Reviewer—AAN	None	None	None	None	None	None	None
Dr. Scott Kinlay	• Organizational Reviewer—SVMB	None	None	None	None	None	None	None
Dr. Gary M. Nesbit	• Organizational Reviewer—ASITN	None	None	None	None	None	None	None
Dr. Bruce A. Perler	• Organizational Reviewer—SVS	None	None	None	None	None	None	None
Dr. Rodney Raabe	• Organizational Reviewer—SIR	• Guidant	None	None	• Guidant • Cordis • Genotech	None	None	• Cook (Royalty from product) • Trainer for Physicians for Carotid Stenting

Name	Representation	Consultant	Research Grant	Scientific Advisory Board	Speakers' Bureau	Steering Committee	Stock Holder	Other
Dr. Lawrence Wechsler	• Organizational Reviewer— AAN	• Astra-Zeneca • NMT Medical • Boston Scientific	• Bristol-Myers Squibb	None	• Bristol-Myers Squibb	• NMT Medical	None	None
Dr. Mark H. Wholey	• Organizational Reviewer— SIR	• Medrad • Mallinckrodt • Edwards	• Bristol-Myers Squibb	• Medrad • Edwards	• Mallinckrodt • Edwards	None	None	None

This table represents the relationships of committee members with industry that were reported by the authors as relevant to this topic. It does not necessarily reflect relationships with industry at the time of publication.

AAN = American Academy of Neurology; PVD = Peripheral Vascular Disease.

ACCF/SCAI/SVMB/SIR/ASITN 2007 Clinical Expert Consensus Document on Carotid Stenting: A Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN Clinical Expert Consensus Document Committee on Carotid Stenting)

American Society of Interventional & Therapeutic Neuroradiology, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, Eric R. Bates, Joseph D. Babb, Donald E. Casey, Jr, Christopher U. Cates, Gary R. Duckwiler, Ted E. Feldman, William A. Gray, Kenneth Ouriel, Eric D. Peterson, Kenneth Rosenfield, John H. Rundback, Robert D. Safian, Michael A. Sloan, Christopher J. White, Robert A. Harrington, Jonathan Abrams, Jeffrey L. Anderson, Eric R. Bates, Mark J. Eisenberg, Cindy L. Grines, Mark A. Hlatky, Robert C. Lichtenberg, Jonathan R. Lindner, Gerald M. Pohost, Richard S. Schofield, Samuel J. Shubrooks, JR, James H. Stein, Cynthia M. Tracy, Robert A. Vogel and Deborah J. Wesley
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CORRECTION

In the article by Bates ER, Babb JD, Casey DE, et al., “ACCF/SCAI/SVMB/SIR/ASITN 2007 clinical expert consensus document on carotid stenting: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN Clinical Expert Consensus Document Committee on Carotid Stenting),” which appeared in the January 2/9, 2007 issue of the journal (*J Am Coll Cardiol* 2007;49:126–70), the following correction should be made:

On page 139, the fifth sentence under the heading “Lipid-Lowering Therapy,” 20 mg should be changed to 80 mg so that the sentence reads, “The SPARCL (Stroke Prevention with Aggressive Reduction of Cholesterol Levels) trial studied atorvastatin 80 mg for secondary prevention of stroke in 4,731 patients without coronary artery disease and documented a 16% relative risk reduction for recurrent stroke (136,136a).”

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