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Medical Policy Manual

Topic: Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease (Atherosclerotic and Aneurysms)

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION[1]

It is estimated that intracranial atherosclerosis causes about 8% of all ischemic strokes. Intracranial stenosis may contribute to stroke in two ways: either due to embolism or low flow ischemia in the absence of collateral circulation. Recurrent annual stroke rates are estimated at 4%–12% per year with atherosclerosis of the intracranial anterior circulation, and 2.5%–15% per year with lesions of the posterior (vertebrobasilar) circulation. Medical treatment typically includes either anticoagulant therapy (i.e., warfarin) or antiplatelet therapy (e.g., aspirin). The WASID trial (Warfarin-Aspirin Symptomatic Intracranial Disease) was a randomized trial that compared the incidence of stroke brain hemorrhage or death among patients randomized to receive either aspirin or warfarin. The report indicated that with a mean 1.8 years of follow-up, warfarin provided no benefit over aspirin and was associated with a significantly higher rate of complications. In addition, if symptoms are attributed to low flow ischemia, agents to increase mean arterial blood pressure and avoidance of orthostatic hypotension may be recommended. However, medical therapy has been considered less than optimal. For example, in patients with persistent symptoms despite antithrombotic therapy, the subsequent rate of stroke or death has been extremely high, estimated in one study at 45%, with recurrent events occurring within a month of the initial recurrence. Surgical approaches have met with limited success. The widely quoted Extracranial-Intracranial (EC/IC) Bypass study randomized 1,377 patients with symptomatic atherosclerosis of the internal carotid or middle cerebral arteries to medical care or EC/IC bypass. The outcomes in the two groups were similar, suggesting that the EC/IC bypass is ineffective in preventing

cerebral ischemia. Due to inaccessibility, surgical options for the posterior circulation are even more limited.

Percutaneous transluminal angioplasty (PTA) has been approached cautiously for use in the intracranial circulation due to technical difficulties in catheter and stent design and due to the risk of embolism, which may result in devastating complications if it occurs in the posterior fossa or brain stem. However, improvement in catheter trackability, allowing catheterization of tortuous veins, and the increased use of stents has created ongoing interest in exploring PTA as a minimally invasive treatment of this difficult-to-treat population. Most of the published studies of intracranial PTA have focused on the vertebrobasilar circulation. Intracranial vessels on which angioplasty has been performed include:

- Anterior cerebral artery
- Basilar artery
- Carotid siphon
- Internal carotid
- Middle cerebral artery
- Ophthalmic artery
- Posterior cerebral artery
- Vertebral artery (distal)

Intracranial stents are also being used in the treatment of cerebral aneurysms. Stent-assisted coil embolization began as an approach to treat fusiform or wide-neck aneurysms in which other surgical or endovascular treatment strategies may not be feasible. As experience grew, stenting was also used in smaller berry aneurysms as an approach to decrease the rate of retreatment needed in patients who receive coiling.

Regulatory Status

Currently, approval of intracranial stents by the U.S. Food and Drug Administration (FDA) has been through the humanitarian device exemption (HDE) process. This form of FDA approval is available for devices used in the treatment or diagnosis of conditions that affect fewer than 4,000 individuals in the United States per year; the FDA only requires data showing “probable safety and effectiveness.” An approved HDE authorizes marketing of the humanitarian use device (HUD). However, an HUD may only be used after an internal review board (IRB) approval has been obtained for the use of the device for the FDA approved indication. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

Stents for Intracranial Atherosclerosis

There are currently two devices that have received FDA approval for humanitarian use in the treatment of intracranial atherosclerosis. Their labeled indications are as follows:

- NEUROLINK® System (Guidant) 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 greater than or equal to 50% stenosis and that are accessible to the stent system."[2]

- Wingspan™ Stent System with Gateway™ PTA Balloon Catheter (Boston Scientific) is “indicated

for improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with greater than or equal to 50% stenosis that are accessible to the system."[3] The Wingspan Stent System consists of a highly flexible, microcatheter delivered self-expanding nitinol stent, which may be suitable for lesions in the distal internal carotid and middle cerebral arteries. These arteries are difficult to access with a balloon-mounted stent, such as the NEUROLINK system.[4]

Stents for Intracranial Aneurysm

There are currently two devices which have received FDA approval for humanitarian use in the treatment of intracranial aneurysms. Their labeled indications are as follows:

- The Neuroform™ Microdelivery Stent System (Boston Scientific) was approved for use with embolic coils for treatment of wide-neck intracranial aneurysms that cannot be treated by surgical clipping.

- The Enterprise™ Vascular Reconstruction Device and Delivery System (Cordis Neurovascular, Inc./DePuy Companies) was approved for use with embolic coils for treatment of wide-neck, intracranial, saccular or fusiform aneurysms.

In 2011, the Pipeline® Embolization Device (Covidien eV3 Neurovascular), which falls into a new device category called "intracranial aneurysm flow diverters," or flow-diverting stent, received FDA premarket approval for endovascular treatment of large or giant wide-necked intracranial aneurysms in the internal carotid artery in adult patients aged 22 years or older. The Pipeline device is a braided, wire mesh device that is placed within the parent artery of an aneurysm to redirect blood flow away from the aneurysm with the goal of preventing aneurysm rupture and possibly decreasing aneurysm size.

MEDICAL POLICY CRITERIA

Note: This policy does not address percutaneous angioplasty and stenting of extracranial carotid arteries or venous vessels, or the use of mechanical embolectomy or thrombectomy devices which are addressed in separate policies (see Cross References below).

I. Intracranial stent placement may be considered **medically necessary** as part of the endovascular treatment of intracranial aneurysms when *all* of the following criteria are met:

   A. Surgical treatment is not appropriate

   B. Standard endovascular techniques do not allow for complete isolation of the aneurysm, e.g., wide-neck aneurysm (4 mm or more) or sack-to-neck ratio less than 2:1

II. All other intracranial endovascular angioplasty and/or stenting is considered **investigational** including but not limited to the following:

   A. Intracranial stent placement in the treatment of intracranial aneurysms except as noted above

B. Intracranial percutaneous transluminal angioplasty with or without stenting in the treatment of atherosclerotic cerebrovascular disease

C. Intracranial angioplasty with or without stenting for acute ischemic stroke

SCIENTIFIC EVIDENCE

Evaluating the safety and effectiveness of intracranial endovascular angioplasty with or without stenting requires evidence from well-designed, well-conducted randomized controlled trials (RCTs) that compare the health outcomes following endovascular procedures with those following treatment with standard medical or surgical treatment.

Intracranial Atherosclerotic Disease

Data Included in U.S. Food and Drug Administration (FDA) Submissions

- NEUROLINK® System[2]

  The clinical study investigating the NEUROLINK device is known as the SSYLVIA study (Stenting of Symptomatic Atherosclerosis Lesions in the Vertebral or Intracranial Arteries), a prospective, nonrandomized, multicenter, international study of 61 patients. Patients were eligible for participation in the study if they were symptomatic (previous stroke or TIA) attributed to an angiographically demonstrated, discrete stenosis ≥50%, in an extracranial or intracranial artery. The primary endpoint was a composite of stroke and death clinical outcomes at 30 days; 4 patients experienced strokes (6.6%) and there were no deaths. Mean follow-up was 216 days and lower bound for ipsilateral stroke at 12 months was estimated to be 11.5%. The FDA summary notes that in the WASID study of aspirin and warfarin therapy, the rate of fatal or nonfatal stroke was 14.6% and total stroke or death was 22.5% with a follow-up of 15-19 months, suggesting a potentially superior outcome with the NEUROLINK device. However, the short length of follow-up in the NEUROLINK study prevents meaningful comparisons. The FDA Summary of Safety and Probable Benefit concludes, "Therefore, it is reasonable to conclude that the probable benefit to health from using the NEUROLINK System for intracranial stenting for recurrent stroke attributable to intracranial atherosclerosis refractory to medical therapy outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment, when used as indicated in accordance with the directions of use."

- Wingspan Stent System[3]

  The Wingspan was studied in a prospective, multicenter, single arm trial of 45 patients enrolled at 12 international centers. Patients were considered eligible if they presented with evidence of recurrent stroke, refractory to medical therapy and thought to be secondary to intracranial stenosis of 50% or greater. The primary safety endpoint was similar to the SSYLVIA study, i.e., a composite of stroke and death clinical outcomes at 30 days, which occurred in 4.5% of patients (2/45), 1 with death following a hemorrhagic stroke and 1 stroke.

The FDA summary provided a comparison of various outcomes of the NEUROLINK and Wingspan device studies as follows:

Clinical study	Follow-up	All Stroke	Death	Stroke + Death	Ipsilateral Stroke
SSYLVIA (n=61)	Mean: 216 days (n=48 at 6 mos)	13.1%	6.6%	13.1%	11.5%
Wingspan (n-45)	Mean: 174 days (n=42 at 6 mos)	9.5%	2.4%	9.5%	7.1%

The FDA offered the following conclusions concerning the Wingspan device and appeared to base its approval, in part, on the favorable comparison to the NEUROLINK device:

"The Wingspan clinical study treated 45 patients with symptomatic atherosclerotic lesions in intracranial arteries who were refractory to medical therapy. The lesions were predilated and stented. Clinical follow-up (42 patients) and angiographic follow up (40 patients) were performed at 6 months. The type and frequency of observed adverse events including stroke are consistent with or lower than similar neurovascular procedures. Therefore, it is reasonable to conclude that the probable benefit to health from using the Wingspan Stent System with Gateway PTA Balloon Catheter for treating in transcranial stenosis outweighs the risk of illness or injury when used in accordance with the Instructions for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment."

Elective Treatment of Symptomatic Intracranial Stenosis

Systematic Reviews

- The 2005 updated Cochrane review of angioplasty and stenting for vertebral artery stenosis focused on randomized controlled trials comparing vertebral artery angioplasty and stenting with medical management alone.[5] Only one trial met inclusion criteria, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) that included 16 participants. This trial is described in more detail below. The authors concluded, "There is currently insufficient evidence to support the routine use of percutaneous transluminal angioplasty (PTA) and stenting for vertebral artery stenosis. Endovascular treatment of vertebral artery stenosis should only be performed within the context of randomized controlled trials." In addition, the authors noted, "[l]ittle is known about the natural history of vertebral artery stenosis and what constitutes best medical treatment. Future trials should concentrate on comparing different medical treatment such as antiplatelet and anticoagulant drugs as well as comparing endovascular intervention with medical treatment."

- A 2006 Cochrane review of randomized or otherwise controlled studies addressed angioplasty for intracranial artery stenosis.[6] The authors identified no randomized controlled trials but 79 publications of interest consisting of case series with 3 or more cases. The safety profile showed an overall perioperative rate of stroke of 7.9% (95% CI: 5.5% to 10.4%) and perioperative stroke or death of 9.5% (95% CI: 7.0% to 12.0%). The authors concluded the evidence was insufficient to recommend angioplasty with or without stent placement in routine practice for the prevention of stroke in patients with intracranial artery stenosis. The descriptive studies showed the procedure feasible although carrying significant morbidity and mortality risks. Evidence from randomized controlled trials is needed to assess the safety of angioplasty and its effectiveness in preventing recurrent stroke.

- Groschel et al. conducted a systematic review on outcomes after stenting for intracranial atherosclerosis.[7] The authors identified 31 studies including 1,177 procedures, which had mainly been performed in patients with a symptomatic (98%) intracranial high-grade stenosis (mean: 78.7%) with high technical success rates (median: 96%; interquartile range: 90% to 100%). The periprocedural minor or major stroke and death rates ranged from 0% to 50%, with a median of 7.7%. Periprocedural complications were significantly higher in the posterior versus the anterior circulation (12.1% vs. 6.6%, p<0.01), but did not differ between patients treated with a balloon-mounted (n=906) versus those who had been treated with a self-expandable stent (n=271; 9.5% vs. 7.7%, p=0.47). Restenosis greater than 50% occurred more frequently after the use of a self-expandable stent (16/92; 17.4%, mean follow-up time: 5.4 months) than a balloon-mounted stent (61/443; 13.8%, mean follow-up time: 8.7 months; p<0.001). The authors concluded that although intracranial stenting appears to be feasible, adverse events vary widely and thus given a high rate of restenoses and no clear impact of new stent devices on outcome, the widespread application of intracranial stenting outside the setting of randomized trials and in inexperienced centers currently does not seem to be justified.

Randomized Clinical Trials (RCTs)

- The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) randomized 16 patients with symptomatic vertebral artery stenoses in a 1:1 ratio to receive best medical treatment plus endovascular therapy (balloon angioplasty or stenting) or best medical treatment alone.[8] Endovascular intervention was technically successful in all 8 patients, but 2 patients experienced transient ischemic attack at the time of endovascular treatment. During a mean follow-up period of 4.7 years, no patient in either treatment group experienced a vertebrobasilar territory stroke, but 3 patients in each treatment arm died of myocardial infarction or carotid territory stroke, and 1 patient in the endovascular arm had a nonfatal carotid territory stroke. The investigators concluded that patients with vertebral artery stenosis were more likely to have carotid territory stroke and myocardial infarction during follow up than have recurrent vertebrobasilar stroke. While they noted that the trial failed to show a benefit of endovascular treatment of vertebral artery stenosis, the small number of patients enrolled severely limits conclusions.

- The Stenting versus Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial was an RCT comparing aggressive medical management alone to aggressive medical management plus stenting in patients with symptomatic cerebrovascular disease and an intracranial stenosis of between 70-99%.[9] This trial used the Wingspan stent system implanted by experienced neurointerventionists who had been credentialed to participate in the trial. The authors had planned for an enrollment of approximately 750 patients based on power calculations. However, the trial was stopped early for futility after 451 patients had been randomized. The trial was terminated due to an excess of the primary outcome, stroke or death, at 30 days in the stenting group. In the stenting group, the rate of stroke or death at 30 days was 14.7% (95% confidence interval [CI] 10.7-20.1) compared to a rate of 5.8% (95% CI 3.4-9.7, p=0.002) in the medical management group.

  At the time of termination, the mean follow-up was 11.9 months. Kaplan-Meier estimates of the primary outcome of stroke or death at one year was 20.5% (95% CI 15.2-26.0) in the stenting group compared to 12.2% (95% CI 8.4-17.6, p=0.009) in the medical management group. These results represented an excess rate of early adverse events with stenting over what was expected together with a decreased rate of stroke and death in the medical management group compared to expected values.

- In 2013, the SAMMPRIS investigators published results from long-term subject follow up.[10] Primary end points included stroke or death within 30 days of enrollment, ischemic stroke in the territory of the qualifying artery beyond 30 days after enrollment, or stroke or death within 30 days after a revascularization procedure of the qualifying lesion. During a median follow up of 32.4 months, 34 of 227 (15%) of patients in the best medical management group and 52 of 224 (23%) of patients in the stenting group had a primary end point event, with a significantly higher cumulative probability of a primary end point in the stenting group than in the best medical management group (p=0.025). Compared with the best medical management group, subjects in the stenting group had higher rates of any stroke (59/224 [26%] vs 42/227 [19%], p=0.047) and major hemorrhage (29/224 [13%] vs 10/227 [4%], p<0.001). The authors concluded that the benefits of aggressive medical management over percutaneous angioplasty and stenting among patients with intracranial stenosis persist over long-term follow up.

Nonrandomized Trials

A number of nonrandomized studies have compared outcomes of endovascular procedures with medical therapy.[11-14] These studies have either been retrospective, or based on registry data, and provide relatively weak evidence on the efficacy of endovascular procedures compared with medical therapy for intracranial atherosclerosis.

Numerous single arm non-comparative case series have also been published.[15-20] These studies provide some information on the success rates and the adverse events that occur with this procedure, but the lack of a control group does not provide evidence on the comparative efficacy of endovascular approaches versus medical therapy.

Stent-Assisted Treatment of Intracranial Aneurysm

Systematic Reviews

- A systematic review by Shapiro et al. identified 39 articles reporting on 1517 patients, most of which were single-arm, retrospective series.[21] The majority of patients treated had unruptured aneurysms, but 22% of patients had ruptured aneurysms. The authors noted a large amount of heterogeneity in reporting outcome data, particularly for adverse events. The periprocedural mortality rate was 2.1%, and the overall complication rate was 19%. Immediately following treatment, approximately 45% of patients had occlusion of the aneurysm. At an average of 13 months posttreatment, the stroke rate in the stented area was 3.2%.

- A systematic review that was restricted to ruptured aneurysms was published by Bodily et al. in 2011.[22] This review included 17 articles that described treatment in 212 patients. Technical success was high at 93%, and 2% of patients required open surgery due to stent failure or intraoperative aneurysm rupture. A total of 63% (130/207) of aneurysms were successfully occluded. The overall mortality rate was 19%, and 14% of patients had poor clinical outcomes. There was a relatively high rate of adverse events reported, with 8% of patients having an acute intracranial bleed related to the procedure, and 6% (16/288) having a clinically significant thromboembolic event.

Randomized Controlled Trials (RCTs)

No RCTs were identified for stent-assisted intracranial aneurysm repair.

Nonrandomized Comparative Studies

Stent-assisted Aneurysm Repair vs. Standard Surgical Treatment

No trials were found in the published literature that compared stent-assisted treatment of intracranial aneurysms with standard neurosurgical treatment (i.e., surgical clipping or endovascular coils). This contrasts with therapy of ruptured aneurysms in which a randomized trial compared treatment with coiling versus surgical clipping.

Coiling with vs. without Stenting

- The largest clinical case series describing use of stents in treating intracranial aneurysms was described by Piotin and colleagues.[23] They reported on a series of 1,137 patients (1,325 aneurysms) treated between 2002 and 2009. In this series, coiling was performed without stent-assist in 1,109 aneurysms (83.5%), and with stent assistance in 216 aneurysms (16.5%) (15 balloon-expandable and 201 self-expandable stents). Stents were delivered after coiling in 55% (119/216) and before coiling in 45% (97/216) of the cases. Permanent neurological procedure-related complications occurred in 7.4% (16 of 216) of the procedures with stents versus 3.8% (42 of 1,109) in the procedures without stents (logistic regression p=0.644; odds ratio: 1.289; 95% CI: 0.439–3.779). Procedure-induced mortality occurred in 4.6% (10 of 216) of the procedures with stents versus 1.2% (13 of 1,109) in the procedures without stents (logistic regression p=0.006; odds ratio: 0.116; 95% CI: 0.025–0.531). Thus far, the authors have followed 53% (114 of 216) of aneurysms treated with stents and 70% (774 of 1,109) of aneurysms treated without stents, with angiographic recurrence in 14.9% (17 of 114) versus 33.5% (259 of 774), respectively (p<0.0001; odds ratio: 0.3485; 95% CI: 0.2038–0.5960). Based on this series, the authors concluded that use of stents was associated with a significant decrease of angiographic recurrences but with more lethal complications compared with coiling without stents.

- Colby et al. reported on 90 consecutive patients undergoing treatment for para-ophthalmic aneurysms, 30 of whom were treated with coil alone versus 60 who were treated with stent-assisted coils.[24] On initial angiography following the procedure, complete occlusion of the aneurysm was achieved in 43.3% of stented patients compared with 31.7% of nonstented patients. At a mean of 14.5 months follow-up the recurrence rate was lower for the stented group at 15.4% (4/26) versus 41.5% (17/41) in the nonstented group (p<0.05).

- A nonrandomized comparative study reported on 126 aneurysms that were treated with stent-assisted coiling compared with 86 patients treated with coil alone.[25] At 2-year follow-up, the authors reported rates of occlusion and recurrence. Progressive occlusion was noted in 42.5% of the stent group (17/40) compared with 39.5% of the nonstented group (34/86), a difference that was not statistically significant. The rates of aneurysm recurrence were also not statistically different between groups. Recurrence occurred in 17.5% of patients in the stent group versus 21.0% in the nonstent group.

Comparisons between Stents

In 2013, Kadkhodayan et al. reported results from a nonrandomized comparison of the Neuroform and Enterprise systems in the treatment of intracranial aneurysms not amenable to surgical clipping based on

evaluation of prospectively collected registry data.[26] Patients who received the Neuroform device (n=160) were enrolled starting in February 2003, and patients who received the Enterprise device (n=98) were enrolled starting in March 2007. Indications for the devices differed slightly based on FDA HDE criteria: both have an indication for wide-necked aneurysms (neck ≥4 mm or a dome-to-neck ratio <2 mm) not amenable to surgical clipping. For the Enterprise, stents were used for saccular or fusiform aneurysms arising from a parent vessel with a diameter of ≥2.5 mm and ≤4 mm; for the Neuroform, stents were used for saccular aneurysms arising from a parent vessel with a diameter of ≥2 mm and ≤4.5 mm. The authors reported that Enterprise deployment success was high (108 of 115 attempts, 93.9%) compared with Neuroform (173 of 214 attempts, 80.8%, p=0.001). Rates of stent movement, misplacement, and symptomatic hemorrhage were similar for the 2 stent types, but symptomatic thromboembolic events were more frequent with the Enterprise stent (8.7% vs 1.4%, p=0.002).

Nonrandomized Single-arm Studies

Since the publication of the Shapiro and Bodily systematic reviews, a number of noncomparative studies evaluating the use of stent-assisted endovascular treatments in intracranial aneurysms have been published.[27-35] In general, these series demonstrate high rates of technical success of stent deployment with high rates of aneurysm occlusion; however, variable complication rates, particularly related to thromboembolic events were observed. Long-term follow up, particularly beyond 1 year, was limited. Interpretation of these studies is limited by significant methodologic limitations, including but not limited to the lack of a control group for comparison, short-term outcomes, and potential selection bias.

Flow-diverting Stents for Intracranial Aneurysm

Systematic Reviews and Meta-analyses

- The largest meta-analysis by Brinjikji et al, published in 2013, included 1451 patients with 1654 aneurysms reported in a total of 29 studies published through 2012.[36] The authors evaluated aneurysmal occlusion rates at 6 months, and procedure-related morbidity, mortality, and complications across studies. They found a high rate of complete aneurysmal occlusion (76% (95% CI, 70% to 81%), but also a high rate of procedure-related morbidity and mortality (5% [95% CI, 4% to 7%] and 4% [95% CI, 3% to 6%], respectively). This systematic review included the study upon which the FDA approval of the Pipeline Embolization Device was made.[37]

- Also in 2013, Arrese et al reported results of a meta-analysis that used somewhat more restrictive inclusion criteria that included 897 patients with 1018 aneurysms reported in a total of 15 studies.[38] All but 2 of the studies were included in the Brinjikji meta-analysis. They authors determined rates of complete or nearly complete occlusion of the treated aneurysm with a patent parent artery and early procedure-related mortality and neurologic morbidity. Similar to the Brinjikji meta-analysis, this study found a high overall rate of complete aneurysmal occlusion (76.2% [95% CI, 72.1 to 80.2]), but also a high rate of procedure-related morbidity and mortality (2.8% [95% CI, 1.7%–3.8%] and 7.3% [95% CI, 5.7% to 9%], respectively). The authors assessed for publication bias using funnel plots and the Egger's test to assess whether the study estimate size is related to the size of the study, and found p<0.001 for the Egger's test for both early and late morbidity and aneurysmal occlusion, suggestive of publication bias.

Randomized Controlled Trials (RCTs)

No RCTs were found in which flow-diverting stents were used for the treatment of intracranial

aneurysms.

Nonrandomized Studies

Since the publication of the 2 systematic reviews summarized above, several additional studies have been published. One was a comparative study based on registry data of health outcomes following insertion of the Pipeline device versus endovascular coiling.[30] They identified a total of 229 patients enrolled during their data collection period from 2004-2013, 54 treated with the Pipeline device and 175 with coiling. Patients treated with the Pipeline device were significantly older and had significantly larger aneurysms that were more likely to be fusiform. Because of this, the authors excluded patients with fusiform or anterior communicating artery aneurysms and conducted their analysis in 160 patients (40 Pipeline and 120 coil patients) who were matched in a 1:3 ratio on the basis of patient age and aneurysm size. Aneurysm neck size, overall size, and anterior versus posterior circulation location were similar between the groups. Of the patients treated with the Pipeline device, 4 patients (10%) also required adjunctive coil placement. Of the patients treated with endovascular coiling, 67 (56%) were treated with coiling, while 52 (43%) were treated with stent-assisted coiling and 1 (1%) with balloon-assisted coiling. Primary outcomes included obliteration of the aneurysm on follow-up imaging and clinical outcomes, measured by Modified Rankin Scale score of 0-2 (vs 3-6).

At the time of latest follow up, a higher proportion of aneurysms treated with the Pipeline device compared with those treated with coiling achieved complete obliteration (30/35 [86%] vs 37/90 [41%], $p<0.001$). However, angiographic follow-up was available for a greater proportion of patients treated with the Pipeline (35 /40 [87.5%]) than those treated with coiling (90/120 [75%]), and the median angiographic follow-up time differed significantly between the groups (7 months in the Pipeline group and 12 months in the coil group, $p<0.001$). In terms of clinical outcomes, similar proportions of the Pipeline and coil groups had a Modified Rankin Scale score 0 to 2 (35/38 [92%] in the Pipeline group vs 97/103 [94%], $p=0.8$). Similar to the angiographic follow up results, the median clinical follow-up time differed significantly between the groups. Treatment type was not significantly associated with rates of procedure-related complications. While this study directly compares patients treated with the Pipeline endovascular device and those treated with coiling, it is limited by its nonrandomized, retrospective design. In particular, patients treated with coiling were treated in an earlier period (2004-2011) than those treated with the Pipeline device (2011-2012); this may have systematically biased the study in favor of the Pipeline device because aspects of neurointerventional care other than the device used may have differed over time.

The remaining studies were single-arm studies showing feasibility and short-term outcomes up to 1 year.[39-44]Interpretation of these studies is limited by significant methodologic limitations, including but not limited to the lack of a control group for comparison, short-term outcomes, and small sample size.

Acute Stroke

There are currently no randomized controlled trials for intracranial angioplasty with or without stenting for acute ischemic stroke. A number of case series have been published including the Stent-Assisted Recanalization for Acute Ischemic Stroke (SARIS) trial.[45] This study was a prospective series of 20 patients with acute ischemic stroke who presented within 8 hours of symptom onset, with a NIH stroke score of at least 8, and for whom thrombolysis was either contraindicated or ineffective. All patients were treated with the Wingspan intracranial self-expanding stent, aspirin, and clopidogrel. At six months follow-up, mortality was 35% (7/20), NIH stroke score was 3 or less in 60% of patients (12/20), and 55% (11/20) had an NIH stroke score of 2 or less. A total of 11/13 (85%) patients who were alive at six

months had a follow-up angiogram and all showed patency of the stent graft with TIMI level 3 flow or greater.

Clinical Practice Guidelines and Position Statements

Intracranial Atherosclerosis

- The Society for NeuroInterventional Surgery (SNIS)

  In 2012, the SNIS published consensus-based recommendations in a clinical standards statement on endovascular angioplasty and/or stenting of intracranial atherosclerosis.[46] The only randomized controlled trial found was the SAMMPRIS trial, described above. This trial was ranked as AHA evidence level B, defined as limited evidence from a single randomized trial or other nonrandomized studies. The remaining included studies were nonrandomized studies that were uncontrolled or did not have objective outcome measures; these were classified as AHA evidence level C, defined as based on expert opinion, case studies, or standard of care. The following recommendations were made:
  - Medical therapy was recommended over angioplasty and stent therapy (Class IIa recommendation: Weight of evidence/opinion is in favor of usefulness/efficacy).
  - For symptomatic 70-99% intracranial stenosis refractory to aggressive maximal medical therapy, angioplasty or stenting may be considered (Class IIb recommendation: Usefulness/efficacy less well-established by evidence/opinion).
  - There is insufficient evidence to recommend between angioplasty and balloon mounted drug eluting or self-expanding stent systems (Class III recommendation: Intervention is not useful/effective and may be harmful).

- The American Society of interventional and Therapeutic Neuroradiology (ASITN), the Society of interventional Radiology (SIR), and the American Society of Neuroradiology (ASNR)

  In 2005 the ASITN, SIR, and ASNR jointly published a position paper on intracranial endovascular procedures.[47] This position statement reviewed a number of case series and also the SSYLVIA and Wingspan studies. It was republished in 2009 without an updated evidence review.[48] The following statement was offered, although the underlying rationale and process for development for the position statement was not provided:

  > "The ASITN, SIR, and ASNR concur that sufficient evidence now exists to recommend that intracranial angioplasty with or without stenting should be offered to symptomatic patients with intracranial stenoses who have failed medical therapy. Endovascular interventions are intensive services provided to patients who are at very high risk for stroke and typically have multiple comorbidities. Similar to revascularization for extracranial carotid artery stenosis, patient benefit from revascularization for symptomatic intracranial arterial stenosis is critically dependent on a low periprocedural stroke and death rate and should thus be performed by experienced neurointerventionists. We recommend reimbursement by third party insurers so that these patients may have access to such interventions. Continued attempts to improve the benefits of endovascular therapy are warranted."

- The American Heart Association (AHA)

  In April 2009, the AHA, along with several other organizations, published a statement on indications

for intracranial endovascular neuro-interventional procedures.[49] The statement recommended that angioplasty and/or stenting be considered for patient with symptomatic severe intracranial stenoses (>70% luminal narrowing) that has been unresponsive to optimal medical therapy (Class IIb, Level of Evidence C, defined above).

Intracranial Aneurysm

No clinical practice guidelines or position statements from U.S. professional societies were found that provided recommendations for stenting in the treatment of intracranial aneurysms. The 2009 AHA statement mentioned that stent deployment is being investigated to assist in coil embolization of certain aneurysms, but did not include stenting in their recommendations.

Acute Stroke

- The American Heart Association (AHA) and the Society for NeuroInterventional Surgery (SNIS)

In separate position statements, the AHA[49] and the SNIS[50] recommended that the usefulness of endovascular devices other than mechanical thrombectomy devices "is not yet established, but may be beneficial and may be considered" (Class IIb, Level of Evidence C, defined above).

Summary

For elective treatment of symptomatic intracranial artery stenosis, the current evidence is insufficient to determine the effectiveness and rate of adverse events of endovascular angioplasty with or without stenting compared with best medical therapy. The evidence suggests that the adverse event rate with endovascular procedures is relatively high and may outweigh the benefit in preventing recurrent ischemic events. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend angioplasty with or without stenting for treatment of intracranial artery stenosis. Therefore, endovascular procedures with or without stenting are considered investigational for the elective treatment of symptomatic intracranial stenosis.

Use of endovascular stents in the treatment of intracranial aneurysms is generally reserved for cases in which successful occlusion of the aneurysm cannot be obtained with standard endovascular techniques, e.g., wide-neck aneurysms. Despite the lack of evidence from well-designed randomized controlled trials, stent-assisted coil embolization is becoming more widely used for certain intracranial aneurysms. Thus, use of stents may be considered medically necessary as part of the endovascular treatment of intracranial aneurysms in selected cases that meet the medical policy criteria.

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Extracranial Carotid Angioplasty/Stenting, Surgery, Policy No. 93

Percutaneous Angioplasty and Stenting of Veins, Surgery, Policy No. 109

Mechanical Embolectomy for Treatment of Acute Stroke, Surgery, Policy No. 158

CODES	NUMBER	DESCRIPTION
CPT	61630	Balloon angioplasty, intracranial (e.g., atherosclerotic stenosis), percutaneous
	61635	Transcatheter placement of intravascular stent(s), intracranial (e.g., atherosclerotic stenosis), including balloon angioplasty, if performed
HCPCS	None	