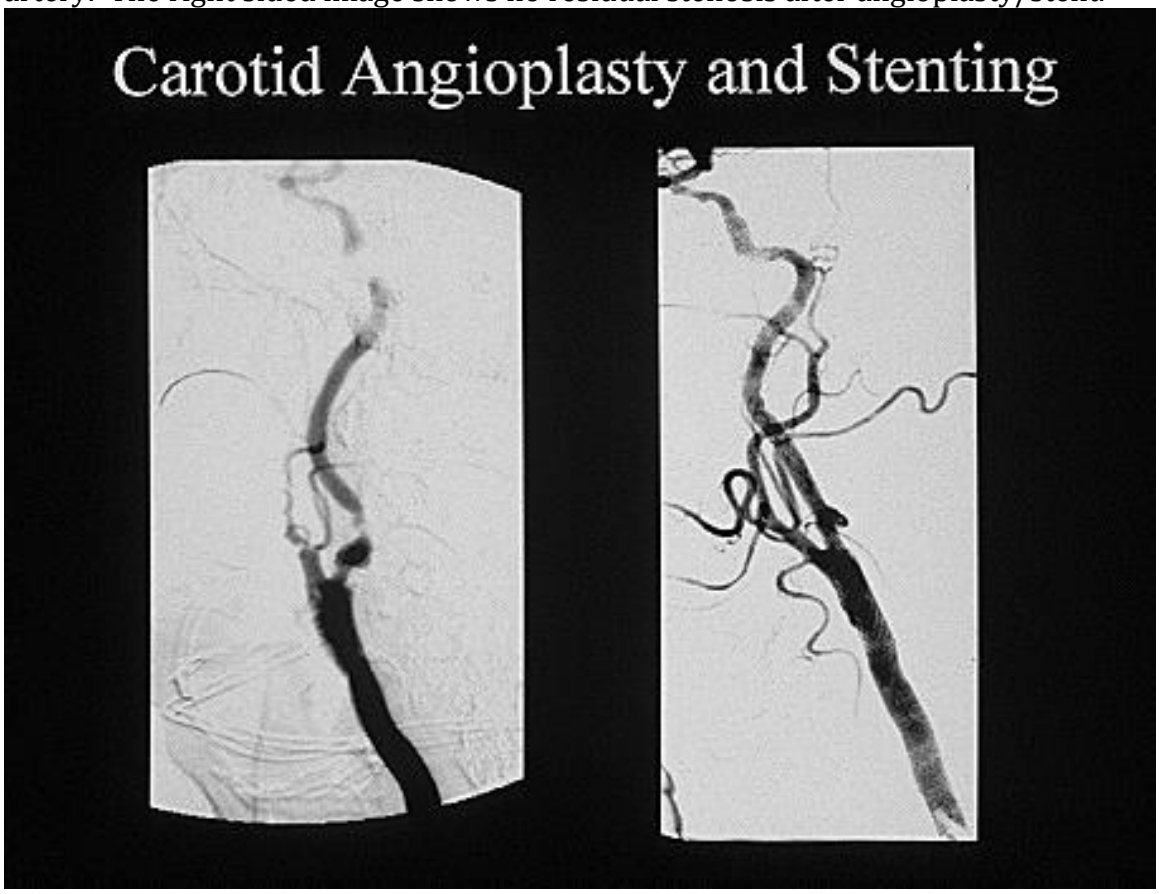
CAROTID STENTING FOR > 70% SYMPTOMATIC OR ASYMPTOMATIC CAROTID STENOSIS

Illustrative Case:

A 70 year old man presented with recurrent but intermittent right sided weakness and right sided visual loss. Visual loss was described as a shade being pulled down over the eye with vision recovering as if the shade was being raised. No cervical bruit was appreciated. Past medical history was notable for 50 pack year history of tobacco use, severe COPD, hypertension treated with a beta blocker and hyperlipidemia managed with a statin agent. The patient had been placed on 81 mg/day ASA at the age of 60 for cardiac prophylaxis. MRI and CT of the brain was negative. Cerebral and cervical angiography was requested. This study demonstrated greater than 90% stenosis of the left cervical internal carotid artery. Because he was considered high risk for pulmonary reasons, he underwent carotid angioplasty and stenting (Figure 1). Following this procedure the patient was placed on dual antiplatelet therapy for 1 month followed by single antiplatelet therapy. No recurrent symptoms were noted.

FIGURE 1: The left sided image shows critical stenosis of the left internal carotid artery. The right sided image shows no residual stenosis after angioplasty/stent.



Topic:

This topic review will address carotid stenting for significant asymptomatic or symptomatic carotid cervical stenosis (≥70%) because studies have shown that 5% of individuals with this degree of stenosis will have a stroke within 5 years (Stroke. 23:1752-1760. 1992). Management of stenosis ≤ 50% is supported by some studies and disputed by others and as such, treatment of this finding is generally carried out on a cases by case basis after maximal medical therapy has failed in symptomatic patients. Maximal medical therapy would include smoking cessation, dietary modification, antihypertensive medications, and antiplatelet and statin agents.

Background:

Stroke (sudden abnormal brain function secondary to a decrease in blood flow to the brain or bleeding in the brain) affects 6-7 million individuals in the US per year, is the second leading cause of all death, and is the greatest cause of premature death and disability. Approximately 20% of all strokes are secondary to atherosclerotic disease and stenosis at the junction of the common carotid artery/external carotid artery/internal carotid artery (aka: common carotid bifurcation). Stenosis can occur anywhere along the common and internal carotid arteries, however, for the purposes of this review we will focus on treatment of disease located at or near the common carotid bifurcation.

Risk Factors For Carotid Stenosis:

Risk factors for the development of carotid stenosis include the following:

Advanced age (≥65)
Atherosclerotic disease elsewhere in the body
Hypertension (SBP >160 mm Hg)
Physical inactivity
Smoking
Hyperlipidemia
Hypertension
Diabetes
Males > Females

What Causes Carotid Stenosis?

Carotid stenosis most commonly develops as a result of atherosclerotic disease. Oxidation of lipid proteins deposited in an artery's intimal layer leads to cytokine release, monocyte deposition, foam cell formation and smooth muscle proliferation (plaque formation). As plaques grow, the arterial lumen can narrow thus reducing

blood flow to the brain. Thrombi can form on these plaques and then mobilize and embolize into intracranial arteries causing occlusion and stroke. Alternatively, rupture of these plaques can lead to cerebrovascular emboli and stroke(Cleveland Clinic Continuing Education Review. 2016).

What Is Considered Significant Stenosis?

Stenosis is generally considered clinically concerning once it exceeds 50 or 60%. Most studies, however, support treatment of stenosis ≥ 70%. Approximately 1-3% of individuals older than 65 harbor such pathology.

Stenosis is formally categorized and measured using the NASCET criteria (N Engl J Med. 325:445-453. 1991). This degree of narrowing is determined by using cerebral angiography to measure the narrowest segment of the internal carotid artery and dividing it by the normal diameter of the internal carotid artery distal to the stenosis and distal to the carotid bulb. Mild stenosis is considered 0-49%, moderate stenosis is considered 50-69%, and severe stenosis is considered 70-99%.

Signs and Symptoms:

Significant carotid stenosis can remain asymptomatic until a stroke occurs. Signs and symptoms of potential carotid stenosis and stroke include:

Unilateral visual loss (aka: amaurosis fugax)
Visual field loss (aka: homonymous hemianopia; homonymous quadrantanopia)
Arm and/or leg weakness
Difficulty understanding speech (aka: receptive aphasia; Wernicke's aphasia)
Difficulty speaking (aka: expressive aphasia; Broca's apahsia)
Unilateral lower facial droop (drooping of the lips/smile on one side)
Altered mental status and altered level of consciousness
A sound heard along the neck where the carotid artery bifurcates (aka: carotid bruit)

Determining the Degree of Carotid Stenosis:

A number of modalities can be used to evaluate for carotid stenosis. These include multiple view catheter angiography (the current gold standard), MR angiography, CT angiography and Duplex Ultrasonography (US). While the first three mentioned technologies utilize the visualization of contrast within various segment of the arterial lumen to measure the degree of stenosis, US uses the speed of blood flow to estimate the underlying degree of stenosis. The greater the stenosis the faster the blood flows through the vessel lumen (Bernoulli's Principle). 70% - 98% stenosis is responsible for creating blood velocities greater than 230 cm/sec through the stenotic segment.

Endovascular Management of Carotid Stenosis:

Stenting for carotid disease was first reported in 1989 when a stent was utilized to treat an intimal flap. Since then, several studies have been performed comparing the efficacy, risks and benefits of carotid artery stenting (CAS) to traditional carotid endarterectomy (CEA). These trials will be summarized below, but in the majority, the overall risks of stroke or death following either treatment are less than 10%.

CAVATAS (2002)	CAS vs. CEA
Postprocedure disabling stroke/death rate	Equivalent
Death/Any stroke rate	Equivalent
8 year ipsilateral stroke rate	Equivalent
Cranial nerve injuries post treatment	Greater for CEA

SAPPHIRE (2004)	
Death/Stroke /MI within 30d post treatment	Equivalent
Death/Stroke/MI 30 days – 3 years	Equivalent
Restenosis rates requiring treatment	Equivalent

EVA-3S (2006)	
Periprocedural stroke/death rate	CAS inferior
5 periprocedural stroke/death rate	CAS inferior
Significant restenosis rate	Equivalent

SPACE (2006)	
Periprocedural death/ipsilateral stroke rate	Equivalent
Ipsilateral stroke at 2 years rate	Equivalent
Recurrent stenosis rate	CAS inferior

ICSS (2010)	
Periprocedural stroke/death/MI within 120 d	CAS inferior
Cranial nerve injuries rate	CEA inferior
5 year stroke rate	CAS inferior
5 year fatal/disabling stroke rate	Equivalent
Long term restenosis rate	Equivalent

CREST (2010)

Periprocedural stroke/death/MI rate	Equivalent
Periprocedural stroke rate alone	CAS inferior
Periprocedural MI rate alone	CEA inferior
10 year stroke/death/MI rate	Equivalent
Restenosis rates	Equivalent

ACT-1 (2016)

Periprocedural stroke/death/MI within 1y	Equivalent
Periprocedural stroke/death rate	Equivalent
5 year stroke free survival	Equivalent

Meta analyses of CEA vs. CAS have also been reported. A 2017 study reviewing 6,526 patients demonstrated CAS to be superior to CEA in terms of periprocedural death, stroke, MI and cranial nerve injury (J Am Coll Cardiol. 69(18):2266-2275, 2017). A prior meta analysis performed in 2012 showed equivalent postprocedural ipsilateral stroke rates between CEA and CAS although restenosis rates were higher for CAS (Cochrane Database Syst Rev. 2012;(9):CD000515).

Current trials evaluating CAS vs CEA include SPACE-2, ACST-2, CREST-2 AND ECST-2. Trial completions are expected between 2019 and 2022.

To reduce the incidence of procedure related embolic strokes during CAS an effort has been made to perform the procedure in conjunction with an embolic protection device (EPD). EPDs come in many forms, but the most common is a wire mounted filter/umbrella that is placed distal to the stenosis and the stent and balloon. The filter's purpose is to capture and remove embolic material that arises during the CAS procedure so as to reduce the incidence of distal ischemic events. While such devices are used in almost all CAS cases, there is currently no evidence that they are in fact beneficial (Stroke. 40(3):841-846, 2009; Cerebrovascular Dis. 29(3):282-289, 2010; Vasc Surg. 47(4):760-765, 2008).

Patients with recurrent carotid stenosis, radiation induced carotid stenosis, tandem cervical and intracranial stenosis, and intracranial ICA stenosis alone are generally treated using CAS although there are no randomized studies that have specifically determined how CEA and CAS compare in these clinical situations.

Post CAS Pharmacology:

While there are no clear studies relating to the use of antiplatelet agents after CAS, it is generally recommended by the American Stroke Association that dual antiplatelet agents (ASA 81-325 mg each day and clopidogrel 75 mg each day) be utilized for

the first month following CAS with single agents being used after 6 months. If patients cannot tolerate clopidogrel then ticlopidine can be used (250 mg twice a day). If CAS is electively scheduled it is also suggested that clopidogrel be used for 3 days prior to the procedure being performed. Some practitioners suggest testing patients for ASA and clopidogrel platelet inhibition when these drugs are used, however, there is no consensus surrounding the necessity or value of such testing.

Conclusion:

CAS and CEA are both very effective treatments for symptomatic, significant carotid stenosis. Current practice seems to support the use of CEA for asymptomatic or symptomatic low risk patients while CAS is best used for symptomatic higher risk populations.