The year 2007 brought further understanding of the risk for subgroups of patients undergoing carotid artery stenting (CAS). For symptomatic patients, both increasing age and treatment within 2 weeks of neurological symptoms were associated with increased risk of perioperative stroke or death.\(^1\) Unfavorable anatomic factors for CAS among octogenarians included aortic arch elongation, calcification, great vessel origin stenosis, tortuosity, and severity of lesion stenosis,\(^2\) and the combined perioperative stroke/myocardial infarction/death rate was 10.8% for this group.\(^2\) Diabetic patients \(\geq 75\) years undergoing CAS have a greater risk for any stroke/death and 12.0\(\times\) greater risk for major stroke/death, whereas diabetics \(< 75\) years have no increased risk.\(^3\) Increasing age was also associated with higher rates of in-hospital stroke or death.\(^4\) There was no significant difference in periprocedural complications after CAS for patients with previous ipsilateral carotid endarterectomy (CEA).\(^5\)

In an attempt to aid decision-making for surgical versus endovascular treatment of carotid artery disease, a single community-based hospital reviewed its contemporary experience with CEs in 1900 patients.\(^6\) High-surgical-risk patients comprised 54% of the total. The perioperative stroke/death rate for this cohort was 1.6% compared with 1.3% for all patients. The 30-day stroke/myocardial infarction/death rate was 3.4%. Severe coronary artery disease and previous ipsilateral CEA were associated with increased risk for complications.\(^6\)

A prospective randomized trial of CAS versus CEA for symptomatic patients reported that despite increased diffusion-weighted imaging lesions on brain MRI after CAS, similar numbers of patients in each treatment group experienced cognitive changes.\(^7\) A study evaluating brain MRI before and after CAS found diffusion-weighted imaging lesions in 41.5%, with no association between microscopic debris captured in the distal embolic protection device and new lesions on MRI.\(^8\) A pre-/post-MRI study of diffusion-weighted imaging changes after CAS with distal embolic protection device or CEA found lesions in 70% of CAS-distal embolic protection device patients and in none of the CEA patients.\(^9\) Among the CAS patients, diffusion-weighted imaging lesions relative to the vessel treated were either bilateral (36%), ipsilateral (47%), or contralateral (16%), and neurological symptoms lasting >36 hours occurred in 11%.\(^9\)

A protocol for comprehensive blood pressure management initiated in conjunction with CAS was shown to significantly reduce the incidence of intracerebral hemorrhage in all patients and both hyperperfusion syndrome and intracerebral hemorrhage in high-risk patients.\(^10\)

A number of industry supported registries continue to supply interesting data. Carotid artery stenting with emboli protection surveillance post-marketing study (CASES-PMS) demonstrated a 30-day stroke/myocardial infarction/death rate of 5.0% for a mixed group of symptomatic and asymptomatic patients.\(^11\) The Carotid ACCULINK/ACCUNET Post-Approval Trial to Uncover Unanticipated or Rare Events (CAPTURE) postapproval registry reported a 30-day stroke/myocardial infarction/death rate of 6.3%, and both registries have shown no difference in outcomes based on level of operator experience.\(^12\) Complication rates in both were similar to Asymptomatic Carotid Atherosclerosis Study (ACAS) and North American Symptomatic Carotid Endarterectomy Trial (NASCET), and there was some relationship to CAS operator experience. Three-year follow-up data from registries using Boston Scientific devices confirmed higher risk of CAS in octogenarians, symptomatic patients, and those with medical comorbidities. In these high-risk cohorts, the incidence of perioperative stroke was up to 7.7%.\(^13\)

Primary stenting consists of carotid stent placement without embolic protection or intentional use of balloon angioplasty. Results among 87 consecutive patients with carotid stenosis treated with primary stent placement revealed 98% procedural success, 2% stroke/death, and 5% with periprocedural transient ischemic attacks.\(^14\)

In the United States, the Centers for Medicare and Medicaid Services (CMS) proposal to expand coverage of CAS essentially maintained the 2005 policy.\(^15\) Coverage continues for high-surgical-risk patients with symptomatic stenosis >70%. High-risk symptomatic patients with 50% to 70% stenosis are covered within FDA-approved clinical trials. The Carotid Revascularization Endarterectomy versus Stent Trial (CREST) study of CEA versus CAS will likely reach its
Intracranial Angioplasty and Stenting

Wingspan stents (Boston Scientific) are now widely used for the treatment of symptomatic intracranial stenosis. In a group of 45 patients, the 30-day stroke/death rate was 4.5%. At 6 months, stenosis improved from 74% to 28%; the rate of all-cause stroke was 9.7% and that of all-cause mortality was 2.3%. Another prospective registry found a 29.7% rate of in-stent restenosis (>50%) plus an additional 4.8% occlusion rate at a mean of 5.9 months follow-up. The restenosis or occlusion was symptomatic in 28% of patients and required retreatment in 52%.

A study comparing symptomatic severe (≥70%) and moderate (50% to 70%) intracranial stenosis in patients treated with balloon-expandable stents found no significant difference in stroke or hemorrhage rates either peripherally or at the 1- and 2-year follow-up. In the multivariate analysis, stent failure was associated with adverse events in the severe stenosis group. In another report, balloon-mounted stent placement for symptomatic vertebralbasilar stenosis resulted in 26.1% periprocedural morbidity and mortality. In-stent restenosis or occlusion occurred in 12.5% by 6 months, all of which were symptomatic.

Acute Stroke Therapy

Several acute stroke therapy trials were reported in 2007. Intervventional Management of Stroke (IMS) II found a 9.9% rate of symptomatic intracerebral hemorrhage after combination IV-intra-arterial (IA) tissue-type plasminogen activator therapy was administered within 3 hours of acute stroke onset, higher than the rate observed in the NINDS tissue-type plasminogen activator trial. A randomized trial is under way (IMS III) to determine whether an IV-IA approach to recanalization is superior to standard IV tissue-type plasminogen activator alone when initiated within 3 hours of stroke onset. Further results from the MERCI and Multi-MERCI investigators have shown that successful recanalization of acute distal ICA and proximal middle cerebral artery occlusions can be achieved in 53% to 63% of patients using the MERCI retriever (Concentric Medical) alone or in combination with IV/IA thrombolitics, yet symptomatic hemorrhages occurred in 6% of those patients who recanalized. Good clinical outcomes (modified Rankin Score ≤2) are more likely in those who recanalize than in those who don’t (39% versus 3%), yet the 90-day mortality rate is still 30%. Another approach in those who fail MERCI retrieval has been to use angioplasty or self-expanding stents to compress friable clot and allow better penetration of thrombolytic agents. Recanalization rates of up to 89% with balloons and 79% with stents have been achieved in small numbers of patients, yet clinical outcomes manifested by modified Rankin Score ≤2 at 3 months remain at approximately 50% or less. Reports of aggressive revascularization of acute ICA and tandem ICA/middle cerebral artery occlusions using stents and intracranial thrombolysis have demonstrated the feasibility of this approach, again in small numbers of patients with recanalization rates of up to 100%, yet good modified Rankin Score scores at 3 and 11 months of only 30% to 40%. Attempts to identify prognostic factors for hemorrhagic complications and eventual clinical outcomes in patients undergoing these aggressive multimodal interventions showed that residual distal occlusions, tandem occlusions, larger initial pretreatment CT infarct size by Alberta Stroke Program Early CT Score (ASPECTS) score, hyperglycemia and use of both IA and IV thrombolytics were all associated with negative results. Novel mechanical revascularization strategies used deflated microballoon catheters and the Alligator retrieval device (Chestnut Medical Technologies) to open vessels that may be refractory to IA thrombolitics or the MERCI device.

Aneurysms

Advances in the endovascular therapy of cerebral aneurysms include the refinement and improved evaluation of current technology, the introduction of several innovative stent devices, more detailed investigation of aneurysm healing mechanisms, and continuing debate on the best management for asymptomatic, unruptured aneurysms. Large, industry supported registries which have been used in the past to promote the use of modified coils have been criticized for their failure to demonstrate advantages over bare platinum. New, randomized trials are underway to determine whether these coils really result in decreased recurrence rates without increased complications. The widespread use of balloon-assisted coiling with low complication rates is allowing better endovascular management of complex aneurysms.

There are new stents being used to assist in the coiling of wide-necked aneurysms, such as the closed-cell design Enterprise (Cordis Neurovascular, Inc), the electrodetachable, fully retrievable Solo (eV3 Neurovascular) and the covered, balloon-expandable Willis (Microport). Development of significant focal stenosis remains a problem, seen in up to 5.8% of stent-assisted cases. A novel approach is to use a high-coverage, endoluminal mesh to divert flow and thus induce aneurysm thrombosis. The Pipeline Neuroendovascular Device (Chestnut Medical Technologies) is a tubular, bimetallic implant with approximately 30% coverage by area. In experimental, elastase-induced aneurysms in rabbits, it was found to be highly trackable, adequately radiopaque and resulted in 88% complete or near complete obliteration without the use of coils. There was minimal neointimal hyperplasia, and patency of small branch arteries covered by the device. Preliminary experience in humans has been encouraging.

New insights into the molecular and genetic factors underlying the healing of experimental swine aneurysms has led to refined evaluation of the effects of different polymers on this process. It is hoped that immunohistochemical and molecular biological data can be used to develop biologically active endovascular devices in the future. A novel method for depositing viable, migration capable fibroblasts on coils and successfully passing them through microcatheters may be a promising technique for endovascular intervention.

Continuing evaluation of data from the International Subarachnoid Aneurysm Trial (ISAT) has shown that late retreatment is almost 7 times more likely in the coiling group.
(17.4% of 1096 patients) than in the surgical cohort, although the incidence of delayed rebleeding was similar up to 8 years. Long-term imaging follow-up is still essential.44,45 There is mounting evidence that this follow-up can be done noninvasively using MR angiography,46-47 thus obviating the need for catheter angiography. Multidetector CT angiography may often be the only investigation needed to detect and plan the treatment of most cerebral aneurysms.48

The debate over best management of asymptomatic, unruptured aneurysms continues, with champions49 and critics50-52 of the International Study of Unruptured Intracranial Aneurysms (ISUIA). Although there is some retrospective data favoring endovascular therapy,53 most investigators agree that a randomized, controlled trial including endovascular and surgical arms is necessary.

AVMs

No new embolic agents for the endovascular therapy of brain AVMs have been used in humans, although an interesting modification to enhance the effects of Onyx (eV3 Neurovascular) with mannitol has been described.54 In this scenario, 25% mannitol was infused before intraarterial injection of Onyx to cause hyperosmotic vessel injury and promote thrombosis of brain, head and neck and dural AVMs in 22 patients. A new nonadhesive liquid embolic agent similar to Onyx has been tested in the swine rete with promising results. Eudragit-E 100 Polymer has a lower viscosity than Onyx, is injected slowly, has no catheter compatibility issues and generates an inflammatory response similar to the cyanoacrylates.55 The treatment decision algorithms for both ruptured and unruptured brain AVMs remain uncertain, and the recently launched A Randomized Trial of Unruptured Brain AVMs (ARUBA) will hopefully provide valid answers for those patients with incidentally discovered lesions.56 There are now 20 participating centers in North America.

Vasospasm

Data from ISAT has confirmed what many investigators have shown in smaller series: that there is no significant difference in the incidence of symptomatic vasospasm between surgical and endovascular groups.44 No new interventional strategies for dealing with symptomatic, posthemorrhagic cerebral vasospasm have been developed, although more compliant balloons for angioplasty are becoming available. An NIH funded, randomized trial of prophylactic balloon angioplasty versus standard medical therapy for vasospasm is currently underway.57

Advances in Technology

Quantitative frequency-domain near-infrared spectroscopy provides continuous, noninvasive information about brain oxygenation, including oxyhemoglobin and deoxyhemoglobin concentrations.58 This can provide valuable information during and following acute interventions for stroke, vasospasm and cerebrovascular atherosclerosis. The diagnostic accuracy of transcranial Doppler imaging and MR angiography was found to compare favorably to catheter angiography in patients with intracranial atherosclerotic stenosis.59 Transcranial Doppler studies may be of value for supplying diagnostic information in acute stroke patients, with good positive predictive value and negative predictive value relative to CT angiography.60 Color-coded duplex sonography has been used to evaluate vessels for recanalization after IV thrombolysis in acute stroke patients.61

Acknowledgments

We thank Rodney M. Samuelson, MD, Babak S. Jahromi, MD, PhD, and Miguel Bussiere, MD, PhD, FRCPC, for reviewing the literature and assistance with the preparation of this manuscript, and Cathy Carlisle for final manuscript preparation.

Sources of Funding

Dr Levy receives grant support from Boston Scientific Corporation and Cordis Corporation, patent royalties from Zimmer Spine, and financial support from Abbott Vascular and ev3 for carotid stent training. Dr Hopkins receives grant support from Boston Scientific Corporation, Cordis Corporation, and Micrus Endovascular.

Disclosures

Dr Hopkins has an ownership interest in APW Holding Inc, Boston Scientific Corporation, and Micrus Endovascular; receives consulting fees from Abbott Laboratories, C. R. Bard, Inc, Boston Scientific Corporation, Cordis Corporation, and Micrus Endovascular; has received honoraria from C.R. Bard, Inc, Boston Scientific Corporation, Cordis Corporation, and Medsn, Inc; and is on the board of, is a trustee of, or is an officer of Access Closure, Inc, marketRX, Inc, and Micrus Endovascular.

References

10. Abou-Chebl A, Reginelli J, Bajzer CT, Yadav JS. Intensive treatment of hypertension decreases the risk of hyperperfusion and intracerebral hem-


54. Feng L. Mannitol as an Adjunct Liquid Embolic Agent for Brain AVMs (a). Proc WFITN, pp 115.


Key Words: interventional neuroradiology advances