Endovascular Therapies for Extracranial Vertebral Artery Disease

Summary

Vertebral artery diseases, including atherosclerotic stenosis, dissections, and aneurysms, can lead to ischemia of the posterior cerebral circulation. Conventional management of extracranial vertebral artery diseases may include medical therapy, including antiplatelet or anticoagulant medications and medications to reduce atherosclerotic disease risk (e.g., statins), and/or surgical revascularization. Endovascular therapies have been investigated as an alternative to conventional management.

Comparative evidence is lacking to determine whether endovascular therapy, including percutaneous transluminal angioplasty (PTA) with or without stent implantation, for extracranial vertebral disease improves outcomes compared with alternatives. For endovascular treatment of extracranial vertebral artery stenosis, there is 1 very small randomized controlled trial comparing endovascular therapy with medical therapy, and this study does not report a benefit for endovascular treatment. Evidence from a large number of small- to moderate-sized noncomparative studies from single institutions indicates that vertebral artery stenting can be performed with high rates of technical success and low periprocedural morbidity and mortality. However, long-term follow-up demonstrates high rates of in-stent stenosis. Given the lack of data comparing endovascular therapy to either medical or surgical management, the evidence is insufficient to determine whether vertebral artery stenting or angioplasty improves the net health outcome.

The evidence related to the use of endovascular therapies for the treatment of extracranial vertebral artery dissections, aneurysms, and arteriovenous (AV) fistulae consists of small case series and case reports. The available cases reports and case series indicate that endovascular therapy for extracranial vertebral artery disorders other than stenosis is feasible and may be associated with favorable outcomes. However, given the lack of evidence comparing endovascular therapies with alternatives, the evidence is insufficient to determine whether endovascular therapy for extracranial vertebral artery dissections, aneurysms, and AV fistulae improves the net health outcome.

Related Policies
7.01.68 Extracranial Carotid Angioplasty/Stenting
2.01.54 Endovascular Procedures for Intracranial Arterial Disease (Atherosclerosis and Aneurysms)
Endovascular therapy, including percutaneous transluminal angioplasty with or without stenting, is considered **investigational** for the management of extracranial vertebral artery disease.

**Policy Guidelines**

The extracranial vertebral artery is considered to be segments V1-V3 of the vertebral artery from its origin at the subclavian artery until it crosses the dura mater.

**Overview of Vertebrobasilar Circulation Ischemia**

Ischemia of the vertebrobasilar or posterior circulation accounts for about 20% of all strokes. Posterior circulation strokes may arise from occlusion of the innominate and subclavian arteries, the extracranial vertebral arteries, or the intracranial vertebral, basilar, or posterior cerebral arteries. Compared with carotid artery disease, relatively little is known about the true prevalence of specific causes of posterior circulation strokes, particularly the prevalence of vertebral artery disease. Reports from 1 stroke registry estimate that in 9% of cases, posterior circulation strokes are due to stenosis of the proximal vertebral artery. Patients who experience strokes or transient ischemic attacks of the vertebrobasilar circulation face a 25% to 35% risk of stroke within the subsequent 5 years. In particular, the presence of vertebral artery stenosis increases the 90-day risk of recurrent stroke by about 4-fold.¹

**Relevant Clinical Anatomy and Pathophysiology**

Large artery disease of the posterior circulation may be due to atherosclerosis (stenosis), embolism, dissection, or aneurysms. In about a third of cases, posterior circulation strokes are due to stenosis of the extracranial vertebral arteries or the intracranial vertebral, basilar, and posterior cerebral arteries. The proximal portion of the vertebral artery in the neck is the most common location of atherosclerotic stenosis in the posterior circulation. Dissection of the extracranial or intracranial vertebral arteries may also cause posterior circulation ischemia. In contrast, posterior cerebral artery ischemic events are more likely to be secondary to embolism from more proximal vessels.

The vertebral artery is divided into 4 segments, V1-V4, of which segments V1-V3 are extracranial. V1 originates at the subclavian artery and extends to the 5th or 6th cervical vertebrae; V2 crosses the bony canal of the transverse foramina from C2-C5; V3 starts as the artery exits the transverse foramina at C2 and ends as the vessel crosses the dura mater and becomes an intracranial vessel. The most proximal segment, V1, is the most common location for atherosclerotic occlusive disease to...
occur, while arterial dissections are most likely to involve the extracranial vertebral artery just before the vessel crosses the dura mater. Compared with the carotid circulation, the vertebral artery system is more likely to be associated with anatomic variants, including a unilateral artery.

Atherosclerotic disease of the vertebral artery is associated with conventional risk factors for cerebrovascular disease. However, risk factors and the underlying pathophysiology of vertebral artery dissection and aneurysms differ. Extracranial vertebral artery aneurysms and dissections are most often secondary to trauma, particularly those with excessive rotation, distraction, or flexion/extension, or iatrogenic injury, such as during cervical spine surgeries. Spontaneous vertebral artery dissections are rare, and in many cases are associated with connective tissue disorders, including Ehlers-Danlos syndrome type IV, Marfan syndrome, autosomal-dominant polycystic kidney disease, and osteogenesis imperfecta type I.2

**Management of Extracranial Vertebral Artery Disease**

The optimal management of occlusive extracranial vertebral artery disease is not well defined. Medical therapy with antiplatelet or anticoagulant medications is a mainstay of therapy to reduce stroke risk. Medical therapy also typically involves risk reduction for classical cardiovascular risk factors. However, no randomized trials have compared specific antiplatelet or anticoagulant regimens.

Surgical revascularization may be used for vertebral artery atherosclerotic disease, but open surgical repair is considered technically challenging due to poor access to the vessel origin. Surgical repair may involve vertebral endarterectomy, bypass grafting, or transposition of the vertebral artery, usually to the common or internal carotid artery. Moderately sized, single-center case series of surgical vertebral artery repair from 2012 and 2013 report rates of overall survival of 90.7% and 77.3% at 3 and 6 years postoperatively, and arterial patency rates of 80% after 1 year of follow-up.3,4 Surgical revascularization may be used in cases of symptomatic vertebral artery stenosis that is not responsive to medical therapy, particularly when bilateral vertebral artery stenosis is present or when unilateral stenosis is present in the presence of an occluded or hypoplastic contralateral vertebral artery. Surgical revascularization may also be considered in patients with concomitant symptomatic carotid and vertebral disease who do not have relief of vertebrobasilar ischemia after carotid revascularization.

The management of extracranial vertebral artery aneurysms or dissections is controversial due to uncertainty about the risk of thromboembolic events associated with aneurysms/dissections. Antiplatelet therapy is typically used; surgical repair, which may include vertebral bypass, external carotid autograft, and vertebral artery transposition to the internal carotid artery, or endovascular treatment with stent placement or coil embolization may also be used.

Given the technical difficulties related to surgical access of the extracranial vertebral artery, endovascular therapies have been investigated for extracranial vertebral artery disease. Endovascular therapy may consist of PTA, with or without stent implantation.
Regulatory Status

There are currently no endovascular therapies approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of extracranial vertebral artery disease. A variety of stents approved for use in the carotid or coronary circulation have been used for extracranial vertebral artery disease, which may be self- or balloon-expandable.

Currently 2 devices have received approval for intracranial atherosclerotic disease from FDA through the Humanitarian Device Exemption process. This form of FDA approval is available for devices used to treat conditions with an incidence of 4000 or less per year; FDA only requires data showing “probable safety and effectiveness.” Devices with their labeled indications are as follows:

1. Neurolink System® (Guidant, Santa Clara, CA). “The Neurolink system is indicated for the treatment of patients with recurrent intracranial stroke attributable to atherosclerotic disease refractory to medical therapy in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with ≥50% stenosis and that are accessible to the stent system.”

2. Wingspan™ Stent System (Boston Scientific, Fremont, CA). “The Wingspan Stent System with Gateway PTA Balloon Catheter is indicated for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system.”

Rationale

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Improvements in intermediate outcome measures may also be adequate to determine efficacy if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.

Appropriate comparators for studies evaluating vertebral artery stenting for vertebral artery stenosis include surgical repair and/or medical management.

Angioplasty and Stenting for Extracranial Vertebral Artery Stenosis

Demonstration of Overall Efficacy

The evidence base for the efficacy of endovascular interventions for vertebral artery stenosis consists of a large number of case series, most of which are small and retrospective. A very small number of controlled trials have been published. The emphasis for this review will be on controlled trials.
Systematic Reviews

Three systematic reviews of published studies were identified. Two of the systematic reviews included all the published studies, while the third was restricted to RCTs.

In 2012, Antoniou et al reported results of a systematic review of studies evaluating percutaneous transluminal angioplasty (PTA), stenting, or both for proximal vertebral artery stenosis.\(^5\) The authors included randomized and nonrandomized trials comparing endovascular treatment with open surgical repair or endovascular treatment with best medical care for proximal vertebral artery stenosis, along with prospective and retrospective case series with at least 5 patients of endovascular treatment for proximal vertebral artery stenosis. The review included 42 publications reporting on unique data sets, 40 of which were retrospective case studies or retrospective reviews of prospectively collected data, and 2 of which were comparative studies (1 RCT by Coward et al.\(^6\) 1 nonrandomized study by Karameshev et al\(^7\)) comparing vertebral artery angioplasty and stenting with medical treatment. The selected studies reported outcomes for endovascular treatment (PTA, stenting, or both) of 1117 vertebral arteries in 1099 patients, with a mean of 26 patients (range, 5-117) per study. Indications for treatment differed across studies, but most included a requirement for vertebral artery stenosis, ranging from at least 50% to at least 70% occlusion, in conjunction with symptoms of posterior circulation disease. Most studies used a definition of “technical success” of less than 20% residual stenosis of the treated segment of the vertebral artery at the end of the procedure. The authors' assessment of the literature was that it was of poor overall quality, and demonstrated heterogeneity in the selection of patients for revascularization, the characteristics of the populations used, and revascularization techniques.

The reported technical success rate was 36% to 100% among the studies, with a weighted mean value of 97%. Thirty-seven studies reported follow-up outcomes at a mean follow-up time of 6 to 54 months. During follow-up, recurrent symptoms of vertebrobasilar insufficiency developed in 65 patients (8%). 21 patients died for a mean late mortality rate of 2%, with 1 death only being reported to be associated with insufficiency of the posterior cerebral circulation. Restenosis in the previously treated segment of the vertebral artery occurred in 183 of the 789 patients who underwent follow-up imaging, for an accumulated restenosis rate of 23% (range, 0%-58%). However, there was inconsistency in the definition of restenosis.

An earlier systematic review from 2011 reflected a smaller evidence base but no difference in conclusions. In this study, Stayman et al reported results of a systematic review of case series of proximal extracranial vertebral artery stenting.\(^8\) The review included 27 articles with a total of 993 patients, of whom 908 (98.7%) underwent primary stenting and 13 (1.3%) underwent primary angioplasty. A total of 712 of 993 (72%) of the cases reviewed involved endovascular treatment of stenoses specifically within the vertebral origins. The technical success rate of stenting procedures was high, with 99.3% of subjects demonstrating less than 20% residual stenosis post procedure. During short-term follow-up (30 days post procedure), 11 subjects had vertebrobasilar strokes (1.2%), and 8 had vertebrobasilar transient ischemic attacks (TIA). Over longer term follow-up, which averaged 21 months, 13 of 980 subjects (1.3%) had a vertebrobasilar strokes (1.3%), while 64 of 980 subjects (6.5%) had recurrent vertebrobasilar TIA symptoms.
These 2 systematic reviews include all of the published evidence available at the time. Conclusions from these reviews are limited largely as a result of the poor quality of the underlying evidence base.

A third systematic review published by the Cochrane Collaboration in 2005, included only studies that randomized patients to endovascular treatment versus best medical therapy in patients with vertebral artery stenosis. This review identified 1 RCT which met the inclusion criteria, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) study. The vertebral artery arm of this trial randomized 16 subjects with symptomatic vertebral artery stenosis to endovascular therapy with best medical care or best medical care alone. The CAVATAS study is described in more detail in the Randomized Controlled Trials subsection. The conclusion of this review was that the single small trial was insufficient evidence to support the routine use of PTA and stenting for vertebral artery stenosis.

Randomized Controlled Trials
CAVATAS incorporated data from 3 separate randomized trials, 2 of which compared endovascular treatment with carotid endarterectomy or medical treatment alone for patients with carotid stenosis who were considered surgical candidates or who were not suitable for endarterectomy, respectively. In the third trial, discussed here, subjects with symptomatic vertebral artery stenosis were randomized to endovascular treatment or best medical management alone. Surgical therapy was not included in this RCT because participating centers were not willing to treat vertebral stenosis surgically. Randomization began in March 1992 and was stopped in July 1997 at the end of the preplanned 5-year recruitment period; stents were in development throughout the trial period and could be used in patients assigned to endovascular therapy from 1994 onward. The study initially randomized 17 patients thought to have vertebral artery stenosis. One patient was excluded from further analysis after angiography showed subclavian artery stenosis, so the final analysis included 8 patients allocated to endovascular treatment and 8 patients allocated to best medical treatment alone. All patients had symptoms attributable to cerebrovascular ischemia in the vascular territory of the stenosed artery, with a mean interval between symptom onset and randomization of 92 days (range, 5-376 days). In the endovascular group, 6 patients underwent PTA alone and 2 underwent primary stenting. Seven endovascular subjects received antiplatelet therapy, while 6 received antihypertensive medications and 5 received statins. Six patients in the medical group received antiplatelet therapy, while 5 received antihypertensive medications and 3 received statins. Endovascular treatment was technically successful in all 8 patients at the first attempt. The severity of vessel stenosis was reduced immediately after angioplasty or stenting, from a median of 73% to a median of 25% (interquartile range, 0%-50%; p=0.003).

During the 30-day post procedure period or post randomization period, 2 subjects in the endovascular group experienced symptomatic posterior circulation TIAs, compared with no subjects in the control group (p=0.47). There were no periprocedural strokes or deaths in either group. After the initial 30-day post procedural or post randomization period, 2 patients from each group had at least 1 additional posterior circulation TIA, with a mean time interval to symptom onset of 10.8 months (range, 6-13.6 months). No patient experienced the primary outcome event of vertebrobasilar territory stroke after randomization. Among the 7 remaining endovascular patients, 6 had follow-up catheter angiography, and 3 of the 6 patients had restenosis greater than 50%. Two of the 6 patients had additional posterior circulation TIAs during follow-up (median stenosis severity, 60%), and 4 had no further TIAs (median...
stenosis severity, 59%; p=0.64). Only 1 patient randomized to best medical therapy had follow-up imaging, which was obtained after the patient had a posterior circulation TIA and underwent successful vertebral artery stenting. Over a mean of 4.7 years of follow-up, 3 patients in each treatment arm died of myocardial infarction (MI), vascular death, or carotid territory stroke, and 1 endovascular patient had a nonfatal carotid territory stroke during follow-up. This study failed to demonstrate a benefit for endovascular intervention, although it was underpowered to detect all but a very large treatment benefit.

Nonrandomized Comparative Studies
One additional nonrandomized study comparing outcomes for patients with symptomatic vertebral ostial stenosis treated with medical therapy alone or vertebral artery stenting, which was included in the Antoniou et al review, was identified.7 The study included 39 consecutive patients at a single institution from 2000 to 2008 treated for vertebral ostial stenosis, 10 stenting and 29 with best medical therapy, with treatment decisions left to the treating physician. All patients had a history of posterior circulation stroke or TIA, with no alternative causes of stroke identified. Patients in the medical therapy group received therapies including aspirin (n=20), clopidogrel (n=1), vitamin K antagonists (n=5), combination of aspirin and clopidogrel (n=3), statin therapy (n=20), and antihypertensive drugs (n=18). All patients receiving vertebral artery stenting received aspirin and clopidogrel for 12 months, with aspirin continued indefinitely. Patients treated medically were older (68 vs 60 years; p=0.04), had less severe neurologic deficits on admission (National Institutes of Health Stroke Score 1 vs 2.5; p=0.03), and were less often current smokers (10% vs 60%; p=0.03). In the medical group, 1 patient died from basilar artery thrombosis 22 days after the index event. In the stenting group, 1 patient experienced a TIA 1 day after the procedure.

There were no hemorrhagic strokes, strokes in the anterior circulation, MI, or reinterventions within 30 days after the index event. At 4-year follow-up, stented patients had a nonsignificantly lower risk of the combined end point of TIA and nonfatal and fatal posterior circulation strokes (10% vs 45%; relative risk, 0.25, 95% confidence interval, 0.03 to 1.85; p=0.095).

Noncomparative Studies
A large number of noncomparative studies, most often with small numbers of patients, have described outcomes for patients treated with endovascular therapies for extracranial vertebral artery disease.

Some of the representative cohort studies of endovascular therapies for vertebral artery stenosis not included in the 2012 Antoniou et al systematic review described above are shown in Table 1.

Section Summary
The evidence related to the overall efficacy of endovascular therapies for extracranial vertebral artery stenosis consists primarily of a number of noncomparative studies and systematic reviews of these studies. Randomized trial evidence is limited to 1 very small RCT comparing endovascular therapy with medical therapy for vertebral artery stenosis, which was underpowered to demonstrate differences between groups. One nonrandomized study reported nonsignificant differences in outcomes between stented and medically treated patients. Evidence from noncomparative studies indicates that vertebral
artery stenting can be performed with high rates of technical success with low periprocedural morbidity and mortality, and that vessel patency can be achieved in a high percentage of cases. However, long-term follow-up demonstrates high rates of in-stent stenosis. Given the lack of data comparing endovascular therapy with either medical or surgical management, the evidence is insufficient to determine whether vertebral artery stenting or angioplasty improves the net health outcome.

### Angioplasty and Stenting for Extracranial Vertebral Artery Aneurysms, Dissections, and Arteriovenous Fistulae

A smaller body of literature has addressed the use of endovascular procedures for extracranial vertebral artery aneurysms, dissections, and arteriovenous (AV) fistulae. These lesions most commonly occur after trauma or iatrogenic injury. Because aneurysms, dissections, and AV fistulae may coexist in the same vessel, studies reporting outcomes for endovascular treatment for these conditions are discussed together. The available literature consists entirely of case reports and case series, and a systematic review of case series.

#### Systematic Reviews

In 2011, Pham et al conducted a systematic review of studies evaluating endovascular stenting for extracranial carotid and vertebral artery dissections that included 8 studies of extracranial vertebral artery stenting with 10 patients (12 vessels). Of the 10 patients included, 70% had associated pseudo aneurysms and 20% had bilateral lesions. Most dissections (60%) were traumatic in etiology, while 20% were spontaneous and 20% were iatrogenic. The indications for stenting were failure of medical management in 40% (defined as a new ischemic event, progression of initial symptoms, or demonstration of an enlarging pseudo aneurysm despite adequate anticoagulation or antiplatelet treatment), contraindication to anticoagulation in 20%, and/or severity of dissection hemodynamics in 60%. No stent-related complications or mortalities were reported in any study. One dissection-related death was reported, although stenting was considered technically successful.

#### Case Series and Case Reports

Since the publication of the 2010 Pham et al systematic review, some additional case series related to the use of endovascular therapies for extracranial vertebral artery dissections have been published.

In 2014, Badve et al retrospectively compared the clinical characteristics of patients with vertebrobasilar dissections with and without aneurysmal dissection treated at a single institution from 2002 to 2010. Thirty patients were identified, 7 with aneurysmal dissections, 1 of which was 1 extracranial, and 23 with nonaneurysmal dissections, 10 of which were extracranial and 12 of which were combined intracranial/extracranial. Patients were treated with antiplatelet agents (aspirin or clopidogrel; n=8) or anticoagulation with warfarin (n=13) or neurointerventional procedures (n=6). One patient in the nonaneurysmal dissection group treated with aspirin died.
## Endovascular Therapies for Extracranial Vertebral Artery Disease

<table>
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<tr>
<th>Study</th>
<th>Study Type</th>
<th>Population/Intervention</th>
<th>FU Period</th>
<th>Main Results</th>
<th>In-Stent Restenosis Rate</th>
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| Kikuchi et al (2014)           | Retrospective review of prospectively collected data | 404 subjects with extracranial vertebral artery stenosis in registry of subjects treated with endovascular therapy for extracranial steno-occlusive disease (total N=1249) | 30 d      | • Postprocedural morbidity: 2.0%  
• Postprocedural mortality: 0.3%  
• Complication rates for entire cohort: 4.2%  
(n=40; 12 with distal embolism, 10 with vessel dissection) | Not reported |
| Sun et al (2014)               | Retrospective review of prospectively collected data | 188 patients with VAO stenosis (≥70%) due to atherosclerosis with vertebral stenting performed for symptomatic posterior circulation TIA or stroke and mRS score ≤2 | Mean, 16.5 mo | • Technical success rate: 100%  
• 34 patients had recurrent TIA after 30 d  
• No cases of stroke or death occurred | >50% ISR in 40 patients (21.2%) |
| Radak et al (2014)             | Cohort; retrospective or prospective not specified | 78 consecutive patients treated with endovascular therapy for symptomatic high-grade (70%-99%) vertebral artery stenosis of the V1 segment unresponsive to 2 mo of best medical therapy | Median, 44.3 mo | • Technical success rate: 93.2%  
• 68.5% underwent direct stenting with BMS;  
16.4% underwent balloon angioplasty with stenting;  
8.2% underwent PTA alone  
• No in-hospital deaths occurred; 1 patient experienced periprocedural TIA  
• 4 patients required secondary endovascular interventions during FU period | 4 cases of symptomatic restenosis; 3 cases of asymptomatic mild/moderate restenosis |
| Li et al (2014)                | Retrospective cohort study           | 32 patients treated with self-expanding stents for symptomatic VAO stenosis               | Mean, 18.3 mo | • Change in mean stenosis (pre- to poststenting): 76.4%-11.4%  
• No cases of verteobasilar stroke, TIA, or death occurred in FU period | 60% ISR was demonstrated on angiography in 1 patient |
| He et al (2014)                | Retrospective cohort study           | 27 consecutive patients treated with endovascular therapy for symptomatic, nonacute VBO (15 vertebral artery occlusions) | Mean, 6.7 mo | • Successful recanalization: 96%.  
• 5 patients had perioperative complications, 3 in those with vertebral artery occlusions (1 ISR, 1 dissection, 1 thrombus translocation) | Not reported for entire cohort |
| Mohammadian et al (2013)       | Prospective interventional study     | 206 subjects with dominant vertebral artery stenosis >50% and clinical signs/symptoms of vertebral occlusion (239 treated lesions, 202 of extracranial) | Mean, 13.15 mo | • Technical success rate: 100%.  
• Of 223 stents placed, 199 (89.2%) were balloon-expandable bare-metal stents; remainder were self-expandable stents  
• Periprocedural complication rate: 7.2% | 15.9% ISR after mean FU of 10.89 mo |
| Edgell et al (2013)            | Retrospective cohort study           | 148 patients treated with PTA and stenting for vertebral artery origin stenosis in institutes participating in | Mean, 8.5 mo | • Drug-eluting balloon-expandable stents used in 56.8%, with BMS in 38.5% and self-expanding stents in 4.7% | Of 58 patients with available FU angiography at |
# Endovascular Therapies for Extracranial Vertebral Artery Disease

<table>
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<tr>
<th>Study</th>
<th>Design</th>
<th>Patient Population</th>
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<th>Outcomes</th>
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| Hatano et al (2011)\textsuperscript{17} | Retrospective review of prospectively collected data | 117 patients treated with stent placement for atherosclerotic VAO stenosis at a single institution (108 symptomatic, 9 asymptomatic) | • Change in mean stenosis (pre- to poststenting): 80.5%-5.3%  
• 1 stroke occurred in 30-d periprocedural period  
Over 3-mo FU, 5/96 patients (5.2%) had TIA | mean 7 mo, 15.5% had ISR ≥50%  
Of 104 patients with angiographic FU at 6 mo, 9.6% had ISR |
| Jenkins et al (2010)\textsuperscript{18} | Retrospective cohort study | 105 consecutive patients treated with stents for symptomatic vertebral artery disease, 91% extracranial | • Successful recanalization (<30% residual stenosis): 99%  
• During FU: 5 patients developed posterior circulation ischemia; 2 patients developed dizziness (resolved after retreatment of ISR); 1 patient developed cerebellar infarction with ISR, 2 patients had posterior circulation strokes without ISR | 7.4% required target vessel revascularization within 1 y postprocedure |

BMS: bare metal stent; FU: follow-up; ISR: in-stent restenosis; MI: myocardial infarction; mRS: modified Rankin Scale; PTA: percutaneous transluminal angioplasty; TIA: transient ischemic attack; VAO: vertebral artery ostium; VBO: vertebrobasilar occlusion.
The use of endovascular therapy for extracranial vertebral artery aneurysms and AV fistulae is similarly limited to small case series and case reports. In an early report from 1996, Horowitz et al described a left-sided vertebral artery pseudoaneurysm with dissection between the vessel media and adventitia at level C-7 that was treated with a balloon-expandable stent. Follow-up angiography 3 months postprocedure showed no filling of the pseudoaneurysm and normal patency of the parent artery. In 2004, Felber et al reported outcomes from endovascular treatment with stent grafts of 11 patients with aneurysms or arteriovenous fistulae of craniocervical arteries, 2 of whom were treated for extracranial vertebral artery disorders with coronary stents (V2; 1 aneurysm and 1 traumatic arteriovenous fistula). The procedure was technically successful in both subjects without complications. At follow-up (5 years and 14 months postprocedure in the aneurysm and fistula patient, respectively), the target vessel was patent without stenosis. In 2008, Herrera et al reported outcomes for a single-center series of 18 traumatic vertebral artery injuries, including 16 AV fistulae (7 of which had an associated pseudoaneurysm) and 2 isolated pseudoaneurysms, treated with endovascular therapy. Endovascular therapy consisted of balloon occlusion of the parent vessel and AV fistula in 12 patients (66.6%), coil embolization in 2 patients (11.1%), detachable balloon and coil embolization, balloon occlusion, and stent delivery with coil and n-butyl cyanoacrylate embolization of a AF fistulae each in 1 patient (5.5% each). Angiography immediately post-endovascular treatment demonstrated complete occlusion in 16 patients (88.9%) and partial occlusion in 2 patients (11.1%). Seventeen patients (94.5%) had complete resolution of symptoms. Other case reports have described the successful use of endovascular treatment with stenting for iatrogenic vertebral artery pseudoaneurysms, iatrogenic vertebral artery AV fistula, extracranial vertebral artery aneurysm with an unknown cause, and extracranial vertebral artery aneurysm with a cervical vertebral arteriovenous fistula.

**Section Summary**
The evidence related to the use of endovascular therapies for the treatment of extracranial vertebral artery dissections, aneurysms, and AV fistulae consists of small case series and case reports. The available case reports and case series indicate that endovascular therapy for extracranial vertebral artery disorders other than stenosis is feasible and may be associated with favorable outcomes. However, given the lack of evidence comparing endovascular therapies with alternatives, the evidence is insufficient to determine whether endovascular therapy for extracranial vertebral artery dissections, aneurysms, and AV fistulae improves the net health outcome.

**Ongoing and Unpublished Clinical Trials**
A search of the online database isrctn.com in January 2015 identified 2 RCTs of endovascular vertebral artery therapy:

- **Vertebral Artery Stenting Trial (VAST) (ISRCTN29597900)**: VAST is a randomized, open-label trial with blinded outcome assessment to compare vertebral artery stenting with best medical therapy among recently symptomatic patients with vertebral artery stenosis (>50%). Enrollment
was planned for 180 subjects, but the trial was stopped for logistical reasons after enrollment of 115 patients, 58 of whom were randomized to stenting. Results have been presented in abstract form, but no published results were identified.

- **Vertebral artery Ischaemia Stenting Trial (VIST) (ISRCTN95212240):** VIST is a multicenter, prospective open-label trial to compare vertebral artery stenting with best medical therapy among patients with recent (within the last 3 months) nondisabling stroke or TIA and vertebral artery stenosis (>50%). Enrollment is planned for 1302 subjects; the estimated study completion date is January 2017.

A search of ClinicalTrials.gov in January 2015 identified 2 additional ongoing studies evaluating endovascular therapies for extracranial vertebral artery disease:

- **Bare-Metal Stents and Drug-Eluting Stents in the Treatment of Patients With Vertebral Artery Ostium Stenosis (NCT02197559):** This is a prospective, observational cohort study to compare outcomes after bare metal or drug-eluting stenting of the extracranial vertebral artery in patients with 70% to 99% vertebral artery ostium stenosis and a history of TIA or nonsevere stroke in the prior 12 months. The primary outcome measures are late loss in lumen diameter and 1- and 12-month rates of death and nonfatal stroke. Enrollment is planned for 172 subjects; the estimated study completion date is December 2015 with follow-up through June 2016.

- **Prospective Evaluation of Safety and Efficacy Vertebral Drug-eluting Stent System (PESS) (NCT02328781):** This is a single-arm interventional study to evaluate a rapamycin-target-eluting stent system in patients with symptomatic vertebral artery stenosis (≥50%) unresponsive to drug therapy. The primary outcome measure is rate of in-stent stenosis at 6 months postprocedure. Enrollment is planned for 150 subjects; the estimated study completion date is August 2016 with follow-up through February 2017.

**Summary of Evidence**

Comparative evidence is lacking to determine whether endovascular therapy, including percutaneous transluminal angioplasty (PTA) with or without stent implantation, for extracranial vertebral disease improves outcomes compared with alternatives. For endovascular treatment of extracranial vertebral artery stenosis, there is 1 very small randomized controlled trial comparing endovascular therapy with medical therapy. Evidence from a large number of small- to moderate-sized noncomparative studies from single institutions indicates that vertebral artery stenting can be performed with high rates of technical success and low periprocedural morbidity and mortality. However, long-term follow-up demonstrates high rates of in-stent stenosis. Given the lack of data comparing endovascular therapy to either medical or surgical management, the evidence is insufficient to determine whether vertebral artery stenting or angioplasty improves the net health outcome.

The evidence related to the use of endovascular therapies for the treatment of extracranial vertebral artery dissections, aneurysms, and arteriovenous (AV) fistulae consists of small case series and case reports. The available cases reports and case series indicate that endovascular therapy for extracranial vertebral artery disorders other than stenosis is feasible and may be associated with favorable outcomes. However, given the lack of evidence comparing
endovascular therapies with alternatives, the evidence is insufficient to determine whether endovascular therapy for extracranial vertebral artery dissections, aneurysms, and AV fistulae improves the net health outcome.

Given the limitations in the evidence base, endovascular therapies are considered investigational for the treatment of extracranial vertebral artery disease.

**Supplemental Information**

**Practice Guidelines and Position Statements**

In 2014, the American Heart Association and American Stroke Association issued guidelines for prevention of stroke in patients with stroke and transient ischemic attack, which make the following recommendations about treatment of extracranial vertebrobasilar disease:

1. Class I Recommendations:
   - Routine preventive therapy with emphasis on antithrombotic therapy, lipid lowering, BP control, and lifestyle optimization is recommended for all patients with recently symptomatic extracranial vertebral artery stenosis (Level of Evidence: C).

2. Class IIb recommendations:
   - Endovascular stenting of patients with extracranial vertebral stenosis may be considered when patients are having symptoms despite optimal medical treatment (Level of Evidence: C).
   - Open surgical procedures, including vertebral endarterectomy and vertebral artery transposition, may be considered when patients are having symptoms despite optimal medical treatment (Level of Evidence: C).

In 2011, a multisociety task force issued guidelines on the management of extracranial vertebral and carotid artery disease with made the following statements about catheter-based revascularization of extracranial vertebral artery disease: “Although angioplasty and stenting of the vertebral vessels are technically feasible, as for high-risk patients with carotid disease, there is insufficient evidence from randomized trials to demonstrate that endovascular management is superior to best medical management.” No specific recommendations are made regarding endovascular therapies.

In 2011, the European Society of Cardiology issued guidelines on the management of peripheral artery disease, including extracranial vertebral artery disease, and made the following recommendations about revascularization for vertebral artery stenosis:

1. Class IIb recommendations:
   - In patients with symptomatic extracranial VA [vertebral artery] stenosis, endovascular treatment may be considered for lesions ≥50% in the case of recurrent ischaemic events despite optimal medical management. (Level of Evidence: C).

2. Class III recommendations:
Revascularization of an asymptomatic VA stenosis is not indicated, irrespective of the degree of severity (Level of Evidence: C).

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

Centers for Medicare and Medicaid Services has a national coverage determination (NCD) for PTA\textsuperscript{31} that addresses the use of PTA in the treatment of atherosclerotic obstructive lesions of the lower extremities or the upper extremities (not including the head or neck vessels), of a single coronary artery, of renal arteries, and of AV dialysis fistulas and grafts. It also addresses the use of PTA concurrent with carotid stent placement in Food and Drug Administration (FDA) investigational device exemption clinical trials, in FDA-approved post approval studies, and in patients at high risk for carotid endarterectomy.

The NCD states that all other indications for PTA, with or without stenting, to treat obstructive lesions of the vertebral and cerebral arteries remain noncovered.

**References**


Policy History

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 19, 2015 and is effective July 15, 2015.

Signature on file
Deborah M. Smith, MD, MPH