Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease

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Management of carotid bifurcation stenosis is a cornerstone of stroke prevention and has been the subject of extensive clinical investigation, including multiple controlled randomized trials. The appropriate treatment of patients with carotid bifurcation disease is of major interest to the community of vascular surgeons. In 2008, the Society for Vascular Surgery published guidelines for treatment of carotid artery disease. At the time, only one randomized trial, comparing carotid endarterectomy (CEA) and carotid stenting (CAS), had been published. Since that publication, four major randomized trials comparing CEA and CAS have been published, and the role of medical management has been re-emphasized. The current publication updates and expands the 2008 guidelines with specific emphasis on six areas: imaging in identification and characterization of carotid stenosis, medical therapy (as stand-alone management and also in conjunction with intervention in patients with carotid bifurcation stenosis), risk stratification to select patients for appropriate interventional management (CEA or CAS), technical standards for performing CEA and CAS, the relative roles of CEA and CAS, and management of unusual conditions associated with extracranial carotid pathology. Recommendations are made using the GRADE (Grades of Recommendation Assessment, Development and Evaluation) system, as has been done with other Society for Vascular Surgery guideline documents. The committee recommends CEA as the first-line treatment for most symptomatic patients with stenosis of 50% to 99% and asymptomatic patients with stenosis of 60% to 99%. The perioperative risk of stroke and death in asymptomatic patients must be <3% to ensure benefit for the patient. CAS should be reserved for symptomatic patients with stenosis of 50% to 99% at high risk for CEA for anatomic or medical reasons. CAS is not recommended for asymptomatic patients at this time. Asymptomatic patients at high risk for intervention or with <3 years life expectancy should be considered for medical management as the first-line therapy. (J Vasc Surg 2011; 54:e1-e31.)

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Management of extracranial carotid disease has been the focus of intense investigation and debate by multiple medical specialists since the introduction of carotid endarterectomy (CEA) as a therapeutic option for the treatment and prevention of stroke more than half a century ago. Initial hopes that CEA could reverse the clinical course of stroke were proven false, and the role of surgical management of extracranial carotid and vertebral obstructions was defined by one of the earliest efforts at a multicentered randomized clinical trial, The Joint Study on The Extracranial Circulation.[1] The results of this decade-long study, involving 5000 patients, established the role of CEA in the treatment of minor stroke, transient ischemic attack (TIA), and amaurosis fugax, confirmed that surgery had a limited role in the treatment of established stroke, and established the limited role of vertebral reconstruction in the treatment of cerebral insufficiency. Over the ensuing decades, surgical results of CEA improved, asymptomatic carotid stenosis was increasingly identified by noninvasive studies, and CEA assumed a primarily prophylactic role as prevention of major stroke in asymptomatic patients or those with evidence of transient cerebral or ocular ischemia. Large randomized trials[2-6] have established the role and efficacy of carotid endarterectomy (CEA) in stroke prevention.

In the last decade, carotid artery stenting (CAS) has emerged as a catheter-based alternative to CEA, and medical therapy for stroke treatment and prevention has evolved. Currently, approximately 135,000 interventions on lesions in the carotid bifurcation are being performed annually in the United States, by a variety of specialists, including vascular surgeons, general surgeons, thoracic surgeons, neurosurgeons, cardiologists, interventional radiologists, and interventional neurologists.[7,8] Approximately 11% of these interventions are catheter-based, and 90% of interventions are in patients without neurologic symptoms.[7]

As in any situation where there are multiple options for the treatment of a single condition, defining optimal treatment can be difficult. This is further compounded when multiple specialists, often with nonoverlapping expertise, are involved in the treatment of the patient. As a result, a voluminous and often conflicting literature has developed around the current standards of diagnosis and management of extracranial carotid stenosis. Recently two large, prospective, randomized trials have been published comparing the efficacy of CEA and CAS in the management of extracranial carotid stenosis.[9,10] A meta-analysis comparing CAS and CEA, including these trials has recently been published in the *Journal of Vascular Surgery*.[11]

In 2008, the Society for Vascular Surgery published clinical practice guidelines for the management of extracranial carotid artery disease in the *Journal of Vascular Surgery*.[12] More recently, a multispecialty document has been published on the "Management of Patients with Extracranial Carotid and Vertebral Artery Disease."[13] This extensive document represents an effort to evaluate the existing literature on extracranial carotid and vertebral disease and is an important reference.

The data contained in the recently published randomized trials has prompted the Society for Vascular Surgery to publish an update of its 2008 guidelines, confined to management of extracranial carotid artery disease. This is particularly appropriate because vascular surgeons play a major if not predominant role in the management of patients with carotid bifurcation disease.

In developing these recommendations, the committee placed more weight on the reduction of stroke and death and less on the importance of nonfatal myocardial infarction (MI). Because the latter end point often represents the main benefit of CAS, the recommendations in this document are more circumspect with regard to the role of CAS and more supportive of the role of CEA than the recom-

mendations of the American Heart Association (AHA) guidelines committee. This document is divided into six major sections:

I. Indications for imaging of the extracranial circulation
II. Selection of imaging modality
III. The importance of medical therapy in the overall management of patients with carotid stenosis, including medical management in the peri-intervention period.
IV. Technical considerations for performing CEA and CAS
V. The relative roles of medical management, CEA and CAS for stroke risk reduction in patients with carotid stenosis based on review of the literature, with particular reference to risk factor stratification and the most recent completed trials
VI. The management of unusual conditions associated with extracranial carotid pathology, including acute neurologic conditions, symptomatic carotid occlusion, carotid dissection, and patients with carotid stenosis in need of coronary artery revascularization

The committee reviewed the literature pertinent to each of the six areas and provided recommendations for treatment using the GRADE (Grades of Recommendation Assessment, Development and Evaluation) system.[14] This system, adopted by more than 40 other organizations, incorporates an evaluation of the strength of the evidence and the risks/benefits of implementing the recommendation. For the purposes of this review, we placed the highest priorities on reducing overall stroke risk, periprocedural stroke risk, and periprocedural mortality. Lesser importance was given to reducing nonfatal MI, cost, and the ability to perform a percutaneous procedure. Recommendations are characterized as *strong* GRADE 1 or *weak* GRADE 2, based on the quality of evidence, the balance between desirable effects and undesirable ones, the values and preferences, and the resources and costs.

GRADE 1 recommendations are meant to identify practices where benefit clearly outweighs risk. These recommendations can be made by clinicians and accepted by patients with a high degree of confidence. GRADE 2 recommendations are made when the benefits and risks are more closely matched and are more dependent on specific clinical scenarios. In general, physician and patient preference plays a more important role in the decision-making process in these circumstances.

In addition to the GRADE of recommendation, the level of evidence to support the recommendation is noted. Evidence is divided into 3 categories: A (high quality), B (moderate quality), and C (low quality). Conclusions based on high-quality evidence are unlikely to change with further study, those based on moderate-quality evidence are more likely to be affected by further investigation, and those based on low-quality evidence are the least supported by current data and the most likely to be subject to change in the future.

It is important to note that a GRADE 1 recommendation can be made based on low-quality (C) evidence by the effect on patient outcome. For example, although there are little data on the efficacy of CEA in asymptomatic patients with <60% stenosis, one can recommend with confidence that CEA not be performed in these patients. A full explanation of the GRADE system is presented in the recent article by Murad et al[14] referenced earlier. It is important to note that this grading system differs somewhat from the one used in the recent American College of Cardiology (ACC)/AHA Task force report.[13]

Each member of the committee was assigned responsibility for compiling information pertinent to a specific area of the document. These data were distributed to all members for review, and each area was subsequently discussed in conference calls. A consensus of the recommendation and level of evidence to support it was reached. Each recommendation in this document represents the unanimous opinion of the task force. Although some recommendations are GRADE 2 with Level 3 data, the task force felt it appropriate to present these as the unanimous opinion of its members regarding optimal current management. This was done with the recognition that such recommendations could change in the future but that it was unlikely that new data would emerge soon. These guidelines are likely to be a "living document" that will change as techniques are further refined, technology develops, medical therapy improves, and new data emerge.

I. INDICATIONS FOR CAROTID BIFURCATION IMAGING

Stroke is the third leading cause of death, behind coronary artery disease (CAD) and cancer, and is the leading cause of disability in the United States and Western Europe. Approximately 80% of strokes are ischemic and 20% are hemorrhagic.[15] Significant carotid stenosis (>50%) is seen in 12% to 20% of all anterior circulation ischemic strokes, which is two to three times higher than the risk for less severe asymptomatic stenosis.[16,17] Unfortunately, only 15% of stroke victims have a warning TIA before stroke, and waiting until symptoms occur is not ideal.[18] The purpose of carotid bifurcation imaging is to detect "stroke-prone" carotid bifurcation plaque and identify a high-risk patient likely to benefit from therapy designed to reduce stroke risk.

Stroke risk is dependent on many factors, but for patients with carotid bifurcation disease, the most important are a history of neurologic symptoms, the degree of stenosis of the carotid bifurcation plaque, and to a lesser extent, plaque characteristics such as ulcerations, intraplaque hemorrhage, and lipid content.

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) clearly demonstrated the efficacy of CEA in reducing stroke in patients with symptoms of carotid territory cerebral ischemia and carotid bifurcation stenosis that reduced luminal diameter by >50%.[2-4] In these studies, the risk of stroke was higher in patients with a clear history of

carotid territory ischemic events (as opposed to amaurosis fugax), and stroke risk increased with the severity of stenosis. Asymptomatic Carotid Atherosclerosis Study (ACAS) and Asymptomatic Carotid Surgery Trial (ACST)[5,6] found that CEA was also effective in reducing stroke risk in patients with asymptomatic carotid stenosis >60%, although the stroke risk inherent in an asymptomatic stenosis was much less than that in a symptomatic lesion. It follows then that neurologically symptomatic patients and neurologically asymptomatic patients at high risk for harboring a carotid stenosis of ≥60% would be candidates for carotid bifurcation imaging.

A. Indications for imaging the neurologically symptomatic patient

Typical carotid territory ischemic symptoms include contralateral weakness of the face, arm, or leg, or both; contralateral sensory deficit or paresthesia of the face, arm, or leg, or both; or transient ipsilateral blindness (amaurosis fugax). If the right cerebral hemisphere is involved, other manifestations may be noted, including anosognosia, asomatognosia, neglect, visual, or sensory extinction. If the left hemisphere is involved, patients may show manifestation of aphasia, alexia, anomia, and agraphesthesia. Symptoms not typically associated with carotid territory events include vertigo, ataxia, diplopia, visual disturbances, dysarthria, nausea, vomiting, decreased consciousness, and weakness, which may include quadriparesis.

The physical examination may show signs of stroke: facial/eyelid drooping, motor or sensory deficits, and speech disturbances. Ocular examinations can occasionally identify Hollenhorst plaques. Neck auscultation may elicit carotid bruit; however, the absence of a neck bruit does not exclude the possibility of a significant carotid bifurcation lesion. Given the incidence of significant carotid stenosis in patients who present with stroke[15,19] and the effectiveness of CEA in reducing stroke in symptomatic patients with >50% carotid stenosis,[2-4] it is important to evaluate the carotid bifurcation in every patient with symptoms of carotid territory ischemia.

Amaurosis fugax or the finding of a Hollenhorst plaque on funduscopic examination, or both, is also correlated with the presence of significant carotid bifurcation stenosis. However, neither amaurosis fugax nor identification of a Hollenhorst plaque are associated with the same stroke risk as transient cerebral ischemia.[20] Identification of carotid stenosis in that clinical scenario implies a stroke risk somewhere between a neurologically symptomatic patient and one who is asymptomatic.

B. Indications for imaging the neurologically asymptomatic patient

Evaluation and treatment of patients who are neurologically asymptomatic is much more controversial. The benefit of carotid endarterectomy for stenosis >60%, although statistically significant in large trials, is much less than for neurologically symptomatic individuals and rests on the premise that intervention can be performed with minimal morbidity.[5,6] Identification of these asymptomatic patients may occur by routine screening using duplex ultrasound (DUS) imaging or selective application of DUS imaging to high-risk individuals.

1. Screening for asymptomatic carotid stenosis. To date, there is no consensus on which patients should undergo carotid screening for the detection of carotid stenosis. The American Society of Neuroimaging[21] concluded that the efficacy of screening would be related to the prevalence of the disease in the screened populations. When the prevalence of stenosis is ≥20%, screening reduced risk of stroke in a cost-effective manner, with intermediate prevalence of between 5% and 20%: screening reduced the risk of stroke in a cost-effective manner in some studies; however, the benefit was usually marginal and was lost if complications of the intervention >5%. With a prevalence of <5%, screening has not been shown to reduce the risk of stroke in a cost-effective manner and may be harmful.

Given these assumptions, screening of the general population is not indicated. This position is supported by multiple professional organizations, including the National Stroke Association,[22] the Canadian Stroke Consortium[23] and the U.S. Preventive Services Task Force.[24] The American Stroke Association/AHA Stroke Council[25] concluded that highly selected patient populations may benefit, but screening of the general population for asymptomatic carotid stenosis was unlikely to be cost-effective and might have the potential adverse effect of false-negative or false-positive results. Finally, the American College of Cardiology Foundation, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and American Society of Interventional & Therapeutic Neuroradiology Clinical Expert Consensus Panel on Carotid Stenting recommended screening for asymptomatic patients with carotid bruit who are potential candidates for carotid intervention and for those in whom coronary artery bypass grafting (CABG) is planned.[26]

a. Screening patients with asymptomatic bruit. Zhu and Norris,[27] in the largest reported study of carotid screening in asymptomatic patients, reported the prevalence of carotid stenosis >75% for those with a carotid bruit was 1.2%. Although the presence of a neck bruit has not been found to predict carotid stenosis >60% in a neurologically asymptomatic population,[27] focal ipsilateral carotid bruits in neurologically symptomatic patients had a sensitivity of 63% and a specificity of 61% for high-grade carotid stenosis (range, 70%-99%).[28] The absence of a bruit did not significantly change the probability of significant stenosis in this group of patients (pretest, 52%; post-test, 40%). Ratchford et al[29] found in a selected high-risk subgroup of asymptomatic patients that if a bruit was heard, 25% had a >60% stenosis. The presence of carotid bruit has been shown to increase the absolute risk of stroke,[30-32] MI, and death.[33] In general population-based studies, the prevalence of severe bifurcation stenosis is not high enough to make bruit alone an indication for carotid screening. With these facts in mind, screening should be pursued only if a

bruit is associated with other risk factors for stenosis and stroke in patients who have a low operative risk[5,6,12,34] and are willing to undergo carotid intervention, whether CEA or CAS.

b. Potential "high-risk groups" who might benefit from screening for asymptomatic stenosis. Two studies have identified specific groups among the general population with a higher prevalence of significant carotid stenosis that may >30%. Jacobowitz et al[35] developed a model identifying patients at high risk for >50% asymptomatic carotid stenosis. The screened patients were aged >60 years and had one or more of the following risk factors: history of hypertension, CAD, current smoking, and a first-degree family relative with a history of stroke. The prevalence of carotid artery stenosis was only 2% if no risk factor was present, 6% with one risk factor, which increased to 14% for two risk factors, to 16% for three risk factors, and to 67% for four risk factors.

Qureshi et al[36] identified the following variables associated with ≥60% asymptomatic carotid stenosis: age >65 years (odds ratio, 4.1), current smoking (odds ratio, 2), CAD (odds ratio, 2.4), and hypercholesterolemia (odds ratio, 1.9). Patients undergoing coronary revascularization are another group with an increased prevalence of carotid stenosis of 2% to 27%.[37,38] Overall, the prevalence of carotid artery stenosis among patients undergoing CABG is higher than the general population. In patients with symptomatic CAD and other risk factors, such as age >65 years, history of stroke or TIA, left main coronary stenosis, diabetes mellitus, carotid bruit, peripheral arterial disease (PAD), and previous carotid operation, it is feasible that a subset of patients with a prevalence >20% can be identified who might benefit from carotid screening.[37,39-45] The ACC/AHA guidelines[46] note that carotid screening before CABG is probably indicated in the following subset of patients: age >65 years, left main coronary stenosis, history of smoking, history of TIA/stroke or carotid bruit, and PAD.

Several studies[47-51] have suggested that the prevalence of ≥60% carotid artery stenosis among patients with symptomatic PAD is >20%, regardless of the patient's age. However, the prevalence of ≥60% carotid artery stenosis among patients with abdominal aortic aneurysms (AAA) is <20%.[52-54] This suggests that screening patients with AAA would have only a modest benefit and only if intervention could be performed with low morbidity and mortality.[23] Because there is no evidence that stroke risk after AAA repair is increased by the presence of carotid stenosis, routine carotid screening of AAA patients is not indicated.

In patients with prior head and neck radiotherapy, the prevalence of significant carotid artery stenosis may be high enough, depending on the time between radiotherapy exposure and screening, to justify routine carotid screening.[55-59] The highest incidence is generally observed 15 years after radiotherapy exposure, with 21.3% and 5.3% rates of ipsilateral and contralateral stenosis, respectively. The data also suggest that the ipsilateral common carotid (CCA) and internal carotid arteries (ICA) are both in-volved. The rate of contralateral carotid artery stenosis may also be higher than that observed in the general population.

Unfortunately, limited data are available regarding carotid screening after radiotherapy among patients with head and neck cancer. However, the distribution of disease and clinical course in patients after radiation for head and neck malignancy is different from that of the typical atherosclerotic population. There is a higher incidence of diffuse disease, often involving the CCA, and many of these patients remain neurologically asymptomatic. Further, CEA in this group is considered relatively "high risk," and prior radiotherapy is a relative indication for CAS rather than CEA. There are no robust data on the long-term results of CAS in asymptomatic stenosis associated with prior radiotherapy. Therefore, issues other than the increased prevalence of disease must be considered in formulating recommendations concerning screening in this group of patients.

Brain imaging will occasionally identify patients who have evidence of focal cerebral infarction despite the absence of any history of neurologic symptoms and a normal result on the neurologic examination. These infarcts can vary in size and are often found in the frontal lobes or the nondominant temporal lobe. They may occur as small symmetric lacunar infarcts, implying small-vessel disease, or they may also be asymmetric, which tends to implicate ipsilateral carotid stenosis. These can be secondary to blood flow changes distal to carotid occlusion, which may increase the risk of lacunar infarcts in those with small vessel disease. However, Kakkos et al[60] reported a higher stroke rate of 4.4% vs 1.3% in patients with 60% to 79% clinically asymptomatic stenosis if a silent infarct was present. Carotid screening is recommended in patients with asymptomatic infarctions.

● **Recommendations for the use of carotid bifurcation imaging**

1. Imaging of the cervical carotid artery is recommended in all patients with symptoms of carotid territory ischemia. This recommendation is based on the significant incidence of clinically relevant carotid stenosis in this patient group and the efficacy of CEA for clinically significant lesions in reducing overall stroke (GRADE 1, Level of Evidence A).

2. Imaging should be strongly considered for patients who present with amaurosis fugax, evidence of retinal artery embolization on funduscopic examination, or asymptomatic cerebral infarction, and are candidates for CEA. This recommendation is based on the intermediate stroke risk in this group of patients and the efficacy of CEA in reducing risk of subsequent stroke (GRADE 1, Level of Evidence A).

3. Routine screening is *not recommended* to detect clinically asymptomatic carotid stenosis in the general population. Screening is *not recommended* for presence of a neck bruit alone without other risk factors. This recommendation is based on the low prevalence of disease in the population at large, including those with neck bruits, as well as the potential harm of indiscriminate

application of carotid bifurcation intervention to a large number of asymptomatic individuals (GRADE 1, Level of Evidence A).

4. Screening for asymptomatic clinically significant carotid bifurcation stenosis should be considered in certain groups of patients with multiple risk factors that increase the incidence of disease as long as the patients are fit for and willing to consider carotid intervention if a significant stenosis is discovered. The presence of a carotid bruit in these patients increases the likelihood of a significant stenosis (GRADE 1, Level of Evidence B). Such groups of patients include:
   a. Patients with evidence of clinically significant peripheral vascular disease regardless of age.
   b. Patients aged ≥65 years with a history of one or more of the following atherosclerotic risk factors: CAD, smoking, or hypercholesterolemia. In general, the more risk factors present, the higher the yield of screening should be expected.

5. Carotid screening may be considered in patients before CABG. This is most likely to be fruitful if the patients are aged >65 years and have left main disease or a history of peripheral vascular disease. The strongest indication for screening these patients from the data available is to identify patients at high risk for perioperative stroke (GRADE 2, Level of Evidence B).

6. Carotid screening is *not recommended* for patients with AAA who do not fit into one of the above categories (GRADE 2, Level of Evidence B).

7. Carotid screening is *not recommended* for asymptomatic patients who have undergone prior head and neck radiotherapy. Although the incidence of disease is increased in this group of patients, the utility of intervention in the absence of neurologic symptoms has not been clearly established (GRADE 2, Level of Evidence B).

II. SELECTING IMAGING MODALITIES FOR CAROTID EVALUATION

The two most important features of carotid bifurcation atheroma are the degree of diameter stenosis and the character of the bifurcation plaque. In addition to information about the carotid bifurcation, there are clinical scenarios where the clinician requires information on the status of the vessels proximal or distal to the cervical carotid artery. These factors need to be considered when choosing between imaging studies. It is common—but not universal—to use multiple modalities when evaluating a patient with suspected cervical carotid stenosis.

In NASCET[2,3] and ECST,[4] a higher degree of stenosis in symptomatic patients was associated with a higher stroke risk. The ACAS[5] found no correlation between the severity of carotid stenosis and the incidence of stroke; however, there were too few strokes in this study to permit a subgroup analysis of the effect of degree of stenosis on the ability to benefit from CEA. Angiographic data from the ECST study[61] on contralateral asymptomatic carotid arteries from 2295 patients demonstrated a <2% annual stroke risk in patients with <70% neurologically asymptomatic

stenosis. Asymptomatic lesions with greater degrees of stenosis had a greater risk of stroke: 9.8% for patients with 70% to 79% stenosis and 14.4% for those with 80% to 99% stenosis. These data suggest that the degree of stenosis is a marker of stroke risk in symptomatic and asymptomatic lesions. Pathologic studies have demonstrated that more stenotic carotid plaques are more likely to have ulceration, intraplaque hemorrhage, and intraluminal thrombus formation, all of which are clearly related to cerebral embolization and stroke.[62]

Plaque morphology is an important feature in assessing future risk of neurologic events. Heterogeneous plaques have been shown to increase the risk of neurologic symptoms (TIA/stroke)[63,64] and were also associated with an incidence of TIA/stroke that was higher than that in homogenous plaques for all grades of stenosis.[64] Using DUS imaging and computerized image analysis[65] quantifying the gray scale median of the plaque, Biasi et al[66] demonstrated that gray scale median values of ≤25 were associated with an increased stroke risk of carotid stenting procedures.

Nicolaides et al[67] recently concluded that morphologic assessment of plaque structure may allow the identification of a subgroup of asymptomatic carotid stenoses with a 4.5-fold increase in the risk of developing ipsilateral neurologic symptoms compared with those with a similar degree of stenosis, which will reduce the number of patients requiring intervention to prevent one stroke. At present, however, this type of plaque analysis[66,67] is not widely available and requires further prospective evaluation to determine its ultimate clinical utility.

The imaging modalities most often used to evaluate patients for cervical carotid stenosis are carotid DUS (CDUS), magnetic resonance imaging (MRI) and angiography (MRA), computed tomography angiography (CTA), and digital subtraction angiography (DSA). Each of these will be discussed in turn.

A. Carotid duplex ultrasound imaging

DUS imaging provides an accurate and reliable noninvasive tool to determine the degree of cervical carotid stenosis and plaque morphology in most patients. It is usually the initial study in patients who present with symptoms or a carotid bruit. Because the study is highly dependent on technique, testing should be done in an accredited vascular laboratory (eg, Intersocietal Commission for the Accreditation of Vascular Laboratories), and the images should be reviewed by physicians experienced in vascular ultrasound interpretation.

Determining the degree of carotid artery stenosis is largely based on an analysis of the peak systolic velocity (PSV) or the end-diastolic velocity (EDV), or both, of the carotid artery. A panel of experts from several medical specialties convened in October 2002 in San Francisco, California, under the auspices of the Society of Radiologists in Ultrasound, to arrive at a consensus regarding the performance of Doppler US imaging to aid in the diagnosis of ICA stenosis.[68] This panel of experts recommended a cutoff PSV of the ICA of ≥125 cm/s for predicting angio-

graphic >50% stenosis and ≥230 cm/s for predicting >70% ICA stenosis. These recommended criteria are based on an analysis of several published studies and the experience of the panelists rather than values validated against other imaging modalities.

AbuRahma et al[69] recently analyzed the CDUS and angiography results of 376 carotid arteries in their institution. Using the consensus criteria, they demonstrated a sensitivity of 93%, specificity of 68%, and overall accuracy of 85% for stenosis between 50% and 69%. A PSV of ≥230 cm/s for ≥70% stenosis had a sensitivity of 99%, specificity of 86%, and overall accuracy of 95%. Receiver operator curves showed that the ICA PSV was significantly better than EDV or ICA/CCA ratio ($P = .036$) in detecting ≥70% stenosis and ≥50% stenosis. There was no improvement in accuracy by adding the EDV values or the ratios, or both, to the PSV values.

Velocity-based estimation of carotid artery stenosis may need to be adjusted in certain circumstances, for example, higher velocities in women than in men and higher velocities in the presence of contralateral carotid artery occlusion.[70,71] High carotid bifurcation, severe arterial tortuosity, extensive vascular calcification, and obesity may also reduce the accuracy of DUS imaging. Carotid stents will decrease compliance of the vessel wall and flow velocity.[72] DUS imaging may also fail to differentiate between subtotal and total carotid occlusion. Intravenous administration of contrast agents may improve diagnostic accuracy,[73,74] but the safety of these agents has been questioned.

Power Doppler and contrast DUS imaging can be used to differentiate between preocclusive stenosis and complete occlusion.[75] Overall, each vascular laboratory should have in place an internal validation process of their own criteria for their internal use.

DUS imaging of the carotid artery has two major limitations: quality dependence on the technician's examination and limitations of visualization of the proximal carotid artery and intracranial portions. Although the intracranial cerebral arteries can be assessed with transcranial Doppler imaging, this technique is not as widely available at most institutions as other imaging modalities.

In addition to determining percent stenosis, DUS, as noted above, has been used to determine plaque characteristics (echogenicity) using gray scale median values, which predict the stroke risk of a particular plaque. Plaque characterization is not routine in every vascular laboratory and requires specific protocols to assure standardization of results.

B. Magnetic resonance imaging and angiography

MRA has the advantage of being noninvasive, does not require iodinated contrast or ionizing radiation, and provides an unlimited number of projections of the carotid lumen from a single acquisition. MRA can also assess intrathoracic and intracranial lesions that are not amenable to DUS interrogation. MRA does not visualize the surrounding soft tissue structures, unless additional MRI is performed, and calcium within the plaque is not defined. It cannot be used in patients with implanted ferromagnetic devices, such as implantable defibrillators and pacemakers, and is of limited use in uncooperative patients and those with claustrophobia. The gadolinium-based compounds used as a contrast agent for MRA have been associated with nephrogenic systemic fibrosis in patients with pre-existing renal disorders.[76]

MRA has a tendency to overestimate the degree of carotid stenosis. The sensitivity and specificity for diagnosing 70% to 99% stenosis with time-of-flight MRA are identical to DUS imaging (88% and 84%, respectively); however, MRA has a tendency to "over-read" stenosis, making it difficult to differentiate more moderate (50% to 69%) from severe stenosis. Similarly, high-grade stenosis will result in a loss of signal on MRA. This does not represent a carotid occlusion when the more distal cervical carotid is visualized. However, when there is no reconstitution of the cervical carotid artery on MRA, the diagnosis of carotid occlusion can be made with a high degree of certainty.[76,77]

MRI can be used to analyze plaque morphology, specifically the structure of the atherosclerotic plaque. It can identify the lipid-rich necrotic core and the fibrous capsule with high sensitivity and specificity[78] and can distinguish between an intact thick, thin, or ruptured fibrous cap.[79] When dedicated protocols are used, MR also can demonstrate specific plaque components, including calcium, lipid, fibrocellular element, or thrombus within the plaques.

C. Computed tomography angiography

CTA is less susceptible than MRA to overestimating the severity of carotid stenosis. The rapid acquisition of spiral CT images allows excellent timing with contrast administration and provides quality images that can be viewed in multiple planes. CTA is extremely fast and offers submillimeter spatial resolution (0.3 vs 0.8 mm for contrast-enhanced MRA), is less expensive than contrast-enhanced MRA, provides a faster processing time, and can visualize soft tissue, bone, and blood vessels at the same time. CTA can also demonstrate vascular anomalies, has the ability to quantify the extent of calcification, and can interrogate the arterial tree from the aortic arch to the circle of Willis. Stenoses can be measured with electronic microcalipers based on NASCET or ECST methods.[80]

A meta-analysis of 28 studies analyzing the diagnostic accuracy of CTA compared with DSA showed a pooled sensitivity of 85% and specificity of 93% for CTA in detecting 70% to 99% carotid stenosis and a sensitivity and specificity for occlusions of 97% and 99%.[81] CTA was also highly accurate in identifying calcification but less reliable in describing carotid plaque morphology, specifically the lipid component, or ulceration. CTA appears less reliable than DUS imaging or MRA for assessing plaque morphology.[82] Other limitations of this technique include cost (compared with DUS), contrast exposure, and the added concern of radiation exposure. In addition, a large calcium burden can limit the ability to distinguish contrast from calcium during postprocessing imaging.

D. Catheter-based DSA

Many authorities still consider carotid conventional digital angiography to be the gold standard against all other imaging modalities in patients with extracranial cerebrovascular disease. Measurement of carotid stenosis using DSA is generally done using the NASCET method.[2] Conventional angiography is generally reserved for patients with conflicting imaging studies before CEA or in patients considered for CAS. DSA provides high-quality imaging that is accurate, objective, and easy to interpret. It can identify lesions from the aortic arch to the intracranial vessels. Major limitations of angiography that make it inappropriate as a screening modality include its cost and associated risks, specifically of stroke.[83-85] Overall, DSA is most useful in patients when less invasive imaging studies produce conflicting results. When DUS imaging is equivocal, DSA is preferred over CT and MR in evaluating patients with renal dysfunction (by minimizing contrast load), obesity, or indwelling ferromagnetic material, which render CTA or MRA technically inadequate or difficult.

E. Comparison of CDUS, MRA, CTA, and DSA

The U.K. Health Technology Assessment concluded that although contrast-enhanced MRA was the most accurate imaging modality overall, it was limited by unavailability, inaccessibility, and delays. Therefore, they concluded that color DUS imaging remained the preferred imaging modality for identifying patients with 70% to 99% stenosis.[86] As such, CDUS is the preferred imaging modality for the identification of asymptomatic stenosis.

This recommendation was based on several factors, including low cost, a much higher number of strokes likely to be prevented in the long-term by the rapid availability of CDUS imaging in contrast with other imaging, and the good sensitivity of imaging in detecting significant stenosis. However, the Health Technology Assessment highlighted the concern of the accuracy of DUS in diagnosing 50% to 69% stenosis, which carries a sensitivity of only 36% and a specificity of 91%.[86]

The utility of CDUS will depend on the clinical presentation of the patient. In neurologically symptomatic patients, a diagnosis by CDUS of stenosis between 50% and 69% is sufficient to proceed with surgery based on its specificity. However, a negative CDUS result would mandate another imaging study because of the low sensitivity of CDUS in this setting. In neurologically asymptomatic patients, a moderate stenosis (50% to 69%) diagnosed by CDUS should be confirmed by another imaging study before intervention is undertaken.

F. Imaging after carotid intervention

The prevalence of carotid artery restenosis after CEA varies between 1% and 37%,[87-90] although symptomatic recurrent stenoses is infrequent (0% to 8%).[87] Factors associated with restenosis include continued smoking, small ICA diameter, operative defect detected at intraoperative assessment, and primary closure after CEA. The aggregate incidence of residual and recurrent carotid stenosis after CEA in ACAS was 13%.[88] Of 136 patients who had restenosis, 8 (5.9%) underwent reoperation, only 1 of whom was symptomatic. There was no correlation between late stroke and recurrent stenosis. Similarly, Cao et al[89] randomized 1353 patients who underwent CEA. Of these, the eversion technique was used in 678, and standard CEA with primary closure was done in 419 and patch closure in 256. The life-table estimate of the cumulative risk of restenosis at 4 years was 4% in the eversion CEA group and 9% in the standard CEA group, and 98% of these patients were asymptomatic.

Several studies have reported the progression of contralateral stenosis after CEA.[91-93] Contralateral carotid stenosis progression was more frequent than ipsilateral recurrent stenosis during the long-term follow-up in these studies. These studies also identified that the risk of contralateral carotid artery stenosis progression depends on the existing disease at the time of the initial CEA.[91-93] The risk of progression for moderate stenosis at the initial surveillance to severe stenosis can be as high as five times.[92]

Several large prospective studies[94-99] have analyzed the rate of carotid in-stent restenosis after CAS. More patients had >70% stenosis of the ipsilateral carotid artery 1 year after CAS than after CEA (19% vs 5%). Use of CDUS to diagnose post-CAS restenosis is confounded by changes in the velocity criterion caused by the stent itself, and standard diagnostic criteria do not apply. Artifacts associated with both CTA and MRA similarly limit the utility of these techniques in the post-CAS patient. DSA is required to confirm restenosis after CAS identified by CDUS when reintervention is contemplated. In contrast, CDUS is sufficient to diagnose and plan therapy for restenosis after CEA.

● **Recommendations for selection of carotid imaging modalities**

1. CDUS in an accredited vascular laboratory is the initial diagnostic imaging of choice for evaluating the severity of stenosis in symptomatic and asymptomatic patients. Unequivocal identification of stenosis of 50% to 99% in neurologically symptomatic patients or 70% to 99% in asymptomatic patients is sufficient to make a decision regarding intervention (GRADE 1, Level of Evidence A).
2. CDUS in an accredited vascular laboratory is the imaging modality of choice to screen asymptomatic populations at high risk (GRADE 1, Level of Evidence B).
3. When CDUS is nondiagnostic or suggests stenosis of intermediate severity (50% to 69%) in an asymptomatic patient, additional imaging with MRA, CTA or DSA is required before embarking on any intervention (GRADE 1, Level of Evidence B).
4. When evaluation of the vessels proximal or distal to the cervical carotid arteries is needed for diagnosis or to plan therapy, imaging with CTA, MRA, or catheter angiography in addition to CDUS is indicated. CTA is preferable to MRI or MRA for delineating calcium. When there is discordance between two minimally invasive

imaging studies (CDUS, MRA, CTA), DSA is indicated to resolve conflicting results. DSA is generally reserved for situations where there is inconclusive evidence of stenosis on less invasive studies or when CAS is planned (GRADE 1, Level of Evidence B).

5. A postoperative DUS study ≤30 days is recommended to assess the status of the endarterectomized vessel. In patients with ≥50% stenosis on this study, further follow-up imaging to assess progression or resolution is indicated. In patients with a normal DUS study result and primary closure of the endarterectomy site, ongoing imaging is recommended to identify recurrent stenosis. In patients with a normal DUS after patch or eversion endarterectomy, further imaging of the endarterectomized vessel may be indicated if the patient has multiple risk factors for progression of atherosclerosis. There are insufficient data to make recommendations on imaging after CAS (GRADE 2, Level of Evidence C). Although the data in this area are not robust concerning intervals for follow-up imaging, the committee was unanimous in this recommendation, recognizing that follow-up DUS carries little risk.

6. Imaging after CAS or CEA is indicated to monitor contralateral disease progression in patients with contralateral stenosis ≥50%. In patients with multiple risk factors for vascular disease, follow-up DUS may be indicated with lesser degrees of stenosis. The likelihood of disease progression is related to the initial severity of stenosis (GRADE 2, Level of Evidence C). Although the data in this area are not robust concerning intervals for follow-up imaging, the committee was unanimous in this recommendation, recognizing that follow-up DUS carries little risk.

III. MEDICAL MANAGEMENT OF PATIENTS WITH CAROTID STENOSIS

Optimal medical management is an important part of overall treatment of all patients with carotid bifurcation disease, regardless of the degree of stenosis or the plan for intervention. This therapy is directed both at the reduction of stroke and overall cardiovascular events, including cardiovascular-related mortality. The best medical management for stroke prevention was highlighted in clinical practice guidelines issued jointly in 2006 by the AHA and the American Stroke Association, and cosponsored by the Council on Cardiovascular Radiology and Intervention and the American Academy of Neurology.[100]

A. Treatment of hypertension

Elevated blood pressure increases the risk for stroke,[101] and reducing blood pressure decreases the risk for stroke.[102] The relationship between blood pressure and stroke risk is "continuous, consistent, and independent of other risk factors."[103] The Framingham Heart study,[104] the Atherosclerosis Risk in Communities (ARIC) study,[105] and the Cardiovascular Health Study[106] each found that hypertension was independently associated with an elevated risk for carotid artery atherosclerosis. Each 10-mm

Hg increase in blood pressure results in an increase in risk for stroke of 30% to 45%. Each 10-mm Hg reduction in blood pressure amongst hypertensive patients decreases the risk for stroke by 33%.[102]

Lowering blood pressure to a target <140/90 mm Hg by lifestyle interventions and antihypertensive treatment is recommended in individuals who have hypertension with asymptomatic carotid atherosclerosis.[100] Aggressive lowering of blood pressure may harm patients who have had a recent stroke by reducing cerebral perfusion. In fact, the Joint National Committee for the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure-VII has remained ambiguous regarding recommendations for antihypertensive management in patients with a recent stroke.[103] However, antihypertensive therapy aimed at reducing blood pressures to <140/90 is recommended for patients who have had an ischemic stroke or TIA and are beyond the hyperacute period.[100]

B. Treatment of diabetes mellitus

In the Cardiovascular Health Study, an elevated fasting glucose level was associated with an increased risk for stroke in patients with carotid atherosclerosis.[107] The Insulin Resistance Atherosclerosis Study[108] and the Atherosclerosis Risk in the Community study[109] showed that diabetes was associated with intima-media thickness of the carotid artery and with progression in intima-media thickness. The United Kingdom Prospective Diabetes Study (UKPDS),[110] the Action to Control Cardiovascular Risk in Diabetes (ACCORD)[111] study, and the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE)[112] trial all tested whether tight control of serum glucose levels in diabetic patients would reduce the risk for stroke. Despite achieving hemoglobin A_{1C} levels <6.5%, no reduction in stroke risk was identified in these trials. Glucose control to nearly normoglycemic levels (target hemoglobin A_{1C} <7%) is recommended among diabetic patients to reduce microvascular complications and, with lesser certainty, macrovascular complications other than stroke.

C. Treatment of lipid abnormalities

The relationship between elevated cholesterol and incident MI in patients with coronary artery atherosclerosis is well established; however, the relationship between hypercholesterolemia and incident stroke is less clear. A meta-analysis of 45 studies of strokes in patients with hypercholesterolemia did not suggest an increased risk for stroke in patients with elevated serum cholesterol.[113] However, several other prospective studies in men and women have subsequently identified an increase in incident stroke associated with elevated cholesterol levels.[114-116]

Patients with known atherosclerosis have demonstrated reduced stroke rates when treated with lipid-lowering therapy. The Multiple Risk Factor Intervention Trial of statin therapy in hypercholesterolemic patients observed that greater reductions in levels of low-density lipoprotein (LDL) were associated with a reduction in stroke risk. A

meta-analysis of 26 trials observed that the risk of stroke decreased by >15% for every 10% reduction in serum LDL[117] in patients with known coronary or other atherosclerosis.

Further meta-analyses of statin trials that also reported on stroke as an outcome have shown that statin therapy reduces the risk of stroke by 15% to 30%.[118] The Stroke Prevention by Aggressive Reduction in Cholesterol trial found that atorvastatin treatment of patients with a recent stroke or TIA resulted in a reduction in stroke rate by 16% over 5 years.[119]

It is less clear if aggressive lipid-lowering therapy results in regression of carotid artery atherosclerosis. Aggressive statin therapy in the Measuring Effects on Intima-Media Thickness: an Evaluation of Rosuvastatin study,[120] the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol[121] study, and the Atorvastatin vs Simvastatin on Atherosclerosis Progression[122] study all showed increased regression of the carotid artery intima-media thickness compared with controls.

Although LDL is the primary determinant of cardiovascular and stroke risk, low levels of high-density lipoprotein (HDL) cholesterol also influence stroke risk, and elevation of HDL has been shown to reduce the risk of stroke.[123] In an analysis of a large (>9200) series of patients, treated by dual therapy aimed at decreasing LDL and raising HDL, elevation of HDL level was independently associated with a reduction of stroke risk by a factor of 0.86. Conversely, an elevated total cholesterol/HDL ratio increased stroke risk by a factor of 1.22. Reducing cholesterol absorption has also been shown to reduce stroke risk in patients with familial hypercholesterolemia.[124] Overall, however, the HDL level had much less effect on stroke risk than did the level of LDL.

Elevated cholesterol, comorbid CAD, or evidence of an atherosclerotic etiology of carotid stenosis should be managed according to National Cholesterol Education Program-Adult Treatment Panel III guidelines,[125] which include lifestyle modification or medications, or both. Statin agents are recommended targeting LDL of 100 mg/dL, for those with coronary heart disease or symptomatic atherosclerotic disease, and LDL of 70 mg/dL for very high-risk persons with multiple risk factors.

D. Smoking cessation

Smoking nearly doubles the risk of stroke.[126,127] Smoking also acts synergistically on other risk factors that are known to increase the risk of stroke, such as CAD and PAD. Conversely, smoking cessation results in a reduction in risk for CAD and for coronary mortality.[128] Cessation also reduces the risk of stroke in men and women.[128-130] Counseling and smoking cessation medications are effective in helping smokers to quit. Physician counseling is an important and effective intervention that reduces smoking in patients by 10% to 20%[131] but continues to be underused.[132] Nicotine replacement therapy, in the form of patches and gums, is effective in reducing smoking.[133]

Patients with extracranial carotid stenosis who are smoking cigarettes should be counseled to quit.

E. Antithrombotic treatment

No adequately powered studies have been performed in asymptomatic patients with carotid atherosclerosis to confirm a benefit with antithrombotic treatment in reducing incident stroke. The US Preventative Services Task Force has recommended daily aspirin as cardiovascular prophylaxis in patients with anticipated cardiac morbidity of >3% for men aged >45 years and in women aged >55 years.[134] These recommendations are based primarily on an observed reduction in overall cardiovascular morbidity and death with aspirin therapy. The AHA Primary Prevention of Cardiovascular Disease and Stroke agrees with this recommendation.[135] There is no evidence to suggest that antiplatelet agents other than aspirin have improved benefit in asymptomatic patients with carotid atherosclerosis.

Evidence for antithrombotic treatment for secondary prevention of recurrent stroke in symptomatic patients with carotid atherosclerosis is more robust.[100,136-139] The choice of antiplatelet therapy among aspirin, clopidogrel, and dipyridamole plus aspirin is not clearly defined because the data are uncertain.

The Clopidogrel in Unstable Angina to Prevent Recurrent Events[140] and Clopidogrel for the Reduction of Events During Observation[141] trials each showed a benefit of clopidogrel plus aspirin compared with aspirin alone in reducing vascular events in patients with prior acute coronary syndromes. The Management of Atherothrombosis with Clopidogrel in High-risk Patients[142] subsequently demonstrated no significant difference in vascular events between symptomatic patients with carotid stenosis treated with clopidogrel plus aspirin compared with clopidogrel alone.

Clopidogrel alone was initially shown to have a small advantage over aspirin in this subset of patients in the Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events[143] trial. However, it costs more than aspirin, and the subsequent Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance[144] trial showed that clopidogrel plus aspirin was equivalent to aspirin alone in preventing vascular events in patients with a prior stroke, TIA, or other cardiovascular disease or in patients with high risk for cardiovascular disease.

Antiplatelet agents are therefore recommended for patients with non-cardioembolic ischemic stroke or TIA associated with carotid atherosclerosis. Aspirin (50-325 mg/d), the combination of aspirin and extended-release dipyridamole, and clopidogrel, are all acceptable options for initial therapy; a combination of aspirin and clopidogrel is not recommended.

Aspirin is currently the most commonly used antiplatelet agent and one of the most frequently prescribed drugs, with as many as 30 million Americans on long-term aspirin regimens. A growing body of evidence suggests that some

patients compliant with aspirin therapy may still develop atherothrombotic complications, such as stroke. Reduced antiaggregant effect is more common in patients taking lower-dose aspirin (81 mg) or 325 mg aspirin with an enteric coating than it is in patients taking 325 mg of noncoated aspirin daily.[145] The lack of consensus for the definition of aspirin resistance and for the specific laboratory test to identify it has led to large variability in its reported prevalence.[146] The routine laboratory evaluation of platelet reactivity is not justifiable. The pharmacologic response to clopidogrel also demonstrates significant interindividual variability.

Patients with reduced platelet inhibition in response to clopidogrel appear to be at increased risk for cardiovascular events. This resistance may result from reduced bioavailability, polymorphisms of cytochrome P450, additional genetic variants, or increased platelet turnover.[147] Prasugrel is an alternate platelet-inhibiting pharmacologic agent of the same class as clopidogrel that does not have these limitations. It has been approved for use in acute coronary syndromes,[148] but no data are available on its use for stroke prevention.

As in the case of aspirin resistance, current evidence does not suggest the routine use of platelet function or genetic testing for clopidogrel resistance. In the absence of randomized trial data, the general approach to patients developing clinical events while taking aspirin or clopidogrel has been to confirm compliance and increase the dosage, followed by the addition or substitution of another antiplatelet agent.[149] However, data in this area are insufficient to allow clear recommendations.

F. Anticoagulant therapy

Parenteral and oral anticoagulants are effective in the prevention of embolic stroke in patients with atrial fibrillation or prosthetic heart valves. However, warfarin anticoagulation has been shown to be less effective than antiplatelet therapy for secondary prevention of neurologic events in patients with carotid atherosclerosis who do not have a history of atrial fibrillation and is not indicated in patients with symptoms of cerebral ischemia.[150,151] The Warfarin-Aspirin Reduced Cardiac Ejection Fraction Study trial is currently investigating the potential advantage in preventing cardioembolic stroke of anticoagulation vs aspirin in patients with chronic congestive heart failure.[152]

G. Medical management for the perioperative period of CEA

Hypertension is a common comorbidity in patients undergoing CEA. Blood pressure fluctuations, both above and below normal, are a significant source of morbidity and may contribute to MI and postoperative reperfusion syndrome. Careful periprocedural blood pressure management is critical to obtaining optimal results from the operation. Although the most recent AHA guidelines do not classify CEA as a high-risk surgical procedure mandating β-blockade, they do indicate that all patients with known CAD should receive β-blockade therapy before CEA to achieve a stable blood pressure and heart rate of 60 to 80 beats/min.[153,154] Given the near ubiquity of this condition in patients with carotid stenosis, β-blockade is nearly universally required in this patient group.

Patients taking combined aspirin and clopidogrel therapy in the perioperative period have a 0.4% to 1.0% higher risk of major bleeding compared with aspirin alone.[155] Aspirin therapy alone does not have to be discontinued before CEA.[156] The risks of periprocedural MI from aspirin withdrawal outweigh the risk of fatal or severe bleeding from aspirin use. The ACC Perioperative Guidelines endorses the continued use of aspirin before and after CEA.[153] A low dose (81 to 325 mg) appears at least as effective as higher doses, and higher doses may in fact be less effective.[157] Patients should continue aspirin therapy after CEA indefinitely, according to recommendations for high-risk patients with atherosclerosis.[100,136-139]

There has been a consensus that preprocedural clopidogrel should be stopped approximately 5 days before elective CABG.[46] Recent data from a large, retrospective, multicentered clinical experience[158] suggest that clopidogrel may be safely continued through the perioperative period without increased bleeding risk. It is therefore reasonable to individualize the management of perioperative clopidogrel therapy. There is no clear information regarding the risks or benefits of continued clopidogrel monotherapy in the periprocedural period for CEA.

One meta-analysis showed preoperative statin therapy resulted in a significant reduction in perioperative mortality in patients undergoing vascular surgery.[159] One small randomized trial found that perioperative death, MI, and stroke in patients undergoing vascular surgery was reduced in the group treated with atorvastatin.[160] In one large observational study of hospital records of 780,591 patients undergoing noncardiac surgery, the risk-adjusted mortality rate was significantly lower in those who received perioperative statins than in those who were not taking statins (odds ratio, 0.62; 95% confidence interval [CI], 0.58-0.67).[161] The evidence for continued use of statin therapy currently remains largely observational. Furthermore, the optimal time for starting therapy, the duration of therapy, dose, or target LDL levels to be achieved still remain to be determined.

H. Medical management for the perioperative period of CAS

Antihypertensive, β-blocker, and lipid-lowering therapy should be initiated in patients undergoing CAS according to the same recommendations for CEA. Patients should be started on dual antiplatelet therapy with aspirin (325 mg) and clopidogrel (75 mg) or ticlopidine (250 mg). No randomized trial has yet compared CAS performed with dual-antiplatelet therapy vs aspirin alone. However, the published periprocedural stroke, MI, and death rates in all recent clinical trials have been achieved with this combination therapy.[9,10,162,163] Dual-antiplatelet therapy should

be continued for 1 month after the procedure, and aspirin should be continued indefinitely.

● **Recommendations for medical management of patients with carotid atherosclerosis**

1. In patients with carotid artery stenosis, treatment of hypertension, hypercholesterolemia, and efforts at smoking cessation are recommended to reduce overall cardiovascular risk and risk of stroke regardless of whether intervention is planned. Targets are those defined by the National Cholesterol Education Program guidelines (GRADE 1, Level of Evidence A).

2. Aggressive treatment of hypertension in the setting of acute stroke is *not recommended*; however, treatment of hypertension after this period has passed is associated with reduced risk of subsequent stroke. The target parameters are not well defined (GRADE 1, Level of Evidence C).

3. Treatment of diabetes with the goal of tight glucose control has not been shown to reduce stroke risk or decrease complication rates after CEA and is *not recommended* for these purposes (GRADE 2, Level of Evidence A).

4. Anticoagulation is *not recommended* for the treatment of TIA or acute stroke, unless there is evidence of a cardioembolic source (GRADE 1, Level of Evidence B).

5. Antiplatelet therapy in asymptomatic patients with carotid atherosclerosis is recommended to reduce overall cardiovascular morbidity, although it has not been shown to be effective in the primary prevention of stroke (GRADE 1, Level of Evidence A).

6. Antiplatelet therapy is recommended for secondary stroke prevention: aspirin, aspirin combined with dipyridamole, and clopidogrel are all effective. Clopidogrel combined with aspirin is not more effective than either drug alone (GRADE 1, Level of Evidence B).

7. Perioperative medical management of patients undergoing carotid revascularization should include blood pressure control (<140/80 mm Hg), β-blockade (heart rate, 60-80 beats/min), and statin therapy (LDL <100 mg/dL) (GRADE 1, Level of Evidence B).

8. Perioperative antithrombotic therapy for CEA should include aspirin (81-325 mg) (GRADE 1, Level of Evidence A). The use of clopidogrel in the perioperative period should be decided case-by-case (GRADE 2 Level of Evidence B).

9. Perioperative antithrombotic management of CAS patients should include dual-antiplatelet therapy with aspirin and ticlopidine or clopidogrel. Dual-antiplatelet therapy should be initiated at least 3 days before CAS and continued for 1 month, and aspirin therapy should be continued indefinitely (GRADE 1, Level of Evidence C).

IV. TECHNICAL RECOMMENDATIONS FOR CAROTID INTERVENTIONS

The efficacy of carotid interventions depends on minimizing perioperative complication rates. This involves appropriate risk factor assessment and patient selection, perioperative therapy, and performance of a technically excellent operation. Perioperative therapy and medical management have been discussed in the previous sections. Specific recommendations on techniques to reduce complications of CEA and CAS are beyond the scope of this report and can be found elsewhere.[164,165] However, some general recommendations can be made regarding the conduct of CEA and CAS.

A. Carotid endarterectomy

Among the variables that have been studied to determine their effect on the outcome of CEA are local vs regional anesthesia, routine vs selective use of shunts, monitoring of brain function during the procedure, routine patch closure after endarterectomy, and completion imaging. Although several authors have suggested that use of regional or local anesthesia is associated with a reduced incidence of perioperative hemodynamic changes and cardiac events, a prospective randomized trial[166] and systematic review of the literature[167] failed to show any difference between the two anesthetic approaches.

An abundant literature exists on the indications identifying patients at risk of flow-related ischemia during CEA and the role of shunting in reducing this complication. Factors associated with increased risk of cerebral ischemia during carotid cross-clamping, and therefore the increased likelihood that a shunt will be needed, during CEA, include recent stroke, contralateral carotid occlusion, and symptoms suggestive of hemodynamic cerebral insufficiency.[168,169] Despite extensive study on the routine or selective use of shunts and cerebral monitoring during CEA, no clear benefit of one approach over the other has emerged.[170]

The routine use of completion imaging after CEA also remains an area of controversy. Although a number of authors have reported detecting abnormalities in 5% to 10% of patients using completion DUS imaging,[171,172] and a cost-benefit analysis suggests completion DUS imaging increases quality-adjusted life-years by 2%,[173] the clinical significance of many of these abnormalities is uncertain, and several series have reported excellent results without use of completion imaging.[174-176] Like the choice of anesthesia and shunting, completion imaging remains a matter of personal preference.

There are, however, data to recommend the use of patch angioplasty or eversion endarterectomy over standard endarterectomy with primary closure. Women and individuals with small ICAs are at most risk of early neurologic events and late restenosis if standard endarterectomy with primary closure is performed. Randomized studies have shown the benefit of patch closure over primary closure in patients undergoing standard CEA.[177] The type of patch material does not appear to have a significant effect on outcome. Prospective comparisons of eversion CEA with primary closure[178] have demonstrated a benefit of the eversion technique for reduction of early and late stroke.

This has been borne out by low rates of early stroke and late restenosis in large single-center reports.[179]

A number of investigations have studied the relationship of operative volume and specialty training with outcome. Although data suggest that there is some relationship between operative volume and outcome, the effect appears less than with other procedures.[180] In a large study of Medicare populations in Maryland and California, surgeons who perform 10 to 15 CEAs per year have better results than those who perform <5 procedures annually, but there was no added benefit to performing more than this relatively low threshold. There has been no consistent relationship between surgical specialty and outcome, and any effect seen is likely related to volume rather than specialty designation.[8,180,181]

B. Carotid artery stenting

The periprocedural management of the CAS patient has been discussed in a previous section. Periprocedural antiplatelet therapy is mandatory, and appropriate attention to access vessels and the status of the aortic arch is required for optimal results. The technical conduct of the CAS involves access of the target vessel, crossing the target lesion, and stent deployment. Technical issues related to carotid stenting include achieving a stable platform for the procedure, use of embolic protection devices, stent dilation before deployment, stent selection, and postdeployment dilation.

Stable sheath access in the proximal CCA is required. This depends on appropriate patient selection, as described above. Once a stable platform is obtained, a decision must be made about use of a cerebral protection device. In general, cerebral protection device deployment has been suggested to reduce the incidence of distal embolization and, potentially, the risk of stroke.[182,183] Although this position is not supported by robust data, it has been generally accepted by the medical community, and use of an embolic protection device has been required by Centers for Medicare and Medicaid Services to qualify for reimbursement.

Several embolic protection devices are available, and selection depends on lesion characteristics and anatomic considerations. Options include proximal or distal occlusion devices designed to interrupt forward flow during the procedure and filter devices placed distal to the lesion designed to trap debris released during the procedure. Distal occlusion devices have the advantage of a smaller diameter than proximal occlusion devices, but the lesion must be crossed before the device is placed in the ICA, a maneuver that can itself cause embolization. At the end of the procedure, suction is applied between the sheath in the CCA and the balloon occluding the distal internal carotid artery to remove debris.

Proximal occlusion devices require placement of two occlusion balloons, one each in the common and external carotid artery, with flow reversal by suction or creation of a proximal arteriovenous connection.[184] Placement of a proximal occlusion device avoids crossing the lesion before protection is in place and has been associated with the lowest incidence of distal embolization as detected by transcranial Doppler imaging or postoperative MRI.[184-186]

The main procedural disadvantages of the current proximal occlusion devices are the relatively large size (9F) of the access sheath, the need to occlude both the common and external carotid artery, and the need to establish venous access for continuous flow reversal. Proximal and distal occlusion devices may both be problematic in patients with poor intracranial collateral circulation because they mandate cessation—and sometimes reversal—of antegrade flow in the ICA. This situation is generally encountered in ≤5% of patients and may be managed by short intermittent inflation times.

Distal filters are deployed in the distal ICA and trap debris released during angioplasty and stent deployment. Like distal occlusion devices, they have the advantage of a smaller diameter (6F), but the lesion must be initially crossed in an unprotected fashion. These filters come in a variety of configurations and pore sizes. Their efficacy is related to the degree with which they can reliably achieve complete apposition to the distal arterial wall. They have the advantage that antegrade ICA flow can be maintained throughout the procedure; however, the filter may become completely occluded if large amounts of debris are released, and debris may escape distally during filter recapture.

The choice of filter device is often related to individual preference and familiarity. Some authors believe proximal occlusion with flow reversal is preferable in nearly all circumstances; however, this technique has its greatest advantage in lesions with a high risk of embolization (markedly irregular plaque, echolucent lesions, active symptoms) or in those that may be difficult to cross due to tortuosity or severe narrowing because protection is in place before the lesion is manipulated. Use of a filter over proximal or distal occlusion is preferred if there is a likelihood that interruption of antegrade ICA flow will not be tolerated. Distal occlusion devices are preferred to filters when the distal ICA anatomy suggests that compete apposition of filter to the distal ICA wall may be difficult due to size or tortuosity.

Direct comparison of proximal occlusion with flow reversal vs distal protection shows that proximal protection with flow reversal results in the lowest embolic load[165,185] However, no device can completely eliminate the risk of embolization during CAS. The fact that no embolic protection is completely effective and that some emboli originate during cannulation of the aortic arch and the proximal great vessels suggests that although improvements to embolization after CAS can be made, the problem cannot be eliminated.

Studies using postoperative diffusion-weighted MRI shown increased 17% incidence of MRI-identified infarcts in patients undergoing CAS compared with CEA (adjusted risk ratio, 5.21).[10] Although these are generally subclinical, recent reports suggest these lesions might be associated with subtle long-term neurologic changes. Echolucent lesions are more likely to be associated with increased embolic risk, whereas recurrent stenoses or fibrous lesions are

associated with a decreased risk of procedural embolization.[66,96,165,184]

Stent predilation is not recommended unless a filter cannot be passed. Stent selection is often based on physician preference. The only large study to test the effect of cell size suggests that closed-cell stents more effectively constrain the carotid plaque and reduce embolization,[187] but there is no consensus on that point. Open-cell stents are more conformable than closed-cell stents and are preferred by some in tortuous anatomy. Once the stent has been deployed, postdilation is used to ensure stent apposition to the plaque, but vigorous postdilation to achieve anatomic perfection is avoided.

The learning curve associated with CAS has been the object of considerable study. The Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis[162] (EVA-3S) study was criticized because of the requirement that interventionalists perform only 25 procedures to qualify for participation in the trial. The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) study required a significant lead-in phase for interventionalists and documentation of low procedural morbidity.[188,189] It is worth noting that CREST is associated with the lowest periprocedural complication rate in the literature. There are data in the literature that suggest achieving a low predictable complication rate after CAS requires a higher level of initial and ongoing experience than current guidelines suggest.[97,190,191]

No relationship has been demonstrated between specialty and outcome. Data from CREST demonstrate that vascular surgeons, cardiologists, interventional radiologists, and interventional neurologists can all achieve comparable results with CAS and that experience is more important than specialty designation in assuring optimal outcomes.[188,189]

● **Recommendations regarding CEA and CAS technique**

1. Patch angioplasty or eversion endarterectomy are recommended rather than primary closure to reduce the early and late complications of CEA (GRADE 1, Level of Evidence A).
2. Use of an embolic protection device (proximal or distal occlusion, distal filter) is recommended during CAS to reduce the risk of cerebral embolization (GRADE 1, Level of Evidence B).

V. SELECTING THE APPROPRIATE THERAPY: MEDICAL MANAGEMENT, CAS, OR CEA

Once a patient with a clinically significant carotid stenosis is identified, appropriate treatment must be selected. Treatment is primarily directed at the reduction of stroke risk. The risks of an interventional treatment must be considered when treatment choices are made. In general, rates of stroke, MI, and death have been used when comparing CAS with CEA. In most clinical trials comparing CAS with CEA, stroke, MI, and death have been given equal weight in determining a composite end point to test overall efficacy.

Data from CREST,[9] however, indicate that stroke has a more significant effect on quality of life at 1 year than nonfatal MI. Because the primary goal of intervention in carotid stenosis is stroke prevention, in developing its recommendations, the committee placed more emphasis on the prevention of stroke and procedurally related death than the occurrence of periprocedural MI. This may result in committee recommendations that differ from the published results of some trials where these three end points were given equal weight in analysis.

Treatment is chosen based on the assessment of risk associated with intervention and the likelihood that a particular intervention will favorably alter the course of the disease. The major determinants of the clinical course of patients with carotid bifurcation stenosis are the presence or absence of neurologic symptoms and the degree of carotid bifurcation stenosis. The threat of stroke in asymptomatic patients with <60% ICA stenosis and in symptomatic patients with 50% stenosis is generally considered to be small and does not warrant intervention. ECST and NASCET[2-4] demonstrated that CEA was unable to reduce the subsequent neurologic event rates in patients with symptoms of cerebral ischemia and bifurcation stenosis of <50% diameter reduction and was actually associated with increased morbidity compared with medical management. Stenoses of <60% diameter reduction were excluded from the asymptomatic studies,[5,6] assuming that asymptomatic patients with stenosis <60% would not benefit from carotid reconstruction. Given the findings of the symptomatic trials, this proved to be an appropriate decision. There have been no studies supporting either CEA or CAS for this cohort of patients.[16]

A. Assessing the risk associated with intervention

CEA and CAS are each associated with specific clinical scenarios that increase their respective risks. This section provides information to identify conditions that pose an increased risk for CAS or CEA and thereby help select the most appropriate therapy. When the risk of intervention is sufficiently increased due to the presence of one or more of these factors, medical therapy may be more appropriate than CEA or CAS.

In the initial CAS trials, a series of anatomic and physiologic criteria were developed by a consensus panel in an attempt to identify "high-risk" CEA patients who might be expected to benefit from CAS.[192] Although these criteria were used to enroll patients in CAS trials and registries, their ability to define "high risk" was never validated in a prospective manner. In fact, some have suggested that CEA could be safely performed in most of these patients.[193,194] As CAS experience matured, certain conditions have been shown to be associated with increased complications after CAS. Risk stratification can generally be divided into two categories: anatomic (including the lesion) characteristics and physiologic characteristics.

1. Anatomic and lesion characteristics.

a. Lesion location. CEA provides excellent access to the cervical carotid artery, but lesions that extend outside this zone can be difficult to treat surgically. Lesions at or above the level of the C2 cervical vertebra or below the clavicle are generally more difficult to expose surgically for CEA without increasing the morbidity of the operation. Lesions of the distal cervical carotid artery can be exposed by division of the digastric muscle and subluxation or division of the mandible, as required.[195,196] Although rarely required, these high carotid exposures may be associated with increased difficulty in directly visualizing the end point of the endarterectomy and with increased incidence of cranial nerve injury, particularly cranial nerve IX.[195,196] Lesions of the very proximal CCAs are difficult or impossible to expose without extending the incision into the chest. This must be considered when evaluating the morbidity of the procedure.

b. Lesion characteristics. Lesion-specific characteristics are thought to increase the risk of cerebral vascular events after CAS[66,197] and include a "soft" lipid-rich plaque identified on noninvasive imaging, extensive (15 mm or more) disease, a preocclusive lesion, and circumferential heavy calcification. A recent publication using multivariate logistic regression analysis of a large patient cohort demonstrated increased periprocedural stroke risk (odds ratios, 2.5-5.6) among patients with lesions >15 mm, excessive calcification, and ulceration.[197] An earlier study has shown a periprocedural stroke risk (odds ratio, 7.1) among patients with a lipid-rich plaque treated with CAS.[66]

The CAS procedure requires manipulation of a wire and a self-expanding stent through the carotid lesion. Unstable plaque increases the risk of embolization during placement of the wire or stent across the carotid lesion. This can be reduced, but not eliminated, by using flow-reversal embolic protection rather than distal filter protection.[185] Long segment lesions may require the placement of multiple stents, and this situation and preocclusive stenoses are both associated with a higher risk of acute or late stent occlusion. Heavy circumferential calcification makes lesion dilation more difficult and also increases the risk of embolization with CAS. There are no lesion specific characteristics that increase the risk of CEA.

c. Other anatomic considerations. Several anatomic situations may increase the difficulty of CEA. These include reoperation after prior CEA, existence of a cervical stoma, history of neck radiotherapy with resultant local fibrotic changes of the skin and soft tissues, and previous ablative neck surgery, such as radical neck dissection and laryngectomy.[193-195,198]

While CEA can be successfully performed in these situations, particularly when the tissues of the ipsilateral neck are not scarred and fibrotic, these situations can increase the risk of wound infection, difficulty of dissection, and potentially, the incidence of cranial nerve injury. The presence of a short, thick neck in an obese patient may make dissection more tedious but has not in itself proven to be associated with increased operative risk.

Anatomic factors to consider with CAS are related to access issues. Successful CAS requires remote access of the ICA artery using a stable platform to avoid the intravascular motion of sheaths, stents, and protection devices during the procedure. Anatomic factors that may complicate this process include aortoiliac tortuosity, a sharply angulated aortic arch (type III), or a carotid lesion with more than two 90° bends within a short distance of the target lesion.[197] Significant distal ICA tortuosity may also complicate the placement and stabilization of a distal embolic protection device. An aortic arch with heavy calcium or a high atherosclerotic burden is also associated with an increased risk with CAS. This is felt to be the main reason that CAS results are worse in patients aged >80 years.[199,200]

2. Patient characteristics. It seems intuitive that the risk of periprocedural events after CEA or CAS might be increased in patients presenting with severe comorbid conditions, including dialysis-dependent renal failure, New York Heart Association class III or IV heart disease, left ventricular ejection fraction <30%, class III or IV angina pectoris, left main or multivessel coronary disease, severe aortic valvular disease, oxygen- or steroid-dependent pulmonary disease, or both, contralateral carotid occlusion, and advanced age. However, little data exist to support one therapy over another in these patients.[162,163] In fact, defining a high-risk patient is much more subjective than defining a high-risk lesion.[193,194,201,202]

As will be seen later, CAS is associated with a lower incidence of cardiac events than is seen in CEA. Therefore, CAS would be preferred over CEA when severe cardiac comorbidities exist in neurologically symptomatic patients. Chronic renal insufficiency has been associated with increased risk of stroke and death after CAS[203,204] and CEA.[205,206] Univariate and multivariate analysis both show that the risk of death, stroke, and MI after CAS at 6 months was associated with hazard ratios >2.5 among patients with chronic kidney disease.[204] Chronic renal insufficiency also increases the risk of stroke after CEA (1.08% to 5.56%). Among asymptomatic patients with cardiac or renal insufficiency, best medical therapy may be preferable to CAS or CEA. CEA or CAS may be considered among symptomatic high-risk patients with moderate to severe carotid stenosis, but the effectiveness over medical therapy is not well established.

There are conflicting data on the influence of contralateral occlusion on the outcome of CEA or CAS. NASCET reported that a contralateral occlusion increased the risk of stroke after CEA from 5.8% to approximately 14%.[207] However, most reports regarding contralateral occlusion do not bear this observation out, and a meta-analysis of the literature suggests a much more modest increase, from 2.4% to 3.7%.[208,209] This was statistically significant, but the results remain within the AHA recommended guidelines. Several single-center studies have shown excellent results in patients with contralateral carotid occlusion.[210,211] A possible explanation for this discrepancy is an

inadequate sample size in the single-center studies. Alternatively, a more consistent technique of intraoperative management in single-center reports, including, algorithms for maintaining intraoperative cerebral perfusion, are more likely to occur in single-center experience than in multicentered studies.

CEA is associated with a lower stroke risk than CAS in patients aged >80 years.[152,161,162] A combined death, stroke, and MI rate of ≥10% has been seen in octogenarians treated with CAS.[152,161] In the CREST study, CAS was associated with an increased stroke risk in patients aged >70 years[9] and appeared to have a benefit compared with CEA in patients aged <70 years, although no other studies have reported this association to date.

Because there is a demonstrable incidence of cranial nerve injury after CEA that is absent after CAS, patients with a history of a contralateral vocal cord paralysis are at increased risk with CEA vs CAS; thus, CAS would be preferred in these patients.

B. Neurologically asymptomatic patients with carotid artery stenosis of 60% or more

1. CEA for asymptomatic lesions. Patients with asymptomatic lesions are currently responsible for nearly all of the carotid interventions performed in the United States.[7] Controlled randomized trials have compared CEA with best medical therapy, but there are a paucity of data on the role of CAS in asymptomatic patients. The results of ACAS[5] and ACST[6] favored CEA in the management of these patients. ACAS demonstrated the superiority of CEA over antiplatelet therapy alone for asymptomatic patients with carotid stenosis of ≥60%. This trial recommended CEA for these patients (aged <80 years) as long as the expected combined stroke and mortality rate for the individual surgeon was not >3%.

The long-term effectiveness of CEA in asymptomatic patients was confirmed by the recently updated results of ACST I, as reported by Halliday et al.[212] Compared with the randomized medical arm, where patients primarily received antithrombotic and antihypertensive therapy, the patients in the CEA arm (aged <75 years) experienced significantly lower perioperative and 10-year stroke rates (13.3% vs 17.9%). The strength of these conclusions have been questioned, based on the relatively modest absolute benefits of CEA and the contention that the medical therapy arm did not reflect contemporary medical management.[213,214]

The question of whether modern medical therapy (including statins) is equivalent or superior to CEA or CAS has not yet been addressed by well-designed, appropriately funded, prospective, multicenter, and randomized trials. An upcoming multicenter randomized trial designed to answer the role of modern pharmacologic therapy in the management of asymptomatic carotid stenosis is the Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis (SPACE-II) study,[215] which will include best medical therapy as the third arm of the trial together with CEA and CAS.

Concerns have also been raised about whether the results of the controlled trials could be attained in general practice. Critics pointed out that these trials were performed in centers of excellence and that the patients were highly selected. However, subsequent reports on patients who would have been excluded from these trials suggest that the exclusion criterion did not falsely lower complication rates. Combined stroke and death rates after CEA in patients defined as high-risk or eligible for high-risk carotid registries varied between 1.4% and 3.6%, well within the AHA guidelines.[193,194,210] Similarly, studies of large National Surgical Quality Improvement Program, state, and Medicare databases of between 4,000 and 35,000 patients[7,8,176,215] demonstrated stroke and death rates as low as 2.2% with a maximum of 6.9% (symptomatic patients only), suggesting that results that conform to national guidelines are achievable across large patient populations.

2. CAS in asymptomatic lesions. Very few studies have specifically addressed the outcome of carotid stenting in asymptomatic patients. CAS has been applied in asymptomatic patients based on the benefit seen for CEA, with the expectation that it would be equivalent or superior to CEA because of its less invasive nature. Many studies of CAS have been in the form of "high-risk" registries.[96,97,163,216-219] Others, such as the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) trial not, only had a small overall usage of stents (26%), but only 16 of 504 patients (<5%) in the study population were asymptomatic.[220] A single-institution study by Brook et al[85] comparing CEA with stenting in asymptomatic patients was also limited by the small number of patients and the lack of major postprocedural complications in either group.[221]

Another trial that suffered from a limited number of patients (<100 asymptomatic CAS) in addition to lack of randomization was the Carotid Revascularization using Endarterectomy or Stenting Systems (CaRESS) study. The primary outcomes were not stratified according to the presence or absence of neurologic symptoms, probably because of the small number of enrollees. The overall 30-day composite of death/stroke/MI was not statistically significantly different for CEA (4.4%) or for CAS (2.1%), and noninferiority of CAS was not demonstrated by statistical methodology.[222]

In 2004, the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, which included "high-risk" patients, 70% of whom were asymptomatic, demonstrated that the results of stenting with cerebral protection devices were not inferior to those obtained with CEA.[94] The primary end point of the study was the 30-day cumulative incidence of death/stroke/MI, which was 5.4% for asymptomatic patients who underwent CAS and 10.2% for CEA (P = .20).

The critics of this study raised several important issues, including the criteria used to define high-risk patients for CEA, the failure to randomize >50% of eligible patients, the unexpected high incidence of postoperative stroke, particularly in the asymptomatic patients, and questions

about reporting bias. A number of critics suggested that the absolute complication rates of both CAS and CEA in this study could not be used to justify either intervention in asymptomatic patients.[223,224] Murad et al[11] found that asymptomatic patients accounted for a minority of all patients entered in 13 trials of CAS vs CEA and that clear conclusions on the treatment of asymptomatic patients were not possible.

CREST[9] has been the only recent multicenter randomized trial that entered a significant number of individuals (1181 patients) with asymptomatic carotid artery stenosis. The published results show that although the risk of stroke with CAS was greater than for CEA in the asymptomatic patients, this was not statistically significant. The difference between CAS and CEA in asymptomatic patients for any periprocedural stroke was 2.5% vs 1.4%, respectively, and any periprocedural stroke, death, or postprocedural ipsilateral stroke was 2.5% vs 1.4%, respectively. These results for CAS and CEA were both within the AHA recommended guidelines.[13] In addition, the primary composite end point of the study that included any periprocedural stroke, death, MI, or postprocedural ipsilateral stroke was 3.5% for CAS and 3.6% for CEA ($P = 0.96$). These results are considerably better than any other large study, including ACAS and ACST for both procedures.[225]

The CREST results confirm that CEA and CAS can be done with relatively low complication rates in asymptomatic patients when performed by highly experienced practitioners who use their best judgment to select the most appropriate patient to be entered into the study. This study provides a benchmark to strive for, but no other large trials have achieved these results.

Unfortunately, the authors did not record the number of patients excluded from the study because they were not considered "good" candidates for any of the proposed procedures. Thus, the true applicability of CEA and CAS in the general population is unknown. This observation may lead one to believe that the CREST results reflect the best possible selection of candidates for CAS. This is particularly true when these results are compared with the considerably worse results presented in SAPPHIRE, the only other extant trial with a large number of asymptomatic patients.

Data published by the Society for Vascular Surgery Outcomes Committee demonstrated that real-world CAS was associated with a significantly higher rate of major complications than CEA in asymptomatic patients.[226] The 30-day outcome analysis of CAS and CEA in 2818 patients revealed the combined death, stroke, or MI rate for 1450 CAS patients was 4.6% vs 1.97% for 1368 CEA patients. Other studies of larger databases[7,8,201,215] have yielded similar results.

Further conclusions on the role of intervention in asymptomatic patients await the results of two additional randomized prospective studies designed to compare the early and long-term results of CEA vs CAS and best medical management: The Carotid Stenting vs Surgery of Severe Carotid Artery Disease and Stroke Prevention in Asymptomatic Patients (ACT I) and, the Asymptomatic Carotid Surgery Trial (ACST-2).[227] Results are not expected until at least 2018.

3. Medical management of asymptomatic carotid stenosis. There has been an increasing call for trials to compare modern medical management of carotid stenosis with both CEA and CAS.[213,214] This is based on the relatively modest absolute stroke reduction in both ACAS and ACST,[5,6] the effect of optimal medical management on stroke risk (see *Section III*), and the rates of stroke reported in SAPPHIRE and many carotid stent registries, all of which contain a significant number of asymptomatic patients. Operation for asymptomatic carotid stenosis should only be undertaken in good-risk patients where excellent results can be documented. In patients with a short life expectancy or multiple risk factors, medical management is likely to be superior to intervention. As noted, several studies have been designed to test the ultimate role of medical vs interventional management in asymptomatic carotid disease.

C. Neurologically symptomatic patients with 50% or greater carotid artery stenosis

1. CEA in symptomatic stenosis. NASCET and ECST both demonstrated the benefit of CEA in neurologically symptomatic patients with carotid stenosis that reduced diameter >50%.[2-4] NASCET demonstrated an absolute risk reduction in stroke of 17% at 2 years (24% in medical arm vs 7% in surgical arm) for patients with >70% carotid stenosis. ECST demonstrated a similar stroke risk in this group after 3 years in the medical arm, 26.5% with a stroke risk in the surgical group of 7%, an absolute reduction of 14.9%. In both studies, the risk of stroke in the medical arm, and therefore the benefit of CEA, increased with the degree of stenosis. The results of these trials firmly established CEA as the treatment of choice for patients with severe carotid stenosis and are widely accepted throughout the medical community. The benefit of CEA in more moderate stenosis of 50% to 69% was more moderate— 15.7% stroke after CEA vs 22.2% stroke with medical therapy at 5 years—but still statistically significant.[3] Stenoses <50% were not benefited by CEA.

2. CAS in symptomatic stenosis. A number of trials have examined the role of CAS in the management of neurologically symptomatic patients with >50% diameter stenosis. As previously mentioned, SAPPHIRE demonstrated overall equivalence of CAS and CEA in the management of carotid stenosis, although the number of symptomatic patients was too small for subgroup analysis.[94] Two large prospective randomized European trials, EVA-3S[162] and SPACE1,[228] examined the role of CAS vs CEA in neurologically symptomatic patients. EVA-3S showed a statistically inferior outcome for CAS compared with CEA (stroke death, 9.5% vs 3.8%) in these patients. This study was criticized because of the relatively low level of experience (minimum of 25 CAS cases) required in the CAS arm.

The Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial was designed to test "equivalence" between CEA and CAS in

patients with neurologic symptoms. This trial stopped after recruitment of 1200 patients due to the futility of proving equivalence between the two treatments. The rate of death or ipsilateral stroke at 30 days was 6.84% for CAS and 6.34% for CEA in 1183 randomized patients. However, the study was not powered appropriately and failed to show noninferiority of CAS compared with CEA (*P* = .09).

Subsequently the International Carotid Stenting Study Trial (ICST),[10] which enrolled 1713 patients, demonstrated an increased stroke risk for CAS (7.7%) compared with CEA (4.1%) in neurologically symptomatic patients. This observed difference was significant (*P* = .002). The rate of any stroke or death ≤30 days of treatment in the stenting group was more than twice the rate the rate recorded in the endarterectomy group (7.4% vs 3.4%, *P* = .0004). In addition, the composite end point of stroke, death, and MI significantly favored CEA (5.2%) vs CAS (8.5%; *P* = .006). It is of interest to note that the authors of this trial highlight the fact that they observed a higher rate of fatal MIs with CAS than with CEA. This observation has not been confirmed in other large studies, including CREST, and in meta-analysis, where the incidence of MI is higher in the CEA group.[11]

D. Meta-analysis: CEA vs CAS

Murad et al[11] recently completed an updated meta-analysis of all published trials comparing CEA and CAS in the management of patients with carotid stenosis. This analysis included data from the most recently completed randomized studies, CREST and ICST, which comprised 56% of all reported patients. Their analysis concluded that, compared with CEA, CAS was associated with a significantly reduced risk of perioperative MI (relative risk reduction [RRR], 0.43) and a significantly increased risk of any periprocedural stroke (RRR, 1.48). CAS was associated with an increased risk of periprocedural death (RRR, 1.40) that did not reach statistical significance. The risk of ipsilateral major stroke did not differ between the two procedures (RRR, 1.00), although the studies were underpowered to test this effect.

- ● **Recommendations for selecting therapy**

1. For neurologically symptomatic patients with stenosis <50% or asymptomatic patients with stenosis <60% diameter reduction, optimal medical therapy is indicated. There are no data to support CAS or CEA in this patient group (GRADE 1, Level of Evidence B).
2. In most patients with carotid stenosis who are candidates for intervention, CEA is preferred to CAS for reduction of all-cause stroke and periprocedural death (GRADE 1, Level of Evidence B). Data from CREST suggest that patients aged <70 years may be better treated by CAS, but these data need further confirmation.
3. Neurologically asymptomatic patients with ≥60% diameter stenosis should be considered for CEA for reduction of long-term risk of stroke, provided the patient has a 3- to

5-year life expectancy and perioperative stroke/death rates can be ≤3% (GRADE 1, Level of Evidence A).
4. CEA is preferred over CAS in patients aged >70 years of age, with long (>15-mm) lesions, preocclusive stenosis, or lipid-rich plaques that can be completely removed safely by a cervical incision in patients who have a virgin, nonradiated neck (GRADE 1, Level of Evidence A).
5. CAS is preferred over CEA in *symptomatic* patients with ≥50% stenosis and tracheal stoma, situations where local tissues are scarred and fibrotic from prior ipsilateral surgery or external beam radiotherapy, prior cranial nerve injury, and lesions that extend proximal to the clavicle or distal to the C2 vertebral body (GRADE 2, Level of Evidence B). CEA may be preferable in situations where ipsilateral tissue planes remain relatively intact.
6. CAS is preferred over CEA in *symptomatic* patients with ≥50% stenosis and severe uncorrectable CAD, congestive heart failure, or chronic obstructive pulmonary disease (GRADE 2, Level of Evidence C). In making this a GRADE 2 recommendation, the committee recognized the difficulty in clearly defining this group of individuals, both in symptomatology and risk assessment, and acknowledged the potential increased role of aggressive medical management as primary therapy in this high-risk group.
7. Neurologically asymptomatic patients deemed "high risk" for CEA should be considered for primary medical management. CEA can be considered in these patients only with evidence that perioperative morbidity and mortality is <3%. CAS should not be performed in these patients except as part of an ongoing clinical trial (GRADE 1, Level of Evidence B).
8. There are insufficient data to recommend CAS as primary therapy for neurologically asymptomatic patients with 70% to 99% diameter stenosis. Data from CREST suggest that in properly selected asymptomatic patients, CAS is equivalent to CEA in the hands of experienced interventionalists. Operators and institutions performing CAS must exhibit expertise sufficient to meet the previously established AHA guidelines for treatment of patients with asymptomatic carotid stenosis. Specifically, the combined stroke and death rate must be <3% to ensure benefit for the patient (GRADE 2, Level of Evidence B).

VI. UNUSUAL CONDITIONS ASSOCIATED WITH CAROTID STENOSIS

Vascular surgeons will encounter a number of clinical scenarios where the role of carotid intervention is not well established. Oftentimes the data regarding treatment are relatively sparse or represent single-center series rather than prospective randomized trials. These conditions, however, may still be associated with the development of cerebral symptoms, particularly cerebrovascular accident (CVA) and consequently warrant analysis and recommendation.[46,229] For the most part, randomized controlled trials

have not been performed to examine these conditions that occur infrequently, and consequently, Level I evidence is often not available to guide physician practice. Nonetheless, the task force members determined that it was appropriate to make some recommendations in areas where they could reach unanimous agreement. These recommendations should be taken as the best opinion of the task force given current available data. As stated earlier, they may well change in the future as therapy evolves and new data emerge.

A. Acute neurologic syndromes

Acute neurologic syndromes can be divided in to several clinical categories: acute stroke, stroke in evolution, and crescendo TIAs. The pathophysiology and concerns in each category are somewhat different, as are the treatment algorithms and outcomes.

Acute stroke is often associated with intracranial thrombosis, although this is less common in patients with the other two clinical presentations. As a consequence, a major management goal is to identify those patients with intracranial occlusion and to reperfuse the ischemic brain as rapidly as possible. Therapy is primarily directed at the intracranial occlusion. Although carotid bifurcation stenosis may be present, occlusion of the ICA in the neck is unusual in patients who are candidates for intervention.

In contrast, patients with crescendo TIA, by definition, have not had a significant volume of brain infarcted but do have a significant amount of brain at risk from a very unstable lesion with multiple small emboli or a large ischemic brain penumbra due to hemodynamic compromise and poor cerebral autoregulation. In these cases attention is directed at the source of symptoms, usually the carotid bifurcation.

Patients with stroke in evolution occupy a middle ground. Often there has been a permanent area of infarction, but the remaining ischemic penumbra is significant and attention is directed at salvaging this ischemic area as rapidly as possible.

In each of these clinical scenarios, expeditious clinical evaluation, brain imaging, and rapid evaluation of the carotid bifurcation is important in optimizing results. Brain imaging, most often by diffusion-weighted MRI, allows a rapid assessment of the amount of brain infarcted and the amount at risk, whereas CDUS imaging can assess the status of the bifurcation. As will be discussed below, this information dictates the branch points in treatment algorithms that follow. In general, patients with preocclusive carotid stenosis or carotid occlusion are considered for emergency intervention, whereas those with lesser degrees of stenosis are initially managed medically with urgent, but not emergency intervention, according to the recommendations for symptomatic patients with carotid stenosis.

1. Management of acute stroke.

a. Presentation within 0-6 hours. The National Institute of Neurological Disorders and Stroke trial established the efficacy of intravenous recombinant tissue plasminogen activator in the treatment of acute stroke, if therapy could be initiated ≤3 hours of the onset of symptoms.[230] Efficacy has also been established for transarterial intracranial infusion.[231] Factors that have been noted to influence results include the extent of hemispheric involvement, time to the initiation of therapy, time to reperfusion, age, blood glucose, and female sex.[232-235] The most important of these appear to be the degree of hemispheric involvement (>30% by volume), time to reperfusion, and age. The more rapidly intracranial reperfusion occurred, the better the neurologic recovery, with minimal improvement seen if reperfusion was not established before 6 hours.[234] Thrombolysis may be given by systemic (intravenous) or local (intracranial) routes, and both routes are used in some cases to facilitate rapid reperfusion.[234]

Intravenous recombinant tissue plasminogen activator (r-tPA) has the advantage of rapid onset of administration but the potential disadvantage of longer time to reperfusion. Administration of r-tPA into the intracranial thrombus requires assembling a neurointerventional team and therefore takes longer to implement but is more efficacious than systemic therapy alone. Data suggest that about 30% of patients will show neurologic improvement with intravenous r-tPA[235] and that recanalization will occur in >50% of patients ≤6 hours when systemic lysis is supplemented by local intra-arterial infusion.[234]

Mechanical thrombectomy, ultrasound-facilitated lysis, and clot fragmentation or extraction have all been proposed as methods to accomplish rapid reperfusion without the increased risk of hemorrhage associated with chemical thrombolysis.[236-238] Experience at this time is limited. The role of extracranial intervention in the form of CAS or CEA must be considered in the context of the treatment of intracranial thrombosis or obstruction. Angioplasty and stenting of the extracranial ICA may be performed as an adjunct to intracranial therapy. Treatment of extracranial disease offers the potential advantages of preventing further embolization from the extracranial carotid atherosclerosis, increasing perfusion to the ischemic penumbra surrounding the area of cerebral infarct, enhancing arterial flow to augment clot-dissolution therapies, improve access for intervention on the intracranial lesions, and potentially improve the patency of the intracranial intervention. The use of CAS as an adjunct to intracranial catheter-directed therapies has been evaluated in several case series.[239] Although the results initially reported have been favorable, the overall experience has been limited.

b. Presentation later than 6 hours. Only about 15% of acute stroke patients will present within the 6-hour time window for acute intervention.[240] Reasons for delay include failure to recognize symptoms, delay in seeking medical assistance, and a lack of nearby facilities capable of emergency intervention. As a result, many patients present outside this therapeutic window. Intervention in these patients is directed at the carotid bifurcation, not the intracranial circulation, with the goal of preventing recurrent

events rather than re-establishing intracranial flow in occluded arteries.

Patients with an acute fixed deficit of more than 6-hours' duration and a mild or moderate deficit may be considered for carotid intervention after a period of medical stabilization. It is generally accepted that intervention is safely performed early (≤2 weeks) after the event and is preferable to a delayed (4-6 weeks) intervention.[241-244] Advances in radiographic imaging have made possible the identification of a subset of patients who may benefit from carotid bifurcation intervention in the setting of acute stroke.[245,246]

Urgent CEA may be considered for patients in whom the distal ICA as well as middle cerebral artery and other intracranial vessels remain patent, who have limited areas of infarct (<30% of hemispheric volume), with significant areas of ischemic penumbra at risk for progression of the infarct, have a mild to moderate neurologic deficit, and are at risk for recurrent embolization and repeat stroke. Patients should be hemodynamically stable, with mild or moderate functional deficit, relatively preserved mental status, and a favorable prognosis.[247-252] Because these are symptomatic patients, CEA would be recommended unless the patients are at high risk for surgery due to medical morbidity or anatomic features.

There are separate groups of patients in whom the neurologic examination fluctuates under observation. These patients can be classified as having unstable neurologic syndromes, a category that includes both stroke in evolution and crescendo TIA. In these clinical syndromes, urgent or emergent therapy is often considered to reverse ischemia or salvage brain at risk.

2. Stroke in evolution (fluctuating neurologic deficits). This is a clinical syndrome that has been characterized by an evolving neurologic condition associated with an acute precipitating neurologic event. In these situations, the initial medical management of stroke, including antiplatelet agents, volume support, and blood pressure management, has not succeeded in stabilizing the patient's neurologic condition, which may "wax and wane" over the early course of disease. Although patients may never return to normal, their neurologic deficits will be mild to moderate in nature. These patients should have brain imaging to exclude hemorrhage as an etiology and to identify ischemic but viable brain. Carotid imaging by DUS, CTA, or MRA should identify a tight lesion in the carotid bifurcation.

The presumption is that optimizing hemispheric blood flow will improve perfusion to the ischemic hemisphere and reduce the ultimate extent of neurologic deficit. This must be balanced by concern that restoring blood flow may result in hemorrhagic conversion of an infarction or a reperfusion injury.

There are no large series of patients treated in a standard manner from which to draw definitive conclusions regarding optimal therapy. In patients where hemorrhage has been excluded by brain imaging, some surgeons use a heparin infusion to try to stabilize these patients and prevent propagation of thrombus as part of their immediate

management. Only a few reports have included outcomes of CEA in patients with stroke in evolution. In general the stroke/death rates range from 9.2% to 26.2%.[230,248,250-252] This reflects the heterogenous group of patients and lack of standard selection criterion for intervention. There are no data on unoperated-on controls for comparison. The lack of high-quality data on the treatment of stroke in evolution precludes any clear conclusions on the management of this group of patients. There has not been a significant experience with CAS in these patients, distinct from what is referenced above for acute stroke, to draw conclusions.

3. Crescendo TIA. This relatively rare clinical syndrome is characterized by repetitive episodes of transient neurologic ischemia, followed by return to a normal neurologic status. The definition of "crescendo" varies, but generally includes multiple repetitive events within a 24-hour period that do not respond to antiplatelet therapy. High-grade stenosis of the carotid bifurcation, often with associated ulceration or thrombus, is a common finding. Brain imaging does not reveal a significant area of infracted brain, and there may or may not be a large ischemic penumbra. Symptoms are thought to arise from an unstable carotid plaque with recurrent emboli despite antiplatelet therapy or from unstable cerebral hemodynamics associated with the bifurcation lesion.

Therapy in these patients is directed at removing the causative lesion at the carotid bifurcation. Again, some surgeons advocate heparin therapy in the immediate preoperative period if intracranial hemorrhage has been excluded, but this is based on personal experience rather than reported data. Urgent CEA in these patients has been associated with an increased risk of stroke compared with "elective" interventions. Overall, however, the results of surgery in patients with crescendo TIA are better than that of stroke in evolution. Systematic reviews of the literature for crescendo TIA report rates of stroke and death of 6.5% (95% CI, 3.4%-10.4%) and stroke, MI, and death of 10.9% (95% CI, 5.5%-17.9%). The comparable end points for stroke in evolution include stroke and death rates of 16.9% (95% CI, 9.2%-26.2%), and stroke, MI and death rates of 20.8% (95% CI, 13.2%-29.6%).[252] Although there are no data comparing CAS and CEA in these patients, the presumptive increase in embolic potential of these plaques suggests that CEA would be preferred to CAS when the former is feasible.

4. Acute postintervention stroke or occlusion. Patients who undergo carotid intervention may suffer stroke in the early postintervention period. Treatment aims at restoring intracranial blood flow to normal levels and depends on identifying the etiology of the stroke. In general, treatment decisions should be made as expeditiously as possible. Stroke that occurs immediately after CEA is considered secondary to a technical defect at the operative site, until proven otherwise. Other etiologies of stroke in the immediate postoperative period include embolization, intraoperative watershed infarction, and intracranial hemorrhage.

Of these four, early thrombosis at the endarterectomy site is the most common.[253] The status of the endarterectomy site should be determined. In most cases, this can be done by emergency bedside ultrasound imaging. If thrombosis is confirmed, then operative exploration with repair of the defect is indicated. Early re-exploration of an occluded endarterectomy site with successful repair may reduce long-term neurologic sequelae. Although there are no control groups available for comparison, re-exploration for symptomatic thrombosis has been associated with resolution of neurologic deficit in half to three-quarters of patients.[254-256]

If imaging shows the endarterectomy site is patent, other etiologies should be considered, specifically, distal embolization or intracranial hemorrhage. Emergency head CT to exclude hemorrhage is followed by anticoagulation and angiography, with intracranial intervention according to acute stroke guidelines. If capability for acute stroke intervention is not available, then anticoagulation and blood pressure support is indicated.

Acute stroke complicating CAS may result from embolization to the intracranial circulation during the procedure, occlusion of the angioplasty and stent site, or intracranial hemorrhage. Because CAS procedures are performed on patients who are awake, ongoing neurologic assessment is possible to guide evaluation and management. Management of acute, symptomatic intracranial embolization commonly reflects the current standard for intervention for acute stroke, as detailed in the previous section. Management options, including catheter-directed intra-arterial thrombolysis, clot dissolution or fragmentation with evacuation, and potentially, intracranial stenting, may be used as appropriate.[233,236-239,257] In selected cases, perfusion imaging may also be of utility in determining which patients will potentially benefit from intracranial revascularization.[245,246]

Acute occlusion of the stent has rarely been reported. A total of 10 cases of stent thrombosis have been reported, with causes being attributed to the use of inappropriate, balloon-expandable stents, inadequate antiplatelet or anticoagulation therapy, or plaque protrusion through the stent or technical failure Options for management are analogous to the techniques used for acute de novo occlusion of the internal carotid artery and include recanalization, intra-arterial thrombolysis, and management of the underlying cause of the occlusion.

● **Recommendations for management of acute neurologic syndromes**

1. Patients who present ≤6 hours of the onset of stroke should be considered for acute intervention to reduce the ultimate neurologic deficit. Interventions may include local or systemic thrombolysis (GRADE 1, Level of Evidence A). The role of endoluminal mechanical lysis or extraction remains to be defined.
2. Patients who present with fixed neurologic deficit >6-hours' duration should be considered for CEA once their condition has been stabilized. CEA should be performed ≤2 weeks of the neurologic event (GRADE 1, Level of Evidence B).
3. Patients who present with repetitive (crescendo) episodes of transient cerebral ischemia unresponsive to antiplatelet therapy should be considered for urgent CEA. The risk of intervention is increased over elective surgery for neurologic symptoms, but not as much as for patients with stroke in evolution. CEA is preferred to CAS in these patients based on the presumptive increased embolic potential of bifurcation plaque in this clinical situation (GRADE 1 Level of Evidence C).
4. For acute stroke after CEA, emergent imaging (ultrasound or fast CTA) is indicated to evaluate the endarterectomy site. When imaging suggests thrombosis, is indeterminate, or not available, immediate operative re-exploration is indicated (GRADE 1, Level of Evidence B).
5. When the endarterectomy site is patent, other modalities such as CT and angiography should be used to better identify the cause of the stroke. If CT excludes intracranial hemorrhage, anticoagulation is reasonable until a definitive decision regarding the appropriate diagnosis and therapy can be made (GRADE 2, Level of Evidence C). The committee acknowledged the lack of robust data in this small group of patients but was unanimous in its endorsement of this recommendation based on the data available and the low likelihood that new data would emerge in the near future.
6. No firm recommendations can be made on treatment of stent thrombosis associated with CAS. It is reasonable to attempt to restore patency by use of chemical lysis or clot extraction (GRADE 2, Level of Evidence C). The committee acknowledged the lack of robust data in this small group of patients but was unanimous in its endorsement of this recommendation based on the data available and the low likelihood that new data would emerge in the near future.

B. ICA occlusion with persistent symptoms and external carotid stenosis

Some patients with documented chronic occlusion of the ICA may develop recurrent neurologic or ocular symptoms. Neurologic symptoms may be secondary to embolization from the distal aspect of the occluded ICA segment, intrinsic disease of the external carotid artery, or from embolization from the proximal aspect of the occluded ICA. Ocular ischemia may arise from stenosis of the external carotid artery.[258] These patients may be managed by endarterectomy of the common and external carotid artery with transection and flush ligation of the ICA to remove the "stump" as a cause of the symptoms.[259,260] Alternatively, angioplasty and stenting of the external carotid artery has been used to enhance cerebral perfusion in patients with external carotid stenosis and occlusion of the ICA.[261]

Oral anticoagulation administration has been used in the treatment of patients with a stroke associated with chronic occlusion of the ICA. On meta-analysis, anticoagulation resulted in a significant reduction in the incidence

of recurrent CVA. In contrast, aspirin administration did not affect the recurrent stroke rate.[262]

● **Recommendations for management of symptomatic ICA occlusion**

1. Patients with known ICA occlusion and persistent ipsilateral neurologic symptoms can be treated by endarterectomy of the common and external carotid artery, with transection and ligation of the ICA origin. The addition of oral anticoagulation is likely to reduce the rate of recurrent CVA (GRADE 1, Level of Evidence C).

C. Carotid dissection

Carotid dissection may occur spontaneously or result from traumatic or iatrogenic injury. Historically, carotid dissection has been treated medically with antiplatelet agents or anticoagulation. Intervention has largely been reserved for patients with recurrent neurologic symptoms despite antithrombotic therapy, those who experience cerebral hypoperfusion due to hemodynamic effects of the dissection, or those in whom antithrombotic therapy is contraindicated. Open surgical therapy may be associated with significant rates of perioperative CVA and cranial nerve injury. The largest case series reported a 12.5% rate of combined recurrent stroke and death and a 58% rate of cranial nerve injury.[263]

More recently, endovascular techniques, including stent placement with or without adjunctive angioplasty, have been evaluated. Relatively few reports have been published on a small number of patients with dissection.[264-266] These initial results provide some encouragement, with the development of new or progressive symptoms occurring infrequently. Endovascular therapies appear to provide significantly superior results compared with open surgical approaches, with lower stroke rates and no cranial nerve injuries.

A comprehensive literature review identified 62 patients treated by endovascular means. The technical success rate reported was 100%, and the 1-year patency rate was 100%. The rate of recurrent CVA was 11% with no deaths.[264-266] No large series have been reported, and a multicenter trial appears to be warranted. With these considerations, endovascular treatment of patients when medical management fails appears to be justified.

● **Recommendations for management of carotid dissection**

1. Patients with carotid dissection should be initially treated with antithrombotic therapy (antiplatelet agents or anticoagulation) (GRADE 1, Level of Evidence C).
2. Patients who remain symptomatic on medical therapy may be considered for intervention. Although data are insufficient to make firm recommendations, the committee unanimously agreed that balloon angioplasty and stenting is currently preferred over open surgery after failed medical management (GRADE 2, Level of Evidence C).

D. Combined carotid and coronary disease

The incidence of concomitant carotid and coronary atherosclerosis is significant. Patients who have coronary disease amenable to percutaneous coronary intervention should be treated in that manner, followed by treatment of the carotid stenosis. The presence of carotid disease has been associated with an increase in the incidence of CVA in the perioperative period for cardiac surgery. The presence of a bruit increases the risk of CVA to 1.6% to 5.5%, and the presence of a carotid stenosis between 50% to 99% increases the risk to 2.0% to 8.4%.[38,46,267] Consequently, the management of concomitant carotid and coronary disease has been the subject of considerable study.

For patients experiencing symptoms related to a carotid stenosis (TIA, CVA), the risk of CVA associated with cardiac surgery is increased to such a degree that concomitant management of the carotid disease is mandatory. Prior CVA or TIA increases the risk of perioperative stroke to 2.2% to 8.5%. If bilateral 50% to 99% stenoses are present, the risk of perioperative CVA increases to 5.2% (95% CI, 0%-10.8%). If carotid occlusion is present, the risk of perioperative CVA increases to 7% to 12% (95% CI, 2.1%-21.2%).[268-271] Alternative treatments, including combined CEA and CABG, staged CEA and CABG, or CAS and CABG have all been reported.

A review of the literature to date suggests that CEA, followed by CABG, is associated with the lowest stroke rate, whereas combined CEA and CABG carries a higher mortality rate, and delayed CEA is associated with the lowest mortality but the highest stroke rate. Most studies are retrospective reviews, and there is no evidence that patient groups are comparable. However, in a meta-analysis, Naylor et al[269] found that the total stroke/MI/death rate associated with any combination CEA and CABG ranges from 9% to 12%.

In contrast to patients with neurologic symptoms and those with severe bilateral carotid bifurcation stenosis, the management of patients requiring cardiac surgery in whom unilateral asymptomatic carotid stenosis has been identified is not established. Documentation of a increase in the perioperative stroke rate in patients undergoing cardiac surgery who have been identified as having concomitant carotid disease has been well established for decades.[272] An increase in the incidence of CVA in the perioperative period for patients undergoing cardiac surgery has been demonstrated for patients with a carotid bruit, carotid stenosis >50%, or a history of TIA or CVA. Stenoses <70% do not appear to be associated with increased stroke.[271,273]

Unfortunately, the literature is not consistent with regard to the degree of stenosis reported as "significant" or the criteria for screening and quantifying stenosis. As a result, accurate assessment of the stroke risk associated with an asymptomatic stenosis in CABG patients is not possible at this time. It remains uncertain if correction of carotid disease before cardiac surgery is effective in lowering the perioperative rate of CVA for those patients. Only two randomized controlled trials have compared combined CEA/CABG with a strategy of CABG first and delayed CEA in patients with unilateral asymptomatic carotid stenosis. Hertzer et al[274] demonstrated reduced combined

stroke/death rates for combined CEA/CABG compared to staged CEA (5.6% vs 17%). The stroke rate associated with the "unprotected" CABG was 7.4%, compared to a stroke rate of 2.8% with combined CEA/CABG. Recently, Illuminati et al[275] reported randomizing 185 patients with unilateral severe (>80%) asymptomatic carotid stenosis, in whom aortic arch disease had been excluded by preoperative CT scan, between "protected" CABG (15 CEA first, 79 combined CEA and CABG) and "unprotected" CABG with CEA performed at a later time (within 3 months) (91 patients). There were no strokes in the "protected" group, compared to 7 strokes (3 early, 4 later) in the "unprotected" group. All strokes were ipsilateral to the stenosis and occurred before CEA was performed. These two reports suggest that patients with asymptomatic unilateral severe stenosis may benefit from CEA before or with CABG in centers with considerable experience. However, further studies are required before a general recommendation can be made. Other factors, including the specific nature of the cardiac surgery being performed, length of cardiopulmonary bypass, and the status of the aortic arch, among a variety of other risk factors, are important in determining overall stroke risk after CABG.[271,276] The best results, stroke/death rates of 2.2%, have been reported for off-pump CABG and synchronous CEA, although there is likely a significant influence of patient selection in these series.[277] It is also possible that the presence of carotid stenosis is a surrogate marker for stroke risk, rather than a preventable, direct cause (as evidenced by patients with unilateral carotid occlusion who exhibit the highest perioperative rates of CVA).[269]

In summary, significant indirect evidence suggests that treatment of neurologically symptomatic carotid stenosis or patients with bilateral asymptomatic severe disease may reduce the incidence of perioperative CVA in patients undergoing cardiac surgery. The data on treatment of unilateral asymptomatic stenosis >70% suggest CEA before or in combination with CABG is reasonable in centers of excellence but the data at this point are insufficient to make a firm recommendation. Local results are critical in determining appropriate therapy.

When coronary intervention can be performed percutaneously, this should precede carotid intervention. Data indicating trends toward improved outcomes for simultaneous performance of the surgical procedures at institutions that manage these conditions regularly are not sufficiently robust to support a definitive recommendation. More recently, some studies suggested a potential role for CAS before CABG, with a trend toward decreased stroke rates in the patients treated with CAS.[278,279] A review of the Nationwide Inpatient Sample found the risk of perioperative stroke was 62% higher for combined CEA and CABG (3.9%) compared with combined CAS and CABG (2.4%), with an OR of 1.62 (95% CI, 1.1-2.5).[278]

If a sequential strategy is planned, CABG may need to be deferred for 2 to 4 weeks because of the need for dual-antiplatelet therapy after CAS. This has resulted in some logistical difficulties in patients who require urgent coronary revascularization. A meta-analysis of all published results[280] suggested that the stroke/death rate of 9.1% seen with CAS and CABG is not significantly different than the results with CEA and CABG. One must conclude that data are insufficient to support a clear recommendation for treating patients with unilateral asymptomatic carotid stenosis who need CABG.

● **Recommendations for management of combined carotid and coronary disease**

1. Patients with symptomatic carotid stenosis will benefit from CEA before or concomitant with CABG. The timing of the intervention depends on clinical presentation and institutional experience (GRADE 1, Level of Evidence B).
2. Patients with severe bilateral asymptomatic carotid stenosis, including stenosis and contralateral occlusion, should be considered for CEA before or concomitant with CABG (GRADE 2, Level of Evidence B).

AUTHOR CONTRIBUTIONS

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