Carotid Artery Stenting: What You Need To Know

Rahul S. Patel, M.D.,¹ and Barry T. Katzen, M.D.²

ABSTRACT

Carotid stenting has become an accepted alternative in patients with carotid stenosis. The purpose of this article is to review the relevant trials, describe the different devices available for stenting, the devices for cerebral protection, as well as describe techniques and tricks for successful carotid artery stenting. Understanding how to appropriately preoperatively evaluate patients and intra- and postoperative procedures, carotid artery stenting can be a safe procedure.

KEYWORDS: Carotid stenosis, carotid artery stenting, stroke, cerebral protection

Objectives: Upon completion of this article, the reader should be able to list the relevant clinical trials as well the appropriate clinical management and selection of patients undergoing carotid artery stenting.

Accreditation: Tufts University School of Medicine (TUSM) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit: TUSM designates this educational activity for a maximum of 1 *AMA PRA Category 1 Credit*TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Stroke is the third leading cause of death and disability in the United States. Approximately 800,000 new or recurrent strokes occur each year.¹ Of these, 20 to 30% are thought to be secondary to carotid artery thromboembolic disease. Since landmark studies in the 1990s, carotid endarterectomy (CEA) has been established as the gold standard for the treatment of carotid artery stenosis.^{2–4} Around the same time, carotid artery stenting (CAS) became a more feasible technique with the introduction of cerebral protection devices. Even though CAS appears to be a safe and feasible method for treatment of CAS, its superiority to CEA in certain situations is unclear.

Initially CAS was intended for use in patients who were loosely determined to be high risk for surgery. This includes a heterogeneous group of patients with both physiological and anatomic risk factors for CEA

(Table 1). These criteria arose from the criteria used to exclude patients for the Asymptomatic Carotid Atherosclerosis Study (ACAS) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) trials.

TRIALS

The first multicenter randomized trial involving CAS, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) trial, began in 1992 before the option of stenting was available. Stenting was eventually added to the trial later, although only ~25% of all patients in the interventional arm received stents.⁵ The trial is therefore primarily one of angioplasty alone compared with CEA, and without any embolic protection. The trial excluded any patients considered high risk by traditional standards and included patients were

¹Division of Vascular and Interventional Radiology, University of Maryland Medical Center, Baltimore, Maryland; ²Baptist Cardiac and Vascular Institute, Miami, Florida.

Address for correspondence and reprint requests: Barry T. Katzen, M.D., Baptist Cardiac and Vascular Institute, 8900 North Kendall Drive, Miami, FL 33176 (e-mail: barryk@baptisthealth.net).

Peripheral Vascular Disease; Guest Editors, Robert A. Hieb, M.D., and Parag J. Patel, M.D.

Semin Intervent Radiol 2009;26:324–332. Copyright © 2009 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI 10.1055/s-0029-1242200. ISSN 0739-9529.

Table 1 High-Risk Criteria

Recurrent stenosis
Contralateral occlusion
Prior neck radiation or radical neck dissection
Surgically inaccessible lesions
Age >80
Significant medical comorbidities
COPD
CHF
LVEF <30%
Unstable angina
Multivessel CAD
Dialysis-dependent CRI

COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; CRI, chronic renal insufficiency.

randomized to endovascular treatment or CEA. For the most part, the patients enrolled in the study were symptomatic (>90% with symptoms within 6 months of randomization). The trial found that there was no significant difference at 30 days or 3 years between the two groups in the incidence of death or stroke. It is important to note that the stroke and death rate for the CEA at 90 days was 9.9%, considerably higher than the 6.5% in a similar population set in the NASCET trial and 7.0% in the European Carotid Surgery Trialists (ECST).⁶

The first U.S.-based multicenter randomized trial was the Carotid Wallstent Trial.⁷ This tested the tracheobronchial Wallstent for the treatment of CAS without embolic protection in symptomatic patients who were considered high risk for CEA. Only 200 patients were enrolled in the study before it was halted in 1999 because it was determined that the noninferiority end points of the trial would not be achieved by the anticipated enrollment of 600 patients. In the enrolled patients, there was no statistical difference between the CAS and CEA arm, although a strong trend favoring CEA was noted.

These early trials had several limitations. End point definitions were problematic. Nondedicated equipment was used for procedures. For example, the Wallstent used at the time required an 8-French sheath and the 0.035-inch lumen didn't match the 0.018-inch wires typically used in the procedure. There was no embolic protection. Also, there was inadequate operator training prior to the study. Many of these limitations and inadequacies were addressed in later studies.

In the late 1990s, feasibility and pivotal trial work began on devices specifically designed for CAS and with embolic protection. Several high-surgical risk registries are still ongoing, although some have been completed (Table 2). All are designed as noninferiority studies, with a direct surgical comparison in the Stenting and Angioplasty with Protection in Patients at high Risk for Endarterectomy (SAPPHIRE) trial.⁸ The other studies used objective performance criteria agreed to by the FDA for registry studies. These were derived specifically for each registry study based on outcomes for endarterectomy based on published results.

SAPPHIRE was the first randomized control trial comparing CEA and CAS using distal protection. The study enrolled 747 high-risk symptomatic and asymptomatic patients. Three hundred thirty-four patients were placed in the randomized arm with the remaining patients placed into either stent or surgical registry. Asymptomatic patients included in the study had a stenosis >80%. A stenosis of >50% was required for symptomatic patients. The 30 day major adverse event rates (stroke, death, and myocardial infarction) was lower in the CAS group (4.8%) than the CEA group (9.8%), although this was not statistically significant ($P=0.09$). The 1-year major adverse event (MAE) rate was 12.2% for CAS compared with 20.1% for CEA patients. Three-year results were published in 2008 with data available for 86% of CAS patients and 70% of CEA patients. The MAE rate was not statistically different between the two groups, 24.6% for CAS and 30.3% of CEA.

Table 2 U.S. Registries

Name of Device	Manufacturer	Trial Name	No. of Patients
Acculink	Guidant/Abbott Vascular, Natick, MA	ARCHer ⁹	581
EXACT	Abbott Vascular, Abbott Park, IL	SECURITY	305
WallStent	Boston Scientific, Natick, MA	BEACH ¹⁰	480
NexStent	Endotex/Boston Scientific, Natick, MA	CABERNET ¹¹	454
Exponent	Medtronic, Minneapolis, MN	MAVERIC II	399
Protégé	Ev3, Plymouth, MA	CREATE ¹²	419
Fibernet (filter)	Lumen Medical, Plymouth, MA	EPIC	237
Gore NPS (flow reversal)	W.L. Gore, Flagstaff, AZ	EMPIRE	245
Vivexx*	BARD, Covington, GA	VIVA	
Mo.Ma*	Invatec, Roncadelle, Italy	ARMOUR	

*Published data unavailable.

Figure 1 Thirty-day carotid stent outcomes in U.S. high-risk trials and SAPHIRE Carotid Endarterectomy arm.

The Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS) trial confirmed the results of the SAPHIRE trial.¹³ This was a large multicenter, prospective trial, but was not randomized; it was designed to prove noninferiority between CAS with protection and CEA. Overall, there were twice as many CEAs compared with CAS. All patients were permitted in the study, symptomatic and asymptomatic, high-risk and low-risk patients. Despite nonrandomization, baseline demographics between the two groups were similar except that patients with previous carotid surgery or stenting were more likely to undergo CAS. There was no statistical difference at 30-day death and stroke rates between CAS and CEA groups (2.1% versus 3.6%) and no difference at 1 year (10.0% versus 13.6%, respectively). Morbidity and mortality rates approached those for the NASCET and ACAS standards. A larger phase II CaRESS trial has been planned but not yet initiated.

The Stent Supported Percutaneous Angioplasty of the Carotid artery versus Endarterectomy (SPACE) trial set out to establish noninferiority for CAS in symptomatic patients with stenosis >50% by NASCET standards and with low surgical risk.¹⁴ It was a randomized trial involving 35 centers across Germany, Austria, and Switzerland. A total of 1200 patients were randomized, 595 to CEA and 605 to CAS. At 30 days, the rate of ipsilateral ischemic stroke or death was not statistically different, 6.84% for CAS and 6.34% for CEA. The incidence of ipsilateral stroke at 30 days was 6.5% for CAS and 5.1% for CEA, with a trend showing superiority of CEA over CAS. It is important to note that embolic protection was not a requirement and was only used in 27% of the CAS cases.

A second European trial with similar design, the Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S), was conducted in France.¹⁵ The inclusion criteria were similar to that of the SPACE trial. The study was stopped pre-

maturely on the basis of safety and futility. MAEs occurred in 9.6% of CAS patients compared with 3.9% of CEA patients ($P=0.01$). The study was limited by deficiencies in the training and low-volume stent operators. CEA operators needed to perform 25 endarterectomies in the year before enrollment, but a stent operator could have as few as five lifetime procedures to be considered qualified. Also, embolic protection devices (EPDs) were not mandated until after four to five excess strokes in the stent arm.

The registries can be discussed as a group because they have similar eligibility, definitions, and end points. All the registries are multicenter; eligibility requirements are similar to those used in the SAPHIRE trial and were designed to prove noninferiority of CAS with a direct surgical comparator in the SAPHIRE study of high-risk patients and objective performance criteria (OPC) agreed to by the FDA. The 1-year primary end points are also similar to SAPHIRE. Device success is very good, with more than 95% of the EPDs and ~99% of stents successfully deployed. A summary of the 30-day stroke rate and MAE compared with the SAPHIRE CEA data is provided in Fig. 1.

Another interesting study was the CASES-PMS registry, which examined the use of distal protection by operators who either had previous experience with the study device (Angioguard XP) or who underwent formal training.¹⁶ The 30-day MAE (5%) did not vary significantly between symptomatic and asymptomatic patients or among operators with high and low volume or with differing levels of experience with the device.

TIPS/TECHNIQUES

Before the Procedure

Treatment of carotid atherosclerotic disease is different from treatment of atherosclerotic disease in other

vascular beds due to the potential of devastating neurological complications as well as significant hemodynamic changes that can occur. CAS requires appropriate patient selection and preplanning.

Noninvasive vascular imaging is the preferred imaging screening method for carotid disease, as it is a quick, relatively inexpensive, noninvasive study and does not require the use of intravenous contrast agents. It can be limited by the presence of dense calcifications. Interpretation can also be limited by the presence of tandem lesions. Also, there can be significant interlaboratory variability.

In patients with abnormal sonographic findings, computed tomographic angiography or magnetic resonance angiography is of added value preprocedurally as it allows the evaluation of tandem lesions as well as the aortic arch anatomy. These studies cannot be done in every patient, as renal insufficiency is a relative contraindication.

It is important to determine aortic arch configuration and arch vessel configuration because these features determine the technical complexity of the procedure. Complex aortic arches maybe the single most limiting factor in successful CAS.¹⁷ There are some studies that show that arch anomalies are associated with a higher risk of neurological complications.¹⁸ The arch types range from a type I arch, where the great vessels arise for the outer curvature of the arch at the same horizontal level (no angulation), to a type IV arch, where the arch vessels arise with severe angulation, accompanied by increased length and transverse diameters of the arch.

A comprehensive neurological exam is important to establish a baseline in case there is a neurological complication. Clopidogrel 75 mg per day dose should be started a few days before the procedure as well as aspirin. This is because during percutaneous interventions, there is injury to the intima causing release of procoagulant tissue factors other platelet-adhesive proteins in the subendothelium.¹⁹ The extent of platelet deposition depends on the degree of vessel wall injury; in some cases, the thrombus can expand to occlude the vessel completely. Distal microemboli during CAS are also indicative of increased platelet activation.²⁰ Some studies suggest a 10-fold relative risk reduction of having >20 emboli in the postoperative period when comparing aspirin and clopidogrel to aspirin alone without an increase in the risk of bleeding complications.²¹

Procedure

The patient should have periodic neurological assessments after various stages of the procedure. This is typically done by placing a noisemaker, such as horn, in the contralateral hand of the carotid artery being treated. It can be squeezed throughout the procedure to assess the patient's motor function and ability to

follow verbal commands. Also, due to the need to assess the patient's speech and cognitive abilities throughout the procedure, the patient should not be oversedated. In patients with native atherosclerotic lesions, antihypertensive medications, especially β -blockers, are used prior to the procedure.

Typically, common femoral access is obtained and a 6-French sheath is placed. If an arch aortogram is required, a pigtail catheter is positioned in the ascending aorta with the tube angulated ~ 25 to 30 degrees left anterior oblique (LAO). If the arch anatomy is relatively straightforward, a 4-French or 5-French angled catheter in conjunction with a 0.035 Glidewire (Terumo, Somerset, NJ) is used to cannulate the appropriate common carotid artery (CCA). If the angled catheter is unsuccessful, a reversed curve catheter, such as a Simmons or sidewinder shape, can be used. A cervical carotid angiogram is performed in both the anteroposterior and lateral projections from a CCA hand injection with a calibrated marker placed on the neck, or with isocenter calibration.

Next, the catheter is placed into the distal external carotid artery (ECA) and the wire is exchange for a stiff 0.035 wire (e.g., Tad-II (Covidien, Hazelwood, MO), Amplatz (Cook Medical, Flagstaff, AZ and Boston Scientific, Natick, MA), stiff angled Glidewire (Terumo, Somerset, NJ), etc.). Over the stiff wire, a 90-cm 6-French Shuttle (Cook Medical, Bloomington, IN) sheath is positioned in the CCA, being careful not to advance the dilator too far into the carotid bifurcation. Alternatively, these sheaths with prefitted shaped catheters (Shuttle Select, Cook Medical, Bloomington, IN) may be used to perform a single-step access to the CCA.

In patients with difficult arch anatomy and tortuous vessels, "buddy-wire" technique can be used to bring an 8-French guide catheter into the CCA. This is done by placing an 8-French guide catheter at the origin of the vessel and then placing multiple wires, usually a 0.035 and at least one 0.014 wire, into the ECA. The guide catheter is then advanced carefully further into the CCA using a telescoping technique. Typically, a 0.014 wire is left in the ECA throughout the procedure.²² In patients with extremely difficult arch anatomy, where the guide sheath may not be able to be placed, some have advocated the use of direct cervical carotid access.²³

Typically before the guide sheath is placed, anticoagulation is initiated. The activated coagulation time (ACT) is used as a guide to heparin administration with a goal ACT of 250 to 300. The usual dose of heparin is 100 U/kg. The dose can be repeated through the procedure as needed. Bivalirudin, a direct thrombin inhibitor, can also be used and is preferred by some because of the short 25-minute half-life and more predictable effectiveness. A bolus of 1 mg/kg is given intravenously followed by an infusion of 0.2 mg/kg per

Figure 2 Image of some of the different distal protection filters available. (A) Angioguard (Cordis, Miami, FL), (B) AccUNET (Abbott Medical, Abbott Park, IL), (C) Rubicon Medical, Salt Lake City, UT), (D) Filterwire EZ (Boston Scientific, Natick, MA), (E) Spiderwire (EV3, Plymouth, MN), (F) Defender* (Medtronic, Minneapolis, MN). *Not available in United States.

hour. The dose should be adjusted for renal failure and dialysis patients.

Once the sheath is securely positioned in the CCA and anticoagulation initiated, the cerebral EPD is selected (Fig. 2). The internal carotid artery (ICA) anatomy must be appropriate for the selected device. There must be sufficient length for the placement of the device and adequate distance from the carotid lesion. Typically, the floppy distal portion of the EPD is shaped and then manipulated across the stenosis and placed in the distal ICA sufficiently so the filter is adequately distal the stenosis in a straight segment of the ICA. The EPD is deployed and care is taken throughout the procedure to avoid movement and repositioning of the EPD as this can cause spasm or vessel injury. An angiogram is performed to verify proper positioning, sizing, and wall apposition of the EPD.

The previously described steps are specific for distal filtration devices. There are two EPD systems that provide protection by either proximal occlusion or flow reversal. The first to be released (in the United States) is the Flow Reversal System from Gore Medical, Flagstaff, AZ. This system does not require the use of a guide sheath. The system consists of an 8-French sheath with a distal balloon around the sheath that is placed into the CCA and an occlusion balloon wire that is placed into the ECA. The ECA balloon is typically inflated proximal to the first branch of the ECA, the superior thyroidal artery. If the ECA is occluded, the system can still be used, just without the need for the ECA balloon wire. The system also requires the placement of a 6-French sheath into the common femoral vein (CFV). The filter port on the arterial sheath is attached to an external filter, which is then attached to the CFV sheath. Once the CCA balloon, which is part of the guide sheath, is inflated, there is active flow reversal (Figs. 3 and 4).

Mo.Ma Ultra (Invatec, Roncadelle, Italy) (Figs. 5 and 6) is a proximal occlusion device. This system is one unit with part of the sheath extending into the ECA, which has a balloon to occlude the ECA. This system requires the ECA be patent. There is no CFV sheath, and therefore no active flow reversal. The disadvantage to this system is that once the CCA balloon is inflated, further angiograms cannot be performed without vigorous aspiration of the sheath (typically 90 to 120 mL).

It is important to note the patient's neurological status once proximal occlusion or flow reversal is established. Some patients are unable to tolerate the flow reversal/occlusion of the CCA, and this is remedied by restoring flow in the CCA. Of the 245 patients enrolled in the EMPiRE trial, 6 (2.4%) were unable to tolerate flow reversal.²⁴

Once the appropriated EPD is placed, typically predilatation of the lesion is performed. Usually this is done with a 3- or 4-mm rapid exchange balloon (e.g., Sterling, Boston Scientific, Natick, MA). Because angioplasty typically occurs at or near the carotid bulb, it is not uncommon for patients to have bradycardia and hypotension. To limit this effect, patients are given 0.5 to 1 mg of intravenous atropine prior to angioplasty. This is not necessary in patients who had a previous CAE. Also, patients should have continuous hemodynamic monitoring during the procedure and at least 24 hours after the procedure.

Stent Selection

Using angiographic measurements, a stent of appropriate diameter and length is selected. Tapered and non-tapered stents are used depending on anatomy. There are inherently two types of carotid stents, open versus closed cell design stents (Table 3). Different carotid stent designs yield different wall scaffolding and plaque

Figure 3 Schematic drawing of the Gore Flow Reversal System (W.L. Gore Medical, Flagstaff, AZ).

Figure 4 Left internal carotid artery (ICA) stenosis in a symptomatic patient (A). Successful deployment of the Gore Flow Reversal system (B) with the balloon wire inflated in the external carotid artery (ECA) (white arrow). Placement of a Precise (Cordis, Miami, FL) stent with no residual stenosis (C).

Figure 5 Mo.Ma Ultra flow reversal system (Invatec, Roncadelle, Italy.)

stabilization properties. This depends on the size of the free cell area between the struts of the stent. Closed-cell stents are characterized by small free cell areas when compared with open-cell stents, which leave larger uncovered gaps. The shortcoming of closed-cell stents is that they are less flexible and conformable to the carotid anatomy and therefore may not be advantageous in certain patients with tortuous anatomy.

Bosiers et al reported the potential impact of carotid stent cell design on the risk for neurological complications, although this difference was only seen

in symptomatic patients. They found that late complication rates are higher for open cell types and increase with larger free cell area,²⁵ although a study published later by Schillinger et al found no difference in the neurological complication, stroke, and mortality rate between the different stent designs.²⁶ It is important to note that both studies are retrospective and nonrandomized, and further study is probably required.

Stent Deployment

In cooperative patients, road mapping techniques may be useful for accurate positioning, or intermittent contrast injections may also be helpful. Stents are generally deployed after centering the lesion on the stent. Self-expanding nitinol stents may have a tendency to migrate cephalad, so it is recommended that slow initial unsheathing be used, with a brief delay after the first segment exits, to allow release of the constraining pressure of the delivery system, and any final repositioning that may be necessary. Each stent has unique aspects of delivery with which the operator should be familiar.

Following the placement of the stent, further balloon expansion can be performed if needed. A post-placement angiogram is performed prior to removal of the EPD to verify patency and flow through the EPD. If there is no flow seen in the ICA, this can be secondary to

Figure 6 Carotid angiogram in a patient with symptomatic internal carotid artery (ICA) stenosis. (B) Angiogram with Mo.Ma Ultra sheath in place with external carotid artery (ECA) balloon (white arrowhead) inflated. (C) Now common carotid artery (CCA) balloon (white arrow) is inflated and therefore flow reversal initiated. (D) Final angiogram with stent in place and no significant stenosis.

Table 3 Overview of Carotid Stent Types

Closed cell

Carotid Wallstent (Boston Scientific Corp., Natick, MA)
X-act (Abbott Vascular Devices, Abbott Park, IL)
NexStent (Boston Scientific Corp., Natick, MA)

Open cell

Precise (Cordis, Miami, FL)
Exponent (Medtronic, Minneapolis, MN)
Protégé (Ev3, Plymouth, MN)
Acculink (Guidant, Natick, MA)

Hybrid

Cristallo Ideale (Invatec, Roncadelle, Italy)*

*Not available in United States.

Table 4 Duplex Sonography Criteria for Evaluation of Carotid Stents

% Stenosis (Diameter Reduction)	PSV (cm/s)	PSV Ratio	EDV (cm/s)	Color/Power Doppler Findings
<50	<150	<2	NA	No or minimal stent luminal reduction
50–75	>150	>2	<125	Turbulent flow
>75	>300	>4	>125	Distal ICA spectral waveform damped
Occlusion	NA	NA	NA	No stent flow visualized

PSV, peak systolic velocity; EDV, end diastolic velocity; ICA, internal carotid artery.

a large burden of thrombus or atherosclerotic debris within the EPD. This is usually cleared by a catheter over the filter wire and aspirating a portion of the debris/thrombus. Any vasospasm that may have occurred can be treated with nitroglycerine. The EPD is removed as instructed by the device-specific instructions. Once the EPD is removed, completion angiograms are performed of the cervical carotid, as well as anteroposterior and lateral intracranial angiograms.

If there are no neurological or technical issues, the catheters and guide sheath are removed. The CFA sheath is removed once the ACT is <150 seconds or with the assistance of a closure device at the end of the procedure.

For 24 hours after the procedure, the patient's neurological and hemodynamic status is monitored closely. Some patients may require vasopressors due to hypotension. Stent patients require antiplatelet therapy, with aspirin and clopidogrel continued for at least 1 month after the CAS procedure, but longer periods of dual antiplatelet therapy are desirable, up to 6 months. CAS is contraindicated in patients who cannot tolerate aspirin. Carotid duplex is usually performed within 1 month then at 6 months and yearly thereafter.

Follow-up

In our practice, patients return in 30 days for follow-up ultrasound duplex evaluation as well as a neurological evaluation. This is typically done again at 6 months and then yearly thereafter. The main concern is restenosis.

Carotid artery in-stent restenosis rates have been reported to be 2.27% at 6 months and 3.36% at 1 year with a residual stenosis rate of greater than 50%.²⁷ The main predictor of restenosis appears to be previous CAE or radiation therapy.²⁸ Most patients are asymptomatic, and restenosis is detected on the follow-up duplex evaluations. The duplex criteria for in-stent restenosis are listed in Table 4.²⁹ Treatment of restenosis is usually done when there is a greater than 75% reduction in luminal diameter. This is done again with distal protection and balloon angioplasty alone. Recurrent in-stent stenosis can be treated with restenting.

Another complication that can be identified on duplex evaluation is stent fracture, although this is a rare complication, with only a few (<5) being reported in the literature (Fig. 7). In limited experience, it appears that treatment is only necessary when associated with >70% reduction in luminal diameter.³⁰

CONCLUSION

CAS still remains a somewhat controversial procedure. In the hands of an experienced operator, with appropriate preprocedure evaluation and preparation, as well as an understanding of potential procedural and post-procedural complications, CAS can be a relatively safe procedure with minimal complications and significant clinical benefit, especially to patients who are considered at high risk for CEA.

Figure 7 Patient status post bilateral internal carotid artery (ICA) stents with Xact stents (Abbott, Abbott Park, IL). Presents for follow-up duplex evaluation and (A) found to have a left ICA stent fracture. The stent fracture was also confirmed (white arrow) with plain film radiograph (B).

REFERENCES

- Lloyd-Jones D, Adams R, Carnethon M, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009;119:e21–e181
- North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445–453
- Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA* 1995;273:1421–1428
- Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1998;339:1415–1425
- CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. *Lancet* 2001;357:1729–1737
- Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;351:1379–1387
- Naylor AR, Bolia A, Abbott RJ, et al. Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. *J Vasc Surg* 1998;28:326–334
- Yadav JS, Wholey MH, Kuntz RE, et al; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493–1501
- Gray WA, Hopkins LN, Yadav S, et al; ARCHEr Trial Collaborators. Protected carotid stenting in high-surgical-risk patients: the ARCHEr results. *J Vasc Surg* 2006;44:258–268
- Iyer SS, White CJ, Hopkins LN, et al; BEACH Investigators. Carotid artery revascularization in high-surgical-risk patients using the Carotid WALLSTENT and FilterWire EX/EZ: 1-year outcomes in the BEACH Pivotal Group. *J Am Coll Cardiol* 2008;51:427–434
- Hopkins LN, Myla S, Grube E, et al. Carotid artery revascularization in high surgical risk patients with the NexStent and the Filterwire EX/EZ: 1-year results in the CABERNET trial. *Catheter Cardiovasc Interv* 2008;71:950–960
- Safian RD, Bresnahan JF, Jaff MR, et al; CREATE Pivotal Trial Investigators. Protected carotid stenting in high-risk patients with severe carotid artery stenosis. *J Am Coll Cardiol* 2006;47:2384–2389
- CARESS Steering Committee. Carotid revascularization using endarterectomy or stenting systems (CARESS): phase I clinical trial. *J Endovasc Ther* 2003;10:1021–1030
- Ringleb PA, Allenberg J, Brückmann H, et al; SPACE Collaborative Group. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. *Lancet* 2006;368:1239–1247
- Mas JL, Chatellier G, Beyssens B, et al; EVA-3S Investigators. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med* 2006;355:1660–1671
- Katzen BT, Criado FJ, Ramee SR, et al; CASES-PMS Investigators. Carotid artery stenting with emboli protection surveillance study: thirty-day results of the CASES-PMS study. *Catheter Cardiovasc Interv* 2007;70:316–323
- Lin SC, Trocciola SM, Rhee J, et al. Analysis of anatomic factors and age in patients undergoing carotid angioplasty and stenting. *Ann Vasc Surg* 2005;19:798–804
- Faggioli GL, Ferri M, Freyrie A, et al. Aortic arch anomalies are associated with increased risk of neurological events in carotid stent procedures. *Eur J Vasc Endovasc Surg* 2007;33:436–441
- Chaturvedi S, Yadav JS. The role of antiplatelet therapy in carotid stenting for ischemic stroke prevention. *Stroke* 2006;37:1572–1577
- Aronow HD, Shishehbor M, Davis DA, et al. Leukocyte count predicts microembolic Doppler signals during carotid stenting: a link between inflammation and embolization. *Stroke* 2005;36:1910–1914
- Payne DA, Jones CI, Hayes PD, et al. Beneficial effects of clopidogrel combined with aspirin in reducing cerebral emboli in patients undergoing carotid endarterectomy. *Circulation* 2004;109:1476–1481
- Wholey MD, Wu W, Toursarkissian B. An alternative technique for complex aortic arch access. *Endovasc Today* 2008;7:61–66
- Feldtman RW, Buckley CJ, Bohannon WT. How I do it: cervical access for carotid artery stenting. *Am J Surg* 2006;192:779–781
- Hopkins LN, Clair D. EMPiRE: A multicenter registry evaluating neuroprotection during carotid stenting with a novel flow reversal system. Paper presented at: Transcatheter Cardiovascular Therapeutics; October 12–17, 2008; Washington, D.C.
- Bosiers M, de Donato G, Deloose K, et al. Does free cell area influence the outcome in carotid artery stenting? *Eur J Vasc Endovasc Surg* 2007;33:135–141; discussion 142–143
- Schillinger M, Gschwendtner M, Reimers B, et al. Does carotid stent cell design matter? *Stroke* 2008;39:905–909
- Wholey MH, Al-Mubarek N, Wholey MH. Updated review of the global carotid artery stent registry. *Catheter Cardiovasc Interv* 2003;60:259–266
- Younis GA, Gupta K, Mortazavi A, et al. Predictors of carotid stent restenosis. *Catheter Cardiovasc Interv* 2007;69:673–682
- Armstrong PA, Bandyk DF. Duplex ultrasound surveillance after carotid stent angioplasty: when to follow-up and what to look for. *Vasc Disease Mgmt*; 2007:460–466
- Diehm N, Baum S, Katzen BT, Kovacs M, Benenati J. Fracture of a carotid stent: a word of caution. *J Vasc Interv Radiol* 2008;19:622–623