Case Presentation

A 64-year-old man with a past medical history of diabetes mellitus, hyperlipidemia, and hypertension presented with acute-onset left hemiparesis, hemisensory loss, and dysarthria. He was diagnosed with a right middle cerebral artery stroke and treated with systemic thrombolysis. His poststroke workup included a carotid duplex ultrasound and computed tomographic angiogram of the carotid arteries (Figure 1), which confirmed a severe (70%–99%) stenosis in the right internal carotid artery (ICA) secondary to a 20-mm-long atherosclerotic plaque extending from the carotid bifurcation to the level of C2-C3 disc space. The left ICA showed moderate (50%–69%) stenosis. Should this patient be recommended for carotid artery revascularization, and, if so, by which method?

Stroke, defined as acute development of a focal neurological deficit attributable to the disruption of blood flow to the brain, is caused by 1 of 2 main causes: ischemia or hemorrhage. The majority (>80%) of strokes are of ischemic etiology, of which ≈15% to 20% are attributable to atherosclerosis of the extracranial carotid arteries. The risk of death and recurrent stroke increases following an ischemic stroke. Transient ischemic attacks, or stroke-like symptoms that last <24 hours, are also associated with an increased risk of early recurrent stroke, particularly in patients with carotid artery atherosclerosis.

The bifurcation point of the common carotid artery, or carotid bulb, is predisposed to the development of atherosclerosis owing to low wall shear stress and resulting flow stagnation. Narrowing or stenosis of the carotid bulb and ICA because of atherosclerosis can lead to ischemic stroke secondary to plaque embolization or hypoperfusion. The prevalence of ICA stenosis is estimated to be 2% to 3% in the general population, with increased prevalence noted in men and the elderly. Other factors associated with ICA stenosis include smoking, hypertension, hyperlipidemia, coronary artery disease (CAD), diabetes mellitus, peripheral arterial disease, abdominal aortic aneurysm, and Native American or white race.

Although evidence for routine radiographic screening for ICA stenosis in asymptomatic patients is lacking, patients who experience a stroke or transient ischemic attack routinely undergo vascular assessment of the carotid arteries. Conventional cerebral angiography is considered the gold standard test for the diagnosis of carotid artery stenosis. However, its use is generally limited in preoperative carotid evaluation because of its invasive nature, financial costs, and a small but real risk of stroke. Noninvasive alternatives such as duplex ultrasound, computed tomographic angiography, and magnetic resonance angiography have essentially replaced cerebral angiography, given their high sensitivity and specificity for identifying high-grade carotid stenosis.

Each year, ≈795 000 people experience a new or recurrent stroke in the United States, and ≈130 000 die of stroke. Furthermore, stroke is a leading cause of

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long-term disability and has substantial economic impact on society, with medical costs of up to $38.6 billion every year in the United States. Therefore, stroke prevention and decreasing the risk of recurrent stroke are important.

The primary goal in carotid artery revascularization is to prevent stroke in patients with carotid artery stenosis. Treatment options include the following:

1. Best medical therapy (BMT)
2. Carotid endarterectomy (CEA)
3. Carotid artery stenting (CAS)

Making a decision among the treatment options is based on the following factors:

1. Patient factors
2. Disease factors
3. Resources

### Patient Factors

#### Age

Age ≥70 years has been associated with increased periprocedural risk with CAS in comparison with CEA. Data from a subanalysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST),1 and a Cochrane meta-analysis of 16 carotid revascularization randomized clinical trials (RCTs)2 consistently reported significantly increased risk of periprocedural stroke or death in CAS-treated patients ≥70 years of age. This observation is likely related to unfavorable anatomy in the elderly, such as increased vessel tortuosity, greater burden of atherosclerosis, and decreased plaque stability.

#### Sex

Most major RCTs have reported that women received less benefit from CEA than men,3–7 although some population-based studies have shown no difference in outcomes. The effect of the female sex on CAS is unclear. A subanalysis of CREST reported an increased risk of stroke or death in symptomatic women who underwent CAS in comparison with CEA,8 whereas a meta-analysis of the 3 European RCTs showed no significant difference.9 Population-based studies have also provided conflicting evidence regarding the effect of sex on CAS in comparison with CEA. Consequently, for now, the female sex should not be considered a high-risk factor for CAS.

#### Comorbidities and Operative Risk

Myocardial infarction is the major non-neurological complication of carotid revascularization. CEA has been associated with an increased risk of periprocedural myocardial infarction in comparison with CAS in recent RCTs.2,10,11 Accordingly, the cardiac status of each patient should be investigated before the selection of the appropriate carotid revascularization procedure. Chronic kidney disease has been associated with an increased risk of complications following both CEA and CAS, whereas the impact of diabetes mellitus on CEA and CAS remains poorly understood, and reports give conflicting results. The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, which showed noninferiority of CAS in high-risk patients, defined patients with clinically significant cardiac disease (congestive heart failure, abnormal stress test, or need for open-heart surgery) and severe pulmonary disease as at high risk for carotid revascularization.10

#### Life Expectancy

A patient’s life expectancy is an important factor in deciding whether to proceed with carotid artery revascularization. The symptomatic carotid artery stenosis RCTs showed a significant reduction in stroke rate with CEA at 2 to 3 years postprocedure.3–5 For asymptomatic patients, the Asymptomatic Carotid Atherosclerosis Study (ACAS) and Asymptomatic Carotid Surgery Trial (ACST) showed a small benefit for CEA in comparison with BMT at 5 years.6,7 Therefore, asymptomatic patients should have a life expectancy of at least 3 to 5 years to gain a significant benefit from carotid revascularization, whereas symptomatic patients benefit almost immediately.

#### Functional Status

Particular attention toward patient functional status is critical to determine whether patients will benefit from carotid revascularization. Patients with dense hemispheric neurological deficits, significant dementia, or severely limited functional status attributable to poor cardiac, renal, or pulmonary reserve are unlikely to benefit from any form of carotid revascularization. Final decisions for the treatment course should include input from the physician, patient, and family.

#### Patient Preference

When carotid artery revascularization is considered, the choice to proceed with CEA or CAS should involve the patient, and an adequate discussion about the advantages and disadvantages...
Each procedure should take place. Furthermore, patient input is essential for the management of asymptomatic carotid disease, because patients may elect to undergo BMT alone given the smaller benefit of carotid revascularization, depending on their personal preference.

### Disease Factors

#### Risk of Stroke

1. Symptomatic status. The North American Symptomatic Carotid

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sample Size</th>
<th>Patient Population</th>
<th>Primary End Point</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPPHIRE</td>
<td>334</td>
<td>Symptomatic &gt;50% stenosis Asymptomatic &gt;80% stenosis High risk</td>
<td>30-d stroke, MI, death + 1-y ipsilateral stroke, death</td>
<td>1-y: 12.2% CAS vs 20.1% CEA; ( P=0.004 ) 3-y: 24.6% CAS vs 26.9% CEA; ( P=0.71 )</td>
<td>CAS noninferior to CEA in high-risk patients</td>
</tr>
<tr>
<td>EVA-3S</td>
<td>527</td>
<td>Symptomatic &gt;60% stenosis Standard risk</td>
<td>30-d stroke, death 4 y/10 y: 30-d stroke, death + ipsilateral stroke</td>
<td>30-d: 9.6% CAS vs 3.9% CEA; ( P=0.01 ) 4-y: 11.1% CAS vs 6.2% CEA; ( P=0.03 ) 10-y: 11.5% CAS vs 7.6% CEA; ( P=0.07 )</td>
<td>Failed to prove noninferiority of CAS in standard-risk symptomatic patients</td>
</tr>
<tr>
<td>SPACE</td>
<td>1196</td>
<td>Symptomatic &gt;70% stenosis Standard risk</td>
<td>30-d stroke, death 2 y: 30-d stroke, death + ipsilateral stroke</td>
<td>30-d: 6.8% CAS vs 6.3% CEA; ( P=0.09 ) 2-y: 9.5% CAS vs 8.8% CEA; ( P=0.62 )</td>
<td>Failed to prove noninferiority of CAS (noninferior margin = &lt;2.5%) in standard-risk patients</td>
</tr>
<tr>
<td>ICSS</td>
<td>1713</td>
<td>Symptomatic &gt;50% stenosis Standard risk</td>
<td>120-d stroke, death, MI 5 y: fatal or disabling stroke</td>
<td>120-day: 8.5% CAS vs 5.2% CEA; ( P=0.006 ) 5-y: 6.4% CAS vs 6.5% CEA; ( P=0.77 ) 5-y any stroke: 15.2% CAS vs 9.4% CEA; ( P&lt;0.001 )</td>
<td>Failed to prove noninferiority of CAS in standard-risk patients; differences attributable to more nondisabling 30-d strokes with CAS</td>
</tr>
<tr>
<td>CREST</td>
<td>2502</td>
<td>Symptomatic &gt;50% stenosis Asymptomatic &gt;50% stenosis Standard risk</td>
<td>30-d stroke, MI, death + 4-y ipsilateral stroke</td>
<td>30-d: 5.2% CAS vs 4.5% CEA; ( P=0.38 ) 4-y: 7.2% CAS vs 6.8% CEA; ( P=0.51 ) 30-d stroke, death in Symptomatic: 6.0% CAS vs 3.2% CEA; ( P=0.02 ) 30-d MI: 1.1% CAS vs 2.3% CEA; ( P=0.03 )</td>
<td>CAS noninferior to CEA in standard-risk patients; Greater risk of MI with CEA and stroke with CAS; CAS in elderly and symptomatic patients at highest risk of stroke</td>
</tr>
</tbody>
</table>

CAS indicates carotid artery stenting; CEA, carotid endarterectomy; CREST, Carotid Revascularization Endarterectomy versus Stenting Trial; EVA-3S, Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; ICSS, International Carotid Stenting Study; MI, myocardial infarction; SAPPHIRE, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; and SPACE, Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy.

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of each procedure should take place. Furthermore, patient input is essential for the management of asymptomatic carotid disease, because patients may elect to undergo BMT alone given the smaller benefit of carotid revascularization, depending on their personal preference.

### Disease Factors

#### Risk of Stroke

1. Symptomatic status. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) established that patients with ipsilateral neurological symptoms within 6 months have the greatest risk of stroke, and benefit most from CEA.\(^3\)-\(^5\) This benefit was greater than that seen for patients in the major asymptomatic trials.\(^6\)-\(^7\) Contemporary RCTs comparing CEA and CAS have demonstrated that CEA is superior to CAS in the treatment of symptomatic patients, with the greatest benefit in the first week after symptom onset.\(^12\)-\(^16\) Data from CREST indicated CAS may be an alternative to CEA in asymptomatic standard-risk patients if performed by experienced interventionalists who have an established stroke rate of <3%.\(^11\) However, other RCTs have yet to confirm the noninferiority of CAS in this asymptomatic population.

2. Degree of stenosis. Carotid artery diameter is used as a surrogate marker for atherosclerotic...
Table 2. Advantages and Disadvantages of Carotid Artery Stenting

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>• Lower risk of perioperative MI</td>
<td>• Higher risk of perioperative stroke</td>
</tr>
<tr>
<td>• Suitable option for high-risk patients</td>
<td>• Associated with worse outcomes in symptomatic</td>
</tr>
<tr>
<td>• Suitable option for patients with hostile neck</td>
<td>• Not a suitable option for patients with lesions at</td>
</tr>
<tr>
<td>or hostile carotid</td>
<td>• Evidence for noninferiority in standard-risk and</td>
</tr>
<tr>
<td>• Can be performed under local/regional</td>
<td>asymptomatic patients is limited</td>
</tr>
<tr>
<td>anesthesia</td>
<td></td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction.

plaque size and volume. NASCET reported an increased risk of stroke in high-grade (≥70%) carotid stenosis in comparison with moderate-grade (50%–69%) stenosis.3,4 Patients with <50% stenosis have minimal risk of stroke.

3. Plaque characteristics. Identifying high-risk carotid plaques in asymptomatic patients can help predict which patients are at highest risk of stroke. Unstable plaques show characteristics of ulceration, intraplaque hemorrhage on MRI, rapid progression, increased plaque area, plaque heterogeneity with increased echolucency, low gray-scale median, and presence of discrete white areas within the plaque.

4. Contralateral disease. Contralateral carotid artery occlusion has been associated with increased risk in patients undergoing CEA, with inadequate intracranial collateral circulation as a potential risk factor. Studies comparing CEA and CAS in patients with contralateral carotid occlusion have been conflicting. Hence, based on the available evidence, one procedure cannot be recommended over another in this population.

Anatomic Considerations

1. Hostile neck. CAS is preferred to CEA in patients with challenging neck anatomy and high operative risk. This includes previous radical neck surgery or external beam radiotherapy, contralateral laryngeal nerve palsy, or tracheostomy. Whether CAS or CEA is preferable for recurrent carotid artery stenosis remains debatable.

2. Hostile carotid. CAS should be considered in patients with carotid lesions distal to the C2 vertebral body or proximal to the clavicle because they are difficult to tackle surgically. However, ICA-common carotid artery angulation >60 degrees, target ICA lesion >10 to 15 mm in length, ostial involvement of the lesion, and excessive calcification have been associated with worse outcomes in CAS-treated patients in comparison with CEA-treated patients.

3. Aortic arch. Particular attention should be given to the configuration, tortuosity, and extent of calcification of the aortic arch, because these factors can increase the risk of stroke with CAS and the technical complexity of the procedure.

Resources

Resource availability is an important factor, particularly when CAS is considered. CAS is a technically demanding procedure that should be performed by experienced operators in specialized centers to minimize poor outcomes and maximize procedural success. The optimal training requirements for CAS are unclear, because several multidisciplinary societal guidelines have proposed a diversity of training standards for CAS, ranging from a minimum of 30 to 150 diagnostic cervicocerebral angiograms, and 25 to 75 CAS procedures. Increased operator and institutional experience has also been associated with lower rates of stroke/death following CAS, with operator volume of ≥6 cases per year and center experience of >150 CAS procedures associated with the best outcomes. Therefore, if CAS is considered, patients should be referred to an operator and center with endovascular expertise in this procedure.

Carotid Endarterectomy Versus Stenting

CEA was established as the gold standard treatment for symptomatic patients with ICA stenosis after 2 large RCTs in the 1990s (NASCET, ECST) demonstrated the superiority of CEA over medical management for stroke prevention.3–5 Two large asymptomatic trials (ACAS, ACST) also showed a small (6%) reduction in stroke rate with CEA at 5 years in comparison with medical therapy.6,7 Therefore, the selection of asymptomatic patients for CEA is guided by a detailed assessment of patient life expectancy, comorbid conditions, surgeon/institution stroke rate, and patient preference.

CAS, since its introduction in 1980, has undergone significant evolution. Technological advances and improved operator experience over the past decade have led to a refined, modern CAS technique. Major innovations in the CAS technique include the routine use of stenting, routine use of embolic protection devices, improved endovascular tools and equipment, and new antiplatelet drugs. To that end, several contemporary RCTs comparing the gold standard CEA with modern CAS have been published since 2000, with conflicting results. Nonetheless, the use of CAS has significantly increased in the United States over the past decade.

Outcomes

Results from the 5 major CEA versus CAS RCTs are presented in Table 1.10–20 Taken as a whole, the current evidence from RCTs has not proven the noninferiority of CAS to CEA. A recent meta-analysis of these RCTs has shown a similar trend: CAS-treated patients have a 1.5- to 2-fold increased risk of peri procedural stroke or death, but
Choosing Between Different Modalities

Choosing the appropriate carotid revascularization procedure is a complex decision that requires consideration of several factors. This is reflected in the diverse set of recommendations made by the major international committee guidelines on this topic. Nonetheless, given the current state of evidence, CEA is generally superior for symptomatic patients with significant ICA stenosis, including those ≥70 years of age. CAS is a reasonable alternative in patients with high operative risk, including those with a hostile neck or significant comorbidities such as uncompensated cardiac or pulmonary disease.

Additionally, the American College of Cardiology/American Heart Association guidelines recommend CAS as an alternative to CEA for symptomatic patients at average or low risk of complications associated with CAS if the anticipated rate of peri-procedural stroke or mortality is <6%. This recommendation is based largely on findings from CREST. However, given a lack of consistent evidence for noninferiority of CAS in other RCTs for symptomatic patients, this recommendation remains debatable, and is not reflected in other guidelines.

In asymptomatic patients, the general recommendation is to consider CEA for significant ICA stenosis in patients who have a life expectancy of at least 3 to 5 years, and low risk of perioperative stroke/death (<3%). The role of CAS in asymptomatic patients remains to be established. However, given the results from CREST, some guidelines suggest that CAS may be considered as an alternative to CEA in highly selected asymptomatic patients treated at high-volume centers by experienced operators with low stroke/death rates (<3%). Several RCTs are planned or underway that will provide more clarity on the role of CAS and modern BMT in asymptomatic patients with ICA stenosis, including: SPACE-2, ECST-2, ACST-2, and CREST-2. Table 2 details the advantages and disadvantages of CAS, and Figure 2 provides a decision-making algorithm for CEA versus CAS.

Conclusion
The patient in the aforementioned case presented with symptomatic, significant right ICA stenosis. Therefore, in this case, carotid artery revascularization in addition to BMT was indicated for stroke prevention. Given the current evidence, CEA was the preferred option because the patient was not at high operative risk attributable to a hostile neck or significant comorbidities. When anatomic factors were considered, the patient had a long 20-mm plaque originating from the carotid bulb, which was unfavorable for CAS. Therefore, CEA was recommended to the patient, which he underwent within 1 week following his stroke. He had an uncomplicated postoperative course and was symptom-free at 6-week follow-up.

Disclosures
None.

References


Carotid Artery Revascularization: What's the Best Strategy?
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