Intracranial atherosclerosis is a major cause of stroke and accounts for 8% to 10% of ischemic stroke in mixed patient populations. The vessels involved are mainly the vessels of the Circle of Willis. Although the pathophysiology of most of these stenoses is thought to be atherosclerosis, when evaluating these patients, consideration should be given to other etiologies such as vasculitis, dissection, embolism undergoing recanalization, moyamoya arteriopathy, postradiation arteriopathy, and infectious vasculitides.

The Warfarin-Aspirin for Symptomatic Intracranial Disease (WASID) trial shows that numerous patients undergoing medical treatment will experience recurrent symptoms. A reason for this finding is likely hypoperfusion due to flow-limiting stenoses for which antithrombotic therapy may not be effective. In such patients, restoring adequate cerebral blood flow should be the primary goal of intervention. Extracranial-to-intracranial bypass surgery has essentially been abandoned due to nearly double the risk of stroke in patients with severe middle cerebral artery (MCA) stenosis compared to medical therapy. With developments in stent technology, endovascular approaches have emerged as a feasible and potentially highly effective therapy for patients in whom medical treatment fails.

**PREOPERATIVE PATIENT SELECTION**

The most crucial indication for intracranial stenting is the presence of symptomatic intracranial atherosclerotic stenoses and failure of medical therapy. Results from the WASID trial show that in patients with high-grade stenosis (> 70%), the risk for subsequent stroke in the territory of the stenotic artery is 23% at 1 year and 25% at 2 years. Although patients with stenoses < 70% are also at an increased risk of stroke, the risk is relatively low compared to that of endovascular intervention; therefore, patients with > 70% symptomatic intracranial stenoses are most likely to benefit from invasive treatment strategies. In addition, patients must be able to tolerate dual-antiplatelet therapy for 30 days or longer, and their symptoms should be attributable to the territory distal to the stenotic segment. This last point is critical because the basilar artery and MCA have many important perforators that originate from their main trunks that often cause clinical syndromes due to parent vessel atherosclerosis. Angioplasty or stenting in such circumstances has a high probability of causing perforator occlusion and stroke.

**ENDOVASCULAR APPROACH**

The endovascular approach for intracranial angioplasty and stenting is similar to that of acute stroke intervention, but pretreatment with dual-antiplatelet agents is critical. A femoral approach is preferred, especially for MCA and internal carotid artery (ICA) procedures. Heparin is administered to achieve an activated clotting time between 250 and 300 seconds. Treatment for vasospasm should be considered during the procedure, although...
there are no data to support this practice except that the cerebral vessels are prone to spasm; because proper stent sizing is essential, antispasm treatment may help improve device sizing. A long sheath (except in the rare patients with no tortuosity and a relatively proximal stenosis in whom a short sheath may be used) should be advanced into the common carotid artery or subclavian artery, and a 6-F guide sheath should be placed distally in the cervical ICA or vertebral artery. The lesion should then be crossed with a hydrophilic, soft microwire with an atraumatic tip. The tip of the guidewire should be positioned distal to the stenosis with great care taken to avoid placing the wire in small branches or perforators. For terminal ICA and MCA treatment, the wire should be passed into the second or proximal third-order branches (Figure 1A). In the posterior circulation, the wire should be in a posterior cerebral artery if possible (Figure 1B). The authors’ approach is to predilate the lesion with an undersized, over-the-wire balloon, keeping in mind that vessel rupture or dissection with subarachnoid hemorrhage are often fatal in this setting (Figure 1C). This practice permits adequate sizing of the vessel and observation of lesion response to angioplasty. Postangioplasty angiography should then be performed, and unless an excellent result with < 30% residual stenosis is seen, stenting should be performed with a stent size no larger than the smallest normal segment into which the stent will be deployed. The length of the stent should be kept to the minimum needed to cover the lesion or particularly the angioplasty segment, because longer stents are more difficult to deliver. Poststenting dilation is rarely needed unless a self-expanding stent is used. This last point is controversial and based on anecdotal experience with the Wingspan stent system (Boston Scientific Corporation, Natick, MA). If a large branch or perforator emanates from the lesion, the increased risk of branch occlusion and consequent stroke should be discussed with the patient before the procedure. If this occurs, the authors have found, acedotally, that intra-arterial infusion of glycoprotein IIb/IIIa antagonist may recanalize the occluded branch.

To improve flow though the stenosis, the increase in lumen diameter need not be significant, because flow is proportional to the fourth power of the radius. The angiographic endpoint of a smooth, normal-caliber lumen—while desirable—is not necessary, because the cerebral vessels are very fragile, and persistent attempts to achieve such a goal may easily lead to tragic complications of arterial rupture or dissection and intracerebral hemorrhage (ICH).

**PERIOPERATIVE MANAGEMENT**

After every maneuver and before removing the equipment, patients should be assessed neurologically; therefore, these procedures should not be performed under general anesthesia.10 If there is any clinical deterioration, angiography of the appropriate vessel should be performed immediately. Vasospasm, embolization, and dissection are the most likely etiologies of intraoperative deficits and should be treated appropriately. If the angiogram reading is normal, an expanding ICH should
be suspected, and appropriate measures need to be taken. If there is frank extravasation of contrast on the angiography, immediate blood pressure lowering, heparin reversal, and even temporary balloon occlusion should be considered. Under these circumstances, the authors have seen only a few patients survive despite all of the measures mentioned. If there are no new neurological deficits, heparin may be discontinued at the end of the procedure but not reversed except in those who are at high risk for hyperperfusion syndrome or ICH. Routine use of glycoprotein IIb/IIIa antagonists is discouraged unless patients are inadequately premedicated with antiplatelet agents.

POSTOPERATIVE CARE

Close observation of neurological status and monitoring of blood pressure are critical. If there is a risk of hyperperfusion syndrome and ICH, blood pressure should be kept in the low normal range for at least 14 days. Dual-antiplatelet therapy needs to be continued for at least 30 days. If drug-eluting stents were placed, prolonged therapy for 6 months up to 1 to 2 years may be necessary. In addition, all patients should have a 30-day follow-up with a transcranial Doppler ultrasound and neurological examination. At 6 months, another follow-up is needed, and unless the stented segment is easily evaluated by transcranial Doppler ultrasound, angiography should be performed to assess stent patency. The authors have found it useful to know if any early, severe, neointimal proliferation occurs; in such cases, more frequent clinical assessments and continued dual-antiplatelet therapy are warranted.

CLINICAL OUTCOMES

Stent delivery is the most challenging single aspect of intracranial interventions, especially stent delivery to the terminal ICA and MCA. The latest generation of coronary stents (particularly the cobalt-chromium platforms) has proven to be highly deliverable, but in 8% to 10% of

Figure 2. The Neurolink stent, which is no longer commercially available in the United States.
patients, even these stents cannot be delivered safely through the cavernous carotid artery. The bulk of published series of intracranial angioplasty and stenting has been series of patients treated with balloon-expandable coronary stents. The reported outcomes with these stents have been highly variable because of differences in patient selection, techniques, and operator experience. Most series have reported 30-day stroke, ICH, and death rates of 8% to 20%, but some have had rates as high as 50%, although the average rate is approximately 10% to 12%.11-14 The authors have reported on the use of drug-eluting stents for intracranial stenoses with excellent success, but the ultimate safety of this approach is unclear.15

The balloon-expandable Neurolink stent system (Guidant Corporation) is the first stent designed specifically for cerebrovascular applications (Figure 2). It was evaluated in 43 intracranial lesions in a multicenter, non-randomized, feasibility study, the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA) study.16 The investigators reported a high procedural success rate of 95% and a low stroke rate of 6.6% at 30 days and 14% at 1-year follow-up. However, in-stent restenosis > 50% occurred in 32.4% of the patients with intracranial stents. Although the stent received a humanitarian device exemption from the United States Food and Drug Administration, it is no longer commercially available.

In 2005, a novel nitinol self-expanding stent system (Wingspan stent system and Gateway percutaneous transluminal angioplasty balloon catheter, Boston Scientific Corporation) was released under a humanitarian device exemption for the treatment of symptomatic intracranial stenoses (> 50%) refractory to medical therapy (Figure 3A). The single-arm, multicenter Wingspan study of 45 qualified patients17 had a 97.7% procedural success rate. The composite ipsilateral stroke or death rates at 30-day, 6-month, and 1-year follow-up were 4.5%, 7.1%, and 9.3%, respectively. The rate of in-stent restenosis of 50% or more at 6 months was 7.5%, and all were asymptomatic. Currently, there are two prospective, multicenter Wingspan stent registries established in the United States. The National Institutes of Health Multicenter Wingspan Intracranial Stent Registry enrolled 129 patients with stenosis of 70% to 99%.18 The initial analysis showed a technical success rate of 96.7% and a stroke or death rate of 9.6% and 14% at 30 days and 6 months, respectively. Restenosis of 50% or more was found in 25% of 52
patients who underwent follow-up angiography. In the United States Wingspan Registry, supported by a research grant from Boston Scientific Corporation, there were 78 patients with 82 intracranial stenoses of 50% or more. The stent was successfully placed in 98.8% of patients. Major periprocedural complications were reported in 6.1% of treatments. In-stent restenosis—defined as stenosis > 50% within or adjacent to the implanted stents and absolute luminal loss > 20%—was seen in 34.5% of patients, 76% of whom were asymptomatic. The major limitation of this stent system is the instructions for use that prohibit poststenting angioplasty, often resulting in significant residual stenoses, in vessels measuring < 3 mm would be expected to have a high risk of early restenosis. The self-expanding nature of the stent, despite high hopes, does not appear to be useful in maintaining vessel patency but has been of great benefit in improving safety and stent delivery compared to balloon-expandable stents (Figure 4).

The Pharos stent (Micrus Endovascular Corporation, San Jose, CA), derived from one of the most flexible balloon-expandable monorail coronary stents (Figure 3B), has been initially evaluated in a German prospective single-center study that enrolled 21 patients with symptomatic intracranial stenosis of 50% or more. At 30 days, a technical success rate of 90.5% was achieved, with a stroke rate of 9.5% and a 9.5% stent thrombosis rate. The Pharos Vitesse second-generation stent, already authorized by the CE for commercial distribution in the European Union, is being investigated in the United States, Europe, and Asia in the Vitesse Intracranial Stent Study for Ischemic Therapy (VISSIT), a prospective, randomized, multicenter study.

All of the published retrospective series and prospective device studies have differed markedly in techniques and outcome definitions; what they all have in common is poor angiographic follow-up, and most have poor clinical follow-up. Therefore, no firm conclusions regarding safety, efficacy, and durability can be drawn from the available data.

CONCLUSION

Due to the lack of efficacy and durability data from prospective, randomized, multicenter trials, intracranial stenting remains investigational and should be used only in carefully selected patients after thorough evaluation of their clinical and anatomical factors. The authors do not recommend stenting in patients with chronic complete occlusion and asymptomatic lesions, and we generally do not advocate stenting in elderly patients, especially those with underlying dementia and severe vessel calcification. However, symptomatic patients with angiographically documented > 70% stenoses who have failed medical therapy are appropriate candidates for intracranial angioplasty and stenting and should be enrolled in clinical trials when possible.

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